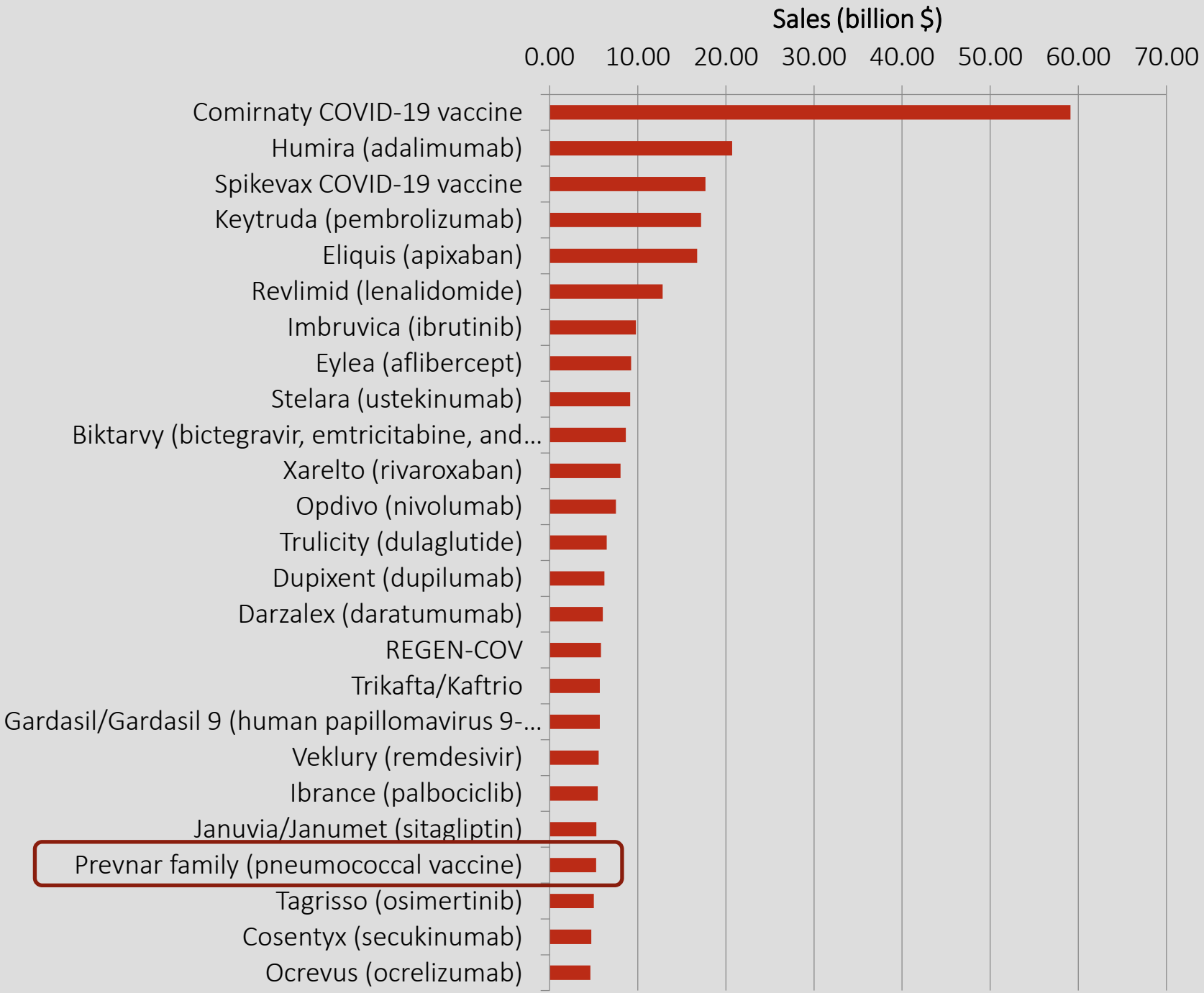

Health Economic Evaluation

1st GENID Summer School onModeling InfectiousDiseases

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MARTIN-LUTHER-UNIVERSITÄT
HALLE-WITTENBERG

Agenda

- → **Introduction to health economic evaluation and decision modeling**
- → Modeling pneumococcal disease dynamics
- → Decision problem and model concept
- → Data
  - → Epidemiology
  - → ~~Vaccine effects~~
  - → Health outcomes (QALYs)
  - → Costs
- → Results
  - → Base case analysis
  - → Sensitivity analysis

A simple decision problem: Which house will I buy (when I become assistant professor in Halle)?

Δ cost

Higher cost

worse and more expensive

better and more expensive

Δ value

Lower cost

worse and less expensive

Lower value

better and less expensive

Higher value

ICER
=
Incremental cost-effectiveness ratio
=
Δcost /Δ value

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Study types

→ Cost-minimization analysis
- Calculate the costs of each relevant intervention
- Intervention with lowest cost is the preferred option
- Only when effectiveness of all relevant interventions is identical!!!

→ Cost-benefit analysis
- Monetarize the effects
- Option with the highest net value is the preferred option
- Monetarization of health effects can be very challenging

→ Cost-effectiveness analysis
- Calculate the relation of costs and effects (avoided hospitalizations, successful amputations, prevented premature death, life years gained,…)
- Options below a defined cost-effectiveness threshold are cost-effective

→ Cost-utility analysis
- Cost-effectiveness analysis with utilities instead of effects
- Very comprehensive outcome measure
- Generic outcome measure

Analysis of costs and benefits of health technologies: assessment and appraisal

→ Value of the health technology

→ Value for money
- Incremental cost-effectiveness ratio

Assessment
(done by researchers)

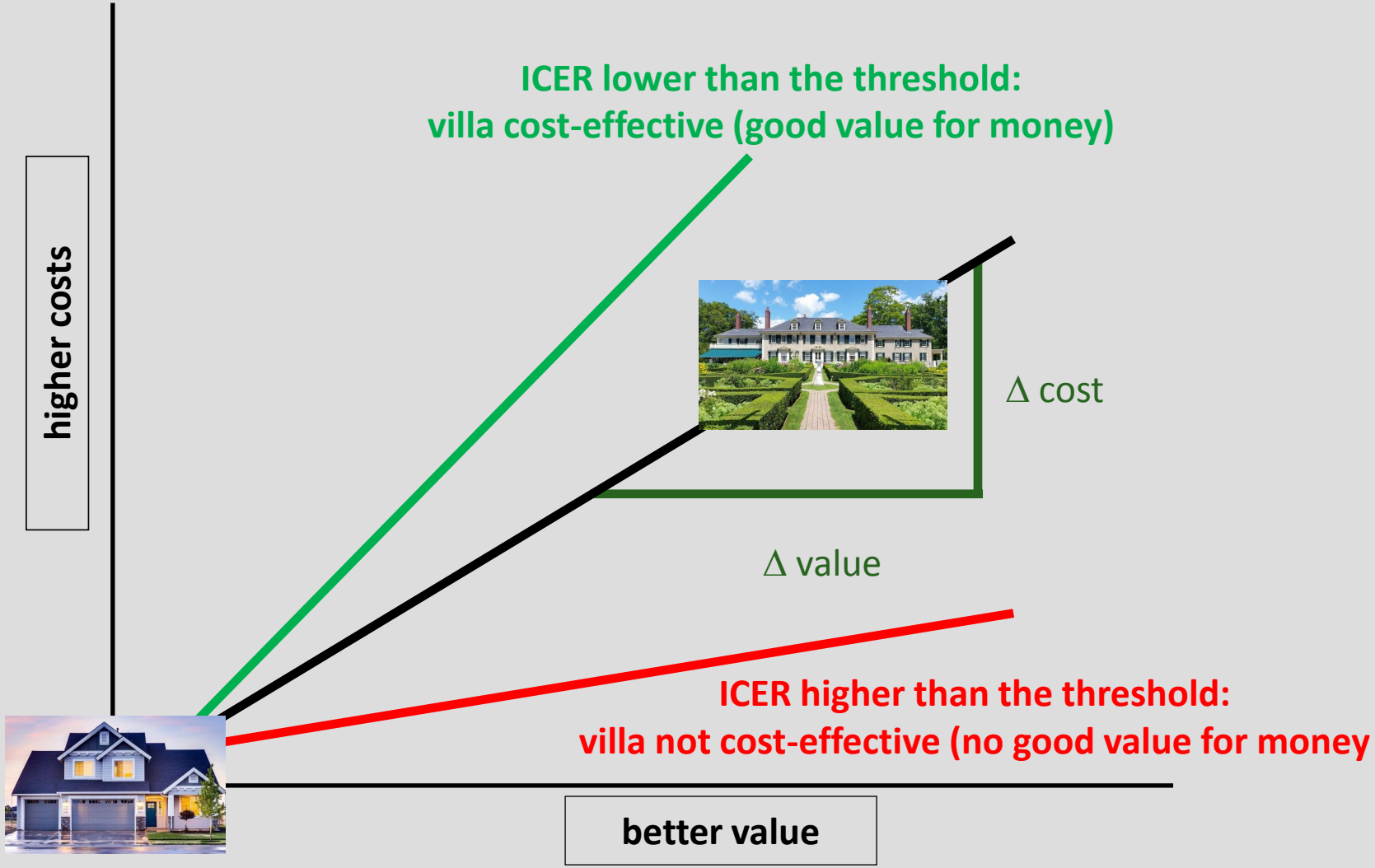
Recommendation possible (not binding)

→ Is the health technology „good value for money“?
- Cost-effective
- Fairness/social preferences

➔(flexible) thresholds

Appraisal
(done by decision makers)

Decision-making based on ICERs



International thresholds

Country	Threshold (national currency)	Comment	Threshold (EURO)
Australia	50,000		32,000
Ireland	45,000		45,000
Japan	5,000,000		38,000
Canada	80,000	Different categories	56,000
Netherlands	20,000		20,000
Norway	500,000		50,000
Poland	146,937	3 x GDP / capita	32,326
Scottland	20,000		23,600
Sweden	500,000		50,000
South Korea	25,000,000	1 x GDP / capita	18,500
Taiwan	1,199,237	1 x GDP / capita	37,176
Thailand	160,000		4,160
Czech Republic	1,355,826	3 x GDP / capita	52,877
UK	20,000	Different categories	23,600
US	50,000		43,000

https://www.ohe.org/publications/international-cost-effectiveness-thresholds-and-modifiers-hta-decision-making

International thresholds (modifier)

Country	Threshold (national currency)	Comment	Threshold (EURO)
Australia	Not defined	Rule of rescue, unmet needs, equity	Not defined
Ireland	100,000	Ultra-rare	100,000
Japan	7,500,000	Rare paediatric, oncology	57,000
Canada	140,000	Oncology	98,000
Netherlands	20,000-80,000	Severity	20,000-80,000
Norway	1,000,000 275,000-825,000	Ultra-rare Severity	100,000 27,500-82,500
Poland	n/a		n/a
Scottland	Not defined	Rare, no alternatives etc.	Not defined
Sweden	2,000,000	Severity, rare	200,000
South Korea	Not defined	rare, no alternatives etc.	Not defined
Taiwan	n/a		n/a
Thailand	Not defined	Equity	Not defined
Czech Republic	Not defined	Innovation, severity	Not defined
UK	50,000 100,000-300,000	End of life Ultra-rare	59,000 118,000-354,000
US	500,000	Ultra-rare	430,000

https://www.ohe.org/publications/international-cost-effectiveness-thresholds-and-modifiers-hta-decision-making

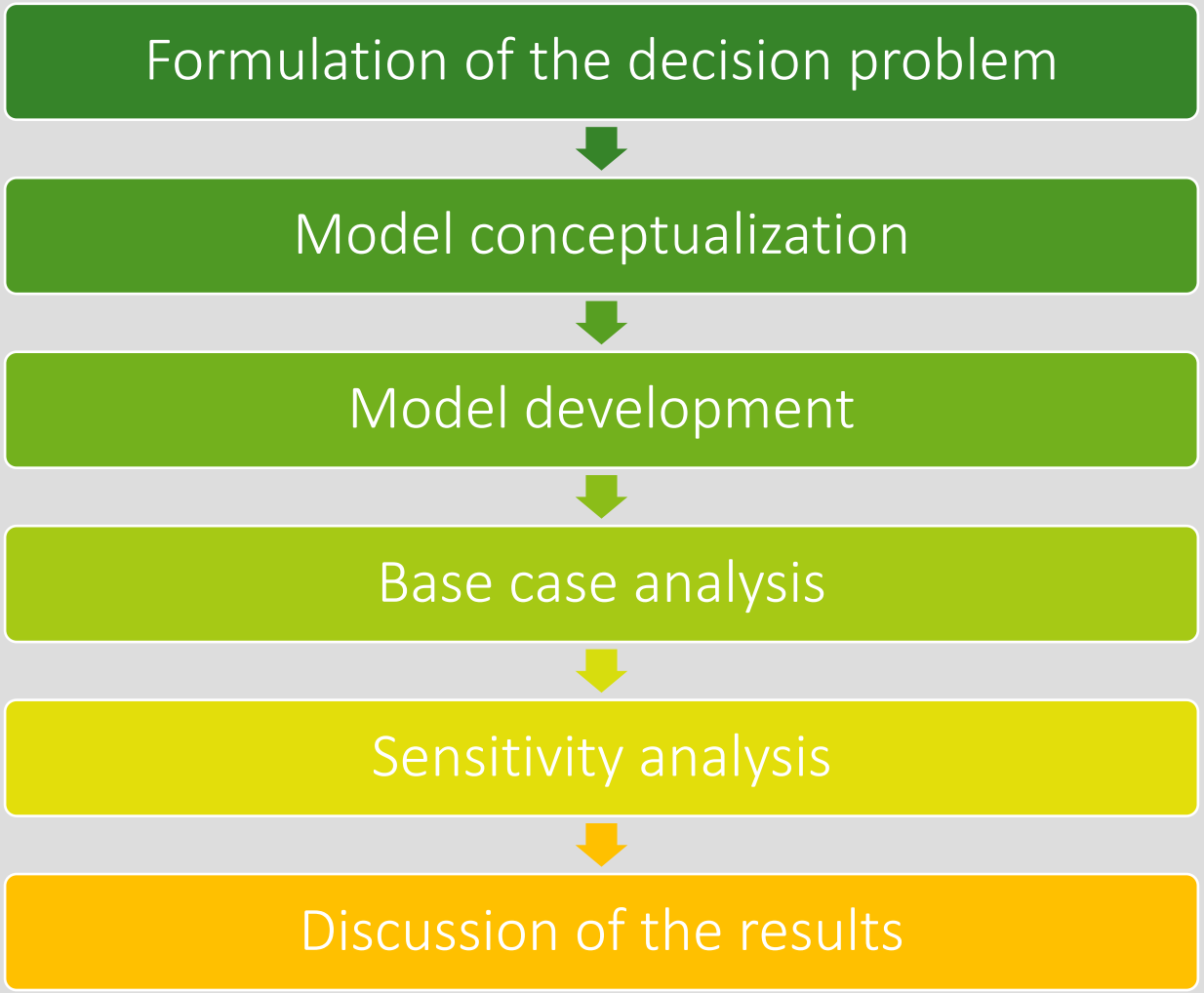
Decision analytic modeling in healthcare

→ **Systematic quantitative** approach to decision making under **uncertainty**

→ Comparing the **consequences** of **at least two alternative options** and evaluating them with respect to their **expected** costs and **expected** outcomes

→ Aim: Support decision making in questions about ressource allocation in healthcare (giving recommendations)

Steps in decision modeling



Formulation of the decision problem

→ What alternative actions?

→ For which population? (e.g., age groups)

→ Primary outcomes?

Model conceptualization I

→ Construction plan for the model

→ Represents the essential elements (alternative courses of action, patients and their health states, resources, etc.) and their relationships, structures, and rules

1. Choose perspective
   - Patients, providers, payers, society, etc.

2. Define time horizon
   - Must include all relevant medical and economic consequences

Model conceptualization II

3. Identify medical alternatives
   - Consider all relevant alternatives
   - If necessary, develop a sequence plan (treatment plan) with "if-then" rules

4. Specify possible clinical and economic consequences
   - All relevant health states must be specified and captured
     - Any state that differs from other states in terms of future mortality rates, morbidity rates, risk rates, quality of life, and costs
   - Descripe all significant cost components, resource consumption in the health states

Model conceptualization III

5. Describe sequence of events, health states and consequences
   - Schematic representation in the form of a flow chart, decision tree, bubble diagram, etc., including branches or connections

6. Determination of the model type and the simulation type
   - Suitability of the model type decisive for the selection
   - As simple as possible, but as complex as necessary

Model development I

→ Develop, program and test the computer model based on current data and findings

1. Program the model structure
   - Selection of software

2. Populate of the model with data
   - Data should be systematically collected and reviewed for quality, relevance, and transferability
   - Epidemiology, clinical parameters, quality of life, costs, resource consumptions

Data sources

- → Epidemiology
  - Epidemiological studies
  - Databases/Registers/Surveillance Systems
  - Claims data
  - ...
- → Clinical parameters
  - Clinical studies
  - Evidence-based medicine
  - ...
- → Health Economics
  - Health economic studies, e.g. on quality of life, cost-of-illness
  - EBM catalog (outpatient treatment) / Lauer-Taxe (drugs)
  - DRG report browser / grouper (inpatient treatment)
  - Claims data
  - ...
- → Expert opinion (only if no other source available)

Model development II

3. Calibration
   - Procedure to determine unknown parameters

4. Verification and validation
   - Internal validation: test the program code (e.g. with extreme value assumptions)
   - External validation: comparison with external data and other models

5. Make assumptions transperent

Base case analysis

→ Run the model with the most likely parameter values

→ Present results in the form of cost-effectiveness ratios and incremental cost-effectiveness analyses

Sensitivity analysis

→ Test the robustness of the results

→ Modify assumptions, parameters and structures systematically

→ Identify parameters whose uncertainty has substantial impact on results

→ Provides information on future research priorities

→ Structural analyses, deterministic univariate and multivariate analyses, scenario analyses, probabilistic analyses

Discussion of the results

→ Discuss the results, taking into account the assumptions made and the data quality

→ Discuss uncertainties

→ Discuss limitations

→ Statements on the generalizability and transferability of the conclusions

Cost categories in health economic evaluations

→ Direct costs

- Doctor visits, hospitalisation, …

→ Indirect costs

- Loss of productivity

→ Intagible costs

- Pain etc.

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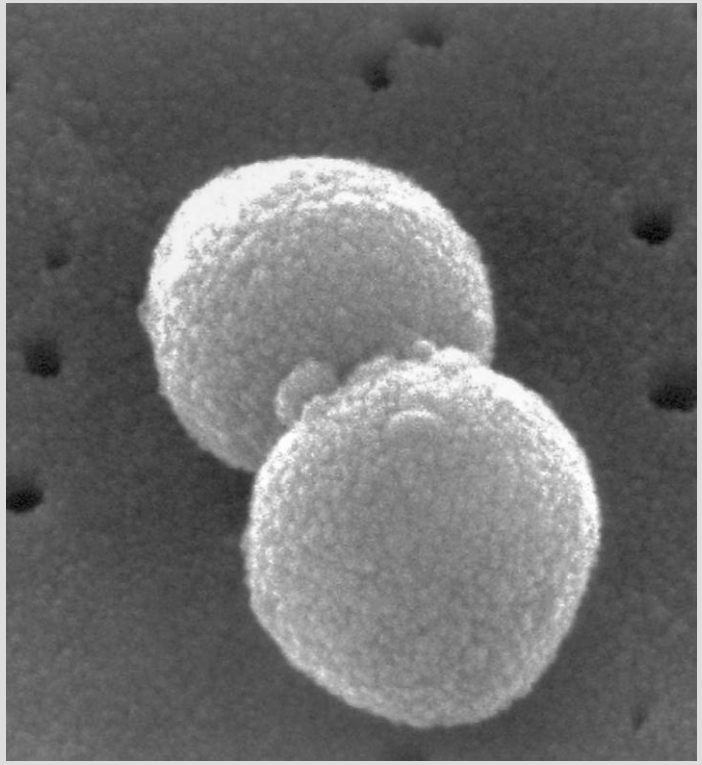
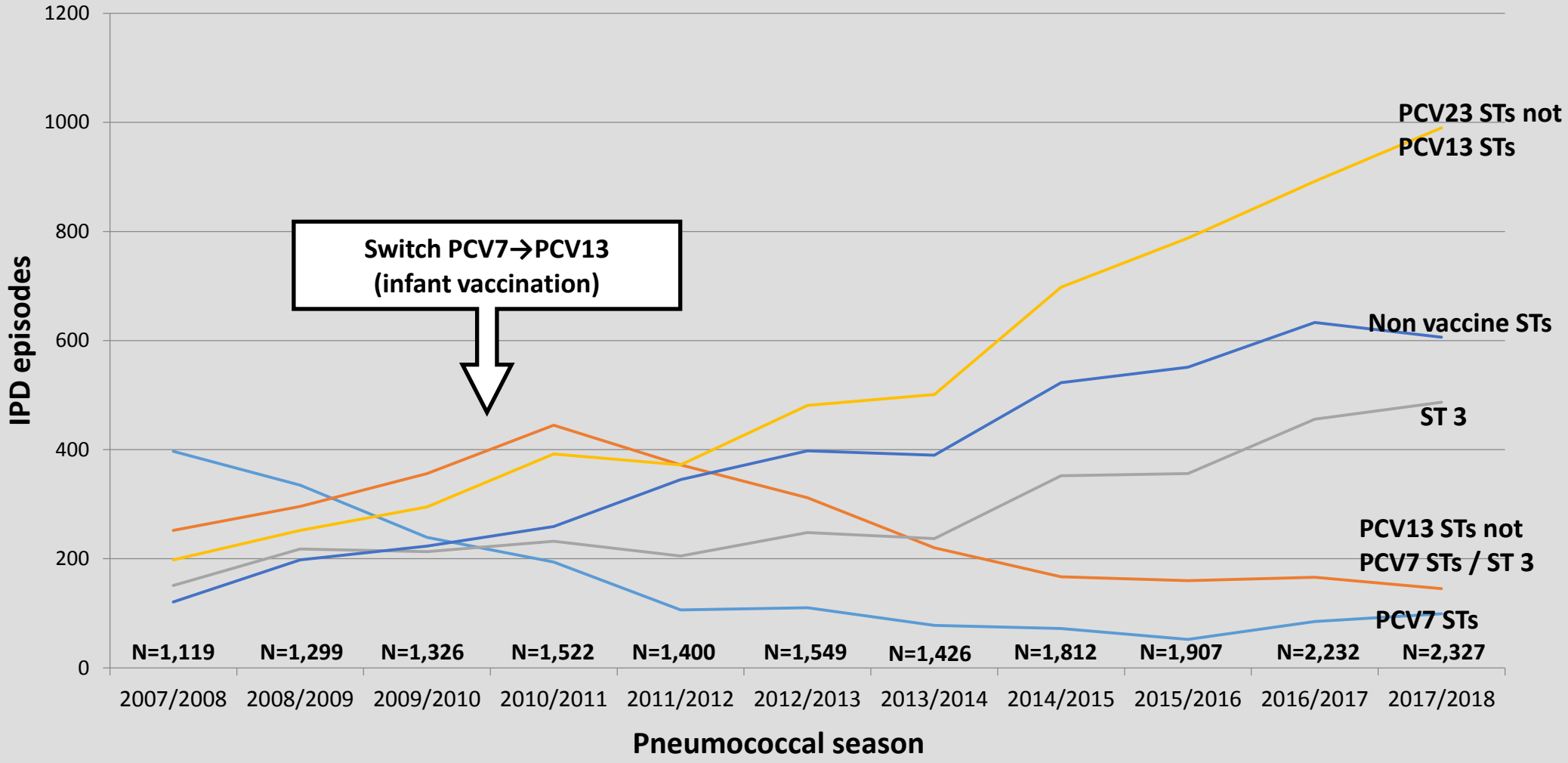
S. pneumoniae

- → Grampositive bacteria
  - 90 serotypes identified
- → Colonize the nasopharinx and can cause local infections (such as pneumonia) and invasive diseases (IPD, such as sepsis, meningitis)
  - About 50% of infants und 5-15% of adults are asymptomatic carrier of S. pneumoniae
- → Vaccination recommendations in Germany
  - Infants with pneumococcal conjugate vaccines (PCV); PCV13 (2+1)
  - Adults over 60 years old with 23 valent polysaccharide vaccine (PPSV23)
  - Specific recommendation for immunocompromised persons

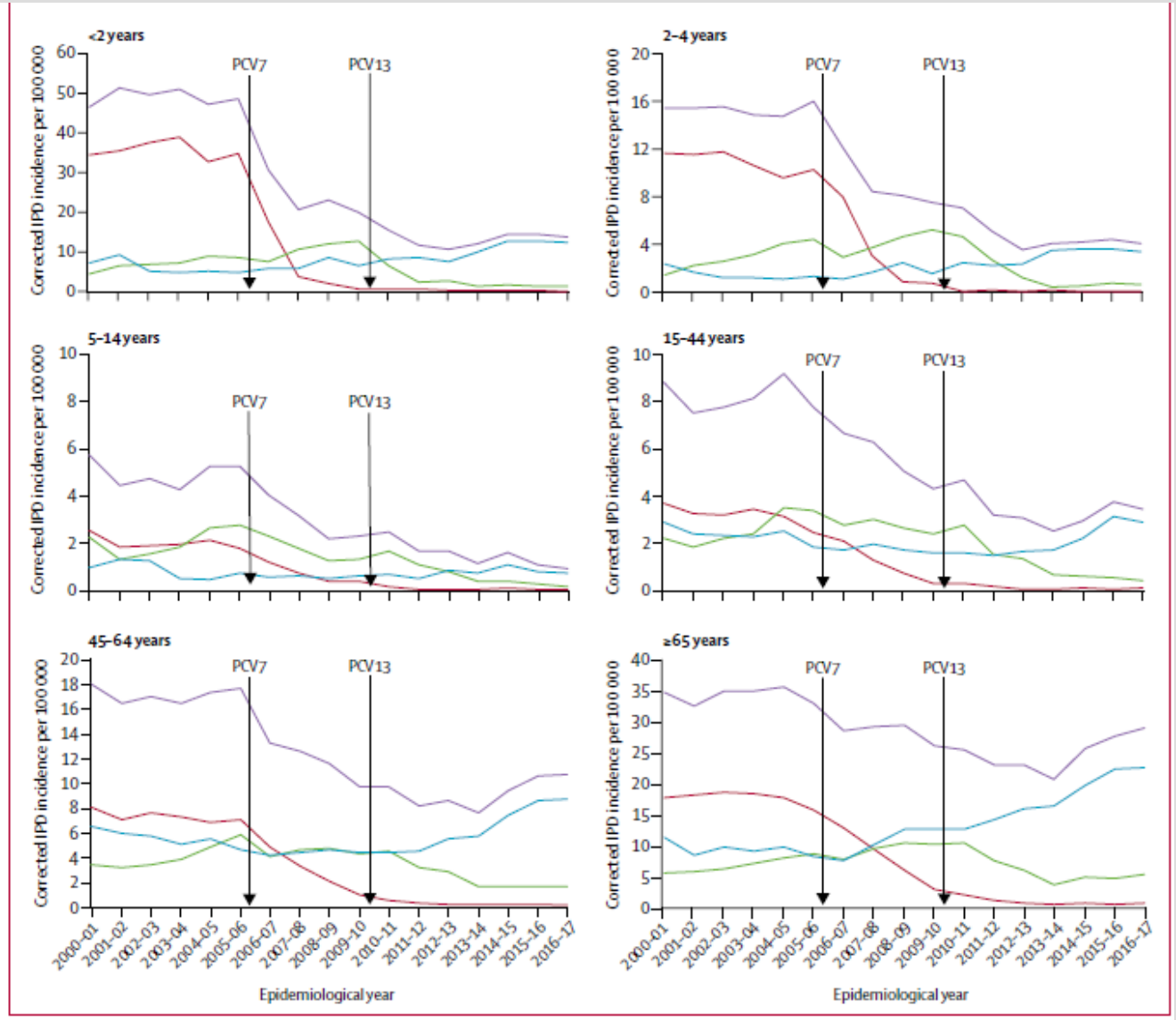


Serotyped IPD cases in age group 60+ years old



Source: Nationales Referenzzentrum für Streptokokken

IPD Incidence in England and Wales



Ladhani et al. 2018

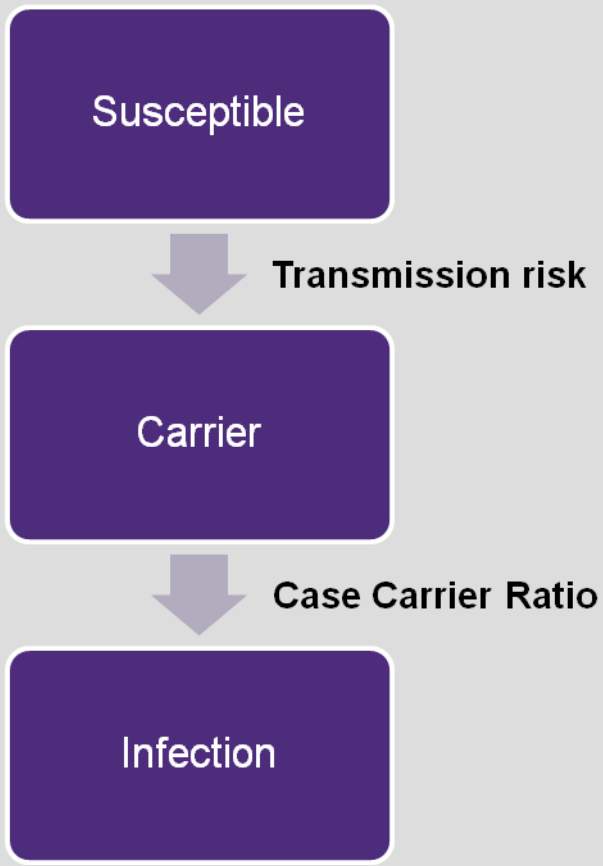
Carriage prevalence in UK

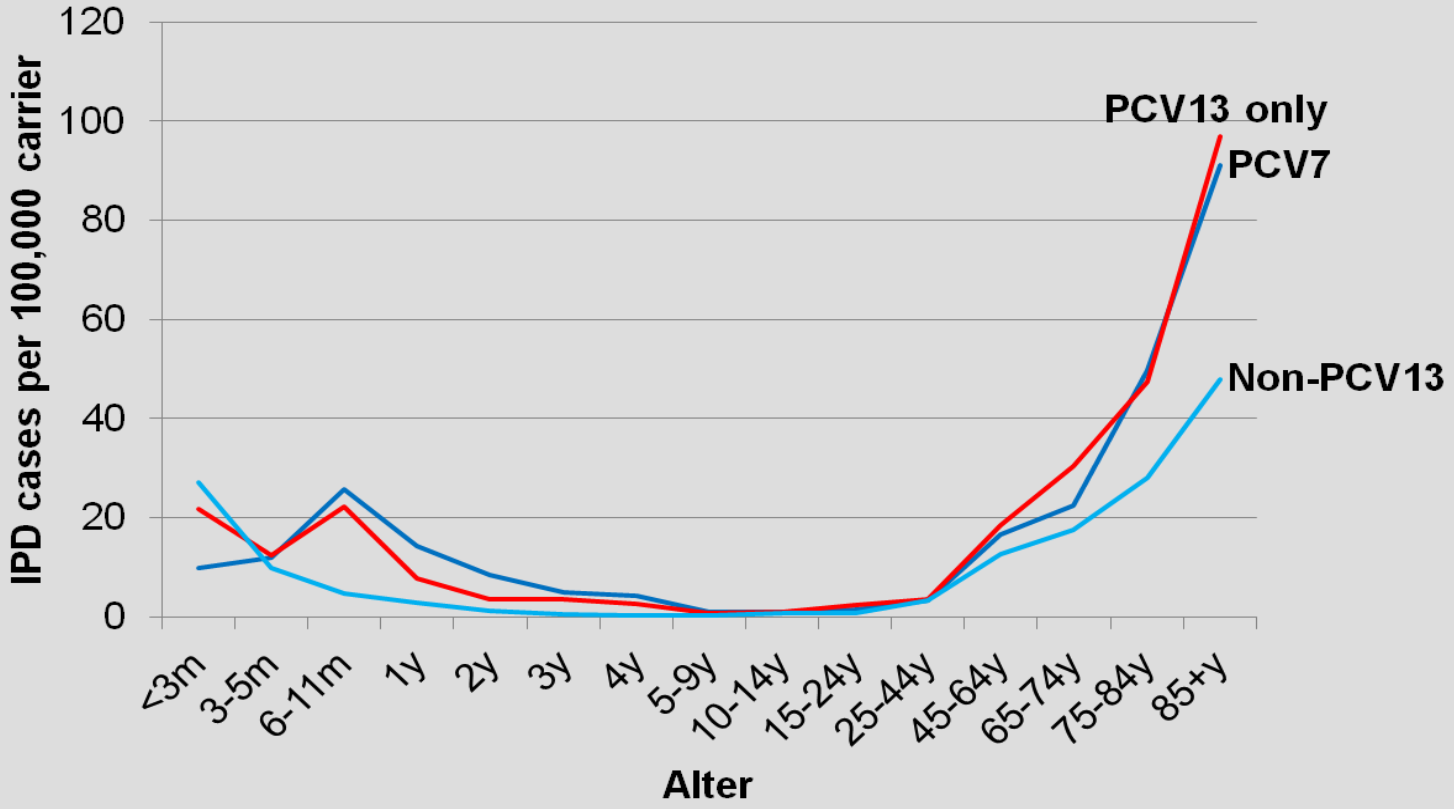
		NVT (95% CI)[1]	PCV7 (95% CI)	Extra 6 PCV13 serotypes (95% CI)	ALL (95% CI)
<5 years	Participants 15/16 (n = 293)	150	0	3	152
	Proportion 15/16	51.1% (45.3–57.0)	0.0% (0.0–1.3)	1.0% (0.2–3.0)	51.9% (46.0–57.7)
	Proportion 12/13	46.9% (41.1–53.5)	0.4% (0.0–2.0)	0.4% (0.0–2.0)	47.7% (41.8–53.5)
	Proportion 08/09	37.0% (30.5–44.0)	4.2% (2.1–8.0)	9.9%(6.4–14.9)	51.0% (44.0–58.0)
	Proportion 01/02	8.5% (6.4–11.1)	31.9% (28.1–36.1)	8.0% (6.0–10.6)	48.4% (44.1–52.7)
5–20 years	Participants 15/16 (n = 73)	18	0	2	20
	Proportion 15/16	24.7% (15.3–36.1)	0.0% (0.0–4.9)	2.7% (0.3–9.5)	27.4% (17.6–39.1)
	Proportion 12/13	19.6% (13.3–28.0)	0.9% (0.0–4.9)	1.8% (0.5–6.3)	22.3% (15.6–30.9)
	Proportion 08/09	22.8% (13.8–35.2)	0.0% (0.0–6.3)	5.3% (1.8–14.4)	28.1% (18.1–40.8)
	Proportion 01/02	8.5% (5.6–12.8)	10.0% (7.5–13.4)	2.0% (1.0–4.1)	21.1% (16.5–26.5)
>20 years	Participants 15/16 (n = 284)	8	0	0	8
	Proportion 15/16	2.8% (1.2–5.4)	0.0% (0.0–1.3)	0.0% (0.0–1.3)	2.8% (1.2–5.5)
	Proportion 12/13	3.1% (1.6–5.7)	0.0% (0.0–1.3)	0.3% (0.0–1.9)	3.4% (1.9–6.1)
	Proportion 08/09	6.0% (3.1–11.4)	2.3% (0.8–6.4)	1.5% (0.4–5.3)	9.8% (5.8–16)
	Proportion 01/02	1.9% (1.3–2.9)	4.0% (3.0–5.4)	1.6% (1.0–2.5)	7.6% (6.1–9.4)
All	Participants 15/16 (n = 650)	176	0	5	180
	Proportion 15/16	27.0% (23.7–30.7)	0.0% (0.0–0.6)	0.7% (0.3–1.8)	27.7% (24.3–31.3)
	Proportion 12/13	23.6% (20.5–26.9)	0.3% (0.1–1.1)	0.6% (0.2–1.5)	24.5% (21.4–27.8)
	Proportion 08/09	24.1% (20.1–28.6)	2.9% (1.6–5.1)	6.3% (4.3–9.2)	33.2% (28.7–38.1)
	Proportion 01/02	5.2% (4.2–6.5)	15.2% (13.2–17.4)	4.1% (3.2–5.2)	24.4% (21.9–27.1)

[1] 6C and non-typeable pneumococci are included in the non-vaccine types. Multiple carriage was detected in 5 individuals. These had 10A/21, 22F/Non-typeable, 23B/Non-typeable, 3/23B and 9N/6C. When assessing the proportion of individuals who carried any VT or NVT serotype, multiple carriage episodes in individuals who carried both a VT and NVT serotype are included. For this reason adding up the number of VT and NVT carriers is one more than the total for carrying any serotype. Non-typeable isolates were counted as NVTs for this analysis to be consistent with the 2012/13 analysis.

https://doi.org/10.1371/journal.pone.0195799.t002

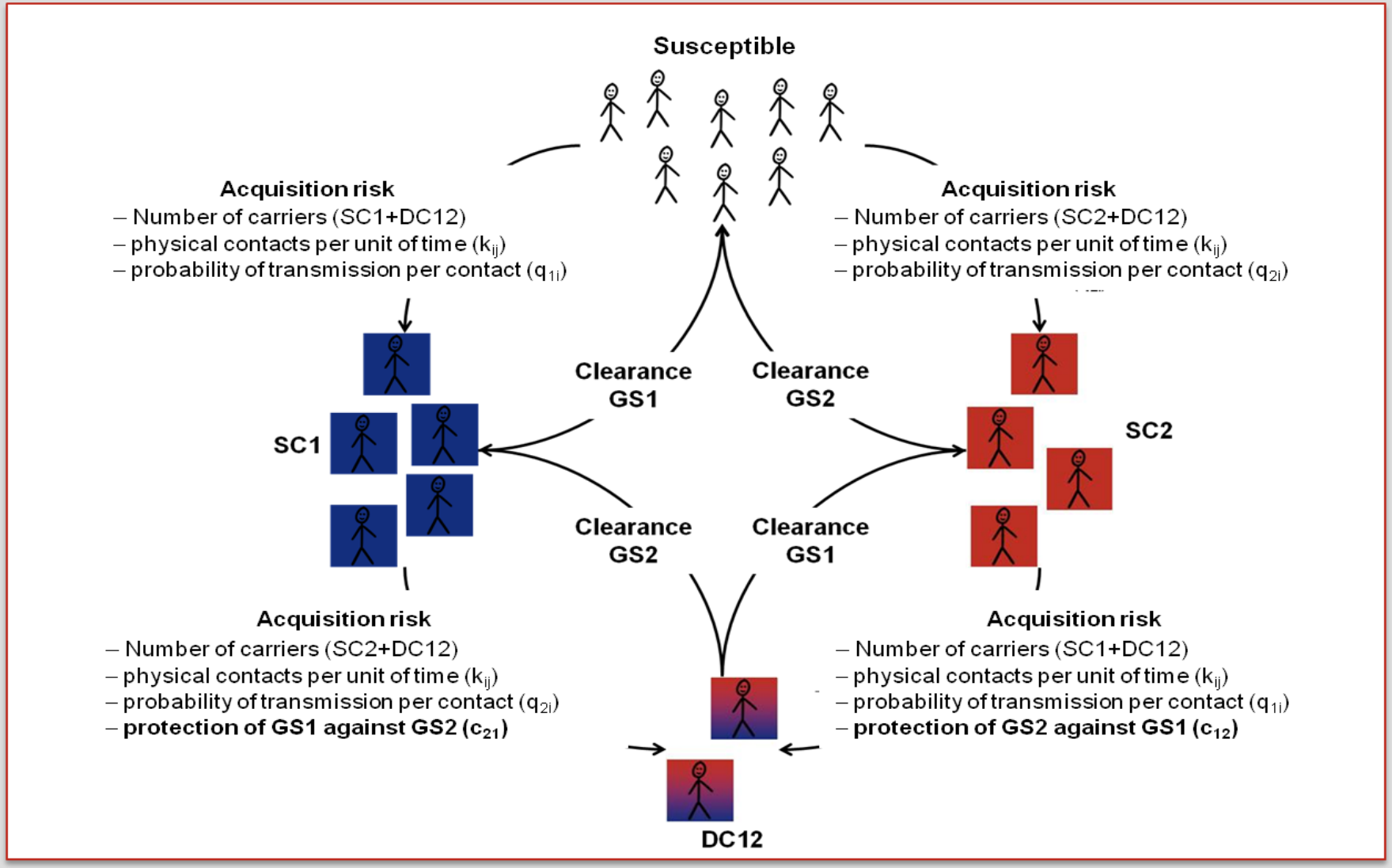
Case-Carrier-Ratios (IPD)





Quelle: Choi et al 2012

Modeling pneumococcal transmission dynamics: indirect herd effects and replacement diseases



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Decision problem

→ What is the most effective and cost-effective vaccination strategy in older adults (60+ years old) for the prevention of pneumococcal diseases
- Initial vaccination at age 60, 65, 70
- Vaccines
  - PCV13
  - PPSV23
  - Sequential vaccination (PCV13 + PPSV23)

→ Taking into account the impact of the infant vaccination on the incidence and serotype distribution of the target population

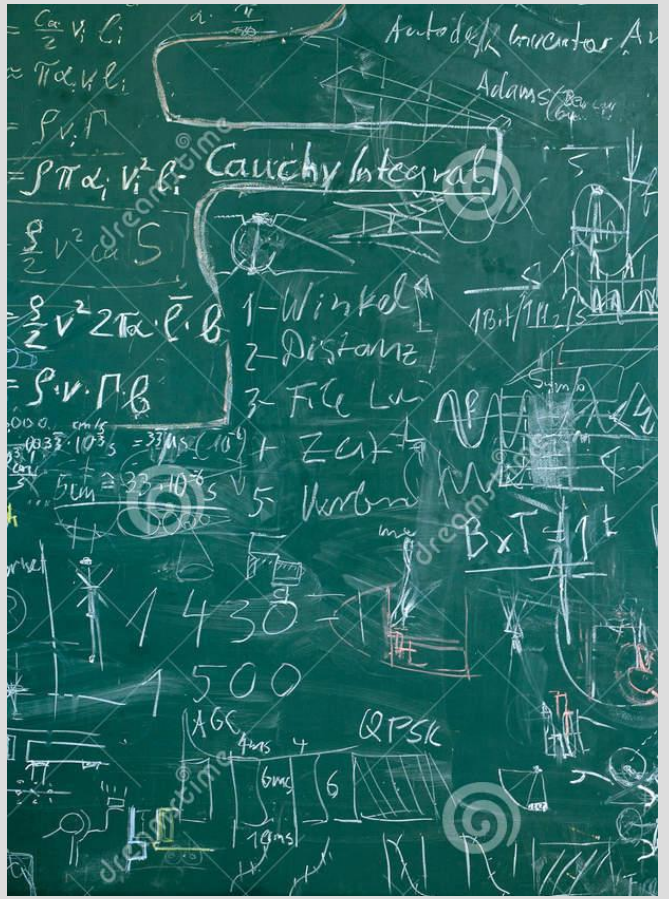
Model concept

→ SIS differential equation model

→ 400 age groups (0; 0,25; … ; 99,75 years old)
- 100,000 individuals per age group; discrete aging
- Contacts weighted with the German population structure
- No mortality

→ 5 groups of serotypes (+ combinations)
- GS1: PCV7 STs
- GS2: PCV13 STs not PCV7 STs / ST 3
- GS3: ST 3
- GS4: PPSV23 STs not PCV13 STs
- GS5: other STs
- 10 combinations (only for carriage)

→ 3 pneumococcal diseases
- Invasive pneumococcal diseases (IPD)
- Non-invasive hospitalized pneumonia (NPPin)
- Non-invasive pneumonia treated in an outpatient setting (NPPout)



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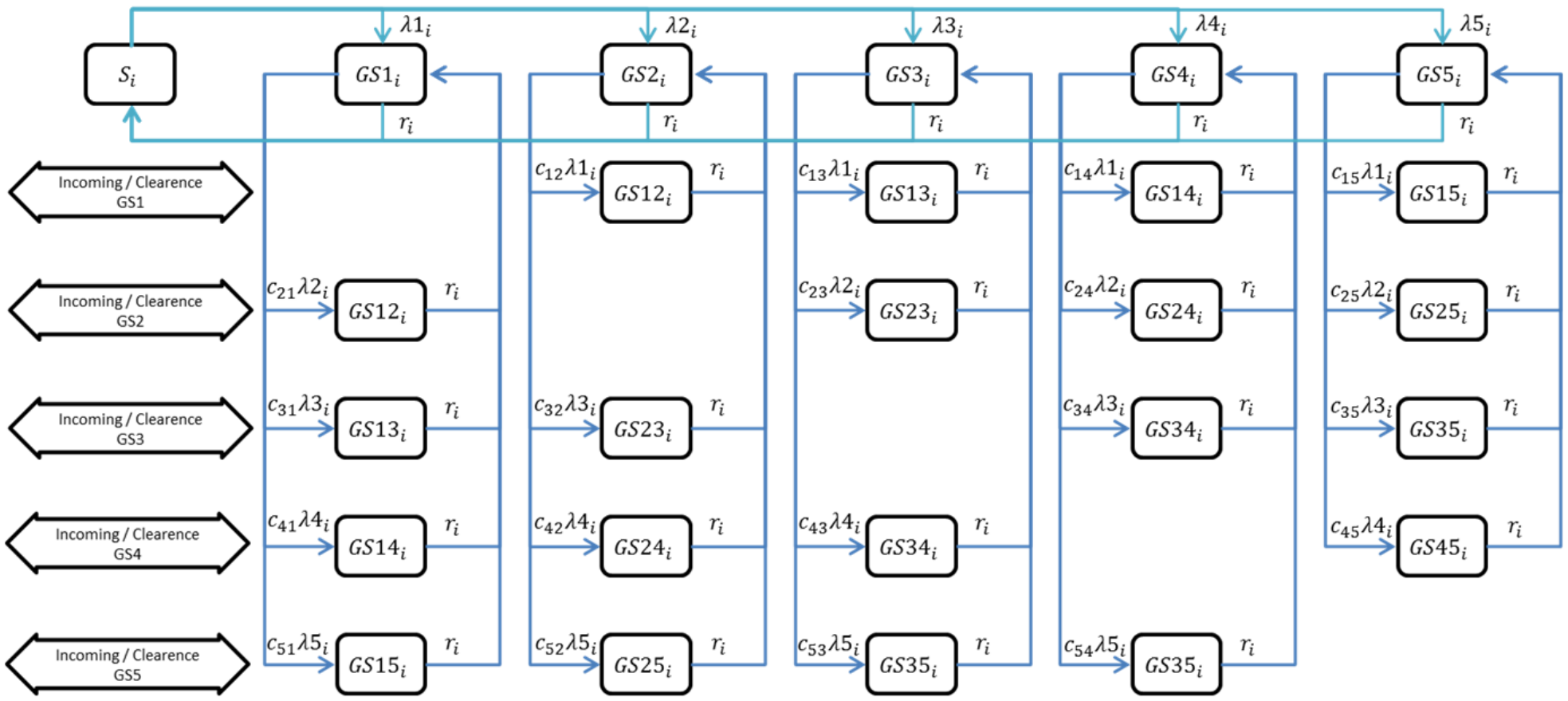
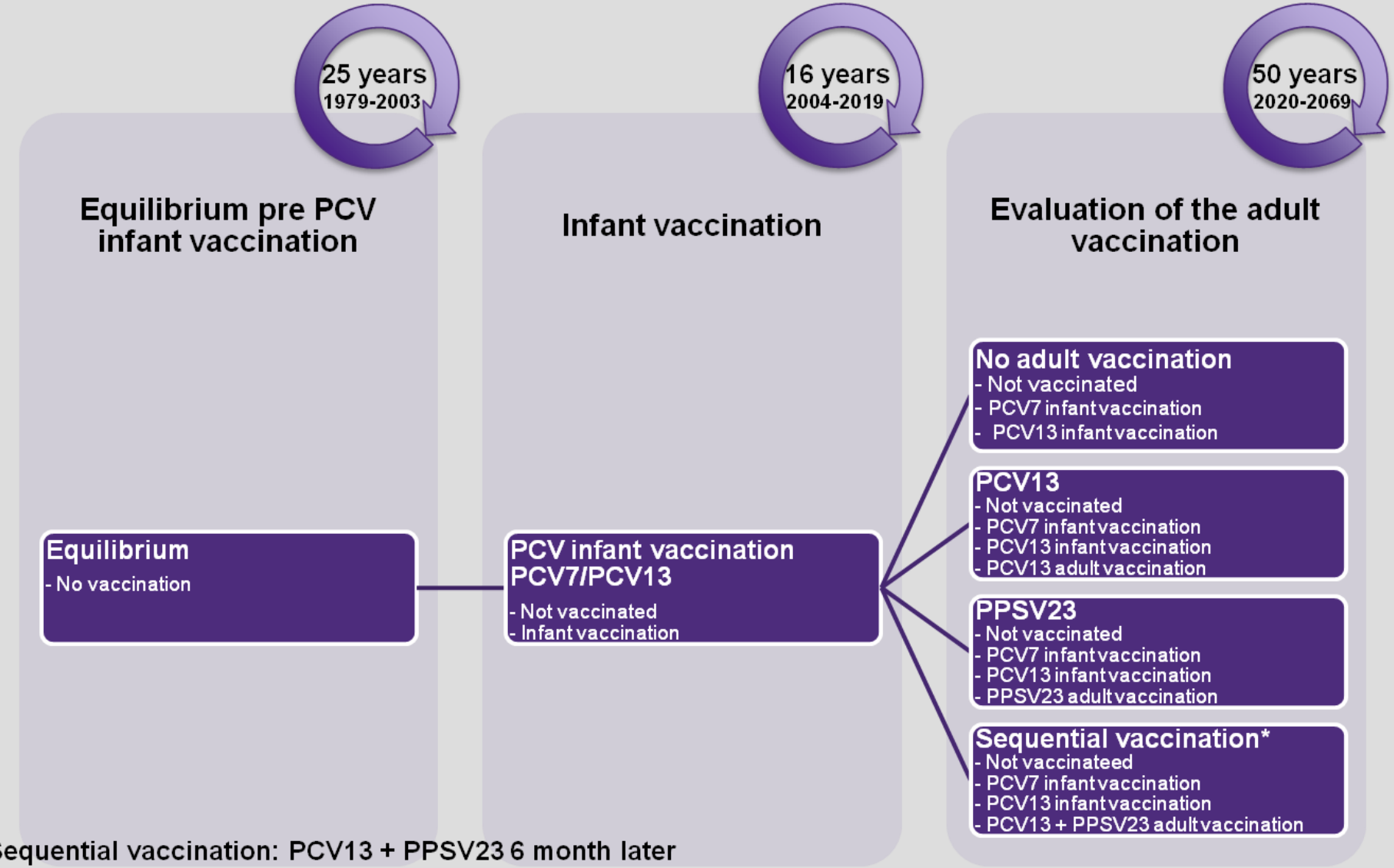
Model core



S_i = Susceptible of age i
$GS1_i$ – $GS45_i$ = Carrier
$\lambda 1_i$ – $\lambda 5_i$ = Force of infection age i
c12 – c54 = Competition parameter
r_i = clearance rate age i

Complete model (time horizon)



* Sequential vaccination: PCV13 + PPSV23 6 month later

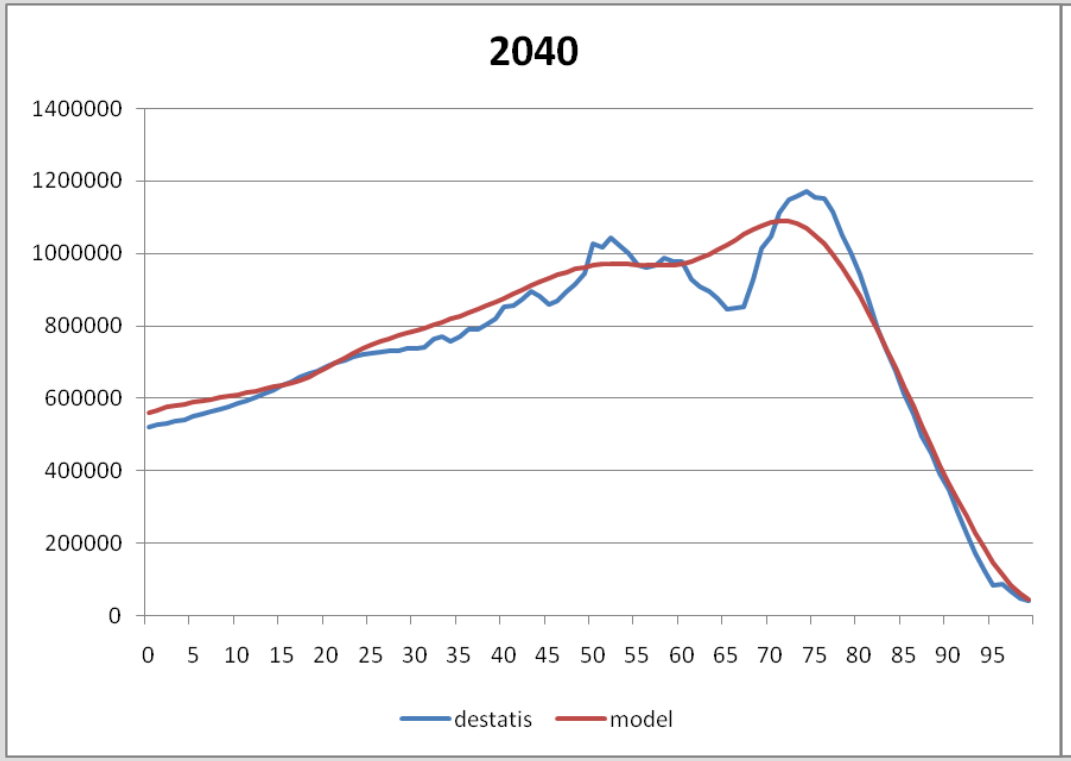
Demography: continues vs. discrete aging

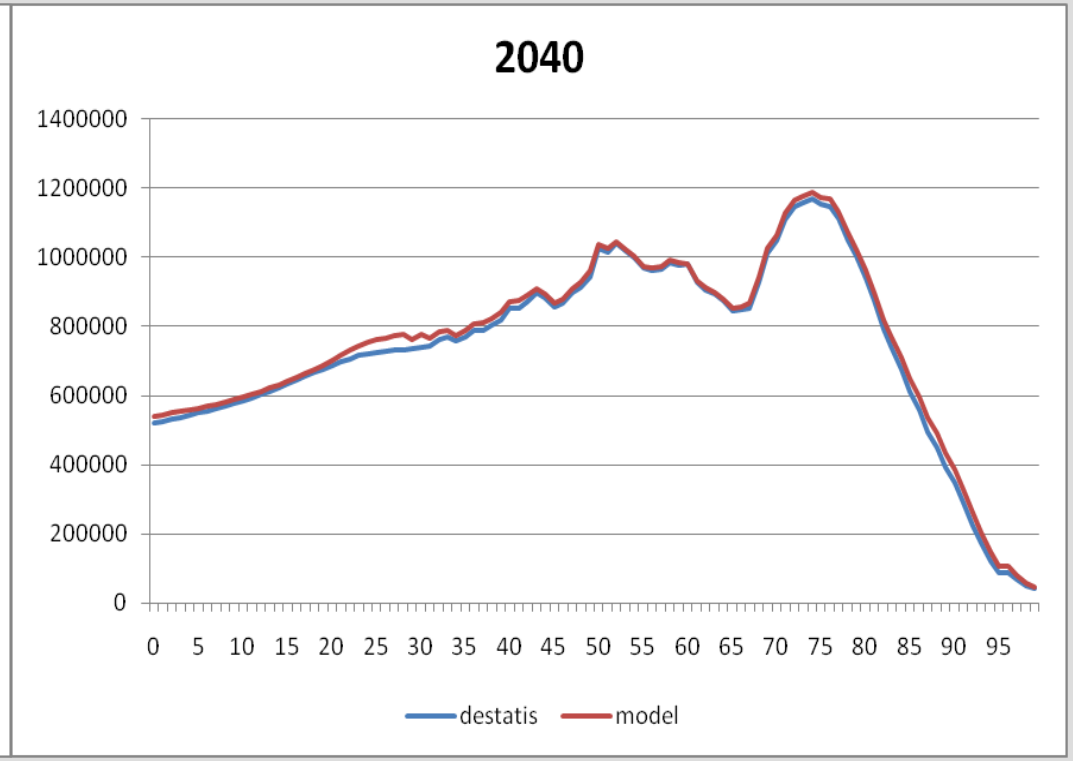
Continues aging

- Apply aging in the ODE system using rates

Discrete aging

- Apply aging outside the ODE system sing a loop
  - Duration of age intervals should be identical and rather short (e.g. one year)



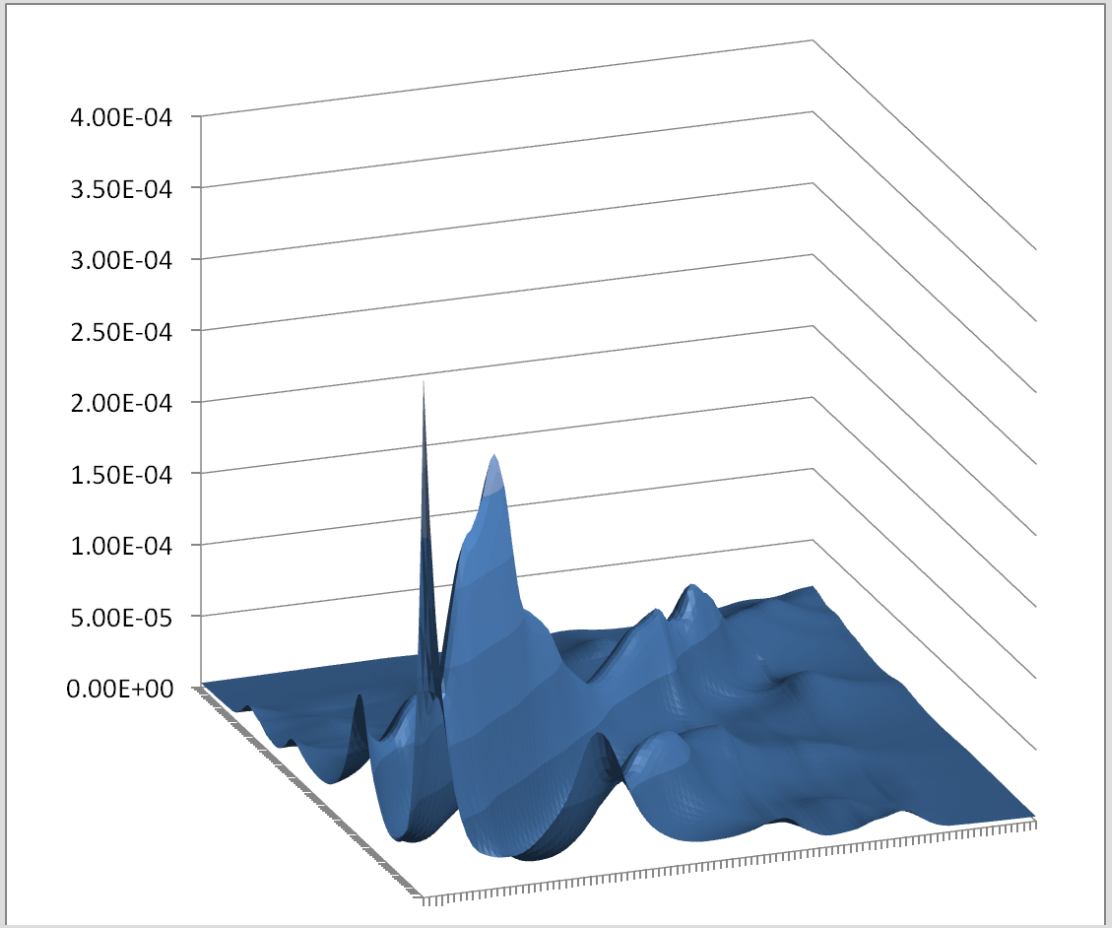


Physical contact rate per year

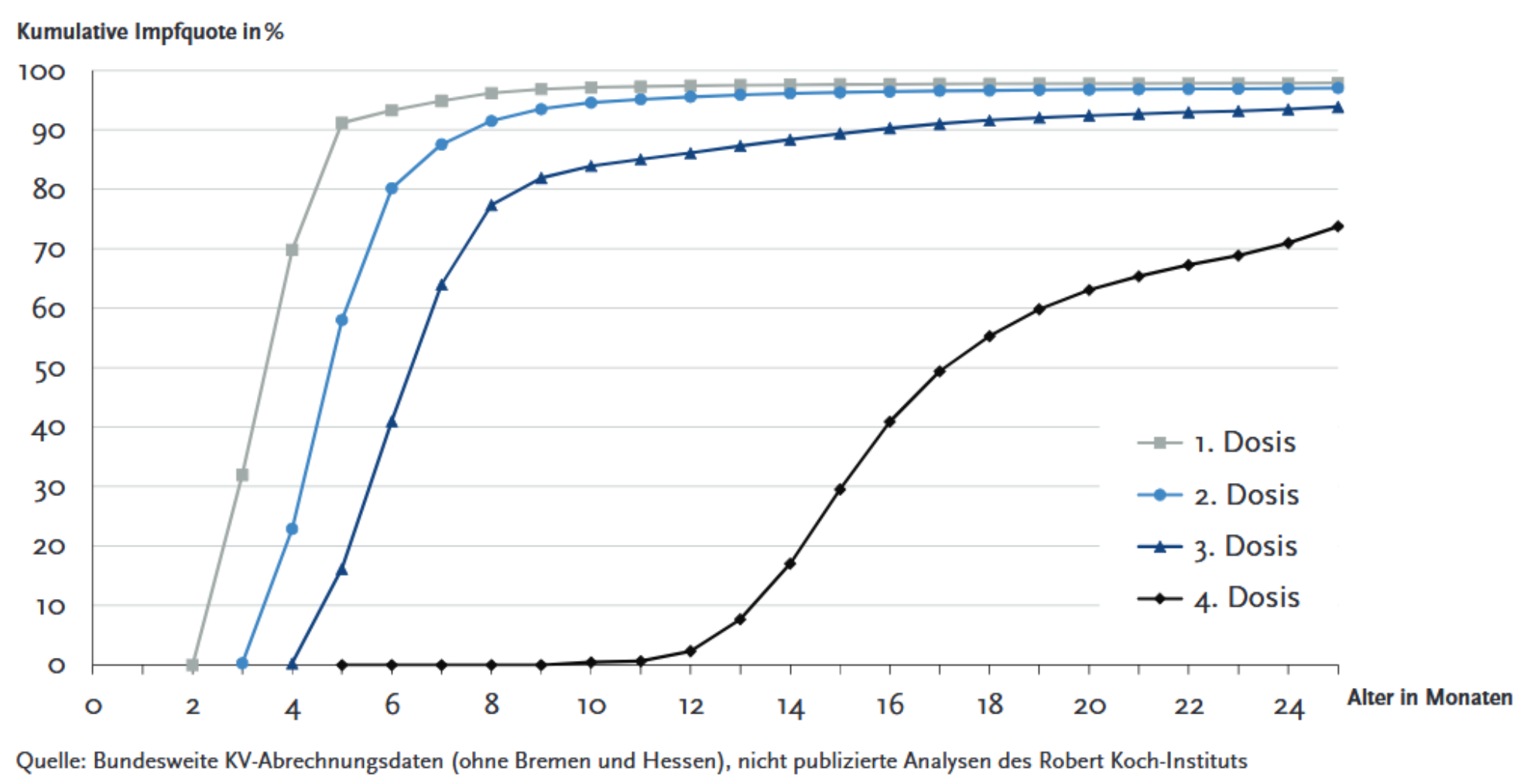
→ Based on Polymod

→ Bivariate smoothing

- Tensor product smoothing
- Marginal smoother: thin plate regression splines
- Contact rate per year
- $$\frac{contacts\ per\ day * 365}{size\ of\ contact\ age\ group}$$
- Symmetric matrix



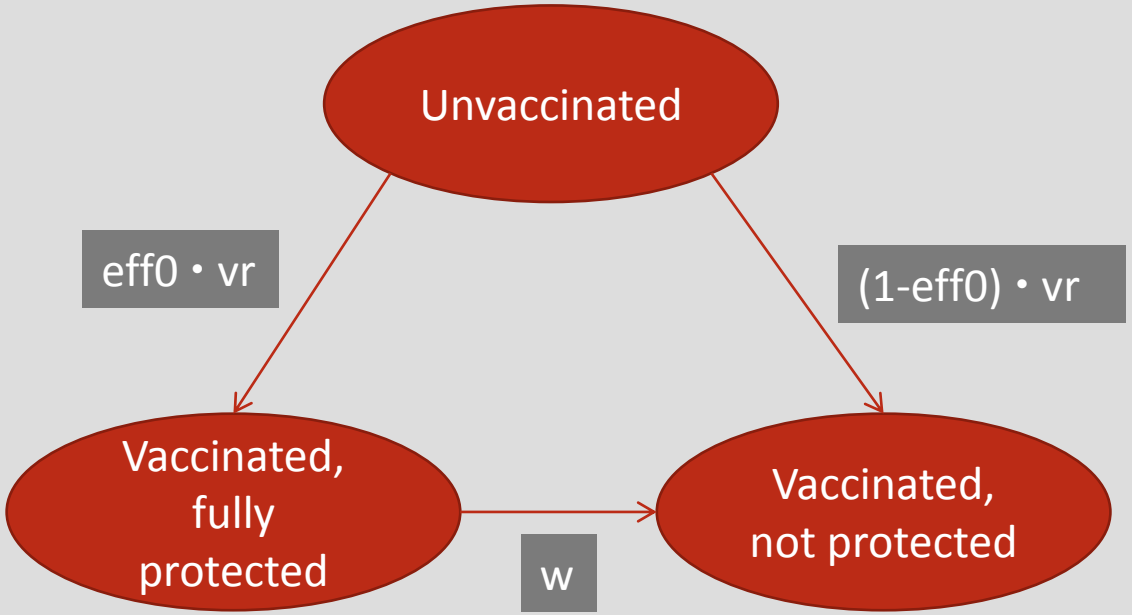
Cumulative vaccine uptake in the 2011 birth cohort

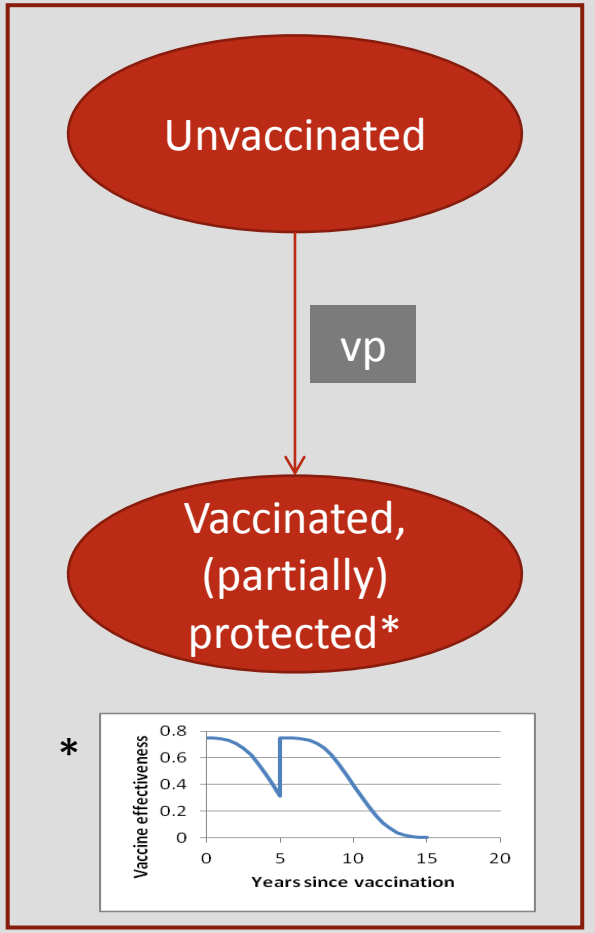


Quelle: Bundesweite KV-Abrechnungsdaten (ohne Bremen und Hessen), nicht publizierte Analysen des Robert Koch-Instituts

Modeling vaccination

→ Many different approaches to modelling vaccination





eff0: initial vaccine efectiveness
vr: vaccination rate
vp: vaccination probability
w: waning

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German data I

→ No carriage studies

→ IPD

- Nationales Referenzzentrum für Streptokokken (NRZ)
  - Serotype distribution
- No incidence data for adults >16 years
  - Pre-PCV incidences from a study conducted in North Rhine-Westphalia (Reinert et al. 2003)
- IPD incidence only for children <15y
  - Capture-recapture based on data from Esped and Pneumoweb
  - Recalculation based on data from ESPED and NRZ
  - Serotype distribution from NRZ

German data II

→ Hospitalized NPP

- All-cause pneumonia incidence: hospital statistics (ICD J12-J18); pneumococci (ICD J13); gbe-bund.de
- Claims data
- Proportion of pneumococci: CAPNETZ
  - 30% but a pathogen is identified in only 50% of samples
- Serotype distribution: CAPNETZ

→ Outpatient NPP

- Prescription data (unpublished)
- Claims data
- No information on the proportion of pneumococci and the serotype distribution

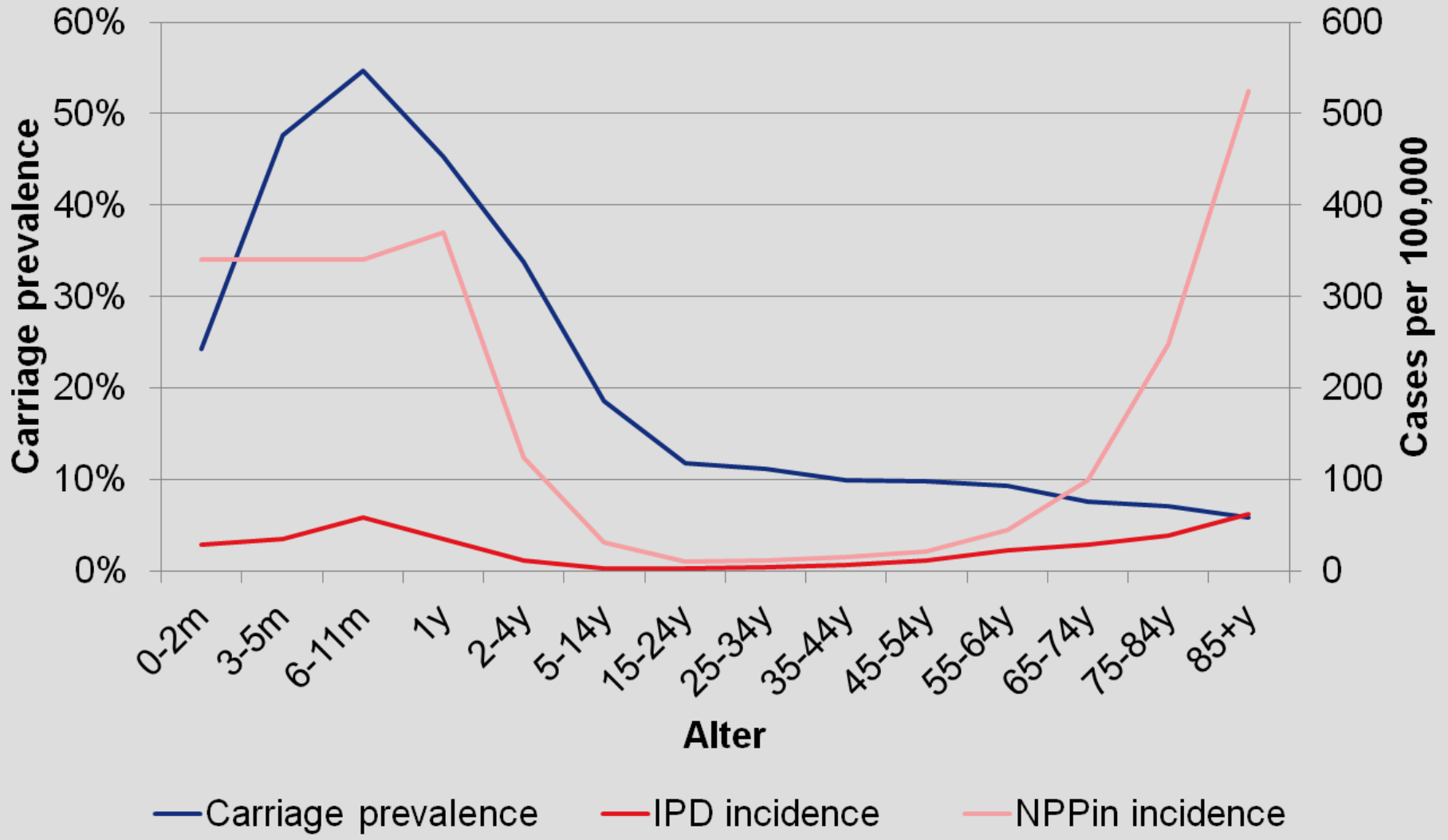
Transmission probability and carriage prevalence

→ Transmission probability per contact is calibrated
- Depends on age and group of serotypes (7 age parameter * 5 groups of serotypes)
- Cubic polynoms

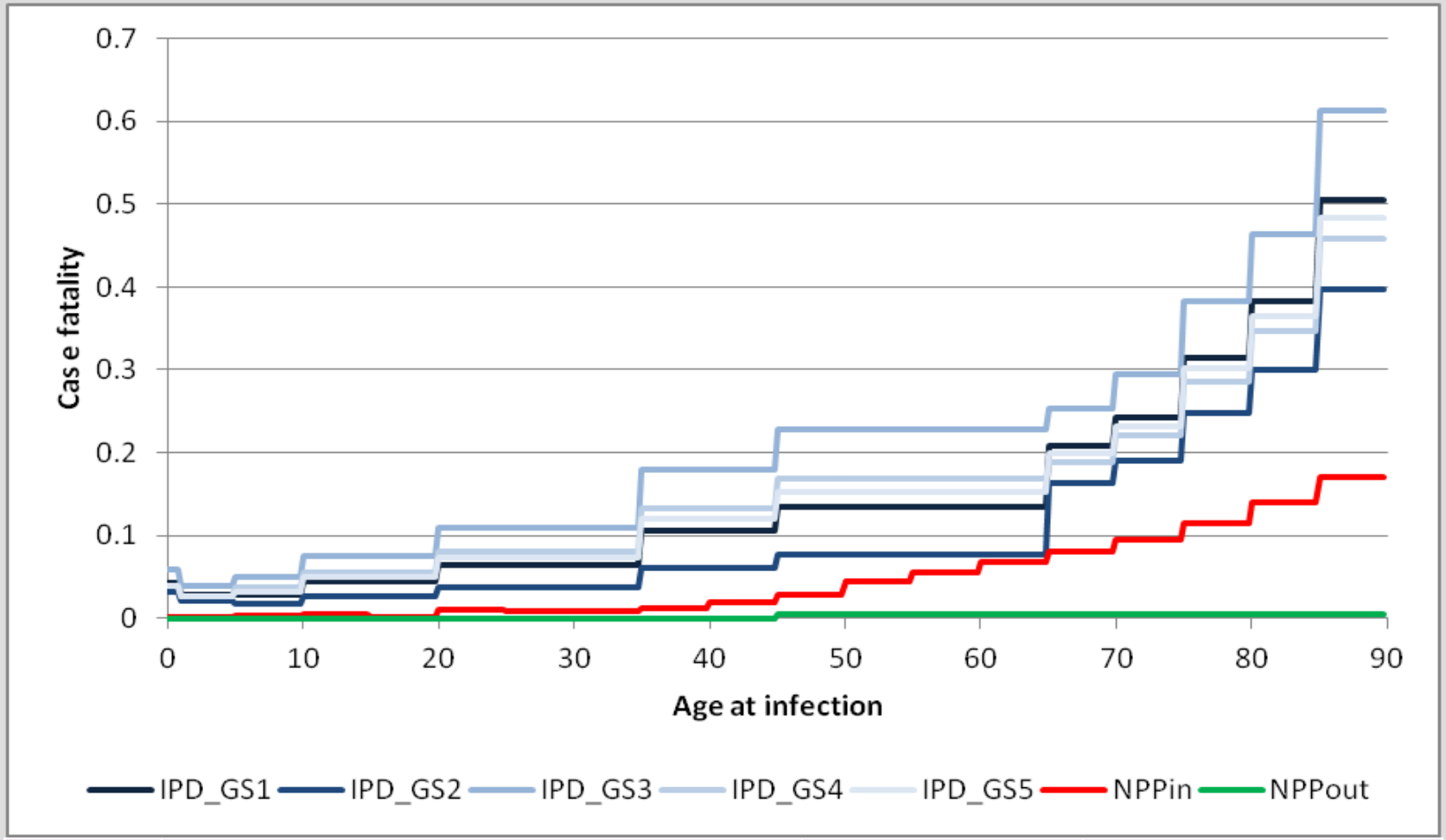
→ IPD incidence, case carrier ratios, average duration of carriage and serotype competition determine the carriage prevalence
- Invasiveness is geographical und temporal stable (Brueggeman 2004)
- Basis: IPD incidence in Germany pro PCV infant vaccination (von Kries 2003, Reinert 2005)
- Case Carrier Ratios based on Choi 2012
- Duration of carriage based on Högberg 2007
- Assumption: Duration of carriage only depends on age

<1 year old	1-2 years old	3-4 years old	5-17 years old	>18 years old
74 days	47 days	34 days	26 days	25 days

Pre-PCV carriage prevalence and disease incidence in Germany



Case fatality %



	IPD	NPPin	NPPout
source	van Hoek 2012, NRZ, gbe-bund.de	gbe-bund.de	CAPNETZ

Health outcomes

	Generic	Disease specific
Patient relevant outcomes	➢ Life years ➢ Prevented death ➢ **Quality-adjusted life years (QALY)** ➢ …	➢ Prevented IPD cases ➢ Prevented pneumococcal pneumonia ➢ …
Surrogates	➢ ???	➢ Increased immune response against pneumococci ➢ …

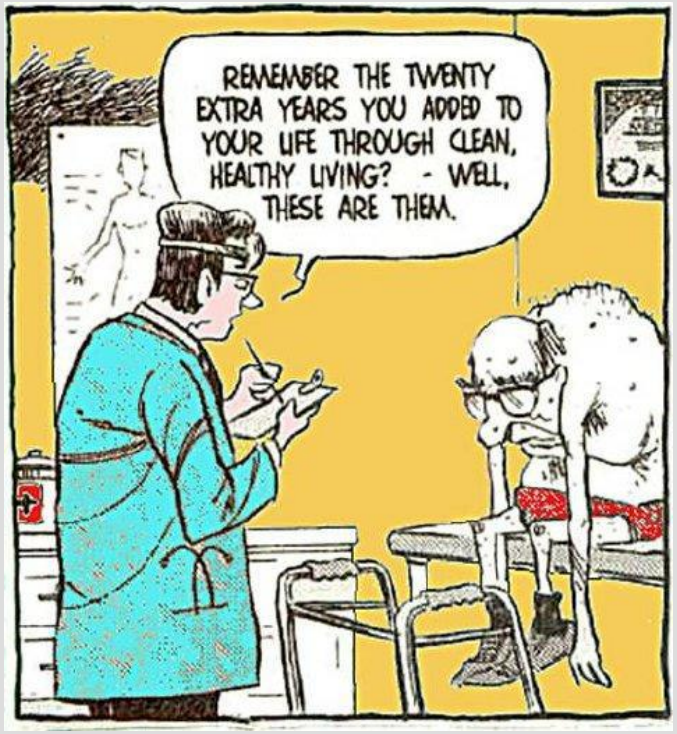
Quality-adjusted life-years (QALYs)

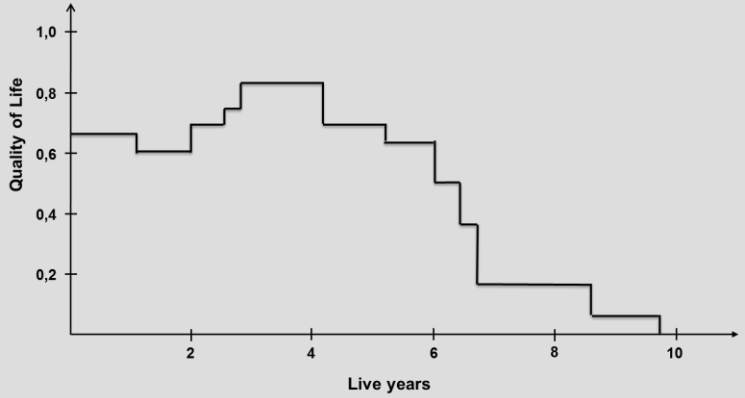
→ Utility measure

→ Two dimensions

- Remaining life expectancy
- Health related quality of life

→ <u>Idea</u>: A life year in perfect health has a higher value than a life year with a disease



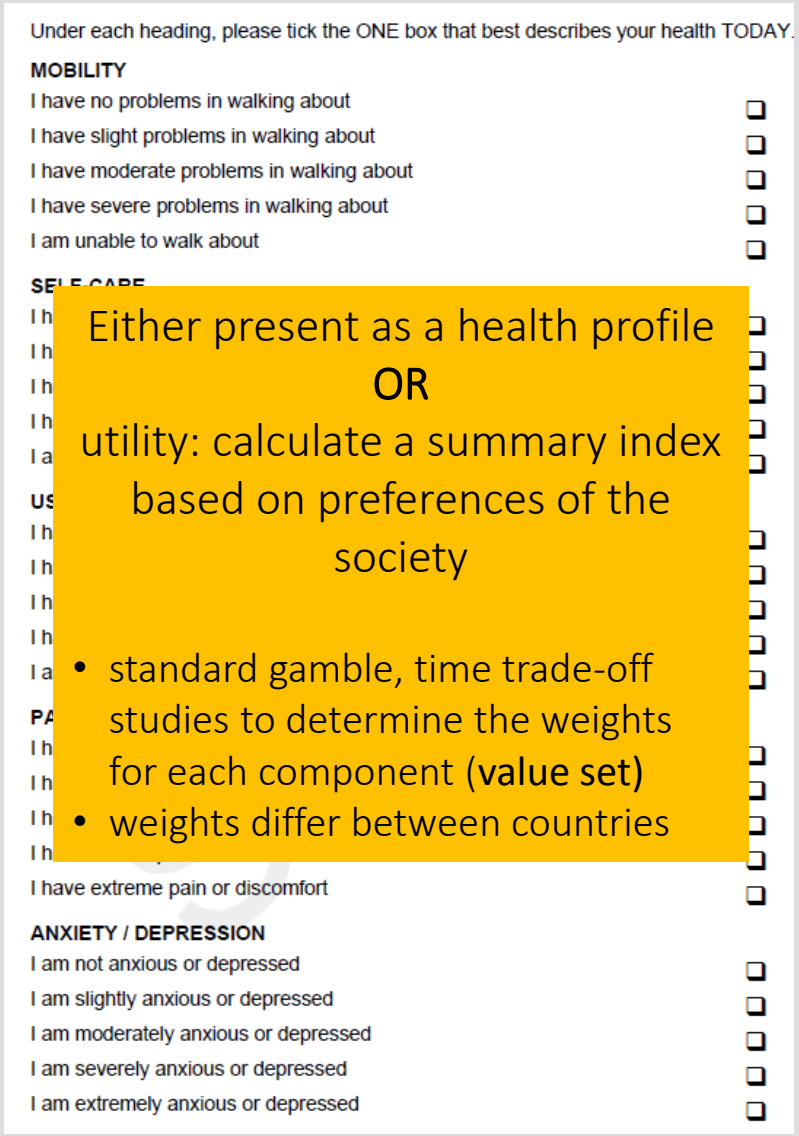


EQ-5D-5L

1 QALY

=

Utility of one life year in perfect health



Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

SELF-CARE

I h ❑
I h ❑
I h ❑
I h ❑
I a ❑

US

I h ❑
I h ❑
I h ❑
I h ❑
I a ❑

PA

I h ❑
I h ❑
I h ❑
I h ❑
I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

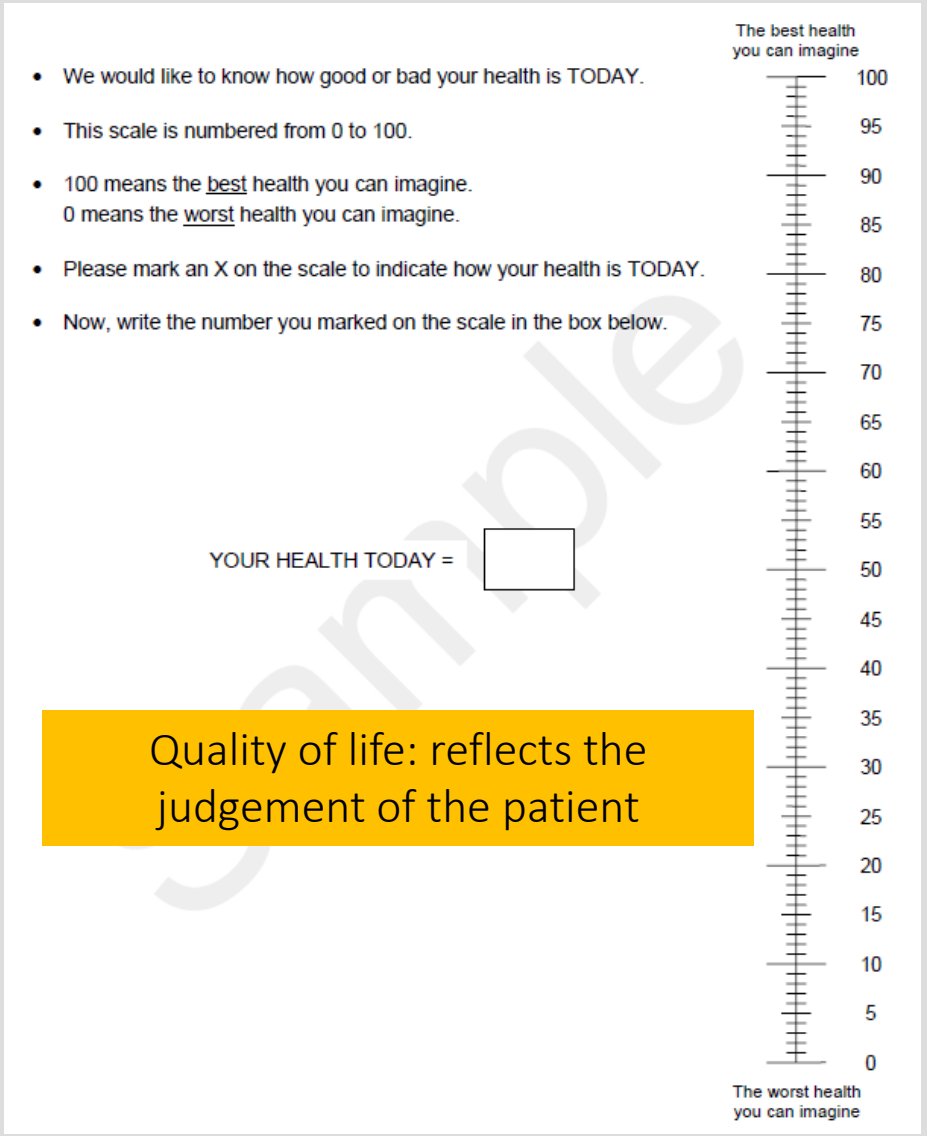
I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

Either present as a health profile

OR

utility: calculate a summary index based on preferences of the society

- standard gamble, time trade-off studies to determine the weights for each component (**value set)**
- weights differ between countries



- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Please mark an X on the scale to indicate how your health is TODAY.
- Now, write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = ☐

The best health you can imagine

100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0

The worst health you can imagine

Quality of life: reflects the judgement of the patient

Source: EuroQol

German EQ-5D-5L value set

Independent variables of the model[a,b]	Model 1: Tobit (cTTO model)		Model 2: Conditional Logit (DCE model)			Model 3a: Hybrid censoring at -1 (cTTO + DCE model)[c]		Model 3b (Value Set): Hybrid censoring at -1 and correcting for heteroskedasticity (cTTO + DCE model)[d,e]	
	β (SE)	p	β (SE)	p	rescaled β	β (SE)	p	β (SE)	p
MO2: slight problems	0.028 (0.015)	0.062	0.135 (0.057)	0.019	0.023	0.028 (0.008)	0.000	0.026 (0.006)	0.000
MO3: moderate problems	**0.015** (0.017)	0.379	0.370 (0.069)	0.000	0.063	0.051 (0.009)	0.000	0.042 (0.009)	0.000
MO4: severe problems	0.130 (0.018)	0.000	0.834 (0.069)	0.000	0.141	0.139 (0.009)	0.000	0.139 (0.009)	0.000
MO5: unable	0.207 (0.017)	0.000	1.349 (0.077)	0.000	0.228	0.216 (0.009)	0.000	0.224 (0.009)	0.000
SC2: slight problems	0.035 (0.014)	0.013	0.408 (0.063)	0.000	0.069	0.058 (0.008)	0.000	0.050 (0.006)	0.000
SC3: moderate problems	0.050 (0.018)	0.006	**0.393** (0.070)	0.000	**0.067**	0.062 (0.009)	0.000	0.056 (0.008)	0.000
SC4: severe problems	0.174 (0.017)	0.000	1.034 (0.072)	0.000	0.175	0.174 (0.009)	0.000	0.169 (0.009)	0.000
SC5: unable	0.244 (0.016)	0.000	1.520 (0.071)	0.000	0.257	0.248 (0.008)	0.000	0.260 (0.008)	0.000
UA2: slight problems	0.034 (0.015)	0.024	0.119 (0.059)	0.044	0.020	0.025 (0.008)	0.001	0.036 (0.006)	0.000
UA3: moderate problems	0.069 (0.016)	0.000	0.232 (0.066)	0.000	0.039	0.049 (0.009)	0.000	0.049 (0.008)	0.000
UA4: severe problems	0.121 (0.017)	0.000	0.669 (0.070)	0.000	0.113	0.117 (0.009)	0.000	0.129 (0.008)	0.000
UA5: unable	0.203 (0.016)	0.000	1.130 (0.073)	0.000	0.191	0.191 (0.009)	0.000	0.209 (0.008)	0.000
PD2: slight problems	0.061 (0.013)	0.000	0.421 (0.063)	0.000	0.071	0.066 (0.008)	0.000	0.057 (0.006)	0.000
PD3: moderate problems	0.098 (0.018)	0.000	0.739 (0.070)	0.000	0.125	0.119 (0.009)	0.000	0.109 (0.009)	0.000

Source: Ludwig et al. 2018

EQ-5D

German Value Set

Ludwig, K., Graf von der Schulenburg, JM. & Greiner, W. German Value Set for the EQ-5D-5L. *PharmacoEconomics* **36,** 663–674 (2018). https://doi.org/10.1007/s40273-018-0615-8
https://link.springer.com/article/10.1007%2Fs40273-018-0615-8#citeas

EQ-5D-5L Crosswalk Index Value Calculator

https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/valuation-standard-value-sets/crosswalk-index-value-calculator/

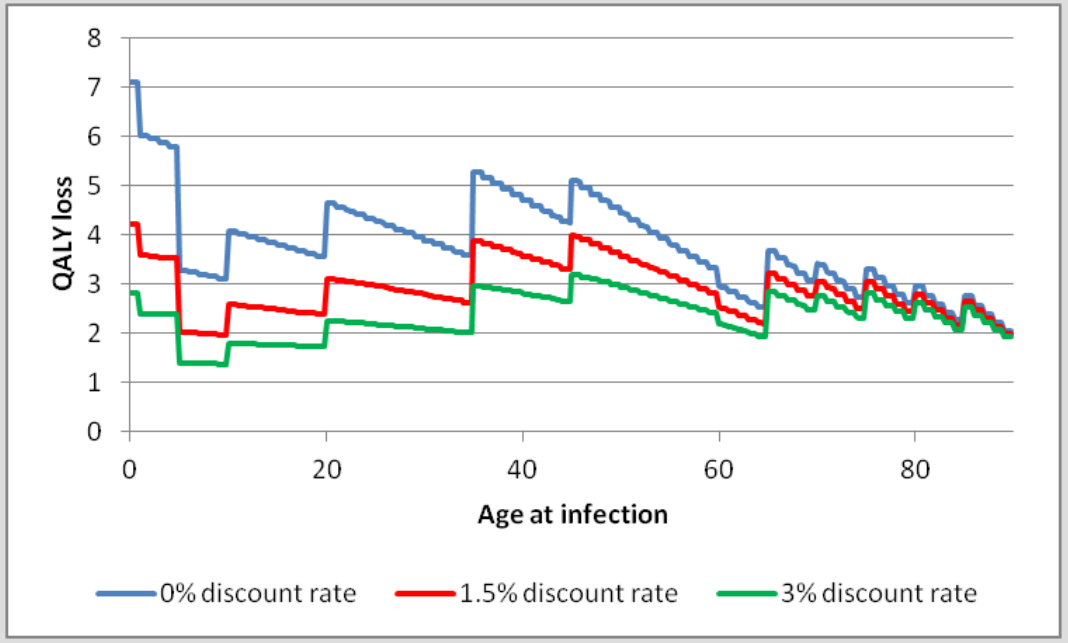
EQ-5D population norms

https://euroqol.org/eq-5d-instruments/population-norms/
https://eq-5dpublications.euroqol.org/download?id=0_54006&fileId=54415

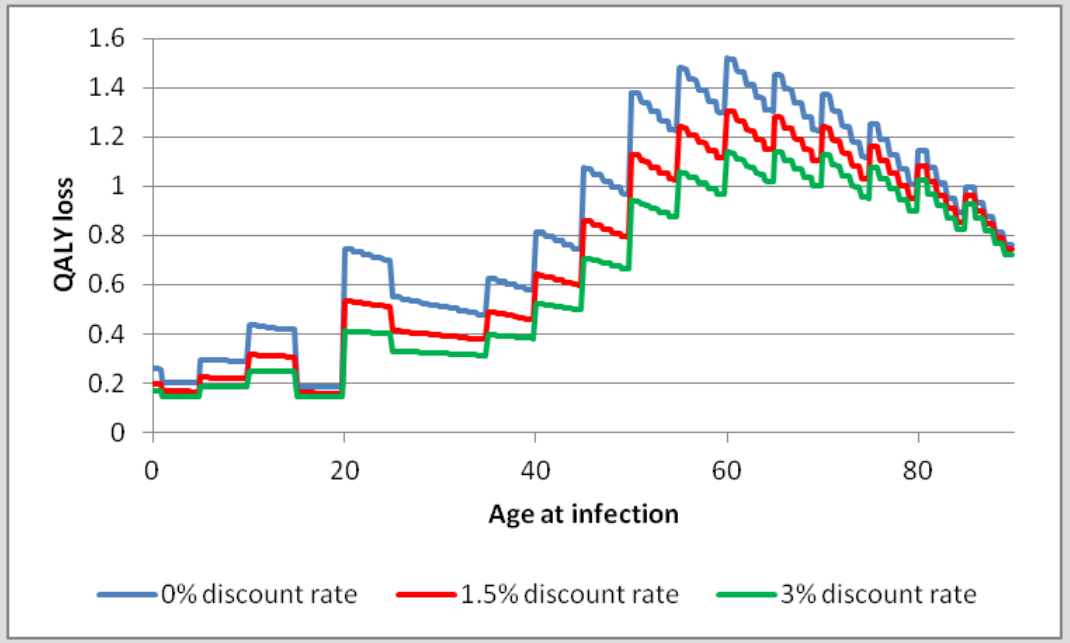
QALY losses due to pneumococcal diseases

→ Includes disutility due to infection, sequelea, premature death

PCV7-IPD



NPPin



Cost categories

→ Direct costs

→ Indirect costs

→ Intangible costs

Direct costs

→ Include all costs that result from a medical intervention and are directly attributable to it

→ **Direct medical costs** include all costs arising from the provision of the healthcare service
- e.g. costs for personnel, diagnostics, therapy (medication)
- including costs arising from treatment / tests
- as well as costs for the treatment of side effects / complications of the therapy

→ **Direct non-medical costs** include all non-medical costs of treatment
- Travel costs, childcare costs, etc.

Indirect costs

→ **Indirect costs** are all productivity losses due to illness and interventions

→ Calculation method
- Human capital approach
- Friction cost approach

Intangible costs

→ **Intangible costs** are disease-associated costs whose monetary value cannot be directly quantified. They include somatic, mental, psychological and social factors.

→ Quantification is associated with major methodological problems

- Often measured in quality of life, QALY losses
- Double counting should be avoided

Perspective

Cost components	Perspective			
	Society	Payer (health insurance)	Patient	Provider
Medical care	Real costs (all)	Reimbursement	Co-payment / self-medication	Costs (own)
Patient time	Yes	No	Yes	No
Productivity loss	Yes	No	Partly (income)	No
Transport cost	Yes (all)	Possible (reimbursement)	Co-payments / costs	Possible (own costs)
Other services	Yes	Possible (reimbursment)	Co-payments / costs	No
Continued pay	administrative costs only	Possible (costs)	No	No

Discounting

→ adjusting future costs and outcomes of health-care interventions to “present value”

→ based on the concept of “positive time preference”
- Other justification: invest in the capital market, uncertainty

→ Uniform vs. differential discounting

→ Can have a substantial impact on the results (in particular in prevention)

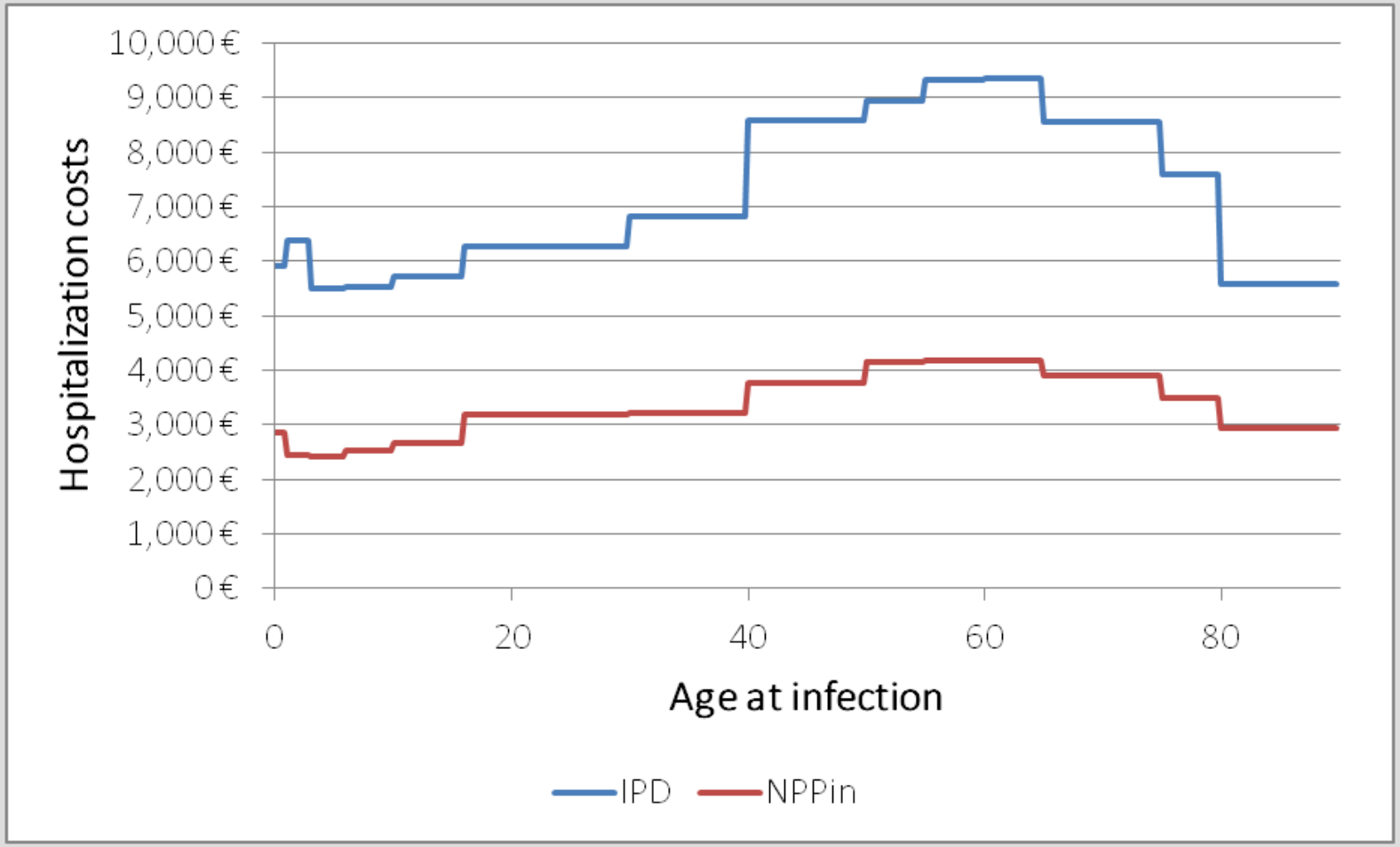
Vaccination costs

Price year 2016	Pharmacy retail price	Discount pharma company	Discount pharmacy	Co-payment	
PREVENAR 13 N2 (10 Stück)	668.42	64.30	1.77	0.00	**60.24**
PREVENAR 13 N1 (1 Stück)	79.85	6.05	1.77	0.00	72.03
PNEUMOVAX 23 N2 (10 Stück)	309.05	16.50	1.77	0.00	**29.08**
PNEUMOVAX 23 N2 (1 Stück)	41.64	1.70	1.77	0.00	38.17

https://www.cgm.com/deu_de/produkte/apotheke/lauer-taxe.html

+ 7.19 Euro application fee (source: vaccination agreements)

Costs of hospitalization



G-DRG Report Browser: https://www.g-drg.de/Datenbrowser_und_Begleitforschung/G-DRG-Report-Browser
G-DRG-Grouper: https://www.drg-research-group.de/index.php?option=com_webgrouper&Itemid=112&view=webgrouper

Direct costs of NPPout

EMB 2015	<4y	5-18y	19-54y	55-75y	76+y
03000 - Versichertenpauschale	24.24	15.41	12.53	16.13	21.57
03040 – Zusatzpauschale	14.79	14.79	14.79	14.79	14.79
03230 - Problemorientiertes ärztliches Gespräch	4.62	4.62	4.62	4.62	4.62
	43.65	34.82	31.94	35.54	40.98

https://www.kbv.de/html/ebm.php

	Pharmacy retail price	Discount pharma company	Discount pharmacy	Co-payment	Costs from the payer‘s perspective	Costs from the societal perspective
AMOXI 1000 1A Pharma N2 (20 Stück)	15.67	0	1.77	5	8.9	13.9

https://www.cgm.com/deu_de/produkte/apotheke/lauer-taxe.html

Indirect costs I

Employment (%)

AGE/TIME	2012	2013	2014	2015	2016
15y-19y	26.0	26.7	26.0	25.5	26.7
20y-24y	64.2	64.4	63.9	63.6	63.6
25y-29y	77.6	77.6	77.7	78.1	78.2
30y-34y	82.3	82.1	82.3	82.5	82.1
35y-39y	83.6	83.7	83.9	84.3	83.8
40y-44y	86.3	86.3	86.1	85.8	86.2
45y-49y	85.9	86.2	86.2	86.7	87.6
50y-54y	82.7	83.0	83.5	84.1	84.9
55y-59y	75.1	76.1	77.2	77.5	79.4
60y-64y	46.6	50.0	52.6	53.3	56.0
65y-69y	11.2	12.6	13.8	14.5	15.5
70y-74y	5.1	5.5	5.9	6.2	6.6
75y-79y	1.5	1.6	1.7	1.8	1.9

Eurostat

Work loss due to infection (days)

	IPD	sCAP	oCAP
<15y	7.00	7.00	3.00
15y-19y	29.20	7.36	7.36
20y-24y	68.50	9.09	9.09
25y-29y	76.20	9.55	9.55
30y-34y	76.40	10.27	10.27
35y-39y	80.10	11.80	11.80
40y-44y	83.70	12.87	12.87
45y-49y	83.90	14.46	14.46
50y-54y	79.70	15.43	15.43
55y-59y	67.50	17.25	17.25
60y-80y	39.30	18.65	18.65
80+y	0.00	0.00	0.00

AOK

Indirect costs II

Average wage per person

	2012	2013	2014	2015	2016
per year	37,035	37,709	38,755	39,789	40,661
per day	101.47	103.31	106.18	109.01	111.40

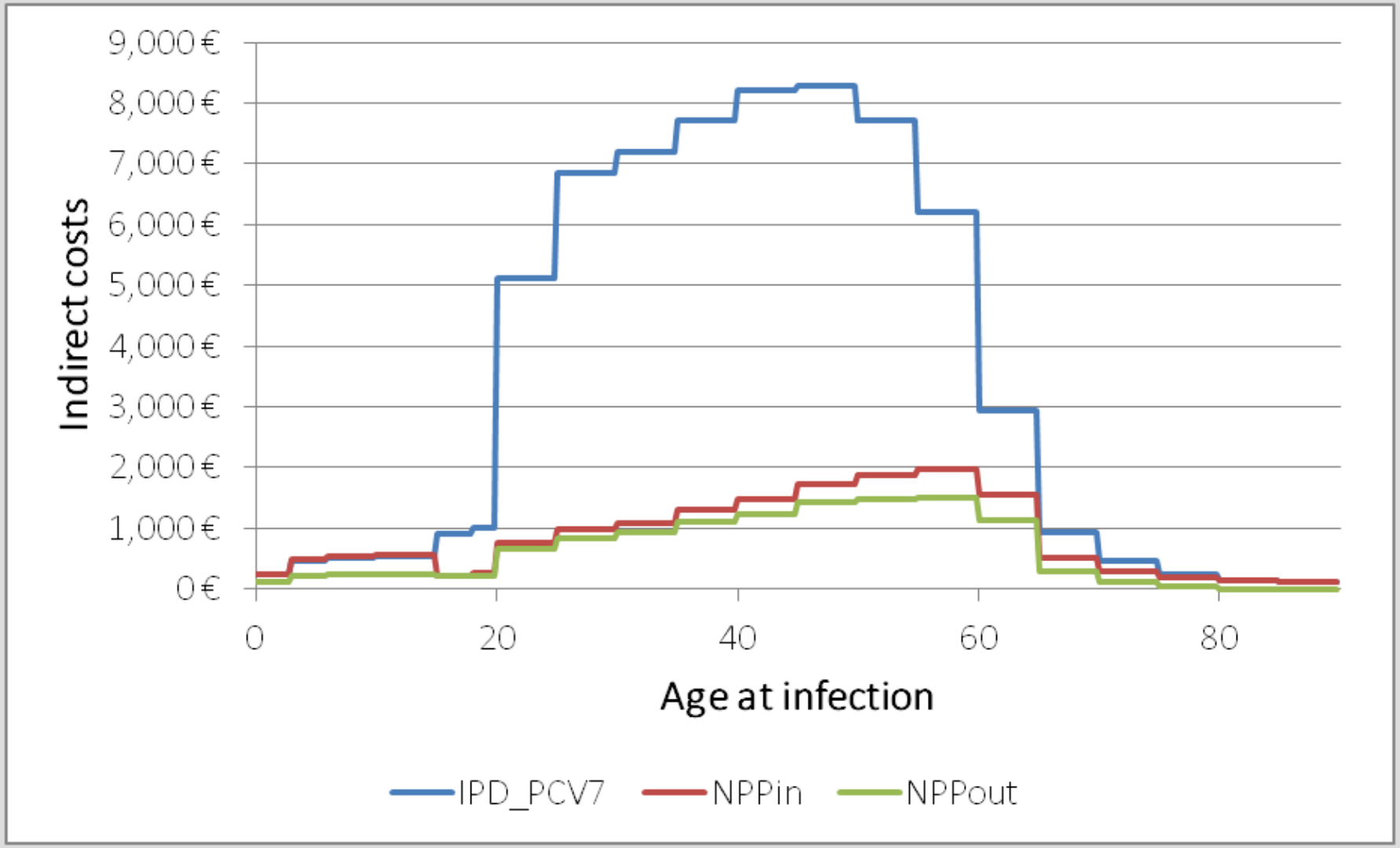
German Federal Statistical Office

Average vacancy time (days)

2012	2013	2014	2015	2016
77.00	78.00	77.00	84.00	93.00

Federal Employment Agency

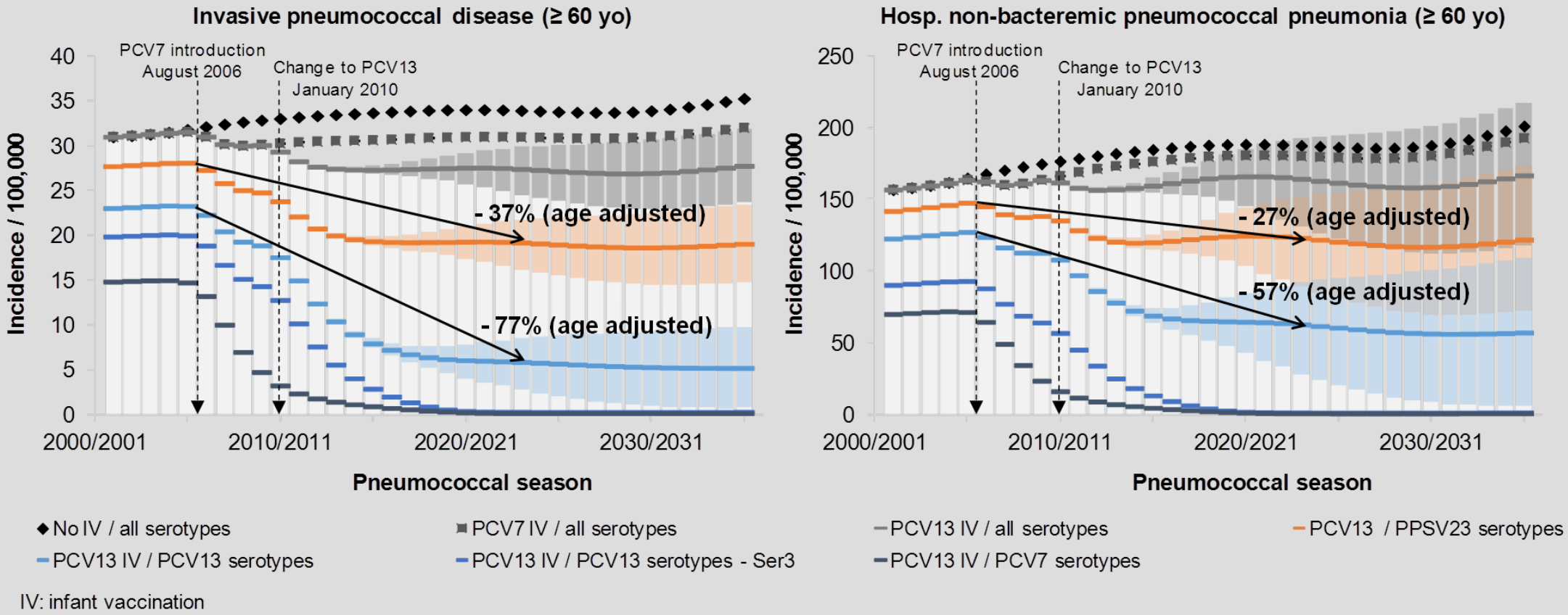
Indirect costs III



Agenda

- → Introduction to health economic evaluation and decision modeling
- → Modeling pneumococcal disease dynamics
- → Decision problem and model concept
- → Data
  - → Epidemiology
  - → Vaccine effects
  - → Health outcomes (QALYs)
  - → Costs
- → **Results**
  - → Base case analysis
  - → Sensitivity analysis

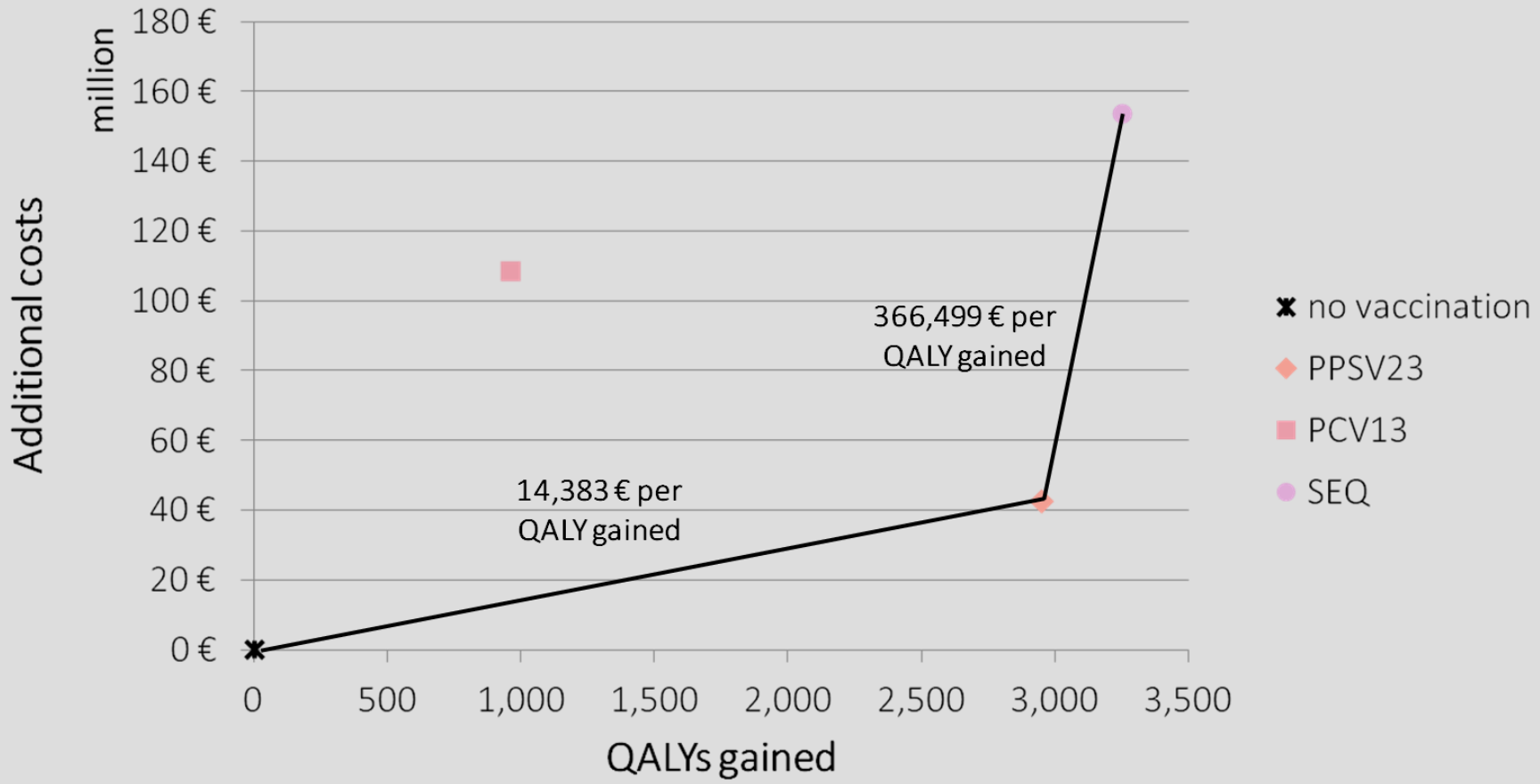
Simulated pneumococcal disease dynamics



IV: infant vaccination

Base case analysis (no revaccination; old results)

- Target population: vaccination of 60 years old
- Vaccination coverage: 30%
- Discount rate: 3%



Probabilistic sensitivity analysis I

→ Model Carlo simulation
- including all relevant parameters

→ Distributions
- Probabilities: beta, dirichlet
- Relative risk: log-normal
- QALY: beta or log-normal
- Costs: gamma or log-normal

Results of the probabilistic sensitivity analysis: visualization

Scatterplot

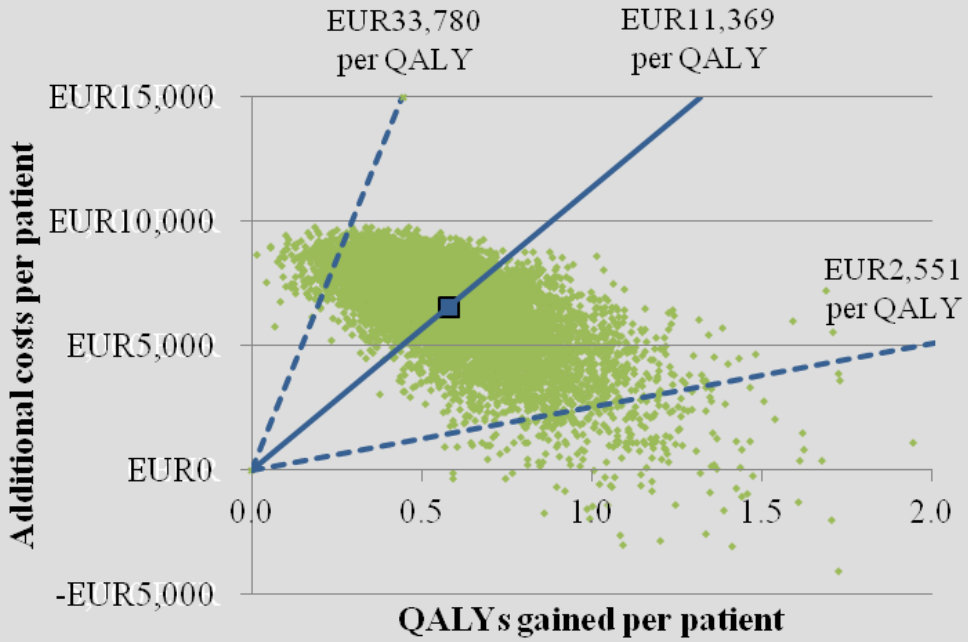


Figure 5a. Scatterplot. The green dots each show the results of one iteration of the Monte Carlo simulation. The larger blue point shows the average QALYs gained as well as the average additional costs of the Kenevo compared to NMPK. The incremental cost-effectiveness ratio (ICER) - additional costs per QALY gained - is shown by the blue lines. The solid lines show the average ICER and the dashed lines the 2,5% and 97,5% quantiles.

Cost-effectiveness acceptability curve

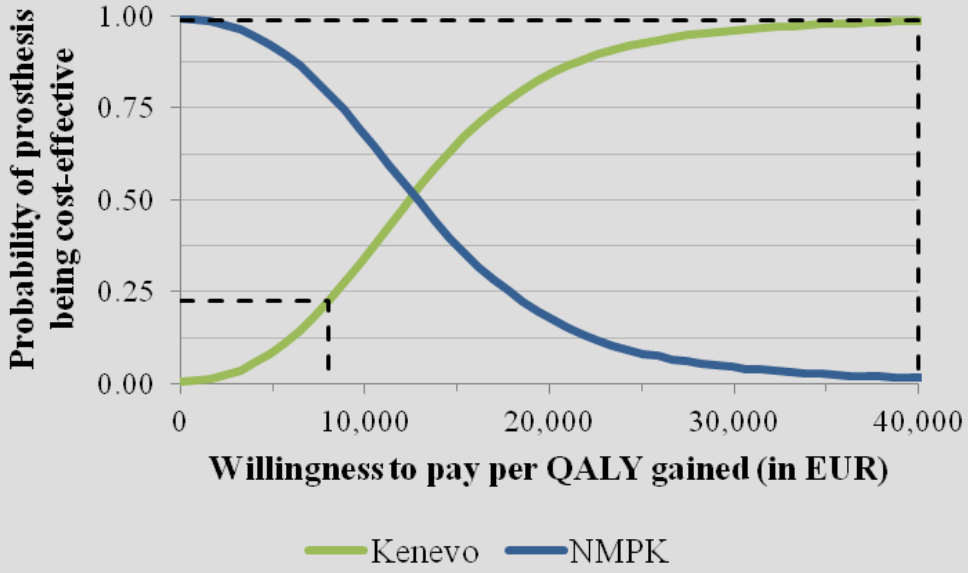
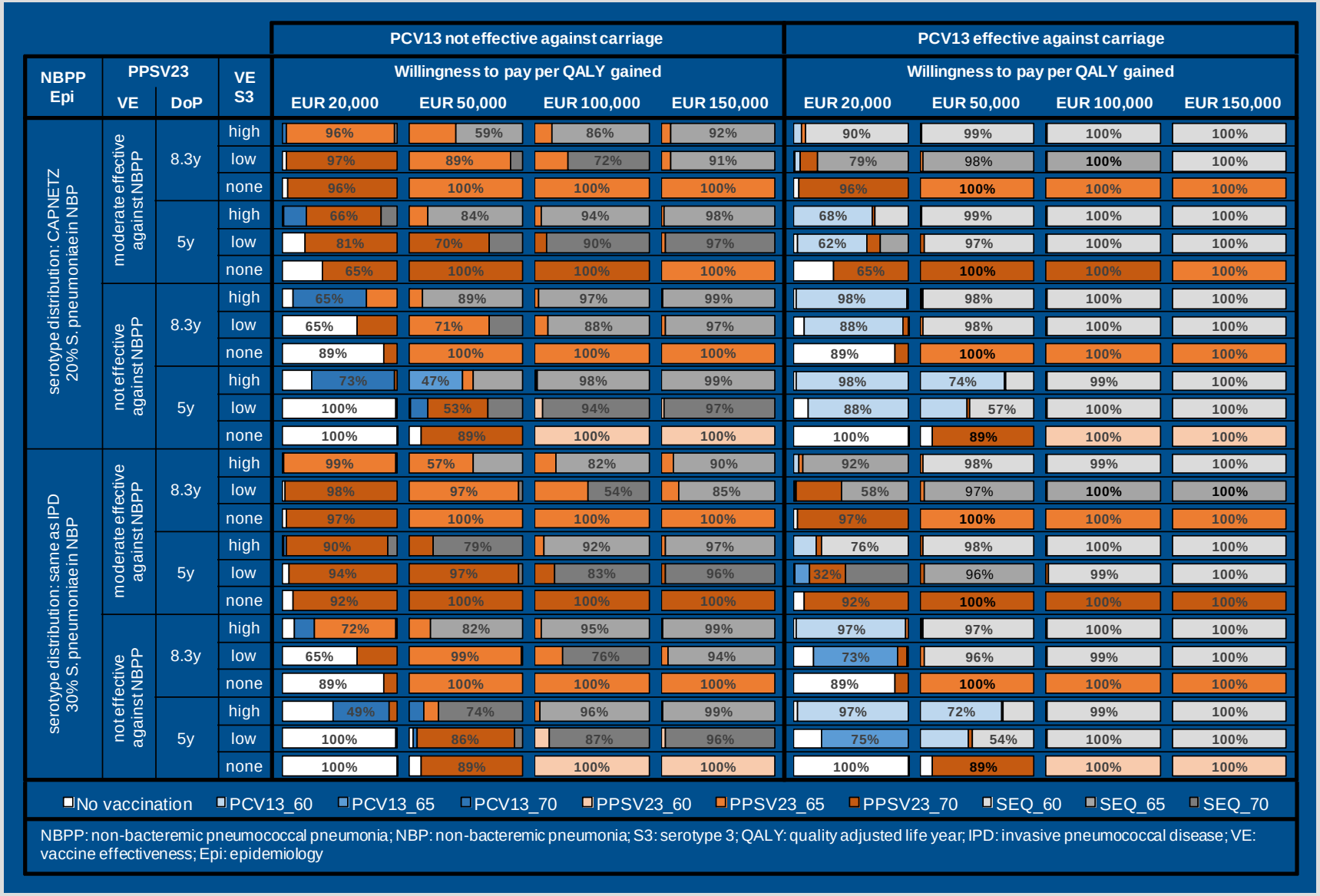


Figure 5b. Cost-effectiveness acceptability curve. The green and blue lines show the cost-effectiveness probabilities of the Kenevo MPK or the NMPK for given willingness to pay thresholds per QALY gained. The black dashed lines mark the cost-effectiveness probabilities of the Kenevo MPK for the Swedish thresholds of EUR8,00 and EUR40,000 per QALY gained. The probabilities are the proportion of Monte Carlo interations with an incremental cost-effectiveness ratio below the given threshold.

Probabilistic sensitivity analysis



NBPP: non-bacteremic pneumococcal pneumonia; NBP: non-bacteremic pneumonia; S3: serotype 3; QALY: quality adjusted life year; IPD: invasive pneumococcal disease; VE: vaccine effectiveness; Epi: epidemiology

Thank you very much

„But, I‘ve learned the value of a Euro,
That‘s why I am asking you for ten,“