Folkhälsomyndigheten
PUBLIC HEALTH AGENCY OF SWEDEN

Health economic evaluation of a herpes zoster vaccination programme for the elderly in Sweden

This title can be downloaded from: www.folkhalsomyndigheten.se/publications.
Some titles may be ordered as printed.

Article number: 24013

About this publication

The Public Health Agency of Sweden has conducted an evaluation of whether to recommend herpes zoster vaccination for the elderly and other adults with increased risk for shingles. This evaluation has been done in conjunction with an evaluation of whether to introduce varicella vaccination into the national vaccination programme for children since both diseases are caused by the varicella zoster virus.

The health economic analysis of herpes zoster vaccination was designed for the evaluation of whether it fulfils the criteria for inclusion in a national vaccination programme. The Swedish Communicable Diseases Act (SFS 2004:168 Section 3 and SFS 2012:452) stipulates three criteria to be assessed and presented in support of a proposal for the introduction of a new vaccine into a national vaccination programme (1). One of these criteria is an economic evaluation of the cost-effectiveness of the vaccination programme from a societal perspective. This report presents the methods and results from this health economic analysis.

The main target group for this publication is the Swedish Regions. The publication may also be of interest to professional societies under the Swedish Society of Medicine, health professionals with responsibility for vaccination, and the international community with responsibilities for evaluating new vaccines.

The analysis was carried out by Frida Kasteng, health economist at the Unit for Analysis at the Public Health Agency of Sweden, in collaboration with a working group consisting of analysts and experts from the Public Health Agency of Sweden as well as external experts (see Appendix A).

The Public Health Agency of Sweden

Karin Tegmark Wisell

Director-General

Table of contents

About this publication 3
Abbreviations 5
Summary 6
Sammanfattning 8
Background 10
Purpose 12
Method 13
Health economic model 13
Parameters and assumptions 14
Incidence of HZ 14
Impact of intervention 14
Resource use and costs 15
Health-related quality of life 18
Sensitivity analyses 19
Budget impact analysis 20
Result 21
Cost-effectiveness 21
Base case results 21
Sensitivity analyses 22
Budget impact 26
Distribution of cost and cost-savings at regional and national levels 26
Vaccination programme budget estimation 27
Discussion 29
References 32
Appendix A: Contributing experts 37

Abbreviations

EQ-5D	EuroQol five dimensions, instrument used to measure health-related quality of life
HTA	Health technology assessment
HZ	Herpes zoster
HZO	Herpes zoster ophthalmicus
ICER	Incremental cost-effectiveness ratio, the difference in costs between two interventions divided by the difference in effect
PHN	Post-herpetic neuralgia
QALY	Quality-adjusted life year, a measure that combines two dimensions of health: length of life and quality of life
RCT	Randomised clinical trials
RZV	Recombinant zoster vaccine (Shingrix®)
SEK	Swedish currency
USD	United States dollar
VZV	Varicella zoster virus
ZVL	Zoster vaccine live (Zostavax®)

Summary

The Public Health Agency of Sweden has conducted an evaluation of whether to recommend herpes zoster vaccination for the elderly and other adults with increased risk of shingles in a two-dose schedule. The cost-effectiveness of a herpes zoster vaccination programme for the elderly was assessed. Our analyses suggest that a herpes zoster vaccination programme for the age group 65 years and older would incur a very high cost per quality-adjusted life year in the Swedish context with the current tentative vaccine price. The budget impact of offering vaccination to this age group as a whole would be considerable and implementation might need to be offered in a phased manner over a number of years.

Herpes zoster (shingles) is caused by the reactivation of the varicella zoster virus, which remains latent in the body following a primary infection causing varicella (chickenpox). The life-time risk of developing herpes zoster is around 35%. The risk increases with age. Herpes zoster is characterised by a painful rash or blisters on the skin or mucosa which usually heals within 2-4 weeks. Approximately 15% of patients develop persistent nerve pain in the affected area that lasts for more than 90 days, and sometimes lasting a life-time.

The first vaccine against herpes zoster, a live-attenuated vaccine, was approved in the EU in 2006. In 2018, it was followed by the EU authorisation of a recombinant adjuvanted subunit zoster vaccine. In some countries, this vaccine has been recommended in vaccination programmes for the elderly and for immunocompromised from 18 years of age in, for example in Australia, Canada, Germany, Italy, New Zealand, Spain, the UK and the USA, in line with the EU authorisation. To date, none of the other Nordic countries has introduced a herpes zoster vaccination programme, but evaluations are on-going.

We carried out a health economic analysis to assess the cost-effectiveness of administering herpes zoster vaccination to the elderly as part of a vaccination programme in Sweden compared with a scenario without vaccination. We modelled vaccine provision to age-specific cohorts ranging from 50 to 85 years old. Parameter estimates in the model were based on national and international scientific publications, data from Swedish national and regional registries, and national guidelines for treatment and prophylaxis of herpes zoster.

Our base case analysis indicates that the cost per quality-adjusted life year gained for the 65-year-old cohort would be around SEK 1,150,000 from a societal perspective, using the tentative price of the vaccine of SEK 1,612 per dose provided by the vaccine producer. This is classified as a very high cost per quality-adjusted life year according to the guidelines used by the National Board of Health and Welfare. At a cost of approximately 30-40% of the current tentative vaccine price - when provided to individuals in the age interval 50-80 years - the cost per quality-adjusted life year gained would come down to a moderate level (below SEK 500,000). For the 85-year-old cohort the cost per quality-adjusted life year

would be classified as high (approximately SEK 600,000) at 30% of the tentative vaccine price.

The annual cost of offering the vaccine to 65-year-olds, with a 60% coverage rate, would be around SEK 240 million per year, using the current tentative vaccine price in the estimation. The total initial cost of a vaccination offer to the entire population aged 65 and above would be considerably higher. We have therefore budgeted for a suggested offer of vaccination to the group 65 years and older in a stepwise manner, phased out over a number of years, starting with the oldest.

Individuals that are immunocompromised due to disease or treatment, aged 18 or older, incur a risk of herpes zoster in line with or higher than that of the elderly. We have not assessed the cost-effectiveness of a vaccination programme for this group due to its heterogeneity in terms of disease risk, vaccine effectiveness and age.

Sammanfattning

Folkhälsomyndigheten har utvärderat huruvida bältrosvaccination bör rekommenderas för den äldre befolkningen och andra vuxna med ökad risk för bältros i ett tvådosschema. I samband med detta har myndigheten genomfört en kostnadseffektivitetsanalys av bältrosvaccination för äldre. Våra analyser visar att införande av ett bältrosvaccinationsprogram for åldersgruppen 65 år eller äldre skulle resultera i en mycket hög kostnad per vunnet kvalitetsjusterat levnadsår med nuvarande tentativa vaccinpris. Budgetpåverkan av att erbjuda vaccination till denna åldersgrupp som helhet skulle bli betydande och vaccination skulle eventuellt behöva introduceras stegvis över ett antal år.

Bältros orsakas av en reaktivering av varicella-zosterviruset, vilket finns kvar latent i kroppen efter en primärinfektion som leder till vattkoppor. Livstidsrisken för att utveckla bältros är runt 35 procent. Risken ökar med åldern. Bältros kännetecknas av smärtsamma utslag på huden eller slemhinnorna. Dessa läker oftast inom 2–4 veckor. I ungefär 15 procent av alla fall leder bältros till långvarig nervsmärta i den drabbade kroppsdelen som kvarstår i mer än 90 dagar, och ibland blir kronisk.

Det första bältrosvaccinet, ett levande försvagat virus, godkändes i EU 2006. 2018 efterföljdes det av ett rekombinant subenhets- och adjuvansinnehållande vaccin. Detta vaccin har rekommenderats i vaccinationsprogram för äldre i till exempel Kanada, Spanien, Storbritannien Tyskland, och USA, samt för personer med ett nedsatt immunförsvar från 18 års ålder, enligt EU-godkännandet. Hittills har inget nordiskt land initierat något vaccinationsprogram för bältros, men utredningar pågår i alla nordiska länder.

Vi har genomfört en hälsoekonomisk analys för att skatta kostnadseffektiviteten av att introducera bältrosvaccination för äldre som del av ett nationellt vaccinationsprogram, jämfört med ett kontrollscenario utan vaccination. Vi modellerade vaccination av åldersspecifika grupper från 50 till 85 år. Modellparametrarna baserades på svenska och internationella vetenskapliga publikationer, data från svenska nationella och regionala register, samt nationella behandlingsriktlinjer för bältros.

Våra analyser visar att kostnaden per vunnet kvalitetsjusterat levnadsår för gruppen 65 år skulle vara runt 1 150 000 kronor från ett samhällsekonomiskt perspektiv, med ett tentativt vaccinpris från vaccinproducenten på 1 612 kronor per dos. Resultatet klassas som en mycket hög kostnad per vunnet kvalitetsjusterat levnadsår enligt Socialstyrelsens metodriktlinjer. Vid en sänkning till 30–40 procent av det tentativa vaccinpriset skulle kostnaden per vunnet kvalitetsjusterat levnadsår hamna på en måttlig nivå (under 500 000 kronor) för åldersgrupperna 50–80 år. För gruppen 85 år beräknas kostnaden per vunnet kvalitetsjusterat levnadsår som hög (cirka 600 000 kronor) vid 30 procent av tentativt vaccinpris.

Den årliga kostnaden för att erbjuda vaccination till 65-åringar, med 60 procents täckningsgrad, skulle vara runt 240 miljoner kronor vid nuvarande tentativa vaccinpris. Den totala initiala kostnaden för att erbjuda vaccinering till alla över 65

års ålder skulle vara betydligt högre. Vi har därför budgeterat för en föreslagen stegvis vaccination i gruppen 65 år och äldre där de äldsta skulle erbjudas vaccinationen först.

Personer med ett nedsatt immunförsvar som är 18 år eller äldre har en risk för bältros som är likvärdig eller högre än den hos äldre. Vi har inte skattat kostnadseffektiviteteten av ett vaccinationsprogram för denna grupp på grund av den stora variationen inom gruppen vad gäller risk för bältros, vaccineffektivitet och ålder.

Background

Herpes zoster (HZ), also referred to as shingles, is caused by the reactivation of the varicella zoster virus (VZV) which remains latent in sensory, cranial and autonomic nerves after a primary infection causing varicella (chickenpox).

The VZV which cause chickenpox is very contagious and most individuals are infected early in life. Most children born and raised in Sweden are infected and develop varicella during their pre-school years and almost 100% of Swedes have been infected by the time they reach adulthood (2, 3). The life-time risk of developing HZ in an individual who has been infected with VZV is around 35% (4, 5). The virus can be reactivated if the immune system is weakened later in life due to age or suppressed because of disease or medication. Approximately 55% of cases, and more than 75% of hospital admissions due to HZ in Sweden occur in individuals aged 65 years or older (4, 6).

HZ is characterised by a painful rash or blisters on the skin or mucosa. The most common site affected is the trunk, on one side of the body. The rash usually heals within 2-4 weeks, but around 15% of patients, increasingly so with age, develop post-herpetic neuralgia (PHN), defined as persistent nerve pain in the affected area lasting for more than 90 days (4, 7-9). PHN can last for several months or even years in some individuals. Further, 10-20% of patients develop HZ ophthalmicus following reactivation of VZV residing in the ophthalmic branch of the trigeminal nerve (8-10). This may result in partial or complete acute or chronic vision loss in the affected eye if not treated vigorously with antivirals. Complications such as pneumonia, pneumonitis, meningitis and encephalitis may occur in HZ patients just as during the primary VZV infection. A 1.8-fold increased risk of stroke has been reported during the first month post HZ, down to a risk of 1.2 one year post the HZ diagnosis (11). HZ may recur, most commonly in individuals with haematological malignancies and long lasting zoster-related pain, but it is relatively rare estimated to 1-5 % in different studies (4, 9, 12, 13). The overall mortality risk due to HZ is around one per thousand cases. Over the 20-year time period 2003-2022 one individual in the age span 45-65 years died on average per year due to HZ diagnosis. Three individuals aged 65-74 years, ten aged 75-84 years and 30 aged 85 years or older (6).

The first vaccine against HZ, Zostavax® (Merck Sharp & Dohme) was approved in the EU 2006. It is a live attenuated vaccine (ZVL) based on the same virus as the currently available varicella vaccines but in a higher titre (14). In 2018, it was followed by the EU authorisation of a second generation recombinant zoster vaccine (RZV), Shingrix® (GlaxoSmithKline). The ZVL vaccine has a 64% (95% CI 56–71) short-term efficacy against HZ in the age group 60-69 years and 38% (95% CI 25–48) in persons aged 70 years or older, as reported from randomised clinical trials (RCT) (15) with estimates in the same range from observational studies (16). RCT data for the RZV vaccine report a 97.7% (95% CI 93.1-99.5) efficacy in protecting individuals 50 years or older against HZ year 1, while long-

term follow-up indicates a 73.2% (95% CI 46.9-87.6) efficacy after 10 years (17). Pooled data from the first observational studies in the USA report a 79% (95% CI 70-89) vaccine effectiveness against HZ year 1 (18-21) down to 73% at 3 to 4 years of follow-up (21). Both vaccines are approved for the elderly from age 50 years. The RZV vaccine is also approved for immunosuppressed individuals from 18 years of age while the live vaccine is contraindicated in this group (14).

The USA was the first country to establish a vaccination programme with the ZVL vaccine, from 50 years of age, followed by Canada (age 50+) and Greece (age 60+) in 2011, South Korea (age 60+) in 2012, the UK (ages 70-79) in 2013 and France in 2015 (ages 65-74) (14). Several of these countries have now switched their recommendation to the RZV vaccine: the USA in 2017, Canada in 2018 and the UK in 2023 (22-24). The RZV vaccine was also recommended in Germany in 2019 and in Spain in 2021 (25, 26). Uptake of the vaccine has been slow in Canada, Germany and the UK due to its considerable budget impact (23, 27). To date, none of the Nordic countries have introduced an HZ vaccination programme. A systematic literature review has been conducted jointly among the Nordic countries during 2023 in preparing for the possible introduction of zoster vaccination in the countries.

The Public Health Agency of Sweden initiated a combined assessment of varicella vaccination for inclusion in the national vaccination programme for children, and HZ vaccination as a vaccination programme for the elderly in 2018. However, due to the COVID-19 pandemic the assessment was paused for a couple of years and resumed late 2022. A health economic assessment of the cost-effectiveness of ZVL, based on this previous work, was published in 2021 (28). It concluded that ZVL vaccination as part of a vaccine programme would not be cost-effective in Sweden, in line with an earlier assessment by the Dental and Pharmaceutical Benefits Agency that withdrew the subsidy for the ZVL vaccine already in 2014 when the company failed to show long-term efficacy (29). In this analysis we only assessed the cost-effectiveness of the RZV vaccine. This is due to its observed superior efficacy and effectiveness when compared with ZVL, as well as the expected discontinuation of ZVL on the European market (communication Merck Sharp & Dohme 20230530). The cost-effectiveness of a RZV vaccination programme in a Swedish context has also been assessed by Region Stockholm in 2023 (30).

Purpose

The purpose of this evaluation was to assess the cost-effectiveness of offering herpes zoster vaccination to different age groups of the elderly population in Sweden and assess its budget impact at regional and national levels.

Method

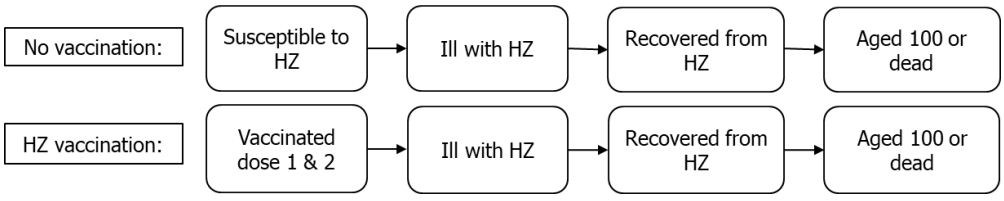
We carried out a health economic analysis to assess the cost-effectiveness of administering HZ vaccination to the elderly compared with a scenario without HZ vaccination. We modelled vaccine provision to age-specific cohorts ranging from 50 to 85 years to assess the cost-effectiveness of different vaccination programs based on age at vaccination. The cost-effectiveness results are presented in terms of cost per quality-adjusted life year (QALY) gained, also commonly referred to as the incremental cost-effectiveness ratio (ICER) in health economic analyses. The base case scenario is a societal perspective, as stipulated in the cost-effectiveness criteria of the Swedish Communicable Diseases Act (1).

The parameter estimates in the model were based on scientific publications, data from Swedish national and regional registries, and national guidelines for antiviral treatment and prophylaxis for disease (31-33). In cases where published data were missing, assumptions from Swedish clinical expertise have been used (Appendix A).

Health economic model

The cohort model used in the health economic analysis was developed in Excel®. The model was a state transition model following a cohort of individuals from time of vaccination until age 100 years or death, whichever occurred first. Since HZ is a reactivation of an earlier varicella infection, with minimal transmission effect, we used a non-transmission model. The cycle length was one year, with age-specific risk of disease, quality of life weights and costs of illness. The age specific mortality was based on Swedish life tables for 2019 (34) and the modelled population was the average of the years 2017-2021 for each age cohort modelled. To perform the health economic analyses, the data were matched with the corresponding resource use, the unit costs of resources use and the quality-of-life impact. Results were calculated for both a societal and a health system perspective. The model structure is depicted in Figure 1.

Figure 1 Flowchart of the cohort model



The healthcare cost data used in the model were updated to 2023 values using the annual increase in the unit value used to calculate diagnostic-related group weights (35). Both health effects and costs were discounted by 3% annually, according to the Dental and Pharmaceutical Benefits Agency's general advice for health economic evaluations (36). The results were also presented without discounting, as recommended in a proposed European standard for the health economic analysis of vaccination programmes (37). Reporting standards for health economic analyses

were used as guidance for presentation of results (38). One-way and two-way sensitivity analyses were carried out to assess the sensitivity of results to variations in key input variables.

There is no explicit threshold for when an intervention is considered to be cost-effective in Sweden (39). Priorities in the Swedish healthcare sector are guided by the three main principles of the ethics platform (human dignity, needs and solidarity, and cost-effectiveness) which is part of the Swedish Health and Medical Services Act (40). In general, what is considered to be an acceptable cost of an intervention in relation to its health benefits is a judgement that takes into account also other factors such as the health impact of the intervention and the severity of the condition to be prevented or treated (41). Meanwhile, decisions about national vaccination programmes are primarily based on the three criteria specified in the Swedish Communicable Diseases Act (1).

The cost per QALY framework against which we present our results in this report was based on the methods guidelines from the National Board of Health and Welfare where a cost of SEK 100,000-499,000 is considered a moderate cost per QALY a cost between SEK 500,000-1,000,000 is a high cost per QALY and a cost above SEK 1,000,000 a very high cost per QALY (32).

Parameters and assumptions

Incidence of HZ

The number of primary care visits due to HZ was used as a proxy for HZ incidence (42). We used primary care data from Region Västra Götaland (4), one of the larger regions in Sweden population-wise, with nearly one-fifth of the national population (33). We assumed the same age-adjusted incidence rates at national level. In the model, we used the average number of visits during the period 2017-2021 in 1-year age intervals.

Impact of intervention

Vaccine efficacy and effectiveness

The RZV has been evaluated in two phase III RCTs. The vaccine efficacy compared with placebo was estimated at 97.2% (95% CI 93.7-99.0) in ZOE-50 (population 50+) (43) and at 89.8% (95% CI 84.2-93.7) in ZOE-70 (population 70+) over a median follow-up of 3.1 and 3.7 years respectively (44). A long-term follow-up of up to 10 years after vaccination published in 2022 showed a 97.7% (95% CI 93.1-99.5) vaccine efficacy year 1 down to 73.2% (95% CI 46.9-87.6) in year 10 using pooled data from both studies (17). These data were used to calculate the annual waning rate of vaccine effectiveness in our model as 3.2%.

Furthermore, we pooled data from three observational studies conducted in populations in the USA. These studies showed a real-life vaccine effectiveness of 79% (95% CI 70-89) year 1 (18-21), reduced to 73% after 3 to 4 years of follow up

(21). We used this vaccine effectiveness rate in our sensitivity analyses as the year 1 effectiveness, thereafter assuming the same waning rate as in the clinical trials.

The risk of PHN and HZO rates were assumed to be the same in post-vaccination HZ-cases as in cases in unvaccinated. The RCTs did not detect a difference in PHN risk when compared with overall HZ risk (44). Observational studies suggest some degree of, but with the present population-base not statistically significant, increased protection against HZO following vaccination (19, 45). Reactogenicity in the form of injection site pain, erythema, and swelling, and systemic symptoms - most commonly fatigue, headache, and myalgia - following the vaccination is not uncommon, but is short-term and usually mild (46). The analysis therefore does not account for resource use nor the health utility impact of these.

Vaccination coverage

The vaccination coverage was assumed to be 60% on the basis of the coverage rates seen for influenza vaccination in the health economic model (47). The coverage assumption does not impact the cost per QALY estimation since we did not use a transmission model as HZ is minimally transmittable. However coverage assumptions impact the total cost of the programme in the model and were varied in the budget impact analysis.

We expected all covered individuals to complete the two-dose vaccine schedule in the base case analysis with information campaigns which explain that reactogenicity is expected but short-term with no long-term sequalae.

Resource use and costs

Cost of vaccination

The RZV is offered in a two-dose schedule. In our analyses we assumed that these are administered within one year. The total vaccination cost within the model includes the expense of two vaccine doses, as well as the costs associated with administering each shot. The current tentative price per dose in Sweden is SEK 1,612 (communication GlaxoSmithKline 20230313). This price may be reduced following price negotiations. We note that in the WHO MI4A vaccine purchase database there is no price listed for the WHO European region but that the price for the American region is on average USD 102.4 (48). This corresponds to approximately 70% of the current tentative price for Sweden, USD 1=SEK 10.6 (average exchange rate 2023 (49)).

For the administration of each dose, a cost of SEK 180 was applied, approximately 30 minutes of healthcare staff time, based on the average salary for nurses in 2022, SEK 40.500 including social fees (50, 51). It did not include the cost of facilities or overheads.

Medical resource use

Primary care need was concordant with the incidence rates since we used primary care as a proxy for HZ incidence (ICD-10 B02) (4). The proportion of patients receiving antiviral treatment for HZ was based on the same study as incidence rates (4), while the risk of Post Herpetic Neuralgia (PHN) and stroke due to HZ came from earlier publications on the burden of HZ in Sweden (42, 52). The number of primary care visits for HZ and PHN was based on the estimates used in the two other Swedish economic evaluations of HZ vaccination (28, 30).

Table 1 Incidence and proportion of patients in need of medical care (4, 42, 52)

Age group	Incidence per 1000 individuals	Primary care HZ, 1 visit per patient	Pharmaceutical need HZ	Primary care PHN, 5 visits per patient	Pharmaceutical need PHN
50-54	3.4	100%	67%	4.2%	79%
55-59	4.5	100%	67%	5.8%	84%
60-64	5.8	100%	67%	5.8%	84%
65-69	7.0	100%	67%	7.9%	93%
70-74	8.8	100%	67%	7.9%	93%
75-79	9.8	100%	67%	12.3%	85%
80-84	11.3	100%	67%	12.3%	85%
85-89	11.2	100%	67%	13.7%	82%
90-94	10.4	100%	67%	13.7%	82%
95+	10.2	100%	67%	13.7%	82%

Rates of specialised outpatient care and hospitalisation covering the same 5-year period as the incidence data (2017-2021) were extracted from the National Patient Register of Sweden (customised data provided by the database holder) (6). In the base case analysis, we only considered the cost of admission and specialised outpatient care where HZ was the main diagnosis as advised by the external expert group (Appendix A).

Due to the relatively low stroke and mortality rates associated with HZ (6, 42) and the fact that the majority of cases occur in individuals aged 85 years or older, i.e. above the average life expectancy in Sweden, stroke and mortality were not accounted for in the base case analysis but we included the QALY loss due to stroke and mortality in the sensitivity analysis.

Table 2 Incidence and proportion of patients in need of medical care (4, 6, 42)

Age group	Incidence per 1000 individuals	Specialised out-patient care	In-patient care	HZ related stroke risk	HZ related mortality (primary and contributing)
50-54	3.4	9.0%	0.6%	0.0000%	0.0000%
55-59	4.5	9.6%	0.7%	0.0002%	0.0001%
60-64	5.8	9.6%	0.7%	0.0002%	0.0001%
65-69	7.0	10.4%	1.0%	0.0007%	0.0004%
70-74	8.8	10.4%	1.0%	0.0007%	0.0004%
75-79	9.8	12.1%	2.4%	0.0018%	0.0013%
80-84	11.3	12.1%	2.4%	0.0018%	0.0013%
85-89	11.2	13.5%	5.3%	0.0040%	0.0161%
90-94	10.4	13.5%	5.3%	0.0040%	0.0161%
95+	10.2	13.5%	5.3%	0.0040%	0.0161%

Cost of care

The unit cost of primary care visits was taken from the ‘‘Cost-per-patient’ database (data shared by the statistics unit of the Swedish Association of Local Authorities and Regions) (53). The unit cost of specialised out-patient care and hospitalisations was extracted directly from the online records of the same database. Average costs over the years 2019-2021 were updated to 2023 values, as previously described. The average cost per visit/admission was multiplied by the average number of corresponding visits/admissions from the online National Patient Register, and the source of mean days admitted (6). Information on pharmaceuticals administered was acquired from national guidelines (31) and the Swedish expert group advice. The cost of pharmaceuticals was taken from the online pricelist of the Swedish pharmacy Apoteket AB (the state-owned pharmaceuticals retailer in Sweden) (54). The model does not account for changes in supportive home care services or informal care due to HZ as we had no information about the potential impact of HZ on home care.

Table 3 Medical unit costs (SEK) (6, 53, 54)

Age group	Primary care visit	Drugs HZ (valaciclovir 500 mg, 42 pcs)	Drugs PHN (amitriptylin 10 mg, 100 pcs + 25 mg, 100 pcs*3) (a)	Specialised out-patient care visit	In-patient care per admission	Mean days admitted to hospital
50-64	1,843	123	348	5,843	59,997	4.0
65+	1,846	123	348	7,077	75,019	5.6

(a) Alternative treatments include gabapentin and topical treatment with lidocaine or capsaicin

Productivity losses (indirect costs)

Indirect costs were included in the analysis in the form of productivity losses in case of illness. The occupational rates by age group were based on year 2022 statistics (55). The cost of productivity losses was calculated on the basis of an

average monthly salary in 2022 of SEK 33,700 (51) and the statutory employers' fee of 31.42% (50). This inferred a productivity loss of SEK 44,289 per month, or SEK 2,109 per working day. The average length of the productivity loss in the model differed among age groups depending on age-specific disease severity states. For sick leave due to herpes zoster, the days of illness were based on available estimates from the literature paired with expert advice (56).

Table 4 Indirect costs (50, 51, 55, 56)

Age group	Employment rate	Average days sick leave	Unit cost per day
50-54	88%	3.5	2,109
55-64	77%	3.9	2,109
65-74	19%	1.0	2,109
75-84	0%	0	2,109
85+	0%	0	2,109

Health-related quality of life

Table 5 presents the QALY loss applied in the model for each respective age group and disease (HZ and PHN respectively, with the denominator for both being HZ incidence) and the resulting total age specific QALY loss per incident case. The short term QALY loss due to HZO is included in these estimated, however we did not find data on the long-term QALY loss of HZO-related eye complications, therefore, this is not included. The utility loss due to different degrees of pain associated with HZ and PHN was derived from a British study (57). This percentile utility loss was multiplied with the age-adjusted utility for the general population in Sweden (58). Furthermore, a UK register study on the burden of PHN was used to quantify the QALY loss due to HZ and PHN in terms of average duration and proportional utility loss due to different degrees of pain (8, 59). The QALY loss associated with HZ-associated stroke was very small due to the low incidence of HZ-related stroke (42, 60, 61). QALY loss due to HZ-related mortality was estimated by multiplying years of life lost due to premature death to the age-adjusted utility in the age group (6, 58). Since mortality associated with HZ is mainly due to other co-morbidities QALY, QALY loss due to stroke and mortality was only added in the sensitivity analysis.

Table 5 Average annual QALY reductions per episode (6, 8, 42, 57-61)

Age group	QALY loss HZ (month 1)	QALY loss PHN	Total QALY loss per HZ case	QALY loss stroke	QALY loss mortality	Total QALY loss per HZ case including stroke and mortality
50-54	0.007	0.221	0.017	0.00000	0.002	0.017
55-64	0.008	0,214	0.027	0.00001	0.002	0.029
65-74	0.010	0.209	0.035	0.00001	0.004	0.039
75-84	0.011	0.205	0.042	0.00001	0.001	0.043
85+	0.011	0.201	0.043	0.00000	0.001	0.045

Tables 6 and 7 list the input parameters used to calculate the QALY loss values applied in the model.

Table 6 Basis for calculation of QALY loss (8, 57-59)

Age group	Mean utility Swedish population	Utility mild pain (%)	Utility moderate pain (%)	Utility severe pain (%)	Mild HZ pain	Mode-rate HZ pain	Severe HZ pain	Duration pain HZ without persisting pain (months)
50-59	0.83	0.91	0.71	0.32	24%	4%	8%	1
60-69	0.80	0.91	0.71	0.32	41%	5%	9%	1
70-79	0.79	0.91	0.71	0.32	41%	5%	9%	1
80-89	0.77	0.91	0.71	0.32	41%	5%	9%	1

Table 7 Basis for calculation of QALY loss (cont.) (8, 57-59)

Age group	Persisting pain following HZ	Mild PHN pain	Moderate PHN pain	Severe PHN pain	Duration mild PHN pain (months)	Duration moderate PHN pain (months)	Duration severe PHN pain (months)
50-59	9%	42%	49%	9%	6.7	10	12.5
60-69	12%	42%	49%	9%	6.7	10	12.5
70-79	17%	42%	49%	9%	6.7	10	12.5
80-89	20%	42%	49%	9%	6.7	10	12.5

The proportions of patients in different age groups with moderate/severe pain in the UK registry study were in line with the proportion of patients with PHN diagnosis and/or analgesics prescription in the Swedish study used to assess healthcare cost associated with PHN (42) (Table 8).

Table 8 Comparison between studies used to estimate PHN-risk and duration in the model (8, 42)

Age group	PHN diagnosis/analgesics prescription at month 3 from HZ diagnosis (Swedish patients, 2008-2010)	Moderate/severe PHN pain at month 3 from HZ diagnosis (British patients, 2000-2006)
50-59	6%	5%
60-69	6%	7%
70-79	10%	10%
80+	14%	12%

Sensitivity analyses

In order to investigate the robustness of the results from our analysis, we conducted several sensitivity analyses as outlined in Table 9.

Table 9 Parameters varied in sensitivity analyses

Parameter	Base case	Alternative values in sensitivity analyses
QALY loss due to HZ and PHN	Values as in Table 5 (8, 57-59)	Values used by Wolff 2021 (28) from (57)
		Values used by Nystrand 2023 (30) from (8, 57, 59)
QALY loss due to HZ-associated stroke and premature death	Not included	Values as in Table 5 (6, 42, 58, 60, 61)
Vaccine effectiveness year 1	97.7% (17, 43, 44)	79% (18-21)
Waning rate	3.2% (exponential) (17)	1.5% / 6.5%
Compliance rate dose 2	100%	85% (with vaccine effectiveness at 58% after 1 dose) (18)
Incidence	Incidence from VGR 2017-2021 (4)	Incidence from VGR 2008-2010 (slightly lower) (42)
Potential vaccine price following price negotiation	Current tentative price (SEK 1,612)	70%, 50%, 30%, 10% of current tentative price
Vaccine administration cost	SEK 180 (50, 51)	SEK 90, SEK 360
Cost of care	Unit costs from national/regional cost database (53)	50%, 200%
Added cost of information campaign during first 2 years	Not included	SEK 20 million (62)
Discount rate QALYs	3% (36)	0%, 5% (36)
Discount rate costs	3% (36)	0%, 5% (36)
Time horizon	Lifelong (until age 99)	10 years (length of vaccine follow-up from the clinical studies (17)

Budget impact analysis

Based on output from the cost-effectiveness model, we present an assessment of cost and potential cost-savings of an HZ vaccination programme at regional and national levels.

The budget impact of a vaccination programme is presented as an annual cost of providing vaccination to one age cohort (65-year-olds). The population size is based on the average cohort of 65-year-olds during the years 2017-2021. The budget impact is presented with different vaccine price assumptions (70%, 50%, 30% and 10% of the current tentative price and different coverage rates (50%, 60%, 70% and 80%). The estimation includes the administrative cost of giving the vaccine but no other programme implementation costs, such as training of healthcare staff and public information campaigns. The budget impact of future years is not discounted (63). We also estimate the budget impact of a phased implementation for individuals aged 65 and older. In this budget we assumed increasing coverage rates with age in line with what is seen for influenza vaccination in the elderly (47).

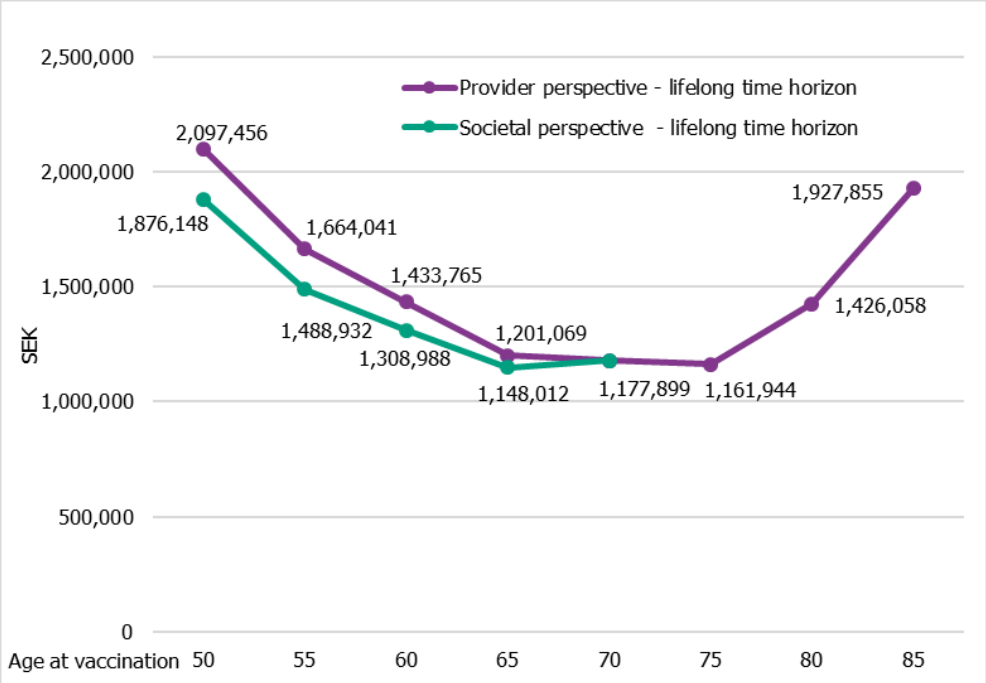
Result

Cost-effectiveness

Base case results

We estimated the lowest cost per QALY gained to be associated with the vaccination of 65-year-olds to 75-year-olds, both from a societal and health system perspective, when we modelled a vaccination programme offered to different age cohorts. From a societal perspective, the estimated costs range from SEK 1,150,000 to 1,180,000 per QALY gained based on the current tentative vaccine price of SEK 1,612 per dose (Figure 2).

Figure 2 Modelled cost per QALY gained for vaccination of different age-cohorts (using the current tentative vaccine price of SEK 1,612)



The total cost of a vaccination programme where 65-year-olds would be offered vaccination with a coverage rate of 60% was calculated to SEK 237 million, using the tentative vaccine price of SEK 1,612 per dose in the estimation. Total societal net costs over the length of the modelled period were SEK 204 million compared to a cost of SEK 70 million in a scenario without vaccination.

The total number of QALYs saved over the 35 years modelled was estimated at 178. The cost per QALY gained from a societal perspective was estimated at SEK approximately 1,150,000 per QALY gained and from a health system perspective at SEK 1,200,000 per QALY gained.

Table 10 Total programme costs and cost consequences, 35-year time horizon, vaccination of adults aged 65 (million SEK), Cost/QALY (SEK)

Category	No vaccination	Vaccination	Difference	Cost difference	Share of cost-savings
Cost of vaccination programme		237	237	+100%	
Direct costs of illness	53	30	-23	-43%	71%
Indirect costs of illness	17	7	-9	-56%	29%
Total costs (health system)	**54**	**267**	**214**	**+399%**	
Total costs (societal)	**70**	**275**	**204**	**+290%**	
Total QALYS	**-391**	**-213**	**178**		
Cost/QALY (health system perspective)			**SEK 1,201,000**		
Cost/QALY (societal perspective)			**SEK 1,148,000**		

Sensitivity analyses

If price negotiations were to reduce the vaccine cost to 70% of its current tentative price, the cost of vaccination per QALY gained from a societal perspective for the age cohorts from 65 to 75 years would be around SEK 800,000 per QALY gained according to our model estimates. If the vaccine price was reduced to 30% of the current tentative price, the cost per QALY gained would be SEK 500,000 or less for the age cohorts from 50 to 80 years. At this price level the cost per QALY would be around SEK 600,000 for the 85-year-olds.

Figure 3 Modelled cost per QALY gained for vaccination of different age cohorts and tentative vaccine prices

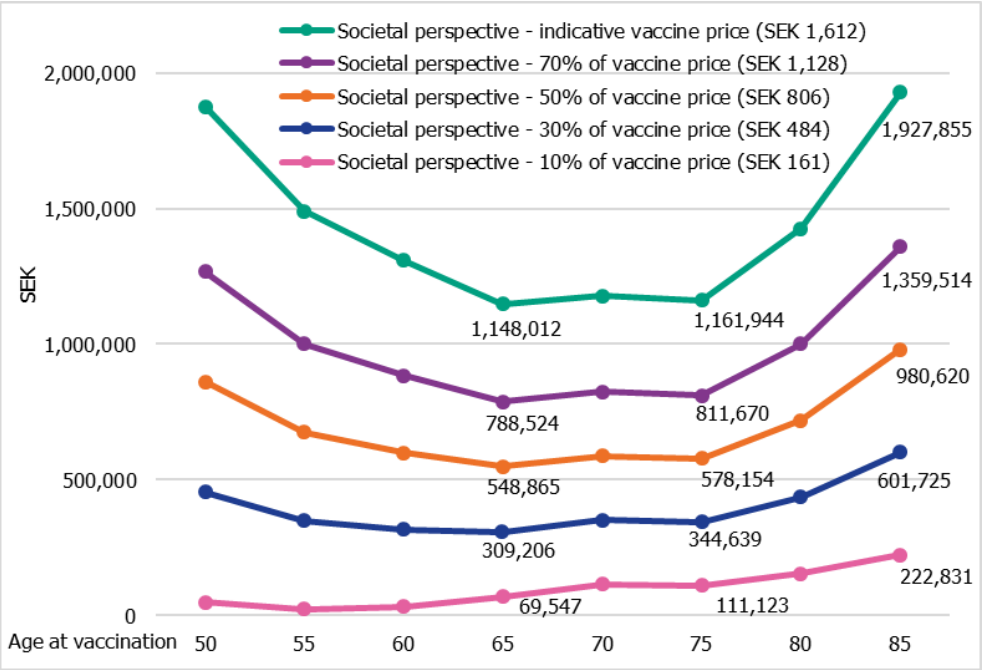
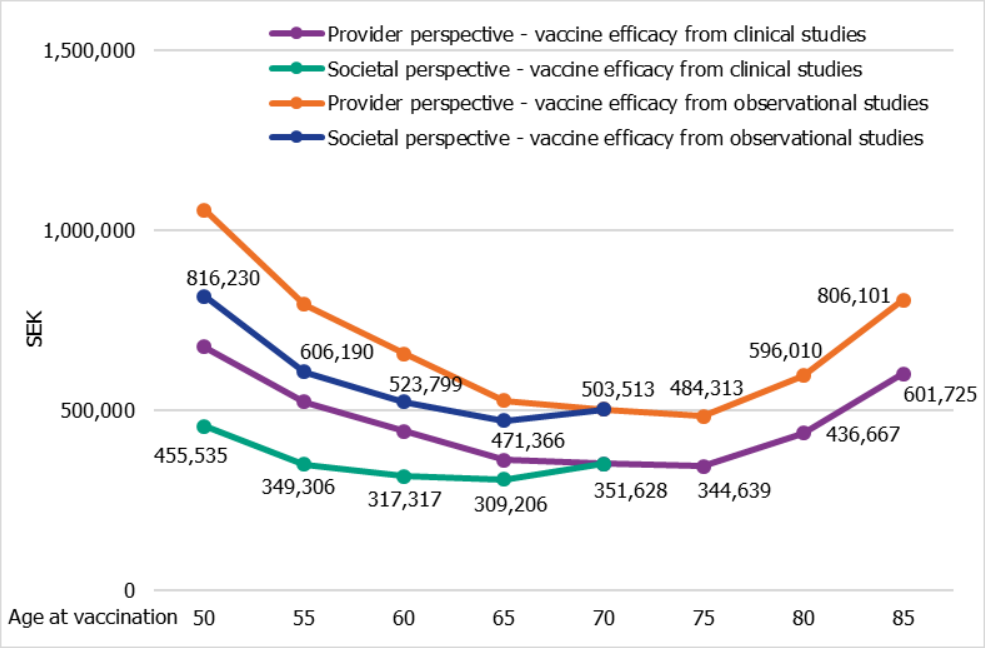


Figure 4 presents the modelled cost per QALY gained with the two different assumptions of vaccine effectiveness: the efficacy measured in the clinical trials and that from the pooled observational studies, with an assumed price reduction to 30% of the current tentative vaccine price. The estimated costs per QALY gained were, as previously presented, below SEK 500,000 for the 50-80 year-olds when we used the clinical trial vaccine efficacy. When we used the vaccine effectiveness from the observational studies in the model, the cost per QALY gained was estimated at approximately SEK 500,000 for the 60-75 years age cohorts. The cost per QALY gained was estimated at approximately SEK 600,000 for the 80-year-olds and at approximately SEK 800,000 for the 85-year-olds.

Figure 4 Modelled cost per QALY gained for vaccination of different age cohorts, vaccine price 30% of tentative price (SEK 484), vaccine effectiveness year 1, 97.7% and 79% respectively



Figures 5-7 provide an overview of how variation in key input parameters in relation to health outcomes (QALYs), vaccine effectiveness, programme design, costs and model design would change the cost per QALY for the 65, 75, and 85-year-old cohorts. The vertical line in the figure illustrates the cost per QALY of the base case analysis and the green and purple staples show how much the cost per QALY is affected by a change in the listed variable. The sensitivity analyses demonstrated that the model results are highly sensitive to different assumptions of the QALY loss caused by HZ, primarily driven by the uncertainty of QALY loss due to PHN. We compared our assumption of QALY loss with the estimates used in two previously published economic evaluations of HZ vaccination programmes in Sweden. When we applied the QALY loss per age group used in the economic evaluation of the zoster vaccine live (ZVL) from Wolff et al (28) (QALY loss from a modelling done by the UK Health Protection Agency (57)), the estimated cost per

QALY gained for 65-year-olds decreased to SEK 487,000 in our model. On the other hand, when we applied the same QALY loss estimates as used in the economic evaluation of the RZV published by Region Stockholm in 2023 (30), which used similar data sources for QALY loss as those we used in our analysis (8, 59) but applied to a different age-adjusted baseline utility (64), the cost per QALY gained for the same group increased to SEK 1,686,000/QALY. The differences are even more accentuated in older age cohorts as the variation in assumptions concerning QALY loss associated with PHN increases with increasing age (Figures 4 and 5).

Shifting our focus to the assumptions related to vaccine effectiveness, by changing the year 1 effectiveness from the clinical efficacy of 97.7% reported from the clinical studies (17, 43, 44) to 79%, the average effectiveness in pooled data from the USA observational studies (18-21), the vaccination cost per QALY gain increased to approximately SEK 1,600,000 for 65-year-olds and to SEK 1,400,000 for 75-year-olds. Different assumptions regarding the vaccine effectiveness waning rate also influenced the results but to a lesser degree.

As already outlined above, we see that the cost per vaccine dose highly influences the cost per QALY. The sensitivity analyses also investigated the impact of varying the discount rate for QALYs and cost as well as using a shorter time horizon of 10 years instead of until age 100 years or death. Ten years is in line with the maximum published follow-up time of the vaccine to date.

Figure 5 Sensitivity analyses 65-year-old cohort (base case cost per QALY gained SEK 1,148,012)

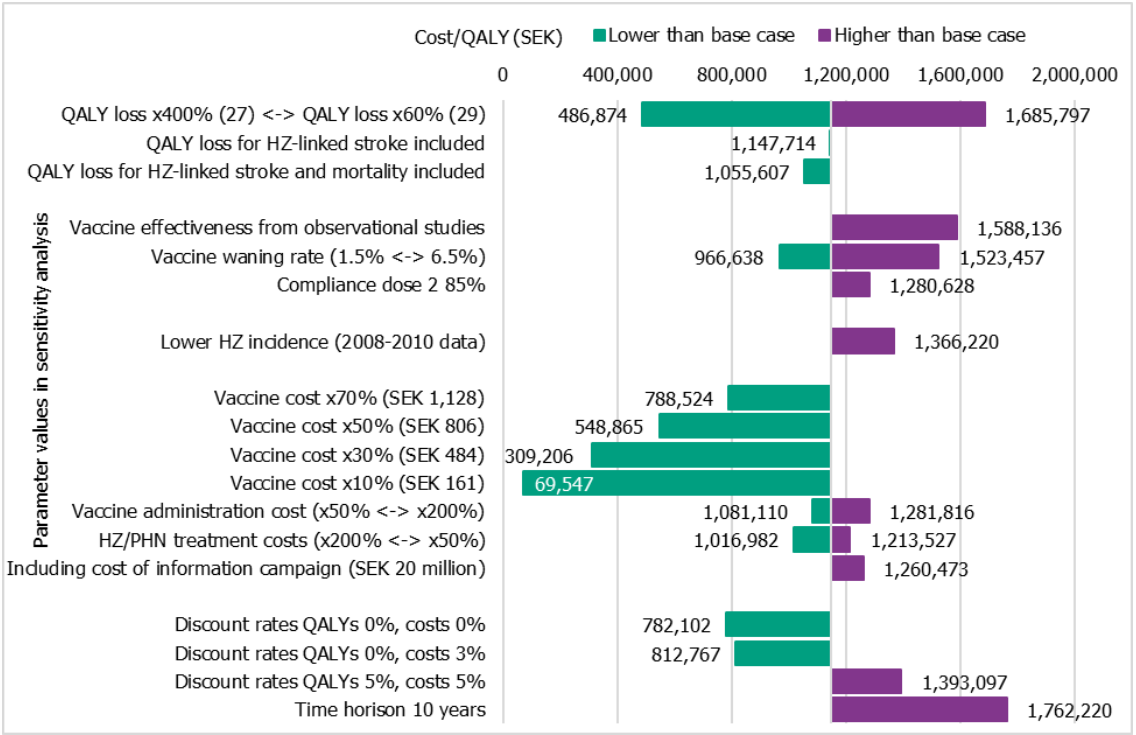


Figure 6 Sensitivity analyses 75-year-old cohort (base case cost per QALY gained SEK 1,161,944)

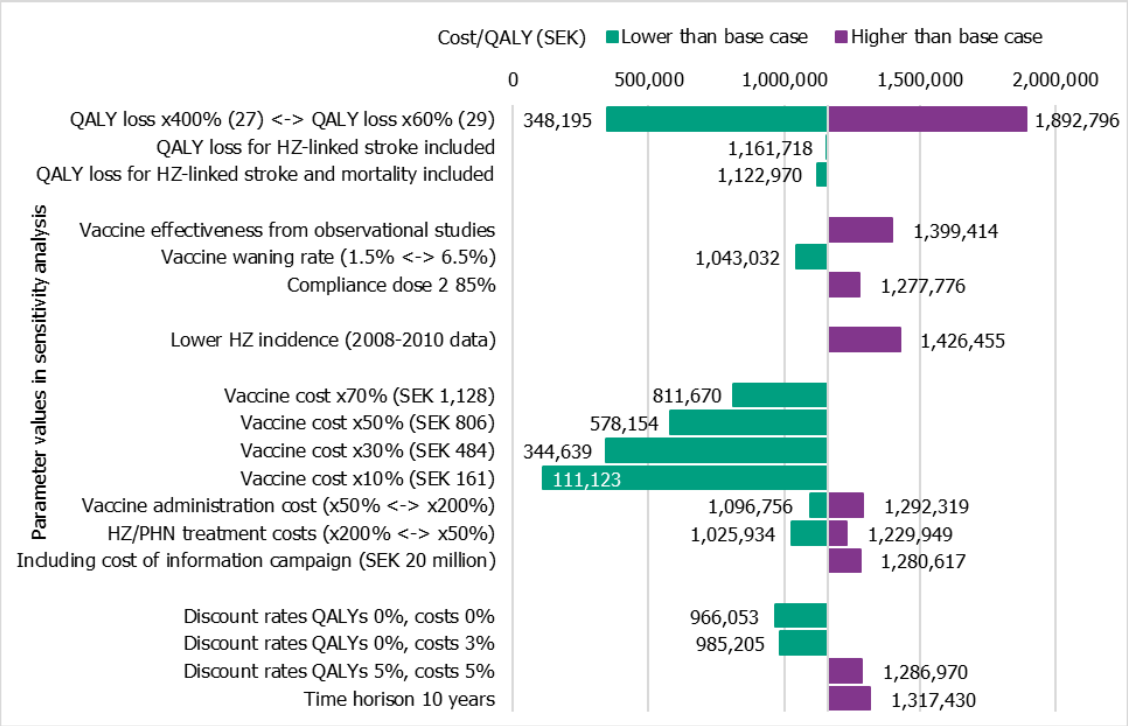
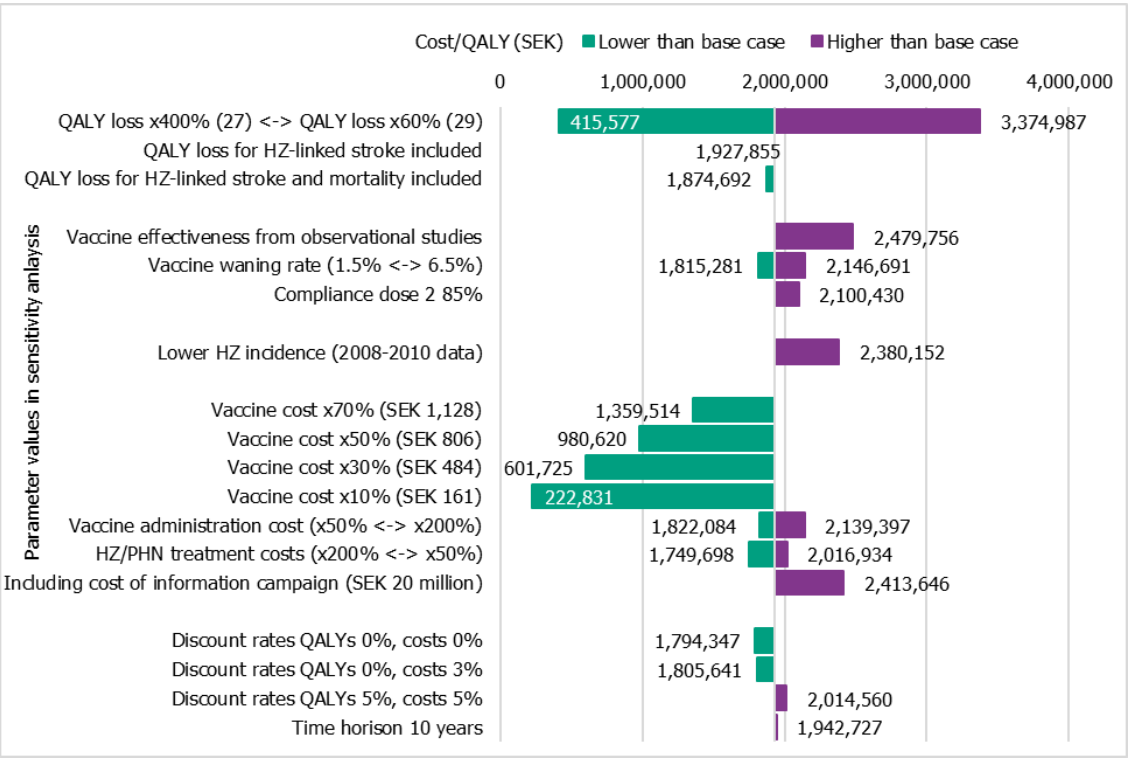


Figure 7 Sensitivity analyses 85-year-old cohort (base case cost per QALY gained (y-axis) SEK 1,927,855)



Budget impact

Distribution of cost and cost-savings at regional and national levels

We assume that the cost of vaccination would be funded from the regional healthcare budgets. A vaccination programme would result in a decrease in healthcare resource utilisation due to HZ, but these cost-savings would be considerable lower than the cost of vaccination at the current tentative price of the vaccine. The cost-savings due to reduced productivity losses would affect the national accounts, but this would be relatively limited for a programme targeted at individuals aged 65 years or older although this may be change over time in those under 70 years with increased retirement age (Figure 8). We have not considered any costs or cost-savings at the municipal level in our model.

Figure 8 Overview of cost and cost-savings as a result of a vaccination programme for 65-year-olds with a 60% coverage rate at regional and national levels

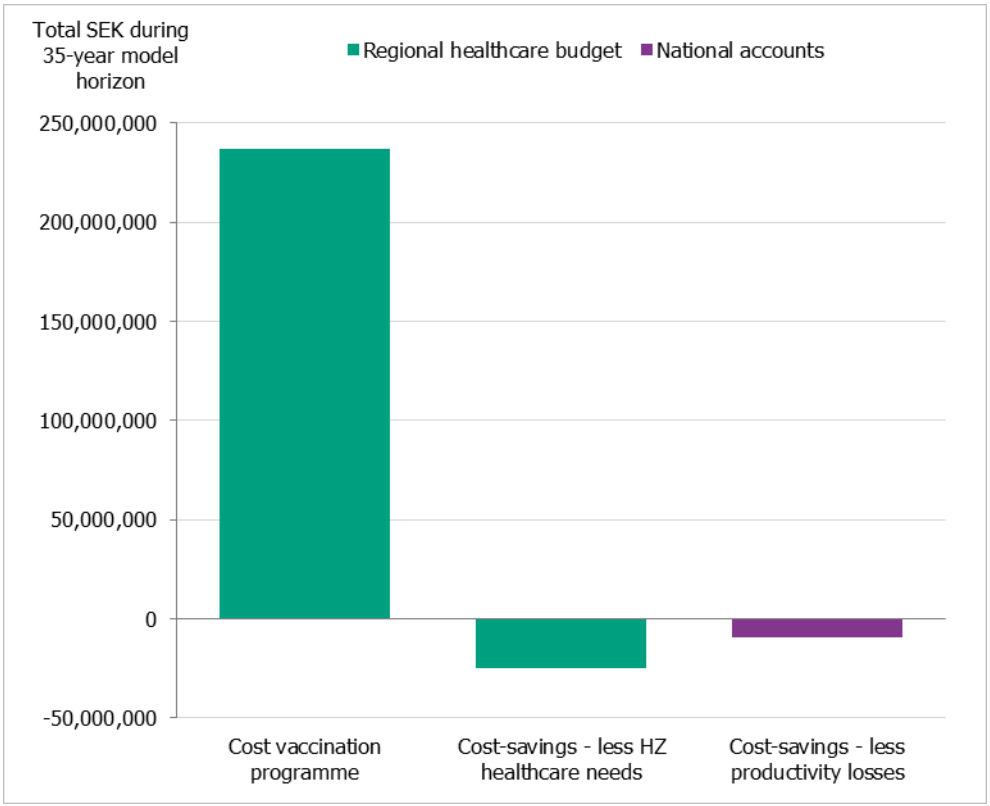


Table 11 presents the discounted cost and cost consequences extracted from the model at different time periods. Since the cost of the vaccination programme and averted productivity losses occur only during the first and first five years respectively these remain the same for all time periods. Due to the discount rate applied in the model, the averted health care costs per year diminishes over time.

Table 11 Discounted cost and cost-savings from a societal perspective as a result of a vaccination programme for 65-year-olds, with a 60% coverage rate, at regional and national levels at different time horizons (million SEK)

Cost category	Cumulative year 5	Cumulative year 10	Cumulative year 20	Cumulative year 35
Cost vaccination programme	237	237	237	237
Averted healthcare costs	-8	-14	-22	-23
Cost difference regional level	**229**	**223**	**215**	**214**
Averted productivity losses	-9	-9	-9	-9
Cost difference national level	**-9**	**-9**	**-9**	**-9**
Total cost difference	**220**	**214**	**206**	**204**

Vaccination programme budget estimation

The budget impact of an HZ vaccination programme for 65-year-olds is presented in Table 12, assuming different costs of the vaccine and different vaccine coverage rates. For example, if the price of the vaccine was halved to around SEK 806 per dose, the cost of vaccinating 65-year-olds with a coverage rate of 60% would be SEK 130 million. The budget impact models do not include the cost of information campaigns, which may amount to an estimated SEK 20 million (62). This cost would likely decrease over time with increased awareness among the population about the vaccine programme.

Table 12 Estimated annual cost of a vaccination programme for 65-year-olds (a) (dose 1 and 2 during the same year (b)) at percentage rates of the current tentative vaccine price (b) (million SEK)

Expected coverage rate	Tentative vaccine price	70% of vaccine price	50% of vaccine price	30% of vaccine price	10% of vaccine price
50%	197	144	109	73	38
60%	237	173	130	88	45
70%	276	202	152	102	53
80%	316	231	174	117	60

(a) Population size (average 2017-2021): 110,165 65-year-olds
(b) The vaccine administration cost was set to SEK 180 per dose in all estimates

Table 13 presents the estimated budget impact of a phased implementation for all individuals aged 65 year and older, with a suggested start of the oldest as has been recommended by the National Council on Medical Ethics, although the cost per QALY is higher for this group. The expected coverage rates are based on what is seen for influenza vaccination for the elderly (47). The total cost over the five years was estimated at SEK 5.6 billion at the current tentative vaccine price and at SEK 2.1 billion if the vaccine price was to be reduced to 30% of the current tentative vaccine price.

Table 13 Estimated cost of a phased implementation for individuals aged 65 or older (dose 1 and 2 during the same year (a)) during a 5-year period (SEK million)

Age groups (b)	Expected coverage rate	Tentative vaccine price	70% of vaccine price	50% of vaccine price	30% of vaccine price	10% of vaccine price
Year 1: 82+ years old	70%	1,032	754	568	382	197
Year 2: 77-82 years old	70%	1,032	754	568	382	197
Year 3: 73-77 years old	65%	1,163	849	640	431	221
Year 4: 69-73 years old	60%	1,195	873	658	443	228
Year 5: 65-69 years old	60%	1,173	856	645	434	223
Total cost		**5,596**	**4,086**	**3,079**	**2,072**	**1,065**

(a) The vaccine administration cost was estimated at SEK 180 per dose
(b) Based on the average population 2017-2021. There is an overlap in age between the groups due to the phased introduction

Discussion

Our base case analysis indicates that the cost per QALY gained for the age cohorts 65-75 years old is around SEK 1,150,000 - 1,180,000 from a societal perspective. This is classified as a very high cost per QALY gained according to the methods guidelines used by the National Board of Health and Welfare (32). However, cost-effectiveness ratios as high as this have been approved for pharmaceuticals in exceptional cases (65). At a cost of approximately 30-40% of the current tentative vaccine price - when provided to individuals in the age interval 50-80 years - the cost per QALY gained would come down to a moderate level (below SEK 500,000) according to the same guidelines. For the oldest age cohort evaluated, 85-year-olds, the cost per QALY would be classified as high (approximately SEK 600,000) at 30% of the tentative vaccine price.

If we assume a lower real-life vaccine effectiveness, in line with what has been reported in observational studies in the USA population (79% year 1 instead of 97.7%), at a vaccine cost of 30% of the current tentative vaccine price, the cost per QALY gain would be around SEK 500,000 for the age cohorts of 60 to 75 year-olds. For 80 to 85-year-olds it would be SEK 600,000-800,000 per QALY gained.

It is important to point out that our base case results are very sensitive to the QALY loss applied in the model associated with HZ, particularly the QALY loss resulting from PHN. A meta-analysis of PHN burden of illness concludes that PHN affects 5-30% of HZ patients (9); hence the span of assumed QALY loss is a result of the variation across studies both of PHN incidence and the measurement of the degree and duration of pain associated with PHN. Consequently, this has resulted in a wide range of assumptions in previous HZ studies, leading to a fourfold variation in QALY loss due to HZ in previous economic evaluations of ZVL vaccination (66).

A recently published cost-effectiveness analysis of a RZV vaccine introduction in Region Stockholm from a health system perspective estimated a cost per QALY gained in the same range as our analysis, at SEK 1,190,000-1,320,000 for 65 to 74-year-olds in an analysis using the vaccine effectiveness of clinical studies, increasing to 1,530,000-1,680,000 when applying the vaccine effectiveness from observational studies (30).

To date, the RZV has been recommended to the general elderly population in a few European countries. In the UK, where a vaccine programme with the ZVL has been in place since 2013, the recommendation was changed to the RZV in 2023. A phased introduction started in September 2023 is planned over a 10-year period (23). Thereafter, the vaccine will be offered at age 60. The German Standing Committee on Vaccination recommended vaccination with RZV in 2019. The cost-effectiveness analysis that was part of the decision concluded that vaccination at age 65 years resulted in the lowest cost per QALY of the age cohort considered, at EUR 24,000, based on a tentative vaccine price of EUR 84 (26). The vaccine uptake in the first years has been approximately 10% of the population aged 60

years or above in Germany (27). The RZV has been recommended in Spain since 2021 for individuals aged 65 years or older (25), based on a cost-effectiveness analysis from 2018 that estimated the cost per QALY gained at EUR 6,930 with vaccination of individuals aged 65 years and at EUR 8,578 with vaccination of 75-year-olds (67). The recommendation proposed a phased introduction, depending on availability, vaccinating one age cohort per year, starting with 80-year-olds, down to 65-year-olds. A vaccine price of EUR 81 per dose was assumed in the analysis. In a Belgian Health Technology Assessment published in 2022, the data on cost-effectiveness were based on an analysis that estimated a cost per QALY gained which ranged between EUR 87,000-108,000 for the age cohorts 50-80 years, with a tentative vaccine price of EUR 140. They concluded that the price needed to be reduced to EUR 37.5 in order for the vaccine to be cost-effective (against a EUR 300,000 per QALY threshold in Belgium) for 50-year-olds (59, 68). The RZV has been recommended for all individuals aged 50 years or older in Canada since 2018 (24). The decision was based on an analysis, published in 2019, which estimated that the vaccination of individuals 50+ with the RZV would range from cost-saving to a cost per QALY of CAD 26,000 (SEK 215,000) at a vaccine price in the range of CAD 100-200 (SEK 800-1,600) (69). However, there have been implementation concerns due to the large budget impact of funding the vaccine to the population 50 years and older (27).

Thus, in summary, cost-effectiveness analyses have resulted in quite diverse cost per QALY assumptions, from cost-saving in Canada for certain age groups, a cost per QALY of less than SEK 100,000 in Spain, a cost per QALY of around SEK 250,000 in Germany to a cost per QALY in the range of SEK 1,000,000 in Belgium. The QALY loss assumptions seem to be an important factor influencing the results, where the Belgian analyses use the same burden of disease study (8) to estimate QALY loss from PHN as our study, as well as the study from Region Stockholm (30). Furthermore, different vaccine prices have been used in published models since national list prices were not available at the time of several of the analyses. Furthermore, the high budget impact of offering vaccination to the entire elderly population in a country is an issue, which may result in substantial costs during the first years if vaccination is not phased in over several years, for example as will be the case in Spain and the UK.

The annual budget impact of a vaccination programme for 65-year-olds in Sweden was estimated to approximately SEK 240 million with the current tentative vaccine price and to approximately SEK 90 million at 30% of the current tentative vaccine price, assuming a 60% vaccine coverage rate in both cases. We estimated that a vaccination offer to the entire population aged 65 years and older would amount to around SEK 5.6 billion with the current tentative vaccine price. If the vaccine price were reduced to 30% of the tentative price the total cost of offering vaccination to all individuals aged 65 or older would be approximately SEK 2.1 billion, or in the range of SEK 400 million per year if vaccination eligibility was to be distributed over a 5-year period with the vaccine offered to different age groups.

Individuals that are immunocompromised due to disease or treatment, aged 18 or older, incur a risk of herpes zoster in line with or higher than that of the elderly. We have not assessed the cost-effectiveness of a vaccination programme for this group due to its heterogeneity in terms of disease risk, vaccine effectiveness and age. Few cost-effectiveness analyses have been published for this group (70). However, the US Centers for Disease Control and Prevention has published an economic evaluation looking at different immunocompromised patient groups aged 19-49 years. The study concluded that RZV vaccination range from cost-saving to a cost of around USD 200,000 per QALY depending on the patient condition (71).

The limitations of this health economic analysis include the fact that the RZV is relatively new, there is only long-term follow-up data for 10 years, the uncertainty associated with PHN-associated QALY loss and that of other sequelae such as stroke and HZO. A limitation on the cost side is that we did not have data that allowed us to include potential costs of changes in home care service needs due to HZ and PHN.

To conclude, our analysis estimated that an HZ vaccination programme using the RZV vaccine would incur a very high cost per QALY in the Swedish context with the current tentative vaccine price. The budget impact of offering vaccination to the entire population aged 65 years or older would be considerable, therefore implementation might need to be offered in a phased manner over a number of years.

References

1. Government of Sweden, Ministry of Health and Social Affairs. The Swedish Communicable Diseases Act (Smittskyddslagen (2004:168)), (2004).
2. Nardone A, de Ory F, Carton M, Cohen D, van Damme P, Davidkin I, et al. The comparative sero-epidemiology of varicella zoster virus in 11 countries in the European region. Vaccine. 2007;25(45):7866-72. DOI:10.1016/j.vaccine.2007.07.036.
3. Widgren K, Persson Berg L, Morner A, Lindquist L, Tegnell A, Giesecke J, et al. Severe chickenpox disease and seroprevalence in Sweden - implications for general vaccination. Int J Infect Dis. 2021;111:92-8. DOI:10.1016/j.ijid.2021.08.012.
4. Södergren E, Mardberg K, Nishimwe M, Bhavsar A, Marijam A, Bergström T, et al. Incidence and burden of herpes zoster in Sweden: a regional population-based register study. Submitted to Infectious Diseases and Therapy. 2023.
5. Brisson M, Edmunds WJ, Law B, Gay NJ, Walld R, Brownell M, et al. Epidemiology of varicella zoster virus infection in Canada and the United Kingdom. Epidemiol Infect. 2001;127(2):305-14. DOI:10.1017/s0950268801005921.
6. National Board of Health and Welfare. National Patient Register of Sweden [Internet]. 2023 [cited September 2023]. From: https://www.socialstyrelsen.se/statistik-och-data/statistik/statistikdatabasen/.
7. Bowsher D. The lifetime occurrence of Herpes zoster and prevalence of post-herpetic neuralgia: A retrospective survey in an elderly population. Eur J Pain. 1999;3(4):335-42. DOI:10.1053/eujp.1999.0139.
8. Gauthier A, Breuer J, Carrington D, Martin M, Remy V. Epidemiology and cost of herpes zoster and post-herpetic neuralgia in the United Kingdom. Epidemiol Infect. 2009;137(1):38-47. DOI:10.1017/S0950268808000678.
9. Kawai K, Gebremeskel BG, Acosta CJ. Systematic review of incidence and complications of herpes zoster: towards a global perspective. BMJ Open. 2014;4(6):e004833. DOI:10.1136/bmjopen-2014-004833.
10. Liesegang TJ. Herpes zoster ophthalmicus natural history, risk factors, clinical presentation, and morbidity. Ophthalmology. 2008;115(2 Suppl):S3-12. DOI:10.1016/j.ophtha.2007.10.009.
11. Marra F, Ruckenstein J, Richardson K. A meta-analysis of stroke risk following herpes zoster infection. BMC Infect Dis. 2017;17(1):198. DOI:10.1186/s12879-017-2278-z.
12. Yawn BP, Wollan PC, Kurland MJ, St Sauver JL, Saddier P. Herpes zoster recurrences more frequent than previously reported. Mayo Clin Proc. 2011;86(2):88-93. DOI:10.4065/mcp.2010.0618.
13. Kim YJ, Lee CN, Lee MS, Lee JH, Lee JY, Han K, et al. Recurrence Rate of Herpes Zoster and Its Risk Factors: a Population-based Cohort Study. J Korean Med Sci. 2019;34(2):e1. DOI:10.3346/jkms.2019.34.e1.
14. Pan CX, Lee MS, Nambudiri VE. Global herpes zoster incidence, burden of disease, and vaccine availability: a narrative review. Ther Adv Vaccines Immunother. 2022;10:25151355221084535. DOI:10.1177/25151355221084535.
15. Oxman MN, Levin MJ, Johnson GR, Schmader KE, Straus SE, Gelb LD, et al. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. N Engl J Med. 2005;352(22):2271-84. DOI:10.1056/NEJMoa051016.
16. Centers for Disease Control and Prevention. Grading of Recommendations, Assessment, Development, and Evaluation (GRADE): Recombinant Zoster Vaccine (RZV) and Herpes Zoster Live-Attenuated Vaccine (ZVL). In: Practices ACoI, editor.: Centers for Disease Control and Prevention; 2018.

17. Strezova A, Diez-Domingo J, Al Shawafi K, Tinoco JC, Shi M, Pirrotta P, et al. Long-term Protection Against Herpes Zoster by the Adjuvanted Recombinant Zoster Vaccine: Interim Efficacy, Immunogenicity, and Safety Results up to 10 Years After Initial Vaccination. Open Forum Infect Dis. 2022;9(10):ofac485. DOI:10.1093/ofid/ofac485.

18. Izurieta HS, Wu X, Forshee R, Lu Y, Sung HM, Agger PE, et al. Recombinant Zoster Vaccine (Shingrix): Real-World Effectiveness in the First 2 Years Post-Licensure. Clin Infect Dis. 2021;73(6):941-8. DOI:10.1093/cid/ciab125.

19. Sun Y, Jackson K, Dalmon CA, Shapiro BL, Nie S, Wong C, et al. Effectiveness of the recombinant zoster vaccine among Kaiser Permanente Hawaii enrollees aged 50 and older: A retrospective cohort study. Vaccine. 2021;39(29):3974-82. DOI:10.1016/j.vaccine.2021.05.056.

20. Sun Y, Kim E, Kong CL, Arnold BF, Porco TC, Acharya NR. Effectiveness of the Recombinant Zoster Vaccine in Adults Aged 50 and Older in the United States: A Claims-Based Cohort Study. Clin Infect Dis. 2021;73(6):949-56. DOI:10.1093/cid/ciab121.

21. Zerbo O, Bartlett J, Fireman B, Lewis N, Goddard K, Dooling K, et al. Effectiveness of Recombinant Zoster Vaccine Against Herpes Zoster in a Real-World Setting. Ann Intern Med. 2024;177(2):189-95. DOI:10.7326/M23-2023.

22. Dooling KL, Guo A, Patel M, Lee GM, Moore K, Belongia EA, et al. Recommendations of the Advisory Committee on Immunization Practices for Use of Herpes Zoster Vaccines. MMWR Morb Mortal Wkly Rep. 2018;67(3):103-8. DOI:10.15585/mmwr.mm6703a5.

23. UK Health Security Agency. UK Health Security Agency. Introduction of Shingrix® vaccine for the whole programme and expansion of eligible cohorts letter. 2023.

24. Warrington R, Ismail S, National Advisory Committee on Immunization. Summary of the NACI Update on Herpes Zoster Vaccines. Can Commun Dis Rep. 2018;44(9):220-5. DOI:10.14745/ccdr.v44i09a06.

25. Spanish Ministry of Health. Recomendaciones de vacunacion frente herpes zoster. In: Grupo de trabajo de herpes zóster de la Ponencia de Programa y Registro de Vacunaciones CdSPdCIdSNdS, editor.: Ministerio de Sanidad; 2021.

26. Siedler A, Koch J, Garbe E, Hengel H, von Kries R, Ledig T, et al. Background paper to the decision to recommend the vaccination with the inactivated herpes zoster subunit vaccine : Statement of the German Standing Committee on Vaccination (STIKO) at the Robert Koch Institute. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2019;62(3):352-76. DOI:10.1007/s00103-019-02882-5.

27. European Centre for Disease Prevention and Control. ECDC NITAG Information Webinar: Herpes Zoster Vaccination, 13 June 2023. 2023.

28. Wolff E, Widgren K, Scalia Tomba G, Roth A, Lep T, Andersson S. Cost-effectiveness of varicella and herpes zoster vaccination in Sweden: An economic evaluation using a dynamic transmission model. PLoS One. 2021;16(5):e0251644. DOI:10.1371/journal.pone.0251644.

29. The Dental and Pharmaceutical Benefits Agency of Sweden. Zostavax utesluts ur högkostnadsskyddet. 2014.

30. Nystrand C HS, Heintz E, Sparring V. Kostnadseffektiviteten av bältrosvaccinering med Shingrix® i Region Stockholm. Stockholm centrum för hälsoekonomi. Centrum för hälsoekonomi, informatik och sjukvårdsforskning, Region Stockholm; 2023. [cited March 2024]. From: https://www.chis.regionstockholm.se/49d8c5/globalassets/verksamheter/chis/stoche/rapport_baltrosvaccinering.pdf.

31. Läkemedelsboken: Hudsjukdomar [Internet]. 2023 [cited March 2024]. From: https://lakemedelsboken.se/kapitel/hud/hudsjukdomar.html#f1_82.

32. National Board of Health and Welfare. National Board of Health and Welfare. Nationella riktlinjer - Metodbeskrivning. 2019. [cited March 2024]. From:

https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/dokument-webb/nationella-riktlinjer/nationella-riktlinjer-metodbeskrivning.pdf.

33. Statistics Sweden. Population statistics [Internet]. 2023 [cited March 2024]. From: https://www.scb.se/en/finding-statistics/statistics-by-subject-area/population/population-composition/population-statistics/#_Tablesandgraphs.

34. Statistics Sweden. Life table by sex and age. Year 1960 - 2022 [Internet]. 2023 [cited March 2024]. From: https://www.statistikdatabasen.scb.se/pxweb/en/ssd/START__BE__BE0101__BE0101I/LivslangdEttariga.

35. The National Board of Health and Welfare. Arbetsprocessen för nationella prospektiva vikter - Uppdatering inför 2023. 2023. [cited March 2024]. From: https://www.socialstyrelsen.se/statistik-och-data/klassifikationer-och-koder/drg/viktlistor/.

36. The Dental and Pharmaceutical Benefits Agency of Sweden. Läkemedelsförmånsnämndens allmänna råd om ekonomiska utvärderingar. 2017.

37. Ultsch B, Damm O, Beutels P, Bilcke J, Bruggenjurgen B, Gerber-Grote A, et al. Methods for Health Economic Evaluation of Vaccines and Immunization Decision Frameworks: A Consensus Framework from a European Vaccine Economics Community. Pharmacoeconomics. 2016;34(3):227-44. DOI:10.1007/s40273-015-0335-2.

38. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. BMJ. 2022;376:e067975. DOI:10.1136/bmj-2021-067975.

39. Swedish Agency for Health Technology Assessment and Assessment of Social Services. Utvärdering av insatser i hälso- och sjukvården och socialtjänsten: En metodbok. Stockholm: Statens beredning för medicinsk och social utvärdering (SBU); 2023. [cited March 2024]. From: https://www.sbu.se/sv/metod/metodboken-2023/.

40. Government of Sweden, Ministry of Health and Social Affairs. Health and Medical Services Act (Hälso- och sjukvårdslag (2017:30)), (2017).

41. Prioriteringscentrum. Förslag till modell för horisontell prioritering inom hälso- ochjukvård - Rapport från Nationell expertgrupp för horisontella prioriteringar. Linköpings Universitet; 2023. [cited March 2024]. From: https://liu.diva-portal.org/smash/get/diva2:1802243/FULLTEXT01.pdf.

42. Sundstrom K, Weibull CE, Soderberg-Lofdal K, Bergstrom T, Sparen P, Arnheim-Dahlstrom L. Incidence of herpes zoster and associated events including stroke--a population-based cohort study. BMC Infect Dis. 2015;15:488. DOI:10.1186/s12879-015-1170-y.

43. Lal H, Cunningham AL, Godeaux O, Chlibek R, Diez-Domingo J, Hwang SJ, et al. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Engl J Med. 2015;372(22):2087-96. DOI:10.1056/NEJMoa1501184.

44. Cunningham AL, Lal H, Kovac M, Chlibek R, Hwang SJ, Diez-Domingo J, et al. Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older. N Engl J Med. 2016;375(11):1019-32. DOI:10.1056/NEJMoa1603800.

45. Lu A, Sun Y, Porco TC, Arnold BF, Acharya NR. Effectiveness of the Recombinant Zoster Vaccine for Herpes Zoster Ophthalmicus in the United States. Ophthalmology. 2021;128(12):1699-707. DOI:10.1016/j.ophtha.2021.04.017.

46. Schmader KE, Levin MJ, Chen M, Matthews S, Riley ME, Woo W, et al. Impact of Reactogenicity After Two Doses of Recombinant Zoster Vaccine Upon Physical Functioning and Quality of Life: An Open Phase III Trial in Older Adults. J Gerontol A Biol Sci Med Sci. 2021;76(3):485-90. DOI:10.1093/gerona/glaa127.

47. Public Health Agency of´Sweden. Vaccinationstäckning bland personer 65 år och äldre, per region och nationellt, säsongen 2022–2023. 2023. From:

https://www.folkhalsomyndigheten.se/folkhalsorapportering-statistik/statistikdatabaser-och-visualisering/vaccinationsstatistik/statistik-for-influensavaccinationer/vaccinationstackning-mot-influensa-20222023/.

48. World Health Organization. MI4A Vaccine Purchase Database [Internet]. 2023 [cited September 2023]. From: https://www.who.int/teams/immunization-vaccines-and-biologicals/vaccine-access/mi4a/mi4a-vaccine-purchase-data.

49. Sveriges Riksbank. Annual average exchange rates (aggregate). 2023. From: https://www.riksbank.se/sv/statistik/sok-rantor--valutakurser/arsgenomsnitt-valutakurser/?y=2023&m=10&s=Comma&f=y.

50. Swedish Tax Agency. Arbetsgivarvgifter (employer's fee). 2023. From: https://www.skatteverket.se/foretag/arbetsgivare/arbetsgivaravgifterochskatteavdrag/arbetsgivaravgifter.4.233f91f71260075abe8800020817.html?q=arbetsgivaravgifter.

51. Statistics Sweden. Average monthly salary by occupation [Internet]. 2023 [cited March 2024]. From: https://www.scb.se/hitta-statistik/statistik-efter-amne/arbetsmarknad/loner-och-arbetskostnader/lonestrukturstatistik-kommuner/pong/tabell-och-diagram/genomsnittlig-manadslon-efter-yrke/.

52. Studahl M, Petzold M, Cassel T. Disease burden of herpes zoster in Sweden--predominance in the elderly and in women - a register based study. BMC Infect Dis. 2013;13:586. DOI:10.1186/1471-2334-13-586.

53. Swedish Association of Local Authorities and Regions. The Cost Per Patient Database (KPP Databas) [Internet]. 2023 [cited September 2023]. From: https://skr.se/skr/halsasjukvard/ekonomiavgifter/kostnadperpatientkpp/kppdatabas.46722.html.

54. Apoteket. Products. 2023 [cited September]. From: https://www.apoteket.se/.

55. Statistics Sweden. Befolkningen 15-74 år (AKU) efter kön, ålder och arbetskraftstillhörighet. År 2001 - 2023 [Internet]. 2023 [cited March 2024]. From: https://www.statistikdatabasen.scb.se/pxweb/sv/ssd/START__AM__AM0401__AM0401A/NAKUBefolkning2Ar/.

56. Nilsson J, Cassel T, Lindquist L. Burden of herpes zoster and post-herpetic neuralgia in Sweden. BMC Infect Dis. 2015;15:215. DOI:10.1186/s12879-015-0951-7.

57. van Hoek AJ, Gay N, Melegaro A, Opstelten W, Edmunds WJ. Estimating the cost-effectiveness of vaccination against herpes zoster in England and Wales. Vaccine. 2009;27(9):1454-67. DOI:10.1016/j.vaccine.2008.12.024.

58. Burstrom K, Johannesson M, Diderichsen F. Swedish population health-related quality of life results using the EQ-5D. Qual Life Res. 2001;10(7):621-35. DOI:10.1023/a:1013171831202.

59. Pieters Z, Ogunjimi B, Beutels P, Bilcke J. Cost-Effectiveness Analysis of Herpes Zoster Vaccination in 50- to 85-Year-Old Immunocompetent Belgian Cohorts: A Comparison between No Vaccination, the Adjuvanted Subunit Vaccine, and Live-Attenuated Vaccine. Pharmacoeconomics. 2022;40(4):461-76. DOI:10.1007/s40273-021-01099-2.

60. Persson J, Levin LA, Holmegaard L, Redfors P, Jood K, Jern C, et al. Stroke survivors' long-term QALY-weights in relation to their spouses' QALY-weights and informal support: a cross-sectional study. Health Qual Life Outcomes. 2017;15(1):150. DOI:10.1186/s12955-017-0724-7.

61. Luengo-Fernandez R, Gray AM, Bull L, Welch S, Cuthbertson F, Rothwell PM, et al. Quality of life after TIA and stroke: ten-year results of the Oxford Vascular Study. Neurology. 2013;81(18):1588-95. DOI:10.1212/WNL.0b013e3182a9f45f.

62. Magnusdottir K GZ, Heintz E, Zethraeus N, Sparring V, Nystrand C. Budgetpåverkansanalys av vaccinationsprogram för äldre. Stockholm centrum för hälsoekonomi. Centrum för hälsoekonomi, informatik och sjukvårdsforskning, Region Stockholmi; 2023. [cited March 2024]. From: https://www.chis.regionstockholm.se/49f0e9/globalassets/verksamheter/chis/stoche/rapport_bia_230627-1.1.pdf.

63. Mauskopf JA, Sullivan SD, Annemans L, Caro J, Mullins CD, Nuijten M, et al. Principles of good practice for budget impact analysis: report of the ISPOR Task Force on good research practices--budget impact analysis. Value Health. 2007;10(5):336-47. DOI:10.1111/j.1524-4733.2007.00187.x.

64. Burstrom K, Johannesson M, Diderichsen F. Health-related quality of life by disease and socio-economic group in the general population in Sweden. Health Policy. 2001;55(1):51-69. DOI:10.1016/s0168-8510(00)00111-1.

65. Svensson M, Nilsson FO, Arnberg K. Reimbursement Decisions for Pharmaceuticals in Sweden: The Impact of Disease Severity and Cost Effectiveness. Pharmacoeconomics. 2015;33(11):1229-36. DOI:10.1007/s40273-015-0307-6.

66. Kawai K, Preaud E, Baron-Papillon F, Largeron N, Acosta CJ. Cost-effectiveness of vaccination against herpes zoster and postherpetic neuralgia: a critical review. Vaccine. 2014;32(15):1645-53. DOI:10.1016/j.vaccine.2014.01.058.

67. L. Vallejo Torres RL, E. Sanromá Ramos, V. Ramos García, A. Toledo Chávarri, E. Herrera Ramos, J.J. Pérez Martín, A. Limia Sánchez, M. Soler Soneira, J. Castilla Catalán, M. García Cenoz, S. Tamames Gómez, I. Imaz Iglesia, J.P. Chalco, A. García Rojas, P.G. Serrano-Aguilar. Coste-efectividad de la vacunación frente a herpes zóster. In: SESCS IdEdTS, editor. Madrid: Ministerio de Sanidad, Consumo y Bienestar Social; 2018.

68. Roberfroid D ZR, Maertens de Noordhout C, Thiry N. Evaluation of shingrix vaccine against herpes zoster. Health Technology Assessment (HTA). Brussels: Belgian Health Care Knowledge Centre (KCE); 2022.

69. Drolet M, Zhou Z, Sauvageau C, DeWals P, Gilca V, Amini R, et al. Effectiveness and cost-effectiveness of vaccination against herpes zoster in Canada: a modelling study. CMAJ. 2019;191(34):E932-E9. DOI:10.1503/cmaj.190274.

70. Giannelos N, Ng C, Curran D. Cost-effectiveness of the recombinant zoster vaccine (RZV) against herpes zoster: An updated critical review. Hum Vaccin Immunother. 2023;19(1):2168952. DOI:10.1080/21645515.2023.2168952.

71. Leidner AJ, Anderson TC, Hong K, Ortega-Sanchez IR, Guo A, Pike J, et al. Cost-Effectiveness Analysis of Vaccination With Recombinant Zoster Vaccine Among Hematopoietic Cell Transplant Recipients and Persons With Other Immunocompromising Conditions Aged 19 to 49 Years. Value Health. 2023;26(2):204-15. DOI:10.1016/j.jval.2022.08.003.

Appendix A: Contributing experts

Internal experts from the Public Health Agency of Sweden

2022-2024

Sören Andersson, professor, head of unit, Unit for vaccine programmes

Annika Ersson, analyst, infectiologist, previous county officer on disease control, Unit for vaccine programmes

Kari Johansen, analyst, pediatrician, clinical virologist, previous senior consultant Vaccine Preventable Diseases/Influenza and other Respiratory Diseases, ECDC, former representative EMA Vaccine Working Party, Unit for vaccine programmes

Frida Kasteng, analyst, health economist, Unit for analysis

Disa Hansson, analyst, mathematical modeller, Unit for analysis

Lisa Brouwers, head of unit, Unit for analysis

Carl Lundberg, analyst, Unit for coordinated public health

Sofie Larsson, analyst, health economist, Unit for analysis

Anna Leetma, communicator, Unit for planned communication

Helene Englund, analyst, epidemiologist, Unit for vaccine programmes

Ingrid Uhnoo, analyst, infectiologist, previously analyst the Swedish Medicine Agency, former representantive EMA Vaccine Working Party, previously Head of programmes, Unit of vaccine programmes

External consultant modelling

GianPaolo Scalia Tomba, guest professor, mathematician, Department of mathematical statistics, Stockholm University

2018-2020

Sören Andersson, analyst, professor

Ellen Wolff, analyst, health economist, Unit for analysis

Tiia Lepp, analyst, Unit for vaccine programmes

Adam Roth, Head of Unit for vaccine programmes

Katarina Widgren, analyst, infectiologist, Unit for vaccine programmes

Rose-Marie Carlsson, analyst

Ingrid Uhnoo, analyst, infectiologist, previously analyst the Swedish Medicine Agency, previously representant EMA Vaccine Working Party, previously Head of programmes, Unit of vaccine programmes

External consultant modelling

GianPaolo Scalia Tomba, guest professor, mathematician, Department of mathematical statistics, Stockholm University

Nordic Collaborating group for systematic literature review

Kari Johansen. Public Health Agency of Sweden

Lene Kristine Juvet. Norwegian Public Health Institute

Silje Lae Solberg. Norwegian Public Health Institute

Eli Heen. Norwegian Public Health Institute

Ingun Heiene Tveteraas. Norwegian Public Health Institute

Hanne Nøkleby. Norwegian Public Health Institute

Joakim Øverbø. Norwegian Public Health Institute

Annika Ersson. Public Health Agency of Sweden

Kamilla Josefsdottir. Centre for Health Security and Communicable Disease Control, Directorate of Health, Iceland

Ida Glode Helmuth. Danish Health Authority

Heini Salo. Finnish Institute for Health and Welfare

External experts from specialist associations and other government agencies

Sveriges Infektionsläkarförening (Fredrik Kahn, infectiologist, Anja Rosdahl, infectiologist, Martin Angelin, infectiologist)

Smittskyddsläkarföreningen (Katarina Widgren, ass. county officer)

Sveriges Förening för Allmänmedicin (Margareta Ehnebom, general practicioner)

Svensk Geriatrisk förening (Dorota Religa, professor in geriatrics)

Svensk Reumatologisk förening (Jon Einarsson, rheumatologist; Meliha Kapetanovic, rheumatologist; Iva Gunnarsson, rheumatologist)

Sveriges läkares intresseförening för primär immunbrist (Fredrik Kahn, infectiologist)

Skolläkarföreningen (Helena Lüning, MD student health)

Skolsköterskeföreningen (Ulrika Brännström, nurse within student health)

Barnhälsovården (Jeanette Björnell, nurse within the child health care)

Barnhälsovårdsöverläkarna (Leif Ekholm, paediatrician)

Barnläkarföreningen (Viktor Peny, paediatrician)

Referensgruppen för antiviral terapi (RAV) (Jan Albert, professor, clinical virology)

Läkemedelsverket (Charlotta Bergquist, head of unit, Unit for efficacy and safety; Bernice Aronsson, analyst, paediatrician)

The National Board of Health and Welfare, Department of registry and statistics, Statistikservice (Henrik Nordin, head of unit; Mattias Åman Svensson, statistician)

Tandvårds- och Läkemedelsförmånsverket (TLV) (Sonny Larsson)

Experts within child oncology, immunodeficiency, infectious diseases, clinical virology and vaccinology with special expertise

2022-2024

Marta Granström, professor emeritus, Karolinska Institutet, specialist in clinical virology and bacteriology, former representative EMA Vaccine Working Party, EMA Paediatric Committee (PDCO)

Per Ljungman, professor, Karolinska Institutet, specialist in internal medicine and hematology

Anna Nilsson, child oncologist, senior lecturer/senior physician, Department of Women's and Children's Health, Karolinska Institutet

Marie Studahl, professor in infectious diseases, infectiologist, Göteborg University

2018-2020

Anna Nilsson, child oncologist, senior lecturer/senior physician, Department of Women's and Children's Health, Karolinska Institutet

Marie Studahl, professor in infectious diseases, infectiologist, Göteborg University

Thomas Bergström, professor, specialist in clinical virology and bacteriology, Göteborg University

Margareta Ehnebom, general practitioner

Kathy Falkenstein-Hagander, paediatrician

Jeanette Björnell, nurse, child health services developer, Region Stockholm

The Public Health Agency of Sweden is an expert authority with responsibility for public health issues at a national level. The Agency develops and supports activities to promote health, prevent illness and improve preparedness for health threats. Our vision statement: a public health that strengthens the positive development of society.

Folkhälsomyndigheten
PUBLIC HEALTH AGENCY OF SWEDEN

Solna Nobels väg 18, 171 82 Solna. **Östersund** Campusvägen 20. Box 505, 831 26 Östersund.

www.folkhalsomyndigheten.se