Examples of how health burden estimates are used to recommend adult vaccines in NIPs

Example NITAG: Germany

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Methodology of the STIKO

Patient relevant endpoints concerning efficacy & safety

P = Population
I = Intervention
C = Comparison
O = Outcome

Systematic reviews

„GRADE-ing“ the quality of evidence

Grade down
1. Risk of bias
2. Inconsistency
3. Indirectness
4. Imprecision
5. Publication bias

Grade up
1. Large effect
2. Dose response
3. Confounders

Randomization increases initial quality

Risk-benefit analysis

Further aspects:
- Burden of illness
- Population effects
- Cost effectiveness
- Vaccine acceptance
- Integration into the vaccine calendar

Overall quality of evidence of vaccine efficacy & safety

Recommendation
(pro / con)

We recommend using …
We suggest using …
We recommend against …
We suggest against using …

Adaptiert nach GRADE

New vaccine recommendation

- **Key questions:**

- Pathogen characteristics
- Characteristics of the target disease
- Vaccine characteristics (efficacy/effectiveness, safety)
- Vaccination strategy (e.g. number needed to vaccinate; vaccination coverage to reach the vaccination goal; potential population-level effects of the vaccination)
- Implementation of the recommendation (possible obstacles; potential acceptance of the vaccine in the population; other preventive measures; if a valid analysis is available: cost-effectiveness of vaccination)

Prioritization process

- Availability of a vaccine

  Any vaccine licensed for the German market qualifies for discussion by STIKO
  For vaccines with a high degree of public interest, a working group can start the assessment process prior to licensure.

- The disease burden in Germany is quantifiable

  Disease incidence (stratified by age group or disease severity)
  Mortality, number of hospitalizations, risk of long-term sequelae

- Data on vaccine efficacy/effectiveness and safety

  Published studies on vaccine efficacy/effectiveness, preferably peer-reviewed, should be available prior to assessment
  Published data on reactogenicity and adverse events following vaccination

Strengths and Limitations

- **Strengths:**

  Well defined process with clear SOP

  No influence of the pharmaceutical industry

  Cost recovery is mandatory
  (Health insurance has to pay!)

  Yearly update of vaccine recommendations

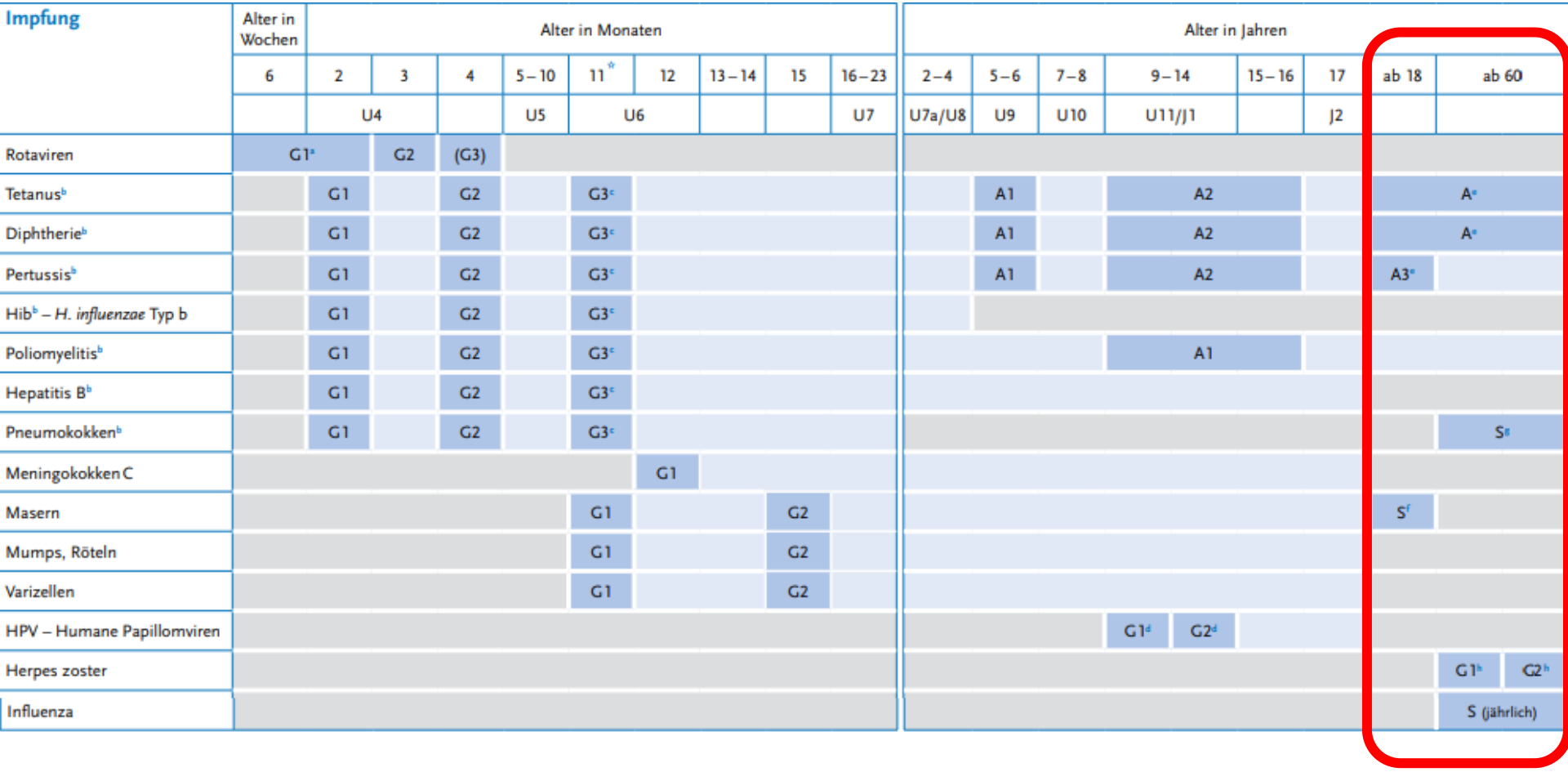
- **Limitations:**

  In COVID times limited personal ressources

  Time consuming process

  Lacking recommendations,
  e.g.: Men B, new PCV vaccines

Standard Immunizations, STIKO 2023



Impfung	Alter in Wochen	Alter in Monaten								Alter in Jahren							
	6	2	3	4	5–10	11*	12	13–14	15	16–23	2–4	5–6	7–8	9–14	15–16	17	ab 18	ab 60
		U4			U5	U6				U7	U7a/U8	U9	U10	U11/J1		J2		
Rotaviren	G1[a]		G2	(G3)														
Tetanus[b]		G1		G2		G3[c]						A1		A2			A[e]	
Diphtherie[b]		G1		G2		G3[c]						A1		A2			A[e]	
Pertussis[b]		G1		G2		G3[c]						A1		A2			A3[e]	
Hib[b] – *H. influenzae* Typ b		G1		G2		G3[c]												
Poliomyelitis[b]		G1		G2		G3[c]								A1				
Hepatitis B[b]		G1		G2		G3[c]												
Pneumokokken[b]		G1		G2		G3[c]												S[g]
Meningokokken C							G1											
Masern						G1			G2								S[f]	
Mumps, Röteln						G1			G2									
Varizellen						G1			G2									
HPV – Humane Papillomviren														G1[d]	G2[d]			
Herpes zoster																		G1[h] G2[h]
Influenza																		S (jährlich)

Published and updated on a yearly basis at the end of January.

Further updates depend on the decision process of the STIKO.

Zoster vaccination, Germany (since Dec. 2018)

S: **Every person > 60 years old**

I: **> 50 years old with underlying comorbidities, e.g.**

- Immuno-deficiency
- HIV-infection
- Rheumatoid arthritis, lupus erythem.
- Inflammatory bowel disease
- COPD, asthma
- chronic renal failure
- Diabetes mellitus

2 shots with an interval from 2-6 months

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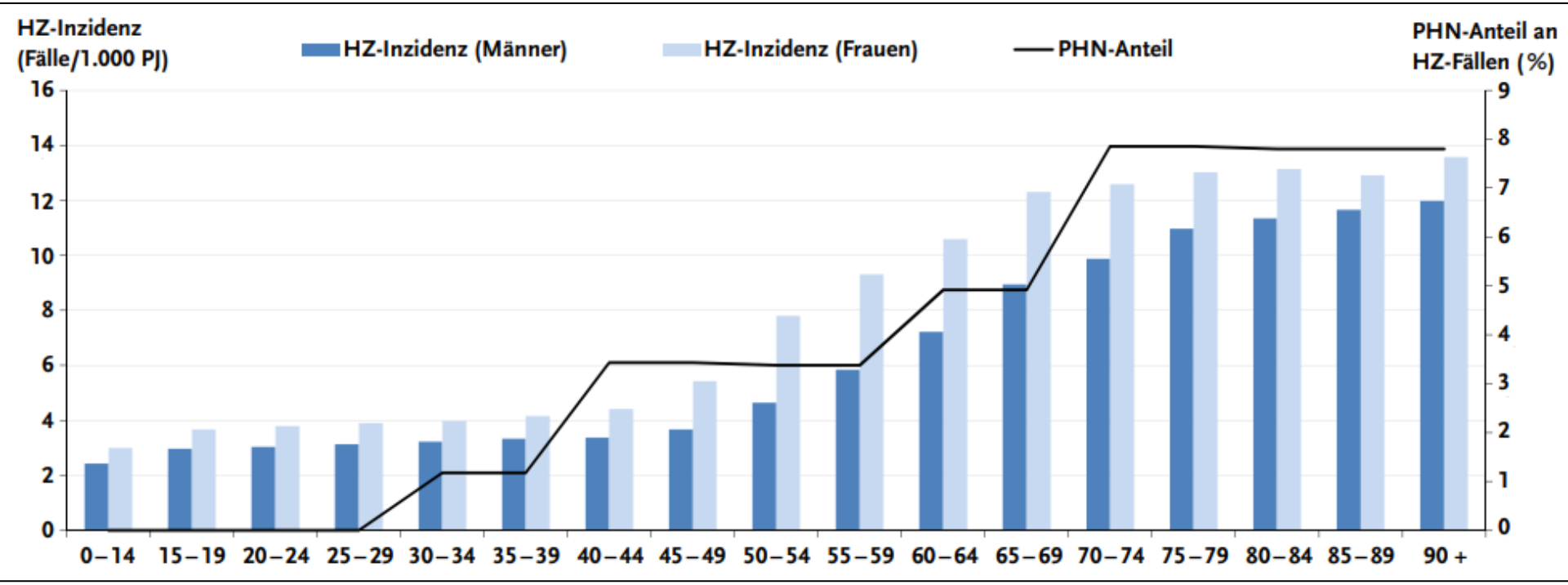
- Immuno-deficiency
- HIV-infection
- Rheumatoid arthritis, lupus erythem. (RR 1,19-4,1)
- Inflammatory bowel disease (RR 1,26-1,5)
- COPD, asthma (RR 1,11-1,7)
- chronic renal failure (RR 1,14-1,6)
- Diabetes mellitus (RR 1,02-1,68)

2 shots with an interval from 2-6 months

Zoster: epidemiology, Germany



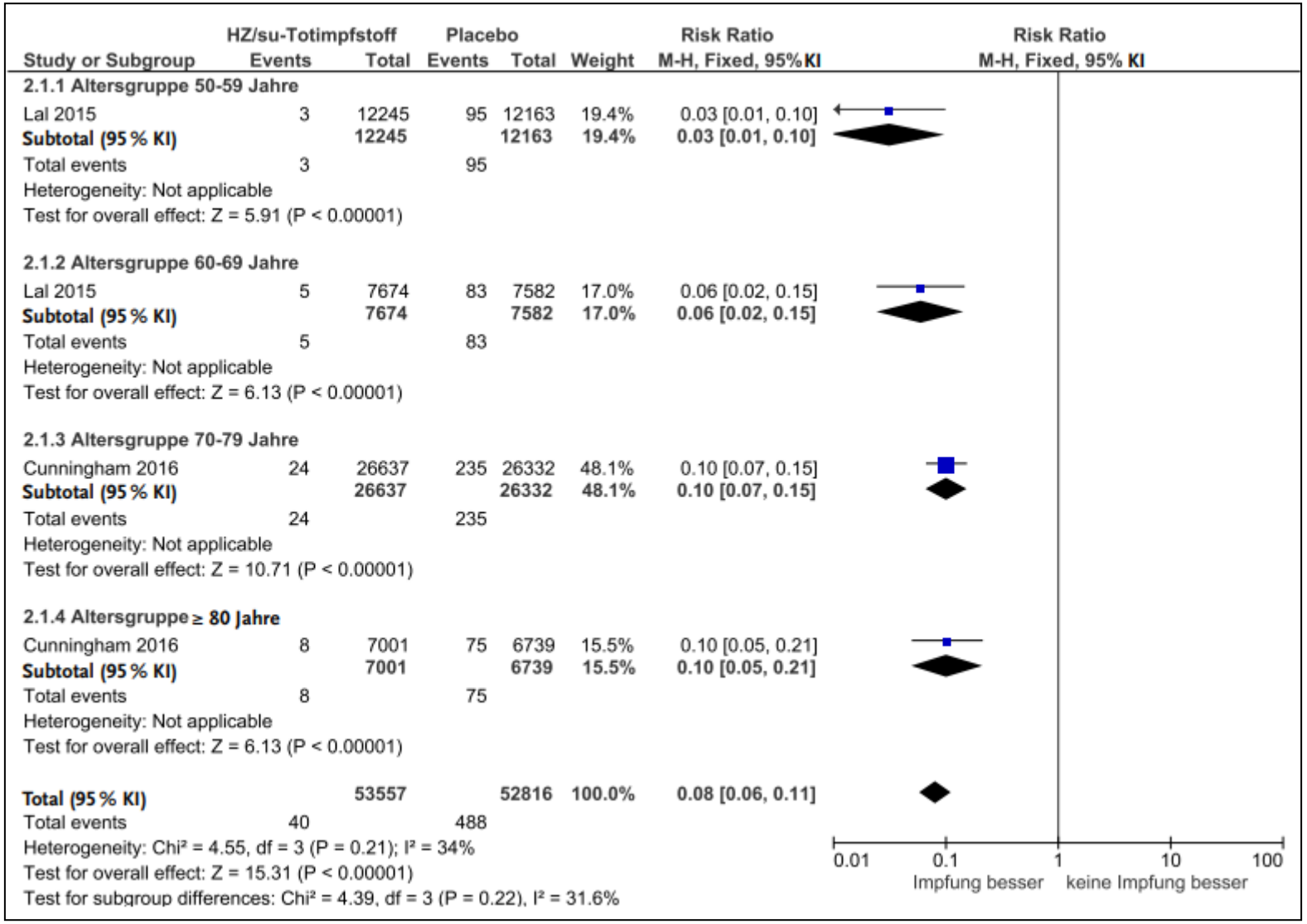
~ 300.000 cases each year (~ 20.000 hospitalized)

Incidence: > 50 years: 6 per 1000 patient-years

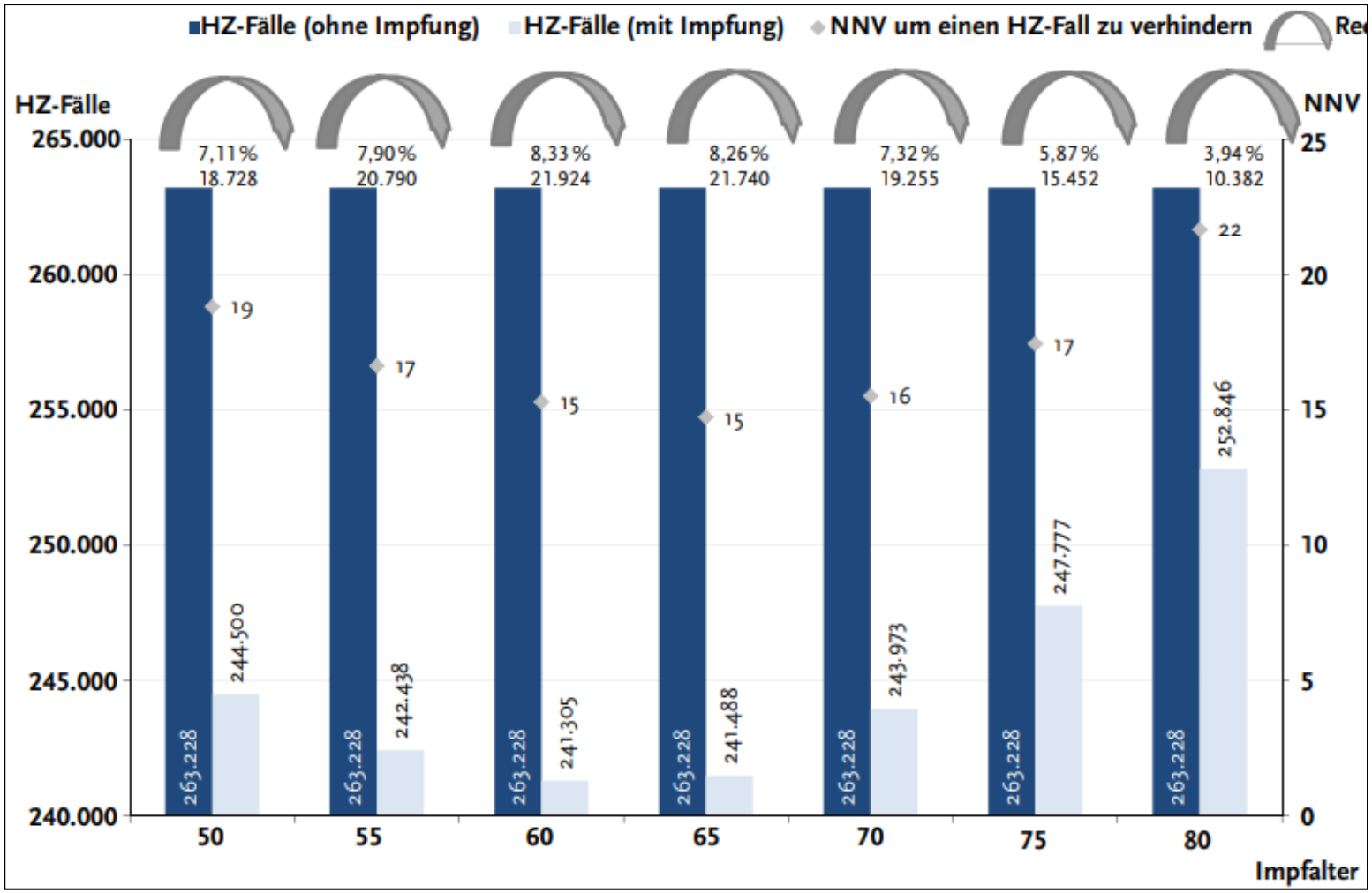
> 70 years: 13 per 1000 patient-years

PHN: 50-54 years 12%, 80-84 years > 20%

Efficacy of the vaccine to prevent Zoster, different age groups

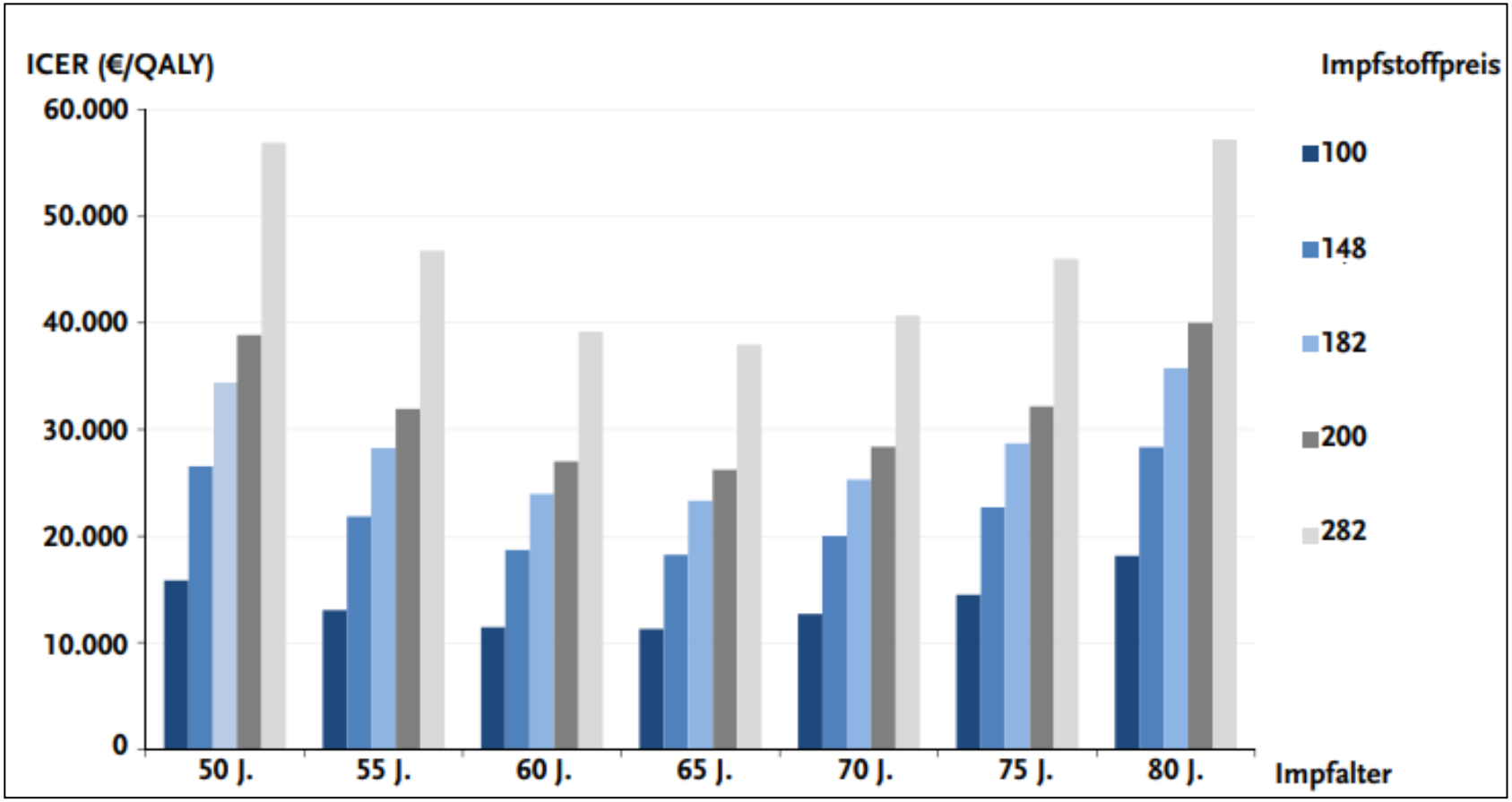


Impact of the vaccine on the epidemiology of Zoster health burden in Germany, modelling



Zoster cases with and without vaccine and NNV by age, Cohort 1.000.000, vaccine uptake 35 %

Cost per gained QUALY and price of the vaccine



Cost per gained QUALY according to price of the vaccine and the age of the vaccine recipient

ICER: Incremental cost-effectiveness ratio

Influenza vaccination, Germany (since Dec. 2018)

S: **Every person > 60 years old, HD 4-valent**

I:
- **Pregnancy, starting in the 2nd trimenon**
- **Underlying comorbidities, e.g.**

Chronic pulmonary diseases

Chronic cardiac, kidney or liver diseases

Chronixc neurological disorders

HIV-infection

Immuno-deficiency

Inactivated 4-valent

Influenza vaccines for the elderly

▸ **adjuvantiert** ▸ Subunit-Vaccine ▸ Ei-basiert ▸ Adjuvants MF-59	▸ **Hochdosis** ▸ Spaltvirus-Vaccine ▸ Ei-basiert	▸ **Zellkultur-basiert** ▸ Subunit-Vaccine ▸ Säugerzellkultivierung ▸ (Ei-basierte Virusseeds bis 2017)	▸ **rekombinant** ▸ Baculovirusvektor ▸ Insektenzellkultivierung
▸ 15 µg HA A(H1N1) ▸ 15 µg HA A(H3N2) ▸ 15 µg HA B(Victoria) ▸ 15 µg HA B(Yamagata) ▸ HA- & NA-Oligomere	▸ 60 µg HA A(H1N1) ▸ 60 µg HA A(H3N2) ▸ 60 µg HA B(Victoria) ▸ 60 µg HA B(Yamagata) ▸ HA- & NA-Oligomere	▸ 15 µg HA A(H1N1) ▸ 15 µg HA A(H3N2) ▸ 15 µg HA B(Victoria) ▸ 15 µg HA B(Yamagata) ▸ HA- & NA-Oligomere	▸ 45 µg HA A(H1N1) ▸ 45 µg HA A(H3N2) ▸ 45 µg HA B(Victoria) ▸ 45 µg HA B(Yamagata) ▸ nur HA-, keine NA-Oligomere
▸ *Fluad Tetra*	▸ *Efluelda/Fluzone HD Quadrivalent*	▸ *Flucelvax Tetra*	▸ *Supemtek/Flublok Quadrivalent*
▸ zugelassen **Ab 65 Jahre**	▸ zugelassen **Ab 65 (60*) Jahre** *erwartete Zulassung für 2021	▸ zugelassen **Ab 9 Jahre**	▸ EU-Zulassung Q4 2020* **Ab 18 Jahre** *erwartete Zulassung in der EU

Effectiveness of the vaccine variable from season to season:

2010/11 – 2019/20 prevention of lab-confirmed medical consultation
H1N1 55%, H3N2 19%, B Yamagata 32%, B Victoria 31%

Immunosenescence and/or comorbidities have an influence

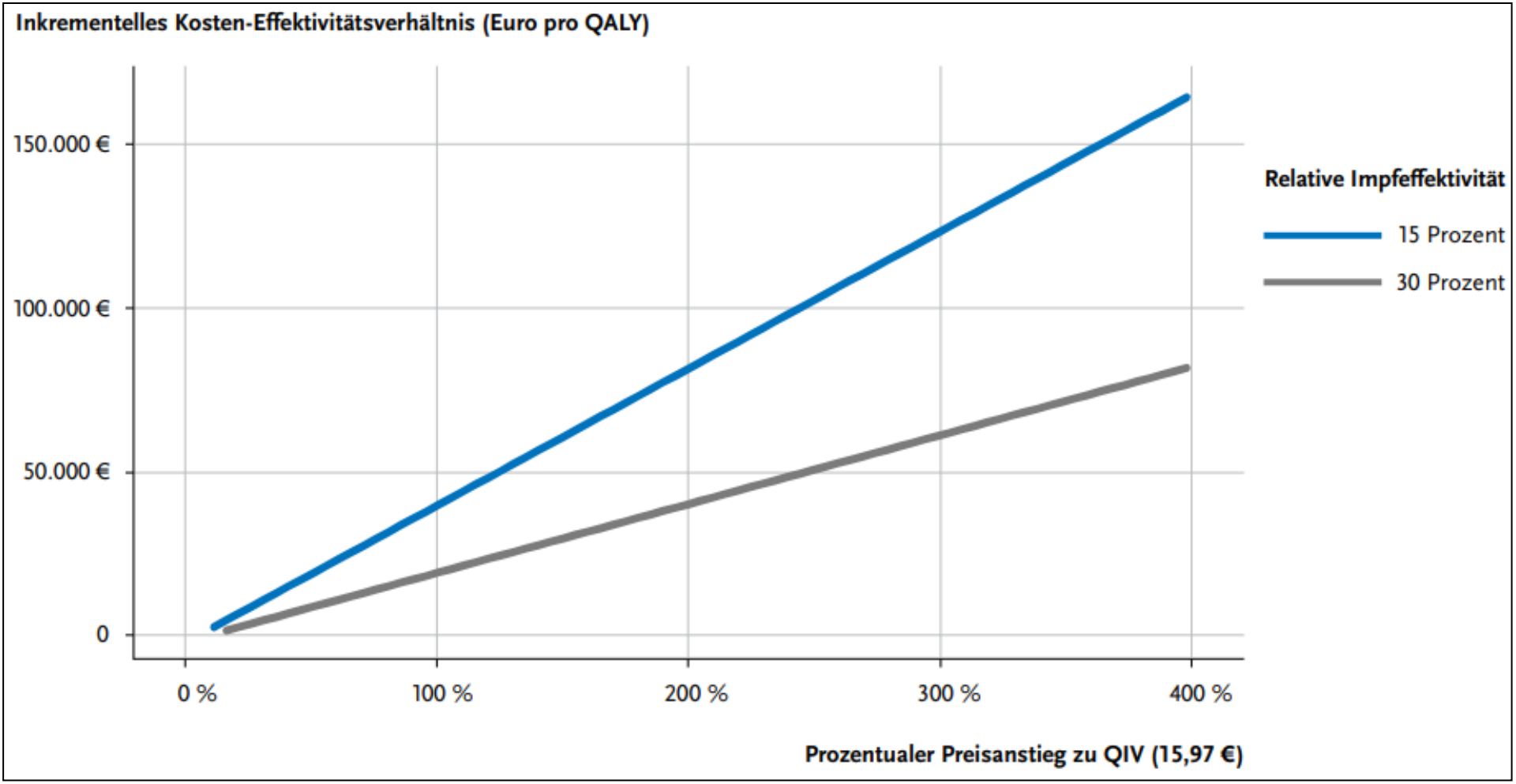
Modelled scenario for influenza disease burden

	Ausgangslage	Modelliertes Szenario mit rVE=15 %		
	durchschnittliche Saison (herkömmliche Impfstoffe)	durchschnittliche Saison	schwache Saison	starke Saison
	Gesamtzahl	Absolute Reduktion		
Infektionen	25.235.159	111.632	12.113	352.951
Sympt. Erkrankungen	16.882.321	74.682	8.104	236.124
Arztkonsultationen	5.150.023	23.013	2.927	54.185
Hospitalisierungen	45.980	314	37	767
Todesfälle	7.002	163	15	564

Modelling the effects of rVE=15%,

Input data for the seasons 2003/04 till 2018/19

Health economics, HD flu vaccine

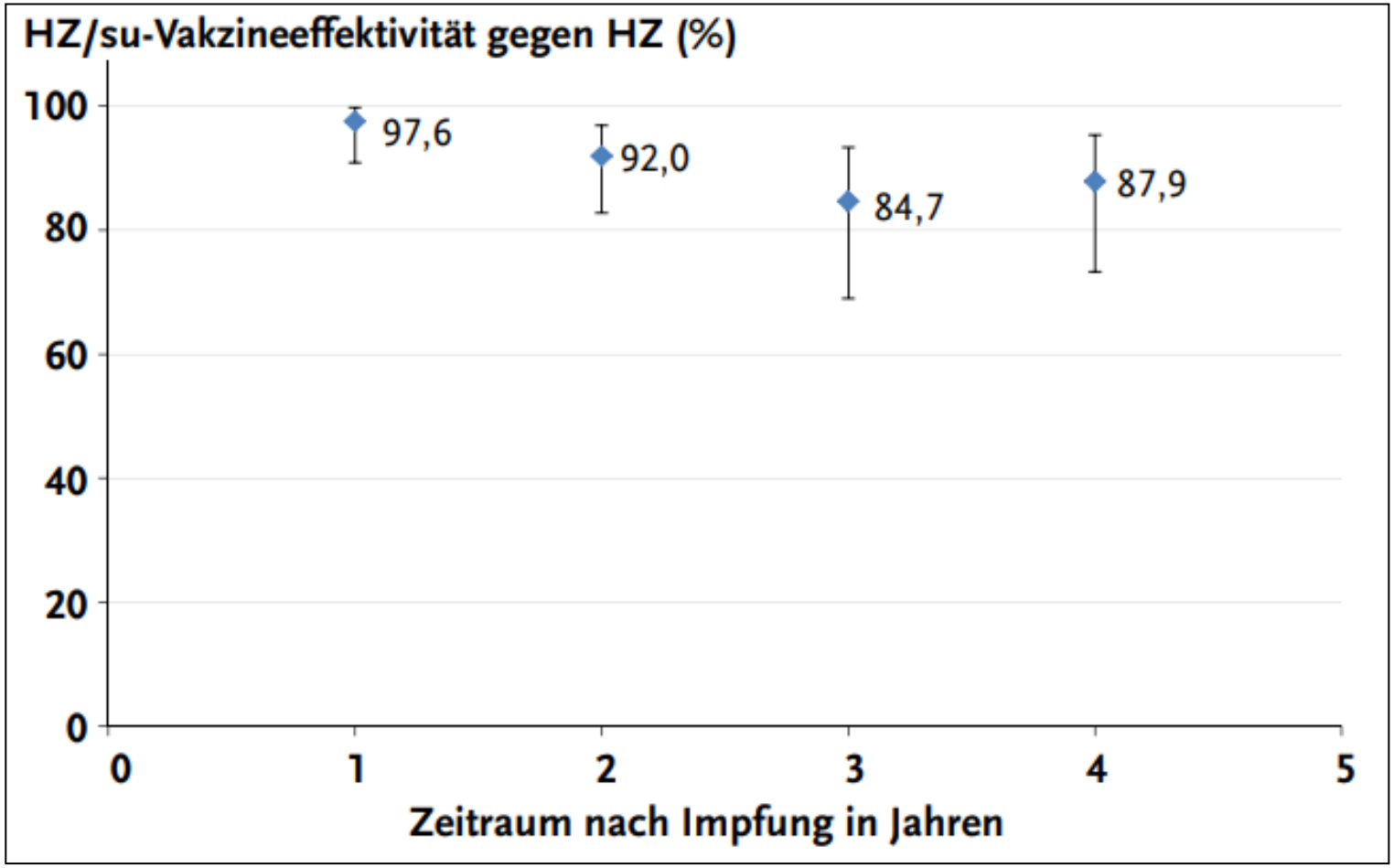


Health economic evaluation for a more effective vaccine (rVE=15% and rVE=30%) on the basis of QUALYs

Thank you!

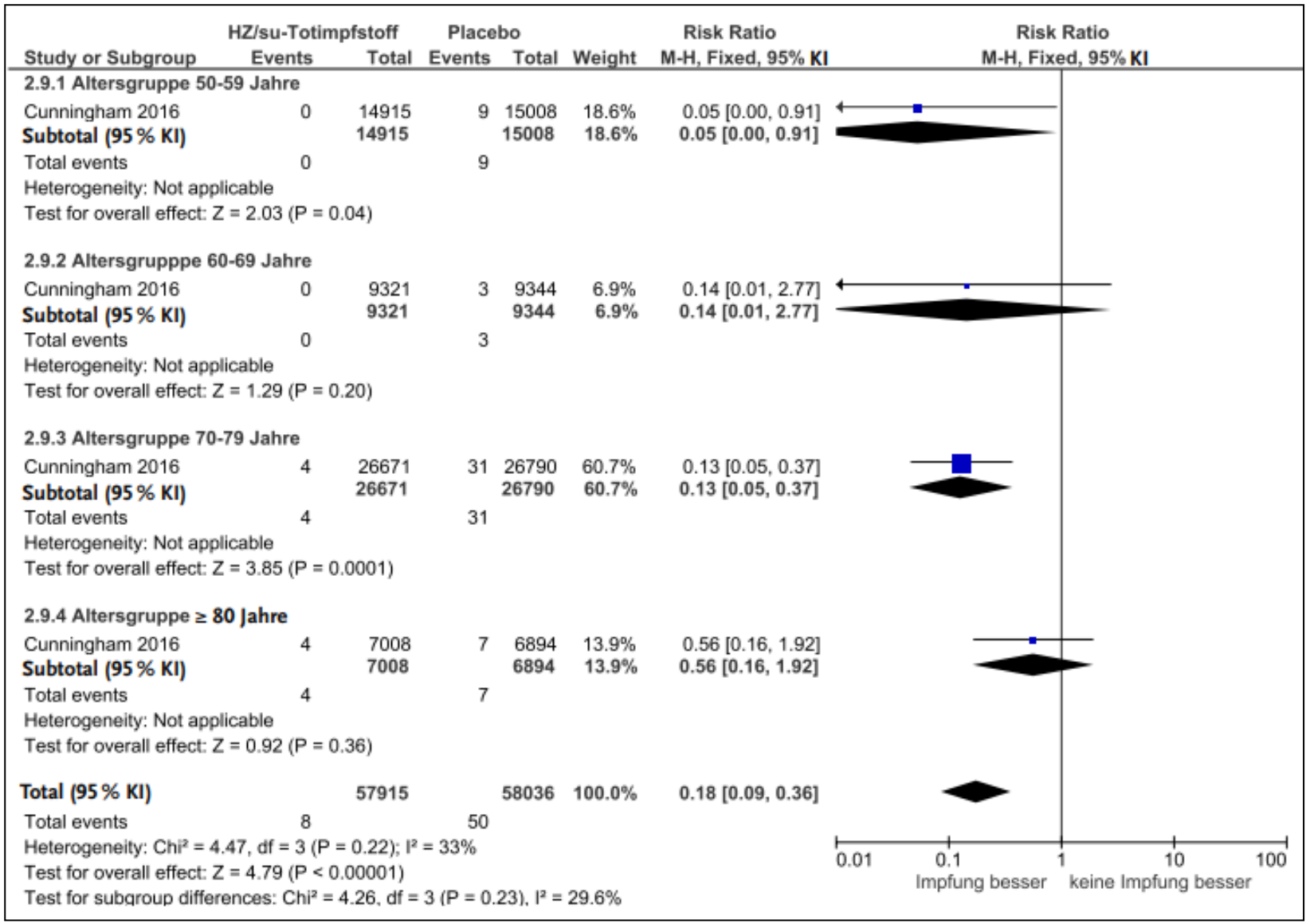
Vielen Dank!

Duration of protection

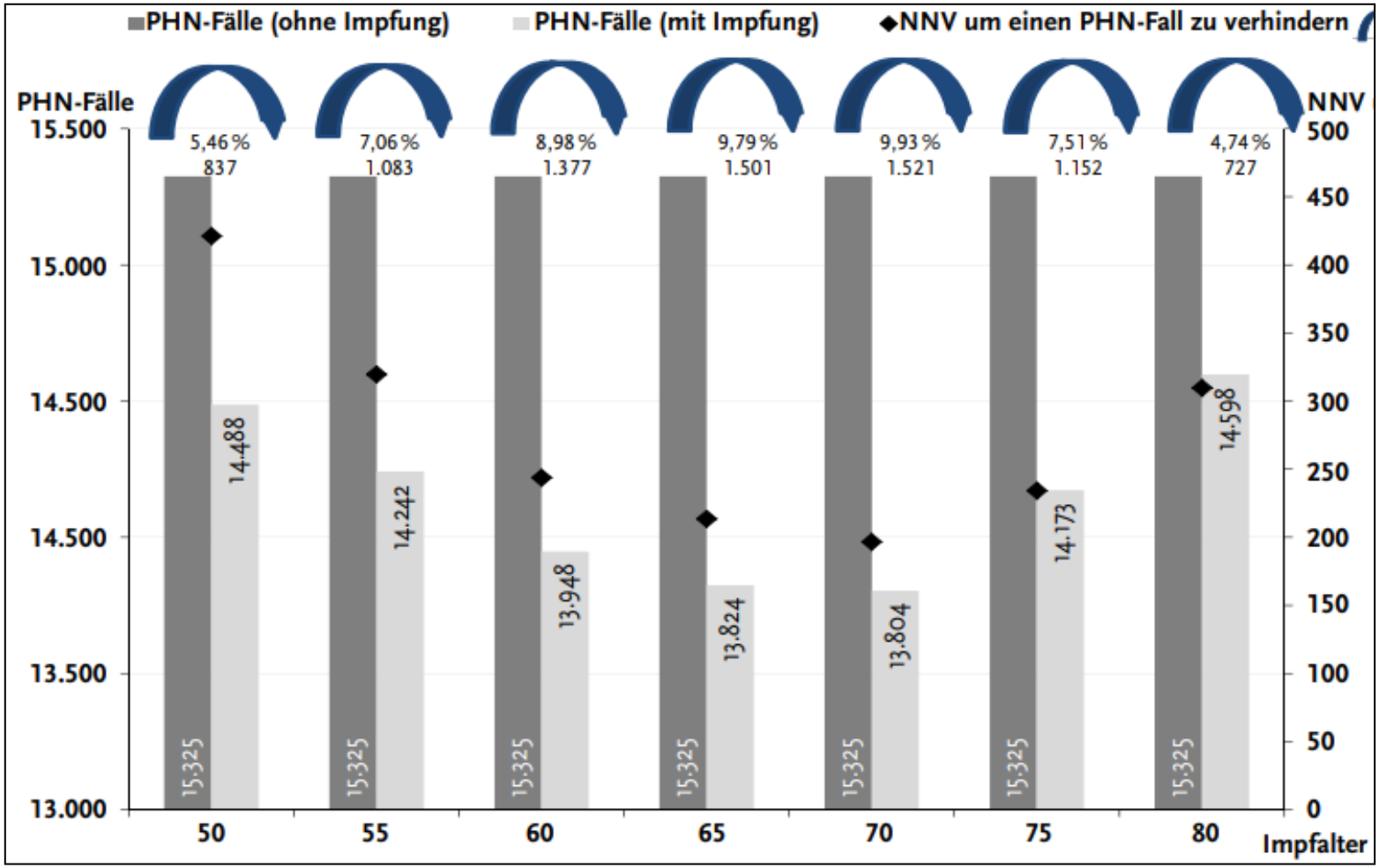


Duration of protection to prevent Zoster, > 70 years

Efficacy of the vaccine to prevent PHN, different age groups



Impact of the vaccine on the epidemiology of PHN health burden in Germany, modelling



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