Disclosure Statement

- I am an employee of the GSK group of companies

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The Predicted Public Health Impact of RZV in Canadian Adults ≥50 Years of Age

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Conflicts of interest
All authors are employees of the GSK group of companies. DC holds shares in the GSK group of companies.

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BACKGROUND AND AIMS

- Herpes Zoster (HZ), also known as shingles, is characterized by a unilateral vesicular rash.[1] It can lead to complications, the most common being postherpetic neuralgia (PHN), a debilitating nerve pain affecting 14%-33% of HZ patients.[2]
- In Canada, approximately 1 in 3 people will develop HZ over their lifetime, with this risk increasing to almost 50% by age 85.[3] HZ and PHN place a significant burden on the Canadian healthcare system[4,5] and with the aging population, the incidence of these are expected to increase.[6,7]

Wikimedia Commons

1. National Advisory Committee on Immunization (NACI). Accessed Aug 2017. 2. Drolet M, *et al*. J Pain 2010; 11:1211-21. 3. Harpaz R, *et al*. MMWR Recomm Rep 2008; 57:1-30. 4. Najafzadeh M, *et al*. Pharmacoeconomics 2009; 27:991-1004. 5. Brisson M, *et al*. Hum Vaccin 2008; 4:238-45. 6. Schmader K, *et al*. J Infect Dis 2008; 197 Suppl 2:S207-S15. 7. Varghese L, *et al*. BMC Geriatr 2017; 17:30.

BACKGROUND AND AIMS

- Two HZ vaccines are licensed for use in Canadian adults ≥50 years old (y):
    1. Adjuvanted Recombinant Zoster Vaccine (RZV)[1]
    2. Zoster Vaccine Live (ZVL)[2]

- This analysis reports the predicted public health impact of both vaccines in adults ≥50y in terms of:

HZ & PHN cases avoided

Number needed to vaccinate (NNV) to prevent one case of HZ or PHN

Hospitalizations and physician visits avoided

1. GSK Canada. http://ca.gsk.com/media/1350788/shingrix_pm-2017-10-13.pdf. Accessed Oct 2017.
2. Merck. https://www.merck.ca/assets/en/pdf/products/ZOSTAVAX_II-PM_E.pdf. Accessed May 2017.

METHODS

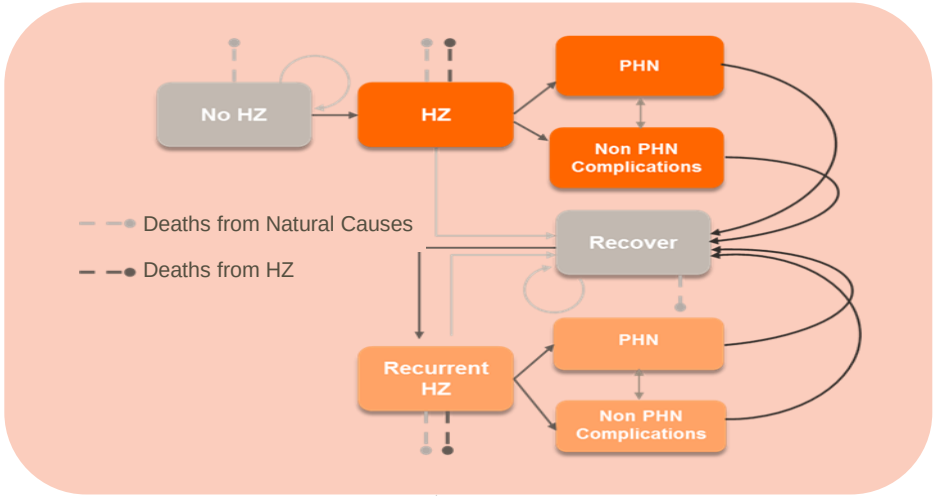
Zoster ecoNomic Analyses (ZONA) Model

Global Inputs

Vaccine Efficacy (VE) for RZV and ZVL

Duration of protection

Static Multi-Cohort Markov Model[1]



Local inputs:

- Demographics
- HZ/PHN incidence
- Compliance 2nd dose
- Utility losses
- Resource utilization

What is the public health impact?

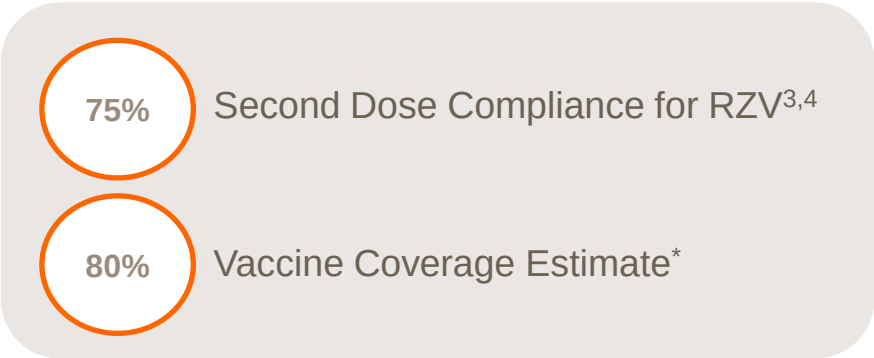
- RZV
- ZVL
- No Vaccination

1. Curran D, et al. HVI 2017; 13 (10): 2213-2221

METHODS

Key Model Input Source Data

Disease incidence	Total					
	50-59y	60-64y	65-69y	70-79y	≥80y	Source / Comments
Annual probability of initial or recurrent HZ case (per 1,000)	6.0	8.7	8.7	10.9	11.1	Marra *et al.* 2016[1]
Proportion of cases developing PHN	14.60%	20.50%	20.50%	33.80%	33.80%	Drolet *et al.* 2010[2]



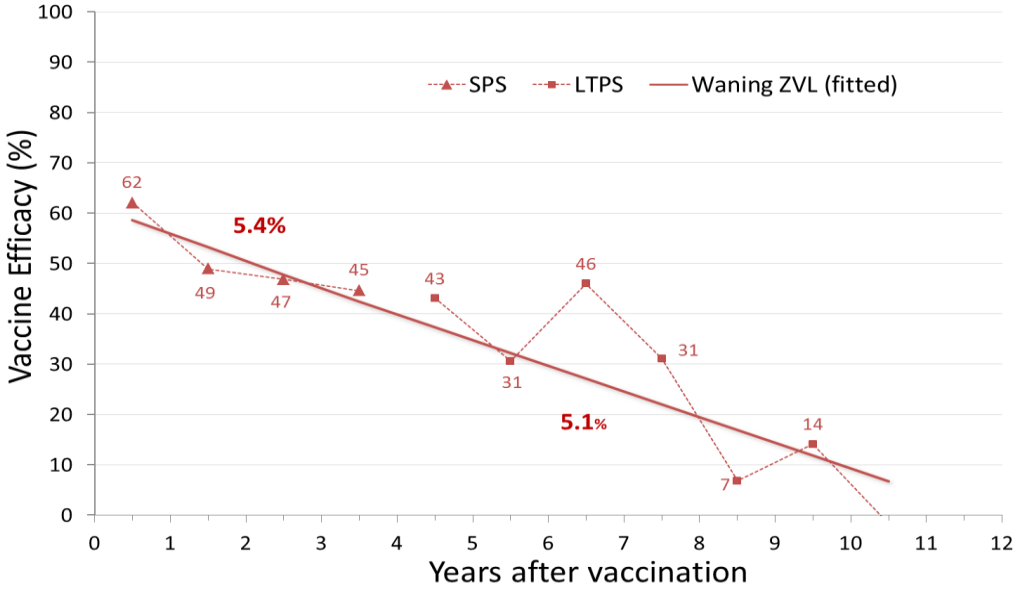
1. Marra F, et al. BMC infect Dis 2016; 16:589. 2. Drolet M, et al. J Pain 2010; 11:1211-21. 3. Assumption based on Lal H, et al. N Engl J Med 2015; 372:2087-96., Cunningham AL, et al. N Engl J Med 2016; 375:1019-32., 4. Nelson, et al. Am J Public Health 2009; 99(S2). * Assumption for both vaccines based on greater uptake than flu for seniors (Public Health Agency of Canada 2017).

METHODS

HZ Vaccine Efficacy Waning Over Time: ZVL

ZVL Results from Clinical Trials[1-3]

VE vs.	HZ	PHN
50-59y	69.80%	-
60-64y	63.89%	65.69%
65-69y	63.89%	65.69%
70-79y	40.85%	73.38%
≥80y	18.25%	39.51%



There are no head to head studies comparing the efficacy of RZV and ZVL.

HZ, Herpes Zoster; LTPS, Long Term Persistence Study; PHN, postherpetic neuralgia; SPS, Shingles Prevention Study , VE, vaccine efficacy; Y, Years-old of age; ZVL, Zoster Vaccine Live

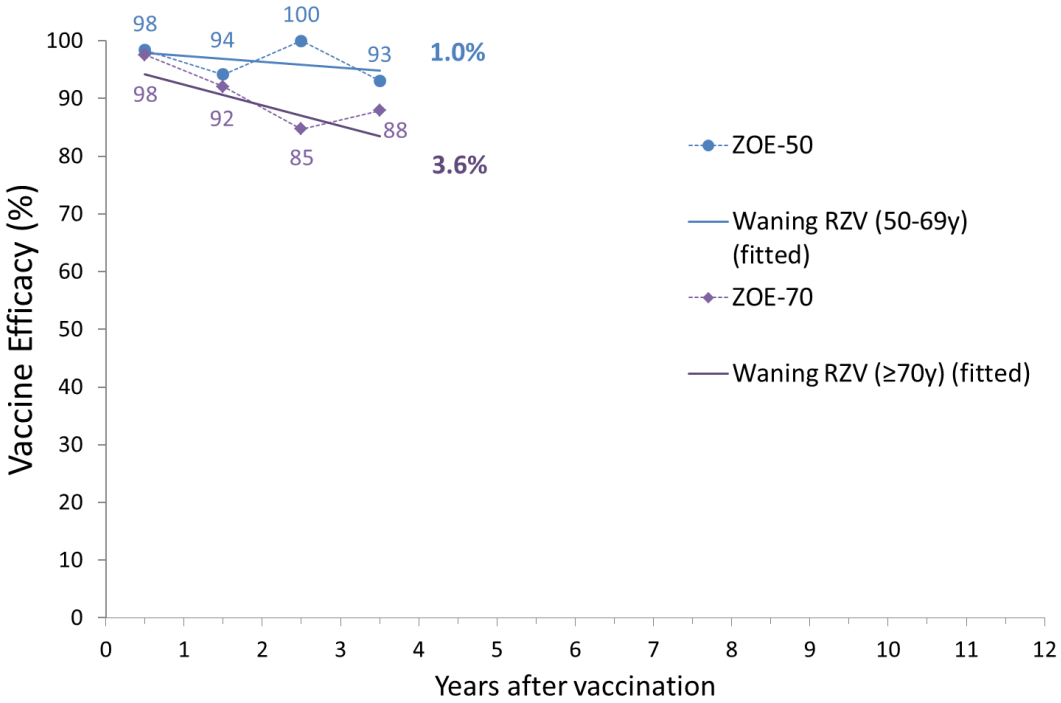
1. ZVL SPS: Oxman MN *et al* NEJM 2005; 352:2271-2284. 2. ZVL ZEST: Schmader KE, *et al.* Clin Infect Dis 2012; 54:922-8. 3. ZVL LTPS: Morrison VA, *et al.* Clin Infect Dis 2015; 60:900-9.

METHODS

HZ Vaccine Efficacy Waning Over Time: RZV

RZV Results from Clinical Trials[1,2]

	VE vs. HZ	CI
≥50y	97.2%	93.7%-99.0%
≥70y	91.3%	86.8%-94.5%



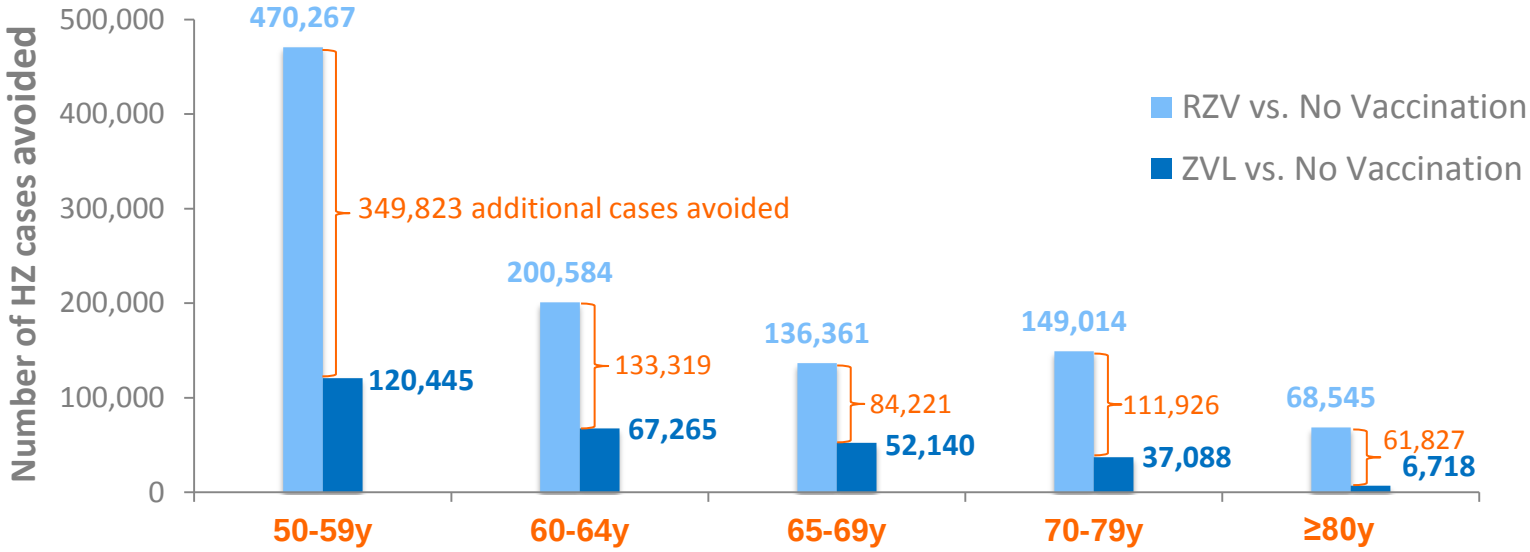
CI, confidence interval; HZ, Herpes Zoster; RZV, Adjuvanted Recombinant Zoster Vaccine; VE, vaccine efficacy

1. ZOE-50: Lal H *et al*. NEJM 2015;372:2087-2096. 2. ZOE-70: Cunningham AL *et al* NEJM 2016;375:1019-1032.

RESULTS

Model-predicted HZ cases avoided by age group for RZV and ZVL, over the lifetime of the cohort.

Amongst the approximately 12 million Canadian adults ≥50 years old, the ZONA model predicts that **RZV immunization would prevent 741,116 additional cases of HZ compared to ZVL** over the lifetime of the cohort.

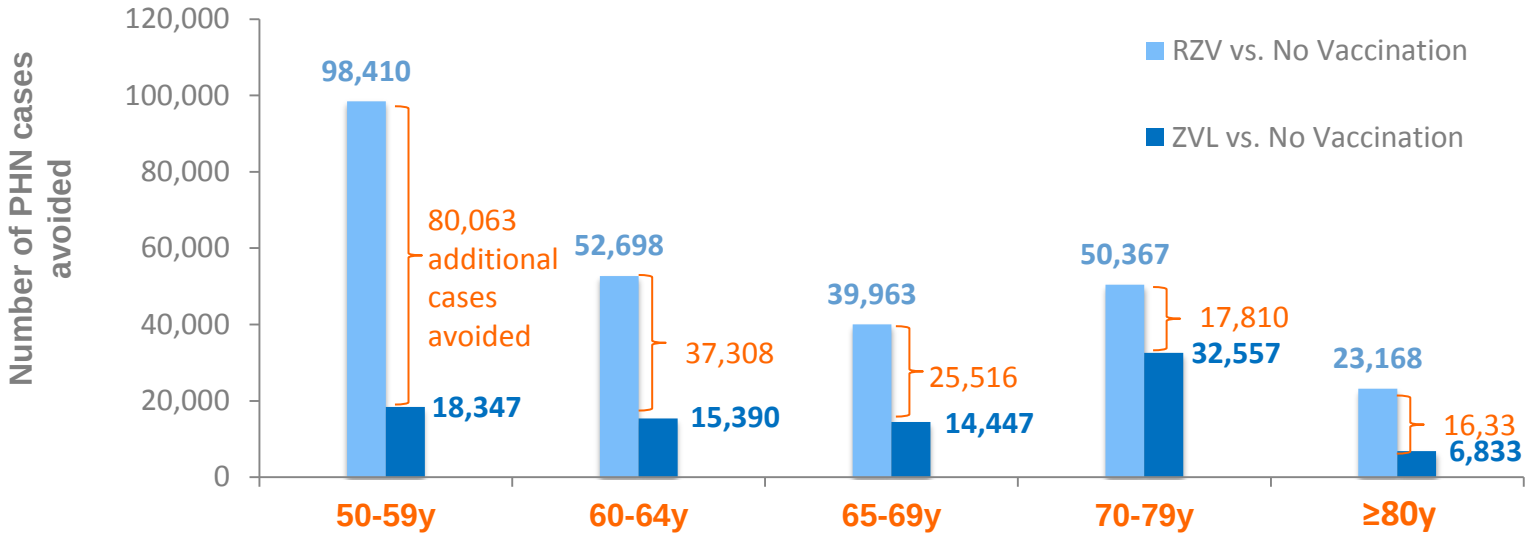


HZ: Herpes zoster; RZV: Adjuvanted Recombinant Zoster Vaccine; ZVL: Zoster Vaccine Live; y: years

RESULTS

Model-predicted PHN cases avoided by age group for RZV and ZVL, over the lifetime of the cohort.

Amongst the approximately 12 million Canadian adults ≥50y, the ZONA model predicts that **RZV immunization would prevent 177,031 additional cases of PHN compared to ZVL** over the lifetime of the cohort.



PHN: postherpetic neuralgia; RZV: Adjuvanted Recombinant Zoster Vaccine; ZVL: Zoster Vaccine Live; y: years.

RESULTS

Model-predicted resource utilization by age group comparing RZV and ZVL, over the lifetime of the cohort.

This would translate into 7,411 additional hospitalizations avoided and 1,845,378 additional general practitioner visits avoided by using RZV compared to ZVL.

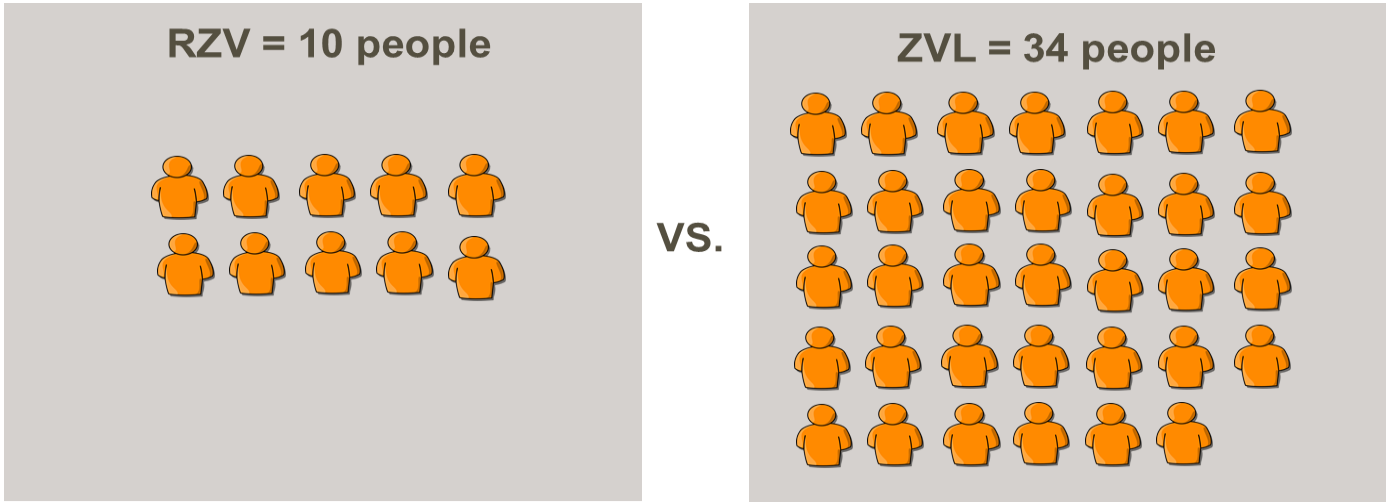
Resource Utilization	50-59y	60-64y	65-69y	70-79y	≥80y	**≥50y combined**
Additional hospitalizations avoided using RZV instead of ZVL	3,498	1,333	842	1,119	618	**7,411**
Additional family practitioner visits avoided using RZV instead of ZVL	871,059	331,965	209,709	278,695	153,949	**1,845,378**

RZV: Adjuvanted Recombinant Zoster Vaccine; ZVL: Zoster Vaccine Live; y: years.

RESULTS

Number needed to vaccinate to prevent one case of HZ in Canadian adults ≥50y.

The model predicts that approximately 3 times as many individuals ≥50y would need to be immunized with ZVL compared to RZV to prevent one case of **HZ**.



HZ: Herpes zoster; RZV: Adjuvanted Recombinant Zoster Vaccine; ZVL: Zoster Vaccine Live.

RESULTS

Number needed to vaccinate to prevent one case of PHN in Canadian adults ≥50y.

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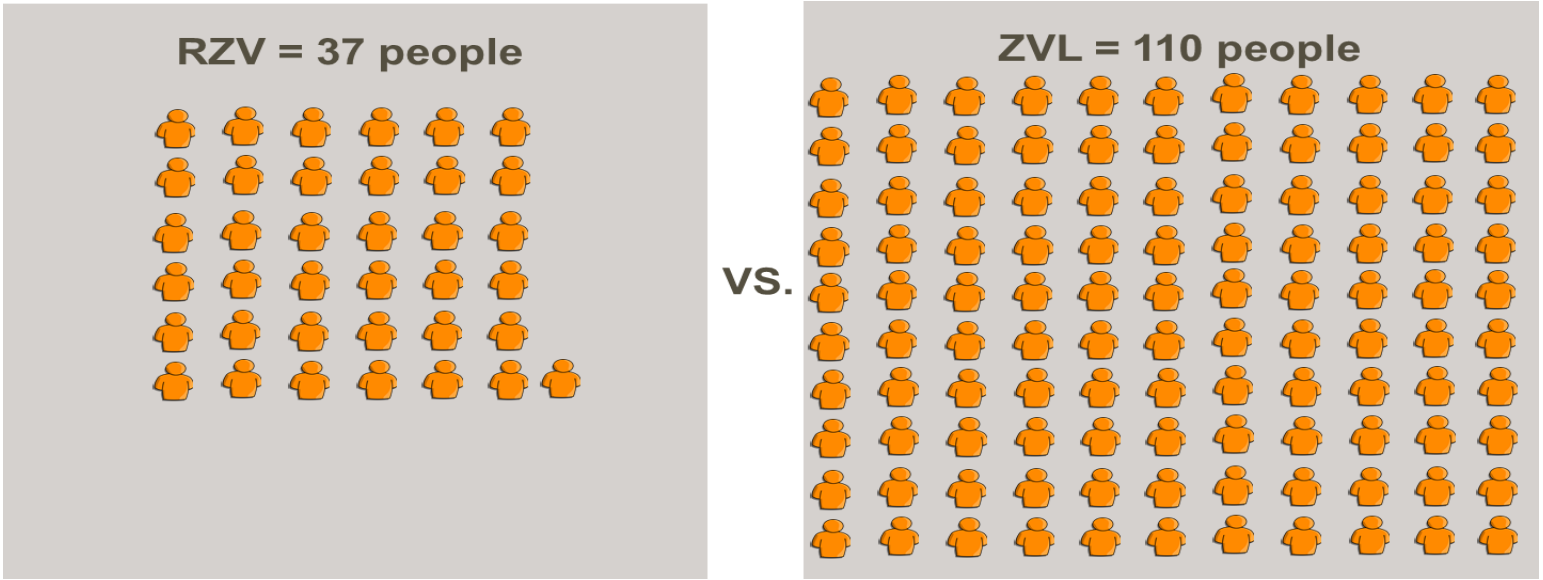


PHN: postherpetic neuralgia; RZV: Adjuvanted Recombinant Zoster Vaccine; ZVL: Zoster Vaccine Live.

DISCUSSION

- While models are not a substitute for epidemiologic data, mathematical models are an important tool to help policy makers and public health officials make informed decisions.

- As with all models, where data were sparse, we were forced to make a number of key assumptions:
  - VE estimates were based on clinical trial data as RZV has only recently been approved and real world evidence has not yet been collected.
  - To evaluate VE over time, a linear approximation was fitted to the yearly VE estimates derived from these trials to extrapolate efficacy beyond four years.
  - Assumptions of coverage rate and second-dose compliance as there are no good proxies for these in Canadian adult immunizations.

- ZONA model predicts that RZV can avoid more cases of HZ and PHN compared to ZVL in Canadian adults.

CONCLUSIONS

- Models allow us to simulate the effects of an immunization program and compare that to other potential immunization programs or to no immunization program.

- This analysis can help healthcare practitioners, policy makers, and public health officials make informed decisions about HZ vaccines.

- The model predicts a greater reduction in HZ and PHN morbidity and healthcare utilization associated with RZV compared to ZVL immunization.

Thank you!

BACK-UP SLIDES

Summary of National Assumptions

	RZV	ZVL
Cohort of Interest	≥ 50 year olds in Canada	≥ 50 year olds in Canada
Vaccine Coverage	80%	80%
Second Dose Adherence	75%	N/A
Vaccine Efficacy	ZOE 50 (Lal *et al.* 2015) ZOE 70 (Cunningham *et. al.* 2016)	SPS (Oxman *et al.* 2005) LTPS (Morrison *et al.* 2015) ZEST (Vesikari *et al.* 2013)
Waning VE	Age and duration since immunization specific estimates based off ZOE-50 and ZOE-70, validated at Global Advisory Board[1]	Linear function of waning immunity from SPS, LTPS, and ZEST studies, as validated at Global Advisory Board[1]

The studies referred to in the above chart are not head to head studies. There are no efficacy studies comparing RZV to ZVL. Comparative claims cannot be made.

1. GSK Global Advisory Board, September 22, 2016, Quebec

Vaccine Efficacy

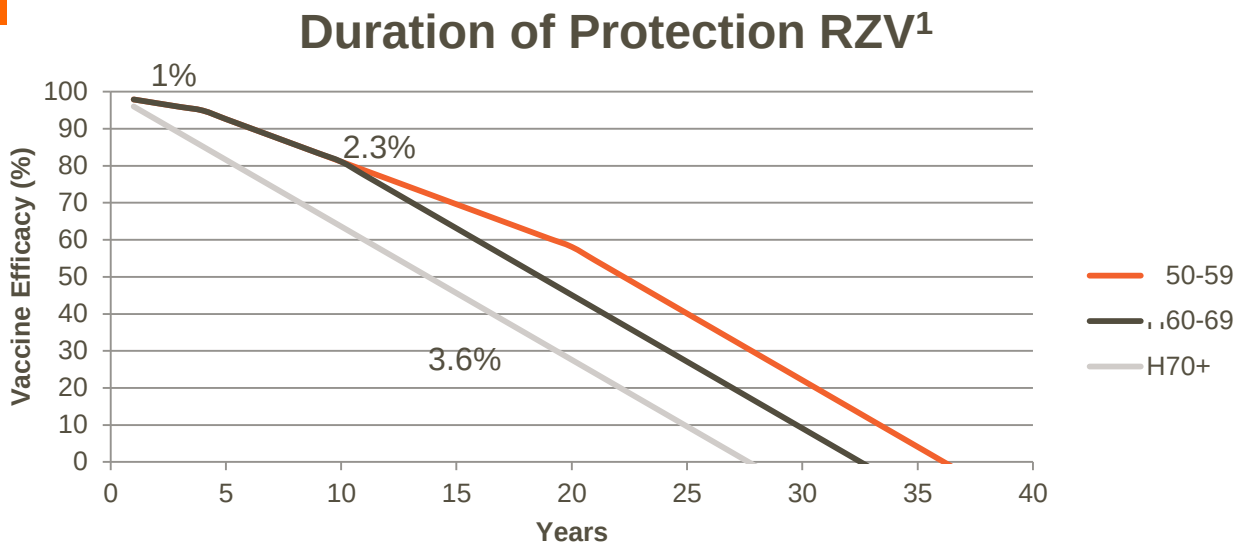
RZV

Vaccine Efficacy HZ
ZOE 50 (Lal *et al.* 2015)
ZOE 70 (Cunningham *et. al.* 2016)

Initial VE RZV

- **Age 50-69**: 98.4% (95%-100%)
- **Age 70+**: 97.8% (94.1%-100%)
- No top-up PHN Efficacy

What does this mean for the model?[1,2]



1. GSK Global Advisory Board, September 22, 2016, Quebec. 2. Curran, D. *et al.* Assessment of the potential public health impact of Herpes Zoster vaccination in Germany. *HVI*, 0, doi:10.1080/21645515.2017.1345399 (2017).

One dose Vaccine Efficacy

RZV

Vaccine Efficacy HZ[2]
ZOE 50 (Lal *et al.* 2015)
ZOE 70 (Cunningham *et. al.* 2016)

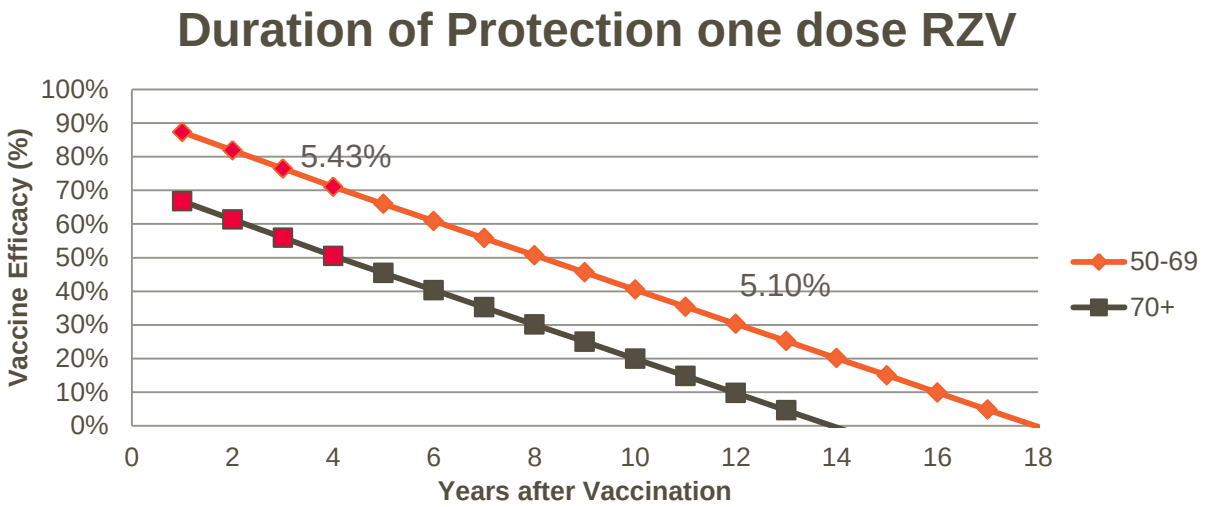
Age strata		95% CI	
	(%)	LL	UL
50–69	**90.09**	58.93	98.88
≥70	**69.51**	24.94	89.11

[2]Follow up time <3 months

[a] Based on 2 subjects with a case of HZ in the RZV group and 19 subjects with a case of HZ in the placebo group.

[b] Based on 7 subjects with a case of HZ in the RZV group and 20 subjects with a case of HZ in the placebo group.

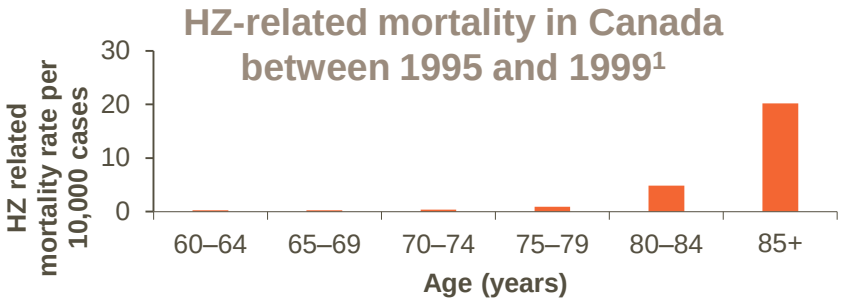
What does this mean for the model?[1,2]

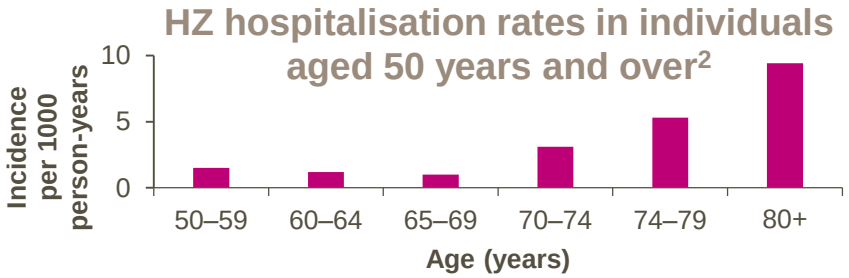


1. GSK Global Advisory Board, September 22, 2016, Quebec. 2. Curran, D. *et al.* Assessment of the potential public health impact of Herpes Zoster vaccination in Germany. *HVI* 0, doi:10.1080/21645515.2017.1345399 (2017).

Burden of Disease in Canada

Hospitalisation, mortality and costs





- $CAN 101 (without PHN)[2]
- $CAN 1559 (with PHN)[1]

Drugs costs per HZ case

- 60–64 y: 2.8
- 65–69 y: 3.9
- 70–74 y: 3.8
- 75–79 y: 4.3
- 80–84 y: 4.8
- All age groups: 4.0

Average number of physicians visits for HZ with PHN[1]

- 60–64 y: 14.2 days
- 65–69 y: 18.2 days
- 70–74 y: 15.9 days
- 75–79 y: 18.5 days
- 80–84 y: 24.1 days
- All age groups: 21.6 days

Average length of stay in hospital for HZ without PHN[1]

- $CAN 821 (min 411, max 1232) (calculated for 2005)[2]
- $CAN 590 (95% CI 531.4–649.5) (calculated for 2008)[1]

Mean cost per day of hospitalisation with HZ

HZ places a significant burden on the Canadian healthcare system

PHN, post-herpetic neuralgia

[1]Najafzadeh *et al. Pharmacoeconomics* 2009;27:991–1004; [2]Brisson *et al. Hum Vaccin* 2008;4:238–45

Impact to Work Productivity and Absenteeism[1]

- Adults 50+ actively employed with HZ or HZ associated pain.
- Measure HZ-related burden of illness, Quality of Life

57.7% Reported work-time loss due to HZ episode

9.1 days Average number of days of work lost due to shingles

66% Reported decreased work productivity

1. Rampakakis et al. Health and QoL Outcomes 2017. 15:11