Human Vaccines & Immunotherapeutics

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/khvi20

Cost-utility analysis of the universal pneumococcal vaccination programme for older adults in Norway

Liv Solvår Nymark, Jacob Dag Berild, Trude Marie Lyngstad, Brita Askeland Winje, Didrik Frimann Vestrheim, Ingeborg Aaberge, Lene Kristine Juvet & Ellen Wolff

To cite this article: Liv Solvår Nymark, Jacob Dag Berild, Trude Marie Lyngstad, Brita Askeland Winje, Didrik Frimann Vestrheim, Ingeborg Aaberge, Lene Kristine Juvet & Ellen Wolff (2022): Cost-utility analysis of the universal pneumococcal vaccination programme for older adults in Norway, Human Vaccines & Immunotherapeutics, DOI: 10.1080/21645515.2022.2101333

To link to this article: https://doi.org/10.1080/21645515.2022.2101333

Published online: 02 Aug 2022.

HUMAN VACCINES & IMMUNOTHERAPEUTICS
https://doi.org/10.1080/21645515.2022.2101333

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

OPEN ACCESS Check for updates

Cost-utility analysis of the universal pneumococcal vaccination programme for older adults in Norway

Liv Solvår Nymark[a], Jacob Dag Berild[a], Trude Marie Lyngstad[a], Brita Askeland Winje[a], Didrik Frimann Vestrheim[a], Ingeborg Aaberge[a], Lene Kristine Juvet[a], and Ellen Wolff[b]

[a]Division of Infection ControL, Norwegian Institute of Public Health, Oslo, Norway; [b]Department of Public Health Analysis and Data Management, Public Health Agency of Sweden, Solna, Sweden

ABSTRACT

The aim of this study was to establish whether the universal pneumococcal vaccination for older adults in Norway is likely to be cost-effective from the perspective of the health care provider. A decision tree model developed by the Public Health Agency of Sweden was adapted to the Norwegian setting. Two cohorts, consisting of 65-year-olds and 75-year-olds grouped into vaccinated and unvaccinated, were followed over a 5-year time horizon. In the base case, the 23-valent polysaccharide vaccine (PPV23) was used while the 13-valent pneumococcal conjugate vaccine (PCV13) was included in scenario analyses only. The costs and health benefits (measured in quality adjusted life years (QALY) gained) were compared in the two cohorts between the vaccinated and unvaccinated groups. The impact of indirect effects of the vaccine, such as herd immunity and serotype replacement, were not investigated. The relative importance of change in price was assessed by performing one-way sensitivity analyses. Under base-case assumptions, the programme for the 75-year-old cohort is expected to be dominant (cost-effective) from the health care perspective at the current maximal pharmacy retail price and at 75% vaccination coverage. In comparison, for the 65-year-old cohort the cost per QALY gained is approximately NOK 601,784 (EUR 61,281) under the base-case assumptions. A reduction in the cost of the vaccine to one quarter of its current level also brings the cost per QALY gained within the acceptable ranges in a Norwegian context for both the 65- and 75-year-old cohorts. There is no exact cost-effectiveness threshold in Norway. However, introducing a vaccination programme against pneumococcal disease for 65-year-olds in Norway is likely to fall within the acceptable range while for the 75-year-old cohort the universal programme appears to be dominant (cost-effective).

ARTICLE HISTORY
Received 7 April 2022
Revised 5 July 2022
Accepted 10 July 2022

KEYWORDS
Pneumococcal vaccine; cost-effectiveness; *Streptococcus pneumonia*

Introduction

Pneumococcal infections are caused by *Streptococcus pneumoniae*, commonly referred to as pneumococcus.[1] *S pneumoniae* is the most common cause of community-acquired pneumonia (CAP), bacterial meningitis, bacteremia, and otitis media.[2] Additionally, it is an important cause of sinusitis, septic arthritis, osteomyelitis, peritonitis, and endocarditis.[3]

Following the introduction of the conjugate pneumococcal vaccine (PCV) in the Norwegian childhood immunization programme, we observed substantial reductions in severe invasive pneumococcal disease (IPD) and pneumonia caused by vaccine serotypes in children targeted for vaccination, as well as in unvaccinated adults through indirect herd protection. However, the burden of pneumococcal disease remains considerable in Norway, especially among the older adults and clinical risk groups[4] due to increases in IPD incidence caused by replacement with non-vaccine serotypes. In Norway, after 2016, a declining incidence of IPD caused by both PCV13 (13-valent pneumococcal conjugate vaccine) and non-PCV13 IPD was observed, though the proportion of non-PCV13 serotypes is increasing compared to PCV13 serotypes.[4]

In Norway, the 23-valent polysaccharide vaccine (PPV23) is not implemented in a universal pneumococcal vaccination programme for older adults. However, all persons 65 years and older, as well as medical risk groups are recommended pneumococcal vaccination.[5] PPV23 is currently the recommended vaccine for medical risk groups and the older adults in Norway. Only a few, selected high-risk groups are recommended PCV13 in series with PPV23.[6] The current uptake of pneumococcal vaccination in Norway is assumed to be suboptimal in adultsat approximately 15%.[4] Currently vaccination outside the childhood immunization programme is only financed for selected medical high-risk groups.[7] In Denmark, a pneumococcal vaccination programme has been administered free of charge for persons aged 65 years and older, as well as for high-risk groups since 2020.[8] In Sweden, people with certain underlying diseases, as well as those who are 75 years-of-age and older, will be offered vaccination against pneumococcal infections within a free-of-charge national vaccination programme from the autumn of 2022.[9]

The continued dissemination of non-vaccine serotypes, as well as the low uptake of pneumococcal vaccination warrants the need to inform health policy makers on the effect and cost-

CONTACT Liv Solvår Nymark livsolvar.nymark@fhi.no Division of Infection Control, Norwegian Institute of Public Health, Postbox 222, Skøyen, NO-0213 Oslo, Norway.

effectiveness of introducing 23-valent polysaccharide vaccine (PPV23) in a universal vaccination programme for older adults in Norway. This study addresses the issue of whether universal vaccination for older adults with PPV23 would be a cost-effective policy from the health care provider perspective. The analysis takes into consideration the uncertainties related to the variation in the vaccine price and coverage but does not consider the potential for indirect protection (herd immunity) among unvaccinated individuals as well as serotype replacement effects in the whole population.

Methods

Decision tree model

A deterministic cohort decision-tree model developed at the Public Health Agency of Sweden was adapted to the Norwegian setting. The model is described in detail elsewhere.[10] A modified schematic from the Swedish analysis using the same model is presented in Figure 1. The base case analysis measures the impact of vaccinating with PPV23 for a hypothetical 65-year-old and 75-year-old cohort in Norway compared to no vaccination. The 13-valent conjugate vaccine (PCV13) was only included in a scenario analysis. The model was constructed to follow a hypothetical cohort of 65-year-olds and 75-year-olds over a five-year time horizon. A cohort size of 55,614 individuals was used for the 65-year-old cohort while a cohort size of 31,925 individuals was used for the 75-year-old cohort. These cohort sizes were based on population data from Statistics Norway from 2015. The cycle length was set to one year. Individuals enter the model in a susceptible state and then progress depending on their risk of disease, vaccination coverage and vaccination effectiveness.

The model was developed in Excel (2016) software. A collaboration working to assess the impact of pneumococcal vaccination on older adults was previously established among the Nordic countries. The work included a systematic literature review,[11] and it was agreed to strive to re-use models and estimates for health economic evaluations where appropriate. In line with the objective of the Nordic collaboration, the Swedish model was chosen.

The number of quality-adjusted life-year (QALY) gained from the vaccination programme is used as the primary outcome measure for the programme. This is compared to its net cost, which is the additional cost of vaccination minus the expected savings from the programme in terms of reduced use of health care resources.

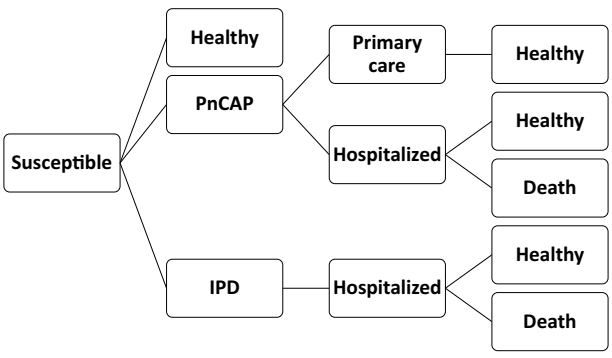

Figure 1. Simplified schematic overview of the decision tree model. Abbreviations: IPD: Invasive pneumococcal disease; PnCAP: Non-invasive pneumococcal community-acquired pneumonia

Pneumococcal infection can lead to a number of outcomes such as invasive disease, pneumonia, ear infections, sinusitis, bronchitis, arthritis, conjunctivitis, and peritonitis. However, the model only considers invasive pneumococcal disease (IPD) and noninvasive pneumococcal community-acquired pneumonia (PnCAP) as randomized and non-randomized observational studies regarding vaccine efficacy are available. All IPD cases were assumed to require hospital admission (100%) while PnCAP cases were assumed to require either hospital admission (25%) or general practitioners (GP) consultation (75%). These assumptions were made in collaboration with clinical experts.

Future benefits and costs were discounted according to the Norwegian guidelines for single technology assessment (STA) at 4% per annum.[12] In the base-case analysis, we assumed vaccination coverage of 75% among both the 65- and 75-year-olds cohorts as this is the target vaccination coverage.

The impact of herd protection, (i.e., changes in disease incidence among unvaccinated individuals), was not considered in this work. Cross-protection (i.e., the protection conferred by a serotype of pneumococci that prevents infection by a closely related serotype of pneumococci) or serotype replacement (i.e., the resistance to sub-types of serotypes if the frequency of a sub-type of serotype declines due to high levels of immunity allowing other serotypes to replace it) were not considered in the analysis.[13] Serotype distribution that may be expected to occur after the introduction of pneumococcal vaccination was, however, considered in the base-case analysis. The impact of changes in vaccine price, vaccination coverage, and inpatient PnCAP incidence were further investigated in one-way sensitivity analyses.

Epidemiological data

No comprehensive community acquired pneumonia (CAP) outpatient data was available from Norwegian sources.[14,15] We assumed that the Swedish register data for outpatient CAP would be similar enough to the Norwegian setting to justify the use of the Swedish dataset.[15] As such, for the base-case analysis the age-specific incidence rates of CAP outpatient for the 65- and 75- year-old cohorts were derived by extracting the data from Swedish register sources[16] and used in line with the methodology in the Swedish model. In the Swedish study CAP was defined as a first-listed discharge diagnosis of pneumonia, or first-listed diagnosis of meningitis, septicemia, or empyema in addition to a pneumonia diagnosis. Analyses were restricted to patients without previous hospital care during the last 30 days to restrict episodes to CAP. The share of CAP which is caused by Streptococcus pneumoniae was estimated as 9% for outpatient CAP based on Leven *et al.* 2018.[17] The model only included the share of CAP that was estimated to be due to pneumococcal infection, i.e. noninvasive pneumococcal community acquired pneumonia (PnCAP).

CAP inpatient estimates were based on hospital discharge data from the Norwegian Patient Register (NPR).[18] CAP was defined as a first-listed discharge diagnosis of pneumonia

according to the listed ICD10-codes. Episodes per person were defined as one or several admissions for CAP within the same 30 days. Further details and description of the data compilation can be found elsewhere[18] In line with the Swedish study, we assumed that 30% of the cases would be caused by pneumococci.[19] Norwegian CAP data including only noninvasive episodes from 2015 was used to estimate the incidence of PnCAP. For the 65-year-old cohort the incidence (per 100.000) was estimated as 815 × 0.3 = 244 and for the 75-year-old cohort the incidence (per 100.000) was estimated as 1770 × 0.3 = 531.

The age-specific incidence of IPD cases per 100.000 population from the Norwegian Surveillance System for Communicable Diseases (MSIS) is based on average estimates over a five-year period from 2015 to 2019.[20] There is variation in the estimates over time and, as such, we think that using average estimates over a five-year period is more representative than using estimates from a single year. MSIS is the most reliable data source on IPD in Norway, as detailed information on laboratory detection of *S. pneumoniae* from sterile area by isolation, nucleic acid, or antigen test (not urine) is available. The epidemiological parameters used are presented in Table 1.

Table 1. Annual incidence of invasive pneumococcal disease (IPD), noninvasive pneumococcal community acquired pneumonia (PnCAP) parameters for a hypothetical cohort of 65 year- and 75-year-olds over a five-year time horizon (year since vaccination).

	Incidence (per 100.000) 65-year-old cohort	Incidence (per 100.000) 75-year-old cohort	Source
IPD	22	37	An average annual incidence is presented using data from the Norwegian Surveillance System for Communicable Diseases for the years 2015 to 2019.
PnCAP*			
Inpatient	244	531	Extracted from the dataset presented in Lyngstad *et al.* 2022
Outpatient	315	525	Swedish register data: Extracted from the dataset presented in Naucler *et al.* 2020 and Wolff *et al.* 2020

**Streptococcus pneumoniae*, the share of CAP which is caused by *Streptococcus pneumoniae* is estimated as 30% for inpatient CAP based on Suzuki *et al.* 2017, and 9% for outpatient CAP based on Leven *et al.* 2018.

Vaccine effectiveness (VE)

The vaccine effectiveness (VE) estimates against pneumococcal disease used in the model for the 65- and 75- year-old cohorts are shown in Table 2. These estimates were based on a combination of data sources which are described in more detail in the subsections below. PPV23 was used in the base-case analysis, while PCV13 was only included in a scenario analysis.

Serotype distribution

Norwegian national data on IPD from 2017 indicates that 127 (23%) of the isolates belonged to serotypes included in PCV13, and 390 (70%) of the isolates belonged to serotypes included in PPV23. In the age group ≥65 years, 226 (68%) of the cases were caused by serotypes included in PPV23, and 74 (22%) of the cases were caused by serotypes included in PCV13.[21] We assumed the same serotype distribution for pneumococcal pneumonia.

PPV23

No comprehensive data from Norway was available for the vaccine effectiveness for the 65-year-old cohort. Thus, we applied the same data as in the study by Wolff et *al.* Estimates of the vaccine effectiveness against IPD for PPV23 following the first year after vaccination were extracted from a review by Kraicer-Melamed et *al.*[22] and a study by Kim et *al.*[23] To obtain the vaccine effectiveness against IPD for Norway, the adjusted PPV23 serotype-specific vaccine effectiveness in the 75-year-old cohort was estimated to be 69.9%. This was then multiplied by the share of IPD that is vaccine type-specific for Norway which is 70%.[21] English data from a study by Djennad et *al.*[24] was used to estimate vaccine effectiveness against IPD in the years 2–5 following vaccination. Similar calculations were applied to estimate the vaccine effectiveness for PPV23 against PnCAP in the 65-year-old cohort. For the first year following vaccination, the estimated vaccine effectiveness of 38.9% was extracted from a Japanese study by Suzuki et *al.*[19] The 38.9% estimate was multiplied by 70% to obtain the estimate of 28%. To obtain the vaccine effectiveness against CAP for the years 2–5 following vaccination similar calculations were conducted (Table 2).

No comprehensive data from Norway was available for the vaccine effectiveness for the 75-year-old cohort. Thus, we applied the same data from Djennad et *al.*[24] to estimate the vaccine effectiveness against IPD in the years 1 to 5 following vaccination. Suzuki et *al.*[19] suggests that the adjusted PPV23 serotype-specific vaccine effectiveness against PnCAP is 28.2%. This estimate was multiplied by the share of PnCAP that is

Table 2. Vaccine effectiveness (VE) on invasive pneumococcal disease (IPD) and noninvasive pneumococcal community-acquired pneumonia (PnCAP) applied in the Norwegian setting*, per year since vaccination, vaccine type; 23-valent polysaccharide vaccine (PPV23) and 13-valent pneumococcal conjugate vaccine (PCV13), and age group.

		PPV23			PCV13		
Age-group	Year since vaccination	VE on IPD*	VE on PnCAP*	Source	VE on IPD*	VE on PnCAP*	Source
65-year-old cohort	1	50%	28%	Kim *et al.* 2019, Suzuki *et al.* 2017, Kraicer-Melamed *et al.* 2016	22%	13%	Bonten *et al.* 2015, Patterson *et al.* 2016
	2	43%	26%	Suzuki *et al.* 2017,	22%	13%	
	3-5	35%	24%	Djennad *et al.* 2019	22%	13%	
75-year-old cohort	1	38%	20%		12%	12%	Van Werkhove *et al.* 2015
	2	38%	20%		12%	12%	
	3-5	39%	20%		12%	12%	

*The VE estimates in Table 4 are based on published estimates for VE, multiplied by the share of IPD or PnCAP caused by PPV23 or PCV13 serotypes respectively.

assumed to be vaccine type-specific in Norway to arrive at an estimate of vaccine effectiveness of PPV23 against PnCAP (20%).

PCV13

In line with the Swedish model, the protective effect against IPD and PnCAP for PCV13, for both the 65-year-old cohort and the 75-year-old cohort, was calculated in the same way as described above and data was collected from the CAPITA trial.[25,26] Vaccine effectiveness against pneumococcal disease was based on intention to treat results of the CAPITA trials and for IPD was adjusted to reflect the serotype distribution in Norway.

Health outcomes

In compliance with the Norwegian guidelines for STA of pharmaceuticals, health-related quality of life (HRQoL) data was based on the standardized generic instrument EQ-5D.[12] The outcome measure QALY gained simultaneously captures gains from reduced morbidity (quality gains) and reduced mortality (quantity gains) and integrates these into a single measure. Reductions in health-related quality of life due to pneumococcal disease (calculated on a scale of 0–1 where 1 is equivalent to perfect health and 0 equates death) were derived from the literature and based on utility values from the Netherlands.[27] For IPD a utility value of 0,694 was used. For inpatient PnCAP a utility value of 0,694 was used while a utility value of 0,761 was used for outpatient PnCAP. No published age or gender-specific EQ-5D data from the general Norwegian population is available. The QALY weight among the healthy population was based on a utility value from a Swedish study (0,765).[28] Severe adverse events are rare and as such we did not consider these in the analysis.[29,30] Therefore, no disutility values were applied in the model.

Cost estimates

Based on past cost-effectiveness analyses of vaccination programmes in Norway,[31–33] the cost per PPV23 vaccine dose was set to the maximum pharmacy retail price as listed by the Norwegian Medicines Agency.[34] The publicly listed maximum pharmacy retail price includes value-added tax (VAT) of 25%.[35] In this analysis (and in line with recommendations for the Norwegian context), the price excluding VAT was calculated and used (see Table 3). The PCV13 vaccine dose was also set to the maximum pharmacy retail price excluding VAT (but only used in a scenario analysis). Vaccines implemented in national immunization programmes (NIP) in Norway are, however, acquired through tenders. The realistic vaccine price is, therefore, typically lower than the maximum pharmacy retail price when included in a NIP. Based on experience with previous tenders for vaccines included in the Norwegian NIP, the rebate varies between 25–75%.[36] In compliance with the Norwegian guidelines for STA of pharmaceuticals,[12] the cost of administering a vaccine is calculated as the renumeration for fee-for-service per the GP Fees List Collective

Table 3. Overview of model input parameters.

Parameter	Value (NOK)	Source/Comments
Vaccination costs		
Cost of vaccine excl. VAT, PPV23[1]	NOK 258	The Norwegian Medicines Agency
Cost of vaccine, PPV23 excl. VAT, with rebate 75%	NOK 64,5	Calculation using the cost of PPV23 excl. VAT NOK 258
Cost of vaccine, PPV23 excl. VAT, with rebate 50%	NOK 129	Calculation using the cost of PPV23 excl. VAT NOK 258
Cost of vaccine, PPV23 excl. VAT, with rebate 25%	NOK 193,5	Calculation using the cost of PPV23 excl. VAT NOK 258
Cost of vaccine excl. VAT, PCV13[2]	NOK 523,5	The Norwegian Medicines Agency
Cost of vaccine, PCV13 excl. VAT, with rebate 75%	NOK 131	Calculation using the cost of PCV13 excl. VAT NOK 523,5
Cost of vaccine, PCV13 excl. VAT, with rebate 50%	NOK 262	Calculation using the cost of PCV13 excl. VAT NOK 523,5
Cost of vaccine, PCV13 excl. VAT, with rebate 25%	NOK 393	Calculation using cost of PCV13 excl. VAT NOK 523,5
Vaccine delivery – a single subcutaneous injection[3]	NOK 150	The Norwegian Medicines Agency
Vaccine administration cost per dose[4]	NOK 336	The Norwegian Medical Association
Treatment costs		
Fee-for-service per consultation	NOK 336	The Norwegian Medical Association
Antibiotics		
Average cost per course of treatment – Phenoxymethylpenicillin	NOK 98,5	The Norwegian Medicines Agency
Average cost per course of treatment – Amoxicillin	NOK 144,75	The Norwegian Medicines Agency
Hospital Admissions		
Average cost per IPD admission	NOK 128 187	Diagnostic Related Group
Average cost per PnCAP admission	NOK 60,812	Diagnostic Related Group

Abbreviations.
VAT: Value-added-tax.
PPV23: 23-valent polysaccharide vaccine.
PCV13: 13-valent pneumococcal conjugate vaccine.
IPD: Invasive pneumococcal disease.
PnCAP: Noninvasive pneumococcal community-acquired pneumonia.
(1) The maximum pharmacy retail price was used (344,40 NOK) and 25% value-added-tax (VAT) was deducted. https://www.legemiddelsok.no/sider/Legemiddelvisning.aspx?pakningId=671a5e74-8144-44fb-8b96-d3991cba8739&searchquery=pneumovax&f=Han;Mtl;Vir;ATC;Var;Mar;Mid;Avr;gen;par;&pane=0.
(2) The maximum pharmacy retail price was used (698,20 NOK) and 25% VAT was deducted. https://www.legemiddelsok.no/sider/Legemiddelvisning.aspx?pakningId=6c87a43e-fbc3-4f77-b4f4-09de265a6fd9&searchquery=Pneumokokk&f=Han;Mtl;Vir;ATC;Var;Mar;Mid;Avr;gen;par;&pane=0.
(3) The cost of a single subcutaneous injection (150 NOK) was added as per the Norwegian Medicines Agency's guidance: https://normaltariffen.legeforeningen.no/book/Fastlegetariffen-2021/m-11 https://legemiddelverket.no/Documents/Offentlig%20finansiering%20og%20pris/Dokumentasjon%20til%20metodevurdering/Retningslinjer%2018.10.2021.pdf.
(4) The fee-for-service for a general practice consultation takst2ad (168 NOK) was multiplied by two as per the Norwegian Medicines Agency's guidance: https://normaltariffen.legeforeningen.no/book/Fastlegetariffen-2021/m-11 https://legemiddelverket.no/Documents/Offentlig%20finansiering%20og%20pris/Dokumentasjon%20til%20metodevurdering/Retningslinjer%2018.10.2021.pdf.

Agreement 2021–2022 (takst2ad)[37] multiplied by two (168 × 2 = 336 NOK/EUR 34). In line with the Norwegian guidelines for STA of pharmaceuticals,[12] an additional cost of 150 NOK (EUR 15) for a single subcutaneous injection is used per vaccine delivery. Thus, the total cost of one vaccination delivery per person includes the vaccine cost, the cost of a single subcutaneous injection and the renumeration of GP fee-for-service multiplied by two. A one-time cost of EUR 127,291 covering implementation and information costs for the first year of the programme was included. This estimate is based on the costing of other vaccination programmes (as laid out in an internal communication from the Norwegian Institute of Public Health).

The average case cost of a hospital admission for either IPD or PnCAP was derived from the Diagnosis Related Group (DRG) which was established based on the International Classification of Diseases (ICD) 10 diagnostic codes.[38] Each DRG code has a relative weight, which determines the reimbursement for that DRG. Each DRG weight represents the average case cost for cases in that DRG relative to the average case cost for all DRGs. The relative weight was multiplied by the unit cost for 2022 (NOK 47 742/EUR 4862).

In the Norwegian guideline for the management of more severe infections in the primary sector a Penicillin or Amoxicillin dosage of 1,3 g 4 times a day for 7 to 10 days is recommended.[39] The cost of antibiotic treatment is based on the official retail prices in Norway as given by the Norwegian Medicines Agency and calculated in the same way as above for the vaccine price. In the Usage of Antimicrobial Agents and Occurrence of Antimicrobial Resistance from Norway report from 2018,[40] it is estimated that, in terms of the number of prescriptions per 1000 inhabitants, penicillin accounts for 25% while amoxicillin accounts for 75%. These estimates were used in the model. All cases which did not require hospitalization were assumed to require treatment with antibiotics.

Costs were measured in 2022 Norwegian kroner (NOK) and converted to € EUR using the average annual 2022 exchange rate (EUR1 = NOK9.820).[41]

Sensitivity and scenario analyses

The most likely parameter values and assumptions were used in the base-case. However, several one-way sensitivity analyses were also performed looking at the effect of changing one parameter at a time. The rebate rates were varied in sensitivity analyses to detect the impact on the vaccine pharmacy retail price for PPV23 if the price was reduced by 25%, 50% and 75%, respectively. The share of PnCAP (inpatient) that is caused by *S. pneumoniae* was varied from 30% in the base case to 20% in a sensitivity analysis. The vaccination coverage was also varied from 75% to 50% in a sensitivity analysis. A scenario analysis in which the PCV13 vaccine price was used instead of the PPV23 vaccine price was performed, in line with the Swedish model. In addition, the impact on the vaccine pharmacy retail price for PCV13 if the price was reduced by 25%, 50% and 75%, respectively, was tested. The share of PnCAP (inpatient) that is caused by *S. pneumoniae* varied from 30% in the base case to 20% for the PCV13 vaccine.

Table 4. Estimated number of Norwegian cases of (invasive pneumococcal disease (IPD) and noninvasive pneumococcal community-acquired pneumonia (PnCAP) in the epidemiological model, with and without vaccination with 23-valent polysaccharide vaccine (PVV23), depending on age and year after vaccination, given the input parameters in Table 2, and 75% vaccination coverage.

	Year 1	Year 2	Year 3	Year 4	Year 5
65-year-old cohort					
IPD					
Not vaccinated	25	25	25	25	25
Vaccinated	16	17	19	19	19
PnCAP Inpatient					
Not vaccinated	279	279	279	279	279
Vaccinated	221	224	228	228	228
PnCAP Outpatient					
Not vaccinated	155	155	155	155	155
Vaccinated	122	124	126	126	126
75-year-old cohort					
IPD					
Not vaccinated	29	29	29	29	29
Vaccinated	22	23	24	24	24
PnCAP Inpatient					
Not vaccinated	415	415	415	415	415
Vaccinated	374	374	374	374	374
PnCAP Outpatient					
Not vaccinated	176	176	176	176	176
Vaccinated	159	159	159	159	159

Results

Base case

PPV23 vaccination would lead to a total decrease in the number of IPD cases by 20% and a decrease of 13% for the CAP cases among the 65-year-old cohort. Among the 75-year-old cohort the IPD cases would be reduced by 20% while the PnCAP cases would be reduced by 10% (See Table 4).

At the current maximal pharmacy retail price for PPV23, vaccinating 65-year-olds would result in a total difference in costs of NOK 9 998 756 million (EUR 1 018 203) over the five-year time horizon and a gain of 16,62 QALY. This results in a cost per gained QALY of approximately NOK 601 784 (EUR 61 281) which falls within the current threshold ranges in Norway which starts at NOK 275 000 (EUR 28 004). The corresponding figures for vaccinating 75-year-olds are a total difference in costs of NOK -503 847 (EUR 51 308) and a gain of 15,84 QALY (See Table 5). This results in a dominant strategy (i.e., a decrease in costs and an increase in effects) for the 75-year-old cohort.

Sensitivity analyses

The impact of changing the share of PnCAP inpatient that is caused by *S. pneumonia* was varied from 30% in the base case to 20% in a sensitivity analysis. This did not have an impact on the incremental cost-effectiveness ratio (ICER) for either the 65-year-old cohort or the 75-year-old cohort. The potential effects of variation in vaccine price for PPV23 from the current price to 25%, 50% or 75% rebate lowered the ICER for the 65-year-old cohort (see Table 6). Changing the vaccination coverage from 75% to 50% for the 65-year-old cohort had minimal impact on the ICER (NOK 601 784 (EUR 61,281) in the base-case versus NOK 626 131/EUR 63,761). Varying the vaccine

Table 5. Base case results (NOK/EUR) – at 75% vaccination coverage.

	No vaccination	Vaccination	Difference
65-year-old cohort			
Cost of acquiring and administrating the vaccine	-	28 229 666	28 229 666
Treatment costs	89 414 214	69 933 303	−19 480 911
Implementation costs, vaccination programme	-	1 250 000	1 250 000
Total costs	89 414 214	99 412 970	9 998 756
QALY	200 607	200 624	16,62
ICER (cost per QALY gained)			**NOK 601 784/ EUR 61,281**
75-year-old cohort			
Cost of acquiring and administrating the vaccine	-	10 803 420	10 803 420
Treatment costs	105 366 067	92 808 801	−12 557 267
Implementation costs, vaccination programme	-	1 250 000	1 250 000
Total costs	105 366 067	104 862 221	−503 847
QALY	115 068	115 084	15,84
ICER (cost per QALY gained)			Dominant

Abbreviations.
QALY: Quality-adjusted life-year.
ICER: Incremental cost-effectiveness ratio.

Table 6. Sensitivity analyses results (NOK/EUR) – varying the price of PVV23 with 25%, 50%, 75% rebate – at 75% vaccination coverage.

	Rebate (%)	ICER (Cost per QALY gained)
65-year-old cohort	25	NOK 439 864/EUR 44,793
	50	NOK 277 945/EUR 28,307
	75	NOK 116 025/EUR 11,815
75-year-old cohort	25	Dominant
	50	Dominant
	75	Dominant

Abbreviations.
QALY: Quality-adjusted life-year.
ICER: Incremental cost-effectiveness ratio.

Table 7. Sensitivity analyses results (NOK/EUR) – varying the price of PCV13 with 25%, 50%, 75% rebate – at 75% vaccination coverage and changing VE data.

	Rebate (%)	ICER (Cost per QALY gained)
65-year-old cohort	25	NOK 940 686/EUR 95,793
	50	NOK 611 826/EUR 62,304
	75	NOK 282 965/EUR 28,815
75-year-old cohort	25	NOK 104 231/EUR 10,614
	50	Dominant
	75	Dominant

Abbreviations.
VE: Vaccine effectiveness.
QALY: Quality-adjusted life-year.
ICER: Incremental cost-effectiveness ratio.

price by 25%, 50% and 75% rebate for the 75-year-old cohort did not change the result of the dominant strategy in the base case (See Table 6). Varying the vaccination coverage rate from 75% to 50% for the 75-year-old cohort did not impact the ICER and the vaccination strategy remained dominant.

Scenario analysis

Using the PCV13 vaccine price and changing the VE data would result in a higher ICER in the base case with a cost per QALY gained of NOK 1 268 291/EUR 129,154 for the 65-year-old cohort and a cost per QALY gained of NOK 235,736/EUR 24,006 for the 75-year-old cohort. However, a rebate of 50% or 75% would result in a dominant strategy for the 75-year-old cohort, while the strategy would fall within the acceptable ranges for the 65-year-old cohort if a rebate of 50% or 75% was used (See Table 7). The impact of changing the share of PnCAP inpatient that is caused by *S. pneumonia* was varied from 30% in the base case to 20% in a sensitivity analysis. This did not have an impact on the ICER.

Discussion

This paper considers the possible health effects and costs associated with a universal vaccination programme with the 23-valent pneumococcal polysaccharide vaccine in older adults in Norway. It establishes baseline information on its effect and cost-effectiveness from the health care perspective.

In Norway, there is no exact cost-effectiveness threshold, and thus the maximum amount a decision-maker is willing to pay for a unit of health outcome is uncertain.[42] However, estimates of the costs that are displaced at the lower end of the scale start at NOK 275 000 (EUR 28 004) per QALY while approaching an upper limit in the upper severity class which is three times this amount i.e., NOK 825 000 (EUR 84 011) per QALY. Vaccinating the 65-year-old cohort with one dose of PPV23 is likely to be cost-effective compared to not vaccinating the cohort as the ICER falls within the recommended ranges. Vaccinating the 75-year-old cohort results in a dominant strategy and is likely to be cost-effective. The sensitivity analyses confirmed the results of the base case vaccinating with one dose of PVV23, implying that varying the input parameters of the model would not alter the conclusions. Vaccinating the 65-year-old cohort with one dose of PCV13 is unlikely to be cost-effective as the cost per QALY falls above (NOK 1 268 291/EUR 129 154) the upper limit on the scale i.e., NOK 825 000 (EUR 84 011) per QALY.

We aimed to use Norwegian data where possible but quality-of life impact, PnCAP outpatient data, vaccine effectiveness and serotype distribution for pneumococcal pneumonia were not available. We acknowledge that using data from other countries with different epidemiology and healthcare systems may have impacted the results in either direction, leading to either under or over-estimation. Since not all data were available from Norway, we had to base our model on other sources. Sweden and Norway are relatively similar countries with subsidized health care services for the population and with a similar burden of pneumococcal disease.

Norway does not have their own local weights and value sets for translating various health states into a quality-of-life score. Therefore, utility values from the Netherlands and Sweden were applied. We acknowledge that transferring utilities from one country to another without an adjustment presents a limitation in the study. However, we would not expect there to be huge fluctuation among weights between Norway and Sweden or the Netherlands.

The health-care perspective was used. Absenteeism from work was ignored in part because of a lack of data on the wider indirect societal costs of pneumococcal disease in

Norway. International guidelines favor using a societal perspective in cost-effectiveness analyses. Nonetheless, following the Norwegian government's guidance using a health-care perspective makes the analysis pertinent and relevant to the Norwegian context.[43] Consequently, we did not consider labor production in the analysis. We do, however, acknowledge using the health care perspective only as a limitation as studies from other countries indicate that including a variety of societal outcomes in the analysis may be essential.[44] Using the health care perspective may imply that we have, in this instance, underestimated the benefits of vaccination.

We are aware that the indirect effects phenomena of herd immunity and serotype replacement are not readily captured via static models.[45] We acknowledge that the decision tree does not accurately represent the nature of the disease and the implied limitation of the work presented here. Nevertheless, most recent cost-effectiveness analyses of either the PPV23 or PCV13 vaccine have used a static approach.[46] Herd immunity from childhood vaccination has substantially reduced the burden of pneumococcal disease in Norway, particularly of pneumonia among older adults. However, serotype replacement has partly offset these benefits. Introduction of newer vaccines with broader serotype protection in the childhood immunization programme could reduce the disease burden in adults further, and thus reduce the cost saving from vaccination of adults. We do not expect PPV23 to reduce nasopharyngeal pneumococcal colonization, and we do not expect indirect effects from vaccination of adults with PPV23. We did not account for either herd immunity effects or serotype replacement. This would require a dynamic approach. However, since the uncertainty of quantifying the long-term impact of indirect effects increases when indirect effects are not implicitly included in the model,[46] we ignored indirect effects in this analysis.

The cost-effectiveness of vaccination (vs. no vaccination) is typically more favorable when indirect effects are included than when indirect effects are not included. However, as unvaccinated people are protected indirectly by those who are vaccinated this does not necessarily mean that the cost-effectiveness of interventions to increase vaccination coverage or interventions to expand vaccination to different population groups is more favorable when indirect effects are included than when indirect effects are not included. In this study, including the ongoing (and increasing) indirect effects of childhood vaccination would likely make the cost-effectiveness results less favorable for vaccinating 65- and 75-year-olds.

Cross-protection between serotypes 6A and 6B and between 19A and 19F may be relevant but no absolute cross-protection has been observed (and some vaccines will contain both 6A and 6B). Thus cross-protection is deemed of limited clinical significance and disregarded in the analysis.[47]

A short time horizon of 5-years was used instead of the generally preferred lifetime time horizon. International guidance recommends a time horizon which is long enough to capture the full spectrum of costs and benefits which in many cases will be the lifetime of the cohorts modeled.[48] A recent report by the Joint Committee of Vaccination & Immunization (JCVI) also emphasized the use of a lifetime time horizon for vaccines.[49] The 5-year time horizon may be too short to capture the impact for PCV13 which has longer lasting protective effects. This may mean that the economic value of PCV13 is underestimated. However, uncertainty about how the epidemiology of *Streptococcus pneumonia* develops over time with universal vaccination favors a short time horizon. Because of changes in the vaccines used in the child vaccination programme, it is likely that serotype replacement will continue to evolve in the future. In addition, new and expanded conjugate vaccines (15 and 20 serotypes) have recently entered the market. The Norwegian Institute of Public Health has started developing recommendations on how these vaccines could replace or supplement the use of PPV23 for older adults and adults with medical risk conditions. This also supports the use of a relatively short time-horizon in our analysis of PPV23.

We have described the limitations of the study above. In the main, this study is limited by the extent to which geographic transferability of data from study populations in other country settings to a target population in Norway is deemed appropriate. The resulting findings should be interpreted carefully in view of this caveat.

Conclusion

A universal PPV23 vaccination programme against pneumococcal disease for the 75-year-old cohort is cost-effective (dominant) in the Norwegian setting. A universal PPV23 vaccination programme against pneumococcal disease for the 65-year-old cohort is likely to be cost-effective in the Norwegian setting, assuming a threshold scale between NOK 275 000 (EUR 28,004) per QALY and NOK 825 000 (EUR 84,011) per QALY.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Author's contributions

The model development was carried out by EW. LSN adapted the model and performed the economic calculations. Data collection and analysis were conducted by TML, BAW, JB and LSN. LSN drafted the manuscript. All authors contributed to the interpretation of the data analyses, revising and approval of the final manuscript.

Funding

The author(s) reported there is no funding associated with the work featured in this article.

ORCID

Liv Solvår Nymark http://orcid.org/0000-0002-4892-4531

References

1. Brooks LRK, and Mias GI . Streptococcus pneumoniae's virulence and host immunity: aging, diagnostics, and prevention. Front Immunol. 2018 Jun 22;9:1366. doi:10.3389/fimmu.2018.01366. PMID: 29988379; PMCID: PMC6023974.

2. File TM Jr. Streptococcus pneumoniae and community-acquired pneumonia: a cause for concern. Am J Med. 2004;117(Suppl 3A):39S–50S. doi:10.1016/j.amjmed.2004.07.007.
3. Pletz MW, Maus U, Krug N, Welte T, Lode H. Pneumococcal vaccines: mechanism of action, impact on epidemiology and adaption of the species. Int J Antimicrob Ag. 2008;32(3):199–206. doi:10.1016/j.ijantimicag.2008.01.021.
4. Winje BA, Vestrheim DF, White RA, Steens A. The risk of invasive Pneumococcal disease differs between risk groups in Norway following widespread use of the 13-valent pneumococcal vaccine in children. Microorganisms. 2021;9(8):1774. doi:10.3390/microorganisms9081774.
5. Pneumokokkvaksine - veileder for helsepersonell [Internet]; [accessed 2022 Mar 27]. https://www.fhi.no/nettpub/vaksinasjonsveilederen-for-helsepersonell/vaksiner-mot-de-enkelte-sykdommene/pneumokokkvaksinasjon—veileder-fo/.
6. Folkehelseinstituttet. Vaksinasjonsveilederen for Helsepersonell (Vaskinasjonsboka) [Internet]. Oslo: Folkehelseinstituttet; 2015 [accessed 2022 Mar 1]. https://www.fhi.no/nettpub/vaksinasjonsveilederen-for-helsepersonell/.
7. The "blue prescription" regulation [Internet]; [accessed 2022 March 27]. https://lovdata.no/dokument/SF/forskrift/2007-06-28-814.
8. Executive order on free pneumococcal vaccination for certain groups of persons. BEK nr 395 af 07/04/2020 [Internet]. The Danish Ministry of Health; [accessed 2022 Mar 1]. https://www.retsinformation.dk/eli/lta/2020/395.
9. Hälsoekonomisk utvärdering av pneumokockvaccination som ett särskilt vaccinationsprogram för personer 75 år och äldre. Public Health Agency of Sweden [Internet]; [accessed 2022 Mar 1]. https://www.folkhalsomyndigheten.se/publicerat-material/publikationsarkiv/h/halsoekonomisk-utvardering-av-pneumokockvaccination-som-ett-sarskilt-vaccinationsprogram-for-personer-75-ar-och-aldre/.
10. Wolff E, Storsaeter J, Ortqvist A, Naucler P, Larsson S, Lepp T, Roth A. Cost-effectiveness of pneumococcal vaccination for elderly in Sweden. Vaccine. 2020;38(32):4988–4995. doi:10.1016/j.vaccine.2020.05.072.
11. Efficacy and effectiveness of pneumococcal vaccination in adults – a second update of the literature. [Effekt av pneumokokkvaksine hos eldre] Report 2019 [Internet]. Oslo: Norwegian Institute of Public Health; 2022. https://www.fhi.no/globalassets/dokumenterfiler/rapporter/2022/efficacy-and-effectiveness-of-pneumococcal-vaccination-in-adults.pdf.
12. Norwegian Medicines Agency. Guidelines for the submission of documentation for single technology assessment (STA) of pharmaceuticals [Internet]. Oslo (Norway): Norwegian Medicines Agency; 2018 [accessed 2022 March 1]. https://legemiddelverket.no/Documents/English/Public%20funding%20and%20pricing/Documentation%20for%20STA/Guidelines%2018.10.2021.pdf.
13. Nymark L, and Vassall A. A comprehensive framework for considering additional unintended consequences in economic evaluation. Cost Effect Resour Alloc. 2020;18:27. https://doi.org/10.1186/s12962-020-00218-8.
14. Holter JC, Muller F, Bjorang O, Samdal HH, Marthinsen JB, Jenum PA, Ueland T, Frøland SS, Aukrust P, Husebye E, et al. Etiology of community-acquired pneumonia and diagnostic yields of microbiological methods: a 3-year prospective study in Norway. BMC Infect Dis. 2015;15(1):64. doi:10.1186/s12879-015-0803-5.
15. Roysted W, Simonsen O, Jenkins A, Sarjomaa M, Svendsen MV, Ragnhildstveit E, Tveten Y, Kanestrøm A, Waage H, Ringstad J, et al. Aetiology and risk factors of community-acquired pneumonia in hospitalized patients in Norway. Clin Respir J. 2016;10(6):756–764. doi:10.1111/crj.12283.
16. Naucler P, Henriques-Normark B, Hedlund J, Galanis I, Granath F, Ortqvist A. The changing epidemiology of community-acquired pneumonia: nationwide register-based study in Sweden. J Intern Med. 2019;286(6):689–701. doi:10.1111/joim.12956.
17. Ieven M, Coenen S, Loens K, Lammens C, Coenjaerts F, Vanderstraeten A, Henriques-Normark B, Crook D, Huygen K, Butler CC, et al. Aetiology of lower respiratory tract infection in adults in primary care: a prospective study in 11 European countries. Clin Microbiol Infect. 2018;24(11):1158–1163. doi:10.1016/j.cmi.2018.02.004.
18. Lyngstad TM, Kristoffersen AB, Winje BA, Steens A. Estimation of the incidence of hospitalisation for non-invasive pneumococcal pneumonia in the Norwegian population aged 50 years and older. Epidemiol Infect. 2022;150. doi:10.1017/S0950268822000607.
19. Suzuki M, Dhoubhadel BG, Ishifuji T, Yasunami M, Yaegashi M, Asoh N, Ishida M, Hamaguchi S, Aoshima M, Ariyoshi K, et al. Serotype-Specific effectiveness of 23-valent pneumococcal polysaccharide vaccine against Pneumococcal pneumonia in adults aged 65 years or older: a multicentre, prospective, test-negative design study. Lancet Infect Dis. 2017;17(3):313–321. doi:10.1016/S1473-3099(17)30049-X.
20. Norwegian Instiute of Public Health. Norwegian surveillance system for communicable diseases [Internet]. Oslo (Norway): Norwegian Instiute of Public Health [accessed 2022 Mar 1]. http://www.msis.no/.
21. Årsrapport for 2017. Invasive infeksjoner [Internet]. Oslo (Norway): Norwegian Instiute of Public Health; 2018. https://www.fhi.no/globalassets/dokumenterfiler/rapporter/2018/arsrapport-invasive-infeksjoner-2017.pdf.
22. Kraicer-Melamed H, O'-Donnell S, Quach C. The effectiveness of pneumococcal polysaccharide vaccine 23 (PPV23) in the general population of 50 years of age and older: a systematic review and meta-analysis. Vaccine. 2016;34(13):1540–1550. doi:10.1016/j.vaccine.2016.02.024.
23. Kim JH, Chun BC, Song JY, Kim HY, Bae IG, Kim DM, Choi YH, Jun YH, Choi WS, Kang SH, et al. Direct effectiveness of pneumococcal polysaccharide vaccine against invasive pneumococcal disease and non-bacteremic pneumococcal pneumonia in elderly population in the era of pneumococcal conjugate vaccine: a case-control study. Vaccine. 2019;37(21):2797–2804. doi:10.1016/j.vaccine.2019.04.017.
24. Djennad A, Ramsay ME, Pebody R, Fry NK, Sheppard C, Ladhani SN, Andrews NJ. Effectiveness of 23-valent polysaccharide Pneumococcal vaccine and changes in invasive pneumococcal disease incidence from 2000 to 2017 in those aged 65 and over in England and Wales. EClin Med. 2018;6:42–50. doi:10.1016/j.eclinm.2018.12.007.
25. Bonten MJ, Huijts SM, Bolkenbaas M, Webber C, Patterson S, Gault S, van Werkhoven CH, van Deursen AMM, Sanders EAM, Verheij TJM, et al. Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults. N Engl J Med. 2015;372(12):1114–1125. doi:10.1056/NEJMoa1408544.
26. van Werkhoven CH, Huijts SM, Bolkenbaas M, Grobbee DE, Bonten MJ. The impact of age on the efficacy of 13-valent Pneumococcal conjugate vaccine in elderly. Clin Infect Dis. 2015;61(12):1835–1838. doi:10.1093/cid/civ686.
27. Mangen MJ, Rozenbaum MH, Huijts SM, van Werkhoven CH, Postma DF, Atwood M, van Deursen AMM, van der Ende A, Grobbee DE, Sanders EAM, et al. Cost-effectiveness of adult pneumococcal conjugate vaccination in the Netherlands. Eur Respir J. 2015;46(5):1407–1416. doi:10.1183/13993003.00325-2015.
28. Burström K, and Rehnberg C. Hälsorelaterad livskvalitet i Stockholms län 2002- 2006; Rapport 2006:1. Enheten för Socialmedisin och Hälsoekonomi. Centrum för Folkhälsa. FORUM för kunnskap og gemensam utvikling. Stockholm, Sweden: Stockholm läns landsting, 2006.
29. Blommaert A, Hanquet G, Willem L, Theeten H, Thiry N, Bilcke J, Verhaegen J, Beutels P.Use of pneumococcal vaccines in the elderly: an economic evaluation – Synthesis. Health Technology Assessment (HTA) Brussels: Belgian Health Care Knowledge Centre (KCE). 2016. KCE Reports 274Cs. D/2016/10.273/78.Please see the link below on page 45: https://kce.fgov.be/sites/default/files/2021-11/KCE_274C_Short-Report_Pneumococcal.pdf, https://kce.fgov.be/sites/default/files/2021-11/KCE_274C_Short-Report_Pneumococcal.pdf.

30. Remschmidt C, Harder T, Wichmann O, Bogdan C, Falkenhorst G. Effectiveness, immunogenicity and safety of 23-valent pneumococcal polysaccharide vaccine revaccinations in the elderly: a systematic review. BMC Infect Dis. 2016;16(1):711. doi:10.1186/s12879-016-2040-y.
31. Jiménez E, Torkilseng EB, Klemp M Cost-Effectiveness of HPV vaccination of boys aged 12 in a Norwegian setting. Report from Kunnskapssenteret no. 2–2015. Oslo: Norwegian Knowledge Centre for the Health Services; 2015.
32. Jiménez E, Wisløff T, Klemp M Cost-Effectiveness of a HPV vaccination catch-up program for females aged 26 years or younger in a Norwegian setting. Report from Kunnskapssenteret no. 5–2012. Oslo: Norwegian Knowledge Centre for the Health Services; 2012.
33. Berg AS, Furuseth E, Greve-Isdahl M, Grosvold IW, Næss LS, Nøkleby H, Stålkrantz J, Tunheim G, Wisløff T, Wolden B, et al. Kikhostevaksine til gravide – aktuelt for Norge? [Maternal Immunization against Pertussis. Evaluation for Norway] Rapport 2019. Oslo: Folkehelseinstituttet.
34. Norwegian Medicines Agency. Oslo (Norway) [Internet]; [accessed 2022 March 1]. https://legemiddelverket.no/english .
35. Norwegian Medicines Agency. Oslo (Norway) [Internet]; [accessed 2022 Mar 27]. https://legemiddelverket.no/offentlig-finansiering/maksimalpris#oversikt-over-maksimalpriser.
36. Watle SV, Naess LM, Tunheim G, Caugant DA, Wisloff T. Cost-Effectiveness of meningococcal vaccination of Norwegian teenagers with a quadrivalent ACWY conjugate vaccine. Hum Vaccin Immunother. 2021;17(8):2777–2787. doi:10.1080/21645515.2021.1880209.
37. Norwegian Medical Association. General practitioner fees list. Collective Agreement; 2021- 2022 [Internet]; [accessed 2022 Mar 1]. https://normaltariffen.legeforeningen.no/asset/pdf/Fastlegetariffen-2021-2022.pdf.
38. Norwegian: (ISF_regulations_2022_DRGlist somatic). Norwegian Directorate of Health [Internet]; 2022 [accessed 2022 Mar 1]. https://www.helsedirektoratet.no/tema/finansiering/innsatsstyrt-finansiering-og-drg-systemet/innsatsstyrt-finansiering-isf/ISF-regelverk%202022.pdf/_/attachment/inline/f7f190ab-33fc-4e07-9d36-fd5fc9e4e17e:9d97d72b2acf5c719d19cde034b6174007b84923/ISF-regelverk%202022.pdf.
39. Antibiotikabruk i primærhelsetjenesten. Oslo (Norway) [Internet]; [accessed 2022 Mar 27]. https://www.antibiotikaiallmennpraksis.no/index.php?action=showtopic&topic=f6000288c623ddf6aa4c.
40. NORM/NORM-VET. Usage of antimicrobial agents and occurrence of antimicrobial resistance in Norway. Tromsø/Oslo. 2019 ISSN:1502-2307 (print)/1890-9965 (electronic); 2018.
41. Exchange rates. Oslo (Norway); 2022 [accessed 2022 Mar 10]. https://www.norges-bank.no/en/topics/Statistics/exchange_rates/Internet.
42. Norwegian Ministry of Health and Care Services. Principles for priority setting in health care - Summary of a white paper on priority setting in the Norwegian health care sector [Internet]. Oslo (Norway): Norwegian Government; 2016. https://www.regjeringen.no/contentassets/439a420e01914a18b21f351143ccc6af/en-gb/pdfs/stm201520160034000engpdfs.pdf.
43. Norheim O, Allgott B, Gjul G, Kjellevold A, Moen A, Sjøli S. Norwegian [Transparent and fair – priorities in health services]. Oslo (Norway): Norwegian Government; 2014. https://www.regjeringen.no/no/dokumenter/NOU-2014-12/id2076730/?ch=1.
44. Nymark LS, Miller A, Vassall A. Inclusion of additional unintended consequences in economic evaluation: a systematic review of immunization and tuberculosis cost-effectiveness analyses. Pharmacoecon Open. 2021;5(4):587–603. doi:10.1007/s41669-021-00269-4.
45. Pitman R, Fisman D, Zaric GS, Postma M, Kretzschmar M, Edmunds J, Brisson M. Dynamic transmission modeling: a report of the ISPOR-SMDM modeling good research practices task force-5. Value Health. 2012;15(6):828–834. doi:10.1016/j.jval.2012.06.011.
46. Nymark LS, Sharma T, Miller A, Enemark U, Griffiths UK. Inclusion of the value of herd immunity in economic evaluations of vaccines. A systematic review of methods used. Vaccine. 2017;35(49):6828–6841. doi:10.1016/j.vaccine.2017.10.024.
47. Madhi SA, Goldblatt D. The duopoly of ten-valent and 13-valent pneumococcal conjugate vaccines: do they differ? Lancet Infect Dis. 2019;19(5):453–454. doi:10.1016/S1473-3099(18)30785-0.
48. Weinstein MC, O'-Brien B, Hornberger J, Jackson J, Johannesson M, McCabe C, Luce BR. Principles of good practice for decision analytic modeling in health-care evaluation: report of the ISPOR task force on good research practices—modeling studies. Value Health. 2003;6(1):9–17. doi:10.1046/j.1524-4733.2003.00234.x.
49. Immunisation and High Consequence Infectious Diseases Team, Global and Public Health Group. Consultation Ron the cost-effectiveness methodology for vaccination programmes and procurement (CEMIPP) report [Internet]; [accessed 2022 Mar 27]. https://www.gov.uk/government/consultations/cost-effectiveness-methodology-for-vaccination-programmes.