

The Socio-Economic
Value of Adult
Immunisation
Programmes
APPENDICES

CONTRACT RESEARCH REPORT
APRIL 2024

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Appendix 1: Country heatmaps of evidence for the value of adult immunisation programmes

TABLE A1: AUSTRALIA

Key

X = Evidence available	No evidence
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Value domain	Population health				Healthcare system		Society				
Value element	Impact on quality of life of vaccinated	Impact on mortality of vaccinated	Impact on quality of life of carers	Transmission value	Cost offsets to healthcare system	Value to other interventions	Impact on productivity of vaccinated	Impact on carer productivity	Social equity value	AMR prevention value	Macroeconomic effects
Influenza	X	X		X	X		X			X	
Pneumococcal	X	X		X	X						
RSV	X										
HZ	X										
All vaccines	X	X		X	X		X			X	



TABLE A2: BRAZIL

Key

X = Evidence available	No evidence
------------------------	-------------

Value domain	Population health				Healthcare system		Society				
Value element	Impact on quality of life of vaccinated	Impact on mortality of vaccinated	Impact on quality of life of carers	Transmission value	Cost offsets to healthcare system	Value to other interventions	Impact on productivity of vaccinated	Impact on carer productivity	Social equity value	AMR prevention value	Macroeconomic effects
Influenza	X	X			X		X				
Pneumococcal											
RSV	X										
HZ	X										
All vaccines	X	X			X		X				



TABLE A3: FRANCE

Key

X = Evidence available	No evidence
------------------------	-------------

Value domain	Population health				Healthcare system		Society				
Value element	Impact on quality of life of vaccinated	Impact on mortality of vaccinated	Impact on quality of life of carers	Transmission value	Cost offsets to healthcare system	Value to other interventions	Impact on productivity of vaccinated	Impact on carer productivity	Social equity value	AMR prevention value	Macroeconomic effects
Influenza	X	X		X	X						
Pneumococcal	X			X							
RSV											
HZ	X										
All vaccines	X	X		X	X						



TABLE A4: GERMANY

Key

X = Evidence available	No evidence
------------------------	-------------

Value domain	Population health				Healthcare system		Society				
Value element	Impact on quality of life of vaccinated	Impact on mortality of vaccinated	Impact on quality of life of carers	Transmission value	Cost offsets to healthcare system	Value to other interventions	Impact on productivity of vaccinated	Impact on carer productivity	Social equity value	AMR prevention value	Macroeconomic effects
Influenza	X	X			X		X				
Pneumococcal	X	X		X	X		X				
RSV	X										
HZ	X	X			X						
All vaccines	X	X		X	X		X				



TABLE A5: ITALY

Key

X = Evidence available	No evidence
------------------------	-------------

Value domain	Population health				Healthcare system		Society				
Value element	Impact on quality of life of vaccinated	Impact on mortality of vaccinated	Impact on quality of life of carers	Transmission value	Cost offsets to healthcare system	Value to other interventions	Impact on productivity of vaccinated	Impact on carer productivity	Social equity value	AMR prevention value	Macroeconomic effects
Influenza	X	X			X		X				
Pneumococcal					X		X				
RSV	X										
HZ	X				X		X				
All vaccines	X	X			X		X				



TABLE A6: JAPAN

Key

X = Evidence available	No evidence
------------------------	-------------

Value domain	Population health				Healthcare system		Society				
Value element	Impact on quality of life of vaccinated	Impact on mortality of vaccinated	Impact on quality of life of carers	Transmission value	Cost offsets to healthcare system	Value to other interventions	Impact on productivity of vaccinated	Impact on carer productivity	Social equity value	AMR prevention value	Macroeconomic effects
Influenza	X	X		X	X		X				
Pneumococcal	X	X			X		X	X			
RSV	X										
HZ	X	X			X		X	X			
All vaccines	X	X		X	X		X	X			



TABLE A8: SOUTH AFRICA

Key

X = Evidence available	No evidence
------------------------	-------------

Value domain	Population health				Healthcare system		Society				
Value element	Impact on quality of life of vaccinated	Impact on mortality of vaccinated	Impact on quality of life of carers	Transmission value	Cost offsets to healthcare system	Value to other interventions	Impact on productivity of vaccinated	Impact on carer productivity	Social equity value	AMR prevention value	Macroeconomic effects
Influenza	X	X		X	X		X	X			
Pneumococcal	X	X			X		X				
RSV	X										
HZ											
All vaccines	X	X		X	X		X	X			



TABLE A10: UNITED STATES OF AMERICA

Key

X = Evidence available	No evidence
------------------------	-------------

Value domain	Population health				Healthcare system		Society				
Value element	Impact on quality of life of vaccinated	Impact on mortality of vaccinated	Impact on quality of life of carers	Transmission value	Cost offsets to healthcare system	Value to other interventions	Impact on productivity of vaccinated	Impact on carer productivity	Social equity value	AMR prevention value	Macroeconomic effects
Influenza	X	X		X	X		X	X			
Pneumococcal	X	X			X				X		
RSV	X	X		X	X						
HZ	X	X			X		X				
All vaccines	X	X		X	X		X	X	X		

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**THE SOCIO-ECONOMIC VALUE OF ADULT IMMUNISATION
PROGRAMMES**

Appendix 2: Benefit-Cost Analysis - Technical Appendix

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1 Background

This Technical Appendix describes the methods and approaches used to analyse the benefits and costs of four adult immunisation programmes across ten countries. A high-level summary of the methods, results and policy implications are presented in Chapter 2: Benefit-cost analysis of adult immunisation programmes. Full results, including sensitivity analyses, are presented in the Appendix 3. A comprehensive list of data inputs and sources is provided in the Supplementary Materials.

2 Objectives

The analysis aims to estimate the aggregable costs and benefits associated with a range of adult immunisation programmes in a diverse set of countries, compared to a state of the world where these programmes are not implemented at all. The adult immunisation programmes analysed are for herpes zoster (HZ), influenza, pneumococcal disease (PD) and respiratory syncytial virus (RSV). Our analysis considers ten countries: Australia, Brazil, France, Germany, Italy, Japan, Poland, South Africa, Thailand, and the US.

3 Approach & Model Framework

3.1 General overview

Our approach is based on the Reference Case Guidelines for Benefit-Cost Analysis in Global Health and Development (Robinson et al., 2019) and therefore distinguishes between monetary inputs into a policy option (i.e. immunisation program) and monetised outputs (i.e. monetised gains in health and wealth) to assess the benefit-cost-profile of a policy option. As we aim to produce aggregable results which are comparable across countries, our approach prioritises consistency in modelling and outcome metrics, which leads to trade-offs with country-specificity.

Two disease-specific considerations are critical to our approach. First, the vaccination programs targeting influenza, PD and RSV differ from HZ, as the former prevent substantial mortality, while the latter is rarely fatal but prevents substantial morbidity and negative impacts on quality of life. The Reference Case Guidelines (Robinson et al., 2019) recommend different approaches to monetising health benefits, which vary in the extent to which they reflect mortality and morbidity, as well as in the associated data requirements. Hence, we apply a different approach to HZ with monetised quality-adjusted life years (QALYs) compared to influenza, PD and RSV, which use the value of statistical life (VSL) and life years (VSLY), as explained in Appendix 2 (sub-section).

Secondly, as vaccines for RSV were first approved in mid-2023 and are therefore emerging rather than established, our modelling for RSV relies on hypothetical programme specifications and coverage rates.

We structure our analysis into two blocks:

1. Publicly provided national programs which generate value mostly from preventing mortality that are either established (Flu, PD) or emerging (RSV)
2. Established publicly provided national programmes which generate value mostly from preventing morbidity

We use disease-specific models applied consistently across countries and based on two archetypes:

- Archetype 1 models for single cohorts: PD and HZ are single cohort models and follow a birth cohort from the eligible vaccination age to the age of 100 or death. Both also only include a one-time vaccination.
- Archetype 2 models for multi-cohort programmes (influenza and RSV) are multi-cohort models that capture all various eligible ages of vaccination. They follow each age cohort at and above the vaccination age until the age

of 100 or death. For RSV, we limit the period of analysis to a two-year analysis for every eligible age cohort because there is no further data from the CDC regarding the efficacy of both currently approved RSV vaccines against our RSV model outcomes.

An overview of the relationship between model choice, programme block, and monetisation approach of benefits is provided in Figure 1, and methodological details are provided in Chapter 5.

		Programme Type 1 <i>Publicly provided national programmes which generate health value mostly from preventing mortality</i>		Programme Type 2 <i>Established, publicly provided national programmes which generate health value mostly from preventing morbidity</i>
		Established	Emerging	
Archetype 1 Models Single Cohort	PD	Mortality: No. of deaths monetised using VSL and no. of LYL monetised VS LY Morbidity: COI Changes in time use: Loss of productivity monetised using human capital approach		HZ Mortality & Morbidity: No. of QALYs lost monetised using VS LY and GDP per capita Changes in time use: Loss of formal productivity using human capital approach
	Archetype 2 Models Multi Cohorts	FLU Mortality: No. of deaths monetised using VSL and no. of LYL monetised VS LY Morbidity: COI Changes in time use: Loss of productivity monetised using human capital approach	RSV Mortality: No. of deaths monetised using VSL and no. of LYL monetised VS LY Morbidity: COI Changes in time use: Loss of productivity monetised using human capital approach	

FIGURE 1: OVERVIEW OF VACCINATION PROGRAM CHARACTERISATION, MODEL CHOICE AND MONETISING OF BENEFITS.

The eligible population for immunisation under each program in each country is modelled on the national life table, an approach that follows previous work by Jit et al. (2014). Each country's official life tables are used for 8 out of 10 countries. No official governmental life tables could be retrieved for South Africa and Thailand; therefore, WHO life tables for these were used instead.

3.2 Established national programmes which generate value mostly by preventing mortality

PD

Model Overview

The model considers the outcomes following the decision tree Talbird et al. (2021) provided. We use a single cohort model, outlined in Figure 2, which follows a cohort at the vaccination age in a country's national schedule until age 100 or death, utilising the national life table. The results are, therefore, over a lifetime time horizon from the vaccination age.

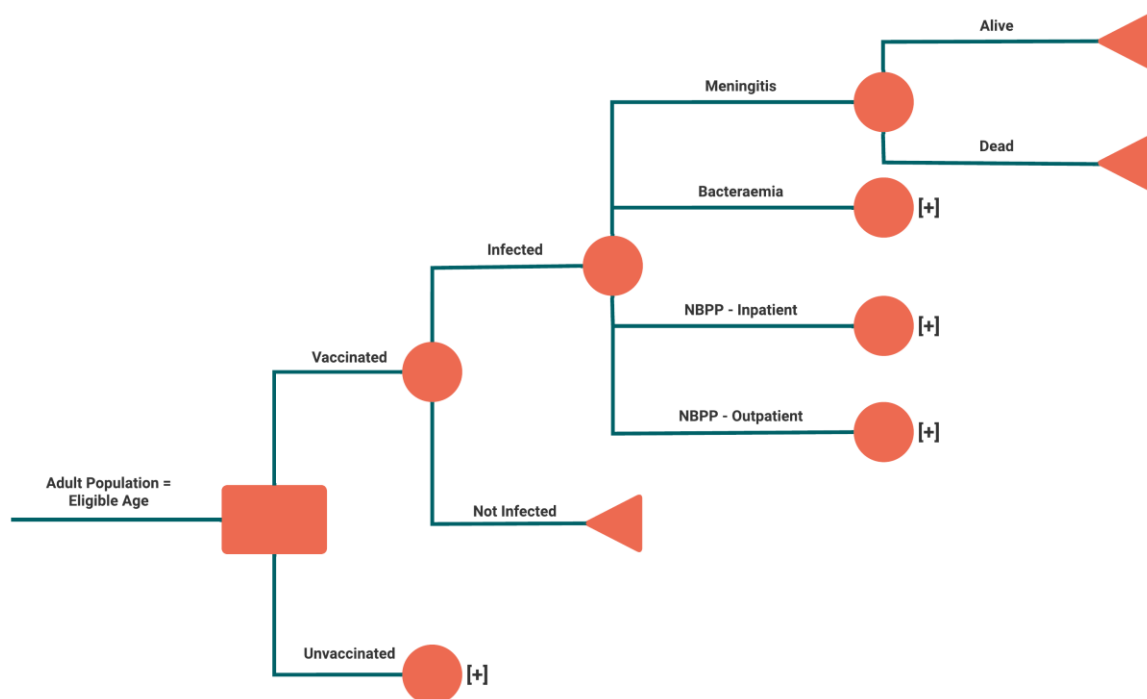


FIGURE 2: PNEUMOCOCCAL DISEASE MODEL

Incidence rates

We aim for country-specific and age-specific incidence and case fatality rates in the absence of vaccination, as specified in the supplementary material. If incidence rates for unvaccinated populations could not be retrieved, we would use country-specific incidence data while the vaccination programs were active. This would lead to underestimating the value of these programs against no vaccination. It should be noted that many programs that were historically in place, from where incidence data would be retrieved, would also use older and less efficacious vaccines in many countries. We adjust the incidences also by vaccine-type specific serotype by multiplying with an adjustment factor, which depends on the serotype distribution of IPD in that nation and the vaccine product being used in the nation's most recent guidelines. We assume this adjustment factor also applies to NBPP in the same way as IPD.

Vaccination program specifications

We model one complete vaccination course based on one dose within the base year and assume specific efficacy rates against the invasive pneumococcal disease (IPD) and non-bacteraemic pneumococcal pneumonia (NBPP) outcomes with IPD including meningitis and bacteraemia as defined in Talbird et al. We aimed to find age-specific and country-specific coverage rates where possible and used the most current recommendation of a nation's national immunisation programme (NIP) to define which vaccine product to use and, thus, which efficacy parameters to use. We do not use local effectiveness rates due to a lack of data availability. Waning rates for each

vaccine product were calculated as simple linear efficacy decrements annually, based on the protection of the duration of the vaccine and the initial efficacy. These are presented in Table 2.

Influenza

Model Overview

The model, outlined in Figure 3, considers the outcomes following the decision tree provided by Talbird et al. (2021). We use a multi-cohort model which follows every age cohort at and above the eligibility age for annual adult flu vaccinations until death or the age of 100 following an official life table. The results are, therefore, over a lifetime time horizon starting at the age of recommended influenza vaccination within a country.

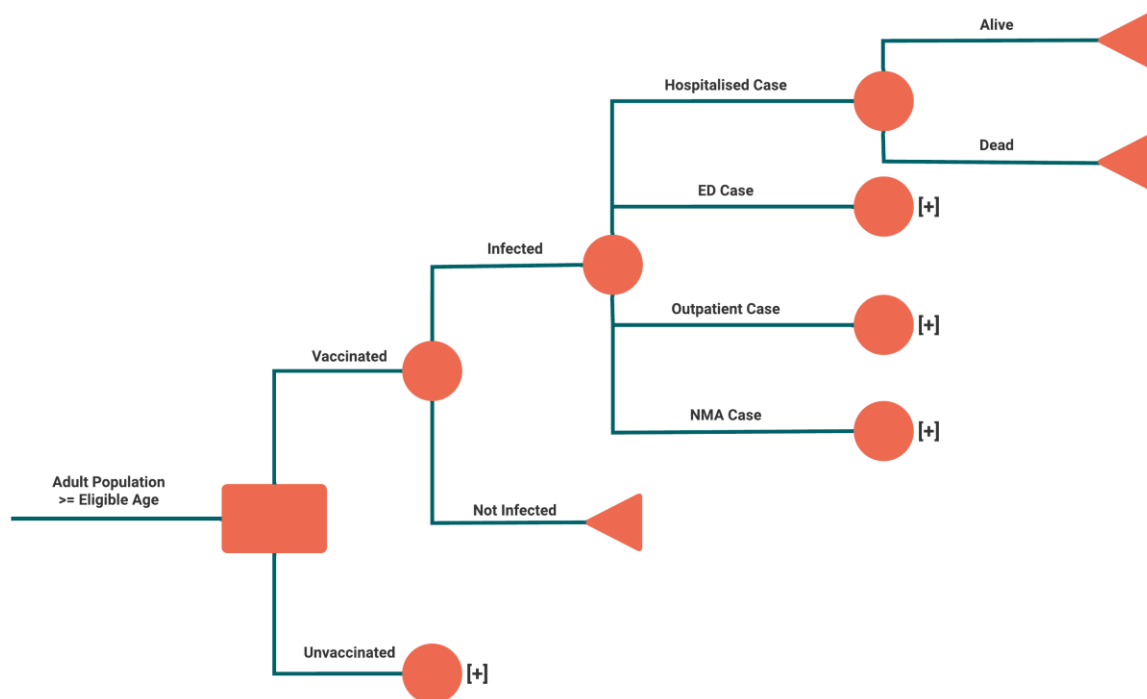


FIGURE 3: INFLUENZA DISEASE MODEL

Incidence Rates

Due to poor data availability amongst our age groups and selection of countries, we standardise incidence rates across all countries using the median point of the WHO global average of influenza attack rates for adults at 7.5% (Influenza, 2024). Further complications with finding localised data included many incidences, including influenza-like illnesses (ILI), a lack of sentinel data collection of influenza notifications, especially in Thailand and South Africa, and possible obfuscation with other respiratory illnesses.

Vaccination program specifications

We model an annual vaccination course based on one dosage and calculate the efficacy against influenza cases based on averages from CDC data (CDC, 2023) involving quadrivalent vaccines and apply this to all countries. This is due to the varying levels of efficacy of flu vaccines, varying products circulating in different parts of the world, and further complications arising from trivalent vaccines in some countries being more effective than quadrivalent vaccines and changing efficacy levels due to local flu serotype distributions. The average efficacy estimated from CDC data was often lower than country-specific effectiveness rates found in the countries where we could find data. However, due to poor data availability across our whole selection of countries and the complications, as stated before, we used the average efficacy as a pragmatic conservative solution to this data discrepancy. We

assume no waning effects with our annual vaccination specification. Due to the seasonality of flu cases, we assume that most flu cases and thus protection against them occur within narrow periods each year, with every subsequent vaccination protecting against the next flu season.

As influenza vaccination coverages differed by age group in the Talbird model, we aimed for age-specific coverage rates in our flu model across all ten countries. These are presented in Table 3.

3.3 Emerging national programmes which generate value mostly from preventing mortality

RSV

Model Overview

The model considers the outcomes as described by the Advisory Committee on Immunization Practices (ACIP), a committee within the US Center for Disease Control and Prevention (Ortega-Sanchez, 2023), which include hospitalisation cases/ED as well as outpatient cases, outlined in Figure 4. These were chosen because they allow for the averaging of the efficacy of the currently available RSV vaccines, Arexvy and Abrysvo since each had a different clinical endpoint in their respective trials. The de-novo model decision tree is presented below in Figure 5.

We use a multi-cohort model that follows every age cohort at and above the eligibility age for RSV vaccination. Due to the limit of vaccine efficacy data, further expanded on below, we use a two-year time horizon with a single vaccination in the first year for all eligible ages. All results are, therefore, a reflection of costs/benefits after a single year of RSV vaccinations. It is likely there are still lingering protection effects after two years, thus we may have an underestimation of the benefits of RSV vaccination. However, due to data uncertainty in this follow-up period, we follow the time horizon of the data provided in the ACIP slides.

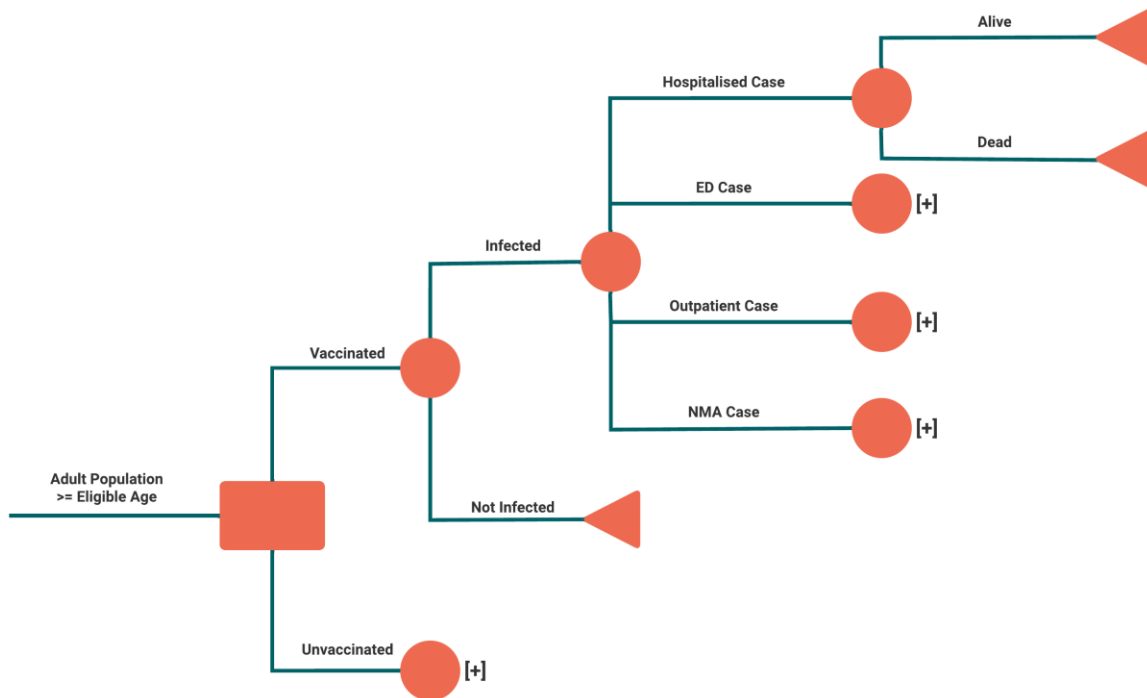


FIGURE 4: RESPIRATORY SYNCYTIAL VIRUS MODEL

Incidence rates

As with the other programs, we aimed for country-specific and age-specific incidence and case fatality rates in the absence of vaccination, as specified in the supplementary material. For RSV, due to there being no existing NIPs for adult RSV vaccination, it was assumed all adult incidence data was for unvaccinated populations, with the possibility of private vaccination being minimal due to many of these RSV vaccines being licensed for sale very recently in 2023.

Vaccination program specifications

We model one vaccination course based on one dose within the US and German setting as these were the only countries within our sample that had already committed to implementing the adult RSV program and had publicly available prices for both currently licensed vaccines, Arexvy (GSK) and Abrysvo (Pfizer). The model assumes a single shot of an “averaged” vaccine and thus uses an averaged efficacy from both products, with the efficacy calculations presented in Table 1. Season 1 corresponds to the first year of vaccination, and season 2 corresponds to year two in our model, after which we assume no more benefits from vaccination.

We average the vaccine efficacy for Arexvy and Abrysvo as outlined in Table 1 based on data published by the CDC (ACIP June 21-23, 2023 Presentation Slides | Practices | CDC, 2023). This approach considers the initial efficacy per season and ignores any waning over one season.

TABLE 1: AVERAGE EFFICACY VALUES FOR AREXVY AND ABRYSVO.

	Hospitalisation	Outpatient
Arexvy endpoint	Severe LRTD	LRTD
Season 1	94.1%	82.6%
Season 2	64.2%	56.1%
Abrysvo endpoint	3 s/s LRTD	2 s/s LRTD
Season 1	88.9%	65.1%
mid-Season 2	78.6%	48.9%
Averages	Hospitalisation Outcome	Outpatient outcome
Season 1	91.5%	73.9%
Season 2	71.4%	52.5%

Due to RSV adult immunisation being hypothetical, we proxy the RSV coverage rates with flu coverage rates for Germany. For the US, we base coverage rates on a RSV vaccination intent analysis conducted by the CDC, (Respiratory Syncytial Virus (RSV) Vaccination Coverage and Intent for Vaccination, Adults 60 Years and Older, United States | CDC, 2024); we only count those who fall into the categories of vaccinated and who “definitely will get a vaccine” in our hypothetical coverage rates. This increases the uncertainty around the coverage rates which could bias the estimated NMBs upwards or downwards. For example, our estimate might be an overestimate due to selection bias since people selected into the survey, and hence do not represent the general population’s desirability of getting the vaccine. On the other hand, the large category of people in the “probably will get a vaccine or are unsure” category, means that many more people might get the vaccine, which would mean we underestimate the potential coverage.

3.4 Established national programmes which generate value mostly from preventing morbidity

Herpes Zoster

Model Overview

The model considers the outcomes following the decision tree provided by Talbird et al. (2021). We use a single cohort model that follows a cohort at vaccination age in a country’s national schedule until age 100 or death following an official life table.

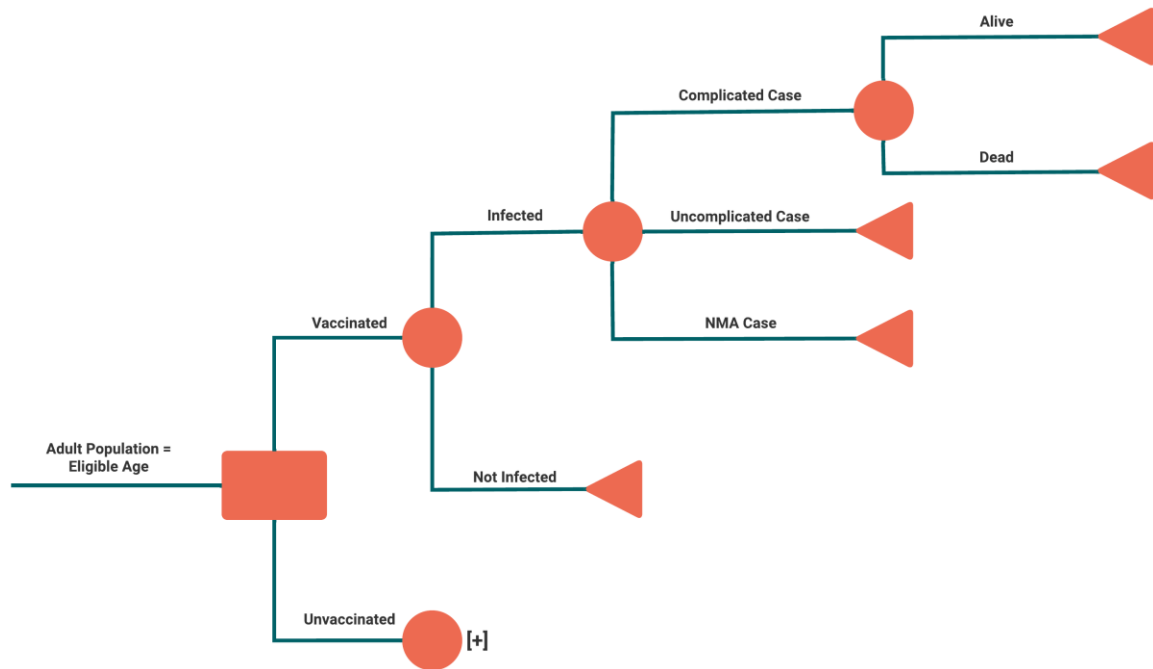


FIGURE 5: HERPES ZOSTER MODEL

Incidence rates

We aim for country-specific and age-specific incidence rates for our outcomes with complicated cases, including post-herpetic neuralgia and other non-pain complications and uncomplicated cases not involving any complications but still requiring some medical involvement, such as visits to a medical facility and/or medicinal prescriptions.

We aimed to use age-specific case fatality rates, which are very low in the context of HZ, a disease which largely impacts quality of life rather than length of life. For this reason, we use a monetised QALY approach that is better suited to capture the impact of preventing morbidity, which we explain in section 5.2.2. In case incidence rates for unvaccinated populations could not be retrieved, we would use country-specific incidence data while the vaccination programs were active, this would lead to an underestimation of the value of these programs against no vaccination. Much like with PD, many programs that were historically in place, from where incidence data would be retrieved, would also use older and less efficacious vaccines than the vaccines we have modelled.

Vaccination program specifications

We model one complete vaccination course based on either one dose (for Zostavax) or two doses (for Shingrix) within the base year and assume efficacy rates against HZ cases as a whole. We aimed to find age-specific and country-specific coverage rates where possible and used the most current recommendation of a nation's national immunisation programme (NIP) to define which vaccine product to use and, thus, which efficacy parameters and dosage to use. We do not use local effectiveness rates due to a lack of data availability, especially for newer products such as Shingrix. We use a simplifying assumption and apply different waning rates for Shingrix based on the age at vaccination derived from the ZOE study outlined in (Van Oorschot et al., 2019), with rates shown in Table 4.

4 Immunisation programme specifications and inputs

For established immunisation programmes (influenza, PD and HZ), we include in our analysis all programmes where there is currently a formal age-based recommendation, and we approximate the programme characteristics specified in these recommendations. For RSV, we model emerging programmes based on any commitments to NIPs by countries and where publicly accessible prices are available for both Abrysvo and Arexvy.

Vaccine coverage, price and administration costs are derived from country-specific data sources where possible. Vaccine prices were only able to be used if they were publicly accessible.

All costs, similar to all monetised benefits, were inflated then converted if required to 2022 international dollars following methodology 2 outlined in (Turner et al., 2019) before being input into the model.

Vaccine efficacy per product was standardised across the country selection to allow for model consistency. For influenza, due to multiple efficacy rates per product per country, we used an averaged vaccine efficacy based on CDC data (CDC, 2023) for consistency. For RSV, we use an averaged vaccine efficacy between Arexvy and Abrysvo, based on ACIP data as outlined above; this reflects the current US recommendation, which is the basis for our specification of the emerging RSV programme in Germany.

4.1 Existing national programmes which generate health value mostly by preventing mortality

TABLE 2: PD IMMUNISATION PROGRAMME SPECIFICATIONS

	Eligible age	Vaccination asset(s)	Vaccination schedule	Vaccine Dosage Cost	Efficacy	Waning Assumptions (Linear efficacy decrement per year based on duration of protection)	Coverage	Incidence adjustment factor for vaccine-type serotypes
Australia	70	PCV-20	Single Dose	81 AUD (2018)	75% against IPD 45% against NBPP	4.69% for IPD efficacy 2.81% for NBPP efficacy	20.10%	49.2%
(Sources)	(Vaccines for Australian adults NCIRS, 2024)	(Pneumococcal disease The Australian Immunisation Handbook, 2023)	(Pneumococcal disease The Australian Immunisation Handbook, 2023)	(Perdrizet et al., 2021)	(Bonten et al., 2015)	(Gourzoulidis, Barmpouni and Vietri, 2023)	(Immunisation coverage and evaluation reports NCIRS, 2024)	(Care, 2023a)
Germany	60	PCV-20	Single Dose	95.96 EUR (2023)	75% against IPD 45% against NBPP	4.69% for IPD efficacy 2.81% for NBPP efficacy	50.89%	58.3%
(Sources)	(Epidemiologisches Bulletin 39/2023, 2023)	(Epidemiologisches Bulletin 39/2023, 2023)	(Epidemiologisches Bulletin 39/2023, 2023)	(APEXXNAR Injektionssuspension i.e.Fertigspritze (1 St) Preisvergleich, PZN 17445189 · MediPreis.de, 2024)	(Bonten et al., 2015)	(Gourzoulidis, Barmpouni and Vietri, 2023)	(Theidel, Kuhlmann and Braem, 2013)	(van der Linden et al., 2015)
Italy	65	PCV-20	Single Dose	55.97 EUR (2022)	75% against IPD 45% against NBPP	4.69% for IPD efficacy 2.81% for NBPP efficacy	65%	68.1%

(Sources)	(EpiCentro, 2024)	(I vaccini offerti, 2024) (15-allegato-b-nota-operativa-antipneumo-20222023.pdf, n.d.)	(I vaccini offerti, 2024) (15-allegato-b-nota-operativa-antipneumo-20222023.pdf, n.d.)	(Polistena et al., 2022)	(Bonten et al., 2015)	(Gourzoulidis, Barmpouni and Vietri, 2023)	(Restivo et al., 2023)	(Surveillance Atlas of Infectious Diseases, 2024)
Japan	65	PPSV-23	Single Dose	4,666 JPY (2017)	73% against IPD 33.50% against NBPP	7.3% for IPD efficacy 3.35% for NBPP efficacy	41.80%	61%
(Sources)	(Vaccination schedule for Japan, 2024)	(Vaccination schedule for Japan, 2024)	(Vaccination schedule for Japan, 2024)	(Jiang et al., 2018)	(Falkenhorst et al., 2017)	(Suzuki et al., 2017)	(Murakami et al., 2019)	(Yanagihara et al., 2021)
United States	65	PCV-20	Single Dose	176.84 USD (2023)	75% against IPD 45% against NBPP	4.69% for IPD efficacy 2.81% for NBPP efficacy	67.50%	56%
(Sources)	(Pneumococcal Vaccination: What Everyone Should Know CDC, 2023)	(Pneumococcal Vaccination: What Everyone Should Know CDC, 2023)	(Pneumococcal Vaccination: What Everyone Should Know CDC, 2023)	(VFC Current CDC Vaccine Price List CDC, 2023)	(Bonten et al., 2015)	(Gourzoulidis, Barmpouni and Vietri, 2023)	(Vaccination Coverage among Adults in the United States, National Health Interview Survey, 2019–2020 CDC, 2023)	(2016-2021 Serotype Data for Invasive Pneumococcal Disease Cases by Age Group from Active Bacterial Core surveillance Data Centers for Disease Control and Prevention, 2024)

TABLE 3: INFLUENZA IMMUNISATION PROGRAMME* SPECIFICATION

	Eligible age	Vaccination asset(s)	Vaccination schedule	Vaccine Dosage Cost	Efficacy (Calculated Average)	Coverages for eligible age groups
Australia	65 and above	Quadrivalent Flu Vaccine	Annual 1 Dose	19.99 AUD (2023)	35.47%	68.60% for 65+

(Sources)	(Adults aged ≥ 65 years are recommended to receive influenza vaccine every year The Australian Immunisation Handbook, 2023, p.65)		(Book a Flu (Influenza) Shot at Chemist Warehouse, 2024)	(CDC, 2023)	(National influenza vaccination coverage - all people NCIRS, 2024)	
Brazil	60 and above	Quadrivalent Flu Vaccine	Annual 1 Dose	33.89 BRL (2019)	35.47%	87% for 60-64 87% for 65+
(Sources)	(Changing the Conversation on Adult Influenza Vaccination: Brazil - Vaccines 4 Life, 2020)		(Crépey et al., 2020)	(CDC, 2023)	(Jamotte et al., 2017)	
France	65 and above	Quadrivalent Flu Vaccine	Annual 1 Dose	11.20 EUR (2017)	35.47%	48.60% for 65+
(Sources)	(Vaccine Scheduler ECDC, 2024)		(Sandmann et al., 2022)	(CDC, 2023)	(Uhart et al., 2016)	
Germany	60 and above	Quadrivalent Flu Vaccine	Annual 1 Dose	11.60 EUR (2019)	35.47%	40% for 60-64 40% for 65+
(Sources)	(RKI - STIKO Recommendations, 2024)		(Cai et al., 2021)	(CDC, 2023)	(Kohli et al., 2022)	
Italy	65 and above	Quadrivalent Flu Vaccine	Annual 1 Dose	6.99 EUR (2017)	35.47%	56.70% for 65+
(Sources)	(Vaccine Scheduler ECDC, 2024)		(de Waure et al., 2019)	(CDC, 2023)	(Copertura vaccinale in Italia, 2024)	
Japan	65 and above	Quadrivalent Flu Vaccine	Annual 1 Dose	3640 JPY (2021)	35.47%	49.30% for 65+
(Sources)	(Changing the Conversation on Adult Influenza Vaccination: Japan - Vaccines 4 Life, 2024)		(vaccine-price-eng202104.pdf, n.d.)	(CDC, 2023)	(Tsuzuki, Schwehm and Eichner, 2018)	
Poland	65 and above	Quadrivalent Flu Vaccine	Annual 1 Dose	51.46 PLN (2023)	35.47%	13.40% for 65+
(Sources)	(Vaccine Scheduler ECDC, 2024)		(Jak wygląda refundacja szczepionek przeciw grypie w sezonie 2023/2024?, 2024)	(CDC, 2023)	(Brydak, Kosek and Nitsch-Osuch, 2012)	
Thailand	65 and above	Quadrivalent Flu Vaccine	Annual 1 Dose	990 THB (2023)	35.47%	30% for 65+
(Sources)	(Vaccination schedule for Thailand, 2024)		(Flu Vaccine Package Bangkok Hospital, 2024)	(CDC, 2023)	(Prasert et al., 2019)	

South Africa	65 and above	Quadrivalent Flu Vaccine	Annual 1 Dose	3.04 USD 2018	35.47%	3.10% for 65+
(Sources)	(Flu vaccines made available for priority groups, 2024)			(Fraser et al., 2022)	(CDC, 2023)	(Edoka et al., 2021)
United States	50 and above	Quadrivalent Flu Vaccine	Annual 1 Dose	15.49 USD	35.47%	44.80% for 50-59 44.80% for 60-64 65.40% for 65+
(Sources)	(Talbird et al., 2021)			(VFC Current CDC Vaccine Price List CDC, 2023)	(CDC, 2023)	(Talbird et al., 2021)

*For seasonal influenza vaccinations, no waning is assumed between annual vaccinations.

4.3 Existing national programmes which generate health value mostly from preventing morbidity

TABLE 4: HZ IMMUNISATION PROGRAMME SPECIFICATIONS

	Eligible age	Vaccination asset(s)	Vaccination schedule	Vaccine Dosage Cost	Efficacy	Waning Assumptions (Linear efficacy decrement per year)	Coverage (for both doses if applicable)
Australia	70	Shingrix	2 Doses	560 AUD (2022) for 2 doses	95.40% for 70+	2.30% for 70+	30.90%
(Sources)	(PBAC, 2023)			(Care, 2023b)	(Strezova et al., 2022)		(Immunisation coverage and evaluation reports NCIRS, 2024)
France	65	Zostavax	1 Dose	104.36 EUR (2022)	64%	4.15% for 50-69	20%
(Sources)	(Vaccine Scheduler ECDC, 2024)			(ZOSTAVAX pdre/solv p susp inj en ser préremplie, 2024)	(Bresse et al., 2013)		
Germany	60	Shingrix	2 Doses	267.24 EUR (2021) for 2 doses	98.90% for 50+	1.50% for 50-69	20%
(Sources)	(RKI - STIKO Recommendations, 2024)			(Curran et al., 2021)	(Strezova et al., 2022)		(Ultsch et al., 2013)
Italy	65	Shingrix	2 Doses	332.20 EUR (2023) for 2 doses	98.90% for 50+	1.50% for 50-69	11.9%
(Sources)	(Volpi et al., 2019)			(Barbieri and Boccacini, 2023)	(Strezova et al., 2022)		(Ceccarelli et al., 2022)
Japan	50	Shingrix	2 Doses	25,920 JPY 2020 for 2 doses	98.90% for 50+	1.50% for 50-69	38%
(Sources)	(Japan's Ministry of Health, Labour and Welfare approves Shingrix for the prevention of shingles in at-risk adults aged 18 and over GSK, 2023)			(Shiragami et al., 2019)	(Strezova et al., 2022)		(Teng et al., 2022)
United States	50	Shingrix	2 Doses	241.85 USD (2023) for 2 doses	98.90% for 50+	1.50% for 50-69	29.40%
(Sources)	(Herpes Zoster Shingrix Vaccine Recommendations CDC, 2023)			(VFC Current CDC Vaccine Price List CDC, 2023)	(Strezova et al., 2022)		(Vaccination Coverage among Adults in the United States, National Health Interview Survey,

				2019–2020 CDC, 2023)
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4.4 Emerging programmes to be rolled out in the future

TABLE 5: RSV IMMUNISATION PROGRAMME SPECIFICATIONS

	Eligible age (according to authorisation)	Vaccination asset(s)	Vaccination schedule	Vaccine Dosage Cost	Efficacy (Averaged)	Coverage (Hypothetical)
Germany	60 and above	Averaged product between Abrysvo and Arexvy	Single dose (Analysis limited to 2 years)	213.61 EUR (2023) for both products	91.50% in Year 1 against hospitalisation 71.40% in Year 2 against hospitalisation 73.85% in Year 1 against outpatient 52.50% in Year 2 against outpatient	40% for 60-64 (Proxied with flu coverage) 40% for 65+ (Proxied with flu coverage)
(Sources)	(News - Authorisation Granted for Respiratory Syncytial Virus (RSV) Vaccine - Paul-Ehrlich-Institut, 2024; Arexvy European Medicines Agency, 2024; Abrysvo European Medicines Agency, 2024)	(ACIP June 21-23, 2023 Presentation Slides Immunization Practices CDC, 2023)	Assumption	(www.shop-apotheke.com, 2024b; a)	(ACIP June 21-23, 2023 Presentation Slides Immunization Practices CDC, 2023)	(Kohli et al., 2022)
United States	60 and above	Averaged product between Abrysvo and Arexvy	Single dose (Analysis limited to 2 years)	198.40 USD (2023) (Averaged price between both Arexvy and Abrysvo, 198.4 & 219.72 respectively when checked)	91.50% in Year 1 against hospitalisation 71.40% in Year 2 against hospitalisation 73.85% in Year 1 against outpatient 52.50% in Year 2 against outpatient	31.20% for 60+ (from CDC intent analysis)

(Sources)	(Commissioner, 2023; RSV (Respiratory Syncytial Virus) Immunizations CDC, 2024)	(ACIP June 21-23, 2023 Presentation Slides Immunization Practices CDC, 2023)	Assumption	(VFC Current CDC Vaccine Price List CDC, 2023)	(ACIP June 21-23, 2023 Presentation Slides Immunization Practices CDC, 2023)	(Respiratory Syncytial Virus (RSV) Vaccination Coverage and Intent for Vaccination, Adults 60 Years and Older, United States CDC, 2024)
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5 BCA Framework

Our benefit-cost analysis (BCA) framework aligns with the Reference Case Guidelines (Robinson et al., 2019) in structuring and valuing costs and benefits, except for the allocation of adverse events costs (see Figure 6).

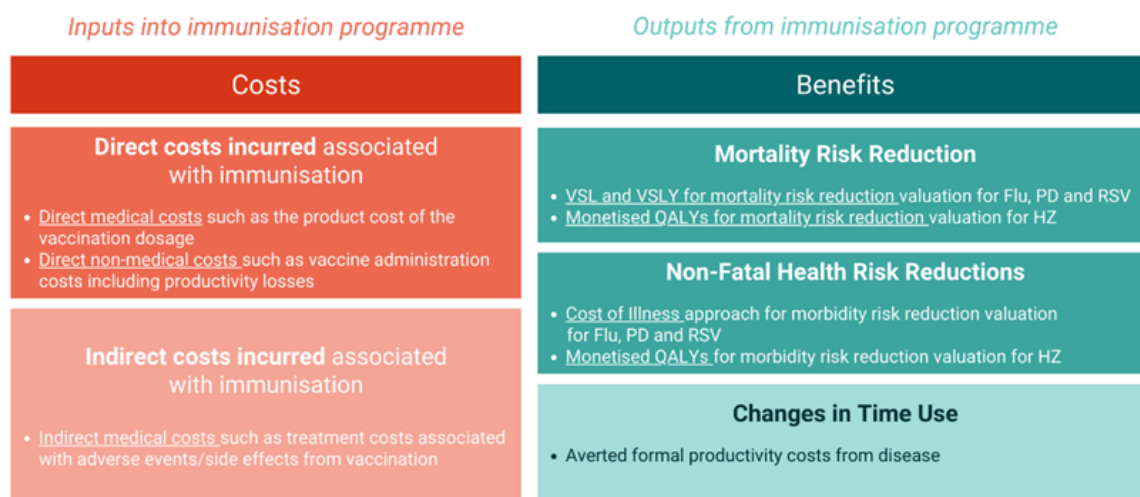


FIGURE 6: STRUCTURE OF COSTS AND BENEFITS INCORPORATED INTO BCA.

5.1 Costs

We include both the direct medical and direct non-medical costs of delivering the immunisation programme as well as part of the indirect costs. This approach ignores the costs associated with setting up the respective program within a country.

Direct medical costs are mainly comprised of vaccine dosage costs, included in all programmes. Direct non-medical costs comprise vaccine administration costs and productivity losses associated with vaccinations, which are included for all programmes modelled. For the latter, we assume 2 hours for all vaccinations in which working productivity is lost. We value this using hourly wages (adjusted by the labour force participation rate and unemployment rate). This is likely an overestimation of productivity losses due to vaccination since not all working adults would use working hours to attend a vaccination and may get vaccinated during appointments for other purposes. However, due to the uncertainty, we opted for a conservative approach and assumed all adults use working hours for vaccination (if they are employed).

We deviate slightly from the reference case as we add the vaccine-attributable adverse events as costs, proxied by the value of two common painkiller tablets per vaccine dose, instead of adding them as offsets to the benefits. While the costs are small and thus the effects marginal, this will lower the BCR since this captures the effect in the denominator rather than the numerator of the BCR ratio. We opt for this more conservative approach of incorporating adverse event costs also due to the lack of being able to include transportation costs across our country selection due to the data availability challenges. We do not include long-term adverse events or more serious adverse events from vaccination as these are low in probability, and data is sparse across our country selection. Instead, we assume all vaccinated individuals use painkillers to treat the localised inflammation of the injection sites.

All costs are presented in 2022 international dollars. Costs found in other currencies are first inflated/deflated using CPI in their country of origin to 2022 levels (OECD, 2023a; Japan Ministry of Health, 2023; IMF, 2023), then converted to international dollars using 2022 USD PPP exchange rates (OECD, 2023b). This follows “Method 2” of (Turner et al., 2019).

5.2 Benefits

Benefits include mortality risk reduction, nonfatal health risk reduction and changes in time use.

5.2.1 Mortality

Multiple approaches to valuing mortality risk reductions substantially impact estimated benefits and overall cost-benefit ratios. Following the BCA Reference Case (Robinson et al., 2019), we present a range of results using a reasonable upper and lower bound of values for averted mortality.

For diseases with a relatively greater impact on mortality (PD, influenza and RSV), the upper bound of our estimated benefit involves multiplying all fatal cases averted with the country-specific estimate for the value of a statistical life (VSL). VSL values for 2022 were only available for the US (US Department of Transportation, 2023) and Australia (Australian Government, 2023). Values for other countries were computed from the US VSL value following the methodology recommended by Nandi et al., 2022, and using GNI per capita values from the World Bank Open Data, 2023, assuming an income elasticity of one. The lower bound multiplies all life years lost (LYL) with a country-specific estimate for the value of a statistical life year (VSLY). VSLY is calculated by dividing the VSL by undiscounted future life expectancy at the average age of the adult population (Robinson, Hammitt and O’Keeffe, 2019). Following the BCA Reference Case (Robinson et al., 2019), we calculate this average using the age at which one would expect half of their life expectancy, from birth, to remain.

For HZ, a disease which creates a large quality of life loss but is rarely fatal, we capture the value of lowering the risk of mortality and morbidity together and explain the approach in section 5.2.2 below.

5.2.2 Morbidity

We apply two different approaches to estimating effects on morbidity, both of which are included in the BCA Reference Case.

For influenza, PD and RSV, we proxy effects on morbidity using the cost of illness (COI) approach due to the lack of high-quality monetary QALY estimates for our countries as a whole and following the BCA Reference Case (Robinson et al., 2019). The COI approach typically captures direct medical costs to third-party funders of health services as well as indirect non-medical costs averted through individual lost productivity and monetary costs such as transport. However, as per our approach to costs, we exclude transportation due to data availability.

For HZ, we value morbidity (and the small percentage of mortality) using monetised QALYs. This is because, unlike the other immunisation programmes considered, most of the health benefits of HZ immunisation programmes are derived from their effects on morbidity as opposed to mortality, which the VSL+COI approach may underestimate.

The Reference Case (Robinson et al., 2019) supports this as a valid methodology, but it does trade off with our ability to use country-specific data. We use age-specific QALY losses calculated for complicated and uncomplicated cases of HZ in the UK, with NMA cases being proxied by uncomplicated cases (Curran et al., 2017). We then apply these to the cases prevented due to vaccination across the eligible countries, all of which are high-income countries similar to the UK.

The number of QALYs is then valued with the VSLY value to obtain the upper bound and with GDP per capita to obtain the lower bound of our benefits. We use the VSLY value as our upper bound due to the reference case (Robinson, Hammitt and O’Keeffe, 2019) where VSLY is presented as a reasonable lower bound to VSL, valuing QALYs the same as to VSLY, in effect, shows the value of our programmes if quality of life was valued equally as highly as VSL/VSLY values mortality alone. Our lower bound of using a nation’s GDP per capita is based on the WHO suggestion of cost-effectiveness thresholds to be 1-3x the GDP per capita of a country. We also use the lowest value in this range to be conservative in our assumptions with supporting evidence, which showed that most cost-effectiveness thresholds were between 0.5 to 1.5 of a country’s GDP per capita (Iino, Hashiguchi and Hori, 2022).

5.2.3 Changes in time use

We include averted productivity costs due to reduced morbidity as benefits of using the human capital approach for all diseases. Given a lack of consistent data availability across our countries on the value of the informal market and the level of participation, we did not explicitly calculate productivity costs within the informal market or non-market productivity costs. Given that these may be significant, particularly for older age groups, our indirect cost

calculation likely underestimates averted productivity costs. Productivity costs were calculated using a standardised approach across the ten countries, adjusted for each disease area.

For labour markets, we used OECD data and official sources when OECD data was not available. We calculated an adjusted population employment rate by multiplying the labour force participation rate (%) by the reciprocal of the unemployment rate (%). Labour force participation rates were categorised for the following OECD age categorisation groups: people aged 50-64 and people aged 65-75. OECD unemployment rates were reported for people aged 25-75; thus, they are not age-specific for the population considered. Given a lack of standardised reporting across our selected countries, we assume no labour force participation for those older than 75. To calculate the expected value per lost work day, we multiply average daily wages (obtained from OECD 2022 data or official sources) by the adjusted population employment rate. Where non-OECD data was used, local currencies were converted to 2022 USD. Given a lack of age-specific data, average daily wages are assumed to be equal across the selected age groups. Details can be found in the supplementary material.

We did not include losses from presenteeism, which is also a notable cause of productivity losses, and hence, a further reason we are likely to underestimate the true productivity losses due to the four diseases in focus.

TABLE 5: SUMMARY OF COSTS AND BENEFITS INCLUDED PER IMMUNISATION PROGRAMME

		PD	HZ	Flu	RSV
Costs	• Direct medical costs such as vaccine costs	Product Costs	Product Costs	Product Costs	Product Costs
	• Direct non-medical costs such as vaccine administration costs and formal productivity losses due to attending vaccination	Administration Costs, Productivity Losses	Administration Costs, Productivity Losses	Administration Costs, Productivity Losses	Administration Costs, Productivity Losses
	• Indirect medical costs such as treatment costs associated with adverse events/side effects	Yes, Minor adverse events	Yes, Minor adverse events	Yes, Minor adverse events	Yes, Minor adverse events
	• Indirect-non-medical costs such as productivity losses due to side effects	No	No	No	No
Benefits	Mortality risk reduction				
	• Prevented cases with the Value per statistical life (VSL) and VSLY	Yes	N/A	Yes	Yes
	• Prevented mortality using monetised QALYs approach	N/A	Yes	N/A	N/A
	Morbidity risk reduction				
	• Prevented direct medical costs associated with most relevant health outcomes and disease costs using Cost of Illness approach	Yes	N/A	Yes	Yes
	• Prevented morbidity using monetised QALYs approach	N/A	Yes	N/A	N/A
	Changes in Time Use				
	• Prevented formal productivity costs	Yes	Yes	Yes	Yes
• Value of time that would be spend by family members and friends to care for affected individual	No	No	No	No	

6 Sensitivity Analyses

For each vaccination program modelled in each respective country, we applied one-way sensitivity analysis to assess the impact of each parameter on the BCR. We varied each parameter relatively to its baseline value by +/-20% and capped the individual value where necessary (e.g. efficacy rates at 100%). Only discount rates were varied by +/- 50%. We excluded varying the vaccination age because, for many countries, we did not have data under the recommended age of their respective NIPs. As the number of input parameters is in the hundreds, we present only the most impactful ones for each programme modelled.

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APRIL 2024

THE SOCIO-ECONOMIC VALUE OF ADULT IMMUNISATION
PROGRAMMES

Appendix 3: Benefit-Cost Analysis – Sensitivity Analysis - Results

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7	Poland.....	12
8	South Africa	13
9	Thailand	14
10	US	15

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Professor Lotte Steuten, PhD

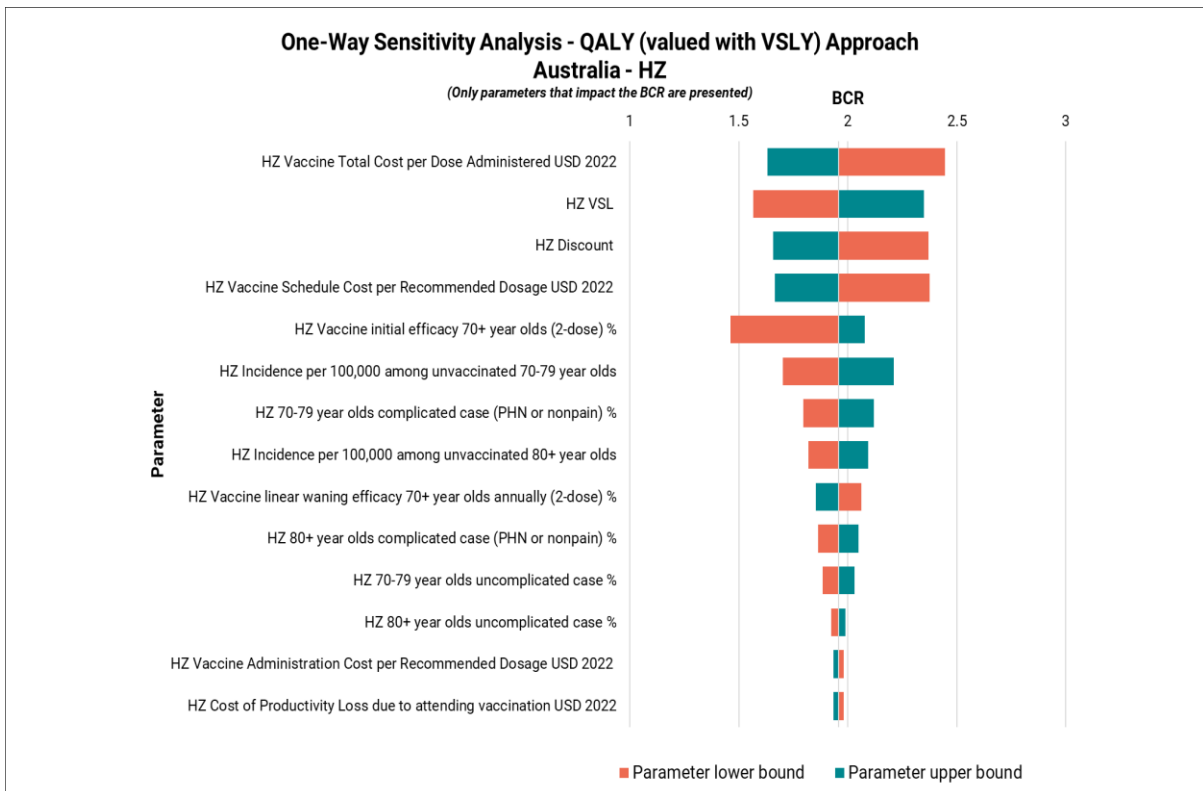
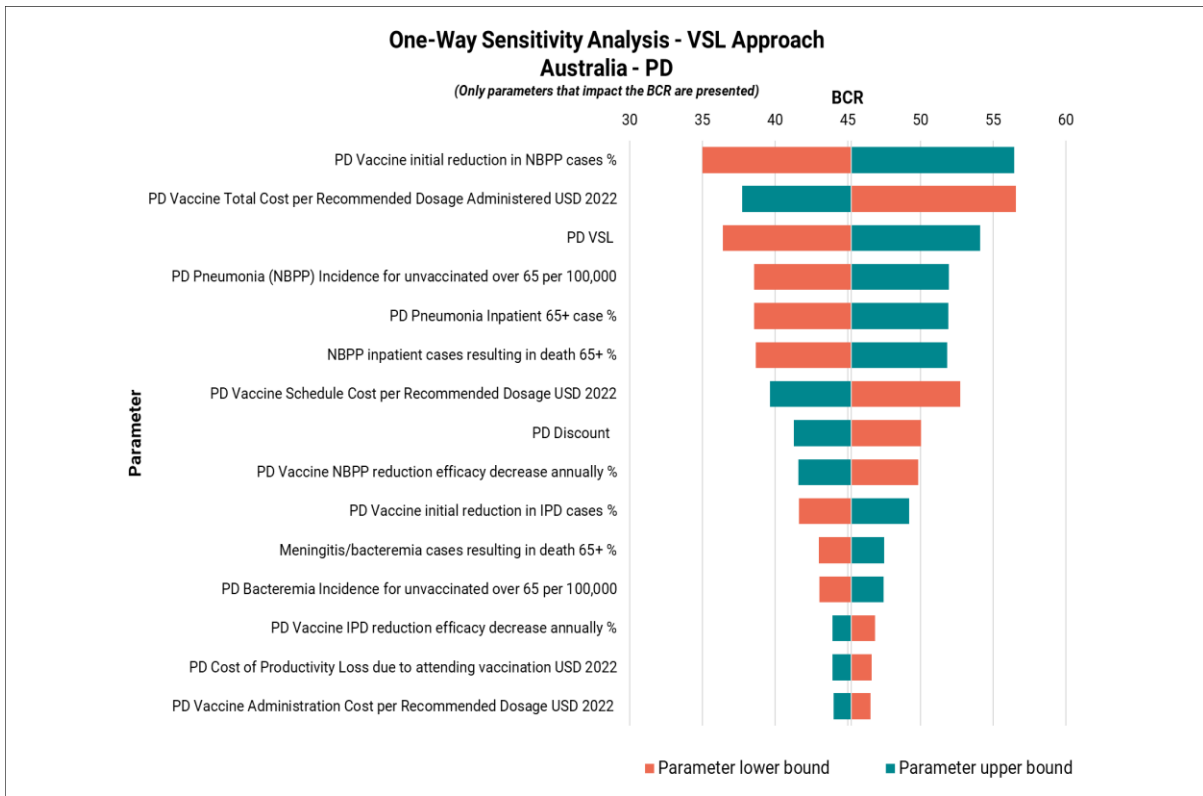
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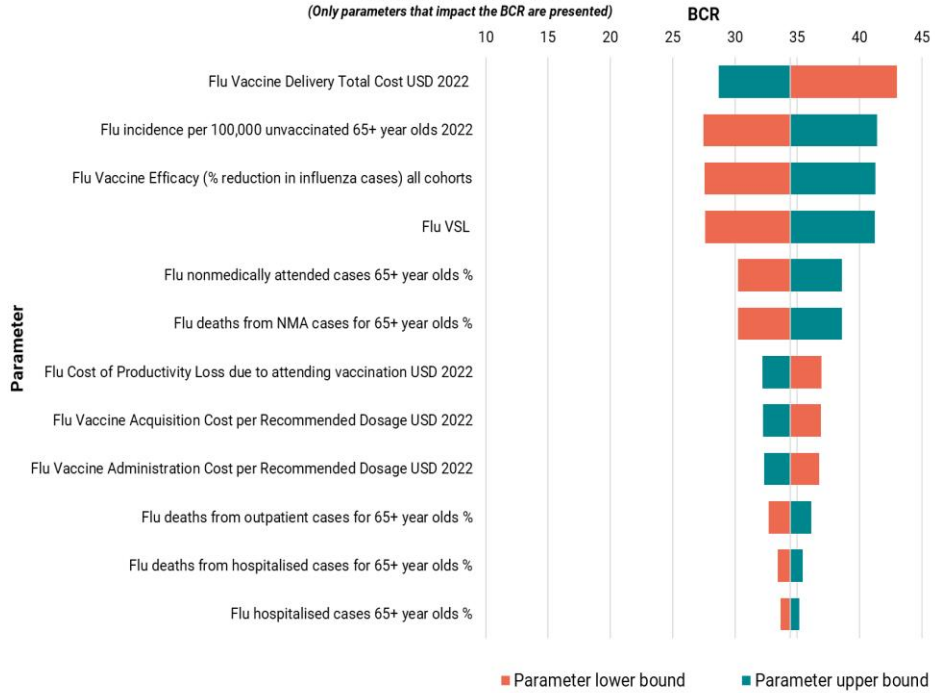
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1 Australia

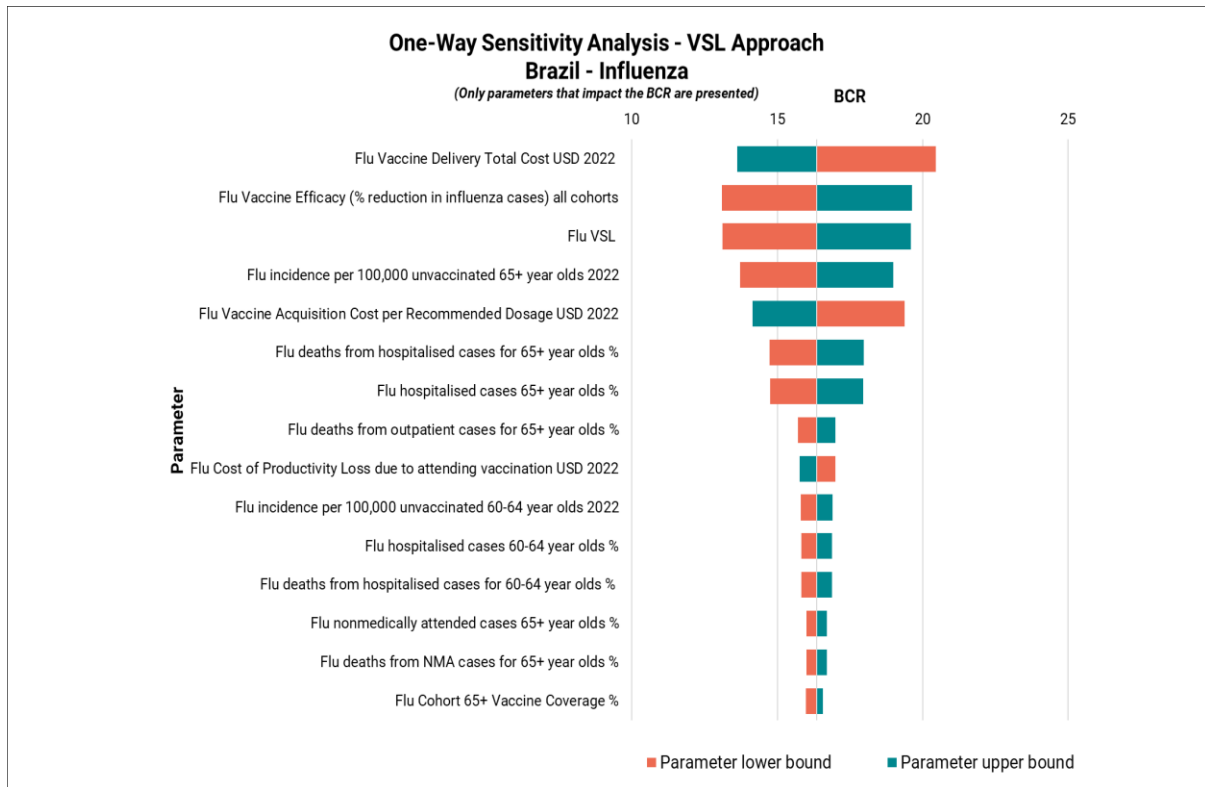


One-Way Sensitivity Analysis - VSL Approach Australia - Influenza

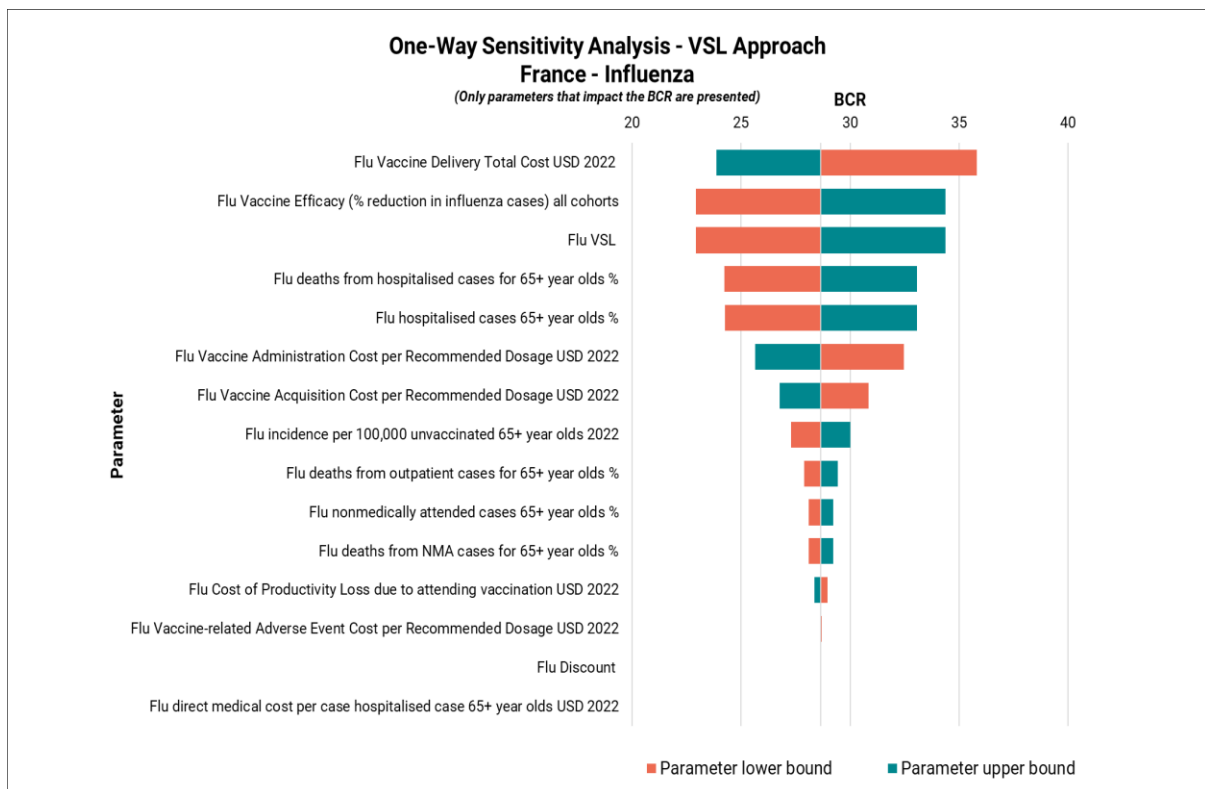
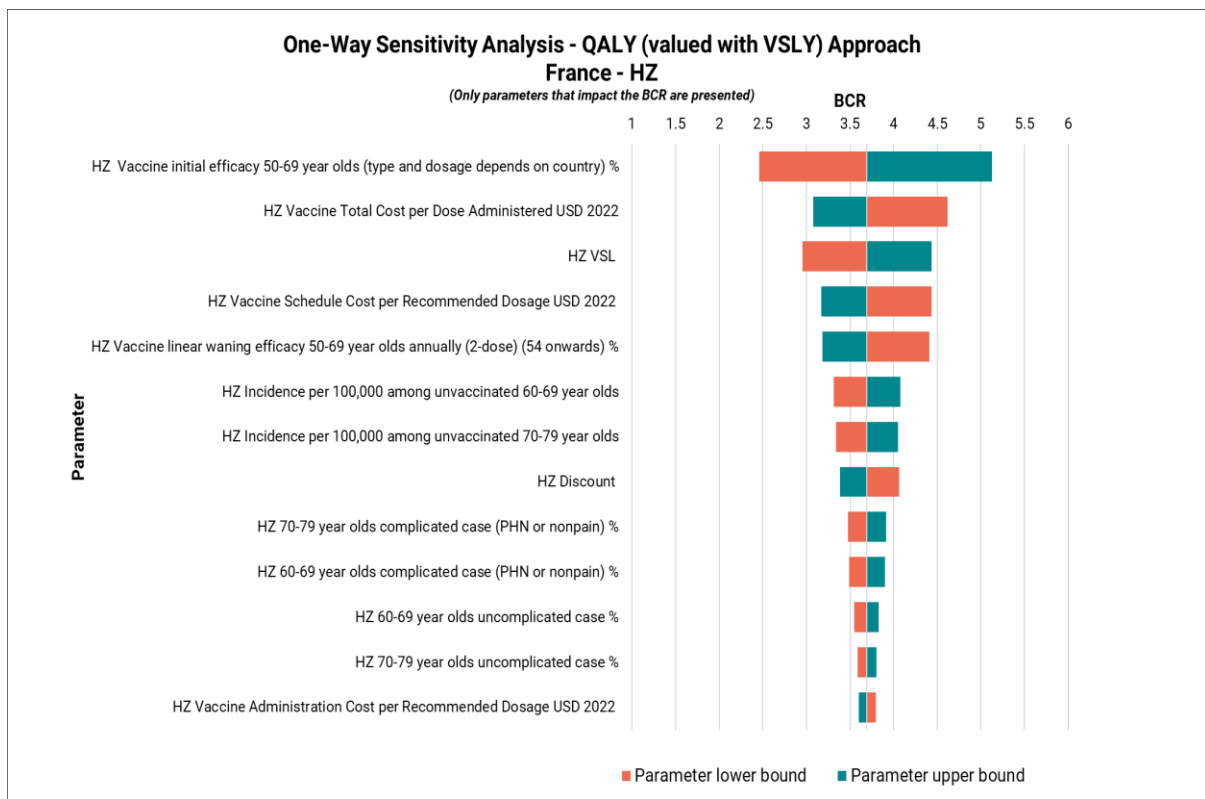
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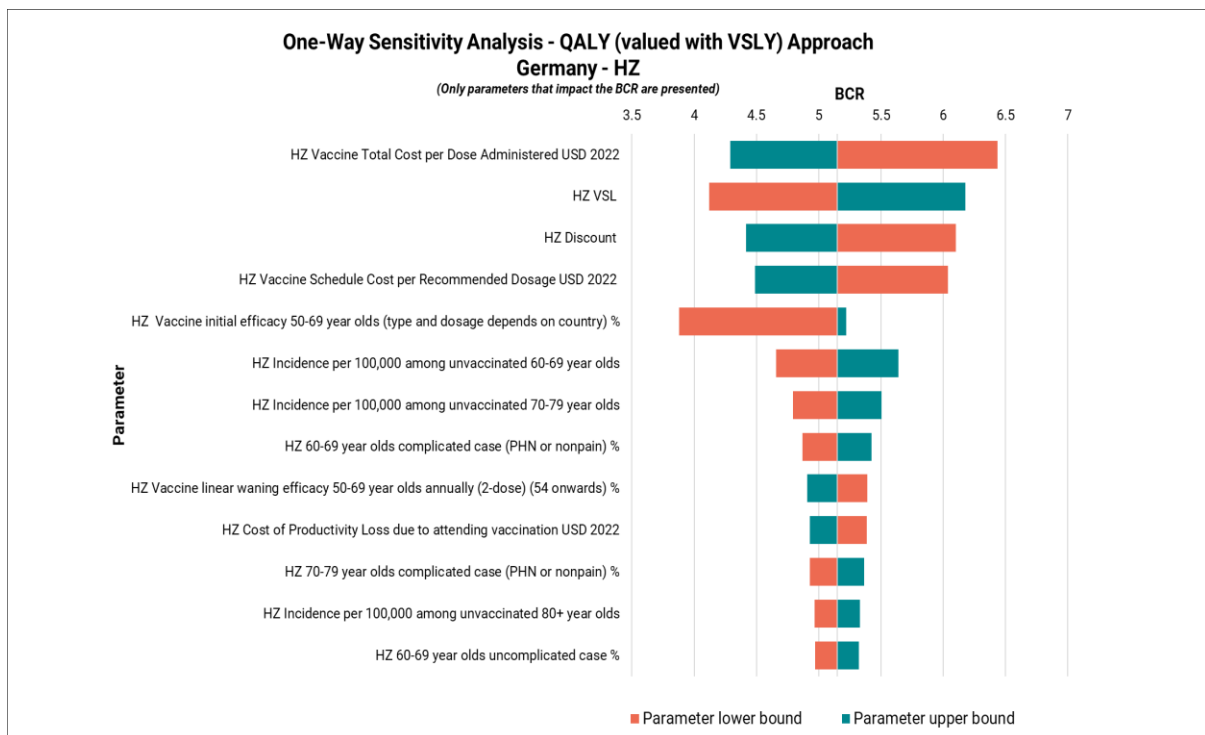
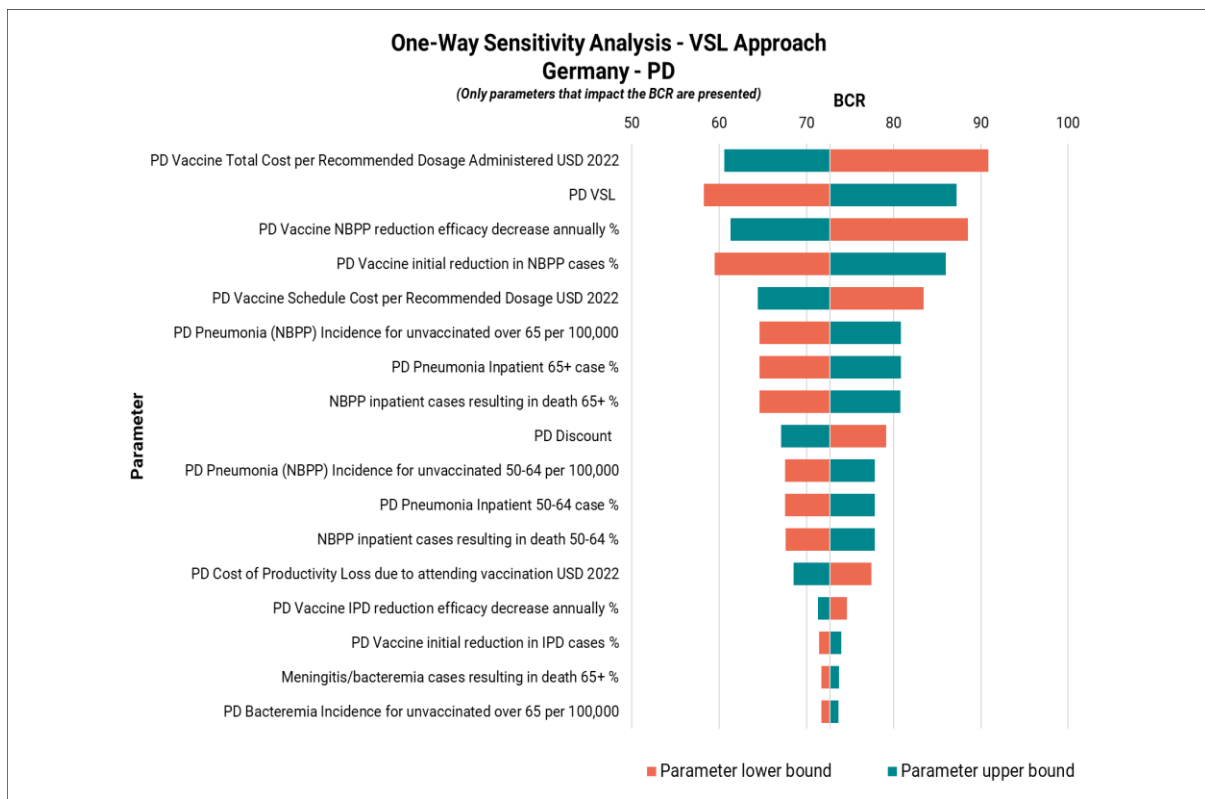
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3 France



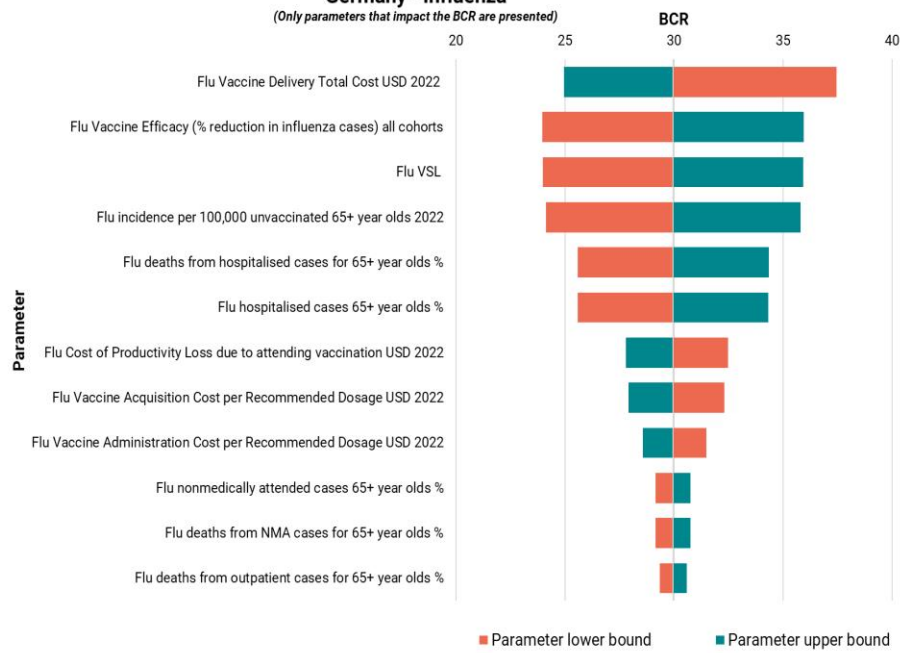
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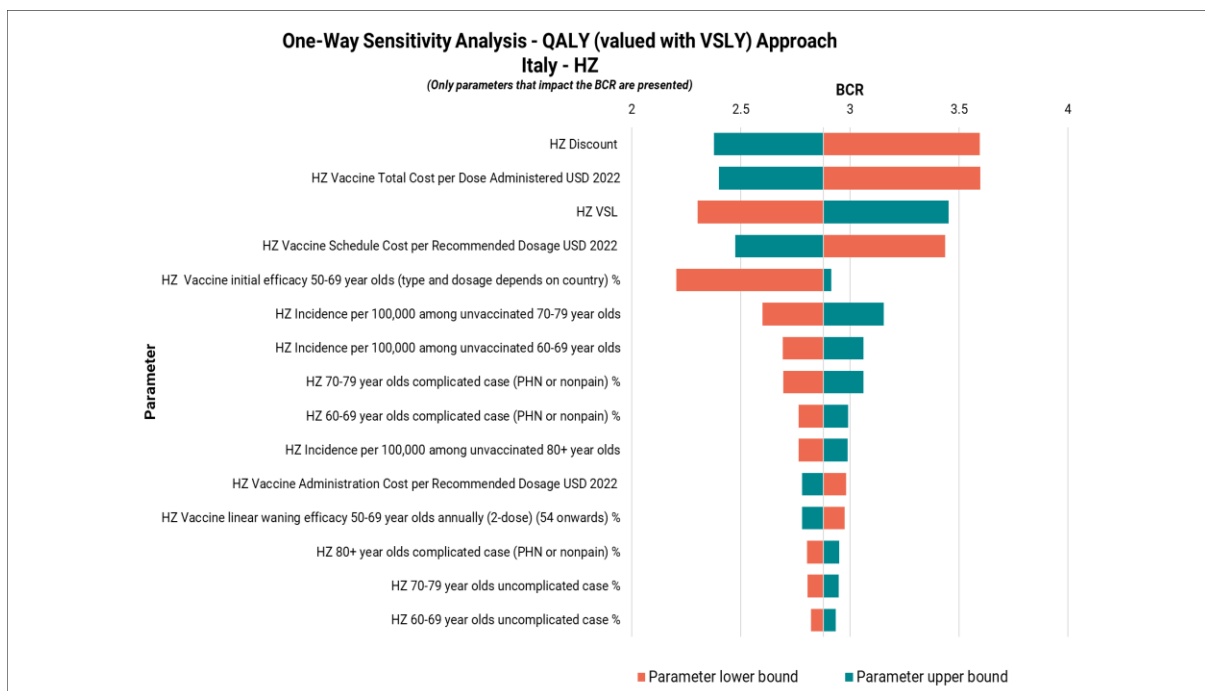
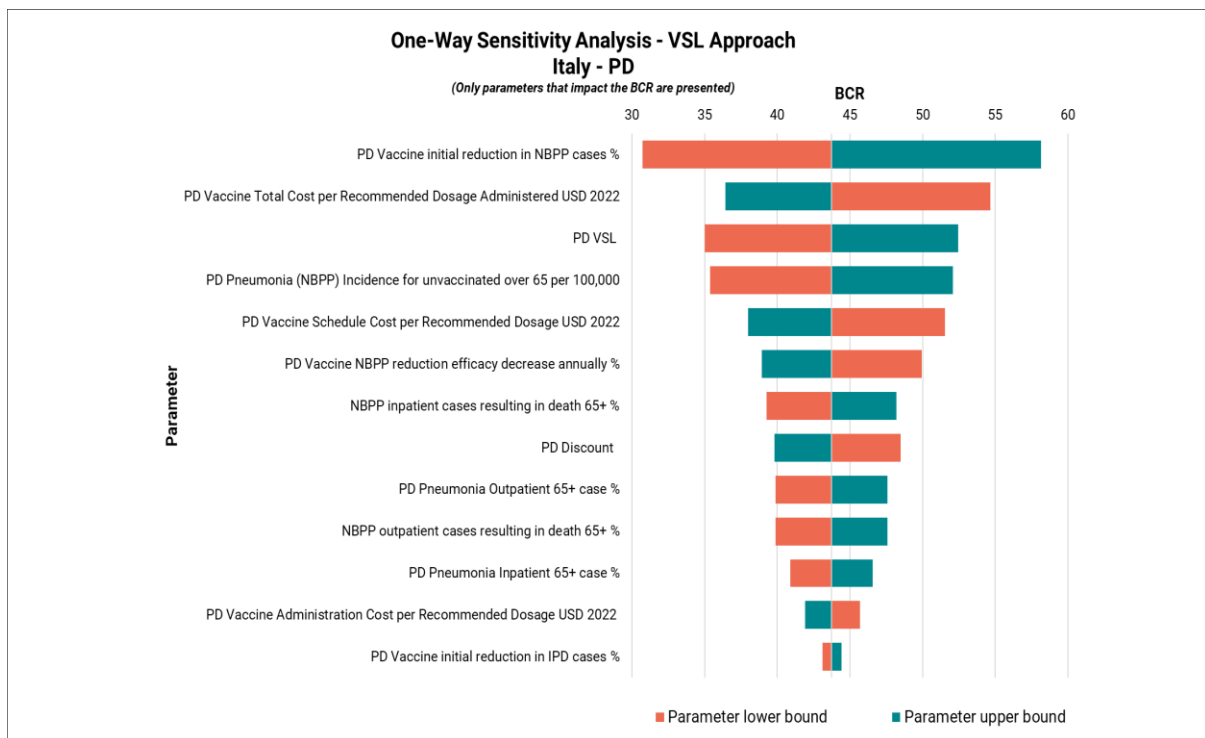
One-Way Sensitivity Analysis - VSL Approach

Germany - Influenza

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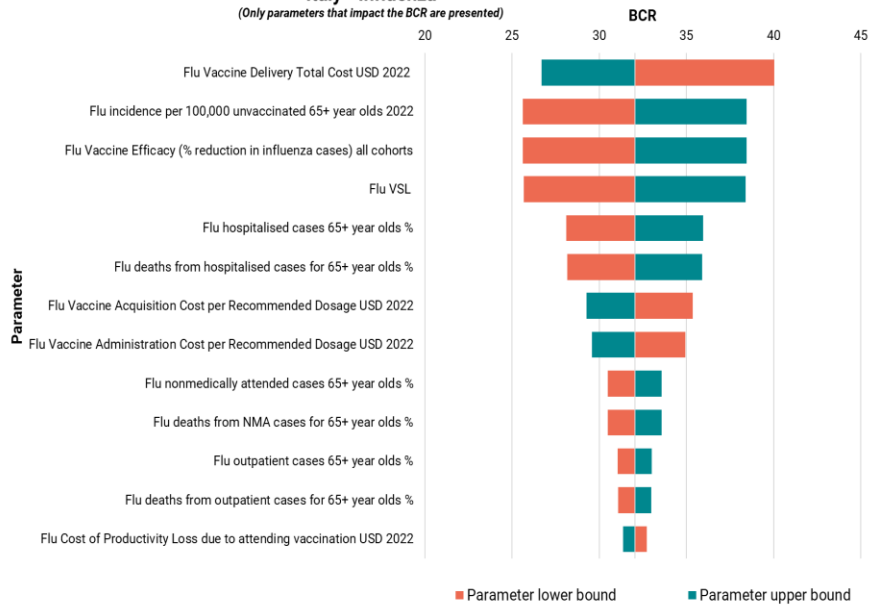


5 Italy

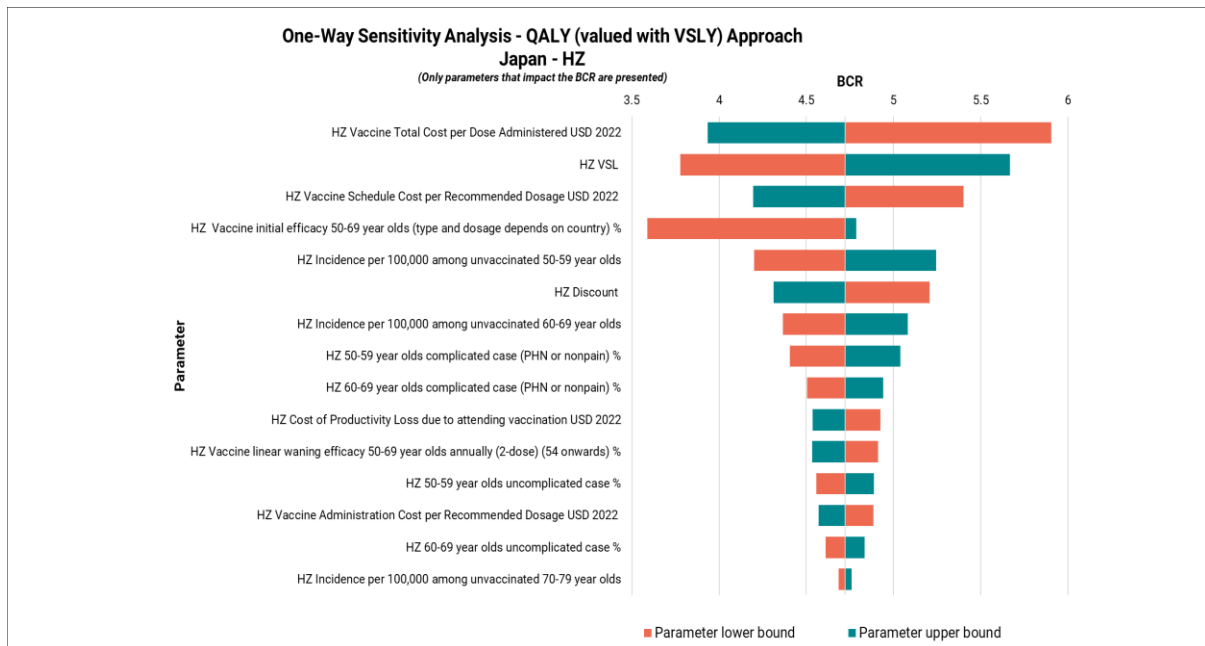
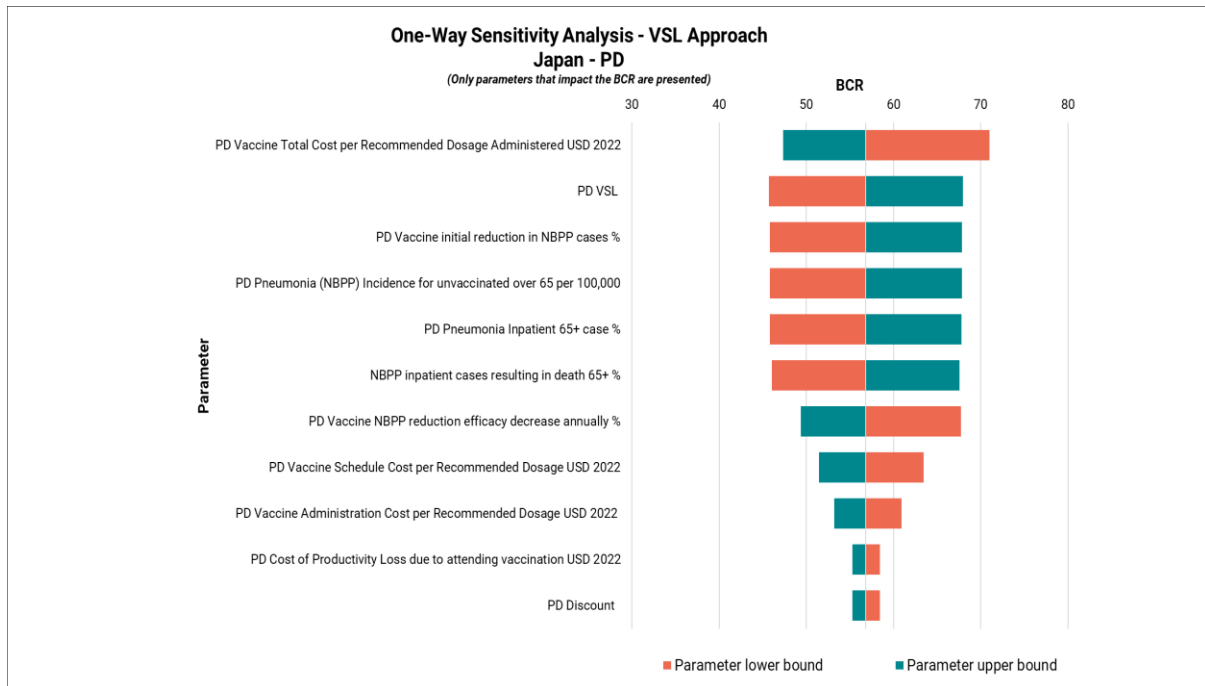


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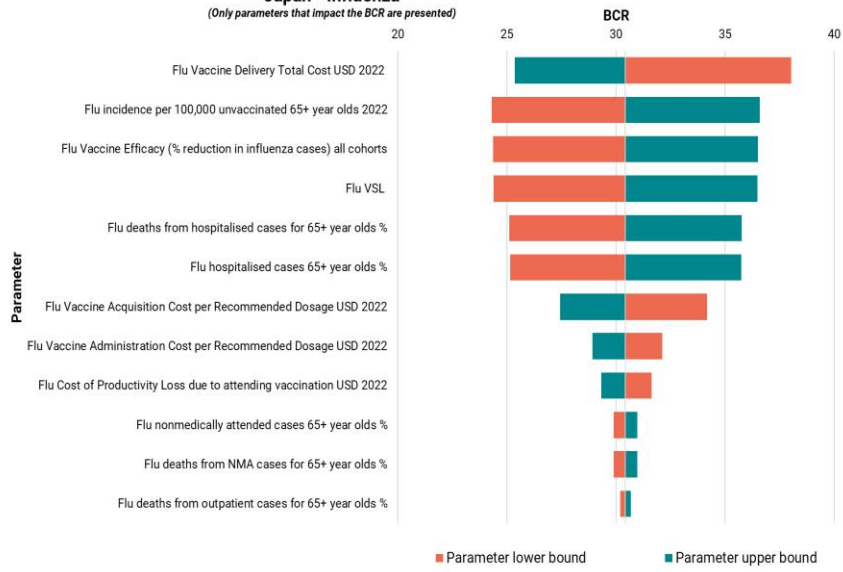


6 Japan

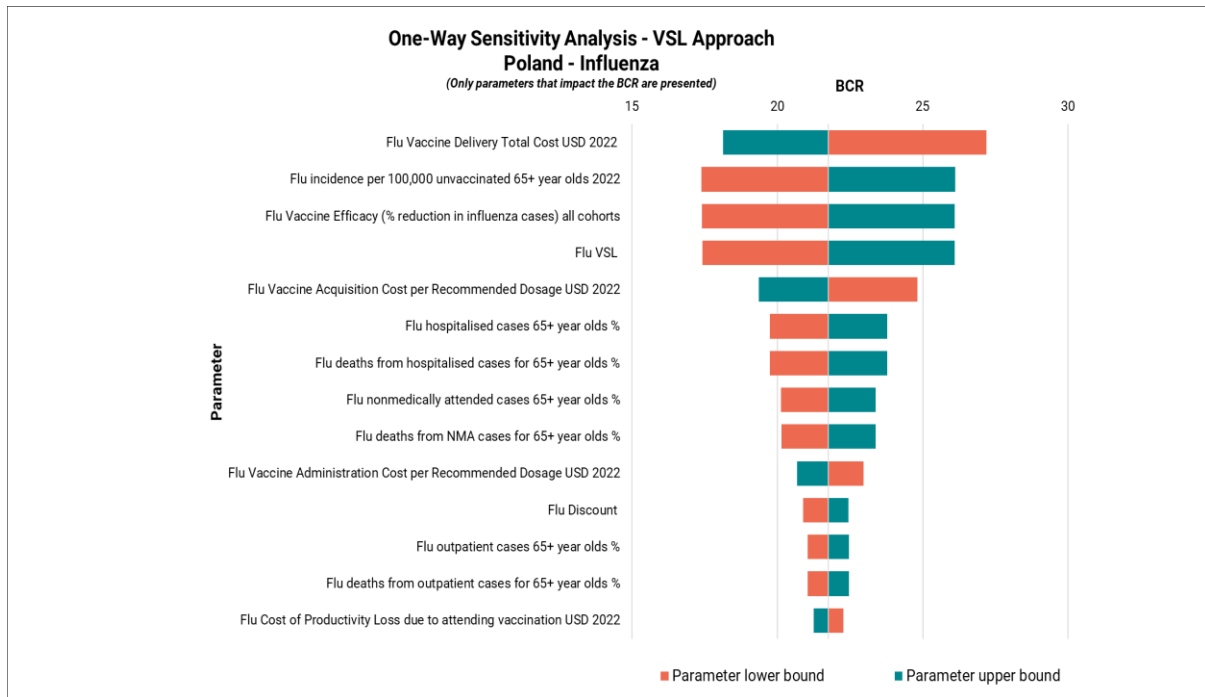


One-Way Sensitivity Analysis - VSL Approach Japan - Influenza

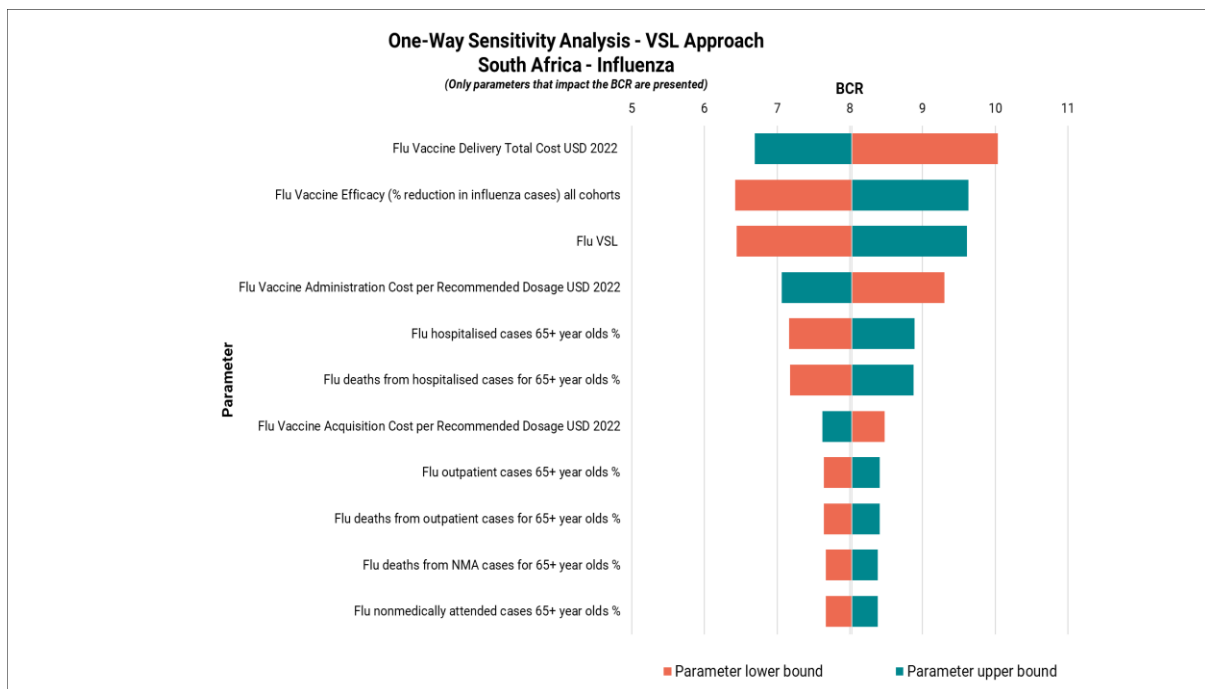
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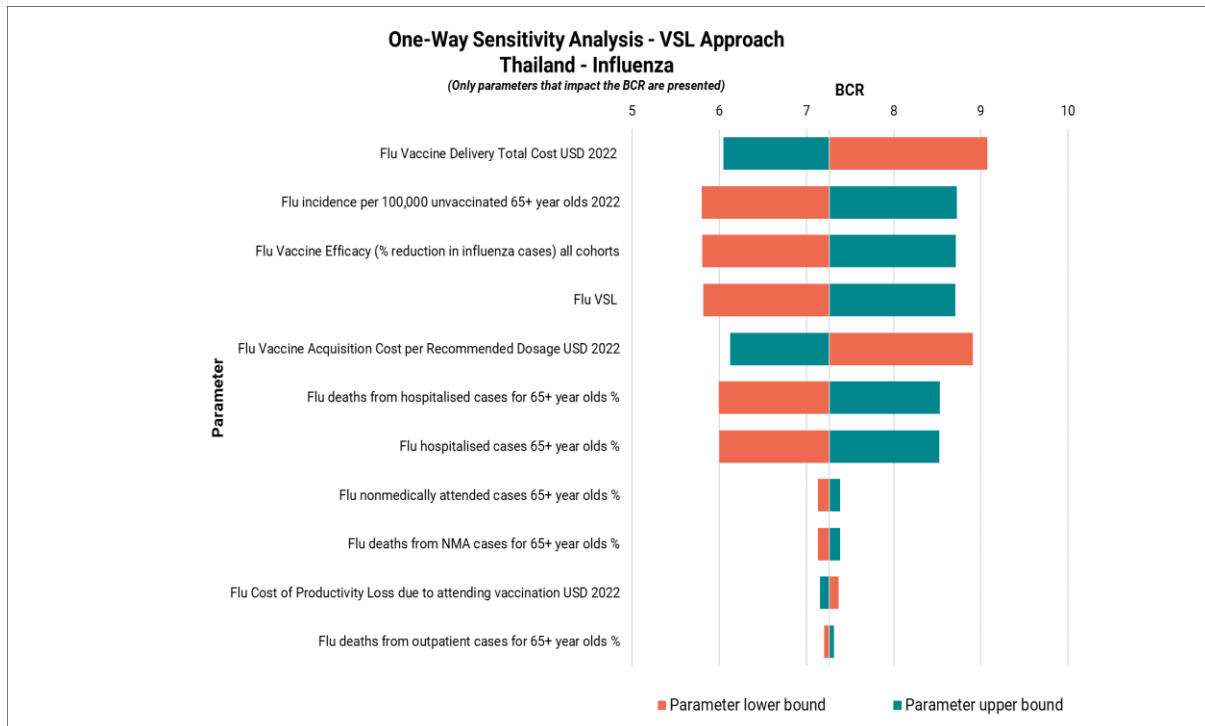
7 Poland

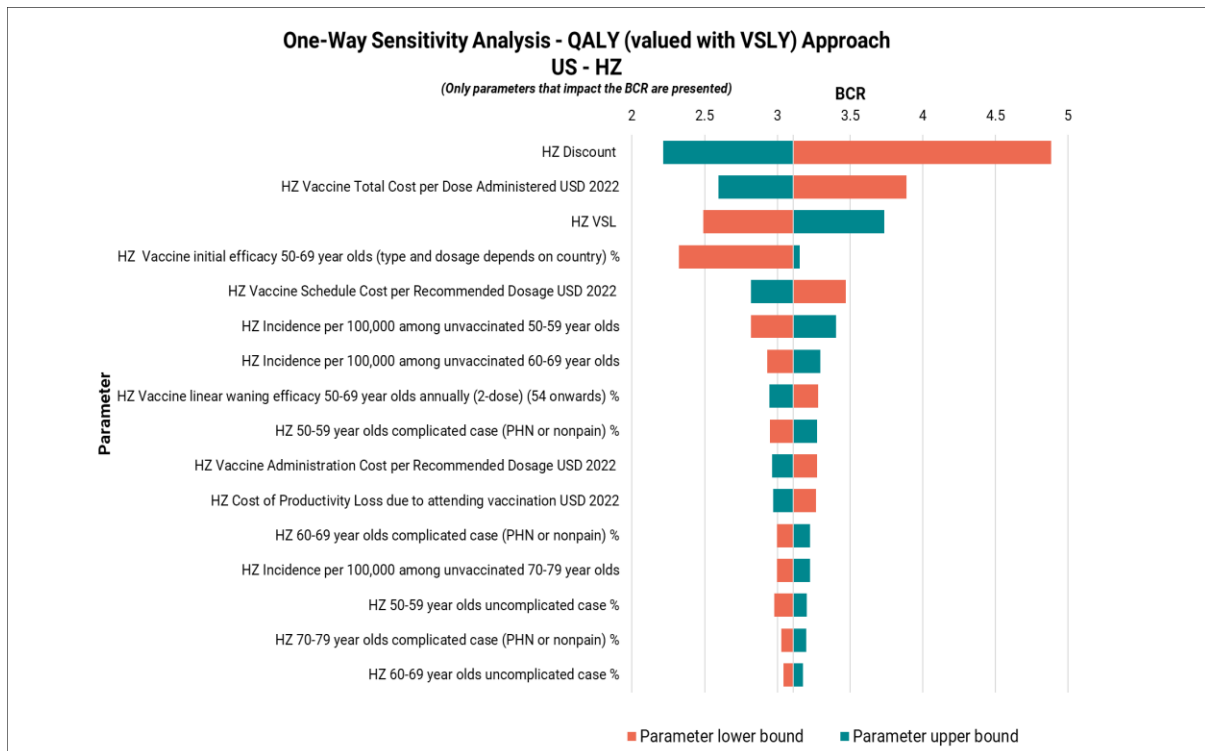
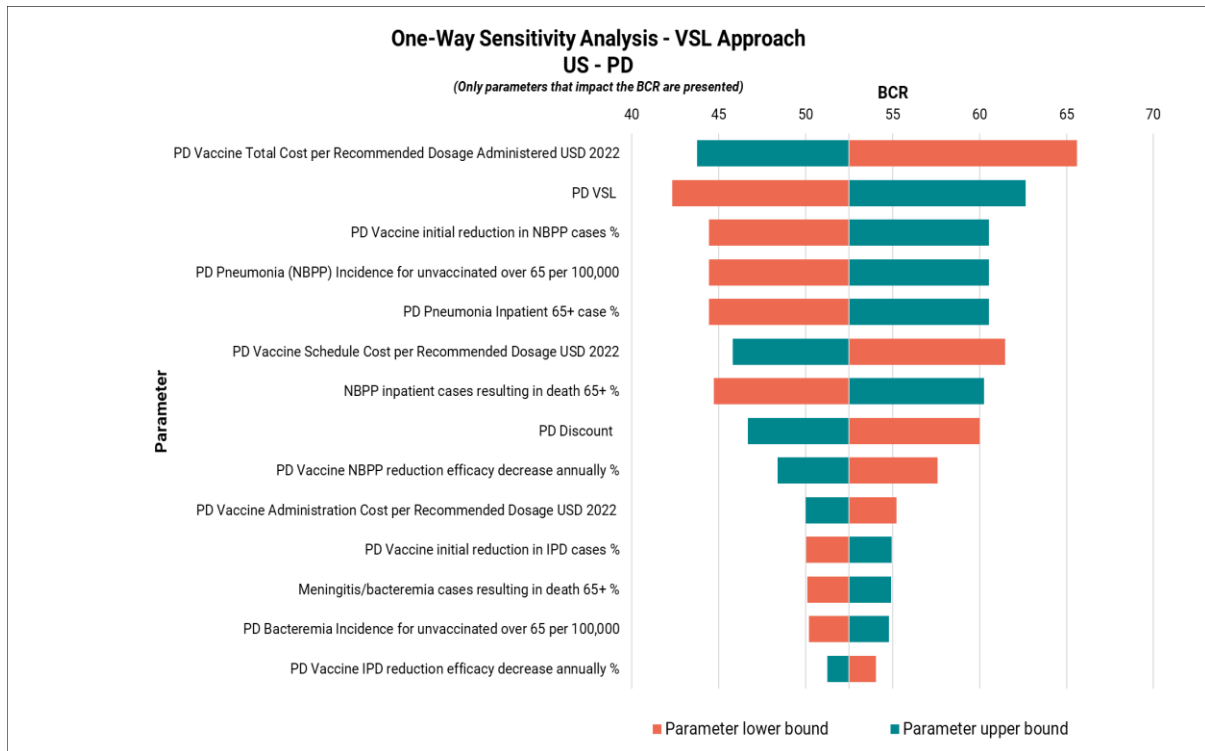


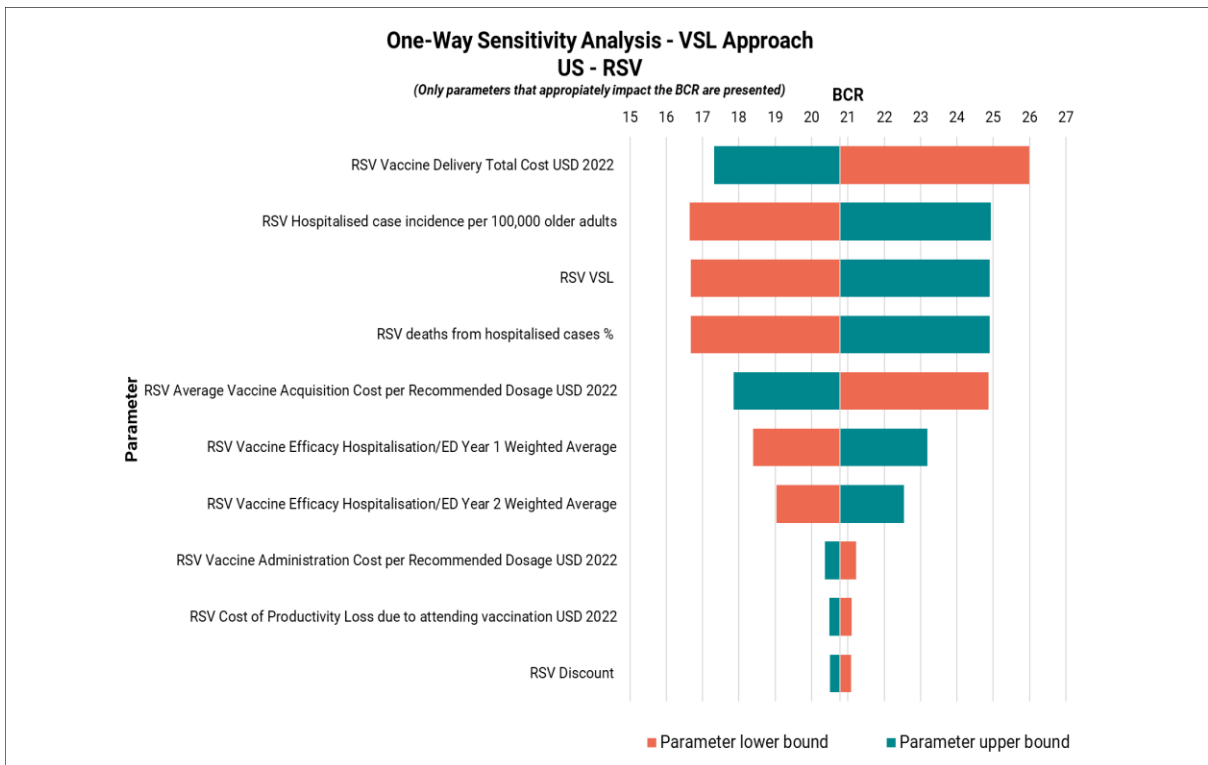
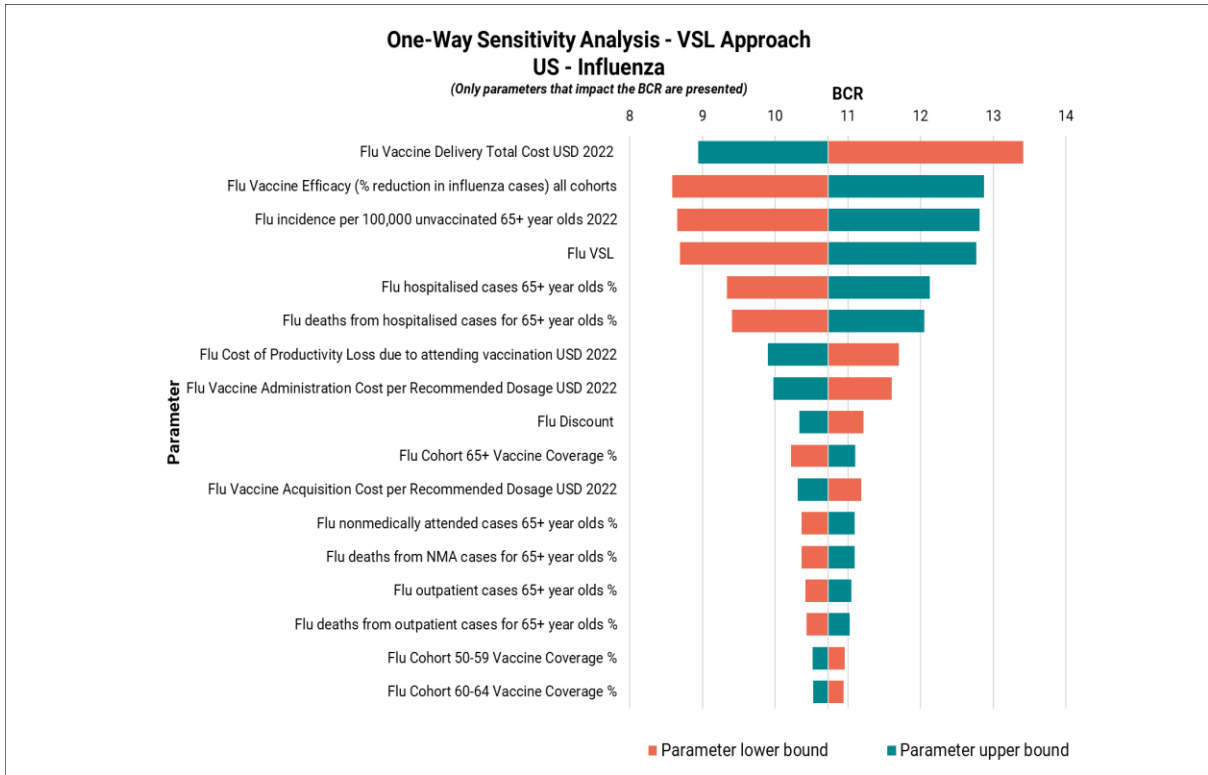
8 South Africa



9 Thailand









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- Drivers of, and incentives for, the uptake of pharmaceuticals and prescription medicines
- Competition and incentives for improving the quality and efficiency of health care
- Incentives, disincentives, regulation and the costs of R&D for pharmaceuticals and innovation in medicine
- Capturing preferences using patient-reported outcomes measures (PROMs) and time trade-off (TTO) methodology
- Roles of the private and charity sectors in health care and research
- Health and health care statistics