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Health Technology Review

The Cost-Effectiveness and Budget Impact of Remdesivir for Outpatient Treatment of COVID-19

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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 remdesivir as an outpatient 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 remdesivir uptake scenarios to treat COVID-19 in outpatients for 3 cohorts: those younger than 65 years, those aged 65 years or older, and/or those in long-term care (LTC).

Results of the CUA suggest that increased use of remdesivir may be cost-effective, depending on treatment uptake, patient cohorts, and considerations of uncertainty.

The mean incremental net monetary benefit (iNMB) ranged from $10 million to $1.21 billion, depending on the scenario and willingness-to-pay threshold per quality-adjusted life-year. The largest iNMB resulted from the scenario that focused on treating individuals at high risk of progressing to severe COVID-19 (those aged ≥ 65 years and those in LTC).

Based on mean estimates for the outpatient use of remdesivir, the budget impact of the scenarios ranged from –$76 million to $246 million. Only the scenario that focused on moderate uptake in populations deemed high-risk was cost-saving. However, when considering uncertainty, we observed all scenarios that focused on the high-risk population to have the potential to be both cost-effective and cost-saving. Total inpatient costs contributed the most to the overall total cost.

The key limitations of this analysis were that the reference scenario included some outpatient use of remdesivir in 2022; mortality impact on long-term care was likely underestimated due to data and model limitations; and the therapeutic effects listed for remdesivir were based on literature before the emergence of the Omicron variant.

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Abbreviations

BIA	budget impact analysis
CCRN	Canadian Collaborative Research Network
CEAC	cost-effectiveness acceptability curve
CI	confidence interval
CIHI	Canadian Institute of Health Information
CrI	credible interval
CUA	cost-utility analysis
FPT	federal, provincial and territorial
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
NA	not applicable
NMB	net monetary benefit
NMV-r	nirmatrelvir-ritonavir
NPI	nonpharmaceutical intervention
PHAC	Public Health Agency of Canada
POSA	probabilistic one-way sensitivity analysis
QALY	quality-adjusted life-year
RR	relative risk
SD	standard deviation
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
WTP	willingness-to-pay

Editorial Note

Canada's Drug Agency (CDA-AMC) completed a Reimbursement Review of remdesivir (Veklury) for nonhospitalized patients, and the Canadian Drug Expert Committee issued a final recommendation on September 4, 2024. It recommended reimbursing remdesivir according to the indication approved by Health Canada for outpatient use, with the same public drug program funding criteria as nirmatrelvir-ritonavir (Paxlovid).

Prior to the reimbursement recommendation, the Public Health Agency of Canada had commissioned the Post-Market Drug Evaluation program to conduct an economic evaluation and budget impact analysis of remdesivir for outpatient use. The research and policy questions defined in this report were developed in advance of the reimbursement recommendation.

The patient population included in this report is broader than the reimbursement recommendation and does not include patients who are immunocompromised. The data used in this economic evaluation are based on the epidemiology of COVID-19 in 2022 and may not reflect the current state of COVID-19.

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 and 14 days before the emergence of the Omicron variant, and between 2 and 4 days following the emergence of the Omicron variant. Individuals with COVID-19 may remain asymptomatic and nonetheless be contagious.[2] 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 for federal, provincial, and territorial (FPT) 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 FPT drug plans' funding decisions. For remdesivir in nonhospitalized patients, CDA-AMC recommended that the public drug programs use the same funding criteria as those for NMV-r.

Prior to the reimbursement recommendations by CDA-AMC for NMV-r and remdesivir, PHAC had commissioned the Post-Market Drug Evaluation program to conduct economic evaluations and budget impact analyses 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. Hence, the research and policy questions defined in this report were developed in advance of the CDA-AMC reimbursement recommendations for remdesivir, and modelling was 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 remdesivir as an outpatient treatment for COVID-19 in Canada on health system costs and health outcomes.

Policy Issue

Health Canada authorized the use of remdesivir in June 2022 for nonhospitalized adults and pediatric patients (weighing at least 40 kg) who have positive results of direct SARS-CoV-2 viral testing and who are at high risk for progression to severe COVID-19, including hospitalization or death, given no drug interactions or side effects. Treatment should be started as soon as possible after diagnosis of COVID-19 and within 7 days of the onset of symptoms.[7-10] Common side effects include nausea, headache, and cough.[10-12] Although there is potential for drug-drug interactions and/or adverse drug events, most patients complete remdesivir treatment as prescribed.[11] Remdesivir is administered intravenously by a health professional for 3 days in an outpatient setting.

Access to outpatient use of remdesivir differs by province and by whether a lab-confirmed diagnosis or a positive rapid test from a primary care provider is required. Lab-confirmed diagnoses are reported and captured in surveillance systems, while cases identified from rapid testing are not.

A systematic review[5] found that outpatient use of remdesivir reduced hospitalizations for COVID-19, but 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 outpatient use of remdesivir for COVID-19, focusing on COVID-19 cases and transitions related to outpatient and inpatient treatment, post–COVID-19 condition, and recovery. We developed a stochastic state-transition model and evaluated 3 cohorts based on data availability and expected differences in disease severity: those younger than 65 years (not in LTC), those aged 65 years or older (not in LTC), and those in LTC. Post–COVID-19 condition was defined as experiencing COVID-19 symptoms for 3 or more months; this occurs in approximately 15% of adults who self-report as having COVID-19.[2] We also address considerations of current testing policies (i.e., using data from the spread of Omicron variants in 2022) and remdesivir's therapeutic effects for outpatient use.

Policy Question

1. What are the health system impacts, uptake, and funding considerations of offering remdesivir as an outpatient 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 remdesivir treatment in the outpatient setting in Canada. Considerations for this policy question include the effectiveness of remdesivir at reducing the proportion of patients who are hospitalized, the potential outpatient use of remdesivir at various uptake levels, the impact on quality of life, health care system costs associated with COVID-19, and treatment costs associated with outpatient remdesivir.

Objective

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

Research Question

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

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

Economic Analysis

Review of Economic Studies

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.[13] Considerations of budget constraints and drug supply can have an important role in resource allocation.[14] In the context of outpatient treatments for COVID-19, factors such as the size of the eligible population over time, prevalence or incidence of the disease, vaccination rates among the eligible population, burden of disease, intervention uptake, and impact on downstream health care resource use (such as inpatient and critical care or intensive care unit [ICU] admissions), should be considered. Based on data from the Council of the Federation Secretariat, it was 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 (including pharmaceuticals and medical supplies), testing, prevention through personal protective equipment, and other health care services and supplies.[15] Treatments and vaccines for COVID-19 in the appropriate patient population, while

considered a major investment, have the potential to substantially save costs due to the downstream health care resource use associated with COVID-19.[16,17]

Prior research on the cost-effectiveness or budget impact of outpatient remdesivir is limited. One study from Canada estimated the cost per patient of remdesivir outpatient treatment at CA$1,872, and that the cost of remdesivir per hospitalization prevented would be CA$52,416 (95% confidence interval [CI], CA$43,056 to CA$149,760).[18] There are a limited number of studies globally that have investigated the cost and budget impacts of remdesivir outpatient treatment. In some jurisdictions, including the US, there are little to no data available to estimate the economic burden of the disease. One study from Turkey found that remdesivir inpatient and outpatient treatment together were determined to be cost-saving in comparison to other existing therapies.[19] An Italian study estimated the daily cost of remdesivir outpatient treatment at €1,348 to €2,359, but also highlighted that outpatient remdesivir service was challenging to provide because of the need for treatment to be given over 3 days, requiring patients to attend multiple treatment visits.[20] While the data described in other jurisdictions have little direct applicability in a Canadian context, these studies offer additional insights into the cost-effectiveness of the outpatient use of remdesivir described in the existing literature.

Economic Evaluation and Budget Impact

We conducted a CUA and BIA examining outpatient treatment strategies for remdesivir based on COVID-19 data for 2022. We developed a stochastic state-transition model that included clinical outcomes associated with COVID-19 cases using data from the Canadian Institute of Health Information (CIHI), Alberta Health, PHAC,[21] and the scientific literature. To reflect the best available data related to remdesivir effect estimates and severity, the patient population in the model was stratified into 3 cohorts: those younger than 65 years (not in LTC), those aged 65 years or older (not in LTC), and those in LTC in any age group. The variation of model inputs allowed for estimates to include 95% credible intervals (CrIs). Costs related to inpatient stay, critical care stay, physician time, and remdesivir (including infusion administration costs) were included in the analysis.

Economic Analyses Overview

We estimated costs, health outcomes, and cost-effectiveness of 5 COVID-19 outpatient treatment scenarios for remdesivir in Canada compared to a baseline of no outpatient treatment. The scope and analytical approach taken in this economic evaluation were 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 Alberta Health and other literature, including reviews by CDA-AMC. CIHI provided COVID-19 data related to severity (inpatient, critical care, death, and length of stay [LOS]) for Canada, and Alberta Health provided case distributions by age group and LTC cohort that were extrapolated to Canadian case data. COVID-19 case data by age group and geography were obtained from the COVID-19 epidemiology update published by PHAC.[21]

The reference scenario was defined as COVID-19 data (lab-confirmed cases and COVID-19 outcomes [mortality and hospitalizations]) representative of 2022 in Canada. While there were likely some regional

differences in outpatient access to remdesivir in 2022, general recommendations included adults with mild to moderate COVID-19 who were at high risk of developing serious disease.[7,22] This defined cohort included considerations for risk factors such as vaccination status, age, comorbidities, and those in LTC.

The 5 remdesivir uptake scenarios were selected to include a focus on high-risk cohorts and assumptions related to outpatient utilization of remdesivir following discussions with the CoLab team. The drug uptake estimates used in the scenarios were selected to represent expected outpatient use of remdesivir if broadly available and with consideration for potential drug interactions and adverse events. These scenarios assumed that all lab-confirmed cases have access to remdesivir as an option for outpatient treatment of COVID-19 at various drug uptakes, to evaluate the overall potential impacts to the health care system. The scenarios defined the cohorts of individuals aged 65 years or older (not in LTC) and of individuals in LTC as "high-risk" for simplicity in naming scenarios. The scenarios are described as follows:

Reference scenario: COVID-19 lab-confirmed cases and hospital dispositions in 2022 in Canada

Scenario 1: Remdesivir treatment of lab-confirmed cases in 5% of those younger than 65 years (not in LTC), 10% of those aged 65 years or older (not in LTC), and 15% of those in LTC (low uptake scenario)

Scenario 2: Remdesivir treatment of lab-confirmed cases in 15% of those aged 65 years or older (not in LTC) and 20% of those in LTC (moderate uptake scenario)

Scenario 3: Remdesivir treatment of lab-confirmed cases in 15% of those in LTC (LTC low uptake scenario)

Scenario 4: Remdesivir treatment of lab-confirmed cases in 50% of those in LTC (LTC high uptake scenario)

Scenario 5: Remdesivir treatment of lab-confirmed cases in 10% of those younger than 65 years (not in LTC), 20% of those aged 65 years or older (not in LTC), and 50% of those in LTC (high uptake scenario)

Economic Evaluation Methods

We developed a stochastic state-transition model that included clinical outcomes associated with COVID-19 infection. The advantage of using a state-transition model compared to other analytical methods is that it captured dynamics related to clinical outcomes — such as transfers between inpatient care, critical care, post–COVID-19 condition, and death — while quantifying costs and quality-adjusted life-years (QALYs) for patient pathways within the health system. The stochasticity implemented in the model (analogous to probabilistic sensitivity analysis) allowed for variations in model inputs and 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 Alberta Health and the literature including reviews by CDA-AMC. The time horizon for this model was 1 year, including impacts on inpatient stay, mortality, and post–COVID-19 condition, along with estimates of projected lifetime QALY losses due to death observed in that year. This approach allowed 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 younger than 65 years (not in LTC), those aged 65 years or older (not in LTC), and those in LTC. As health systems

began to reduce community testing for COVID-19 in 2022, the model simulation was stratified into 2 periods: January 2022 to August 2022 (period 1) and September 2022 to December 2022 (period 2) to better adjust for differences in testing policies and 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 remdesivir uptake estimates for outpatients based on a reasonable coverage (i.e., the percent of outpatients offered remdesivir as informed by the CoLab team) and therapy completion rates (related to drug-drug interactions and/or adverse events). This economic evaluation did not consider COVID-19 rebound; however, this occurs minimally.[5]

Model data were either directly obtained and/or combined from multiple data sources. LTC cases and LOS were extrapolated from other data sources (refer to the Data Inputs section).

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

BIA Methods

The BIA quantified the health system impacts related to remdesivir outpatient treatment retrospectively using Canadian COVID-19 data in 2022, including lab-confirmed cases as well as the number of patients admitted to hospital, both in critical care and not in critical care. These data exclude Quebec due to limitations related to the release of severity data from CIHI. The time horizon for the model was 1 year, while lifetime QALY losses due to death were also included in this analysis, with an assumed discount rate of 1.5%.
The analytical approach aimed to answer a counterfactual question about remdesivir outpatient treatment strategies (i.e., if we had a remdesivir outpatient treatment strategy in 2022, what would be the difference in health care system costs and quality of life outcomes compared to the reference scenario [COVID-19 cases and hospital dispositions in 2022 in Canada]).

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 remdesivir (including infusion administration costs) were included in the analysis. Administration costs related to the implementation of the outpatient 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 had lab-confirmed COVID-19 in 2022. The state-transition model stratified COVID-19 lab-confirmed cases according to the following cohorts: those younger than 65 years (not in LTC), those aged 65 years or older (not in LTC), and those in LTC.

Table 1 provides the hospital case rate per 100 lab-confirmed cases using hospitalization and mortality data obtained from CIHI, and case data obtained from PHAC. As we did not have case rates by LTC, only by age group, we used the proportion of cases that were in LTC from Alberta Health to calculate the severity rates (i.e., hospitalization, ICU, and mortality). The severity rates per 100 lab-confirmed cases were generally higher for those in the cohorts of individuals aged 65 years or older and those in LTC. The transition to reduced community testing aligned with other respiratory viruses was reflected in magnitude differences of hospital disposition outcomes between period 1 and period 2 among those younger than 65 years and in LTC.

Table 1: Hospital Case Rates per 100 Lab-Confirmed Cases in 2022 (Including Inpatient and Critical Care Admissions) in Canada

Hospital disposition	Age < 65 years (not in LTC)	Age ≥ 65 years (not in LTC)	LTC
Period 1: January 2022 to August 2022			
Inpatient admission case rate per 100 lab-confirmed cases	2.8	35.9	5.0
Critical admission case rate per 100 lab-confirmed cases	0.6	5.5	0.3
Death case rate per 100 lab-confirmed cases	0.1	6.3	0.4
Period 2: September 2022 to December 2022			
Inpatient admission case rate per 100 lab-confirmed cases	14.3	28.0	21.7
Critical admission case rate per 100 lab-confirmed cases	3.3	3.8	1.5
Death case rate per 100 lab-confirmed cases	0.8	4.4	1.4

LTC = long-term care.

Treatment

The outpatient COVID-19 treatment considered was remdesivir. Remdesivir aims to stop the virus from multiplying in cells in the body.[12] Remdesivir is indicated for the treatment of COVID-19 in "non-hospitalized adults and pediatric patients (weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death."[23] This drug is administered intravenously by a health professional in an outpatient setting within 7 days of onset of symptoms.[7] In adults, remdesivir 200 mg is administered on day 1 followed by 100 mg on day 2 and day 3.[23]

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 remdesivir, 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 1-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 the COVID-19 Cases state 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. In addition, the use of case and hospitalization data before 2022 (or before the emergence of Omicron) may not be representative of current disease severity rates (including mixed population immunity) and endemic management of COVID-19 (i.e., reduced community testing aligned with other respiratory viruses).

Model Structure (CUA and BIA)

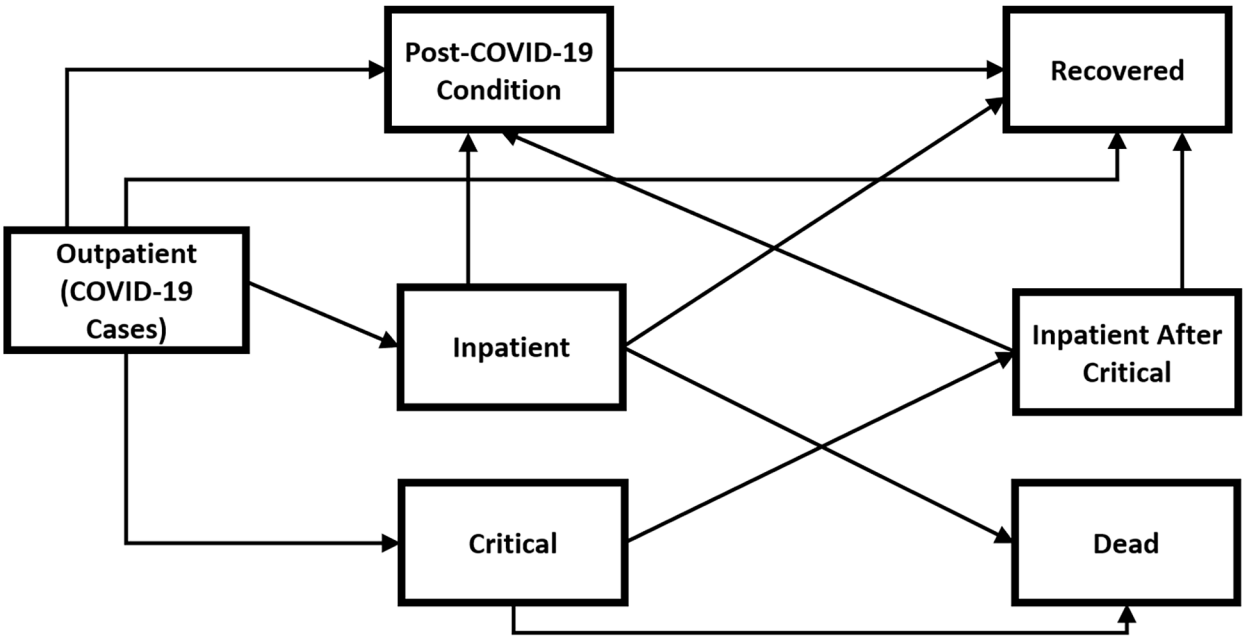
The model used to conduct both the CUA and the BIA was a stochastic state-transition Markov model representing clinical outcomes associated with COVID-19 infection, with states defined as follows:

- **Outpatient (COVID-19 Cases)**: individuals with lab-confirmed COVID-19, but not in hospital
- **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.[24]: “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 beginning in the Outpatient (COVID-19 Cases) state may move to 1 of the hospitalized states (Inpatient or Critical), after which they progress either into the Dead or Recovered states. If outpatients are not hospitalized, they move either to the Post–COVID-19 Condition or Recovered state. Transitions occur on a daily basis in the model. Individuals in the model do not move directly from inpatient to critical. While inpatient to critical care is a realistic transition, there are insufficient data to determine what proportion of patients entered critical care immediately upon hospitalization rather than after a delay. Therefore, in the model, patients who were at some point in critical care spend all their time in the ward after their stay in critical care. This nonetheless consistently depicts the average total time spent in hospital states of patients, and thus accurately captures costs and health-related utilities accrued by their hospital stay. Modelled individuals enter the Dead state from either the Inpatient or Critical states; however, in reality, deaths occurred in individuals that were not admitted to hospital as well, especially those in LTC. The data on deaths directly from LTC were not available and therefore not included in this model. Patients who do not die either recover fully or may first spend time in the Post–COVID-19 Condition state. The proportion of individuals that move to the Post–COVID-19 Condition state differs depending on whether they were in outpatient, inpatient, or critical care, consistent with proportions reported in Hanson et al.[24] Figure 1 shows model states and transitions.

The stochastic state-transition model described in Figure 1 was stratified into 3 cohorts (not shown): those younger than 65 years (not in LTC), those aged 65 years or older (not in LTC), and those in LTC, with the latter 2 cohorts being considered at higher risk for developing severe COVID-19. The transition to endemic management of COVID-19 in 2022, and therefore changes in community testing, highlights a need to stratify the data into 2 periods (not shown): January 2022 to August 2022 (period 1) and September 2022 to December 2022 (period 2). The age cut-offs were used to better align with case and severity data. The model simulated each cohort and period independently.

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



Data Sources

Table 2 provides key data sources and transformations that were used to estimate model inputs for the BIA. The case data obtained from PHAC likely included reinfections and LTC distribution among cases obtained from Alberta Health. They were extrapolated to Canadian case totals due to data limitations. Disease severity data obtained from CIHI did not include information from Quebec.

Table 2: Data Source, Transformations, and Additional Comments

Data source	Data transformations	Additional comments
CIHI data (2022) Datasets:	• Hospital disposition (inpatient, critical care, LOS, and death) and costs • Total costs were transformed to daily	• Data provided at the Canadian level excluded Quebec due to limitations in reporting. • The LTC cohort was based on the discharge

Data source	Data transformations	Additional comments
• Discharge Abstract Database • Canadian MIS Database (costs)	per patient cost using inpatient LOS and critical care LOS.	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 die are accounted for). Deaths that occurred outside discharge were not included. • Costs in the CIHI data did not include physician fees; therefore, we added physician costs using a study by Lau et al.[25] • Costs related to post–COVID-19 condition were not included in the analysis due to limitations in the literature.
PHAC data	• COVID-19 cases for Canada in 2022 by age group and period (January 2022 to August 2022 and September 2022 to December 2022) (Data Inputs, Table 4, Table 5, and Table 6)	• We estimated cases in Canada (excluding Quebec) from the overall total because we did not have severity related data for Quebec from CIHI.
Alberta Health data Datasets: • Provincial Surveillance Information • Communicable Disease Reporting System • Communicable Disease and Outbreak Management • Pharmaceutical Information Network • Continuing Care Reporting System	• Alberta Health LTC case distributions in 2022 were used to extrapolate cases by cohort from the Canadian case data obtained from PHAC. • Drug utilization data were used to estimate baseline use and effect estimates.(Data Inputs and Clinical Inputs in Economic Evaluation)	• Due to data limitations, Alberta LTC case distributions were extrapolated to case distributions in Canada. This may have an impact on the results if the contribution of LTC cases (high-risk cohort) is overestimated. Sensitivity analysis was conducted to evaluate the impact of this assumption.
Wang et al.[5]	• Remdesivir effect estimates against hospitalizations (inpatient only)	• Potential effects of remdesivir on post–COVID-19 condition were not directly included; this was indirectly included since transition proportions to post–COVID-19 condition differed based on outpatient and/or inpatient state (refer to Clinical Parameters in Economic Evaluation).

CIHI = Canadian Institute of Health Information; LOS = length of stay; LTC = long-term care; MIS = management information system; PHAC = Public Health Agency of Canada.

Data Inputs

Table 3 provides the stochastic state-transition model parameters related to outpatient and inpatient transitions with sample distributions and standard deviations (SDs) among COVID-19 cases (refer to Table 20 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 LTC). Two periods were selected to adjust for differences in community testing across different time periods in 2022 (as COVID-19 testing became more

aligned with testing efforts for other respiratory viruses). Across both time periods, the Omicron variant was the main variant in circulation. Data sources used in this analysis include data from CIHI, Alberta Health, PHAC,[21] and the COVID-19 Immunity Task Force.[26] Because COVID-19 severity parameters obtained from CIHI for Canada did not include Quebec, COVID-19 cases used to populate the model and model input parameters were also adjusted to not include Quebec (refer to Table 4, Table 5, and Table 6). All model parameters, except for time to symptom resolution, were 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.

LOS for the Inpatient and Critical states was estimated directly and indirectly (refer to Table 20) from CIHI data. Bayesian inference was used to estimate the distribution of the rate at which 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 standard deviation, s, given by the hospital and critical care data from CIHI, 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 data from CIHI. 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 at which patients leave the hospital and critical care.

Death rates were estimated from CIHI data. Due to data availability, in this analysis, deaths in LTC represent those who died during hospitalization and did not capture LTC residents who died outside hospital facilities.

The therapeutic effect of remdesivir was obtained from Wang et al. (refer to the Clinical Parameters section).[5] The therapeutic effect of remdesivir was applied to hospital admissions (Inpatient and Critical states).[5] 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 8). Baseline health utilities associated with healthy individuals in the Recovered state were obtained from health-adjusted life expectancy (HALE) tables published by Statistics Canada,[27] and cross-referenced with the average age of cases[28] in modelled cohorts. Health utilities immediately following hospital discharge and for post–COVID-19 condition were obtained from Poudel et al.[29] and were further used to infer health utilities for inpatients and outpatients, respectively.

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

Symbol	Quantity	Source	Sample distribution	Mean (SD): age < 65 years	Mean (SD): age ≥ 65 years	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)
$\vec{p}_{o-h}$	Proportion of all lab-confirmed cases that are admitted to inpatient hospital	CIHI	Beta	0.028 (± 5%)	0.359 (± 5%)	0.05 (± 5%)
$\vec{p}_{o-c}$	Proportion of all lab-confirmed cases that are admitted to critical care	CIHI	Beta	0.006 (± 5%)	0.055 (± 5%)	0.003 (± 5%)
$\vec{p}_{c-d}$	Proportion of critical care patients who die	CIHI	Beta	0.169 (± 5%)	0.332 (± 5%)	0.135 (± 5%)
$\vec{p}_{h-d}$	Proportion of inpatients who die	CIHI	Beta	0.016 (± 5%)	0.126 (± 5%)	0.072 (± 5%)
Initial total lab-confirmed COVID-19 cases		CIHI	NA	1,113,626	131,443	114,427
Period: September 2022 to December 2022						
$\vec{T}_{ah}$	LOS hospital (days)	CIHI	Weibull	15 (40)	19 (36)	57 (73)
$\vec{T}_{c}$	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)
$\vec{p}_{o-h}$	Proportion of all lab-confirmed cases that are admitted to inpatient hospital	CIHI	Beta	0.143 (± 5%)	0.280 (± 5%)	0.217 (± 5%)
$\vec{p}_{o-c}$	Proportion of all lab-confirmed cases that are admitted to critical care	CIHI	Beta	0.033 (± 5%)	0.038 (± 5%)	0.015 (± 5%)
$\vec{p}_{c-d}$	Proportion of critical patients who die	CIHI	Beta	0.161 (± 5%)	0.294 (± 5%)	0.073 (± 5%)

Symbol	Quantity	Source	Sample distribution	Mean (SD): age < 65 years	Mean (SD): age ≥ 65 years	Mean (SD): LTC
$\vec{p}_{\mathrm{h}-d}$	Proportion of inpatients who die	CIHI	Beta	0.022 (± 5%)	0.118 (± 5%)	0.060 (± 5%)
Initial total lab-confirmed COVID-19 cases		CIHI	NA	62,932	85,129	15,929
Period: January 2022 to December 2022						
$\vec{T}_{sr}$	Total time to symptom resolution (days)	Siemieniuk et al.[30]	Gamma	9.9	9.9	9.9
$\vec{p}_{orl-l}$	Proportion of outpatients who develop post–COVID-19 condition	Wulf Hanson et al.[24]	Beta	0.057 (± 5%)	0.057 (± 5%)	0.057 (± 5%)
$\vec{p}_{hrl-l}$	Proportion of hospitalized patients who develop post–COVID-19 condition	Wulf Hanson et al.[24]	Beta	0.275 (± 5%)	0.275 (± 5%)	0.275 (± 5%)
$\vec{p}_{crl-l}$	Proportion of critical patients who develop post–COVID-19 condition	Wulf Hanson et al.[24]	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.[24]	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; NA = not applicable.

Estimation of the Population in Canada by Cohort

Because CIHI data for severity did not include data from Quebec, we also adjusted COVID-19 cases used in the model to not include Quebec. Data sources from Alberta Health, PHAC, and the National Institute of Public Health Quebec were used to estimate lab-confirmed COVID-19 cases for all of Canada for model periods in 2022 by the model cohorts (those aged < 65 years, those aged ≥ 65 years, and those in LTC). Table 4 provides the proportion contributions by age distribution of COVID-19 cases in Quebec since 2020. These age-specific proportions were used to distribute total COVID-19 cases for Quebec across the model periods (January 2022 to August 2022 and September 2022 to December 2022) and age (refer to Table 4). Note that, for the age group of individuals aged 60 years to 69 years, the midpoint was used to distribute between the age cohorts. Table 5 provides the estimation of COVID-19 cases in Canada with and without the Quebec cases. These totals were stratified by LTC status using the estimates obtained from Alberta Health provided in Table 6 (refer to initial total lab-confirmed cases in Table 3).

Table 4: Estimation of Lab-Confirmed COVID-19 Cases in Quebec

Age group, in years	Proportion of total COVID-19 cases in Quebec (since 2020)	Number of COVID-19 cases in Quebec (January 2022 to August 2022)	Number of COVID-19 cases in Quebec (September 2022 to December 2022)
0 to 9	0.066	34,111	7,204
10 to 19	0.083	43,150	9,113
20 to 29	0.155	80,209	16,939
30 to 39	0.161	83,456	17,625
40 to 49	0.157	81,363	17,183
50 to 59	0.127	65,848	13,906
60 to 69	0.080	41,741	8,815
70 to 79	0.069	35,722	7,544
80 to 89	0.068	35,037	7,399
90+	0.035	18,363	3,878
Total	**1.000**	**518,998**[21]	**109,608**[21]

PHAC = Public Health Agency of Canada.

Sources: National Institute of Public Health Quebec[31] and PHAC.[21]

Table 5: Estimation of Lab-Confirmed COVID-19 Cases in Canada

Period	Age < 65 years	Age ≥ 65 years	Total
Cases (Canada)			
January 2022 to August 2022	1,529,746	348,749	1,878,495
September 2022 to December 2022	150,356	123,243	273,598
Cases (Quebec)			
January 2022 to August 2022	409,006	109,992	518,998
September 2022 to December 2022	86,379	23,229	109,608
Cases (Canada excluding Quebec)			
January 2022 to August 2022	1,120,740	238,757	1,359,497
September 2022 to December 2022	63,977	100,013	163,990

PHAC = Public Health Agency of Canada.

Sources: National Institute of Public Health Quebec[31] and PHAC.[21]

Table 6: Case Distribution by LTC Status in Alberta

Period	Age < 65 years (LTC cases out of total cases)	Age ≥ 65 years (LTC cases out of total cases)
January 2022 to August 2022	0.006 (1,210 out of 190,638)	0.449 (16,371 out of 36,423)
September 2022 to December 2022	0.016 (176 out of 10,776)	0.149 (1,544 out of 10,375)

LTC = long-term care.

Source: Alberta Health.

Clinical Parameters

Therapeutic Effect Estimates: Remdesivir for Outpatient Treatment of COVID-19

Wang et al. was used to obtain a range of effect estimates for remdesivir as an outpatient treatment for COVID-19.[5,11] Remdesivir mainly had an impact on hospitalization, specifically on inpatient admission rates. These effects were reported as *all ages*[32] and *age stratified* (those aged ≥ 60 years)[11] (refer to Table 21 for an overview of studies considered in this analysis). The effect estimate for those aged 60 years or older was extrapolated to the cohorts of those aged 65 years or older and those in LTC in the model.[11]

Table 7 provides the relative risk estimates obtained from Wang et al.[5] The effect estimates for hospitalization include studies that were limited to those eligible for remdesivir treatment and/or had a prior risk factor for severe disease. This effect estimate was only applied to those within inpatient units because no statistical difference was observed among those in critical care.[5] The study periods for Mazzitelli et al.[32] and Gottlieb et al.[11] were February 2022 to May 2022 and September 2020 to April 2021, respectively. Although the study by Gottlieb et al. was conducted before the emergence of the Omicron variant, the estimate from the study by Mazzitelli at al.[32] (which was conducted in 2022, during Omicron) was within the 95% CI reported by Gottlieb et al.[11] (refer to Table 21). In Table 7, remdesivir treatment effects are assumed to be the same for people aged 65 years or older and people in LTC. The *all ages* estimate from Gottlieb et al.[11] was used to parameterize the cohort of individuals younger than 65 years.

Table 7: Effect Estimates for the Outpatient Treatment of COVID-19 With Remdesivir

Symbol	Quantity	Hazard ratio (95% confidence interval)			Source
		Age < 65 years	Age ≥ 65 years	LTC	
$\vec{p}_{o-h\_therapy}$	Proportion of all cases that are admitted to inpatient unit	0.13 (0.03 to 0.59)	0.11 (0.01 to 0.86)	0.11 (0.01 to 0.86)	Wang et al.,[5] Gottlieb et al.[11]

LTC = long-term care.

Utilities

The health utility associated with the Recovered state was assumed to be that of healthy individuals; it was estimated from HALE tables published by Statistics Canada[27] and assigned to model cohorts according to the average age of COVID-19 cases 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 equally to the average HALE for individuals in the modelled cohort, thereby capturing the loss of expected lifetime QALYs. Poudel et al.[29] reported health utilities for COVID-19 patients immediately upon discharge from hospital, as well as for post–COVID-19 condition. Due to 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.,[29] we inferred that the utility during non critical hospitalization (i.e., the Inpatient and Inpatient After Critical states) is equal to that immediately after discharge. Additionally, health utilities during the period of infection of outpatients were not available from published studies, so we assumed the health utility of the Outpatient state to be the same as that of the Post–COVID-19 Condition state, as reported by Poudel et al.[29] Additionally, individuals in critical care are often either unconscious or have a very low health-related quality of life; therefore, the utility for the Critical health state was assumed to be 0 for simplicity. The utility estimates for the stochastic state-transition model are provided in Table 8.

Table 8: Utility Estimates for the Stochastic State-Transition Model

Symbol	States	Daily utility (SD)	Entry utility (SD)	Source
$\overrightarrow{Ut}_o$	Outpatient	0.76 (0.076)	0	Poudel et al. (2021)[29]
$\overrightarrow{Ut}_c$	Critical	0	0	Estimate
$\overrightarrow{Ut}_h$	Inpatient	0.60 (0.06)	0	Poudel et al. (2021)[29]
$\overrightarrow{Ut}_{d1a}$	Period 1: Dead (age < 65 years)	0	–27.6 (0.04)	Statistics Canada,[27] PHAC[33]
$\overrightarrow{Ut}_{d1b}$	Period 1: Dead (age ≥ 65 years or LTC)	0	–6.4 (0.03)	Statistics Canada,[27] PHAC[33]
$\overrightarrow{Ut}_{d2a}$	Period 2: Dead (age < 65 years)	0	–27.3 (0.03)	Statistics Canada,[27] PHAC[33]
$\overrightarrow{Ut}_{d2b}$	Period 2: Dead (age ≥ 65 years or LTC)	0	–6.0 (0.03)	Statistics Canada,[27] PHAC[33]
$\overrightarrow{Ut}_i$	Inpatient After Critical	0.60 (0.06)	0	Poudel et al. (2021)[29]
$\overrightarrow{Ut}_l$	Post–COVID-19 Condition	0.76 (0.076)	0	Poudel et al. (2021)[29]
$\overrightarrow{Ut}_{r1a}$	Period 1: Recovered (age < 65 years)	0.89 (0.089)	0	Statistics Canada,[27] PHAC[33]
$\overrightarrow{Ut}_{r1b}$	Period 1: Recovered (age ≥ 65 years or LTC)	0.73 (0.073)	0	Statistics Canada,[27] PHAC[33]
$\overrightarrow{Ut}_{r2a}$	Period 2: Recovered (age < 65 years)	0.89 (0.089)	0	Statistics Canada,[27] PHAC[33]
$\overrightarrow{Ut}_{r2b}$	Period 2: Recovered (age ≥ 65 years or LTC)	0.70 (0.070)	0	Statistics Canada,[27] PHAC[33]

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.[34] Table 9 provides the 2022 hospital resource and drug costs used in the health economic evaluation, including the costs associated remdesivir purchasing and dispensation. 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 were not included in the total costs reported by CIHI.[25] Costs related to the implementation of the outpatient strategy (e.g., office administration costs) and health care costs related to post–COVID-19 condition were not included in this analysis.

The administration of remdesivir as an outpatient treatment for COVID-19 includes 3 daily infusions (1.5 hours per infusion) using 4 100 mg vials (2 vials for the first infusion followed by 1 vial each for the second and third infusions).[7,12] The total costs based on US and UK prices range between CA$2,335[35,36] and CA$2,852.[37] Infusion costs based on iron infusions and outpatient parenteral antibiotic therapy were included as additional costs. Overall, these infusion costs adjusted to 2022 Canadian dollars and 1.5 hours (where possible) ranged from CA$331 to CA$438 per infusion.[38,39] The estimated cost for remdesivir outpatient treatment ranged from the lower cost estimate of the drug (assuming no additional administration costs) to the high drug and infusion cost estimate. This range was estimated to be from CA$2,335 to CA$4,166 (i.e., $2,852 [drug cost] + $438 × 3 [3-day infusion cost]).

Table 9: Hospital Resource and Drug Costs

Hospital resource or drug	Cost (SD or range)	Treated state	Source
Period 1: Hospital stay, inpatient (per day)		Inpatient or Inpatient After Critical	CIHI
Age < 65 years	$1,368 (SD = 68.39)		
Age ≥ 65 years	$1,118 (SD = 55.92)		
LTC	$913 (SD = 45.66)		
Period 1: Hospital stay, critical care (per day)		Critical	CIHI
Age < 65 years	$3,713 (SD = 185.66)		
Age ≥ 65 years	$3,640 (SD = 182.01)		
LTC	$4,573 (SD = 228.65)		
Period 2: Hospital stay, inpatient (per day)		Inpatient or Inpatient After Critical	CIHI
Age < 65 years	$1,182 (SD = 59.09)		
Age ≥ 65 years	$1,042 (SD = 52.10)		
LTC	$874 (SD = 43.69)		
Period 2: Hospital stay, critical care (per day)		Critical	CIHI
Age < 65 years	$3,668 (SD = 183.40)		

Hospital resource or drug	Cost (SD or range)	Treated state	Source
Age ≥ 65 years	$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.[25]
Critical care physician (per patient-day)	$254.70 (SD = 128.22)	Critical	Lau et al.[25]
Remdesivir treatment	$3,250.50 (range, $2,335 to $4,166)	COVID-19 Cases: Outpatient	Alberta Health Services[7] Government of Canada[12] Von Scheel[38] Yadav et al.[39]

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

Notes: Period 1 = January 2022 to August 2022 and period 2 = September 2022 to December 2022.

The cost conversion to US dollars was US$1 = CA$1.37.

Scenario Analysis and Sensitivity Analysis

Five treatment scenarios and 1 reference scenario were considered in this health economic evaluation, all of which are described in Table 10. All scenarios described in Table 10 targeted outpatient treatment of remdesivir to the cohorts of individuals aged 65 years or older and those in LTC, as it is understood that these cohorts are at a higher severity risk for COVID-19. However, scenario 1 and scenario 5 included outpatient remdesivir utilization among those younger than 65 years (not in LTC) to evaluate its impact if accessible to a broader population. The 5 scenarios were selected following discussion with the CoLab team. Uptake was defined as a reasonable estimate of remdesivir use if funded publicly for outpatient treatment of COVID-19. Therefore, the scenarios were selected to represent expected outpatient use of remdesivir if broadly available and with consideration for potential drug interactions and adverse events. These scenarios assumed that a fraction of reported cases in 2022 had remdesivir as an option for outpatient treatment of COVID-19, and evaluated the impact of that access to the health care system.

Furthermore, probabilistic sensitivity analyses were undertaken to address parameter uncertainty associated with cost-effectiveness of scenarios compared to the reference scenario, 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 provided in Table 3, Table 7, Table 8, and Table 9. 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).

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 10: Scenario Descriptions for Remdesivir as an Outpatient Treatment

Scenario	Justification
Reference scenario: Lab-confirmed COVID-19 cases and hospital dispositions in 2022 assuming minimal use (≤ 5%) of remdesivir	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): Remdesivir treatment of lab-confirmed cases in 5% of those aged < 65 years (not in LTC), 10% of those aged ≥ 65 years (not in LTC), and 15% of those in LTC	Scenario 1 included outpatient treatment of those aged < 65 years (not in LTC) along with those that have a higher risk of severe COVID-19. Utilization was informed from the study by Mazzitelli et al.,[32] where 12.9% of the eligible cohort that attended an outpatient clinic for COVID-19 received remdesivir. This was also arbitrarily adjusted based on model cohorts.
Scenario 2 (moderate uptake): Remdesivir treatment of lab-confirmed cases in 15% of those aged ≥ 65 years (not in LTC) and 20% of those in LTC	In scenario 2, the magnitude of outpatient uptake of remdesivir among those aged ≥ 65 years and those in LTC was increased to capture potential for higher uptake of the drug; specifically, the uptake increased by 5% in both cohorts.
Scenario 3 (LTC low uptake): Remdesivir treatment of lab-confirmed cases in 15% of those in LTC	Scenario 3 had a focus on outpatient uptake of remdesivir in the LTC cohort with low uptake (consistent with scenario 1).
Scenario 4 (LTC high uptake): Remdesivir treatment of lab-confirmed cases in 50% of those in LTC	Scenario 4 had a focus on outpatient high uptake of remdesivir in the LTC cohort with high uptake (consistent with scenario 5).
Scenario 5 (high uptake): Remdesivir treatment of lab-confirmed cases in 10% of those aged < 65 years (not in LTC), 20% of those aged ≥ 65 years (not in LTC), and 50% of those in LTC	Scenario 5 was a combined scenario of the highest projected outpatient uptake of remdesivir in those aged < 65 years (not in LTC), those aged ≥ 65 years (not in LTC), and those in LTC.

LTC = long-term care.

Uncertainty

As model simulations incorporate uncertainty within model inputs, a probabilistic one-way sensitivity analysis (POSA)[40] (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: LTC 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 remdesivir uptake from moderate to high. Table 11 provides the key model inputs examined for the POSA using total costs as an outcome.

The POSA can assess whether the budget impact (scenario cost minus reference scenario cost) will cost (a strategy that costs more compared to no strategy or reference) or save (a strategy that costs less compared to no strategy or reference) the health care system money. The POSA for remdesivir drug cost used a wide range of costs, from $1,000 to $10,000 per 3-day treatment course, to estimate an optimal price (i.e., where total health care costs are the same for the scenario and reference scenario).

Limitations related to LTC data were examined through a POSA for key model inputs such LTC case distribution and inpatient admission. This will provide insights to budget impact estimates related to parameters that had a higher degree of uncertainty because of limitations in the data source.

Model Validation

Overall, the validation of the model structure and model inputs occurred through discussions with the Canadian Collaborative Research Network (CCRN), the CoLab team, Alberta Health, CIHI, and a clinical expert 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 CCRN. Methods for obtaining model inputs included clarifications from Alberta Health and CIHI (related to a data request), the literature, and discussions with the CoLab team, and a clinical expert where necessary.

Internal validity for the reference scenario as described in Table 12 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), total inpatient admissions, critical care admissions, and deaths, including 95% CrIs. The total inpatient and critical care admissions and deaths from model simulations compared well to the data. Deaths were captured over 1 year, which provided 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 remdesivir on cost-effectiveness outcomes. This included creating scenarios focusing on 1 cohort and the therapeutic effect of remdesivir to determine if the results were reasonable compared to crude estimates. Overall results were compared to other similar economic evaluations (if available) for external validity.

Table 12: 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 inpatient admissions	120,803	120,743 (119,128 to 122,284)
Total critical care admissions	19,635	19,692 (18,233 to 21,234)
Total deaths	14,923	14,927 (13,997 to 15,901)

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 13.

Table 11: POSA of Key Model Inputs

Model parameter	Cohort (age < 65 years, age ≥ 65 years, LTC, and all)	Range (total discrete points within the range)
Remdesivir drug cost (per treatment course)	All	$1,000 to $10,000 (10)
Remdesivir effect on critical care admission	All	0.01 to 1.0 (10)
Total per patient cost: inpatient unit	All	$10,000 to $25,000 (10)
Relative overreporting adjustment of LTC cases (i.e., 0.4 of initial LTC cases of COVID-19 are redistributed to those aged ≥ 65 years to account for the overestimation)	LTC	0.4 to 1.0 (10)
Mean hospital LOS for LTC and those aged ≥ 65 years	Age ≥ 65 years, LTC	20 days to 35 days (10)

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

Table 13: Key Model Assumptions

Related model parameter or structure	Assumption	Additional comments
Cases	• Cases were defined as those detected through laboratory testing by the surveillance system.	• This methodological approach may not account for those infected individuals that have sought treatment if broadly available. This assumption may overestimate the cost-effectiveness and break-even costs of remdesivir as an outpatient treatment option.
Time horizon	• The 1-year time horizon was structured around the availability of data. The use of case and hospitalization data before 2022 (or pre-Omicron) may not be representative of 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 outpatient 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 transitions toward management policies of COVID-19 as an endemic disease.	NA
CIHI data	• COVID-19 severity data reported by CIHI include reinfections. • COVID-19 severity data reported by CIHI do not include data from Quebec.	• The reinfections in the data were not adjusted.
PHAC data	• PHAC data were used for estimating initial cases excluding Quebec data. • It is assumed that the distribution of LTC cases in the PHAC data is similar to data obtained from Alberta Health.	NA

Related model parameter or structure	Assumption	Additional comments
Costs	• Costs related to the implementation of the outpatient strategy (e.g., administration costs) and health care costs related to post–COVID-19 condition were not included in this analysis. • The reference scenario may have included minimal baseline outpatient use of remdesivir and those costs and effect considerations were not included. • The costs considered beyond outpatient treatment included acute care facilities only.	• Health care costs related to COVID-19 management within LTC facilities for patients who could benefit from remdesivir were not captured in the analysis. This may underestimate the cost-effectiveness of remdesivir in the LTC cohort.
Death transition: from outpatient, recovered, and LTC	• Deaths were only modelled from 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.	• LTC cases were more likely to die outside of hospital and therefore, not capturing these deaths could limit the cost-effectiveness of remdesivir in this population.
Post–COVID-19 condition transition from outpatient	• Incidence of post–COVID-19 condition following recovery from nonhospitalized acute infection was calculated with the probability of post–COVID-19 condition per case.	• NA
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 outpatient treatment of the LTC cohort.
Case hospitalization rates	• To calculate case hospitalization rates, it is assumed that all cases were reported to the surveillance system before hospitalization. However, the number of cases detected and reported at hospitalization is unknown, and would therefore not have been subject to outpatient treatment.	• This assumption may overestimate the impact of outpatient remdesivir treatment in the scenarios described.
Remdesivir therapeutic effects	• Due to data limitations, remdesivir therapy effects were assumed to be the same for people aged ≥ 65 years and people in LTC. • We indirectly accounted for remdesivir therapy effects on post–COVID-19 condition because proportion transitions differed by outpatient and in-hospital states.	NA
Remdesivir outpatient scenarios	• Costs related to the implementation of the outpatient strategy (e.g., administration of the program) were not included in this analysis. However, remdesivir procurement costs and dispensation were captured.	• Including additional administration costs would reduce the cost-effectiveness of the outpatient remdesivir program.

Related model parameter or structure	Assumption	Additional comments
	• All scenarios assume those treated with remdesivir will complete the 3-day treatment course.	
LTC case distribution	• The distribution of lab-confirmed COVID-19 cases in Canada did not include an additional stratification by LTC cohort. The LTC case distribution estimated using Alberta Health data was used to stratify these cases at the Canadian level.	• The Alberta Health data describes a high proportion of lab-confirmed cases in the LTC population in Period 1 i.e., approximately 45% of cases (refer to Table 6). This assumption was evaluated using a POSA.
Utilities	• Utilities for model states were the same across cohorts and periods except for the Recovered state. Utilities also do not differ by treatment arm.	NA
Utilities: Outpatient and Post–COVID-19 Condition states	• Due to a lack of studies reporting health utilities for COVID-19 outpatients during their period of infection we assumed utilities in the Outpatient and Post–COVID-19 Condition state would be the same.	NA
Utilities: Inpatient, Inpatient After Critical states	• Due to 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 outpatient remdesivir.
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 zero for simplicity.	• As we assumed no treatment effect of remdesivir outpatient on critical care admission, this assumption would not impact the cost-effectiveness of outpatient remdesivir.
Utilities: Deaths	• Estimated lifetime QALYs lost due to 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%, accounting for the lifetime impact of mortality.

BIA = budget impact analysis, CIHI = Canadian Institute of Health Information; CUA = cost-utility analysis; LTC = long-term care; NA = not applicable; PHAC = Public Health Agency of Canada; QALY = quality-adjusted life-year.

Assumptions Related to the BIA

A complete list of model assumptions is described in Table 13. In Table 14, we provide the BIA model assumptions that were addressed using a POSA.

Table 14: Model Assumptions Addressed by POSA for Remdesivir as an Outpatient Treatment for COVID-19

Assumption	How it was tested in the scenario analysis	Additional comments
LTC case distribution was extrapolated from Alberta to the population in Canada	A POSA was conducted for the LTC case distribution that included a lower bound informed by grey literature.[41] The lower bound was considered using a relative overreporting adjustment reduction (i.e., 0.4 of initial LTC cases of COVID-19 compared to baseline estimates [refer to Table 3] are redistributed to those aged ≥ 65 years to account for the overestimation of initial LTC cases). With fewer LTC cases overall, the rate of severe disease increases in the LTC population.	NA
Remdesivir drug cost was assumed to range between $1,000 and $10,000.	A POSA was conducted to examine a wider range of remdesivir cost to determine a price point where costs would break even (with model uncertainty included in the simulations) when compared between scenarios and the reference scenario.	NA

LTC = long-term care; NA = not applicable; POSA = probabilistic one-way sensitivity analysis.

Results

Cost-Effectiveness Analysis Results

Main Take-Aways

The results of the CUA suggest that outpatient use of remdesivir may be cost-effective at various WTP thresholds. This is supported by positive mean iNMB and ICERs either dominant relative to the reference scenario or below $30,000 per QALY. We observed consistency across scenarios focusing on high-risk cohorts and all cohorts, with the highest iNMB observed in scenarios with moderate uptake in the high-risk cohorts (those aged ≥ 65 years and those in LTC). However, there is considerable uncertainty in results, as the 95% CrIs of all iNMBs cross zero, except for scenario 2 with a WTP threshold greater than $50,000 per QALY.

Detailed results of the CUA are provided in Table 15 (NMB) and Table 17 (ICERs) with disaggregated results described in Table 16 and Table 18. COVID-19 is a highly prevalent disease, with PHAC data on lab-confirmed cases showing 1,523,487 total reported cases in a 1-year period during 2022, and serology

data indicating that many more were infected with COVID-19 than were reported. Most infected people only experience a brief illness and temporary loss of quality of life.

While this may be a small effect at an individual level, given the high prevalence of COVID it represents a significant health burden at a population level. This is reflected in our results when presented as the NMB. 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 1,143,224 total QALYs over 1 year for the population of reported cases. If we assume a WTP per QALY of $50,000, then the total value of the health of the reference scenario population is $57,161,200,000, or $37,520 per lab-confirmed case. 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 $228 million (95% CrI, –$174 million to $506 million) at a WTP threshold of $50,000 per QALY, when compared to the reference scenario. The full set of results for all scenarios is presented in Table 15 (with 95% CrIs). Disaggregated results are described in Table 16 and Table 18 to highlight the breakdown by state and scenario of QALY and health care costs. The largest contribution of QALY and health care costs is from the Recovered and Inpatient states, respectively.

In Table 17, we present ICERs when scenarios are compared to a common baseline (the reference scenario). Because we analyzed potential future states, not treatment strategies to be implemented, we did not calculate ICERs when all scenarios were compared to 1 another, as would be typical in a cost-effectiveness analysis. Rather, our aim was to illustrate the cost-effectiveness of remdesivir under different possible usage patterns and not to identify a single cost-effective strategy.

Key Results

The NMB across all modelled scenarios, including the reference scenario, was in excess of $30 billion, $53 billion, and $110 billion, for a WTP threshold per QALY of $30,000, $50,000, and $100,000, respectively (refer to Table 15). These numbers resulted from the fact that simulations depicted a year of outcomes for all reported cases in Canada (excluding Quebec), as well as the HALE loss due to all COVID-19 related deaths, where these QALY totals are valued at the given a WTP threshold.

The NMB per reported case for the reference scenario was $20,306, $35,314, and $72,834 for a WTP threshold per QALY of $30,000, $50,000, and $100,000, respectively.

The iNMB showed the difference for each modelled scenario relative to the reference scenario (refer to Table 15). There was an increase in total QALYs in all scenarios (refer to Table 17), with the iNMB showing the relative change in the valuation of QALYs versus costs. Across all WTP thresholds, the mean iNMB for all scenarios was positive and ranged from $10 million to $1.21 billion. However, there is considerable uncertainty in these results, with the majority of 95% CrIs from the probabilistic sensitivity analysis crossing zero, suggesting there is the potential for each scenario to not be cost-effective. Only scenario 2 at both the $50,000 and $100,000 WTP per QALY thresholds had 95% CrIs that did not cross zero (refer to Table 15 and Table 16).

At a WTP per QALY of $30,000, the largest iNMB results from scenario 2 that included treated cases within the high-risk cohort (those aged 65 years and older), followed by the 2 scenarios that focus on all 3 cohorts (scenarios 1 and 5).

Scenario 3 (LTC low uptake) and scenario 4 (LTC high uptake) had the lowest mean iNMB and lowest positive ICER estimates. We present our results from the point of view of a hospital setting, and deaths within LTC facilities were not captured in our model. The potential benefits of an outpatient COVID-19 treatment, in this context, may not be fully captured in these cost-effectiveness results.

Reference Scenario

The reference scenario was defined as COVID-19 cases and hospital disposition in Canada in 2022, assuming most outpatients would not be treated with remdesivir. Based on the review by CDA-AMC, utilization of outpatient remdesivir for Ontario and Saskatchewan in 2022 was less than 3% of total COVID-19 cases.[42]

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 6, Table 7, Table 8, and Table 9. In Table 17, we present the ICERs for each of the scenarios relative to a common baseline of the reference scenario. Based on Table 15, scenario 2 would be cost-effective (with consideration of the 95% CrI) when compared to the reference scenario at a WTP threshold of at least $50,000 per QALY. Moreover, Table 17 shows that scenario 2 had the only ICER that was dominant. Disaggregated results stratified by model states are described in Table 16 and Table 17 and highlight that most of the QALY costs independent of WTP were in the Recovered state, and the highest QALY cost decrement was in the Dead state.

Table 15: NMB and iNMB Estimates for Remdesivir Outpatient 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)	$30,936 ($23,728 to $34,526)	$53,801 ($41,785 to $59,784)	$110,962 ($86,923 to $122,951)
iNMB (95% CrI)	NA	NA	NA
Scenario 1 (low uptake)			
NMB (95% CrI)	$31,026 ($23,738 to $34,630)	$54,029 ($41,886 to $60,007)	$111,536 ($87,284 to $123,494)
iNMB (95% CrI)	$89.4 (–$210 to $281)	$228 (–$174 to $506)	$574 (–$89 to $1,070)
Scenario 2 (moderate uptake)			
NMB (95% CrI)	$31,280 ($24,055 to $34,866)	$54,322 ($42,267 to $60,313)	$111,929 ($87,761 to $123,915)

Cost-effectiveness estimate	WTP threshold: $30,000	WTP threshold: $50,000	WTP threshold: $100,000
iNMB (95% CrI)	$343 (–$43 to $493)	$521 ($10 to $725)	$967 ($126 to $1,320)
Scenario 3 (LTC low uptake)			
NMB (95% CrI)	$30,947 ($23,720 to $34,549)	$53,823 ($41,809 to $59,815)	$111,014 ($86,988 to $123,006)
iNMB (95% CrI)	$10 (–$49 to $46)	$22 (–$49 to $65)	$52 (–$48 to $118)
Scenario 4 (LTC high uptake)			
NMB (95% CrI)	$30,971 ($23,723 to $34,573)	$53,874 ($41,791 to $59,880)	$111,134 ($87,016 to $123,120)
iNMB (95% CrI)	$34 (–$152 to $119)	$73 (–$143 to $165)	$171 (–$115 to $289)
Scenario 5 (high uptake)			
NMB (95% CrI)	$31,127 ($23,834 to $34,759)	$54,283 ($42,136 to $60,309)	$112,172 ($87,920 to $124,202)
iNMB (95% CrI)	$191 (–$436 to $503)	$482 (–$333 to $875)	$1,210 (–$82 to $1,840)

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

Note: Cases include only lab-confirmed cases (i.e., 1,523,487 total cases [excluding Quebec] [4.9%] of the total population in Canada excluding Quebec) in 2022.

Table 16: Disaggregated Results (Mean Values Only) of NMB and iNMB Estimates for Remdesivir Outpatient 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	Scenario 1 (low uptake)	Scenario 2 (moderate uptake)	Scenario 3 (LTC low uptake)	Scenario 4 (LTC high uptake)	Scenario 5 (high uptake)
Total value of QALYs (WTP: $30,000) (A)	$34,297	$34,504	$34,564	$34,314	$34,356	$34,733
By health state						
Outpatient	$938	$938	$938	$938	$938	$938
Inpatient	$100	$91	$88	$97	$90	$78
Critical	$0	$0	$0	$0	$0	$0
Inpatient After Critical	$12	$12	$12	$12	$12	$12
Dead	–$4,169	–$3,982	–$3,929	–$4,154	–$4,117	–$3,775
Post–COVID-19 Condition	$923	$909	$907	$921	$917	$893
Recovered	$36,492	$36,535	$36,547	$36,499	$36,515	$36,587
Total value of QALYs (WTP: $50,000) (B)	$57,161	$57,507	$57,607	$57,191	$57,259	$57,889
By health state						
Outpatient	$1,564	$1,564	$1,564	$1,564	$1,564	$1,564
Inpatient	$167	$152	$147	$162	$150	$130

Parameter	Baseline	Scenario 1 (low uptake)	Scenario 2 (moderate uptake)	Scenario 3 (LTC low uptake)	Scenario 4 (LTC high uptake)	Scenario 5 (high uptake)
Critical	$0	$0	$0	$0	$0	$0
Inpatient After Critical	$20	$20	$20	$20	$20	$20
Dead	–$6,949	–$6,636	–$6,548	–$6,923	–$6,862	–$6,292
Post–COVID-19 Condition	$1,539	$1,515	$1,512	$1,536	$1,528	$1,488
Recovered	$60,821	$60,892	$60,912	$60,832	$60,858	$60,979
Total Value of QALYs (WTP: $100,000) (C)	$114,320	$115,010	$115,210	$114,380	$114,520	$115,780
By health state						
Outpatient	$3,127	$3,127	$3,127	$3,127	$3,127	$3,127
Inpatient	$333	$303	$294	$323	$301	$260
Critical	$0	$0	$0	$0	$0	$0
Inpatient After Critical	$41	$41	$41	$41	$41	$41
Dead	–$13,897	–$13,272	–$13,096	–$13,845	–$13,723	–$12,583
Post–COVID-19 Condition	$3,078	$3,031	$3,023	$3,071	$3,057	$2,975
Recovered	$121,640	$121,780	$121,820	$121,660	$121,720	$121,960
Total Costs (D)	$3,360	$3,478	$3,285	$3,368	$3,385	$3,606
By health state						
Outpatient	$0	$325	$190	$63	$212	$734
Inpatient	$2,387	$2,180	$2,121	$2,331	$2,200	$1,898
Critical	$662	$663	$662	$662	$662	$663
Inpatient After Critical	$311	$311	$311	$311	$311	$311
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 $[(A_{Sc} – D_{Sc}) – (A_{Base} – D_{Base})]$	—	$89	$343	$10	$34	$191
$50,000 $[(B_{Sc} – D_{Sc}) – (B_{Base} – D_{Base})]$	—	$228	$521	$22	$73	$482
$100,000 $[(C_{Sc} – D_{Sc}) – (C_{Base} – D_{Base})]$	—	$574	$967	$52	$171	$1,210

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 17: ICERs for Remdesivir Outpatient Treatment Scenarios, Relative to a Common Baseline

Scenarios	Cost (millions)	Incremental cost (millions)	QALYs	Incremental QALYs	ICER
Reference scenario	$3,360	—	1,143,224	—	NA
Scenario 1 (low uptake)	$3,478	$118	1,150,141	6,917	$17,074
Scenario 2 (moderate uptake)	$3,285	–$76	1,152,131	8,907	Dominant
Scenario 3 (LTC low uptake)	$3,368	$7	1,143,813	589	$12,472
Scenario 4 (LTC high uptake)	$3,385	$25	1,145,186	1,962	$12,631
Scenario 5 (high uptake)	$3,606	$246	1,157,777	14,553	$16,885

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

Table 18: Disaggregated Results of the ICERS for Remdesivir Outpatient Treatment Scenarios, Relative to a Common Baseline

Scenarios	Cost (millions)	Incremental cost (millions)	QALYs	Incremental QALYs	ICER
Reference scenario	$3,360	—	1,143,200	—	NA
Outpatient	$0	$0	31,272	0	—
Inpatient	$2,387	$0	3,332	0	—
Critical	$662	$0	0	0	—
Inpatient After Critical	$311	$0	407	0	—
Dead	$0	$0	–138,970	0	—
Post–COVID-19 Condition	$0	$0	30,775	0	—
Recovered	$0	$0	1,216,400	0	—
Scenario 1 (low uptake)	$3,478	$118	1,150,100	6,917	$17,074
Outpatient	$325	$325	31,272	0	—
Inpatient	$2,180	–$207	3,031	–302	—
Critical	$663	$0	0	0	—
Inpatient After Critical	$311	$0	407	0	—
Dead	$0	$0	–132,720	6,255	—
Post–COVID-19 Condition	$0	$0	30,305	–469	—
Recovered	$0	$0	1,217,800	1,432	—
Scenario 2 (moderate uptake)	$3,285	–$76	1,152,100	8,907	Dominant
Outpatient	$190	$190	31,272	0	—

Scenarios	Cost (millions)	Incremental cost (millions)	QALYs	Incremental QALYs	ICER
Inpatient	$2,121	–$266	2,937	−395	—
Critical	$662	$0	0	0	—
Inpatient After Critical	$311	$0	407	0	—
Dead	$0	$0	–130,960	8,009	—
Post–COVID-19 Condition	$0	$0	30,233	–541	—
Recovered	$0	$0	1,218,200	1,834	—
Scenario 3 (LTC low uptake)	$3,368	$7	1,143,800	589	$12,472
Outpatient	$63	$63	31,272	0	—
Inpatient	$2,331	–$56	3,235	−98	—
Critical	$662	$0	0	0	—
Inpatient After Critical	$311	$0	407	0	—
Dead	$0	$0	–138,450	523	—
Post–COVID-19 Condition	$0	$0	30,712	–63	—
Recovered	$0	$0	1,216,600	226	—
Scenario 4 (LTC high uptake)	$3,385	$25	1,145,200	1,962	$12,631
Outpatient	$212	$212	31,272	0	—
Inpatient	$2,200	–$187	3,008	–324	—
Critical	$662	$0	0	0	—
Inpatient After Critical	$311	$0	407	0	—
Dead	$0	$0	–137,230	1,741	—
Post–COVID-19 Condition	$0	$0	30,568	–207	—
Recovered	$0	$0	1,217,200	752	—
Scenario 5 (high uptake)	$3,606	$246	1,157,800	14,553	$16,885
Outpatient	$734	$734	31,271	–1	—
Inpatient	$1,898	–$489	2,600	–732	—
Critical	$663	$0	0	0	—
Inpatient After Critical	$311	$0	407	0	—
Dead	$0	$0	–125,830	13,140	—
Post–COVID-19 Condition	$0	$0	29,752	–1,022	—
Recovered	$0	$0	1,219,600	3,167	—

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

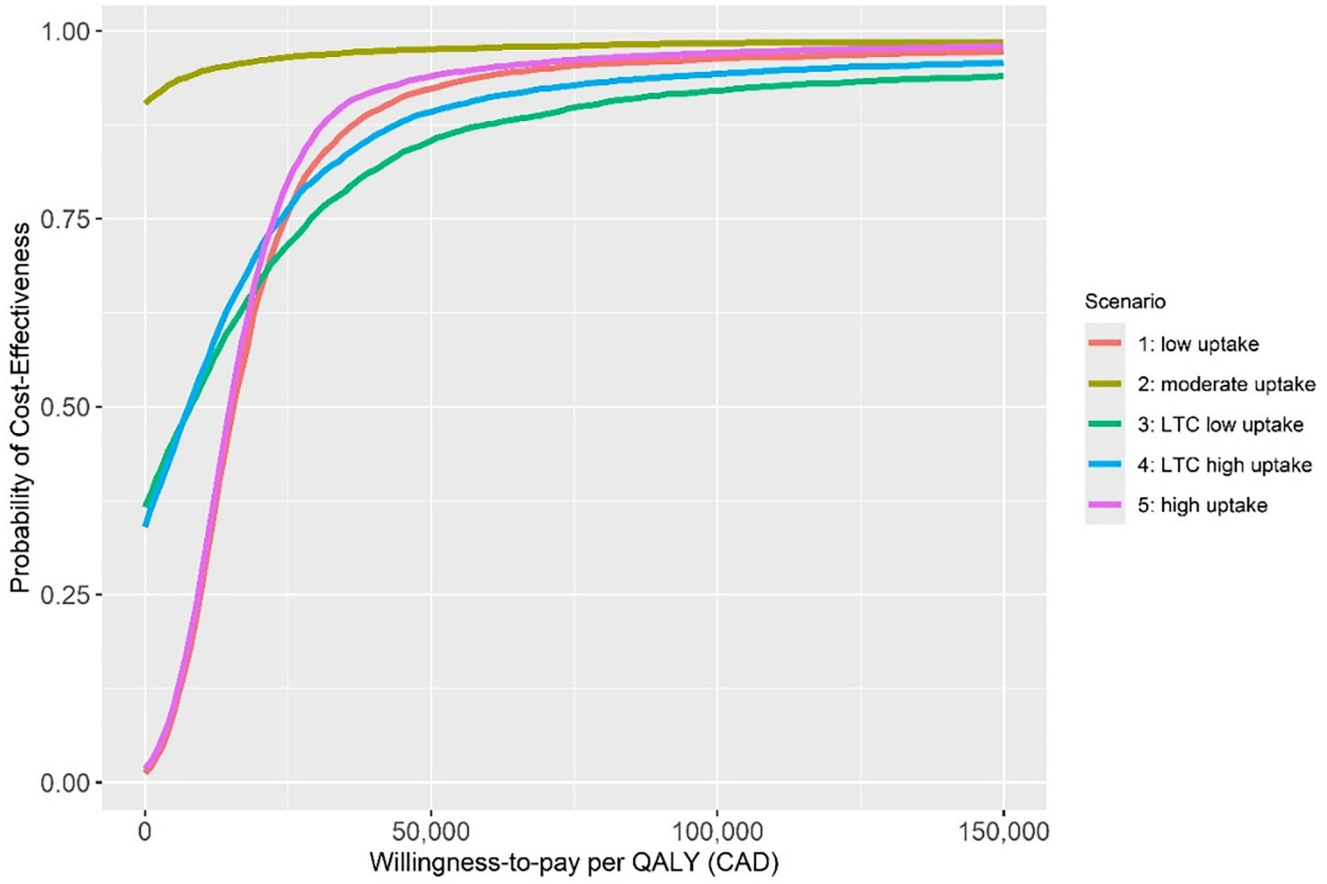
Cost-Effectiveness Acceptability Curves

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 was 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

increases, there is an increase in the number of scenario simulations that have higher expected NMB than the reference scenario due to better QALY outcomes. Although the reference scenario is not shown for each pairwise comparison, graph lines crossing 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 scenario. The moderate uptake scenario (scenario 2) has the highest probability of being cost-effective at conventional estimates of WTP; however, all scenarios have a probability of at least 0.75 of being cost-effective compared to the reference scenario at an approximate WTP threshold greater than $29,000 per QALY.

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; LTC = long-term care; NMB = net monetary benefit; QALY = quality-adjusted life-year; WTP = willingness to pay.

BIA Results

Main Take-Aways

The results of the BIA suggest the majority of uptake scenarios for remdesivir in outpatients would cost the health system. However, scenario 2, which is focused on the high-risk groups, was cost-saving on average. While a proportion of model simulations found that remdesivir for outpatients would be cost-saving (especially when focused on high-risk cohorts), the majority of simulations found it would cost the system money when considering uncertainty. We found that scenarios focused on all cohorts (scenarios 1 and 5) had the highest health system costs and were not considered cost-saving.

The results of the BIA are presented in Table 19. Total costs for the scenarios considered ranged from $3.3 billion to $3.6 billion. Additional outcomes in the BIA included inpatient admissions, critical care admissions, overall number of deaths, and patients developing post–COVID-19 condition. Scenario 2 had the lowest expected cost, and scenario 5 had the highest. The costs for scenario 5 were mainly driven by the cost of the outpatient treatment since it had the highest uptake across all 3 cohorts. When accounting for parameter uncertainty, scenarios 1 and 5 had a positive budget impact compared to the reference scenario.

Results Highlights

- Results of the BIA are presented in Table 19 for the reference scenario and 5 remdesivir outpatient treatment scenarios for all cohorts (those aged < 65 years, those aged ≥ 65 years, and those in LTC) and 2 periods (January 2022 to August 2022 and September 2022 to December 2022).
- Based on the mean estimates, the budget impact of the scenarios ranged from –$75.8 million (95% CrI –$163 million to $121 million) for Scenario 2 (moderate uptake) to $246 million (95% CrI, $14.3 million to $612 million) for scenario 5 (high uptake).
- There were observed reductions in total inpatient admissions, post–COVID-19 condition cases, and deaths across the 5 scenarios. For scenario 5 (high uptake), the mean reduction in these 3 outcomes was the greatest with 20,300 fewer inpatient admissions, 3,920 fewer post–COVID-19 condition cases, and 1,890 fewer deaths.
- Total inpatient costs contributed the most to the overall total cost.
- Mean results for all scenarios, except scenario 2 (moderate uptake), show an increased cost to the health system when compared to the reference scenario. However, for scenario 3 (LTC low uptake) and scenario 4 (LTC high uptake), the average health system costs were the lowest compared to scenarios 1 and 5.
- The BIA showed that the scenarios focused on the high-risk populations had a potential for cost-savings based on parameter uncertainty (95% CrIs) results (without the consideration of utility). However, scenarios 1 and 5 did not have potential to be cost-saving, with the 95% CrIs greater than zero, suggesting that, across the probabilistic sensitivity analysis, these scenarios would cost the health system money.

- The break-even drug cost per treatment was an additional result estimated from the POSA, given the model assumptions used (refer to Table 13) in this analysis. The break-even drug costs per treatment for scenario 2 (moderate uptake), scenario 4 (LTC high uptake), and scenario 5 (high uptake) were $4,752, $2,962, and $2,266, respectively. Costs per treatment less than the break-even estimate would indicate cost-savings for the health care system.
- Because the average budget impact estimate for scenario 2 was cost-saving, its break-even estimate was greater than the treatment cost used in the analysis ($2,335 and $4,166). For scenario 4 and scenario 5, the break-even estimate was within the treatment cost used in the analysis. The key risk groups most impacted by reductions in inpatient admissions from outpatient remdesivir treatment included individuals aged 65 years and older (not in LTC) and individuals in LTC (refer to Table 1), as described in scenario 2.

Table 19: BIA Across 5 Remdesivir Outpatient Treatment Scenarios

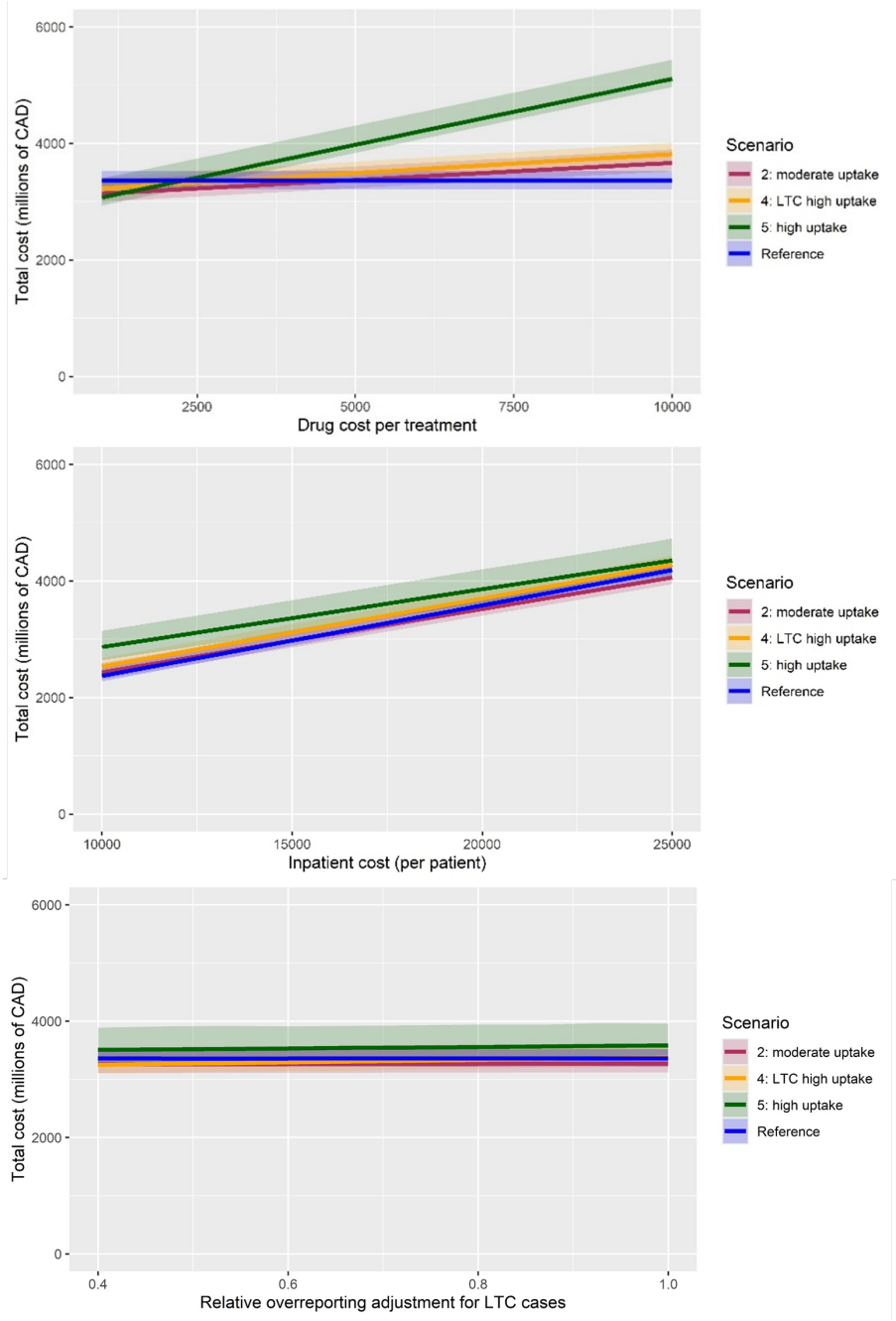
Description	Reference scenario	Scenario 1 (low uptake)	Scenario 2 (moderate uptake)	Scenario 3 (LTC low uptake)	Scenario 4 (LTC high uptake)	Scenario 5 (high uptake)
COVID-19 disposition (95% CrI)						
Total inpatient	120,750 (119,080 to 122,280)	111,420 (109,110 to 116,920)	109,620 (106,980 to 117,670)	119,510 (117,790 to 121,170)	116,640 (114,660 to 119,840)	100,450 (97,100 to 112,340)
Total critical care	19,690 (18,260 to 21,240)	19,700 (18,260 to 21,270)	19,690 (18,250 to 21,280)	19,690 (18,270 to 21,240)	19,690 (18,250 to 21,240)	19,700 (18,230 to 21,260)
Total post–COVID-19 condition	115,680 (107,160 to 124,180)	113,890 (105,400 to 122,440)	113,600 (105,070 to 122,260)	115,430 (106,930 to 123,900)	114,860 (106,370 to 123,400)	111,760 (103,230 to 120,520)
Total deaths	14,920 (14,000 to 15,910)	14,030 (13,130 to 15,060)	13,650 (12,750 to 14,790)	14,840 (13,910 to 15,820)	14,650 (13,710 to 15,640)	13,030 (12,140 to 14,490)
Costs (in millions) (95% CrI)						
Total inpatient	$2,390 ($2,260 to $2,520)	$2,180 ($2,050 to $2,350)	$2,120 ($1,990 to $2,340)	$2,330 ($2,200 to $2,470)	$2,200 ($2,060 to $2,380)	$1,900 ($1,750 to $2,230)
Total critical care	$973 ($878 to $1,080)	$974 ($880 to $1,080)	$973 ($878 to $1,080)	$973 ($878 to $1,080)	$973 ($878 to $1,080)	$974 ($877 to $1,080)
Total inpatient and critical care	$3,360 ($3,210 to $3,520)	$3,150 ($3,000 to $3,340)	$3,090 ($2,940 to $3,320)	$3,300 ($3,160 to $3,460)	$3,170 ($3,020 to $3,360)	$2,870 ($2,710 to $3,210)
Total Remdesivir cost	$0 ($0 to $0)	$384 ($384 to $384)	$225 ($225 to $225)	$75 ($75 to $75)	$250 ($250 to $250)	$868 ($868 to $868)
Total costs	$3,360 ($3,210 to $3,520)	$3,480 ($3,310 to $3,690)	$3,280 ($3,120 to $3,520)	$3,370 ($3,220 to $3,530)	$3,390 ($3,220 to $3,580)	$3,610 ($3,340 to $3,990)
Budget impact: Scenario cost – reference scenario	NA	$118 ($10.9 to $272)	–$75.8 (–$163 to $121)	$7.35 (–$21.8 to $52.1)	$24.8 (–$50.9 to $168)	$246 ($14.3 to $612)

BIA = budget impact analysis; CrI = credible interval; LTC = long-term care; NA = not applicable.

Note: The BIA is estimated based on 1,523,487 total cases (4.9% of the total population excluding Quebec) in 2022.

In Figure 3, a POSA was conducted for the reference scenario, scenario 2 (moderate uptake), scenario 4 (LTC high uptake), and scenario 5 (high uptake) (refer to Table 11 for POSA ranges) for remdesivir cost per treatment course, inpatient cost per patient, and relative overreporting adjustment of LTC cases. Note that the fraction of LTC cases is redistributed to those aged ≥ 65 years.

Figure 3: POSA Results



CAD = Canadian dollars; CrI = credible interval; LTC = long-term care; POSA = probabilistic one-way sensitivity analysis.

For the POSA for remdesivir cost per treatment, the intersection of the reference to other scenario lines describes where the budget impact is zero (i.e., total costs are the same) and the break-even drug cost per treatment course. The break-even drug costs per treatment course for scenario 2, scenario 4, and scenario 5 were $4,752, $2,962, and $2,266, respectively. Costs per treatment less than the break-even costs would indicate cost-savings for the health care system. Although not all scenarios are shown in the POSA, scenario 2 (moderate uptake), scenario 4 (LTC high uptake), and scenario 5 (high uptake) include a range of treatment options impacting each cohort. Figures shown were computed with 1,000 simulations each. Solid lines show mean cost, and shaded ribbons show the 95% CrI.

Summary of Findings

Main Take-Aways

Overall, the CUA and BIA suggest that an outpatient program focused on the high-risk cohorts (those aged ≥ 65 years and those in LTC) may be both cost-effective and cost-saving. In comparison, programs focused on all cohorts, or just those in LTC, while potentially cost-effective at a variety of WTP threshold cut-offs, are less likely to be cost-saving. It is important to note that limitations in the LTC data — specifically, an inability to capture deaths outside of the hospital — may have reduced the cost-effectiveness of remdesivir in this population. There also remains a relatively large amount of uncertainty in these findings with almost all 95% CrIs crossing zero.

It is important to interpret these results bearing in mind that the CUA differs from a typical CUA, in that we did not compare a set of treatment alternatives to identify the cost-effective option. Rather, we projected cost and health outcomes for a range of possible uptake scenarios to understand under what conditions using remdesivir in a community setting would be cost-effective. The CUA and BIA analysis included 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 outpatient remdesivir may be cost-effective, although this is dependent on model uncertainty and the maximum WTP per QALY. When we accounted fully for parameter uncertainty through probabilistic sensitivity analysis, at a WTP threshold of at least $50,000 per QALY, all scenarios would have the potential to be cost-effective compared to the reference scenario, while scenario 2 (moderate uptake) had more certainty because iNMB estimates do not have 95% CrIs that cross zero. Moreover, we found scenario 2 was dominant relative to the reference scenario (it was more effective and less costly than the reference scenario) (refer to Table 17) and the average BIA results also described cost-savings to the health system (refer to Table 19). Scenarios 3 (LTC low uptake) and 4 (LTC high uptake) that focused only on LTC have the lowest positive ICER estimates and lowest iNMB. The average BIA results for these 2 scenarios show they had the smallest increase in health system costs compared to the reference scenario (scenario 3 = $7.35 million and scenario 4 = $24.8 million). When interpreting the results for the LTC scenarios, it is important to remember that the model did not capture deaths within LTC facilities, and

therefore the potential benefits of outpatient remdesivir treatment may not be fully captured in this cost-effectiveness analysis.

Results of the BIA indicate that increased use of remdesivir may lead to increased health system costs, but it also showed reductions in inpatient admissions, post–COVID-19 condition cases, and deaths. However, while the average results show that all scenarios except scenario 2 would increase health system costs relative to the reference scenario, there is parameter uncertainty in the model where 95% CrIs of health system costs cross zero.

Overall, the CUA and the BIA suggest that if the future state were to resemble scenario 2 (moderate uptake: remdesivir treatment of lab-confirmed cases in 15% of those aged ≥ 65 years [not in LTC] and 20% of those in LTC), it is most likely to be cost-effective and will reduce inpatient admissions, post–COVID-19 condition cases, and deaths.

Limitations

Model assumptions and limitations are described in Table 13. Some of the key limitations included:

- Data on the price paid in Canada for outpatient remdesivir treatment were not available, so the treatment costs were estimated based on publicly available sources.
- The therapeutic effects for outpatient remdesivir were based on literature before the emergence of the Omicron variant (refer to Table 21).[11] However, a study conducted in 2022 (refer to Table 21) among those at high risk for hospitalization reported a therapeutic estimate for progression to hospitalization within the range described by Gottlieb et al.[11] Additional studies are needed to verify that the therapeutic effects used in this analysis remain the same considering the new variants in circulation. If remdesivir is less effective against new variants, this would reduce its overall cost-effectiveness.
- The mortality impact in LTC is likely underestimated due to data and model limitations, which only capture deaths in health care facilities and not deaths in LTC facilities. This would reduce the cost-effectiveness of the outpatient use of remdesivir in this population.
- The scenarios described in this analysis would also depend on an anticipated voluntary uptake if the treatment is publicly available. This was not captured as the model incorporated only cases confirmed through laboratory testing in 2022; this may overestimate the cost-effectiveness and break-even costs of remdesivir as an outpatient treatment option. In essence, the more people treated with the drug as a result of greater access, the higher the likelihood that the increased costs of treatment would outweigh the benefits of treatment.
- When calculating the treatment effect on hospitalization rates, it was assumed that all reported cases appeared first in the Outpatient state before admission to the hospital and that all cases could therefore have been treated with remdesivir in the outpatient setting. However, individuals may have been detected as a case on admission, and therefore there would be no opportunity to provide

them remdesivir in the outpatient setting. The distribution of where cases were detected (i.e., within the community or on admission) is unknown. Due to this data limitation, the scenarios assume all reported cases are in the Outpatient state and would likely overestimate the impact of remdesivir as an outpatient treatment option if broadly available.

- Utilities for patients admitted to hospital are likely overestimated in the CUA due to limited data related to in-hospital estimates. This would lead to an underestimation of the cost-effectiveness of scenarios presented in the CUA. Research is ongoing to estimate the quality of life in patients with COVID-19 in different settings, and this may provide more robust utility estimates for future evaluations.
- For provinces and territories that have different cohort criteria for accessing outpatient remdesivir treatment beyond our model structures and scenarios, if case severity rates are similar to those observed in other high-risk cohorts, then differences and/or trends in the BIA should be generally consistent with the results in the report.

Conclusions and Implications for Decision- or Policy-Making

This report evaluated the costs and benefits associated with outpatient use of remdesivir at various potential uptake levels across 3 cohorts (those aged < 65 years, those aged ≥ 65 years, and those in LTC). Overall, we found that outpatient use of remdesivir may be cost-effective across a range of uptakes and cohorts. However, the scenario with the best mean iNMB and budget impact, was the scenario focused on high-risk cohorts (those aged ≥ 65 years and those in LTC) with moderate uptake. Key parameters that may impact these results include the therapeutic effects estimates of remdesivir on hospitalization admission and how this may change with new variants, remdesivir costs, inpatient costs, and lifetime QALY loss associated with mortality from COVID-19.

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 this time, this may impact the cost-effectiveness of remdesivir. Moreover, the effect estimate of remdesivir were based on studies conducted before the Omicron variant, and therefore we assumed the effects would be similar as COVID-19 infections following the emergence of the Omicron variant. Finally, the QALY gains associated with outpatient remdesivir in scenarios focused on LTC may have been reduced based on the lack of death data outside of hospital.

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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, interpretating results, and writing of the report.

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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

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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-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 present): Related to modelling infectious diseases, including COVID-19

Jeff Round disclosed the following.

Research Funding or Grants Paid 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/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): Auto-Injector Device for Trauma Patients

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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 20: Stochastic State-Transition Model Related Parameters as Examples (Among COVID-19 Cases) From CIHI Data With Key Data Transformations

Symbol	Transformation	Quantity	Source	Estimate: age < 65 years	Estimate: age ≥ 65 years	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 care (days)	CIHI	9	9	9
$\vec{T}_{i}$	$\vec{T}_{ah\_c} - \vec{T}_{c}$	LOS for inpatient after critical care (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 care 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 care	CIHI	29	27	71
$\vec{T}_{c}$	NA	LOS critical care (days)	CIHI	9	8	8
$\vec{T}_{i}$	$\vec{T}_{ah\_c} - \vec{T}_{c}$	LOS for inpatient after critical care(days)	CIHI	19	19	63

Symbol	Transformation	Quantity	Source	Estimate: age < 65 years	Estimate: age ≥ 65 years	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 care 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 care cost per day	CIHI	$3,668	$3,366	$4,107

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

Table 21: Overview of Studies Used for Remdesivir Outpatient Effect Estimates (Relative Risk and/or Hazard Ratio)

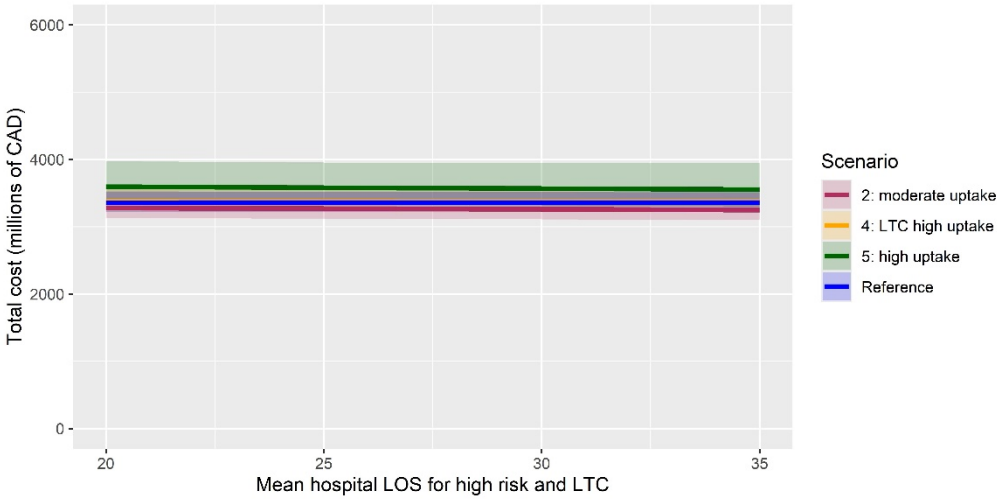
Characteristics or therapeutic effect (point estimates of relative risk)	Mazzitelli et al.[32]	Gottlieb et al. [11]
Study period	February 2022 to May 2022	September 2020 to April 2021
Cohort	Those eligible for remdesivir treatment: 65 years and older, mild or moderate symptoms < 7 days, body mass index ≥ 30, chronic kidney disease (estimated glomerular filtration rate > 30 mL/min), cardiovascular disease, immune suppression, cancer, and other	12 years and older: Had at least 1 prior risk factor for progression to severe COVID-19 or 60 years and older. Risk factors included: hypertension, cardiovascular or cerebrovascular diseases, diabetes, obesity (body max index ≥ 30), immune compromise, chronic mild or moderate kidney disease, chronic liver disease, chronic lung disease, current cancer, or sick cell disease
Location	Italy	US
Progression to hospitalization (all ages)	0.062[a]	NA
COVID-19 related hospitalization or death[b] (all ages)	NA	0.13 (95% CI, 0.03 to 0.59)
COVID-19 related hospitalization or death (60 years and older)	NA	0.11 (95% CI, 0.01 to 0.86)

CI = confidence interval; NA = not applicable.

[a]Estimated from study results.

[b]No deaths by 28 days reported within the study as part of this outcome.

Figure 4: POSA Showing Total Cost (in Millions) Versus Hospital LOS for Patients Treated with Remdesivir Deemed High-Risk and in LTC



CAD = Canadian dollars; CrI = credible interval; LOS = length of stay; LTC = long-term care; POSA = probabilistic one-way sensitivity analysis.

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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.