CoLab Network

CDA-AMC Canada's Drug Agency
L'Agence des médicaments du Canada

March 2025

Drugs Health Technologies Health Systems

Health Technology Review

The Cost-Effectiveness and Budget Impact of Tocilizumab for COVID-19

Authors: Marie Betsy Varughese, Karsten Hempel, Ellen Rafferty, Weston Roda, Danica Wolitski, Jeff Round

This technology review was conducted by the Alberta Drug and Technology Evaluation Consortium (ADTEC) through the Post-Market Drug Evaluation CoLab Network.

Key Messages

This report aims to estimate the impacts of providing tocilizumab as an inpatient treatment for COVID-19 in Canada on the health care system, drug access and uptake, and funding considerations.

We used a state-transition model to conduct a cost-utility analysis (CUA) and budget impact analysis (BIA) of various potential tocilizumab uptake scenarios to treat COVID-19 in hospital in 3 cohorts: those younger than 65 years, those aged 65 years and older, and/or those in long-term care (LTC).

The results of the CUA and BIA suggest that increased use of tocilizumab is likely to be cost-saving, though this is dependent on the treatment effect and uptake, patient cohort, and considerations of uncertainty.

The mean incremental net monetary benefits (iNMB) for all main scenarios were positive, ranging from $123 million to $1,080 million depending on willingness to pay threshold per quality-adjusted life-year (QALY). The largest iNMB was seen from a scenario that included treating individuals in all cohorts.

The mean budget impact estimates ranged from –$72 million to –$296 million across all main scenarios, suggesting tocilizumab will decrease health system costs. Total inpatient costs contributed the most to the overall total cost. While there remains uncertainty in the health care system costs associated with inpatient use of tocilizumab, the majority of model runs found it was cost-saving.

The key limitations of this analysis were that the reference scenario included some inpatient use of tocilizumab in 2022, the mortality impact in LTC was likely underestimated because of data and model limitations, and the therapeutic effects listed for tocilizumab were based on literature released before the emergence of the Omicron variant.

Table of Contents

List of Tables

List of Figures

Abbreviations

BIA	budget impact analysis
CI	confidence interval
CIHI	Canadian Institute of Health Information
CrI	credible interval
CUA	cost-utility analysis
HALE	health-adjusted life-expectancy
iNMB	incremental net monetary benefit
ICER	incremental cost-effectiveness ratio
ICU	intensive care unit
LOS	length of stay
LTC	long-term care
NMB	net monetary benefit
NMV-r	nirmatrelvir-ritonavir
PHAC	Public Health Agency of Canada
POSA	probabilistic one-way sensitivity analysis
QALY	quality-adjusted life-year
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
WTP	willingness to pay

Introduction and Rationale

Background

The main symptoms of COVID-19 include fever, sore throat, runny nose, cough, fatigue, and shortness of breath.[1] The incubation period of COVID-19 ranged between 2 to 14 days (before the emergence of the Omicron variant), and between 2 and 4 days following the emergence of Omicron. Individuals with COVID-19 may remain asymptomatic and nonetheless be contagious.[2] The clinical features of COVID-19 related to severity differ by age, vaccination status, variants of concern, and comorbidities, with COVID-19 disproportionately impacting older adults and those with weakened immune systems (e.g., those with comorbidities).[2]

In Canada, several drug treatments have received approval for the management of COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Initially, the federal government, specifically the Public Health Agency of Canada (PHAC), was responsible for overseeing the procurement and allocation of these drugs to ensure their availability for federal, provincial, and territorial health care systems. The following drugs were funded by PHAC: nirmatrelvir-ritonavir (NMV-r) (Paxlovid), remdesivir (Veklury), and tocilizumab (Actemra).

To provide reliable and evidence-based guidance, Canada's Drug Agency (CDA-AMC) conducted comprehensive evidence reviews for NMV-r, remdesivir (outpatient and inpatient use), and tocilizumab.[3-6] The primary objective of these reviews was to assess the available evidence on the safety, efficacy, and overall benefits of these drugs in the context of COVID-19 treatment. Subsequently, reimbursement recommendations from CDA-AMC were issued for NMV-r, remdesivir for inpatients, and remdesivir for outpatients to support federal, provincial, and territorial drug plans' funding decisions.

Before the reimbursement recommendations by CDA-AMC, PHAC had commissioned the Post-Market Drug Evaluation Program to conduct economic evaluations and BIAs of drugs used to treat COVID-19, including NMV-r, remdesivir, and tocilizumab to inform policy decisions related to the continued inpatient and/or outpatient purchase and use of these therapies. The research and policy questions defined in this report are based on COVID-19 conditions in Canada in 2022.

Main Take-Aways

Several drug treatments have been authorized for use in Canada to manage COVID-19. This report aims to estimate the impacts of providing tocilizumab as an inpatient treatment for COVID-19 in Canada on health system costs and health outcomes.

Policy Issue

Health Canada authorized the use of tocilizumab for COVID-19 in October 2022. It is "indicated for the treatment of hospitalized adult patients with COVID-19 who are receiving systemic corticosteroids, and require supplemental oxygen, non-invasive or invasive mechanical ventilation or extracorporeal membrane

oxygenation."[7,8] The recommended dose of tocilizumab is a single IV infusion of 8 mg/kg not exceeding 800 mg.[8] Common side effects include upper respiratory tract infections, headaches, and increase in blood pressure.[7]

A systematic review found that inpatient use of tocilizumab reduces the length of hospitalization and progression to mechanical ventilation or death. These findings were based on 12 randomized controlled trials.[6] The scope of that review did not include questions of cost-effectiveness or budget impact. To address these, we conducted an economic evaluation and BIA of the use of tocilizumab for COVID-19, considering costs and outcomes associated with inpatient treatment, post–COVID-19 condition, death, and recovery. We developed a stochastic state-transition model and evaluated 3 cohorts within the hospital setting based on data availability and expected differences in disease severity: those aged younger than 65 years (not in LTC), those aged 65 years and older (not in LTC), and LTC cohorts. Post–COVID-19 condition, (also known as post–COVID-19 condition) was defined as those who experience COVID-19 symptoms for 3 or more months; it occurs in approximately 15% of adults following COVID-19 infection.[2] We also addressed considerations of current testing policies (i.e., using data from the spread of the Omicron variants in 2022), and tocilizumab's therapeutic effects.

Policy Question

What are the health system impacts, uptake, and funding considerations of offering tocilizumab as an inpatient treatment option for COVID-19 in Canada?

Main Take-Aways

This report aims to estimate the health system impacts (i.e., health system costs and health outcomes) of access to and funding for tocilizumab treatment in the inpatient setting in Canada. Considerations for this policy question include the effectiveness of tocilizumab at reducing length of stay and mortality for both inpatients and those in the critical care unit, the potential use of tocilizumab if access is expanded, the impact on quality of life, and the health care system treatment costs associated with COVID-19 and tocilizumab.

Objective

The objective was to conduct a CUA and BIA of tocilizumab for inpatient treatment of COVID-19 in Canada.

Research Question

We addressed the previously cited policy question by exploring the following research question:

What is the cost-effectiveness, budget impact, and health system impact of tocilizumab as an inpatient treatment for COVID-19 in populations understood to be at increased risk of severe outcomes?

Economic Analysis

Review of Economic Literature

A BIA is required to assess the affordability of implementing the intervention across the entire eligible population, accounting for the resources required to administer the intervention.[9] Considerations of budget constraints and drug supply can have an important role in resource allocation.[10] In the context of inpatient treatments for COVID-19, factors such as the size of the eligible patient population, dose size and timing, 28-day survival, length of stay (LOS), and critical care or intensive care unit (ICU) admissions should be considered. In 2020, data from the Council of Federation Secretariat estimated that in the first 5 months of 2020 more than $11 billion was spent to address the COVID-19 pandemic in Canada. This included costs for treatment, such as pharmaceuticals and medical supplies, testing, prevention through personal protective equipment, and other health care services and supplies.[11] Treatments and vaccines for COVID-19 in the appropriate patient population, though considered a major investment, have the potential to substantially save costs because of the downstream health care resource use associated with COVID-19.[12,13]

The potential of tocilizumab to be cost-saving for patients hospitalized with acute COVID-19 is supported by evidence from several countries including the US,[14] Britain,[15] Canada,[16] Spain,[17] and Russia.[18] Petrov et al. (2022)[18] found that tocilizumab was the least expensive drug to treat severe and extremely severe COVID-19, with prices ranging from US$468 to US$916 per dose (based on 2022). Garcia-Molina and Alos-Alminana (2023)[17] found that tocilizumab was associated with a total budget impact of €206,466 with marginal costs of €467 per life-year gained and €478 per survivor for individuals aged 18 to 71.5 years and €701 per life-year gained and €726 per survivor for those aged older than 71.5 years old. Dijk et al. (2022)[14] found that tocilizumab was cost-effective and had an iNMB of US$52,378 (based on 2020) from a US health care perspective using a lifetime horizon and a willingness-to-pay (WTP) threshold of $100,000 per QALY. Sinha and Linas (2021)[15] found that tocilizumab in combination with dexamethasone was cost-effective in reducing mortality compared to both dexamethasone and supportive care alone with an incremental cost-effectiveness ratio (ICER) of US$16,520 per QALY (95% credible interval [CrI], US$10,760 to US$51,530) compared to dexamethasone alone. These findings were based on studies that were conducted before the Omicron variants with 4 studies conducted between 2020 and 2021[15-18] and 1 in 2020.[14] Research indicates that tocilizumab compared to standard of care for patients hospitalized with COVID-19 costs between US$468 and US$916 (CA$642 to CA$1,256) per dose (based on 2022),[18] with marginal costs per life-year gained ranging from €467 to €726 (CA$688 to CA$1,070),[17] an ICER of US$16,520 (CA$22,653) per QALY,[15] and an iNMB of US$52,378 (CA$71,844) (based on 2022).[14]

Economic Evaluation and Budget Impact

We conducted a CUA and BIA examining inpatient treatment strategies for tocilizumab based on COVID-19 data from the year 2022. We developed a stochastic state-transition model that included clinical outcomes associated with COVID-19 hospitalization using data from the Canadian Institute of Health Information (CIHI), the Public Health Agency of Canada (PHAC),[19] and the scientific literature. To reflect the best available data related to tocilizumab effect estimates and severity of COVID-19 infection, the patient

population in the model is stratified into 3 cohorts: those aged younger than 65 years (not in LTC), those aged 65 years and older (not in LTC), and those in LTC of any age group. The variation of model inputs allows for estimates to include 95% CrI. Costs related to inpatient stay, critical care stay, physician time, and tocilizumab were included in the analysis.

Economic Analyses Overview

We estimated the costs, health outcomes, and cost-effectiveness of 5 COVID-19 inpatient treatment scenarios for tocilizumab in Canada compared to a baseline. The scope and analytical approach taken in this economic evaluation was based on the best available data identified from clinical reviews, scientific literature, and data repositories. This evaluation was based on Canadian data obtained from CIHI and supplemented with data from the literature, including CDA-AMC reviews. CIHI provided COVID-19 data related to COVID-19 disease severity (inpatient, critical care or ICU, death, and LOS) for Canada.

The reference scenario was defined as COVID-19 hospitalizations representative of 2022 in Canada. Data used to define the reference scenario include some inpatient tocilizumab use, as tocilizumab was approved for use in October 2022 for adults receiving corticosteroids.[7,8] The proportion of patients in Canada with COVID-19 treated with tocilizumab in 2022 within the hospital setting was not available in literature and represents a limitation in the data.

The 5 tocilizumab uptake scenarios were selected following discussions with the CoLab team. The drug uptake estimates used in the scenarios were selected to represent expected inpatient use of tocilizumab with consideration for potential drug interactions and adverse events. These scenarios assumed that patients who are hospitalized had access to tocilizumab as an option for inpatient treatment for COVID-19 at various drug uptakes, to evaluate the overall potential impacts to the health care system. The scenarios define the 65 years and older (not in LTC) and LTC cohorts as “high risk” for simplicity for naming scenarios. These scenarios are described as follows:

Reference scenario: COVID-19 hospital dispositions in 2022 in Canada (reference scenario)

Scenario 1: Tocilizumab treatment of patients who are hospitalized in 10% of those aged younger than 65 years (not in LTC), 15% of those aged 65 years and older (not in LTC), and 15% of those in LTC (low uptake scenario])

Scenario 2: Tocilizumab treatment of patients who are hospitalized in 20% of those aged younger than 65 years (not in LTC), 30% of those aged 65 years and older (not in LTC), and 30% of those in LTC (moderate uptake scenario)

Scenario 3: Tocilizumab treatment of patients who are hospitalized in 15% of those aged 65 years and older (not in LTC) and 15% of those in LTC (high-risk low uptake scenario)

Scenario 4: Tocilizumab treatment of patients who are hospitalized in 50% of those aged 65 years and older (not in LTC) and 50% of those in LTC (high-risk high uptake scenario)

Scenario 5: Tocilizumab treatment of patients who are hospitalized in 30% of those aged younger than 65 years (not in LTC), 50% of those aged 65 years and older (not in LTC), and 50% of those in LTC (high uptake scenario)

Economic Evaluation Methods

We developed a stochastic state-transition model that includes clinical outcomes associated with COVID-19 hospitalization. The advantage of using a state-transition model compared to other analytical methods is that it captures dynamics related to clinical outcomes such as transfers between inpatient, critical care, post–COVID-19 condition, and death, while quantifying costs and QALYs for patient pathways within the health system. Stochasticity in model transitions, along with probabilistic sensitivity analysis in model inputs, allowed reporting of 95% CrIs or standard errors as part of the results. This evaluation was based on data mainly from Canada (excluding Quebec) obtained from CIHI and supplemented with data from the literature, including CDA-AMC reviews. The time horizon included 1 year of simulation, including impacts on inpatient outcomes and post–COVID-19 condition, along with estimates of projected lifetime QALY losses due to death observed in that year. This approach allows for estimating differences in QALY benefit gains or losses compared to the reference scenario.

The state-transition model was stratified into 3 cohorts related to risk of severe outcomes: those aged younger than 65 years (not in LTC), those aged 65 years or older (not in LTC), and those in LTC. The model simulation was stratified into 2 periods: January 2022 to August 2022 (period 1) and September to December 2022 (period 2) to better adjust for differences in severity of COVID-19 observed in the CIHI data. Overall, these results were combined at the end of the simulations across the 3 cohorts and 2 periods.

The intervention scenarios considered various possible tocilizumab uptake estimates based on reasonable coverage (i.e., the percent of inpatients offered tocilizumab as informed by the CoLab team) and therapy completion rates (related to drug-drug interactions and/or adverse events). Model data were either directly obtained and/or combined from multiple data sources, including for the effect estimates of inpatient use of tocilizumab.

We estimated net monetary benefit (NMB) defined as the monetary value of an intervention for a given WTP threshold for an additional unit of health, and it was used to scale both costs and benefits in the same unit. The NMB is estimated for the following 3 WTP thresholds: $30,000, $50,000, and $100,000. We also presented the ICER of each scenario compared to baseline.

BIA Methods

This BIA quantified the health system impacts related to tocilizumab inpatient treatment retrospectively using Canadian COVID-19 data in 2022, including the number of patients admitted to hospital who were in critical care and who were not. This data excludes Quebec because of data limitations related to the release of severity data from CIHI. The time horizon included 1 year of simulation, while lifetime QALY losses due to deaths were also included in this analysis, with an assumed discount rate of 1.5%. The analytical approach aimed to answer a counterfactual question about the inpatient use of tocilizumab (i.e., if we retrospectively treated a specified fraction of patients with tocilizumab in 2022, what would be the difference in health care

system costs and quality of life outcomes compared to the reference scenario [i.e., COVID-19 hospital dispositions in Canada in 2022]).

For the reference and 5 scenarios described previously, the variation of model inputs allowed for budget impact estimates to include 95% CrIs. Costs related to inpatient units, critical care units, physician time, and tocilizumab treatment were included in the analysis. Costs related to corticosteroids (taken with tocilizumab), administration costs related to the implementation of the inpatient treatment strategy, and health care costs related to post–COVID-19 condition were not included.

Target Populations and Setting

Based on the best available data, the target population and setting for the state-transition model was the population in Canada who were hospitalized with COVID-19 in 2022. The state-transition model stratified COVID-19 hospitalizations according to the cohorts: those aged younger than 65 years (not in LTC), those aged 65 years and older (not in LTC), and those in LTC. Hospital dispositions from 2022 related to COVID-19 in Canada were obtained from CIHI and are described in Table 1, stratified across cohorts and time periods (period 1 and period 2). Total hospital admissions include those admitted to the critical care unit.

Table 1: Hospital Dispositions From CIHI Related to COVID-19 in Canada (2022)

Hospital disposition (2022)	Age < 65 years (not in LTC)	Age ≥ 65 years (not in LTC)	LTC
Period 1: January 2022 to August 2022			
Total hospital admissions	38,062	54,433	6,132
Total critical care admissions	6,457	7,261	370
Total deaths[a]	1,601	8,341	465
Period 2: September 2022 to December 2022			
Total hospital admissions	11,062	27,053	3,696
Total critical care admissions	2,068	3,246	233
Total deaths[a]	532	3,758	226

LTC = long-term care; CIHI = Canadian Institute for Health Information.

Note: Total hospital admissions may include repeat hospitalizations and do not represent total people hospitalized.

[a]Within-facility deaths reported from CIHI based on the Discharge Abstract Database.

Treatment

The inpatient COVID-19 treatment considered was tocilizumab. Tocilizumab is used for the treatment of COVID-19 and can help reduce inflammation.[7] The recommended dose of tocilizumab is a single IV infusion of 8mg/kg not exceeding 800 mg given no drug-drug interactions and/or adverse drug events.[7,8] This drug is also administered to those receiving corticosteroids.

Perspective

The CUA and BIA were conducted from a Canadian health care payer perspective.

Time Horizon and Discounting

Based on the availability of data and the time-limited impact of tocilizumab, we used a 1-year time horizon. However, to capture the full impact of preventing deaths, lifetime QALY losses due to death were also included in this analysis, with an assumed discount rate of 1.5%. As all other events were only simulated over a year time horizon, no other discounting was applied, as the impact of discounting over the course of a single year is minimal. Simulated individuals were initialized within hospital at the starting time, and after 1 year most were in the Recovered or Dead state, with a very small proportion (< 0.1%) in the Post–COVID-19 Condition state.

Model Structure (CUA and BIA)

The model used to conduct both the CUA and the BIA was a stochastic state-transition Markov model representing acute care clinical outcomes associated with COVID-19, with states defined as follows:

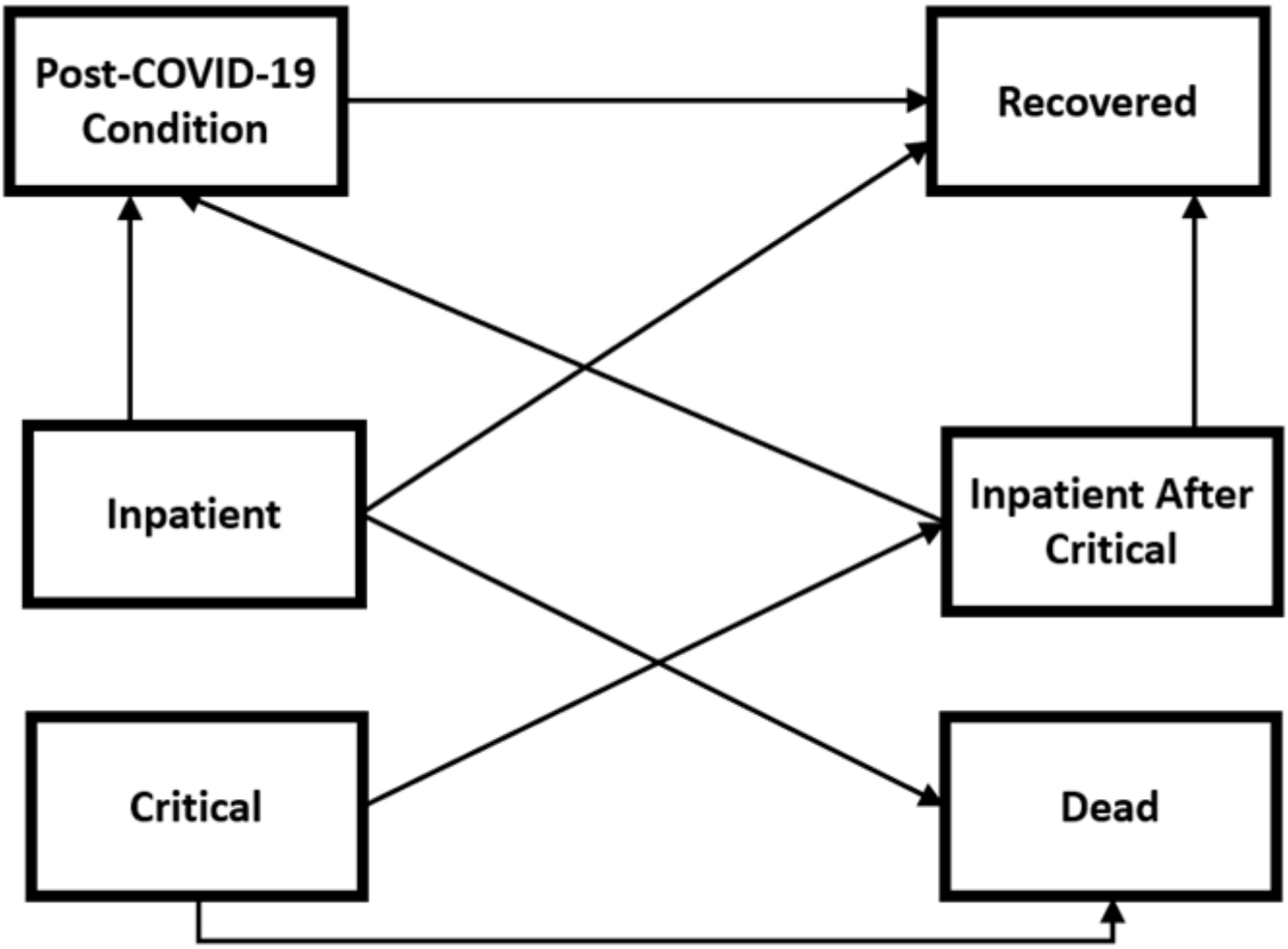
- **Inpatient:** individuals hospitalized but not in critical care
- **Critical:** individuals in critical care requiring ICU admission
- **Inpatient After Critical:** individuals having recovered from the critical state and being monitored before discharge from hospital
- **Post–COVID-19 condition:** defined consistently with Hanson et al.,[20] "Having at least 1 of the 3 symptom clusters (persistent fatigue with bodily pain or mood swings; cognitive problems; or ongoing respiratory problems) 3 months after symptomatic SARS-CoV-2 infection."
- **Recovered**: individuals having recovered from disease states (COVID-19 Cases, Inpatient, and Inpatient After Critical)
- **Dead**: end state; there were no costs associated with this state

Individuals begin in either the Inpatient or Critical state and may progress either to the Death or the Recovered state. Transitions occur on a daily basis in the model. Individuals in the model do not move directly from the Inpatient to the Critical state. Though inpatient to critical is a realistic transition, there is insufficient data to determine what proportion of patients entered critical care immediately upon hospitalization rather than after a delay. Instead, we initialized individuals in both of the Inpatient and Critical states in accordance with admission data from CIHI. To capture the time patients spend in critical care, individuals in the model move from the Critical state to the Inpatient After Critical state. Nonetheless, this accurately depicts the average total time patients spend in each hospital state, and thus accurately captures the costs and health-related utilities accrued by their hospital stay. Modelled individuals enter the Dead state from either the Inpatient or Critical states. This does not include deaths that occurred in individuals who were not admitted to hospital, especially those in LTC. Patients either recover fully or may first spend time in the Post–COVID-19 Condition state. The proportion of individuals who move to Post–COVID-19 Condition differs depending on whether they were an inpatient or critical case, consistent with the proportions reported in Hanson et al.[20] Figure 1 shows the model states and transitions.

The stochastic state-transition model, as described in Figure 1, was stratified into 3 cohorts (not shown): those aged younger than 65 years (not in LTC), those aged 65 years and older (not in LTC), and those in

LTC, and interventions for inpatient treatment targeted all 3 cohorts. The 2022 COVID-19 data were further stratified into 2 periods (not shown) to account for differences in COVID-19 severity outcomes: January to August 2022 (period 1) and September to December 2022 (period 2). The model simulates each cohort and period independently.

Figure 1: Model Diagram of the State-Transition Model for COVID-19



Data Sources

Table 2 describes the key data sources and transformations used to estimate model inputs for the CUA and BIA.

Table 2: Data Source, Transformations, and Additional Comments

Data source	Data transformations	Additional comments
CIHI data (2022) Datasets: • Discharge Abstract Database • Canadian MIS Database (costs)	• Hospital disposition (inpatient, critical, LOS, and death) and costs • Total costs were transformed to daily per-patient costs using inpatient LOS and critical LOS	• Data provided for Canada excluded Quebec because of limitations in reporting. • The LTC cohort was based on the discharge disposition. Estimates such as deaths in facility would be based on institution transfer from type code (i.e., those transferred to an acute hospital facility who subsequently dies is accounted for). Deaths that occurred outside discharge are not included. • Costs did not include physician fees, and this was included using a study by Lau et al.[21] • Costs related to post–COVID-19 condition were not included in the analysis (limitations in literature).
Riad et al.[6] (CDA-AMC systematic review)	• Tocilizumab effect estimates for hospital LOS	• Studies considered from the systematic review for effect estimates had study periods before the Omicron variant (i.e., 2020 to 2021).
WHO[22,23]	• Tocilizumab effect estimates for hospital death	• The WHO living guideline for therapeutics and COVID-19 provides various therapeutic effects for available COVID-19 treatments.

CIHI = Canadian Institute of Health Information; LOS = length of stay; LTC = long-term care.

Data Inputs

Table 3 describes the stochastic state-transition model parameters related to inpatient transitions with sample distributions and standard deviations (SDs) among COVID-19 hospitalizations (refer to Table 17 for additional data transformations used in the model). These transitions are stratified by period 1 (January 2022 to August 2022) and period 2 (September 2022 to December 2022) and cohorts (age < 65 years and not in LTC, age ≥ 65 years and not in LTC, and in LTC). Two periods were selected to adjust for differences in COVID-19 severity outcomes. Data sources include data from CIHI and CDA-AMC systematic reviews (refer to Table 2). Although the target population is Canada, severity parameters obtained from CIHI for Canada did not include data from Quebec; therefore, they were not included in the modelling. All model parameters except for time to symptom resolution varied based on the SD. This simulation method is analogous to a probabilistic sensitivity analysis. Proportion- and time-related transition parameters were assumed to follow the beta and gamma distributions, respectively. For parameters that did not have SDs, assumed SDs of plus or minus 5% of model inputs were used.

The LOS for the Inpatient and Critical states was estimated from CIHI data (refer to Table 17). Bayesian inference was used to estimate the distribution of the rate patients leave the hospital and critical care. This was determined by first using the method of moments to estimate the Weibull distribution that has the LOS mean, $\bar{\theta}$, and LOS SD, s, given by the hospital and critical care CIHI data, respectively. Next, a random

sample of n LOS values were taken from the estimated Weibull distribution, where n is the number of observations given by the hospital and critical care CIHI data. Then an exponential distribution, $EXP(\lambda)$, with an inverse gamma distributed rate, $\lambda \sim INVGAM\left(\frac{n}{\theta}, n\right)$, was fit to the n random samples from the estimated Weibull distribution to determine the distribution of the rate patients leave the hospital and critical care.

Death rates were estimated from CIHI data. Therefore, because of the data available from CIHI, in this analysis, deaths in LTC represent those who died during hospitalization and do not capture LTC residents who died outside of hospital facilities.

The therapeutic effect of tocilizumab was obtained from Riad et al. (refer to the Clinical Parameters section).[6] The therapeutic effect for the inpatient use of tocilizumab was applied to hospital LOS[6] and death[22] (inpatient and critical). Per patient-day costs were estimated using LOS and total cost estimates from CIHI.

Health utilities were assigned to each state to calculate QALYs from model simulations (refer to Table 5). Baseline health utilities associated with healthy individuals in the Recovered state were obtained from health-adjusted life-expectancy (HALE) tables published by Statistics Canada,[24] and cross-referenced with the average age of cases[25] in modelled cohorts. Health utilities immediately following hospital discharge (assumed to be the same as the utilities for inpatients) and for post–COVID-19 condition were obtained from Poudel et al.[26]

Table 3: Stochastic State-Transition Model Parameters Related to Inpatient Transitions, Including Sample Distribution and SD Among COVID-19 Cases

Symbol	Quantity	Source	Sample distribution	Mean (SD): < 65 years old	Mean (SD): ≥ 65 years old	Mean (SD): LTC
Period: January 2022 to August 2022						
$\vec{T}_{ah}$	LOS hospital (days)	CIHI	Weibull	10 (26)	16 (25)	43 (55)
$\vec{T}_{c}$	LOS critical care (days)	CIHI	Weibull	9 (16)	9 (14)	9 (17)
$\vec{T}_{ah\_c}$	LOS hospital among those admitted to critical care (days)	CIHI	Weibull	22 (44)	23 (30)	58 (72)
$\vec{p}_{c-d}$	Proportion of critical patients who die	CIHI	Beta	0.169 (± 5%)	0.332 (± 5%)	0.135 (± 5%)
$\vec{p}_{\mathrm{h}-d}$	Proportion of inpatients who die	CIHI	Beta	0.016 (± 5%)	0.126 (± 5%)	0.072 (± 5%)
Period: September 2022 to December 2022						
$\vec{T}_{ah}$	LOS hospital (days)	CIHI	Weibull	15 (40)	19 (36)	57 (73)

Symbol	Quantity	Source	Sample distribution	Mean (SD): < 65 years old	Mean (SD): ≥ 65 years old	Mean (SD): LTC
$\vec{T}_c$	LOS critical care (days)	CIHI	Weibull	9 (18)	8 (16)	8 (9)
$\vec{T}_{ah\_c}$	LOS hospital among those admitted to critical care (days)	CIHI	Weibull	29 (64)	27 (58)	71 (103)
$\vec{p}_{c-d}$	Proportion of critical patients who die	CIHI	Beta	0.161 (± 5%)	0.294 (± 5%)	0.073 (± 5%)
$\vec{p}_{\mathrm{h}-d}$	Proportion of inpatients who die	CIHI	Beta	0.022 (± 5%)	0.118 (± 5%)	0.060 (± 5%)
Period: January 2022 to December 2022						
$\vec{T}_{sr}$	Total time to symptom resolution (days)	Siemieniuk et al.[27]	Gamma	9.9	9.9	9.9
$\vec{p}_{hrl-l}$	Proportion of hospitalized patients that develop post–COVID-19 condition	Wulf Hanson et al.[20]	Beta	0.275 (± 5%)	0.275 (± 5%)	0.275 (± 5%)
$\vec{p}_{crl-l}$	Proportion of critical patients that develop post–COVID-19 condition	Wulf Hanson et al.[20]	Beta	0.431 (± 5%)	0.431 (± 5%)	0.431 (± 5%)
$\vec{T}_l$	Mean duration of post–COVID-19 condition (days)	Wulf Hanson et al.[20]	Gamma	139.903 (7)	139.903 (7)	139.903 (7)

CIHI = Canadian Institute of Health Information; LOS = length of stay; SD = standard deviation; LTC = long-term care.

Clinical Parameters

Therapeutic Effect Estimates: Tocilizumab for Inpatient Treatment of COVID-19

Table 4 describes the therapeutic effects for the inpatient use of tocilizumab for hospital LOS and death as a relative risk measure. Based on Riad et al.,[6] 4 studies[28-31] were considered that provided therapeutic estimates for LOS in hospitals. These studies were conducted among cohorts that included those aged 18 years and older in high-income countries, and used standard of care comparators. All these studies were conducted between 2020 and 2021 (before the Omicron variant) and represent the best available evidence in the literature. Out of these studies, Rosas et al.[29] was selected for the model input as this study included a hazard ratio based on a cohort from multiple countries, including Canada. The estimated hazard ratio from this study reported in Riad et al. was 0.74 (95% CI, 0.56 to 0.98) of the baseline hospital LOS.[6,29]

The WHO living guideline for therapeutics and COVID-19 provides various therapeutic effects for available COVID-19 treatments.[22,23] This report provided evidence (before the Omicron variant) for mortality among those with severe or critical COVID-19 treated with Interleukin 6 receptor blockers, which included tocilizumab compared to standard care. The certainty of evidence was reported as high, and the relative risk estimate for mortality was 0.88 (95% CI, 0.82 to 0.95).

Overall, the previously mentioned studies were mainly from COVID-19 that occurred before the Omicron variants, which represents a limitation in the data used in this analysis. In addition, these therapeutic effects

were applied similarly in the model across all 3 cohorts. We did include a range of values around each estimate to account for uncertainty.

Table 4: Effect Estimates for the Inpatient Treatment of COVID-19 With Tocilizumab

Symbol	Quantity	Inpatient tocilizumab therapy effect			Therapy effect source
		Age < 65 years (95% CI)	Age ≥ 65 years (95% CI)	LTC (95% CI)	
Relative Risk					
$\vec{T}_{ah}$	LOS hospital (days)	0.74 (0.56 to 0.98)	0.74 (0.56 to 0.98)	0.74 (0.56 to 0.98)	Riad et al.[6] and Rosas et al.[29]
$\vec{T}_{c}$	LOS critical (days)	0.74 (0.56 to 0.98)	0.74 (0.56 to 0.98)	0.74 (0.56 to 0.98)	
$\vec{p}_{c-d}$	Proportion of critical patients that die	0.88 (0.8 to 0.95)	0.88 (0.82 to 0.95)	0.88 (0.82 to 0.95)	WHO[22,23]
$\vec{p}_{\mathrm{h}-d}$	Proportion of inpatients that die	0.88 (0.82 to 0.95)	0.88 (0.82 to 0.95)	0.88 (0.82 to 0.95)	

CI = confidence interval; LOS = length of stay; LTC = long-term care.

Utilities

The health utility associated with the Recovered state was assumed to be that of healthy individuals and is estimated from HALE tables published by Statistics Canada[24] and assigned to model cohorts according to the average age of those with COVID-19 in that cohort. We estimated recovered utilities separately for the 2 time periods captured in the model. Within the model simulated time of 1 year, the accrued QALYs lost due to death did not fully account for the overall QALYs lost from patient deaths, which extended beyond 1 year. As a result, upon entry into the Dead state in the model, a fixed QALY decrement (accounting for discounting) was applied equal to the average HALE for individuals in the modelled cohort, thereby capturing the loss of expected lifetime QALYs. For the purpose of taking the difference between treatment and reference scenarios, this approach produced the same result as adding QALYs to all surviving individuals at the end of simulation equal to their HALE, but had the advantage of requiring only data describing individuals who died. However, total simulated QALYs will include the QALYs accrued during 1 year of simulation and the negative quantities equal to the lost lifetime HALE of individuals who died (refer to Table 14). Poudel et al.[26] reported health utilities for COVID-19 patients immediately upon discharge from hospital, as well as for post–COVID-19 condition. Because of a lack of published studies providing health utilities during hospitalization and with the observation that the recovery of health utility back to baseline is slow following hospitalization, as reported by Poudel et al.,[26] we inferred that the utility during noncritical hospitalization (inpatient and inpatient after critical) is equal to that immediately after discharge. Additionally, individuals in the Critical state are often either unconscious or have a very low health-related quality of life; therefore, the utility for critical was assumed to be 0. The utility estimates for the stochastic state-transition model are described in Table 5.

Table 5: Utility Estimates for the Stochastic State-Transition Model

Symbol	States	Annual utility (SD)	Entry utility (SD)	Source
$\overrightarrow{Ut}_c$	Critical	0	0	Estimate
$\overrightarrow{Ut}_h$	Inpatient	0.60 (0.06)	0	Poudel et al. (2021)[26]
$\overrightarrow{Ut}_{d1a}$	Period 1: Dead (age < 65 years)	0	–27.6 (0.04)	Statistics Canada (2018),[24] PHAC (2023)[32]
$\overrightarrow{Ut}_{d1b}$	Period 1: Dead (age ≥ 65 years and/or LTC)	0	–6.4 (0.03)	Statistics Canada (2018),[24] PHAC (2023)[32]
$\overrightarrow{Ut}_{d2a}$	Period 2: Dead (age < 65 years)	0	–27.3 (0.03)	Statistics Canada (2018),[24] PHAC (2023)[32]
$\overrightarrow{Ut}_{d2b}$	Period 2: Dead (age ≥ 65 years and/or LTC)	0	–6.0 (0.03)	Statistics Canada (2018),[24] PHAC (2023)[32]
$\overrightarrow{Ut}_i$	Inpatient After Critical	0.60 (0.06)	0	Poudel et al. (2021)[26]
$\overrightarrow{Ut}_l$	Post–COVID-19 Condition	0.76 (0.076)	0	Poudel et al. (2021)[26]
$\overrightarrow{Ut}_{r1a}$	Period 1: Recovered (age < 65 years)	0.89 (0.089)	0	Statistics Canada (2018),[24] PHAC (2023)[32]
$\overrightarrow{Ut}_{r1b}$	Period 1: Recovered (age ≥ 65 years and/or LTC)	0.73 (0.073)	0	Statistics Canada (2018),[24] PHAC (2023)[32]
$\overrightarrow{Ut}_{r2a}$	Period 2: Recovered (age < 65 years)	0.89 (0.089)	0	Statistics Canada (2018),[24] PHAC (2023)[32]
$\overrightarrow{Ut}_{r2b}$	Period 2: Recovered (age ≥ 65 years and/or LTC)	0.70 (0.070)	0	Statistics Canada (2018),[24] PHAC (2023)[32]

LTC = long-term care; PHAC = Public Health Agency of Canada; SD = standard deviation.

Costs

All costs were reported in 2022 Canadian dollars and, where needed, were inflated to 2022 Canadian dollars using the Consumer Price Index for all items in Canada.[33] Table 6 describes the 2022 Canadian dollar hospital resource and drug costs used in the health economic evaluation, including the costs associated with purchasing tocilizumab. Costs from CIHI were scaled from total to per-day costs using LOS estimates for inpatient and critical care cases. We added per patient-day costs for inpatient and critical care physicians from the literature because these costs are not included in the total costs reported by CIHI. Costs related to the implementation of the inpatient strategy and health care costs related to post–COVID-19 condition were not included in this analysis.

The administration of tocilizumab as an inpatient treatment for COVID-19 is a 1-time IV infusion with corticosteroids.[7] Although patients could receive an additional infusion of tocilizumab, the proportion who do so is unknown. Therefore, costs were estimated based on a 1-time IV infusion of tocilizumab. Total costs for

tocilizumab do not include corticosteroids (taken with tocilizumab) and treatment within the hospital ranged from $959 to $1,919 for a dose of 400 mg to 800 mg.[34]

Table 6: Hospital Resource and Drug Costs

Hospital resource or drug cost	Cost	Treated state	Source
Period 1: Hospital stay, inpatient (per day)			
Age < 65 years old	$1,368 (SD = 68.39)	Inpatient or Inpatient After Critical	CIHI
Age ≥ 65 years old	$1,118 (SD = 55.92)		
LTC	$913 (SD = 45.66)		
Period 1: Hospital stay, critical (per day)			
Age < 65 years old	$3,713 (SD = 185.66)	Critical	CIHI
Age ≥ 65 years old	$3,640 (SD = 182.01)		
LTC	$4,573 (SD = 228.65)		
Period 2: Hospital stay, inpatient (per day)			
Age < 65 years old	$1,182 (SD = 59.09)	Inpatient or Inpatient After Critical	CIHI
Age ≥ 65 years old	$1,042 (SD = 52.10)		
LTC	$874 (SD = 43.69)		
Period 2: Hospital stay, critical (per day)			
Age < 65 years old	$3,668 (SD = 183.40)	Critical	CIHI
Age ≥ 65 years old	$3,366 (SD = 168.31)		
LTC	$4,107 (SD = 205.34)		
Inpatient physician (per patient-day)	$48.73 (SD = 16.30)	Inpatient or Inpatient After Critical	Lau et al. (2022)[21]
Critical care physician (per patient-day)	$254.70 (SD = 128.22)	Critical	Lau et al. (2022)[21]
Tocilizumab treatment (excluding corticosteroids)	$1,439 (SD = 244.90)	Inpatient or Critical	Government of Alberta (2024)[34]

CIHI = Canadian Institute of Health Information; LTC = long-term care; SD = standard deviation.

Notes: Period 1 was January to August 2022 and period 2 was September to December 2022. Cost conversion to US dollars was US$1 = CA$1.36.

Scenario Analysis and Sensitivity Analysis

Five treatment scenarios and 1 reference scenario were considered in the main health economic evaluation, all of which are described in Table 7. We included both scenarios targeting inpatient treatment of tocilizumab to all cohorts, as well as those focused on cohorts considered at higher risk of severe COVID-19, specifically those aged 65 year and older and in LTC. The reference scenario represents the standard of care during 2022 and included some inpatient use of tocilizumab in adults receiving corticosteroids. The baseline use of tocilizumab within the hospital was not available in the literature. Therefore, scenarios described in Table 7 would include additional tocilizumab use above what was provided to patients in the reference scenario. The 5 scenarios were selected following discussions with the CoLab team. Uptake was defined as a reasonable

estimate of tocilizumab use if broadly available for the inpatient treatment of COVID-19 with consideration for potential drug interactions and adverse events.[35] Therefore, these scenarios assumed that a fraction of hospitalizations had tocilizumab as an inpatient option for COVID-19 treatment and evaluated the impact of that access to the health care system.

We also included 2 additional scenarios as part of a scenario sensitivity analysis where we focused tocilizumab treatment in individuals in critical care; these additional scenarios are presented in Table 7. We reanalyzed the low uptake in high-risk cohorts (aged ≥ 65 years and LTC) and the high uptake in all cohorts but with the costs and benefits of tocilizumab only being captured in the critical care population, these were labelled additional scenario 6 and additional scenario 7, respectively.

Furthermore, probabilistic sensitivity analyses were undertaken to address parameter uncertainty associated with cost-effectiveness of scenarios compared to reference case, across the 3 cohorts and 2 time periods (5,000 simulations). The probabilistic results describe the extent to which parameter uncertainty affected the cost-effectiveness estimates in the model. The SDs for the model parameters used in the stochastic state-transition model are described in Table 3, Table 4, Table 5, and Table 6. Standard distributional forms were taken to describe probability distribution functions relating to input parameters (proportions and utilities were characterized by the beta distribution and costs were characterized by gamma distributions).

The results of the probabilistic analysis are presented using a cost-effectiveness acceptability curve that highlights the probability that each scenario was optimal compared to baseline ($NMB_{scenario} > NMB_{baseline}$). Scenario analysis results include NMB, iNMB, and ICERs, including quadrant location.

Table 7: Scenario Descriptions for Tocilizumab for the Inpatient Treatment of COVID-19

Scenario	Justification
Reference scenario: COVID-19 hospital dispositions in 2022 (Canada) Note: The standard of care during 2022 would include inpatient treatment of tocilizumab. The overall proportion of inpatient use of tocilizumab was unavailable in literature.	The reference scenario focused on representing COVID-19 epidemiology in 2022. Data from 2022 were selected to conduct an economic evaluation as these were the data that were available at the time the analysis was undertaken. During this period, there was a transition of management policies toward COVID-19 as an endemic disease.
Scenario 1 (low uptake): Tocilizumab treatment of patients who were hospitalized in 10% of those aged < 65 years (not in LTC), 15% of those aged ≥ 65 years (not in LTC) and 15% of those in LTC	Scenario 1 included inpatient treatment of those aged < 65 years (not in LTC) along with those who have a higher severity risk and represented the lowest reasonable uptake.
Scenario 2 (moderate uptake): Tocilizumab treatment of hospitalized patients in 20% of those aged < 65 years (not in LTC), 30% of those aged ≥ 65 years (not in LTC) and 30% of those in LTC	In scenario 2, the magnitude of inpatient uptake of tocilizumab was increased to capture the potential for higher uptake of the drug; specifically, uptake was doubled in all cohorts.
Scenario 3 (high-risk low uptake): Tocilizumab treatment of hospitalized patients in 15% of those aged ≥ 65 years (not in LTC) and 15% of those in LTC	Scenario 3 had a focus on inpatient uptake of tocilizumab in individuals at highest risk of severe COVID-19, specifically those aged ≥ 65 years (not in LTC) and those in the LTC cohort, with uptake consistent with scenario 1.

Scenario	Justification
Scenario 4 (high-risk high uptake): Tocilizumab treatment of hospitalized patients in 50% of those aged ≥ 65 years (not in LTC) and 50% of those in LTC	Scenario 4 had a focus on high inpatient uptake of tocilizumab in individuals at highest risk of severe COVID-19, specifically those aged ≥ 65 years (not in LTC) and those in the LTC cohorts.
Scenario 5 (high uptake): Tocilizumab treatment of hospitalized patients in 30% of those aged < 65 years (not in LTC), 50% of those aged ≥ 65 years (not in LTC) and 50% of those in LTC	Scenario 5 was a combined scenario of the highest inpatient uptake of tocilizumab in those aged < 65 years (not in LTC), aged ≥ 65 years (not in LTC), and in the LTC cohorts.
Additional scenarios focused only on critical care	
Additional scenario 6 (high-risk low uptake — critical care only): Tocilizumab treatment of hospitalized patients in 15% of those aged ≥ 65 years (not in LTC) and 15% of those in LTC for individuals in critical care	This scenario was to capture health and cost outcomes if health systems were to focus tocilizumab treatment on individuals in critical care. We looked at the lowest and highest uptake scenarios to see the range of possible impacts in this population.
Additional scenario 7 (high uptake — critical care only): Tocilizumab treatment of hospitalized patients in 30% of those aged < 65 years (not in LTC), 50% of those aged ≥ 65 years (not in LTC) and 50% of those in LTC for individuals in critical care only	This scenario was to capture health and cost outcomes if health systems were to focus tocilizumab treatment on individuals in critical care. We looked at the lowest and highest uptake scenarios to see the range of possible impacts in this population.

LTC = long-term care.

Uncertainty

As model simulations incorporate uncertainty within model inputs, a probabilistic one-way sensitivity analysis (POSA)[36] (n = 1,000 simulations) was used to estimate impacts of changing a key model input on total costs of selected treatment scenarios (scenario 2 — moderate uptake, scenario 4 — high-risk high uptake, and scenario 5 — high uptake) and the reference scenario through systematic sampling between a given range of the model input. Scenario 2, scenario 4, and scenario 5 were selected to provide a range of tocilizumab uptake from moderate to high. Table 8 describes the key model inputs examined for the POSA using total costs as an outcome.

The POSA can assess whether the budget impact (scenario cost – reference scenario cost) will cost (a strategy that costs more compared to the reference scenario) or save (a strategy that costs less compared to the reference scenario) the health care system money.

Table 8: POSA of Key Model Inputs

Model parameter	Cohort (aged < 65 years, aged ≥ 65 years old, LTC, and all)	Range (total discrete points within the range)
Therapy effect of tocilizumab for inpatient use on LOS in hospital	All	0.55 to 0.98 (10)
Therapy effect of tocilizumab for inpatient use on mortality	All	0.81 to 0.98 (10)
Mean hospital LOS of patients who were in critical care for LTC and those ≥ 65 years old	≥ 65 years old, LTC	25 to 40 days (10)
Total per-patient cost: inpatient unit	All	$10,000 to $25,000 (10)

LOS = length of stay; LTC = long-term care; POSA = probabilistic one-way sensitivity analysis.

Model Validation

Overall, the validation of the model structure and model inputs occurred through discussions with the Canadian Collaborative Research Network and the CoLab team to ensure that the model was consistent with current clinical knowledge and practice in Canada. The structure of the stochastic state-transition model was extended from previous work that included multiple iterations and discussions with the Canadian Collaborative Research Network. Methods for obtaining model inputs included clarifications from CIHI (related to a data request), the literature, and discussions with the CoLab team, where necessary.

Internal validity for the reference scenario as described in Table 9 included a comparison of data and model simulations (across the 3 cohorts and 2 periods) for initial model conditions (defined as the starting values for the population cohorts) and total deaths including 95% CrIs. The total deaths in hospital from model simulations compared well to the data. Deaths were captured over 1 year, which provide the total that was validated; however, lifetime impacts of those deaths were captured using QALYs.

Internal validity for scenarios (or treatment effects) was assessed by evaluating simulations at extreme values, such as nullifying the cost of tocilizumab on cost-effectiveness outcomes. This included creating scenarios focusing on 1 cohort and the therapeutic effect of tocilizumab to determine if the results were reasonable compared to the crude estimates. Overall the results were compared to other similar economic evaluations (if available) for external validity.

Table 9: Internal Model Validation of Initial Conditions and Reference Scenario

Internal model validation	Reference scenario (data)	Reference scenario (model, with 95% CrI): n = 5,000 simulations
Total deaths	14,923	14,920 (13,650 to 16,240)

CrI = credible interval.

Model Assumptions

There were several model assumptions required to either supplement missing information or to simplify the model. These assumptions are listed in Table 10.

Table 10: Key Model Assumptions

Related model parameter or structure	Assumption	Additional comments
Time horizon	• The 1-year time horizon was structured around the availability of data. We did not have data available after 2022, and the case and hospitalization data from before 2022 (or before the Omicron variants) may not be representative to current severity rates (including mixed population immunity) and endemic management of COVID-19 (i.e., reduced community testing aligned with other respiratory viruses).	• If COVID-19 severity rates after 2022 are lower (or higher) compared to those used in this report, overall results would overestimate (or underestimate) the overall cost-effectiveness of the inpatient strategy.
Overall model structure	• Stratified model into 2 periods (Period 1: January 2022 to August 2022; Period 2: September 2022 to December 2022) to account for differences in COVID-19 severity estimates.	NA
CIHI data	• COVID-19 severity data reported by CIHI include people with repeat hospitalizations. • COVID-19 severity data reported by CIHI do not include data from Quebec.	NA
Costs	• Costs related to the implementation of the inpatient strategy (e.g., administration costs) and health care costs related to post–COVID-19 condition were not included in this analysis • The reference scenario assumed minimal use of tocilizumab and those cost and effect considerations are not included.	• Health care costs related to COVID-19 management within LTC facilities for patients who could benefit from tocilizumab were not captured in the analysis. This may underestimate the cost-effectiveness of tocilizumab in the LTC cohort.
Death transition: from Recovered, and LTC	• Deaths were only modelled from the Inpatient and Critical states. Death transitions from other model states are challenging to estimate from death data (i.e., interpretations of cause of death as primary, secondary, and contributing cause and location of death) (for LTC data). The LTC cohort was based on the discharge disposition. Estimates such as deaths in facility would be based only on institution transfer from type code. Deaths that occurred outside discharge are not included.	• People in LTC can also die outside of the hospital; therefore, not capturing these deaths could limit the cost-effectiveness of tocilizumab in this population.
Inpatient and critical care model inputs for LTC	• The LTC data obtained from CIHI have limitations related to how LTC is defined by administrative data, and model inputs for this cohort have more uncertainty.	• If inpatient model inputs for LTC are underestimated (a model input that has a therapeutic effect); this would likely also underestimate the cost-effectiveness of scenarios that focus on treatment for the LTC cohort.
Tocilizumab treatment	• Additional treatment beyond the 1-time IV infusion was not accounted for in the costs used in the analysis.	• Adding these additional treatment costs may reduce the cost-effectiveness of tocilizumab.
Tocilizumab therapeutic effects	• Due to data limitations, tocilizumab therapy effects were assumed to be the same for all cohorts (< 65	NA

Related model parameter or structure	Assumption	Additional comments
	years old [not in LTC], ≥ 65 years old [not in LTC], and in LTC)	
Tocilizumab inpatient scenarios	• Costs related to infusion administration and corticosteroids were not included in this analysis.	NA
Tocilizumab reference scenario	• The reference scenario represents the standard of care during 2022 and included some inpatient use of tocilizumab in adults. The baseline use of tocilizumab within the hospital was not available in the literature. Therefore, scenarios described in Table 7 would include some baseline tocilizumab (Health Canada approval in October 2022).	• For the LTC cohort, which is a very high-risk and accessible population, it is possible patients were more likely to have received tocilizumab in 2022, and therefore the treatment effects may already have been seen in the reference population (reducing overall hospitalization and mortality rate in this population).
Utilities	• Utilities for model state were the same across cohorts and periods except for the Recovered state. Utilities also do not differ by treatment arm.	NA
Utilities: Inpatient, Inpatient After Critical states	• Because of a lack of studies reporting health utilities for COVID-19 while in hospital, we assume the health utility of inpatients (noncritical) to be that reported immediately after discharge. This was justified by the fact that recovery of utility back to baseline is very slow after discharge.	• If utilities are lower during hospitalization, this could improve the cost-effectiveness of tocilizumab.
Utilities: Critical state	• Individuals are either unconscious or have a very low health-related quality of life, and the utility for *critical* was assumed to be 0 for simplicity.	• If utilities for those in critical care are higher than 0, this could reduce the cost-effectiveness of tocilizumab.
Utilities: deaths	• Estimated lifetime QALYs lost because of death are subtracted from QALY totals estimated from the 1-year model simulation. These projected lifetime QALYs are assumed to be equal to the average for a given cohort and do not account for possible correlations with age and recovery from COVID-19.	• We discounted lifetime QALY losses associated with mortality at a rate of 1.5% to account for the lifetime impact of mortality.

CIHI = Canadian Institute of Health Information; QALY = quality-adjusted life-year; LTC = long-term care; NA = not applicable.

Assumptions Related to the BIA

A complete list of model assumptions is described in Table 10. In Table 11, we describe the BIA model assumptions that were addressed using POSA.

Table 11: Model Assumptions Addressed by POSA for Tocilizumab

Assumption	How it was tested in the scenario analysis	Additional comments
Tocilizumab therapeutic effect on LOS in hospital	A POSA was conducted to evaluate the impact of the therapeutic effect of LOS in hospital.	This assumption was assessed to explore the impacts on total costs across the uncertainty interval.

LOS = length of stay; POSA = probabilistic one-way sensitivity analysis.

Results

Cost-Effectiveness Analysis Results

Main Take-Aways

The results of the CUA suggest that increased use of tocilizumab in the inpatient setting is likely to be cost-effective at different WTP thresholds. This is supported by a positive mean iNMB and dominant mean ICERs for all tocilizumab uptake scenarios compared to the reference scenario. Both scenarios that focused on high-risk cohorts and those focused on all cohorts were likely to be cost-effective, with higher uptakes yielding greater iNMBs than the reference scenario. These findings were robust even considering uncertainty, as the majority of 95% CrIs for the iNMBs were above 0. The only exception was scenario 1 at WTP thresholds of $50,000 and $100,000, where the credible intervals for the iNMB crossed 0.

Detailed results of the CUA are provided in Table 12 (NMB) and Table 14 (ICERs) with disaggregated results described in Table 13 and Table 15. In Canada (excluding Quebec), COVID-19 hospitalizations during 2022 totalled about 140,000, with 14,900 deaths in hospital. People in hospital with COVID-19 experience a temporary loss of quality of life; we also captured, for those who died, a loss of lifetime QALYs (refer to Table 5).

Approximately 11% of patients admitted to hospital with COVID-19 (14,923 deaths out of 140,438 hospitalizations) died during 2022 (refer to Table 1), and this QALY loss in the reference scenario is reflected in our NMB results (refer to Table 12 and Table 14). The NMB represents the value of a treatment scenario in dollars for a given WTP per unit of outcome, minus the cost of providing care. For our reference scenario, we estimate −41,683 total QALYs over 1 year, which includes a QALY decrement with discounting for the estimated lifetime QALYs lost due to deaths among those hospitalized. Total QALYs reported were negative because the loss of lifetime QALYs due to deaths in patients who were hospitalized exceeded positive QALYs accrued during 1 year of simulation.

If we assume a WTP per QALY of $50,000 then the total dollar value of QALYs lost in the reference scenario population is –$2,084,000,000, or –$14,839 per hospital admission. We then estimate the expected QALYs and NMB for each of the 5 alternate scenarios. From this, we can calculate the iNMB of each scenario relative to the reference scenario. For example, in scenario 1, the iNMB is $214 million (95% CrI, –$15.4 million to $449 million) in when compared to the reference scenario. The full set of results for all main scenarios is presented in Table 12 (with 95% CrIs). Disaggregated results described in Table 13 and Table 15 highlight the breakdown by state and scenario of QALY and health care costs. The largest positive contribution of QALY and health care costs are from the Recovered and Inpatient states, respectively. However, the QALY loss due to death was greater than the QALY gain within the Recovered state (refer to Table 13).

In Table 14 we present ICERs for the tocilizumab uptake scenarios compared to a common baseline (the reference scenario). As we are analyzed potential future states and not treatment strategies to be implemented, we did not calculate sequential ICERs when all main scenarios were compared to 1 another as would be typical in cost-effectiveness analysis. Rather, our aim was to illustrate the cost-effectiveness of tocilizumab under different possible usage patterns and not to identify a single cost-effective strategy.

Key Results

- The NMB of the reference scenario was –$4.6 billion, –$5.4 billion, and –$7.5 billion for WTP per QALY values of $30,000, $50,000, and $100,000, respectively (refer to Table 12). These numbers were estimated from approximately 140,000 hospital admissions related to COVID-19 during 2022 in Canada (excluding Quebec). The negative NMB was a result of lifetime QALYs lost associated with COVID-19 deaths.
- The NMB per reported hospital admission for the reference scenario was –$32,809, –$38,745, and –$53,585 for WTP per QALY values of $30,000, $50,000, and $100,000, respectively.
- iNMB shows the difference for each modelled scenario relative to the reference scenario (refer to Table 12). Although there was a QALY loss in the reference scenario, there was an increase in total QALYs in all main scenarios (refer to Table 14), with iNMB showing the relative change in valuation of QALYs versus overall health care costs.
- Across the 3 WTP thresholds, all main scenarios had a positive mean iNMB. When considering uncertainty, all main scenarios had 95% CrIs for iNMB that where higher than 0, with the exception of scenario 1 (low uptake all cohorts) at WTP thresholds of $50,000 and $100,000 (refer to Table 12 and Table 13). The largest iNMB results occurred in those that had moderate and high uptake (scenarios 2, 4, and 5). Scenarios 2 and 5 included all population groups, while scenario 4 focused on the those aged 65 years and older and/or LTC cohort. As the QALY loss due death was greater for those aged younger than 65 years compared to other cohorts (refer to Table 1), the prevention of those deaths in scenario 5 (high uptake for all cohorts) resulted in an iNMB comparable to scenario 4 (high-risk high uptake) for WTP thresholds of $30,000, $50,000, and $100,000.
- The mean ICER results were comparable across all main scenarios; with lower costs and higher QALY gains then the reference scenario. Scenario 1 saved the least money per QALY gained followed by scenario 2 (refer to Table 12 and Table 14).
- All mean ICER results demonstrate that all tocilizumab scenarios were cost-saving (i.e., dominant) compared to the reference scenario, with more QALYs gained and lower costs. The disaggregated results in Table 15 show that the greatest savings in incremental costs compared to the reference scenario occurred in the Inpatient state. The greatest QALYs gained compared to the reference scenario occurred in the Dead state followed by the Recovered state.
- The iNMB associated with additional scenarios 6 and 7 are presented in Table 18. Overall, we found focusing on critical care resulted in lower iNMBs than the same scenarios that focused on all inpatients. For instance, scenario 7 (high uptake for critical care patients only) had an iNMB (based on a WTP threshold of $50,000) of $239 million (95% CrI, $5 million to $463 million) while scenario

5 (high uptake) had a mean iNMB of $690 million (95% CrI, $240 million to $1,100 million). The scenarios focused on all inpatients resulted in fewer deaths and lower inpatient costs, in comparison to those focused on critical care only.

Reference Scenario

The reference scenario represents the standard of care during 2022 and included some inpatient use of tocilizumab in adults receiving corticosteriods.[8] The baseline use of tocilizumab within a hospital was not available in the literature.

Sensitivity Analysis

The model simulations incorporated a probabilistic sensitivity analysis and the results in Table 15 include 95% CrIs to account for parameter uncertainty. Model inputs, including parameter ranges, SDs, and sampling distributions, are provided in Table 3, Table 4, Table 5, and Table 6. In Table 14 we present the ICERs for each of the scenarios relative to a common baseline of the reference scenario. Based on Table 12, although scenarios 2, 4, and 5 had the largest mean iNMB for WTP thresholds of at least $30,000, with considerations of uncertainty, all these results showed a positive iNMB (i.e., incremental value is more than the cost of the intervention compared to the reference scenario). Disaggregated results stratified by model states are described in Table 13 and Table 15, and highlight that most of the QALY increases and decreases are accrued in the Recovered (positive) and Death (negative) states.

We also included 2 additional scenarios as part of a scenario sensitivity analysis where we focused tocilizumab treatment on individuals in critical care. We reanalyzed the low uptake in high-risk cohorts (aged ≥ 65 years and those in LTC) and the high uptake in all cohorts but with the costs and benefits of tocilizumab only being captured in the critical care population, these were labelled additional scenario 6 and additional scenario 7, respectively. The iNMB and ICERs associated with these additional scenarios are presented in Table 18 and Table 19. Overall, while we found these additional scenarios remained cost-effective with ICERs that were dominant compared to the reference scenario, they produced lower iNMBs to the comparable scenarios that were focused on all inpatients.

Table 12: NMB ($) and iNMB ($) Estimates for Tocilizumab Inpatient Treatment Scenarios (in Millions) by 3 WTP per QALY Thresholds: $30,000, $50,000, and $100,000 (n = 5,000 Simulations per Scenario)

Cost-effectiveness estimate	WTP threshold: $30,000	WTP threshold: $50,000	WTP threshold: $100,000
Reference scenario			
NMB (95% CrI)	–$4,608 (–$5,083 to -$4,183)	-$5,441 (–$6,167 to –4,803)	–$7,525 (–$8,906 to –$6,288)
iNMB (95% CrI)	NA	NA	NA
Scenario 1 (low uptake)			
NMB (95% CrI)	–$4,443 (–$4,926 to –$4,011)	–$5,227 (–$5,954 to –4,587)	–$7,187 (–$8,581 to –$5,979)
iNMB (95% CrI)	$165 ($4, $323)	$214 (–$15, $449)	$338 (–$95, $767)

Cost-effectiveness estimate	WTP threshold: $30,000	WTP threshold: $50,000	WTP threshold: $100,000
Scenario 2 (moderate uptake)			
NMB (95% CrI)	–$4,280 (–$4,786 to –$3,818)	–$5,015 (–$5,781 to –4,340)	–$6,854 (–$8,281 to –$5,600)
iNMB (95% CrI)	$328 ($76, $561)	$426 ($112, $732)	$671 ($146, $1,190)
Scenario 3 (high-risk low uptake)			
NMB (95% CrI)	–$4,485 (–$4,964 to –$4,057)	–$5,285 (–$6,016 to –4,639)	–$7,285 (–$8,663 to –$6,047)
iNMB (95% CrI)	$123 ($19 to $221)	$156 ($26 to $288)	$241 ($12 to $472)
Scenario 4 (high-risk high uptake)			
NMB (95% CrI)	–$4,200 (–$4,733, –$3,709)	–$4,923 (–$5,703, –4,222)	–$6,728 (–$8,135 to –$5,456)
iNMB (95% CrI)	$407 ($120, $669)	$519 ($193, $817)	$797 ($346 to $1,230)
Scenario 5 (high uptake)			
NMB (95% CrI)	–$4,075 (–$4,648 to –3,553)	–$4,752 (–$5,550 to –4,030)	–$6,442 (–$7,899 to –$5,127)
iNMB (95% CrI)	$532 ($149 to $877)	$690 ($240 to $1,100)	$1,080 ($413 to $1,760)

CrI = credible interval; iNMB = incremental net monetary benefit; NA = not applicable; NMB = net monetary benefit; QALY = quality-adjusted life-year; WTP = willingness to pay.

Table 13: Disaggregated Results (Mean Values Only) of NMB and iNMB Estimates for Tocilizumab Inpatient Treatment Scenarios (in Millions) by 3 WTP per QALY Thresholds: $30,000, $50,000, and $100,000 (n = 5,000 Simulations per Scenario)

Parameter	Baseline, (in millions)	Scenario 1 (low uptake), (in millions)	Scenario 2 (moderate uptake), (in millions)	Scenario 3 (LTC low uptake), (in millions)	Scenario 4 (LTC high uptake), (in millions)	Scenario 5 (high uptake), (in millions)
Total value of QALYs (WTP = $30,000) (A)	–$1,251	–$1,176	–$1,104	–$1,200	–$1,083	–$1,014
By health state						
Inpatient	$100	$96	$93	$97	$89	$88
Critical	$0	$0	$0	$0	$0	$0
Inpatient After Critical	$12	$12	$11	$12	$11	$11
Dead	–$4,166	–$4,099	–$4,032	–$4,121	–$4,017	–$3,952
Post–COVID-19 Condition	$293	$294	$295	$294	$296	$296
Recovered	$2,511	$2,520	$2,530	$2,519	$2,538	$2,542
Total value of QALYs (WTP = $50,000) (B)	–$2,084	–$1,960	–$1,839	–$2,000	–$1,806	–$1,691
By health state						
Inpatient	$167	$161	$154	$161	$149	$146
Critical	$0	$0	$0	$0	$0	$0

Parameter	Baseline, (in millions)	Scenario 1 (low uptake), (in millions)	Scenario 2 (moderate uptake), (in millions)	Scenario 3 (LTC low uptake), (in millions)	Scenario 4 (LTC high uptake), (in millions)	Scenario 5 (high uptake), (in millions)
Inpatient After Critical	$20	$20	$19	$20	$19	$18
Dead	–$6,944	–$6,831	–$6,721	–$6,869	–$6,696	–$6,586
Post–COVID-19 Condition	$489	$490	$492	$490	$493	$493
Recovered	$4,184	$4,201	$4,216	$4,198	$4,229	$4,237
Total value of QALYs (WTP = $100,000) (C)	–$4,168	–$3,921	–$3,678	–$4,000	–$3,611	–$3,381
By health state						
Inpatient	$333	$321	$309	$323	$298	$293
Critical	$0	$0	$0	$0	$0	$0
Inpatient After Critical	$41	$39	$38	$40	$38	$37
Dead	–$13,888	–$13,662	–$13,441	–$13,738	–$13,391	–$13,172
Post–COVID-19 Condition	$977	$980	$983	$980	$986	$987
Recovered	$8,368	$8,401	$8,433	$8,396	$8,458	$8,474
Total costs (D)	$3,357	$3,267	$3,176	$3,285	$3,117	$3,061
By health state						
Inpatient	$2,387	$2,323	$2,260	$2,332	$2,202	$2,177
Critical	$660	$642	$624	$649	$623	$603
Inpatient After Critical	$310	$301	$292	$305	$292	$281
Dead	0	0	0	0	0	0
Post–COVID-19 Condition	0	0	0	0	0	0
Recovered	0	0	0	0	0	0
iNMB by WTP						
$30,000 $[(A_{Sc} – D_{Sc}) – (A_{Base} – D_{Base})]$	—	$165	$328	$123	$407	$532
$50,000 $[(B_{Sc} – D_{Sc}) – (B_{Base} – D_{Base})]$	—	$214	$426	$156	$519	$690
$100,000 $[(C_{Sc} – D_{Sc}) – (C_{Base} – D_{Base})]$	—	$338	$671	$241	$797	$1,083

Base = baseline; iNMB = incremental net monetary benefit; LTC = long-term care; NMB = net monetary benefit; QALY = quality-adjusted life-year; Sc = scenario; WTP = willingness to pay.

Table 14: ICERs for Tocilizumab Inpatient Treatment Scenarios, Relative to a Common Baseline

Scenarios	Cost (millions)	Incremental cost (millions)	QALYs	Incremental QALYs	ICER
Reference scenario	$3,357	—	–41,683	—	NA
Scenario 1 (low uptake)	$3,267	–$91	–39,207	2,476	Dominant
Scenario 2 (moderate uptake)	$3,176	–$181	–36,783	4,900	Dominant
Scenario 3 (high-risk low uptake)	$3,285	–$72	–39,998	1,685	Dominant
Scenario 4 (high-risk high uptake)	$3,117	–$240	–36,112	5,571	Dominant
Scenario 5 (high uptake)	$3,061	–$296	–33,810	7,873	Dominant

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year; NA = not applicable.

Note: Total QALYs are negative because of the estimated loss of lifetime QALYs from deaths (refer to the Utilities section for details).

Table 15: Disaggregated Results of the ICERs for Tocilizumab Inpatient Treatment Scenarios, Relative to a Common Baseline

Scenarios	Cost (millions)	Incremental cost (millions)	QALYs	Incremental QALYs	ICER
Reference scenario	$3,357	—	–41,683	—	NA
Inpatient	$2,387	—	3,333	—	—
Critical	$660	—	0	—	—
Inpatient After Critical	$310	—	406	—	—
Dead	$0	—	–138,880	—	—
Post–COVID-19 Condition	$0	—	9,774	—	—
Recovered	$0	—	83,683	—	—
Scenario 1 (low uptake)	$3,267	–$91	–39,207	2,476	Dominant
Inpatient	$2,323	–$64	3,210	–123	—
Critical	$642	–$18	0	0	—
Inpatient After Critical	$301	–$9	394	–12	—
Dead	$0	$0	–136,620	2,257	—
Post–COVID-19 Condition	$0	$0	9,802	27	—
Recovered	$0	$0	84,010	326	—
Scenario 2 (moderate uptake)	$3,176	–$181	–36,783	4,900	Dominant
Inpatient	$2,260	–$127	3,087	–245	—
Critical	$624	–$36	0	0	—
Inpatient after critical	$292	–$18	382	–24	—
Dead	$0	$0	–134,410	4,466	—
Post–COVID-19 Condition	$0	$0	9,831	57	—

Scenarios	Cost (millions)	Incremental cost (millions)	QALYs	Incremental QALYs	ICER
Recovered	$0	$0	84,329	646	—
Scenario 3 (high-risk low uptake)	$3,285	–$72	–39,998	1,685	Dominant
Inpatient	$2,332	–$55	3,226	–106	—
Critical	$649	–$11	0	0	—
Inpatient After Critical	$305	–$5	398	–8	—
Dead	$0	$0	–137,380	1,503	—
Post–COVID-19 Condition	$0	$0	9,799	25	—
Recovered	$0	$0	83,955	271	—
Scenario 4 (high-risk high uptake)	$3,117	–$240	–36,112	5,571	Dominant
Inpatient	$2,202	–$185	2,978	–355	—
Critical	$623	–$37	0	0	—
Inpatient After Critical	$292	–$18	380	–26	—
Dead	$0	$0	–133,910	4,969	—
Post–COVID-19 Condition	$0	$0	9,857	83	—
Recovered	$0	$0	84,583	900	—
Scenario 5 (high uptake)	$3,061	–$296	–33,810	7,873	Dominant
Inpatient	$2,177	–$210	2,929	–404	—
Critical	$603	–$58	0	0	—
Inpatient After Critical	$281	–$29	367	–38	—
Dead	$0	$0	–131,720	7,162	—
Post–COVID-19 Condition	$0	$0	9,868	93	—
Recovered	$0	$0	84,743	1,059	—

ICER = incremental cost-effectiveness ratio; NA = not applicable; QALY = quality-adjusted life-year.

Cost-Effectiveness Acceptability Curves

For each $1,000 increment of WTP per QALY from $0 to $150,000, we computed the probability (calculated as the proportion of 5,000 simulations) of each of the scenarios shown in Table 15 having the highest NMB when compared pairwise to the reference scenario. Figure 2 shows the probability that a scenario is cost-effective across this range of WTP per QALY values when compared to the reference scenario. At a WTP of $0, this analysis simply shows the proportion of simulations for which the scenario in question has the lowest cost. As WTP threshold increases, greater weight is given to incremental QALYs between the therapy and reference scenario. In Figure 2, the probability of cost-effectiveness is always high across all tocilizumab scenarios. At low WTP thresholds, this is due to cost-saving and at high WTP thresholds, this is due to gain in QALYs. The latter is largely due to the prevention of death. Small trends in probability of cost-effectiveness across the WTP range, such as scenario 1 (low uptake) and scenario 3 (high-risk low uptake), result from the interaction between simulation variance and this probability of cost-effectiveness. Although the reference

scenario is not shown for each pairwise comparison, graph lines of 0.5 and greater for “probability of cost-effectiveness” indicate when each scenario has a higher probability of cost-effectiveness (highest NMB) compared to the reference. Overall, 96% of all simulations across scenarios had a greater NMB compared to the reference scenarios at $0 per QALY (not including the QALY gain). Most scenarios had a probability of greater than 96% when the WTP per QALY was increased up to $150,000 per QALY.

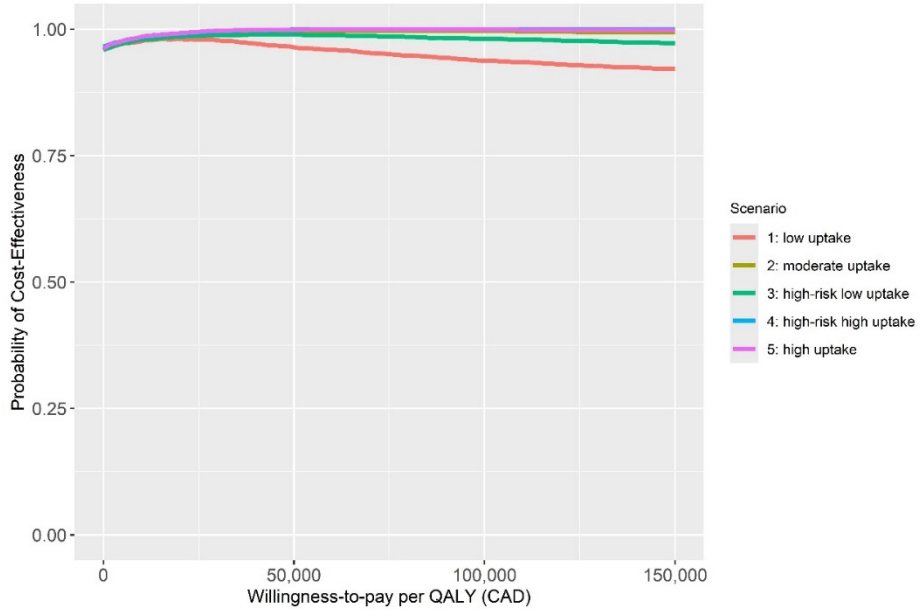
BIA Results

Main Take-Aways

The results of the BIA suggest that tocilizumab has the potential to be cost-saving for all cohorts and under a range of possible uptake scenarios. While there remains uncertainty in health system costs associated with inpatient use of tocilizumab, the majority of model runs found that inpatient use of tocilizumab was cost-saving. Scenarios 4 and 5, which represent the highest uptake scenarios, were found to have the greatest cost-savings to the health care system.

The results of the BIA are presented in Table 16. Total average costs for the main scenarios considered ranged from $3.06 billion to $3.29 billion. Additional outcomes in the BIA included overall number of deaths and patients developing post–COVID-19 condition. Scenario 5 had the lowest expected cost and scenario 3 the highest. Overall, the average cost-savings observed across all main scenarios were driven mainly by

Figure 2: Cost-Effectiveness Acceptability Curves Estimating the Probability of the Scenario Having a Greater NMB at a Given WTP Than the Reference Scenario (N = 5,000 Simulations, Each With Different Parameter Samples)



CAD = Canadian dollars; NMB = net monetary benefit; QALY = quality-adjusted life-year; WTP = willingness to pay.

the therapeutic effect on LOS, where reductions of total inpatient and critical care costs compared to the reference scenario were more than the total cost of treatment. When accounting for parameter uncertainty, no scenarios have an unambiguously positive or negative budget impact compared to the reference case; however, the results in all main scenarios were skewed toward cost-savings to the health care system.

The iNMB associated with additional scenarios 6 and 7 are presented in Table 18. Overall, we found focusing on critical care resulted in negative mean budget impacts, suggesting they were likely to save the health system money. However, they had worse budget impacts overall than the scenarios focused on all inpatients. For instance, while the low uptake high-risk scenario resulted in a budget impact of –$72 million (95% CrI, –$145 million to $10.6 million), the same scenario focused on critical care (additional scenario 6) resulted in a budget impact of –$16.6 million (95% CrI, –$42.7 million to $12 million).

Key Results

- The results of the BIA are presented in Table 16 for the reference scenario and 5 tocilizumab treatment scenarios for all cohorts (those aged < 65 years, those aged ≥ 65 years, and in LTC) and 2 periods (January 2022 to August 2022 and September to December 2022).
- Based on the mean estimates, the budget impact of the main scenarios ranged from –$296 million (95% CrI –$590 million to $33 million) for scenario 5 (high uptake) to –$72 million (95% CrI, –$145 million to $10.6 million) for scenario 3 (high-risk low uptake).
- There were observed increases in number of post–COVID-19 condition cases in the treatment scenarios compared to the reference scenario, this was because more deaths are averted in the treatment scenarios. There were reductions in deaths across the 5 scenarios with scenario 5 (high uptake) having the greatest mortality reduction, with 880 expected deaths averted.
- Total inpatient costs contributed the most to the total cost.
- Mean results for all main scenarios showed a decreased cost to the health system when compared to the reference scenario.
- While scenario 5 had the greatest cost-savings with a BIA of –$296 million (95% CrI, –$590 million to $33 million), scenario 4 (high-risk high uptake) followed closely at –$240 million (95% CrI, –$476 million to $23.1 million). For scenario 4, the total average cost of treatment was $21 million lower than scenario 5.
- The BIA shows that all main scenarios have a potential for cost-savings based on the mean and parameter uncertainty (95% CrI) results (without the consideration of utility). The lower limit of the 95% CrI of budget impact ranged from –590 million (scenario 5) to –$145 million (scenario 3).
- The BIA estimates for additional scenarios 6 and 7 are presented in Table 20. Overall, we found focusing on critical care resulted in lower cost-savings to the health system. For instance, scenario 7 (high uptake for critical care patients) had a mean BIA estimate of –$86.3 million (95% CrI, –$189 million to $6.6 million), while scenario 5 (high uptake for inpatients including critical care) had a mean BIA estimate of –$296 million (95% CrI, –$590 million to $33 million). These differences were largely driven by preventing fewer inpatient stays and their associated costs.

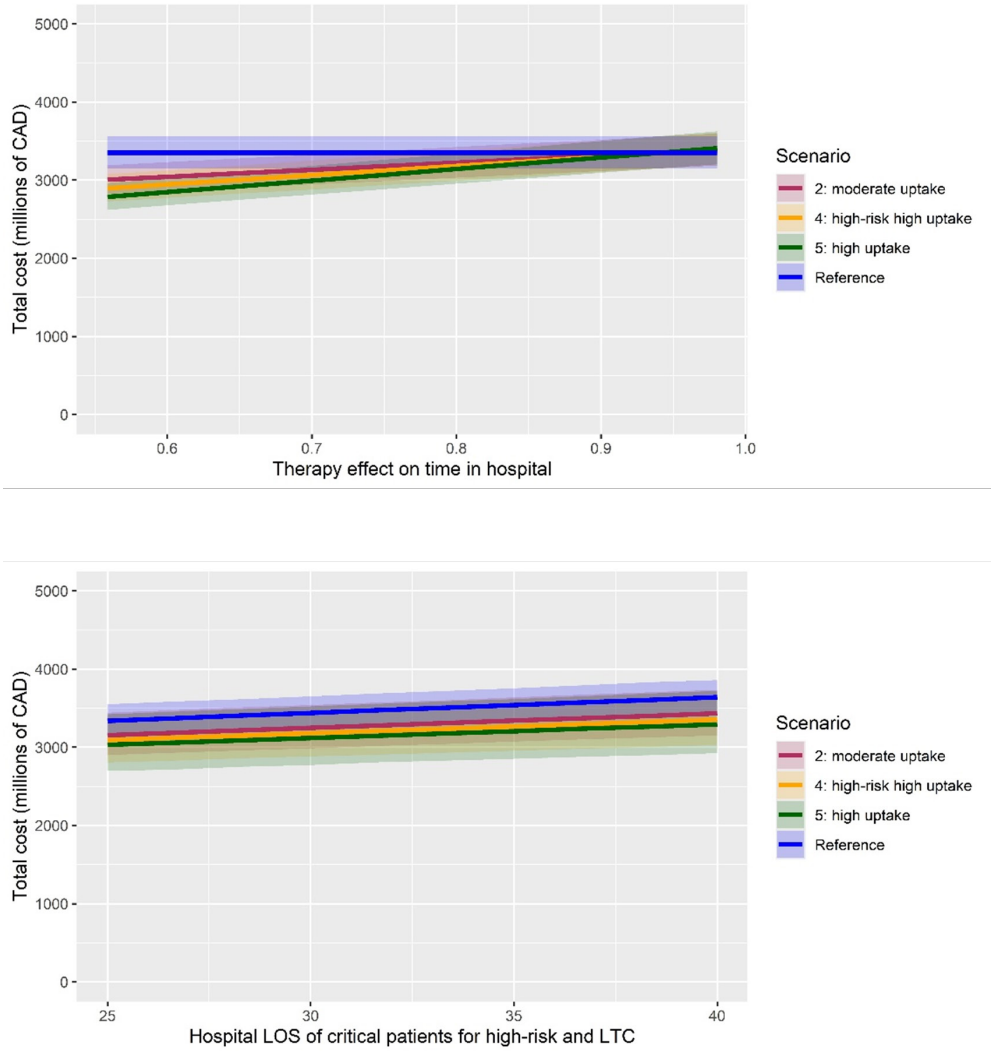
Table 16: BIA Across 5 Tocilizumab Inpatient Treatment Scenarios

Description	Reference scenario	Scenario 1 (low uptake)	Scenario 2 (moderate uptake)	Scenario 3 (high-risk low uptake)	Scenario 4 (high-risk high uptake)	Scenario 5 (high uptake)
COVID-19 disposition (95% CrI)						
Total post–COVID-19 condition	36,820 (33,410 to 40,467)	36,903 (33,510 to 40,600)	36,993 (33,576 to 40,639)	36,894 (33,497 to 40,604)	37,076 (33,633 to 40,756)	37,106 (33,681 to 40,783)
Total deaths	14,920 (13,650 to 16,290)	14,650 (13,390 to 16,040)	14,390 (13,130 to 15,780)	14,680 (13,420 to 16,060)	14,120 (12,870 to 15,520)	14,040 (12,770 to 15,450)
Costs (in millions) (95% CrI)						
Total inpatient	$2,390 ($2,200 to $2,580)	$2,320 ($2,140 to $2,530)	$2,260 ($2,050 to $2,500)	$2,330 ($2,150 to $2,530)	$2,200 ($1,960 to $2,480)	$2,180 ($1,910 to $2,480)
Total critical	$970 ($891 to $1,060)	$943 ($861 to $1,040)	$917 ($827 to $1,020)	$954 ($873 to $1,050)	$915 ($823 to $1,020)	$884 ($776 to $1,010)
Total inpatient and critical	$3,360 ($3,160 to $3,570)	$3,270 ($3,060 to $3,490)	$3,180 ($2,920 to $3,460)	$3,290 ($3,090 to $3,500)	$3,120 ($2,830 to $3,440)	$3,060 ($2,720 to $3,440)
Total tocilizumab cost	$0 ($0 to $0)	$27.2 ($25.5 to $29.3)	$54.4 ($51 to $58.6)	$20.1 ($20.1 to $20.1)	$66.8 ($66.8 to $66.8)	$88.2 ($83.1 to $94.5)
Total costs	$3,360 ($3,160 to $3,570)	$3,270 ($3,060 to $3,490)	$3,180 ($2,920 to $3,460)	$3,290 ($3,090 to $3,500)	$3,120 ($2,830 to $3,440)	$3,060 ($2,720 to $3,440)
Budget impact: scenario cost – reference scenario	NA	–$90.6 (–$183.0 to $14.7)	–$181.0 (–$365.0 to $24.4)	–$72.0 (–$145.0 to $10.6)	–$240.0 (–$476.0 to $23.1)	–$296.0 (–$590.0 to $33.0)

CrI = credible interval; NA = not applicable.

Note: Total costs shown for Inpatient and Critical include the cost of treatment with tocilizumab. Patients are treated in these states.

Figure 3: POSA Results



CAD = Canadian dollars; CrI = credible interval; LOS = length of stay; LTC = long-term care; POSA = probabilistic one-way sensitivity analysis.
Note: Solid lines show mean cost, and shaded ribbons show the 95% CrI.

In Figure 3, a POSA analysis was conducted for the reference scenario, scenario 2 (moderate uptake), scenario 4 (high-risk high uptake), and scenario 5 (high uptake) (refer to Table 8 for POSA ranges) for tocilizumab effect (relative risk compared to the reference scenario) on LOS in hospital, total hospital LOS for critical patients, tocilizumab effect (relative risk compared to the reference scenario) on mortality, and inpatient cost (per patient).

In the POSA analysis we find that tocilizumab's effect on LOS has the biggest effect on the budget impact results. As we see in Figure 3, a reduction in this effect reduces the difference of total costs between scenarios and the reference case. As inpatient costs contribute the most to total costs, reduction in LOS offsets the cost of the treatment considering mean results. Tocilizumab's effect on mortality did not impact

total costs as there are no costs associated with mortality, these benefits are observed through QALYs gained from deaths averted, which is described in the CUA. Although not all scenarios are shown in the POSA analysis, scenario 2 (moderate uptake), scenario 4 (high-risk high uptake), and scenario 5 (high uptake) include a range of treatment options impacting each cohort. The figures shown were computed with 1,000 simulations each.

Summary of Findings

Main Take-Aways

Overall, both the CUA and BIA suggest that, at a range of uptakes, tocilizumab is likely to be cost-effective and may be cost-saving as an inpatient treatment. Both scenarios looking at high-risk cohorts and those focused on all cohorts had similar outcomes, with the scenarios with the highest uptakes having the most favourable results. These findings were robust when considering uncertainty, with the majority of model simulations finding that tocilizumab was cost-saving to the health care system.

It is important to interpret these results considering that the CUA presented in this analysis differs from a typical CUA, in that we do not compare a set of treatment alternatives to identify the cost-effective option. Rather we project cost and health outcomes for a range of possible future scenarios to understand under what conditions using tocilizumab in an inpatient setting would be cost-effective relative to the reference case. The CUA and BIA analysis include a probabilistic sensitivity analysis of 5,000 model simulations to provide a distribution of results reported as 95% CrIs.

The CUA and BIA results suggest that the use of tocilizumab is likely to be cost-effective, though this is dependent on model uncertainty and the maximum WTP per QALY. When we account fully for parameter uncertainty through probabilistic sensitivity analysis, at a WTP threshold of $50,000 or more per QALY, all main scenarios, except scenario 1 (low uptake), were cost-effective compared to the reference scenario (i.e., iNMB estimates are positive in the 95% CrIs) (refer to Table 12). As the therapeutic effect of tocilizumab has an impact on reducing deaths, the overall results included a consideration of the differential impact of death on lifetime QALY loss in those aged younger than 65 years and those aged 65 years or older, and/or those in LTC. While total deaths among those younger than aged 65 years is lower than those aged 65 years or older and/or in LTC, the lifetime QALY loss is greater for those aged younger than 65 years. This is likely why we observe similarities in iNMB for scenario looking across all 3 cohorts and those focused on high-risk cohorts.

All ICERs were dominant compared to the reference case, and therefore, demonstrate incremental cost-savings with QALYs gained compared to the reference scenario. The scenarios that focused on high-risk populations saved more Canadian dollars per QALY gained than scenarios that focused on all cohorts.

The average BIA results also indicate that the treatment scenarios are cost-saving for the health system (refer to Table 16). When considering uncertainty, all main and additional scenarios also showed the potential

for increased costs to the health care system; however, the 95% CrI was skewed toward cost-saving results. Overall, scenarios 4 and 5 had the lowest average BIA result (i.e., had the highest cost-savings to the health system). Across all treatment scenarios, we found reductions in COVID-19 deaths compared to the reference scenario. Overall, the CUA and BIA suggest that if the future state were to resemble any of the scenarios modelled here, especially scenarios with higher uptake, it would likely lead to lower health system costs and a greater reduction in deaths.

Limitations

Model assumptions and limitations are described in Table 10. Some of the key limitations include:

- The reference scenario represents the standard of care during 2022 and includes some inpatient use of tocilizumab in adults. The baseline use of tocilizumab within the hospital were not available in the literature. Therefore, scenarios described in Table 7 would include additional tocilizumab use above what was provided to patients in the reference scenario.
- Although tocilizumab is generally administered with corticosteroids, the additional costs for corticosteroids were not included. This cost is minimal when compared to the overall drug cost.
- The mortality impact in LTC is likely underestimated because of data and model limitations, which only capture deaths in health care facilities and not death in LTC facilities. This would reduce the cost-effectiveness of tocilizumab in this population.
- The tocilizumab costs assume a recommended 1-time infusion with a dose of up to 800 mg.[8] The simulations do not account for a secondary infusion. The proportion of those who needed an additional infusion was not available in the literature. While a range of costs are used, considerations for a higher cost could impact the total costs to the health care system.
- The therapeutic effects of tocilizumab within the hospital setting were based on literature before the Omicron variants. Additional studies after the Omicron variants were discovered are needed to verify that the therapeutic effects used in this analysis remain the same considering the new variants in circulation. If tocilizumab is less effective against new variants, this would reduce its overall cost-effectiveness.
- Utilities for patients admitted to the hospital are likely overestimated in the CUA because of limited data related to in-hospital estimates. This would lead to an underestimation of the cost-effectiveness for scenarios presented in the CUA. Research is ongoing to estimate quality of life in patients with COVID-19 in different settings, and this may provide more robust utility estimates for future evaluations.

Conclusions and Implications for Decision- or Policy-Making

This report evaluated the costs and benefits associated with inpatient use of tocilizumab at various potential uptake levels across 3 cohorts (those aged < 65 years, those aged ≥ 65 years old, and in LTC). Overall, we found that tocilizumab is likely to be cost-effective and has the strong possibility of being cost-saving to the health care system even when considering uncertainty in parameter estimates using probabilistic sensitivity analysis and POSA. Key parameters that may impact these results include the therapeutic effect estimates of tocilizumab on LOS and mortality, tocilizumab costs, inpatient costs, and lifetime QALY loss associate with mortality from COVID-19. Our results were consistent with the findings in the literature, which overall found that tocilizumab had the potential to be cost-saving for patient who are hospitalized in a number of countries, with multiple studies finding it cost-effective.[14-18]

Our analysis also had to make some overall modelling assumptions that could impact these results. Specifically, we modelled COVID-19 hospitalization from the year 2022; therefore, if there are changes to the severity outcomes associated with COVID-19 hospitalization over time, this may impact the cost-effectiveness of tocilizumab. Moreover, the effect estimate of tocilizumab were based on studies conducted before the Omicron variant; therefore, we assumed the effects would be similar as COVID-19 infection following the emergence of the Omicron variant.

References

1. Alberta Health. COVID-19 info for Albertans. 2023; https://www.alberta.ca/coronavirus-info-for-albertans. Accessed 2023 Dec 1.
2. Government of Canada. COVID-19 signs, symptoms and severity of disease: A clinician guide. 2022; https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/guidance-documents/signs-symptoms-severity.html. Accessed 2023 Dec 1.
3. Eze N, Asante B, Spry C, Clement F. *Nirmatrelvir-Ritonavir for the Treatment of COVID-19.* Ottawa (ON): CADTH; 2023: https://www.cadth.ca/nirmatrelvir-ritonavir-paxlovid-treatment-covid-19.
4. Wang X, Kelly S, Peterson J, et al. *Remdesivir for the Treatment of COVID-19 in the Inpatient Setting.* Ottawa (ON): CADTH; 2023: https://www.cadth.ca/remdesivir-veklury-treatment-covid-19-inpatient-setting.
5. Wang X, Kelly S, Peterson J, et al. *Remdesivir for the Treatment of COVID-19 in the Outpatient Setting.* Ottawa (ON): CADTH; 2023: https://www.cadth.ca/remdesivir-veklury-treatment-covid-19-outpatient-setting.
6. Riad J, Wadie L, Spry C, Aves T, Tadrous M. *Tocilizumab for the Treatment of Hospitalized Patients With COVID-19.* Ottawa (ON): CADTH; 2023: https://www.cadth.ca/tocilizumab-actemra-treatment-hospitalized-patients-covid-19.
7. Government of Canada. Actemra (tocilizumab). *COVID-19 vaccines and treatment portal* 2023; https://covid-vaccine.canada.ca/actemra/product-details. Accessed 2024 Jun 19.
8. Actemra (tocilizumab): tocilizumab for injection (20 mg/mL) vials; tocilizumab injection (162 mg/ 0.9 mL) pre-filled syringe and Autoinjector [product monograph]. Mississauga (ON): Hoffmann-La Roche Limited; 2022 Oct 13: https://covid-vaccine.canada.ca/info/pdf/actemra-pm-en.pdf.
9. U.S. Department of Veteran Affairs Health Economics Resource Center (HERC). Budget Impact Analysis. https://www.herc.research.va.gov/include/page.asp?id=budget-impact-analysis. Accessed 2023 Dec 8.
10. Savinkina A, Paltiel AD, Ross JS, Gonsalves G. Population-Level Strategies for Nirmatrelvir/Ritonavir Prescribing-A Cost-effectiveness Analysis. *Open Forum Infect Dis.* 2022;9(12):ofac637. PubMed
11. Health care cost drivers in Canada: Pre-and Post-COVID-19. Ottawa (ON): The Conference Board of Canada; 2020: https://www.conferenceboard.ca/wp-content/uploads/woocommerce_uploads/reports/10816_25078_impact-paper_health-care-cost-drivers.pdf. Accessed 2024 Aug 13.
12. Padula W, Malaviya S, Reid N, et al. PIN150 Economic value of treatment and vaccine technologies to address the COVID-19 pandemic: a cost-effectiveness and budget impact analysis. *Value Health.* 2020;23:S568.
13. Padula WV, Malaviya S, Reid NM, et al. Economic value of vaccines to address the COVID-19 pandemic: a U.S. cost-effectiveness and budget impact analysis. *J Med Econ.* 2021;24(1):1060-1069. PubMed
14. Dijk SW, Krijkamp EM, Kunst N, Gross CP, Wong JB, Hunink MGM. Emerging Therapies for COVID-19: The Value of Information From More Clinical Trials. *Value Health.* 2022;25(8):1268-1280. PubMed
15. Sinha P, Linas BP. Combination therapy with tocilizumab and dexamethasone cost-effectively reduces Coronavirus disease 2019 mortality. *Clin Infect Dis.* 2021;73(11):2116-2118. PubMed
16. Stukas S, Goshua G, Kinkade A, et al. Reduced fixed dose tocilizumab 400 mg IV compared to weight-based dosing in critically ill patients with COVID-19: A before-after cohort study. *Lancet Reg Health Am.* 2022;11:100228. PubMed
17. Garcia-Molina A, Alos-Alminana M. [Translated article] Efficacy and marginal cost of treatment with tocilizumab in COVID-19 patients. *Farm Hosp.* 2023;47(1):T10-T15. PubMed
18. Petrov VI, Ryazanova AY, Ponomareva AV, Shatalova OV, Levina YV. Clinical and economic analysis of genetically engineered biologics consumption by patients with COVID-19. *Pharmacy & Pharmacology.* 2022;10(2):198-206.
19. Government of Canada. Current situation. *COVID-19 epidemiology update* 2024; https://health-infobase.canada.ca/covid-19/current-situation.html?stat=num&measure=deaths_total&map=pt. Accessed 2024 Apr 8.
20. Wulf Hanson S, Abbafati C, Aerts JG, et al. Estimated Global Proportions of Individuals With Persistent Fatigue, Cognitive, and Respiratory Symptom Clusters Following Symptomatic COVID-19 in 2020 and 2021. *JAMA.* 2022;328(16):1604-1615. PubMed

21. Lau VI, Fowler R, Pinto R, et al. Cost-effectiveness of remdesivir plus usual care versus usual care alone for hospitalized patients with COVID-19: an economic evaluation as part of the Canadian Treatments for COVID-19 (CATCO) randomized clinical trial. *CMAJ Open.* 2022;10(3):E807-e817. PubMed

22. Therapeutics and COVID-19: living guideline. *(WHO/2019-nCoV/therapeutics/2022.4)*. Geneva (CH): World Health Organization; 2022 Jul 14: https://iris.who.int/bitstream/handle/10665/359774/WHO-2019-nCoV-therapeutics-2022.4-eng.pdf.

23. Domingo P, Mur I, Mateo GM, et al. Association between administration of IL-6 antagonists and mortality among patients hospitalized for COVID-19: a meta-analysis. *JAMA.* 2021;326(6):499-518. PubMed

24. Statistics Canada. Table A: Life expectancy (LE) and health-adjusted life expectancy (HALE) at selected ages, by sex, Canada, 1994/1995, 1998/1999, 2001, 2005, 2009/2010 and 2015. 2018; https://www150.statcan.gc.ca/n1/pub/82-003-x/2018004/article/54950/tbl/tbla-eng.htm. Accessed 2023 Dec 8.

25. Government of Canada. Summary, Cases and Deaths. *COVID-19 epidemiology update* 2023 Dec 8; https://health-infobase.canada.ca/covid-19/#a2.

26. Poudel AN, Zhu S, Cooper N, et al. Impact of Covid-19 on health-related quality of life of patients: A structured review. *PLoS One.* 2021;16(10):e0259164. PubMed

27. Siemieniuk RA, Bartoszko JJ, Zeraatkar D, et al. Drug treatments for covid-19: living systematic review and network meta-analysis. *BMJ.* 2020;370. PubMed

28. Broman N, Feuth T, Vuorinen T, et al. Early administration of tocilizumab in hospitalized COVID-19 patients with elevated inflammatory markers; COVIDSTORM—a prospective, randomized, single-centre, open-label study. *Clin Microbiol Infect.* 2022;28(6):844-851. PubMed

29. Rosas IO, Bräu N, Waters M, et al. Tocilizumab in patients hospitalised with COVID-19 pneumonia: Efficacy, safety, viral clearance, and antibody response from a randomised controlled trial (COVACTA). *EClinicalMedicine.* 2022;47. PubMed

30. Rutgers A, Westerweel PE, van der Holt B, et al. Timely administration of tocilizumab improves outcome of hospitalized COVID-19 patients. *PLoS One.* 2022;17(8):e0271807. PubMed

31. Stone JH, Frigault MJ, Serling-Boyd NJ, et al. Efficacy of tocilizumab in patients hospitalized with Covid-19. *N Engl J Med.* 2020;383(24):2333-2344. PubMed

32. Government of Canada. Additional COVID-19 data resources. *COVID-19 epidemiology update* 2023; https://health-infobase.canada.ca/covid-19/#a2. Accessed 2023 Dec 1.

33. Statistics Canada. Table 18-10-0005-01: Consumer Price Index, annual average, not seasonally adjusted. 2024 Jan 16; https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1810000501.

34. Government of Alberta. Interactive Drug Benefit List: Tocilizumab. 2024; https://idbl.ab.bluecross.ca/idbl/drugsList;jsessionid=4Jnyqnescz1_je2KmBk9G3g1aH28VoVSXLfpD5BoUElERNHzAmzx!292429862?searchTerm=toc&category=&genericName=TOCILIZUMAB&brandName=&ptc=&mfgCode=. Accessed 2024 Jun 24.

35. Verma AA, Pai M, Saha S, et al. Managing drug shortages during a pandemic: tocilizumab and COVID-19. *CMAJ.* 2021;193(21):E771-E776. PubMed

36. McCabe C, Paulden M, Awotwe I, Sutton A, Hall P. One-Way Sensitivity Analysis for Probabilistic Cost-Effectiveness Analysis: Conditional Expected Incremental Net Benefit. *Pharmacoeconomics.* 2020;38(2):135-141. PubMed

Authors

Health Economics

Marie Betsy Varughese contributed to the methodology, analysis of model inputs, interpretation of results, writing, editing, and reviewing of the report.

Karsten Hempel constructed the model (including methods), ran simulations, and contributed to model inputs, interpretation, and writing, editing, and reviewing the report.

Ellen Rafferty contributed to the methodology, analysis of model inputs, interpretation of results, writing, editing and reviewing of the report.

Weston Roda contributed to the methodology, interpreting results, and writing the report.

Danica Wolitski conducted the literature review and contributed to the writing of the report.

Jeff Round contributed to the conceptualization and design of the model and analysis, reviewing and interpreting analysis results, and writing and editing the report.

Contributors

Acknowledgements

CIHI. Parts of this report are based on data and information provided by CIHI. However, the analyses, conclusions, opinions, and statements expressed herein are those of the authors and not necessarily those of CIHI.

Conflicts of Interest

Marie Betsy Varughese disclosed the following:

Research Funding or Grants paid to My Institution

CIHR: Long Covid impact on nurse work safety

PHAC and NSERC: One Society Network – Pandemic Preparedness Research Network

Simon Fraser University (2023 to 2024): Methods: Model Uncertainty

Involvement With Projects or Scientific Advice

PHAC-EMNID Working group (2020 to Current) – related to Modelling infectious diseases including COVID-19

Jeff Round disclosed the following:

Research Funding or Grants Aid to My Institution

Canadian Clinical Research Network: Modelling the value of research using COVID-19 treatments as an example

Canadian Immunization Research Network: Health-related quality of life in individuals with COVID-19

PHAC and NSERC: One Society Network – Pandemic Preparedness Research Network

CIHR: Long COVID impact on nurse workforce supply

AstraZeneca Canada Inc. (September 2021 to March 2023): Health Technology Innovation Platform (HTIP)

Boehringer Ingelheim (Canada) Ltd. (July 2020 to July 2022): HTIP

Novartis Pharma Canada Inc. (April 2020 to April 2022): HTIP

Takeda Canada Inc. (April 2020 to April 2022): HTIP

GlaxoSmithKline Canada (June 2020 to June 2022): HTIP

MACH32 Medical Devices (2022): Autoinjector device for trauma patients

Rostrum Medical Innovations Inc. (2022): Lung protection ventilation in ICU patients

Involvement With Projects or Scientific Advice

CADTH and Health Canada RWE Reporting Guidance expert committee member (2022 to 2023)

Weston Roda declared the following:

Research Funding or Grants Aid to My Institution

Children's Hospital Eastern Ontario: Newborn screening SMA

Involvement With Projects or Scientific Advice

PHAC-EMNID Working Group: related to Modelling infectious diseases including COVID-19

Health Care Sector Stocks

Cotrustee of a family trust with Health Care sector stock shares in MRK, ABBV, JNJ, LLY, and CI.

Ellen Rafferty declared the following:

Research Funding or Grant Paid to My Institution

CIHR: Long COVID Impact on Nurse Workforce Supply

PHAC/NSERC: One Society Network – Pandemic Preparedness Research Network

Canadian Immunization Research Network: Estimation of long-term COVID-19 health state utility values

Involvement With Projects or Scientific Advice

PHAC-EMNID Working Group (2020 to Present): Related to modelling infectious diseases, including COVID-19

Karsten Hempel disclosed the following:

Research Funding or Grants Paid to My Institution

CIHR: Long COVID Impact on Nurse Workforce Supply

Canadian Clinical Research Network: Modelling the value of research using COVID-19 treatments as an example

Characterization of COVID-19 vaccine safety epidemiology and safety signal detection for adverse events following immunization in Alberta

No other conflicts of interest were declared.

Appendix 1: Supplementary Material

Note that this appendix has not been copy-edited.

Table 17: Stochastic State-Transition Model Related Parameters as Examples (Among COVID-19 cases) From CIHI data With Key Data Transformations

Symbol	Transformation	Quantity	Source	Estimate: < 65 years old	Estimate: ≥ 65 years old	Estimate: LTC
Period: January 2022 to August 2022						
$\vec{T}_{ah}$	NA	LOS hospital (days)	CIHI	10	16	43
$\vec{T}_{ah\_c}$	NA	LOS hospital among those admitted to critical care	CIHI	22	23	58
$\vec{T}_{c}$	NA	LOS critical (days)	CIHI	9	9	9
$\vec{T}_{i}$	$\vec{T}_{ah\_c} - \vec{T}_{c}$	LOS for inpatient after critical (days)	CIHI	13	14	49
p_{ah_c}	NA	Proportion of critical of total hospitalizations	CIHI	0.170	0.133	0.060
$\vec{p}_{c-d}$	NA	Proportion of critical patients that die	CIHI	0.169	0.332	0.135
$\vec{T}_{h}$	$\frac{(\vec{T}_{ah} - p_{ah\_c} \times \left(\vec{T}_{c} + \left(1 - p_{c\_d}\right) \times \vec{T}_{i}\right)}{1 - p_{ah\_c}}$	LOS inpatient (days)	CIHI	8	16	42
$Cost_{h}$	$Total\ inpatient\ cost \div \vec{T}_{h}$	Inpatient cost per day	CIHI	$1,368	$1,118	$913
$Cost_{i}$	$\left(Total\ ICU\ cost - (Cost_{h} \times \vec{T}_{i})\right) \div \vec{T}_{c}$	Critical cost per day	CIHI	$3,713	$3,640	$4,573
Period: September 2022 to December 2022						
$\vec{T}_{ah}$	NA	LOS hospital (days)	CIHI	15	19	57
$\vec{T}_{ah\_c}$	NA	LOS hospital among those admitted to critical	CIHI	29	27	71
$\vec{T}_{c}$	NA	LOS critical or ICU (days)	CIHI	9	8	8
$\vec{T}_{i}$	$\vec{T}_{ah\_c} - \vec{T}_{c}$	LOS for inpatient after critical (days)	CIHI	19	19	63

Symbol	Transformation	Quantity	Source	Estimate: < 65 years old	Estimate: ≥ 65 years old	Estimate: LTC
p_{ah_c}	NA	Proportion of critical of total hospitalizations	CIHI	0.190	0.120	0.063
$\vec{p}_{c-d}$	NA	Proportion of critical patients that die	CIHI	0.161	0.294	0.073
$\vec{T}_h$	$\frac{(\vec{T}_{ah} - p_{ah\_c} \times \left(\vec{T}_c + \left(1 - p_{c\_d}\right) \times \vec{T}_i\right)}{1 - p_{ah\_c}}$	LOS inpatient (days)	CIHI	13	19	57
$Cost_h$	$Total\ inpatient\ cost \div \vec{T}_h$	Inpatient cost per day	CIHI	$1,182	$1,042	$874
$Cost_i$	$\left(Total\ ICU\ cost - (Cost_h \times \vec{T}_i)\right) \div \vec{T}_c$	Critical cost per day	CIHI	$3,668	$3,366	$4,107

CIHI = Canadian Institute of Health Information; LOS = length of stay; NA = Not applicable; LTC = long-term care.

Table 18: NMB and iNMB Estimates for Tocilizumab Treatment for Patients in Critical Care Only (in Millions) by 3 WTP per QALY Thresholds: $30,000, $50,000, and $100,000 (n = 5,000 Simulations per Scenario)

Cost-effectiveness estimate ($ in millions)	WTP threshold: $30K	WTP threshold: $50K	WTP threshold: $100K
Reference scenario			
NMB (95% CrI)	-$4,608 (-$5,083, -$4,183)	-$5,441 (-$6,167, −4,803)	-$7,525 (-$8,906, -$6,288)
iNMB (95% CrI)	NA	NA	NA
Scenario 6 (high-risk low uptake – critical care only)			
NMB (95% CrI)	-$4,577 (-$5,053, -$4,151)	-$5,401 (-$6,135, −4,758)	-$7,462 (-$8,852, -$6,225)
iNMB (95% CrI)	$31 (-$33, $95)	$40 (-$61, $143)	$63 (-$134, $264)
Scenario 7 (high uptake – critical care only)			
NMB (95% CrI)	-$4,430 (-$4,907, -$3,996)	-$5,202 (-$5,930, −4,556)	-$7,133 (-$8,523, -$5,907)
iNMB (95% CrI)	$178 ($17, $330)	$239 ($5, $463)	$392 (-$51, $821)

CrI = credible interval; iNMB = incremental net monetary benefit; N/A = not applicable; NMB = net monetary benefit; QALY = quality-adjusted life-year; WTP = willingness-to-pay.

Table 19: ICERs for Tocilizumab Treatment for Patients in Critical Care Only, Relative to a Common Baseline

Scenarios	Cost (millions)	Incremental cost (millions)	QALYs	Incremental QALYs	ICER
Reference scenario	$3,357	–	−41,683	–	NA
Scenario 1 (low uptake)	$3,341	-$17	−41,216	467	Dominant
Scenario 2 (moderate uptake)	$3,271	-$86	−38,626	3,057	Dominant

ICER = incremental net monetary benefit, QALY = quality-adjusted life-year.

Table 20: BIA Across 2 Additional Tocilizumab Inpatient Treatment Scenarios Focused on Critical Care

Description	Reference scenario	Scenario 6 (high risk low uptake – critical care only)	Scenario 7 (high uptake – critical care only)
COVID-19 disposition (95% CrI)			
Total post–COVID-19 condition	36,820 (33,410, 40,467)	36,846 (33,449, 40,542)	36,939 (33,525, 40,598)
Total deaths	14,920 (13,650, 16,290)	14,850 (13,580, 16,260)	14,650 (13,390, 16,050)
Costs (in millions) (95% CrI)			
Total inpatient	$2,390 ($2,200, $2,580)	$2,390 ($2,200, $2,580)	$2,390 ($2,200, $2,580)
Total critical	$970 ($891, $1,060)	$954 ($873, $1,050)	$884 ($776, $1,010)
Total inpatient and critical	$3,360 ($3,160, $3,570)	$3,340 ($3,150, $3,550)	$3,270 ($3,060, $3,490)
Total tocilizumab cost	$0 ($0, $0)	$2.36 ($2.36, $2.36)	$11.6 ($10.7, $12.6)
Total costs	$3,360 ($3,160, $3,570)	$3,340 ($3,150, $3,550)	$3,270 ($3,060, $3,490)
Budget impact: Scenario cost – reference scenario	NA	-$16.6 (-$42.7, $12)	-$86.3 (-$169, $6.62)

BIA = budget impact analysis; CrI = credible interval; NA = not applicable.

Note: Total costs shown for Inpatient and Critical include the cost of treatment with tocilizumab, patients are treated in these states.

For more information on CoLab and its work, visit colab.cda-amc.ca.

This work was conducted by the Alberta Drug and Technology Evaluation Consortium (ADTEC) through the Post-Market Drug Evaluation CoLab Network. It was supported by Canada's Drug Agency (CDA-AMC) and its Post-Market Drug Evaluation Program through funding provided by Health Canada.

CDA-AMC is a pan-Canadian health organization. Created and funded by Canada's federal, provincial, and territorial governments, we're responsible for driving better coordination, alignment, and public value within Canada's drug and health technology landscape. We provide Canada's health system leaders with independent evidence and advice so they can make informed drug, health technology, and health system decisions, and we collaborate with national and international partners to enhance our collective impact.

CoLab is a pan-Canadian network of experts in applied research, scientific methods, and data analysis. CoLab members work with the Post-Market Drug Evaluation Program to produce credible and timely evidence on postmarket drug safety and effectiveness.