



IMMUNISATION
COALITION



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The economic and individual value of Shingrix vaccination in older individuals and the immunocompromised

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Immunisation Coalition ASM Feb 2024

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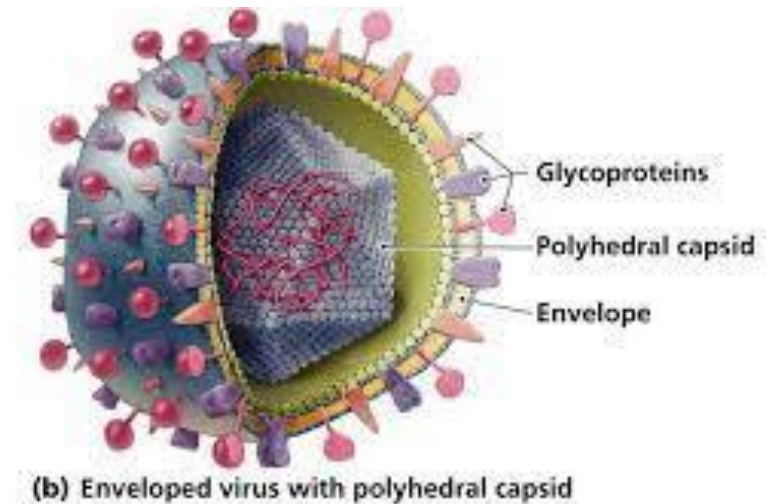
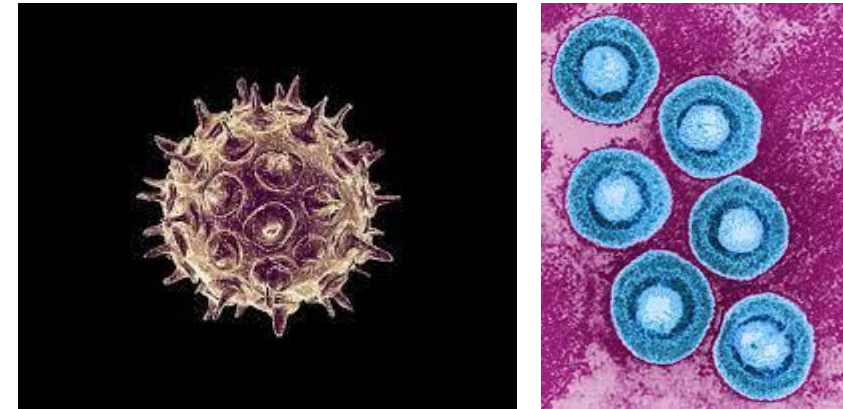
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Declarations

- Member of the Australian Technical Advisory Group on Immunisation
- This is my personal perspective

Herpes Zoster or Shingles – Clinical Aspects

- Caused by reactivated varicella zoster virus infection in dorsal root or cranial nerve ganglia in a person who has previously had chicken pox
- Herpes zoster virus (HZV) = a polyhedral DNA herpes virus
- Causes an itchy rash in a dermatomal distribution which then develops into vesicles, papules, pustules of varying size and stage
- Pain is a major feature (painful neuritis)
- Can persist as post herpetic neuralgia (PHN) = pain persisting ≥ 90 days after rash resolution (can last for years)
- The economic and clinical burden of HZV is substantial



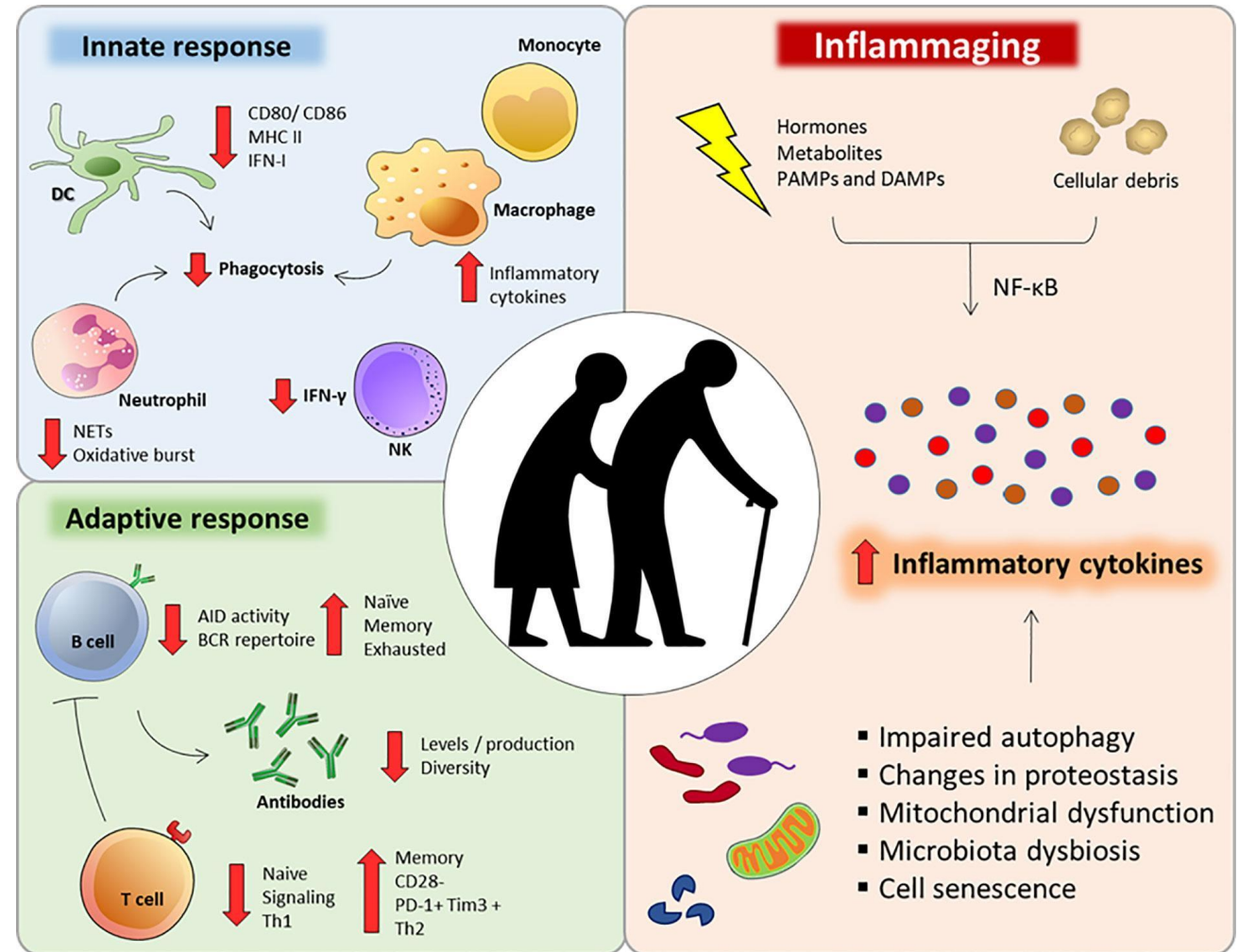
Keeping the Elderly Healthy

- The world's population is aging with the number of people >60 years expected to double by 2050
- Healthy elderly people make a huge contribution to the economy:
 - Care of grandchildren
 - Voluntary work
 - International travel
 - Spending their pensions
- The elderly are more prone to severe outcomes and death from multiple infections
- Sick elderly people are a major drain on resources
- Healthy aging is therefore a major public health priority



Immunosenescence

- Innate and adaptive arms of the immune system deteriorate with increasing age leading to suboptimal immune response to infections and vaccination
- Inflammaging also occurs characterised by enhanced immune activation and cellular decline
- Predicts frailty, cognitive impairment, mortality
- Shingles incidence and severity increases with age





Shingles Vaccines



Zostavax (Merck) ZVL	Shingrix (GSK) RZV
Live attenuated Oka VZV strain	Recombinant subunit vaccine containing VZV glycoprotein E
No adjuvant	Adjuvanted with liposome-based ASO1 _B
Single dose	Two doses 2-6 months apart (1-2 months if immunocompromised)
Contraindicated in immunocompromised & pregnancy	Safe in immunocompromised & pregnancy
Registered in Australia since 2007 for people ≥50 yrs Added to the NIP in Nov 2016 for immunocompetent people aged 70 yrs (with catchup for 71-79 yr olds) No longer available in Australia	Registered in Australia 2018 for people ≥50 yrs Extended to immunocompromised for people ≥18 yrs in 2021 On Australian market since June 2021 Added to the NIP in Nov 2023
~\$190 a dose	~\$560 for 2 doses

Efficacy of Zostavax (ZVL)



- Zostavax Efficacy is moderate as shown in Shingles Prevention Study (SPS) in ≥ 60 yr olds (Oxman et al NEJM 2005) and Zoster Vaccine Efficacy and Safety Trial (ZEST) in 50-59 yr olds (Schmader et al. CID 2012)
 - 51.3% efficacy against HZV and 66.5% against post-herpetic neuralgia over median of 3.1 yrs
 - Efficacy decreased with age being 69.8% efficacy in 50-59 yr olds and 37.6% in those ≥ 70 yrs
 - Efficacy not sig at ≥ 80 yrs impacting cost-effectiveness
 - Wanes over time (e.g., 31.1% [CI 11.2-47.6] at 8 yrs in 1 study and other studies showed 16.5% at 8 yrs)
- Difficult to assess impact due to challenges ascertaining all cases and no systematic evaluation plan in Australia
- Modest reductions in the incidence of HZ and its complications since Zostavax program introduction
- Challenges include:
 - Suboptimal uptake (only 16.2% for 70 yr olds in yr 1 and $\sim 32\%$ since)
 - Safety concerns re. inadvertent use in immunocompromised persons
- 3 vaccine related deaths due to disseminated zoster in Australia

Efficacy of Shingrix

The **NEW ENGLAND**
JOURNAL of MEDICINE

ESTABLISHED IN 1812

MAY 28, 2015

VOL. 372 NO. 22

Efficacy of an Adjuvanted Herpes Zoster Subunit Vaccine
in Older Adults

Randomised placebo-controlled phase III trial in 18 countries
Efficacy and safety in adults aged 50-59 yrs, 60-69 yrs and ≥70 yrs
N = 15,411, 2 doses im 2 months apart

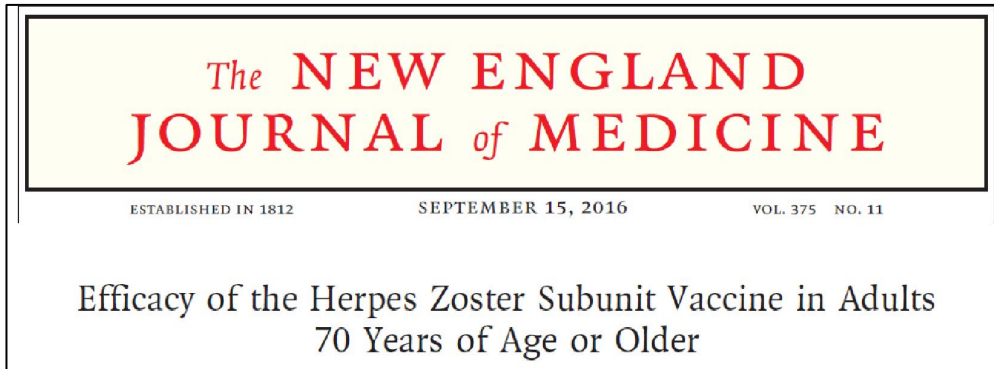
Table 2. Vaccine Efficacy against the First or Only Episode of Herpes Zoster Infection.*

Cohort and Age Group	HZ/su Group				Placebo Group				Vaccine Efficacy†
	No. of Participants	No. of Confirmed Cases	Cumulative Follow-up Period ‡	Rate of Herpes Zoster no./1000 person-yr	No. of Participants	No. of Confirmed Cases	Cumulative Follow-up Period ‡	Rate of Herpes Zoster no./1000 person-yr	
Modified vaccinated cohort									
All participants in cohort	7344	6	23,297.0	0.3	7415	210	23,170.5	9.1	97.2 (93.7–99.0)
50–59 yr	3492	3	11,161.3	0.3	3525	87	11,134.7	7.8	96.6 (89.6–99.3)
60–69 yr	2141	2	7,007.9	0.3	2166	75	6,952.7	10.8	97.4 (90.1–99.7)
70 yr or older	1711	1	5,127.9	0.2	1724	48	5,083.0	9.4	97.9 (87.9–100.0)

6 cases of herpes zoster in vaccine group
210 cases HZV in the placebo group
0.1 vs 9.1 per 1,000 person years
97.2% efficacy (95% CI 93.7–99.0, p<0.001)
96.6% to 97.9% efficacy across all age groups
No SAEs

Lal et al. NEJM 2015; 373(22): 2087

Efficacy of Shingrix at ≥ 70 years



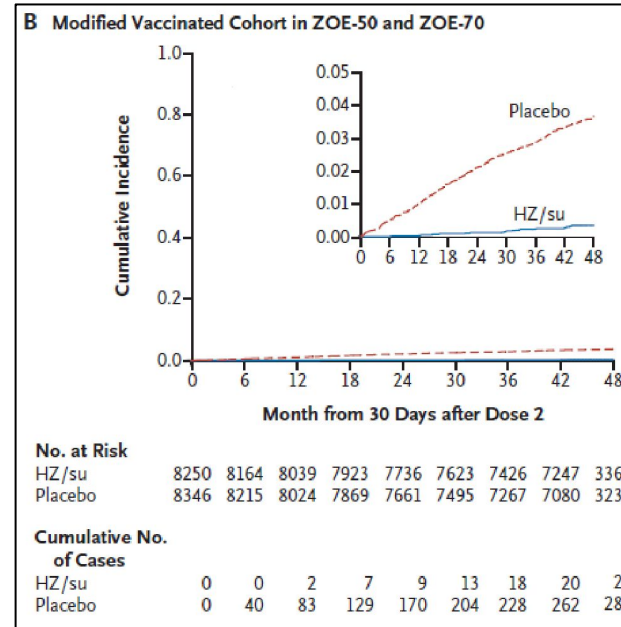
Second trial performed concurrently at same sites in those ≥ 70 yrs

Efficacy against HZV and post-herpetic neuralgia in 13,900 participants

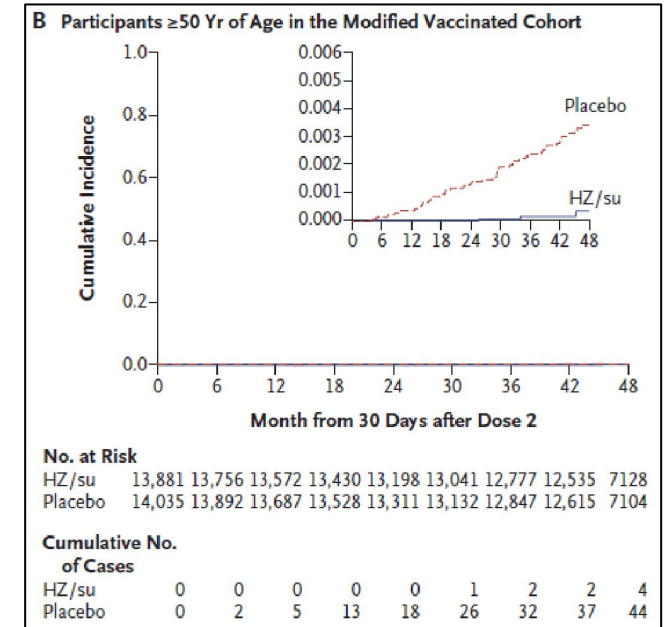
Efficacy against HZV: 89.8% (95% CI 84.2-93.7)

Efficacy against PHN: 88.8% (95% CI 68.7-97.1)

90% efficacy in 70-79 yrs and 89.1% in ≥ 80 yrs



HZV Infection



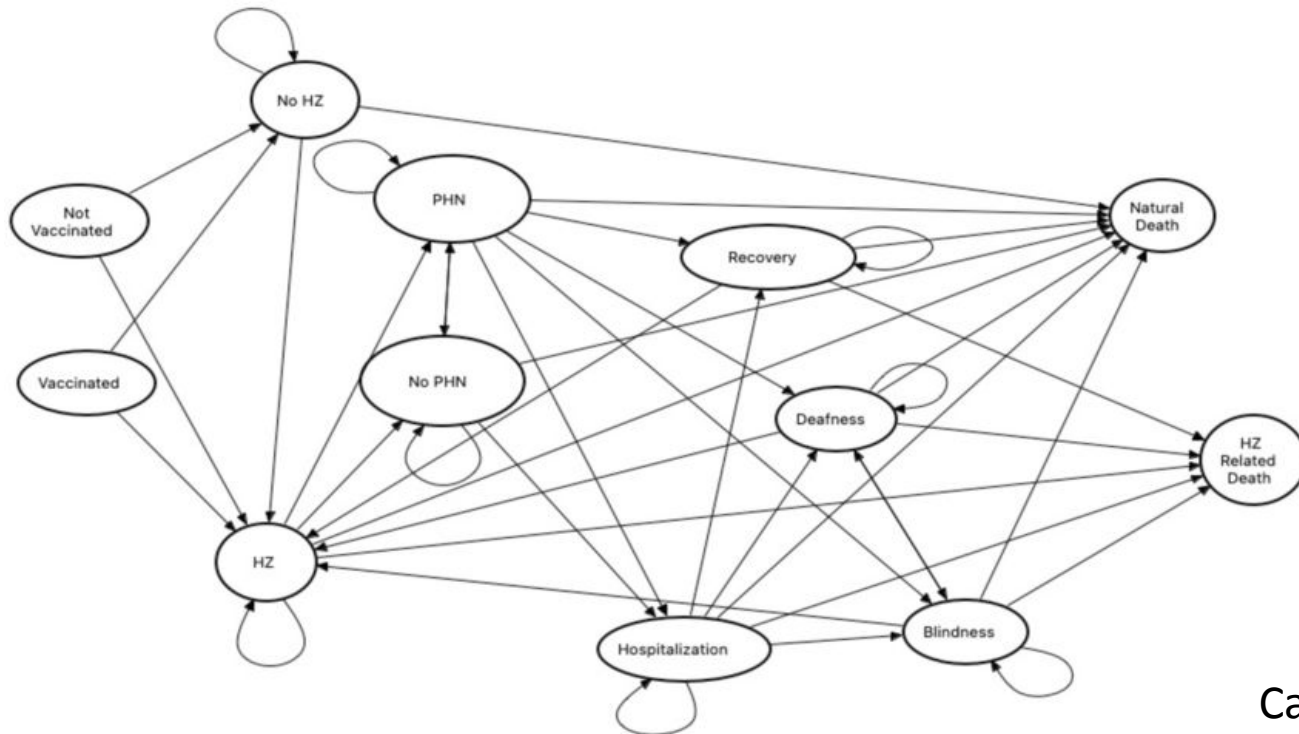
Post herpetic neuralgia

Overall, these 2 studies suggest that the increase in vaccination costs with Shingrix would be partially offset by reduced healthcare visit and medication expenses.

Economic Evaluation

Determining the economic value of a vaccine program is complex

Most published studies use a Markov model

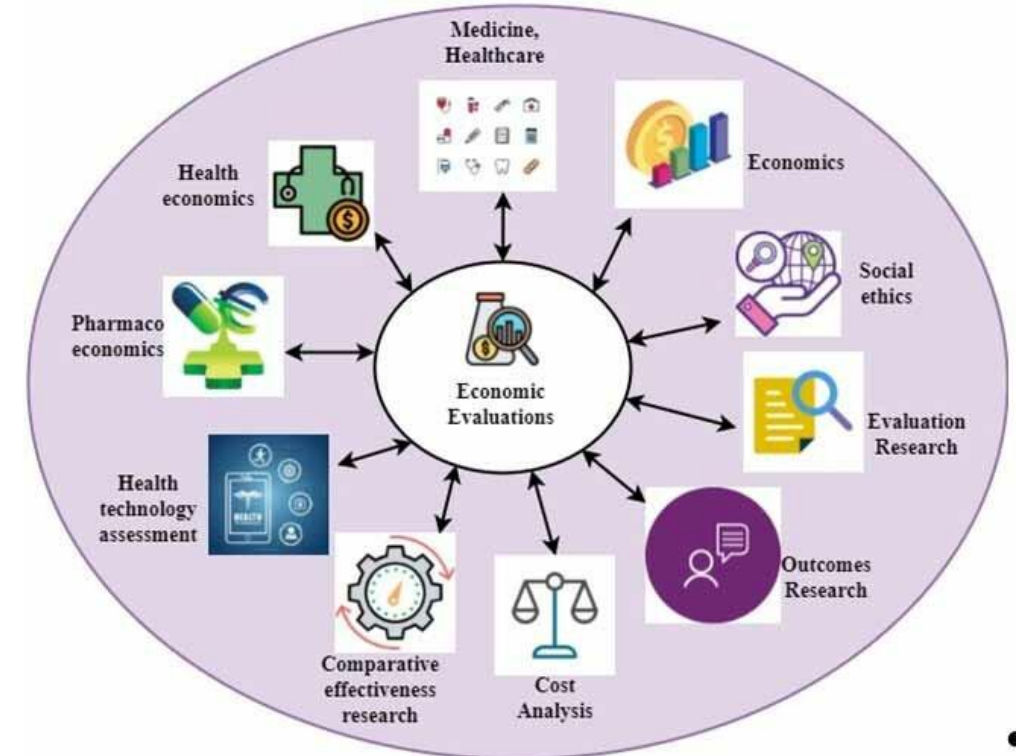


A stochastic (random probability) model describing a sequence of possible events in which the probability of each event depends only on the state attained in the previous event

Economic Evaluation

Factors that need to be taken into account:

- Epidemiology: Incidence and severity of the disease, hospitalisation, sequelae including PHN. Precise data generally not available
- Vaccine efficacy, duration of protection and adverse events following immunisation
- Impact of aging on immunity, disease severity and vaccine effectiveness (need to evaluate different age groups) noting the considerable heterogeneity in the health status of older people
- Co-morbidities e.g. immunosuppression, chronic diseases
- Health sector costs – major factor is vaccine price (Shingrix is expensive), other implementation costs, hospitalisation costs for those affected (higher in older people) e.g. cost per bed day by age, medication, GP visits
- Productivity costs – e.g. time off work for patient / carers / family, inability to do voluntary work or care for grandchildren

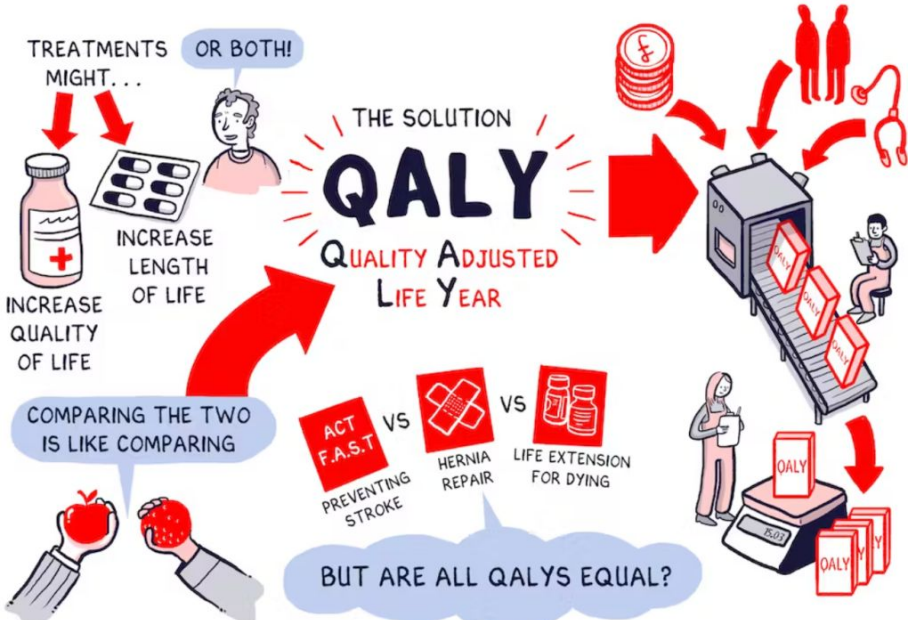
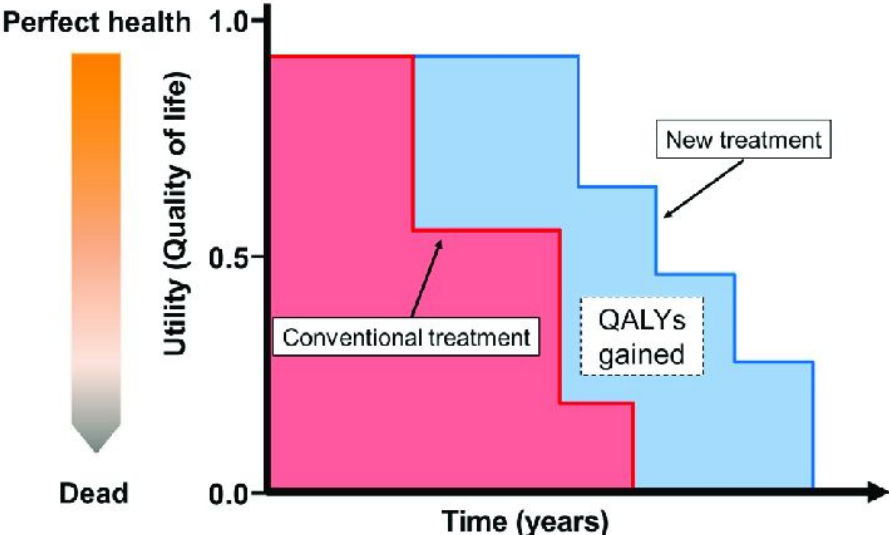


Quality Adjusted Life Years

QALYs combine quantity gains (reduced mortality) and quality gains (reduced morbidity)

Biases towards younger age groups who have longer life expectancy

Quality adjusted life-years (QALYs) = Area under the curve

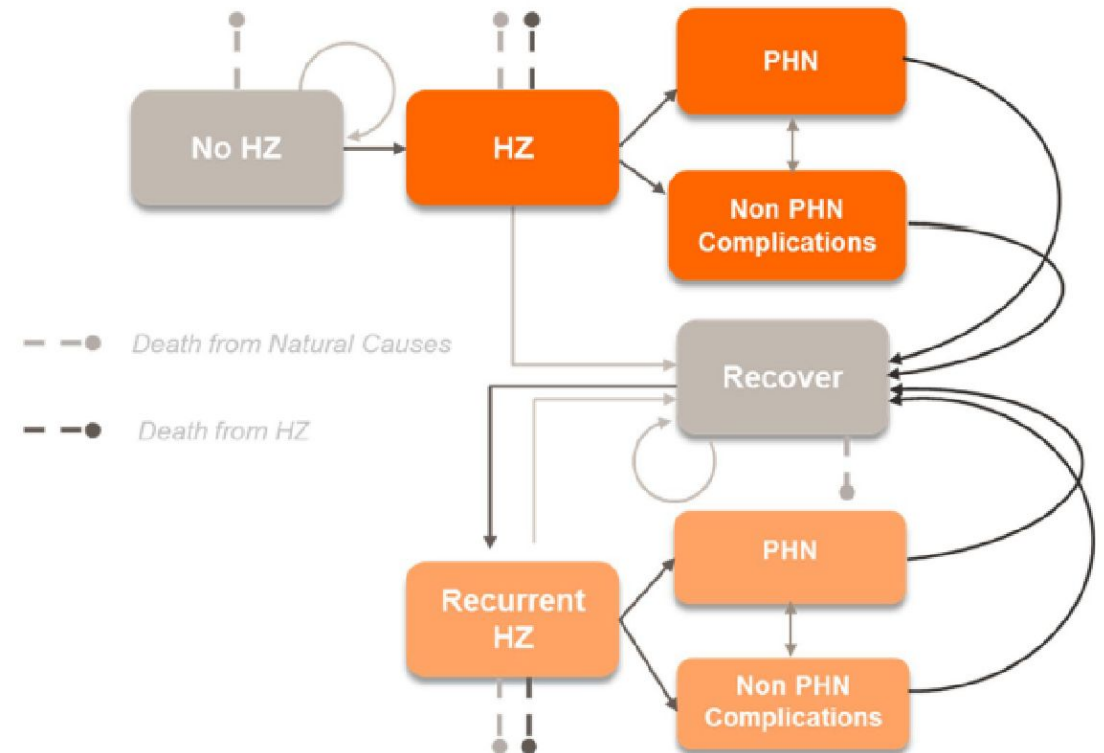


Generally, QALYs are considered equivalent across all ages but incorporating a social value judgement about the value of the health outcome is a useful form of sensitivity analysis

Shingrix Cost-Effectiveness Analysis Canada

Shingrix Recombinant zoster vaccine (RZV) cf no vaccination cf Zostavax live attenuated vaccine (ZVL) in Canadians aged 60 years and older

- Multi-cohort Markov model (single dose static state transition model) applied to Canadian population using recent demographic and epidemiologic data.
- Simulations consisted of age-cohorts (50-59, 60-64, 65-69, 70-79, ≥ 80) annually transitioning between health states.
- Health outcomes and costs were discounted at 1.5% per year.
- The perspective of the Canadian healthcare payer was adopted.
- A coverage of 80% for the first RZV and ZVL dose and a compliance of 75% for the second RZV dose were assumed



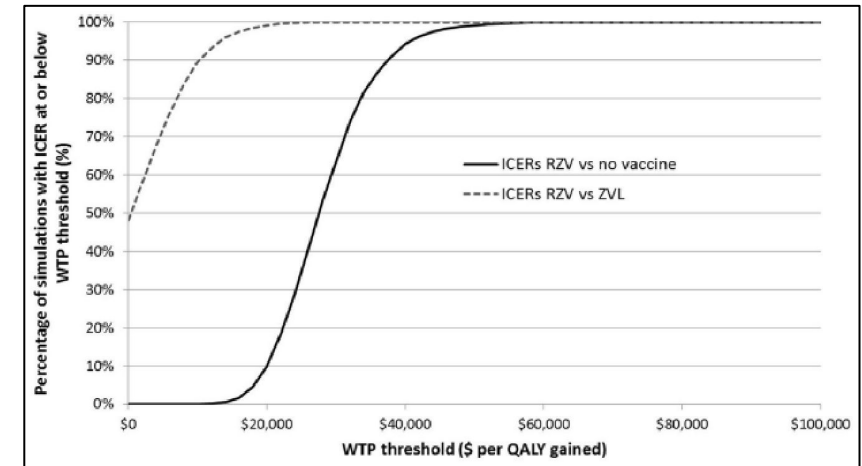
Shingrix Cost-Effectiveness Analysis Canada

- RZV was estimated to be cost effective compared with no vaccination
 - Incremental cost-effectiveness ratio (ICER) of \$28,360 (Canadian dollars) per QALY in persons aged ≥ 60 years
 - Avoiding 554,504 HZ and 166,196 PHN cases with associated costs
- Compared with ZVL, RZV accrued more QALYs through the remaining lifetime
 - An increase in costs of approximately \$50 million resulting in an average ICER of \$2,396 for QALY
- Figures well below Canadian WTP threshold of \$50k /QALY = std threshold used in Canadian cost effectiveness studies
- HZ incidence rate and persistence of vaccine efficacy had the largest impact on cost-effectiveness.

ICERs for base case scenario at ≥ 60 YOA

Outcomes	RZV	No vaccination	ZVL	Difference ^a (RZV vs no vaccination)	Difference ^a (RZV vs ZVL)
Life-years/QALYs (discounted at 1.5%)					
Life-years	107,495,705	107,494,014	107,494,305	1691	1401
QALYs	96,578,202	96,544,742	96,556,869	33,460	21,334
Costs associated with vaccine program, (\$, discounted at 1.5%)					
Vaccination costs	1,286,463,213	0	1,024,290,348	1,286,463,213	262,172,865
Direct costs due to HZ and complications	427,855,341	765,404,926	638,908,525	- 337,549,585	- 211,053,184
Total direct costs	1,714,318,554	765,404,926	1,663,198,873	948,913,628	51,119,681
Cost-effectiveness, \$ per QALY gained (discount rates in parenthesis)					
Base-case: incremental cost per QALY (1.5%)				28,360	2396
Incremental cost per QALY (0%)				24,139	801
Incremental cost per QALY (3%)				32,688	4100
Incremental cost per QALY (5%)				38,577	6516

Cost effectiveness acceptability curve



Shingrix Cost-Effectiveness Analysis Germany

Shingrix vs No Vaccination

- Static multi-cohort Markov model to German population ≥ 60 yrs using recent demographic and epidemiologic data.
- Health outcomes and costs were discounted at 3% per year
- A coverage of 40% for the first RZV dose and 70% compliance for dose 2
- Age cohorts analysed: 60-64, 65-69, 70-79, ≥ 80 yrs

- Vaccinating the population aged ≥ 60 YOA would result in 45,000 HZV cases avoided, 1,713 QALYs gained at a total cost of approximately €63 million compared to 38,000 cases avoided, 1,545 QALYs gained at a total cost of approximately €68 million in the population ≥ 70 YOA.
- Results in an ICER of ~€37,000 and €44,000/QALY, for the age cohort ≥ 60 and ≥ 70 YOA, respectively.
- Number needed to vaccinate (NNV) was similar for three age cohorts analysed (60, 65 and 70 yrs) (range 7–9) but the NNV for PHN was higher (48) for the cohort 70 YOA than for other age cohorts
- Scenario analyses demonstrated that vaccinating at age 60 or 65 YOA would show greater public health impact and would result in the lowest observed ICER compared to vaccinating at 70 YOA

Conclusion: Starting vaccination with RZV in the German population ≥ 60 YOA would demonstrate the best value from a public health and economic standpoint.

Shingrix Cost-Effectiveness Analysis USA

- Cost-effectiveness analysis of RZV, ZVL or no vaccine conducted by CDC
- This comparative analysis informed the Advisory Committee on Immunization Practices (ACIP) and reported outcomes showing cost-effectiveness in both populations ≥ 50 and ≥ 60 YOA.
- Modelled 100% compliance to 2nd dose but used lower values in sensitivity analyses

October 2017, the Advisory Committee on Immunization Practices (ACIP) made the following three recommendations:

- 1) Recombinant zoster vaccine (RZV) is recommended for the prevention of herpes zoster and related complications for immunocompetent adults aged ≥ 50 years.
- 2) RZV is recommended for the prevention of herpes zoster and related complications for immunocompetent adults who previously received zoster vaccine live (ZVL).
- 3) RZV is preferred over ZVL for the prevention of herpes zoster and related complications.

NB Zostavax discontinued in USA in Nov 2020

National Immunisation Program



NIP listing of Shingrix for ≥ 60 yrs rejected by PBAC in 2018 due to uncertainties about cost-effectiveness

Shingrix available for free under the NIP since Nov 2023 for those at greatest risk of complications of shingles (~ 5 million people):

- People aged 65 years and over
- First Nations people aged 50 years and over
- Immunocompromised people aged 18 years and over with the following medical conditions:
 - haematopoietic stem cell transplant
 - solid organ transplant
 - haematological malignancy
 - advanced or untreated HIV

National Immunisation Program



- If previously received free Zostavax shingles vaccine under the NIP, not eligible for a free Shingrix vaccine for at least 5 years.
- If you purchased Zostavax vaccine privately, can receive Shingrix for free under the program if eligible
- Wait at least 12 months between receiving Zostavax and getting the Shingrix vaccine.

Concluding Remarks

- The economic and public health burden of VZV and PHN is considerable
- The recombinant zoster vaccine Shingrix is highly effective and provides long-lasting immunity and protection
- Cost-effective analyses are complex
- Published cost-effectiveness analyses support the use of Shingrix over the live Zostavax vaccine or no vaccine in high socioeconomic countries



A joint Australian, State and Territory Government Initiative

National Immunisation Program Changes to shingles vaccination from 1 November 2023

Answers to commonly asked questions

From 1 November 2023, the shingles vaccine Shingrix® will replace Zostavax® on the National Immunisation Program (NIP) for eligible people.

Who can get the free vaccine?

A 2-dose course of Shingrix® will be available free for:

- people aged 65 years and over
- Aboriginal and Torres Strait Islander people aged 50 years and over, and
- immunocompromised people aged 18 years and over with the following medical conditions:
 - haemopoietic stem cell transplant
 - solid organ transplant
 - haematological malignancy (blood cancer)
 - advanced or untreated HIV.

What is shingles?

Shingles is a viral infection that causes a painful blistering rash. It is caused by reactivation of the same virus that causes chickenpox. While most symptoms typically last 2-3 weeks, shingles can become serious. It can lead to nerve pain that can last for months (called post-herpetic neuralgia or PHN). Other serious complications include pneumonia, hearing problems, blindness and swelling of the brain.

About 1 in 3 people will get shingles in their lifetime. Shingles usually affects older people, and the risk of complications increases with age, particularly for:

- those over the age of 65
- Aboriginal and Torres Strait Islander people aged 50 and over
- some people with weakened immune systems.

How and where can I get the free shingles vaccine?

Check with your vaccination provider if you can get a free shingles vaccine. The vaccine and eligibility will change from 1 November 2023.

While the vaccine is free under the NIP for eligible people, your vaccination provider **may charge a consultation fee** for the visit. Check if there are any fees when making your appointment.

You can book a vaccine appointment at a range of health services including:

- local doctor/general practices
- local council immunisation clinics (available in some states and territories)
- community health centres (available in some states and territories)
- Aboriginal health services
- participating pharmacies.

Not all these vaccination providers will have the free NIP vaccines so it's best to call ahead and check.

If you are not eligible to receive the free Shingrix® vaccine under the NIP, talk to your doctor about your needs and whether you can buy it privately. You may need a prescription. Talk to your local vaccination provider to find out how much it will cost.