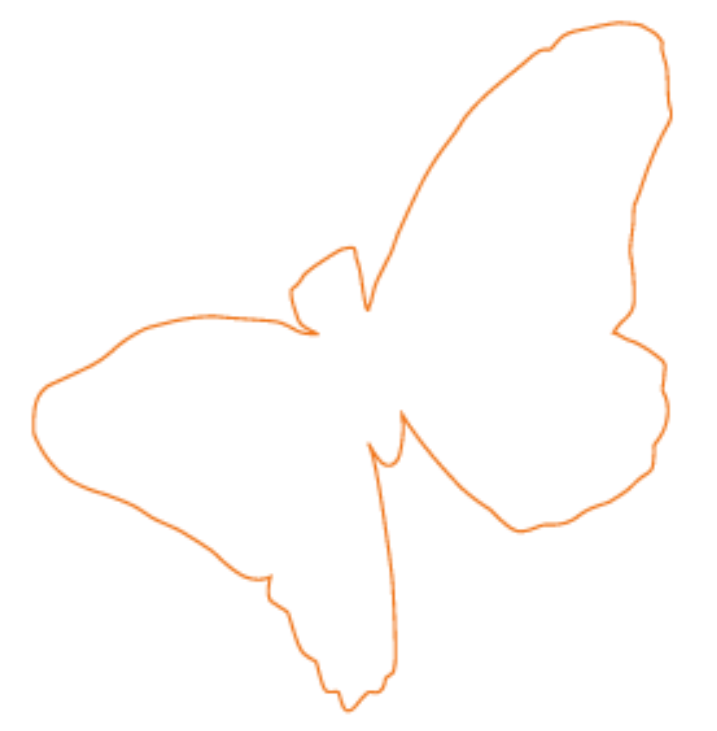


A Cost-effectiveness Analysis of Vaccinating the Elderly with 23-valent Pneumococcal Polysaccharide Vaccine (PPV23) in Germany

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BACKGROUND & OBJECTIVES

- Streptococcus pneumoniae* can cause non-invasive (pneumonia) and invasive pneumococcal diseases (IPD: meningitis, bacteraemic pneumonia and bacteraemia) and results in high morbidity and mortality worldwide, including 1.6 million deaths annually. In Germany, approximately 1,200 death occur each year due to IPD [1,2,3].
- Children, people with immunodeficiency or chronic diseases and the elderly are particularly vulnerable to *S. pneumoniae* infection. Vaccination appears to be the only public health action that could reduce the impact of IPD [1,2,4,5].
- In Europe, the 23-valent pneumococcal polysaccharide vaccine (PPV23) is the only pneumococcal vaccine indicated in adults, and it covers 80% to 90% of serotypes causing IPD. In Germany, it has been recommended and funded in individuals aged 60 and over since 1998 [6-9].
- In the US, the implementation of the PCV (pneumococcal conjugate vaccine) vaccination programme in children led, ten years after its introduction, to a decrease in the incidence of IPD caused by the serotypes included in the PCV vaccine, and to an increase in IPD caused by the non-PCV serotypes [10].
- This study aimed to assess the cost-effectiveness of PPV23 in the elderly in Germany, accounting for the decreased IPD incidence induced by the PCV7/13 vaccination of children.

METHODS

Target population:

- All individuals aged 60 years and older, including low-risk, immunosuppressed and immunocompetent individuals.

Modelling approach:

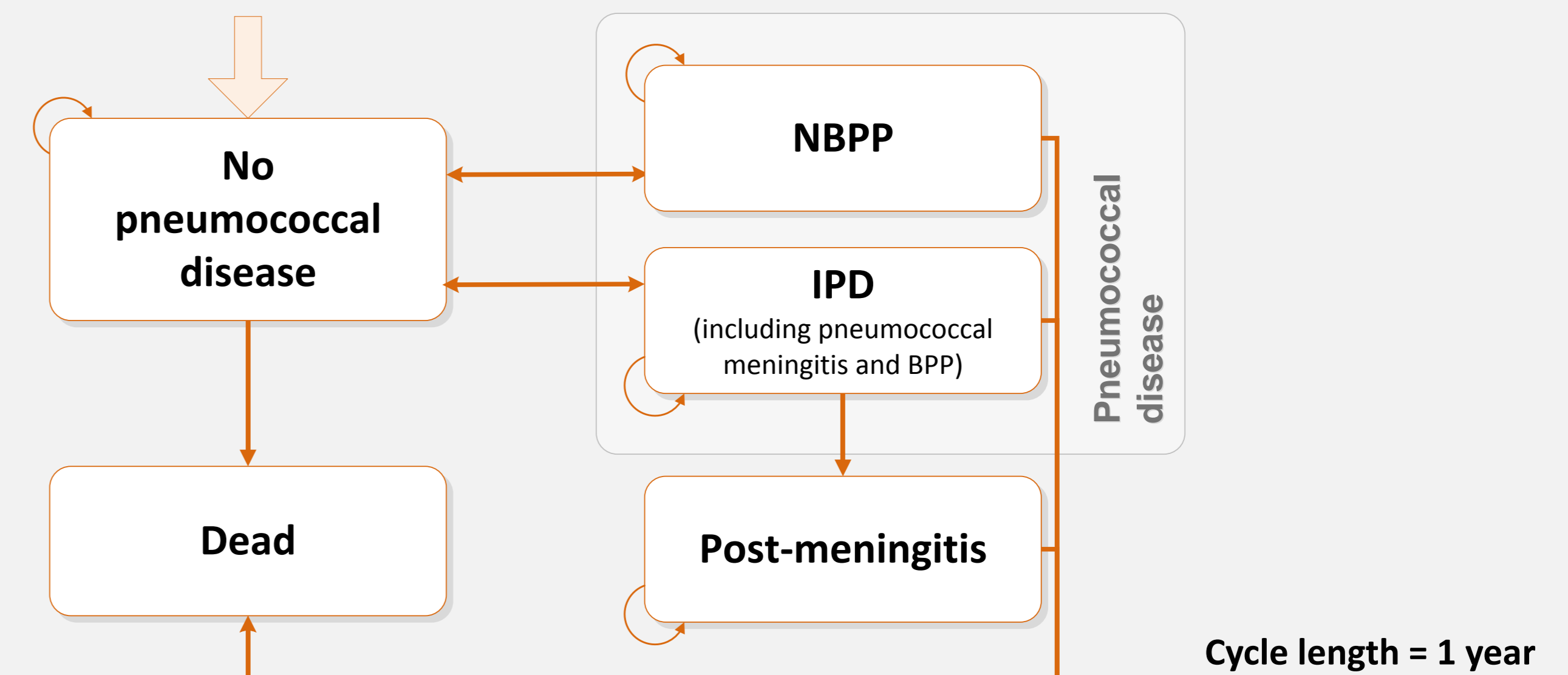
- A population-based Markov model was developed, consisting of five health states: no pneumococcal disease, IPD, non-bacteraemic pneumococcal pneumonia (NBPP), post-meningitis sequelae and death (Figure 1). The approach was in line with the official recommendations [11] as well as published literature [12].
- The model accounted for changes in the incidence of IPD. After the introduction of PCV7/13 in infants and children in Germany, the incidence of IPD associated with the PCV7/13 serotypes was assumed to decrease in adults while the incidence associated with serotypes covered by PPV23 but not PCV7/13 was assumed to increase. The assumptions were based on data observed in the US, where the increase and decrease in incidence observed in adults were fitted using a gamma distribution as a function of cumulative coverage rate observed in the children [10].
- The model followed a cohort of individuals receiving initial vaccination in 2011 until 100 years of age. The cohort consisted of 651,532 individuals, corresponding to 3% of the German population aged 60 years and older.
- The model compared PPV23 to no vaccination.
- Costs were estimated from the third-party payers' perspective. Both costs and utilities (in QALYs) were discounted at 3.0%.

Data sources: the following parameters were applied in the model.

Data point	Description
Demography	Population size and life tables by age and by year were obtained from Statistisches Bundesamt Deutschland [13].
Size of the target population by risk group	Estimated based on the size of the eligible population of influenza vaccination (LR: 86.93%; i.c.: 12.82%; i.s.: 0.25%) [14].
IPD and NBPP incidence	The model applied the incidence of IPD observed in North-Rhine Westphalia, Germany (from 8.5 to 24.1 per 100,000 in different age groups) [3] and distribution by serotype [8]. Relative risks of developing IPD by risk group (LR: 0.3; i.c.: 4.9; i.s.: 35.5) were estimated from a US study [15]. NBPP incidence was estimated based on the German CAPNETZ study (from 298 to 3,581 per 100,000 person-years in different age groups) [16] and it was assumed 40% of community-acquired pneumonia were attributable to <i>S. pneumoniae</i> [17].
Vaccine effectiveness	Vaccine effectiveness was obtained from published literature [18-20]: 74% against IPD in LR and i.c., 35% against IPD in i.s. and 39% against NBPP in LR and i.c. Vaccine waning function was estimated from a previously published cost-effectiveness study (no protection after 9 years from the initial vaccination) [21,22]. Revaccination was not accounted for as it was not recommended in the elderly.
Meningitis	The proportion of meningitis in IPD (8.2%) was estimated based on German data [23]. Proportion of patients developing post-meningitis complications (52%) was estimated based on the published literature [24].
Mortality	Case-fatality rate of IPD (from 21% to 39%) [25] and NBPP (from 9% to 30%) [26] and the relative mortality risk by serotype for IPD (PCV13: 0.953; PPV23 not PCV13: 1.132; not PPV23/6A: 1.127) [8,27] were estimated from European sources.
Costs	Costs were estimated from a previously published cost-effectiveness study and other German sources (BPP: 8,075 €; meningitis: 11,664 €; NBPP [inpatient]: 5,762 €; NBPP [outpatient]: 78 €; NBPP hospitalisation rate ranges from 16.6% to 34.5%; post-meningitis sequelae: 1,552 € for hearing loss and 862 € for others) [23,28,29]. The price of PPV23 was 30.25 € per dose and the administration cost was 6.95 € per dose.
Utilities	Baseline utilities (ranging from 0.51 to 0.77) and utility value associated with IPD (0.20 for 34 days) were obtained from a US cost-effectiveness study as no German data was identified [30]. Disutility due to NBPP was not accounted for in the model as in a previously published German cost-effectiveness study [28]. Utility multipliers associated with post-meningitis complications were obtained from a published study (0.80 for hearing loss and 0.60 for others) [31].

LR: low-risk; i.c.: high-risk immunocompetent; i.s.: high-risk immunosuppressed

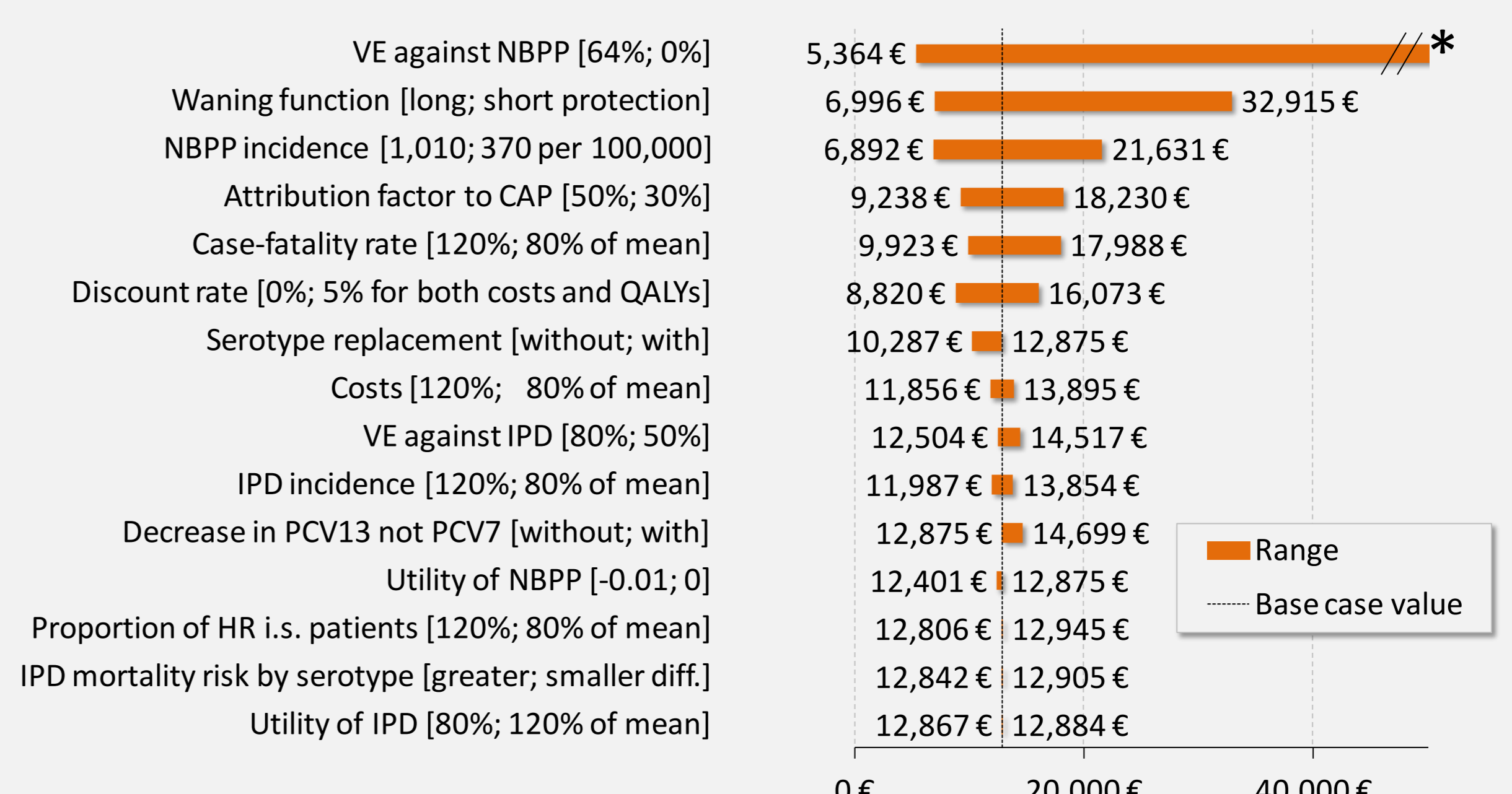
FIGURE 1: MODEL STRUCTURE



RESULTS

- Vaccinating the cohort of individuals aged 60 or older in 2011 was associated with an incremental cost-effectiveness ratio (ICER) of 12,875 € per QALY gained.
- Despite the decrease in IPD incidence among adults due to universal childhood vaccination with PCV7/13, vaccinating the elderly with PPV23 is still cost-effective. Assumptions on future trends on incidence led to an ICER ranging from 10,287 € to 14,699 € per QALY gained.
- A deterministic sensitivity analysis was conducted and demonstrated that vaccinating the elderly with PPV23 remained a cost-effective option in all cases except when assuming no effect against NBPP (85,569 € per QALY gained, see Figure 2). A vaccine effectiveness of 7.3% against NBPP was sufficient to reach an ICER of 50,000 € per QALY gained.
- Results were not sensitive to utility values associated with the IPD and NBPP health states.

FIGURE 2: DETERMINISTIC SENSITIVITY ANALYSIS



* The maximum value obtained in the sensitivity analyses was 85,569 € per QALY gained, when vaccine effectiveness of PPV23 against NBPP was assumed to be 0%.

CONCLUSION

- Although the vaccination of children against the pneumococcal diseases has resulted in a decreased IPD incidence in adults, vaccinating adults aged 60 or older with PPV23 remains cost-effective in Germany.
- A broad serotype coverage is important to prevent from IPD in a context of changing epidemiology among adults.

ACKNOWLEDGEMENT & REFERENCES

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