ORIGINAL RESEARCH ARTICLE

Updated Public Health Impact and Cost Effectiveness of Recombinant Zoster Vaccine in Canadian Adults Aged 50 Years and Older

Sydney George[1] · Justin Carrico[2] · Katherine A. Hicks[2] · Dessi Loukov[1] · Cheryl Ng[3] · Jessica Regan[1] · Nikolaos Giannelos[4]

Abstract

Objectives The aim of this study was to update previously estimated public health impact and cost effectiveness of recombinant zoster vaccine (RZV) for the prevention of herpes zoster (HZ) in Canadians aged ≥50 years using longer-term RZV efficacy and waning data and real-world coverage and completion.

Methods A multicohort Markov model was used to conduct a cost-utility analysis comparing RZV with no HZ vaccination among Canadians aged ≥50 years. Real-world data were used for first-dose coverage (17.5%) and second-dose completion (65%). Vaccine efficacy and waning data were applied from up to 8-year follow-up from the ZOE-50 and ZOE-70 clinical trials. Incremental costs and benefits were calculated using a lifetime horizon from the healthcare payer (base case) and societal perspectives. A discount rate of 1.5% was applied to costs and quality-adjusted life-years (QALYs).

Results The model estimated that RZV would prevent 303,835 HZ cases, 83,256 post-herpetic neuralgia (PHN) cases, 39,653 other complications, and 99 HZ-related deaths compared with no HZ vaccination. Incremental cost-effectiveness ratios (ICERs) were estimated to be $27,486 and $22,097 per QALY (2022 Canadian dollars [CAN$]) from the healthcare payer and societal perspectives, respectively. The base-case ICER was most sensitive to a lower percentage of initial HZ cases with PHN. Almost all probabilistic sensitivity analysis simulations (98.1%) resulted in ICERs <CAN$50,000 per QALY.

Conclusions RZV is expected to remain a cost-effective option for Canadian adults aged ≥50 years when using longer-term RZV efficacy and waning estimates, although the estimated public health impact was smaller than in the previous analysis (due to lower coverage/completion estimates).

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Graphical Abstract

PharmacoEconomics Open

PEER-REVIEWED FEATURE

Updated Public Health Impact and Cost-Effectiveness of Recombinant Zoster Vaccine in Canadian Adults Aged 50 Years and Older

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Background

1/3 of Canadians will develop herpes zoster (HZ) in their lifetime

RISK ↑ Age / IC status

Age-related decline in immunity and immuno-compromised status (IC) increase the risk of HZ

20% of HZ patients develop post-herpetic neuralgia (PHN), a long-term pain complication

Methods

The **ZONA model** was used to estimate the impact of recombinant zoster **vaccine (RZV) vs no HZ vaccination** for Canadians aged ≥50 y
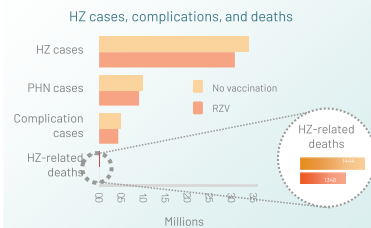A previous model (2017) used vaccine coverage assumptions, but the current (2022) model used real-world evidence (RWE) after 5 years of RZV availability

KEY UPDATES

1. **LONGER-TERM RZV efficacy and waning data** (based on data up to 8 years) against HZ and its complications

2. RWE of lower 1st dose **VACCINATION COVERAGE**

   2017 — **80%** Assumed Vaccination coverage
   2022 — **17.5%** RWE-based Vaccination coverage

3. RWE of lower 2nd dose **COMPLIANCE** (75% in 2017 vs 65% in 2022)
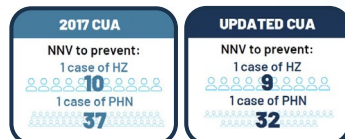
4. Updated **COSTS** and **DEMOGRAPHICS**

Public Health Impact (PHI) Analysis

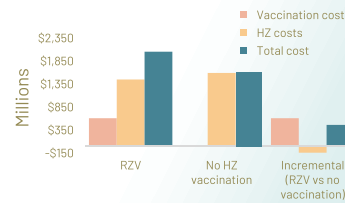Assuming 17.5% coverage, RZV is predicted to **PREVENT** **303,835 HZ** cases and **99 HZ-related deaths**

HZ cases, complications, and deaths

- HZ cases
- PHN cases
- Complication cases
- HZ-related deaths

No vaccination / RZV

HZ-related deaths

Millions

Numbers Needed to Vaccinate (NNV)

Improved waning rates explain smaller NNV in the updated model

2017 CUA
NNV to prevent:
1 case of HZ — **10**
1 case of PHN — **37**

UPDATED CUA
NNV to prevent:
1 case of HZ — **9**
1 case of PHN — **32**

Cost-Effectiveness Analysis

DIRECT COSTS FOR CANADIAN ADULTS AGED ≥50 Y WITH RZV VS NO HZ VACCINATION (PAYER PERSPECTIVE)

- Vaccination costs
- HZ costs
- Total cost

Millions
$2,350
$1,850
$1,350
$850
$350
–$150

RZV / No HZ vaccination / Incremental (RZV vs no vaccination)

Although VACCINATION could cost $ 606 million, $ 144 million DIRECT COSTS could be SAVED with substantial INCREASES IN quality of life and DECREASES in PRODUCTIVITY LOSS due to avoided HZ cases

INCREMENTAL COST-EFFECTIVENESS RATIOS (ICERs)

CAD/QALY*
$30,000
$20,000
$10,000
$0

$27,486 / $22,097 / $30,402

- Payer perspective
- Societal perspective
- 2017 (payer)

*Canadian dollars per quality-adjusted life year

Nearly all probabilistic sensitivity analysis simulations (98.1%) showed ICERs <$50,000/QALY

The base-case ICER was most sensitive to a lower % of initial HZ cases with PHN

Conclusions

These results indicate an opportunity to increase the PHI of RZV (relative to 2017) if coverage can be improved. This is a result of the improved waning of RZV efficacy and the aging of the Canadian population

RECOMBINANT ZOSTER VACCINATION is predicted to remain a COST-EFFECTIVE OPTION for preventing HZ among Canadian adults aged ≥50 years

△ Adis

Key Points for Decision Makers

A 2017 analysis predicted that recombinant zoster vaccine (RZV) would be cost effective for the prevention of herpes zoster (HZ) among adults aged ≥50 years in Canada. However, longer-term vaccine efficacy and waning data were not available and first-dose coverage and second-dose compliance had to be assumed since RZV was not available on the Canadian market.

The current analysis used longer-term RZV efficacy and waning data (based on up to 8 years of follow-up) and real-world Canadian first-dose coverage and second-dose compliance.

In the current study, RZV was predicted to be slightly more cost effective than in the 2017 study. However, coverage and compliance rates would need to be improved to obtain a similar predicted public health impact as the 2017 study.

1 Introduction

Most Canadian adults will have been infected with varicella-zoster virus (VZV) during childhood, leaving them at risk for developing herpes zoster (HZ) later in life, following reactivation of VZV due to a decline in immune system function from older age or compromised immune systems due to disease or immunosuppressive therapy [1]. The incidence of HZ increases with age, from approximately 5 per 1000 people aged 50–54 years to around 11 per 1000 people aged ≥85 years [2]. The incidence of HZ also increases among immunocompromised patients, e.g. 12 per 1000 people with cancer or rheumatoid arthritis and 43 per 1000 people who have undergone bone marrow or stem cell transplantation [3]. The overall lifetime risk of HZ in Canada is nearly one in three [4]. As the incidence of HZ appears to be increasing over time due to an aging Canadian population, the burden of HZ is likely to increase [5].

HZ is characterized by a painful dermatomal rash lasting up to 4 weeks [1]. Approximately 20% of patients with HZ go on to develop post-herpetic neuralgia (PHN) [6], defined as pain that lasts for >3 months after the HZ rash has healed [1] but that can last for considerably longer. Around 10–20% of patients with HZ will develop HZ ophthalmicus [7], which can result in vision loss without prompt treatment [8]. HZ and its complications can therefore have a profound effect on the quality of life of affected patients [9, 10].

Canada's National Advisory Committee on Immunization (NACI) first recommended vaccination with zoster vaccine live (ZVL) in 2010 for the prevention of HZ and its complications in people aged ≥60 years without contraindications [11]. NACI's recommendations were updated in 2018: recombinant zoster vaccine (RZV; *Shingrix*, GSK) should be offered to people aged ≥50 years without contraindications, while ZVL may be considered for immunocompetent people aged ≥50 years without contraindications when RZV is contraindicated or not available/accessible [12]; however, ZVL has since been discontinued in Canada (in 2022) [13].

RZV for Canadian adults aged ≥60 years was estimated by McGirr et al. [14] to be a cost-effective intervention versus no HZ vaccination, with an incremental cost-effectiveness ratio (ICER) of 28,360 Canadian dollars (CAN$) per quality-adjusted life-year (QALY) gained, and for adults aged ≥50 years with an ICER of CAN$30,402 per QALY gained (2016). However, at the time of the McGirr et al. study, RZV efficacy data were only available up to 4 years post-vaccination and assumptions for first-dose RZV coverage and second-dose completion rates were required as RZV was not yet available in Canada. The publication of an interim analysis [15] of follow-up for up to 8 years since initial vaccination from Zoster Efficacy Study in Adults 50 Years of Age or Older (ZOE-50) and Zoster Efficacy Study in Adults 70 Years of Age or Older (ZOE-70) RZV pivotal clinical trial populations [16, 17] has provided longer-term vaccine efficacy (VE) and waning data. Moreover, the publication of real-world evidence for several data inputs for RZV has prompted an updated analysis. In order to ensure that cost-effectiveness models are relevant for policy decision making, it is important that they are updated with new inputs when these become available. The primary objective of the analysis was therefore to apply the new VE and waning data and other updated data inputs that have become available since the McGirr et al. [14] study in the ZOster ecoNomic Analysis (ZONA) 50+ model to update the cost effectiveness and public health impact estimates for Canada.

2 Methods

2.1 Model Overview

The structure of the ZONA model (Online Resource Fig. 1) has already been described [14, 18–26] and the ZONA model used by McGirr et al. underwent external, technical validation [14]. The ZONA model is a static multicohort Markov model developed in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) and considers five age cohorts (50−59, 60−64, 65−69, 70−79, and ≥80 years).

The analysis was conducted over the remaining lifetimes of the cohorts from the year of vaccination, with annual cycles. States in the model were no HZ, HZ, PHN, other complications, recovery, recurrent HZ, death from HZ, and death from other causes. Two strategies were considered: vaccination with two doses of RZV, or no HZ vaccination. Comparisons with ZVL were not conducted because ZVL has been discontinued in Canada [13].

2.2 Input Parameters

Updated population estimates from 2021 [27] and annual all-cause mortality rates from 2020 [28] from Statistics Canada were used (Online Resource Table 1). Inputs from McGirr et al. [14] were used for the annual probability of HZ [29]; the risk of developing PHN [30] and ocular, neurological, cutaneous, and other non-pain complications [6]; and the case fatality rates for HZ [31] as no new data were identified.

First-dose RZV coverage was updated from the 80% assumed by McGirr et al. [14] (which was based on influenza vaccine uptake rates) to 17.5%, based on first-dose real-world coverage data up to 2022 [32] (Table 1). Second-dose completion was updated from an assumed 75% [14] to 65%, based on a Canadian retrospective database study [33]. McGirr et al. [14] used VE and waning data for two doses of RZV from two randomized controlled trials (ZOE-50 and ZOE-70) with mean follow-up durations of 3.2 and 3.7 years, respectively [16, 17]. VE and waning rates in the current analysis were updated with longer-term follow-up data from these two studies, for up to 8 years since initial vaccination (Table 1). VE and waning rates for one dose of

RZV [18] were not changed from the McGirr et al. analysis [14].

The costing methods for HZ cases with and without PHN were consistent with those used by McGirr et al. [14], but used the most recent available data for resource utilization and unit costs for general practitioner (GP) visits, hospitalizations, and prescription drugs [34–37], which resulted in slightly lower costs (Online Resource Table 2). The price per dose of RZV was updated to CAN$130.14, which reflects the IMS Canada Price List on 18 April 2022. Vaccine administration costs were assumed to be CAN$4.95 for the first dose of RZV and CAN$10.55 for the second dose (including a CAN$5.60 premium for an immunization-only visit) [36]. RZV adverse event (AE) costs were estimated based on the proportions of patients in the ZOE studies [16, 17] who required a GP visit, emergency room (ER) visit, or hospitalization (as per McGirr et al. [14]) and the latest unit costs [35, 36], which were inflated to 2022 CAN$ when necessary [38, 39].

Utility values at baseline (i.e. without HZ) were updated from the McGirr et al. analysis [14] using data obtained from Szende et al. [40], who reported EuroQol 5 Dimensions (EQ-5D) index values for Canada, which were weighted for each age group based on Statistics Canada 2021 population estimates [27] (Online Resource Table 3). QALY losses per HZ-only case and per HZ with PHN case were updated using input data from a modeling study by Drolet et al. [41], who estimated QALY losses using data from a Canadian study of patients aged ≥50 years with HZ or PHN. QALY losses for RZV AEs [42] were not updated as no new data were identified since the analysis by McGirr et al. [14].

2.3 Base-Case Analysis

The base-case analysis used the updated values presented in Table 1 and Online Resource Tables 1–4 and an annual discount rate of 1.5% for costs and QALYs, in line with recent guidelines from Canada's Drug and Heath Technology Agency (CADTH) [43]. To incorporate potential uncertainty and assess the sensitivity of results to changes in the discount rate, additional analyses using rates of 0% and 3% were conducted.

2.4 One-Way and Probabilistic Sensitivity Analyses

One-way sensitivity analysis, where inputs were varied one at a time across defined ranges, was conducted to examine the sensitivity of the ICER to the value of each input. The first-dose coverage was varied by ±20% of the base-case value. The range for second-dose completion was 55–75%, with the upper bound consistent with the percentage of adults who received a second vaccine dose in the '12-month cohort' of McGirr et al. [33]. The ranges for the

Table 1 Vaccine coverage, completion, and VE-related inputs

	Base-case value (range)	
	50–69 years	≥70 years
First-dose coverage[a], % [32]	17.5 (14–21)	
Second-dose completion[b], % [33]	65 (55–75)	
VE (two doses)[c], % [15, 24]	98.9 (94.0–100)	95.4 (89.7–100)
Annual waning (two doses),[c] % [15, 24]	1.5 (0.0–3.4)	2.3 (0.3–4.4)

RZV recombinant zoster vaccine, *VE* vaccine efficacy, *ZOE-50* Zoster Efficacy Study in Adults 50 Years of Age or Older, *ZOE-70* Zoster Efficacy Study in Adults 70 Years of Age or Older

[a]Updated based on IQVIA data [32]. Range is ±20% of the base-case value

[b]Updated based on a retrospective database study [33]. Base-case value is the percentage of adults who received a second RZV dose within 2–6 months of a first dose; upper bound is the percentage who received a second RZV dose within 2–12 months. Lower bound was assumed

[c]Updated based on values and ranges estimated in the study by Curran et al. [24] based on longer-term ZOE-50 and ZOE-70 data from the study by Boutry et al. [15]

baseline utility values obtained from Szende et al. [40] were assumed to be ±20% of the base-case values. The ranges for QALY losses were equal to the limits published in Drolet et al. [41]. The vaccine price was not varied in sensitivity analyses because vaccine prices are fixed in Canada. Further details on the ranges for the one-way sensitivity analysis are presented in Table 1 and Online Resource Tables 2 and 3.

A probabilistic sensitivity analysis (PSA) was conducted to examine the impact of uncertainty about the values of model inputs on the ICER estimate. For each PSA, ICERs were estimated from 5000 Monte Carlo simulations in which input values were simultaneously sampled from appropriate probability distributions. Costs and vaccine coverage rates were varied using gamma and uniform distributions, respectively. All other inputs were varied using beta distributions. The base-case values and standard errors (SEs) were used to estimate beta and gamma distribution parameters, while ranges were used to define upper and lower bound values for the uniform distributions. All inputs with SEs and/or ranges (as detailed in Table 1 and Online Resource Tables 2 and 3) were varied in the PSA. Age-dependent parameters that varied across age groups were assumed to be correlated.

Inputs that were not updated were varied in the one-way sensitivity analysis and the PSA as per the study by McGirr et al. [14].

2.5 Scenario Analyses

First-dose coverage values of 40%, 60%, and 80% were tested in three scenario analyses. A fourth scenario analysis estimated the cost effectiveness of RZV versus no HZ vaccination from the societal perspective. Indirect costs of HZ were estimated from absenteeism and presenteeism losses for HZ cases from Drolet et al. [44]. These were multiplied by age-specific employment rates as of February 2022 [45] and total compensation per hour worked in 2020 [46] inflated to 2022 CAN$ using the consumer price index for all items [38, 39] (Online Resource Table 4). Indirect costs for vaccination administration were estimated similarly, based on an assumed 1 h lost. Indirect costs for AEs were based on AE incidences in the ZOE-50 and ZOE-70 studies [16, 17], employment rates and compensation as above, and 4, 12, and 40 h of lost productivity for an AE resulting in a GP visit, ER visit, or hospitalization, respectively. Hours of lost productivity for vaccine administration and AEs were based on the opinion of clinical experts.

2.6 Outcomes

Health and economic outcomes included cases of HZ, PHN, and other complications (ocular, neurological, cutaneous, and other non-pain) avoided; HZ-related deaths avoided; life-years and QALYs gained; direct costs (vaccination, HZ costs, and total); and ICERs. For most analyses, these were from the perspective of the publicly funded healthcare system, and the willingness-to-pay threshold was assumed to be CAN$50,000 per QALY gained, as is commonly used in Canada [47]. All costs are in 2022 CAN$.

3 Results

3.1 Base-Case

In the base case, the model estimated that RZV at a first-dose coverage of 17.5% versus no HZ vaccination would prevent 303,835 cases of HZ, 83,256 cases of PHN, 39,653 complications, and 99 HZ-related deaths, and save 751 life-years and 16,814 QALYs (Table 2). Vaccination costs were estimated to be approximately CAN$606 million, with a direct cost saving of around CAN$144 million, for a total incremental direct cost of CAN$462 million. These outcomes equate to an ICER of CAN$27,486 per QALY gained. Discount rates of 0% and 3% resulted in ICERs of CAN$21,519 and CAN$33,816 per QALY gained, respectively. The number needed to vaccinate (NNV) to prevent one HZ case was 9 and the NNV to prevent one PHN case was 32.

3.2 One-Way and Probabilistic Sensitivity Analyses

In the one-way sensitivity analysis, the ICER was most sensitive to the percentage of initial HZ cases with PHN, the QALY loss per unvaccinated HZ case with PHN, the annual waning of RZV second-dose VE against HZ, and the annual incidence of initial HZ (Fig. 1). The highest ICER was observed when the percentage of initial HZ cases with PHN was at its lower bound (CAN$44,724 per QALY gained).

Stochastic results from 5000 Monte Carlo simulations estimated total median incremental direct healthcare costs of CAN$456 million and an incremental gain of 16,800 QALYs for RZV versus no HZ vaccination (Fig. 2). The runs had a median ICER of CAN$27,174 per QALY gained. Almost all simulations (98.1%) resulted in ICERs below the assumed willingness-to-pay threshold of CAN$50,000 per QALY gained (Fig. 3).

3.3 Scenario Analyses

As first-dose RZV coverage was increased to 40%, 60%, and 80%, the estimated numbers of HZ cases prevented also increased, to 694,481, 1,041,721, and 1,388,962, respectively (Table 3). The estimated numbers of PHN cases, other complications, and HZ-related deaths prevented at various first-dose coverage rates increased similarly (Table 3), as did

Table 2 Results for Canadian adults aged ≥50 years vaccinated with RZV vs. no HZ vaccination from a payer's perspective

	RZV	No HZ vaccination	Incremental (RZV vs. no vaccination)
Health outcomes			
HZ cases	3,077,137	3,380,973	−303,835
PHN cases	906,339	989,595	−83,256
Complication cases	435,531	475,183	−39,653
Ocular	159,807	174,218	−14,411
Neurological	143,606	156,987	−13,381
Cutaneous	64,944	70,726	−5782
Other non-pain	67,174	73,252	−6078
HZ-related deaths	1346	1444	−99
Life-years/QALYs			
Life-years	289,210,749	289,209,999	751
QALYs (discounted)	264,086,045	264,069,232	16,814
Direct costs, CAN$[a]			
Vaccination	605,803,049	0	605,803,049
HZ costs	1,446,473,430	1,590,141,671	−143,668,241
Total	2,052,276,479	1,590,141,671	462,134,808
ICERs, CAN$[a]/QALY			
1.5% discount rate (base case)	–	–	27,486
0% discount rate	–	–	21,519
3% discount rate	–	–	33,816

CAN$ Canadian dollars, *HZ* herpes zoster, *ICERs* incremental cost-effectiveness ratios, *PHN* post-herpetic neuralgia, *QALY* quality-adjusted life-year, *RZV* recombinant zoster vaccine

[a]Costs are in 2022 CAN$

life-years and QALYs gained, vaccination costs, HZ costs averted, and total direct costs. However, as increasing coverage increased vaccination costs and HZ cases averted to the same extent, the ICER remained the same in all scenarios.

From a societal perspective (but otherwise, as per the base case), overall vaccination costs were estimated to increase to approximately CAN$695 million, but there were estimated savings of around CAN$179 million in indirect cost savings of HZ cases prevented (Table 4). These outcomes equate to an ICER of CAN$22,097 per QALY gained, which is more favorable than in the base-case analysis from the healthcare system perspective (CAN$27,486). Discount rates of 0% and 3% resulted in ICERs of CAN$16,061 and CAN$28,594 per QALY gained, respectively.

4 Discussion

This study provides updated results compared with a previous cost-effectiveness analysis for RZV in Canada by McGirr et al. [14], which are shown side-by-side in Online Resource Table 5. When compared with no HZ vaccination, the current analysis estimated that vaccination of adults aged ≥50 years with RZV at recent coverage (17.5%) and completion (65%) rates for an age-appropriate population

approaching 15 million would prevent 303,835 cases of HZ, 83,256 cases of PHN, and 99 deaths, and save 16,814 QALYs. Although the direct vaccination costs would be approximately CAN$606 million, the prevention of HZ cases would save approximately CAN$144 million in direct medical costs due to HZ, resulting in an incremental direct cost of CAN$462 million and an ICER of CAN$27,486 per QALY saved. When societal costs relating to indirect costs of HZ were estimated from absenteeism and presenteeism losses, the ICER was reduced to CAN$22,097.

The most notable data input changes for this analysis were values for first-dose RZV coverage, RZV VE waning, QALY losses per case of HZ alone and HZ with PHN, and RZV AE costs (see Online Resource Table 6 for a side-by-side comparison of all updated input parameters). We also updated the age of the vaccinated population in the base case from ≥60 to ≥50 years because at the time of the analysis by McGirr et al. [14], HZ vaccination (with ZVL) was only recommended for people aged ≥60 years in Canada [11, 48], but this was updated by NACI in 2018 to recommended vaccination (with RZV) for Canadians aged ≥50 years [12].

In the analysis by McGirr et al. [14], 80% first-dose RZV coverage was assumed, along with 75% second-dose completion. Assumptions were used because RZV had not yet been introduced in the Canadian market and were assumed
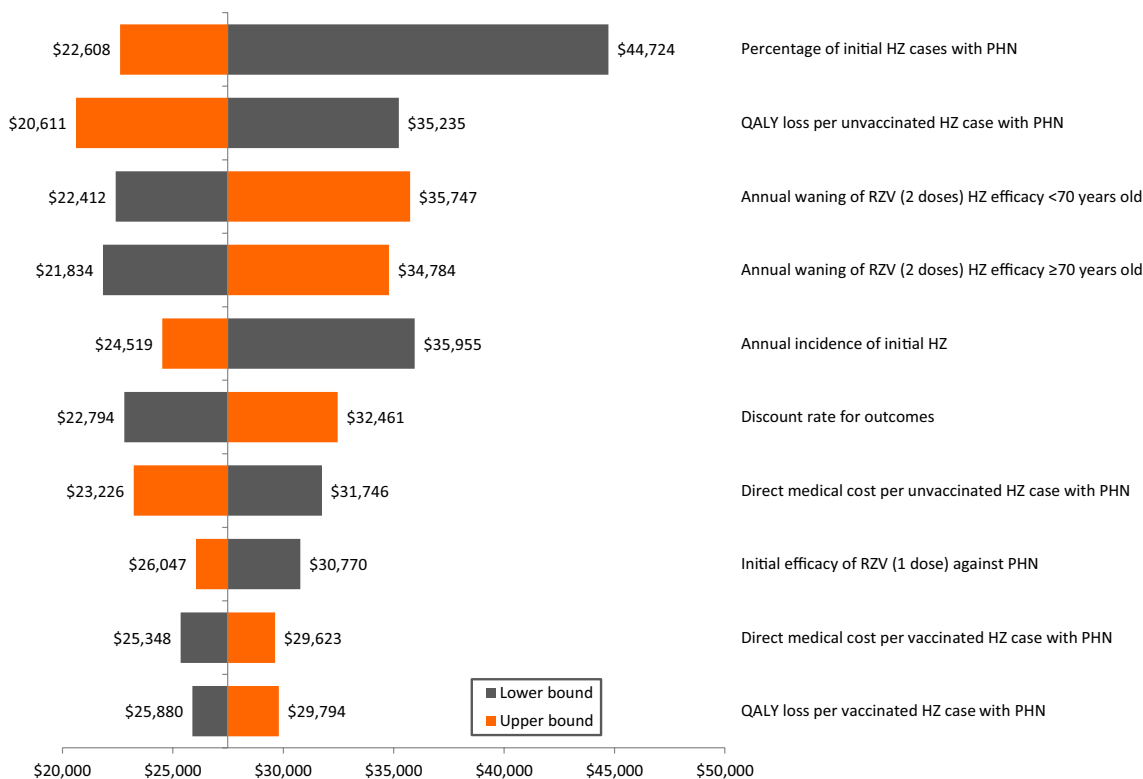
Fig. 1 One-way sensitivity analysis results[a] for the ICERs of RZV vs. no HZ vaccination for Canadian adults aged ≥50 years from a payer's perspective (base-case ICER: CAN$27,486). [a]Costs are in 2022 CAN$. The 10 most influential inputs are shown. *CAN$* Cana-dian dollars, *HZ* herpes zoster, *ICERs* incremental cost-effectiveness ratios, *PHN* post-herpetic neuralgia, *QALY* quality-adjusted life-year, *RZV* recombinant zoster vaccine

Fig. 2 Incremental costs[a] vs. incremental QALYs from 5000 PSA simulations of RZV vs. no HZ vaccination for Canadian adults aged ≥50 years from a payer's perspective. [a]Costs are in 2022 CAN$. *CAN$* Canadian dollars, *HZ* herpes zoster, *PSA* probabilistic sensitivity analysis, *QALYs* quality-adjusted life-years, *RZV* recombinant zoster vaccine
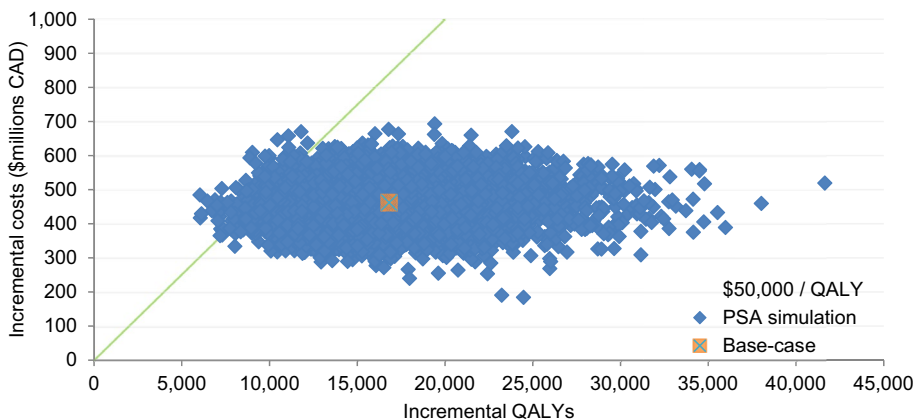
to be higher than influenza vaccine coverage rates. The updated analysis used real-world data for the Canadian population and applied 17.5% first-dose RZV coverage (up to 2022) [32], and, among first-dose recipients, 65% second-dose completion within the 2- to 6-month recommended time period [33]. The lower first-dose coverage resulted in lower estimated reductions in HZ in comparison with results in a ≥50-year-old population in the 2017

analysis (303,835 vs. 1,024,771 [14]) and PHN (83,256 vs. 264,605 [14]). Scenario analyses demonstrated that reductions in HZ (1,388,962) and PHN (380,598) cases were estimated to be greater in the current analysis than in the analysis by McGirr et al. [14] when first-dose RZV coverage was assumed to be the same as in the analysis by McGirr et al. (80%). This opportunity for an increased public health impact for RZV relative to the estimates by McGirr et al.

Fig. 3 Cost-effectiveness acceptability curve from PSA for RZV vs. no HZ vaccination for Canadian adults aged ≥50 years[a] from a payer's perspective. [a]Costs are in 2022 CAN$. *CAN$* Canadian dollars, *HZ* herpes zoster, *ICER* incremental cost-effectiveness ratio, *PSA* probabilistic sensitivity analysis, *QALY* quality-adjusted life-year, *RZV* recombinant zoster vaccine, *WTP* willingness-to-pay
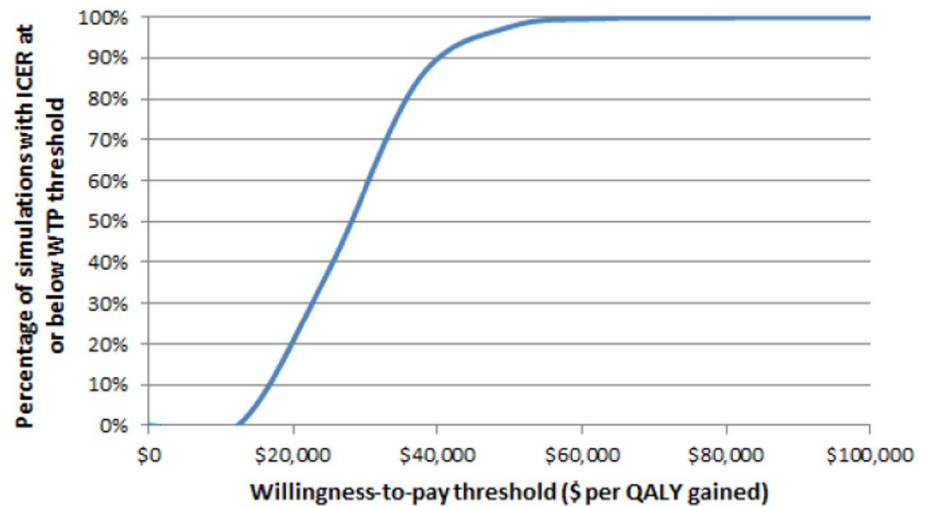

Table 3 Incremental results from a payer's perspective for Canadian adults aged ≥50 years vaccinated with RZV vs. no HZ vaccination based on various first-dose coverage rates

First-dose coverage	Incremental (RZV vs. no vaccination)			
	17.5% (base case)	40%	60%	80%
HZ cases	−303,835	−694,481	−1,041,721	−1,388,962
PHN cases	−83,256	−190,299	−285,449	−380,598
Complication cases	−39,653	−90,634	−135,952	−181,269
HZ-related deaths	−99	−225	−338	−450
Life years	751	1716	2574	3432
QALYs (discounted)	16,814	38,431	57,646	76,862
Vaccination costs, CAN$[a]	605,803,049	1,384,692,684	2,077,039,026	2,769,385,368
HZ costs, CAN$[a]	−143,668,241	−328,384,551	−492,576,826	−656,769,102
Total direct costs, CAN$[a]	462,134,808	1,056,308,133	1,584,462,200	2,112,616,266
ICERs, CAN$[a]/QALY (1.5% discount rate)	27,486	27,486	27,486	27,486

CAN$ Canadian dollars, *HZ* herpes zoster, *ICERs* incremental cost-effectiveness ratios, *PHN* post-herpetic neuralgia, *QALYs* quality-adjusted life-years, *RZV* recombinant zoster vaccine

[a]Costs are in 2022 CAN$

Table 4 Cost results[a] for Canadian adults aged ≥50 years vaccinated with RZV vs. no HZ vaccination from a societal perspective

	RZV	No HZ vaccination	Incremental (RZV vs. no vaccination)
Costs, CAN$[b]			
Vaccination costs (direct and indirect)	694,498,235	0	694,498,235
Direct costs due to HZ	1,446,473,430	1,590,141,671	−143,668,241
Indirect costs due to HZ	1,335,308,137	1,514,612,939	−179,304,802
Total societal costs	3,476,279,802	3,104,754,609	371,525,193
ICERs, CAN$[b]/QALY			
1.5% discount rate (as per the base case)	–	–	22,097
0% discount rate	–	–	16,061
3% discount rate	–	–	28,594

CAN$ Canadian dollars, *HZ* herpes zoster, *ICERs* incremental cost-effectiveness ratios, *QALY* quality-adjusted life-year, *RZV* recombinant zoster vaccine

[a]Health outcome and life-years/QALY results were the same as from the payer perspective (Table 2)

[b]Costs are in 2022 CAN$

[14] is driven by less waning of RZV VE and aging of the Canadian population.

RZV VE and waning estimates were updated in the current analysis based on up to 8 years of follow-up of the ZOE clinical trial populations [15], compared with up to 4 years of follow-up [16, 17] used in the analysis by McGirr et al. [14]. Among people aged 50–69 years, waning was reduced from 1% for the first 4 years and 2.3% thereafter to 1.5% overall, while among people aged ≥70 years, waning was reduced from 3.6 to 2.3%, as estimated by Curran et al. [24]. The changes also impacted the NNV to prevent one HZ case, which was reduced from 10 [14] to 9, and to prevent one PHN case, which reduced from 37 [14] to 32.

QALY losses per HZ case were reduced from 0.036 in the analysis by McGirr et al. [14] to 0.009 (age 50–59 years) or 0.01 (≥60 years), and were updated per PHN case from 0.1357 [14] to 0.041 (age 50–59 years), 0.192 (60–69 years), and 0.234 (≥70 years) based on data published in 2019 by Drolet et al. [41]. This would have reduced the numbers of QALYs saved due to HZ cases but increased the numbers of QALYs saved due to PHN cases, resulting in similar overall QALYs saved per HZ case avoided (55,361/1,024,771 = 0.054 [14] and 16,814/303,835 = 0.055). As the same HZ and PHN probabilities were used in both analyses, these QALY loss changes had little impact on the overall outcomes.

Overall, the updated data inputs between the analysis by McGirr et al. [14] and the current analysis resulted in an updated cost per QALY saved of CAN$27,486 (2022 costings) in comparison with CAN$30,402 (2016 costings) [14], indicating that RZV for adults aged ≥50 years in Canada remains a cost-effective option at a willingness-to-pay threshold of CAN$50,000 per QALY gained. We also evaluated the cost effectiveness of RZV from a societal perspective, which was not performed in the analysis by McGirr et al. [14]. The cost per QALY was lower in comparison with the healthcare payer perspective when indirect costs for vaccination and HZ were included (CAN$22,097). These findings are aligned with results from other ZONA model analyses that have predicted RZV to be cost effective versus no HZ vaccination in the United States (US) [19], Japan [22, 26], and Germany [24]. Three recent reviews have examined the cost effectiveness of RZV [49–51]. A 2022 meta-analysis of 12 studies (from the US, Asia, Canada, and Europe) that compared RZV versus no HZ vaccination concluded that RZV was cost effective for people aged 60–79 years from a societal perspective, and for those aged 60–69 years from a third-party payer perspective [49]. A 2023 review of 18 studies (from the US, Europe, Asia, and Canada) reported that RZV vaccination was predicted to be cost effective in 15 of the 18 included studies [50]. A 2022 systematic review of seven US studies concluded that RZV was a cost-effective strategy but that

second-dose compliance is important [51]. Recent research has shown that barriers to the completion of RZV two-dose regimens include out-of-pocket costs, insurance coverage, accessibility, and patient forgetfulness, while healthcare provider encouragement, reminders, and self-motivation can improve completion [52]. Interventions addressing these factors could therefore help to improve the magnitude of the public health impact of RZV.

In the current one-way sensitivity analysis, the factors that increased the ICER to the largest values were a lower proportion of HZ cases developing PHN, lower HZ incidence, and higher RZV VE waning, but the ICER remained below the CAN$50,000 willingness-to-pay threshold. ZONA analyses from other countries also showed that higher waning [22, 24, 26], a lower proportion of HZ cases developing PHN [22, 24, 26], and a lower HZ incidence [24, 26] were key factors that increased ICER estimates. Given that the incidence of HZ is increasing with an aging Canadian population [5], a higher HZ incidence should result in lower ICERs.

Increasing first-dose coverage had a large impact on the potential public health impact of RZV. Research has shown that barriers to HZ vaccination include vaccine distrust [53], cost concerns [54, 55], and low perceived risk [55]. However, uptake and/or completion could potentially be improved by provider education [56, 57], physician's recommendations [55], nurse/pharmacy administration [56], and use of prompts/reminders [56, 58]. Interventions such as these could help to improve uptake and/or completion, thus improving the public health impact of RZV in Canada.

4.1 Strengths and Limitations

The main strengths of the current analysis are the availability of Canada-specific first-dose coverage [32] and second-dose compliance data [33], and new RZV VE and waning estimates [15, 24]. The latter were based on the availability of up to 8 years of follow-up data [15], compared with up to 4 years of follow-up [16, 17] that were used in the McGirr et al. analysis [14]. However, estimating the QALYs lost for HZ and PHN is challenging, as evidenced by the rather different values used in the analysis by McGirr et al. [14] and the current study, which used newer values [41]. Moreover, the QALYs lost per case of HZ and PHN were assumed to be the same among vaccinated and unvaccinated individuals, but breakthrough HZ tends to be shorter [59]. Thus, the ICERs may have been overestimated. We also did not consider a larger indirect cost per case of HZ with PHN compared with HZ alone, which could have resulted in an underestimation of the value of RZV. Lastly, we assumed a willingness-to-pay threshold of CAN$50,000 per QALY, but this is not explicitly stated by Canadian health technology

assessment bodies, such as CADTH, although there is some evidence to support this threshold [47].

5 Conclusions

RZV presents a cost-effective option, robust to a variety of sensitivity and scenario analyses, for vaccinating Canadian adults aged ≥50 years against HZ compared with no HZ vaccination (ICER CAN$27,486 per QALY gained from the healthcare payer perspective). Compared with the previous analysis [1], cost effectiveness was retained and the estimated public health impact was smaller (due to lower coverage/completion estimates). However, the potential public health impact was estimated to be greater when first-dose RZV coverage was assumed to be the same as the previous analysis driven by less waning of RZV VE and aging of the Canadian population.

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