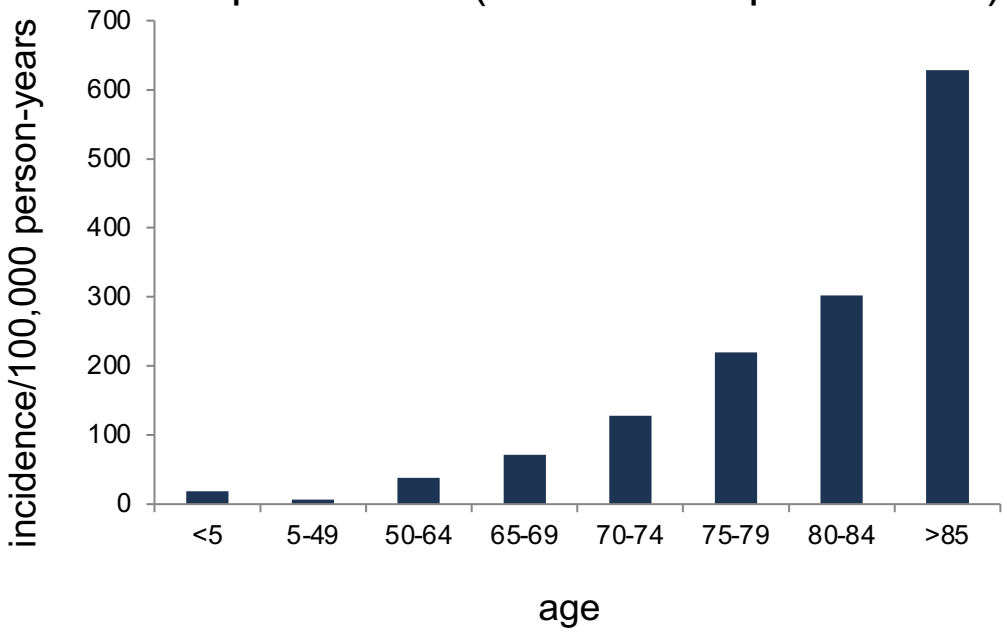
universität innsbruck

Vaccines for older adults: Challenges and Developments

Univ.-Prof. Dr. Birgit Weinberger

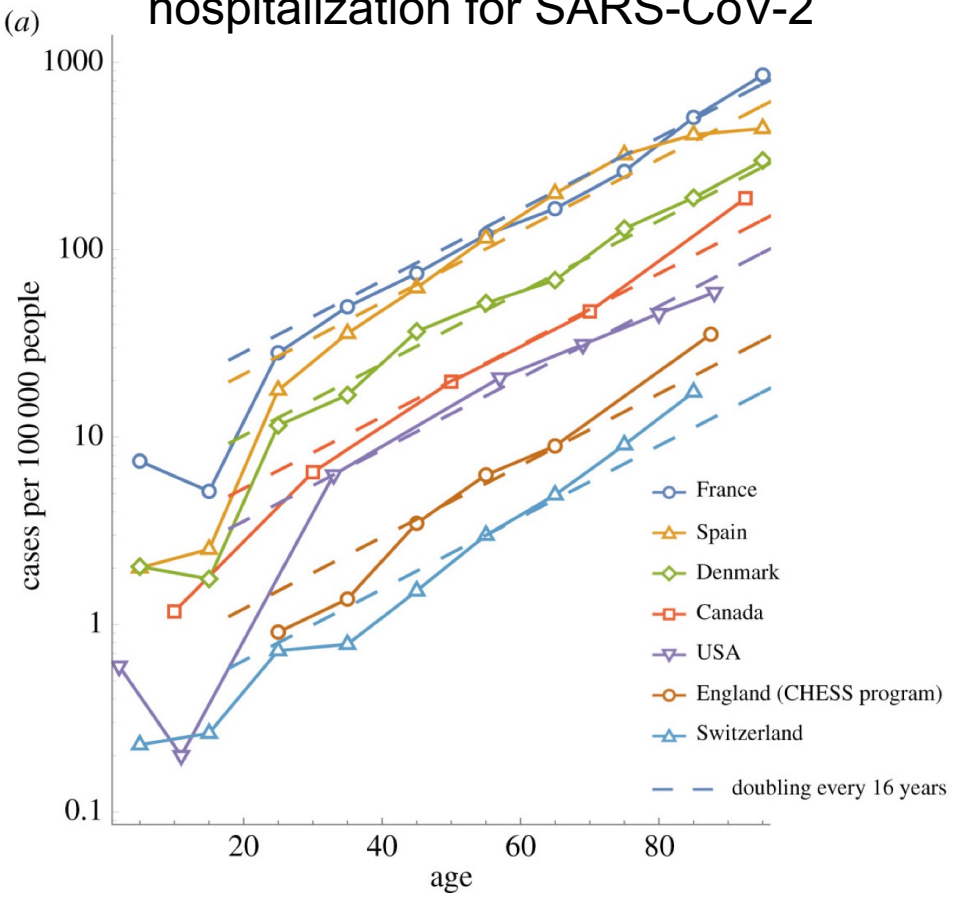
Incidence and severity of infections

hospitalization (influenza or pneumonia)



data from:
Thompson et al., *JAMA,* 2004

hospitalization for SARS-CoV-2

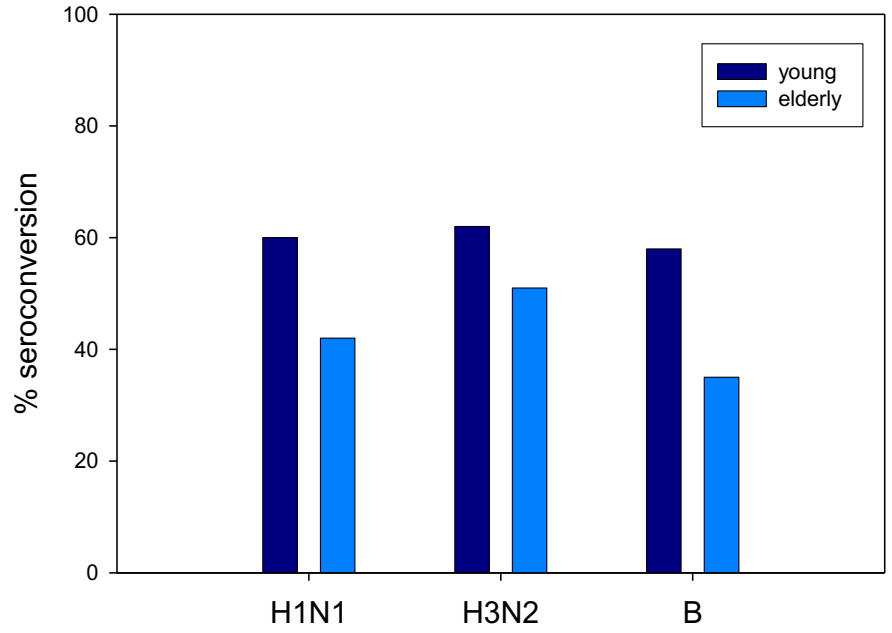


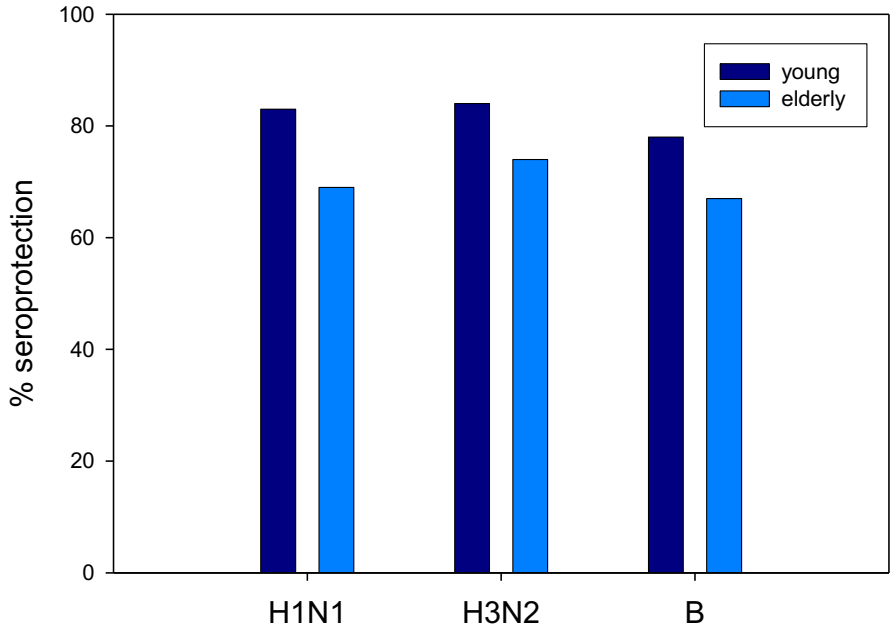
Palmer et al. *J R Soc Interface*, 2021

Influenza

Decreased immunogenicity of influenza vaccines in older adults

meta-analysis of 31 studies (1986-2002)





data from: Goodwin et al., *Vaccine*, 2006

Vaccine recommendations for influenza

	2018/2019	2019/2020	2020/2021	2021/2022	2022/2023
A/H1N1	Michigan/45/2015	Brisbane/02/2018	Guangdong-Maonan/SWL1536/2019	A/Victoria/2570/2019	A/Victoria/2570/2019
A/H3N2	Singapore/INFIMH-16-0019/2016	Kansas/14/2017	Hong Kong/2671/2019	Cambodia/e0826360/2020	A/Darwin/9/2021
B	Colorado/06/2017	Colorado/06/2017	B/Washington/02/2019	B/Washington/02/2019	B/Austria/1359417/2021
B	Phuket/3073/2013	Phuket/3073/2013	Phuket/3073/2013	Phuket/3073/2013	Phuket/3073/2013

quadrivalent vaccines available:

- standard
- high-dose
- adjuvanted

→ many countries recommend the use of high-dose and/or adjuvanted vaccine for older adults

Increased antigen dose

60µg HA per strain instead of 15µg
registered in the US since 2010/2011

→ higher antibody titers, higher seroconversion rate

→ increased clinical efficacy

randomized clinical trial: Fluzone High-Dose vs Fluzone

Variable	Laboratory-Confirmed Influenza†		
	IIV3-HD (N=15,990)	IIV3-SD (N=15,993)	Relative Efficacy (95% CI)
	no. (%)		%
Protocol-defined influenza-like illness	228 (1.4)	301 (1.9)	24.2 (9.7 to 36.5)‡

→ now available as quadrivalent vaccine
recently approved in the US and Europe

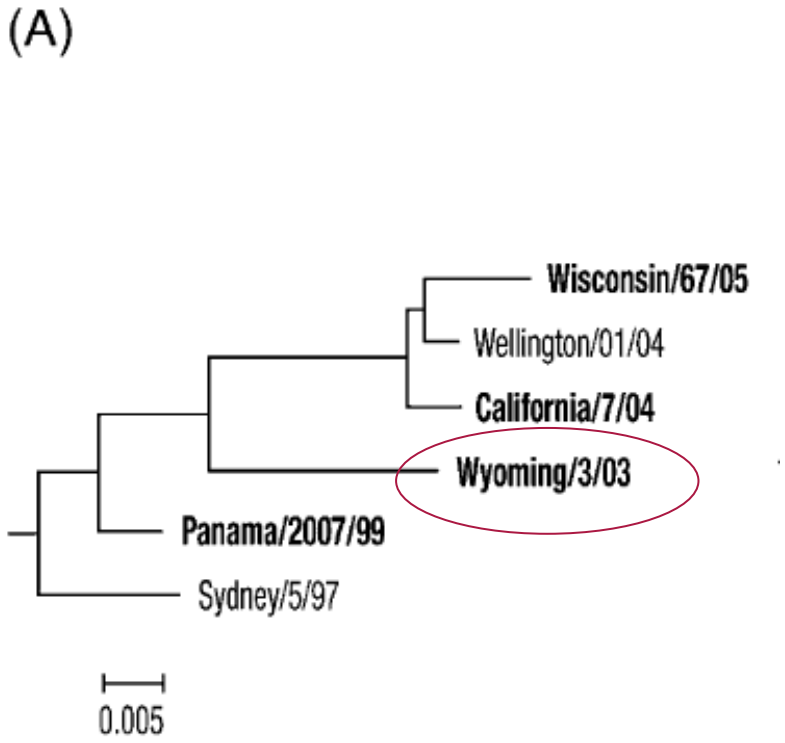
→ immunogenicity identical to trivalent formulation

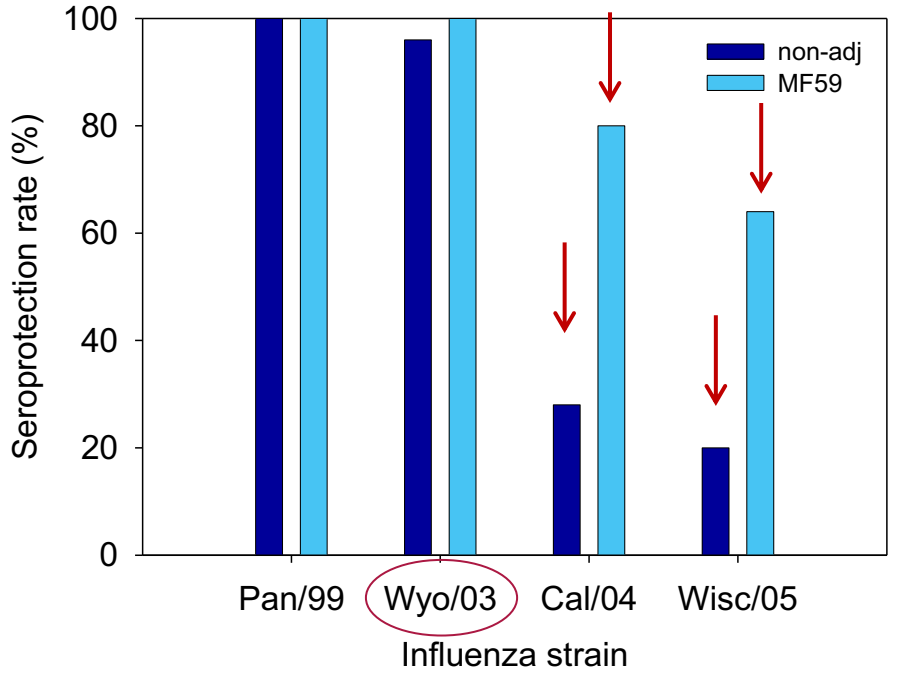
DiazGranados et al., *NEJM, 2014*
Chang et al., *Vaccine, 2019*

Adjuvanted vaccine

MF59: oil-in-water emulsion, squalene-based

→ licensed in Europe for older adults since 1997 (trivalent)





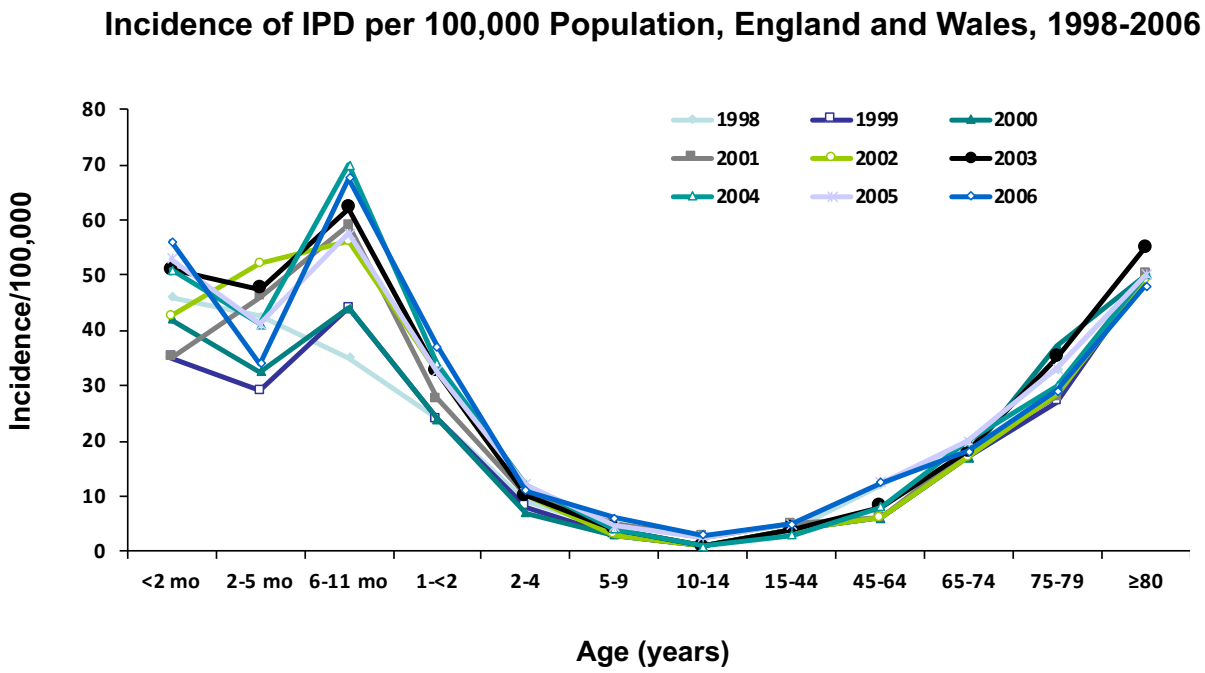
antibodies against heterologous virus strains

data from Ansaldi et al., *Vaccine*, 2008

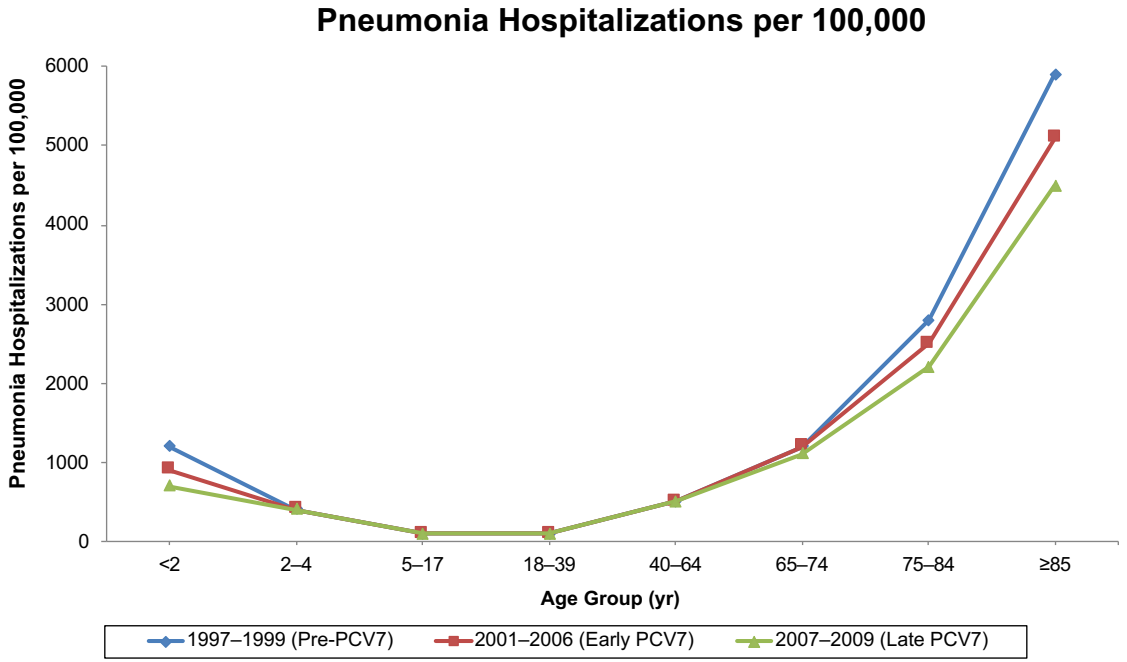
Streptococcus pneumoniae

Pneumococcal disease

Invasive pneumococcal disease (IPD)



Pneumococcal pneumonia



Vaccines need to prevent IPD at the extremes of age and pneumonia in the elderly

Adapted from: Kaye P et al.
Poster presented at: ESPID Brussels, June 2009.

Griffin MR et al. *NEJM* 2013;396:155-163

Vaccination against *S. pneumoniae*

Streptococcus pneumoniae

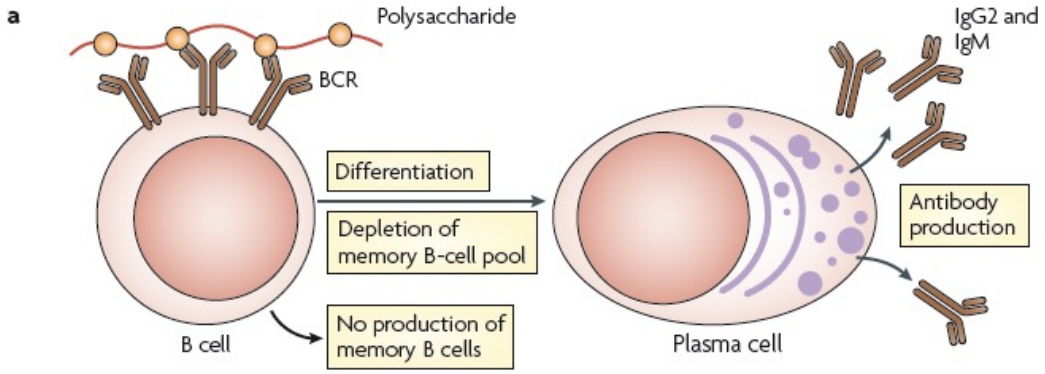
more than 90 serotypes, based on polysaccharide capsule

polysaccharide vaccine

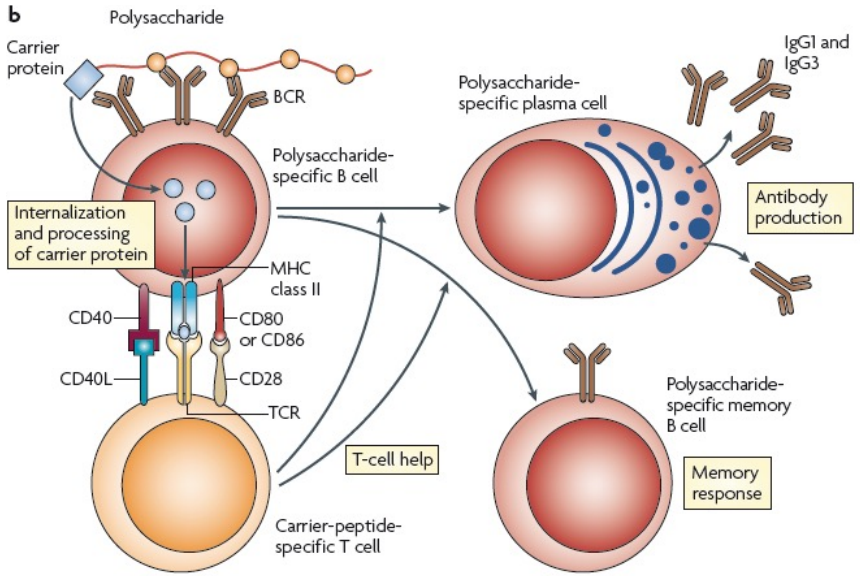
23-valent
T-cell independent antigen
mainly IgM response
not immunogenic in infants

conjugate vaccine

13/15/20-valent after 7-and 10-valent vaccines for children
T-cell dependent antigen
antibody switch
suitable for infants



Pollard et al., *Nat Rev Immunol*, 2009



Vaccination against *S. pneumoniae*

Serotyp	1	2	3	4	5	6A	6B	7F	8	9N	9V	10A	11A	12F	14	15B	17F	18C	19A	19F	20	22F	23F	33F
PPV-23																								
PCV-7																								
PCV-10																								
PCV-13																								
PCV-15																								
PCV-20																								

Polysaccharide vaccine
PPV-23 (Pneumovax, MSD)

Conjugate vaccines
PCV-13 (Prevenar, Pfizer)
PCV-15 (Vaxneuvance, MSD)
PCV-20 (Apexxnar, Pfizer)

Heterogenous vaccination recommendations in Europe:

- only PPV-23
- only PCV-13
- PCV-13 followed by PPV-23
- usually only once, some countries recommend repetition after 5-6 years for patients at risk

Vaccination against *S. pneumoniae*

Efficacy Endpoint	Vaccine Group		VE (%)	95.2% CI	p-value
	PCV-13 (n=42,240)	Placebo (n=42,256)			
Vaccine-type pneumonia	**49**	**90**	**45.56**	**(21.82,62.49)**	**0.0006**
Vaccine-type invasive disease	**7**	**28**	**75.00**	**(41.43, 90.78)**	**0.0005**

Bonten MJ et al. *NEJM* 2015

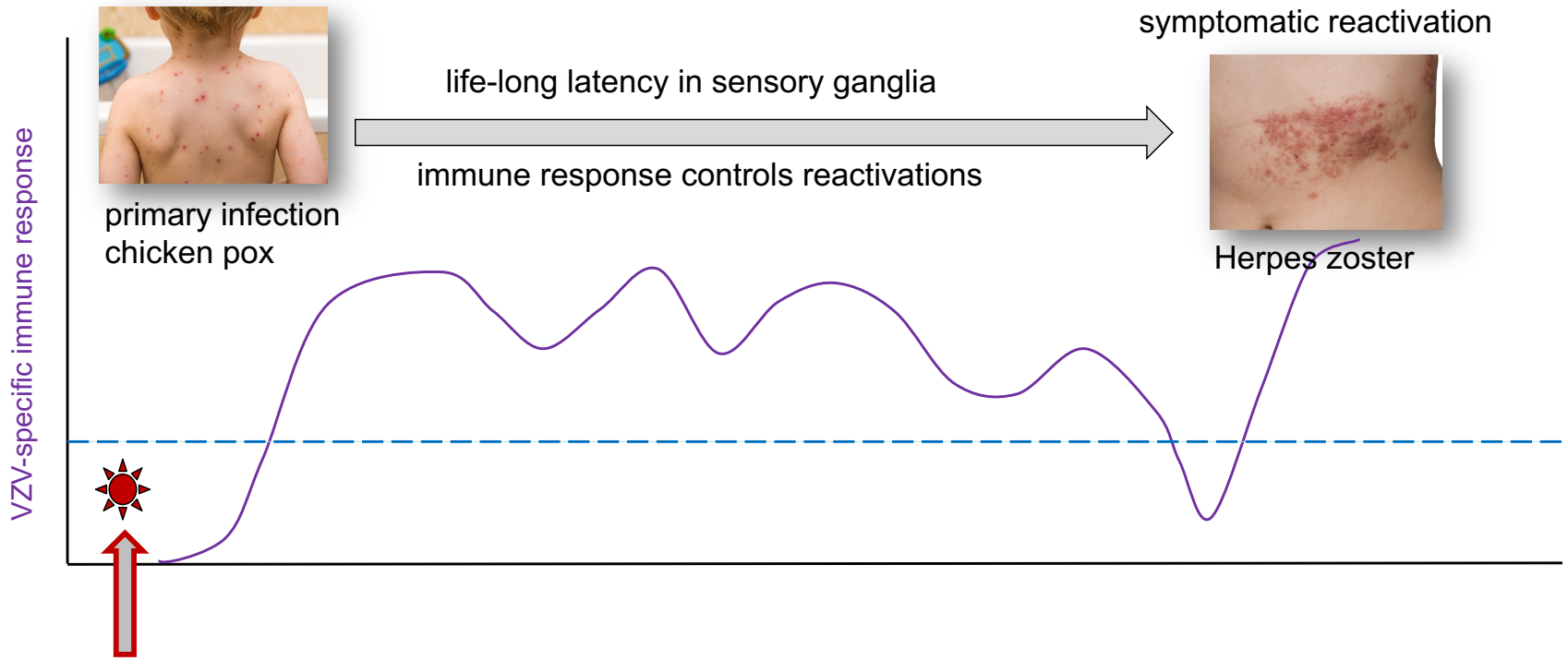
Herpes zoster

Herpes zoster

Varizella-Zoster virus

Herpesvirus
primary infection: chickenpox
latency in sensory ganglia
reactivation: herpes zoster (shingles)

Herpes zoster
1.7 Mio cases per year in Europe
post-herpetic neuralgia (PHN)
long-lasting pain, inefficient therapy
significant limitations in daily-life activities



Photos: Shutterstock
Figure freely adapted from Hope-Simpson, 1965

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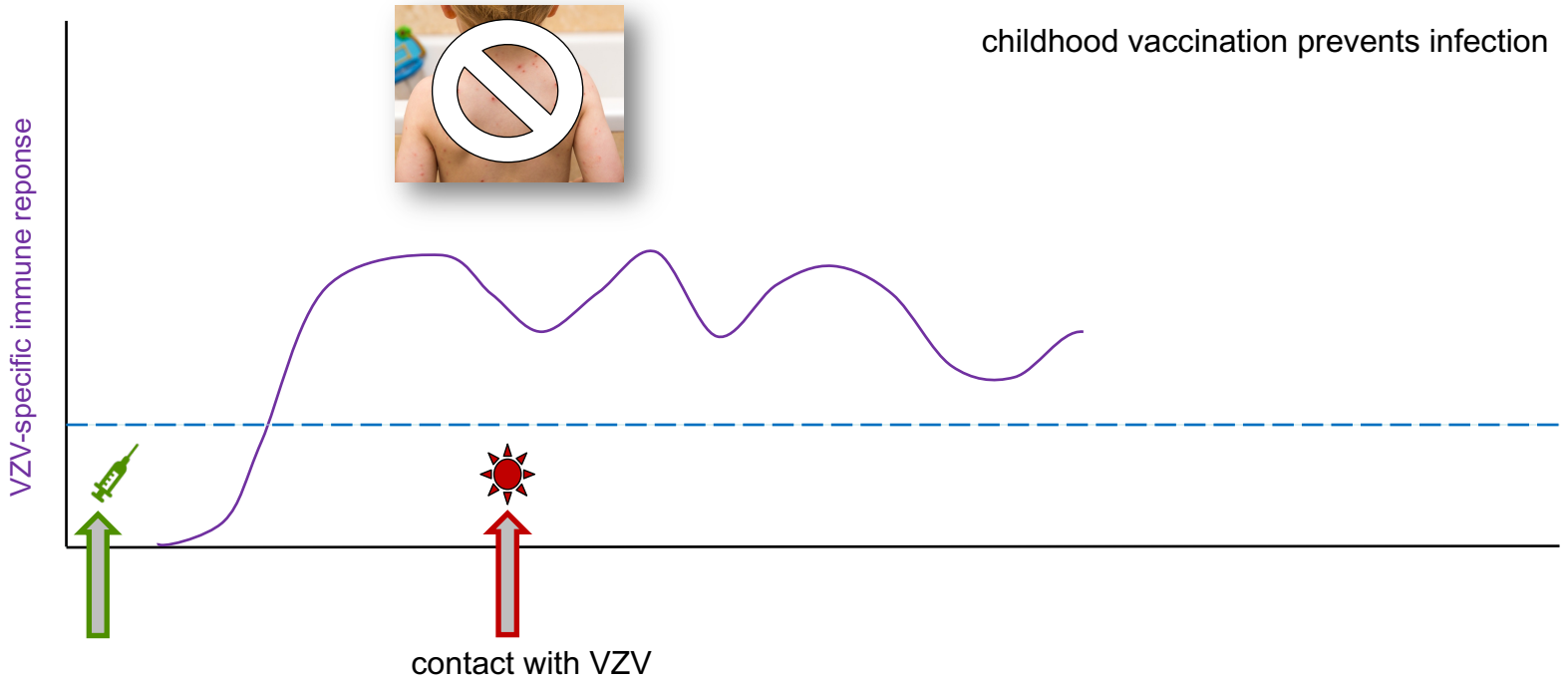
Vaccine
childhood vaccine prevents chickenpox



Photos: Shutterstock
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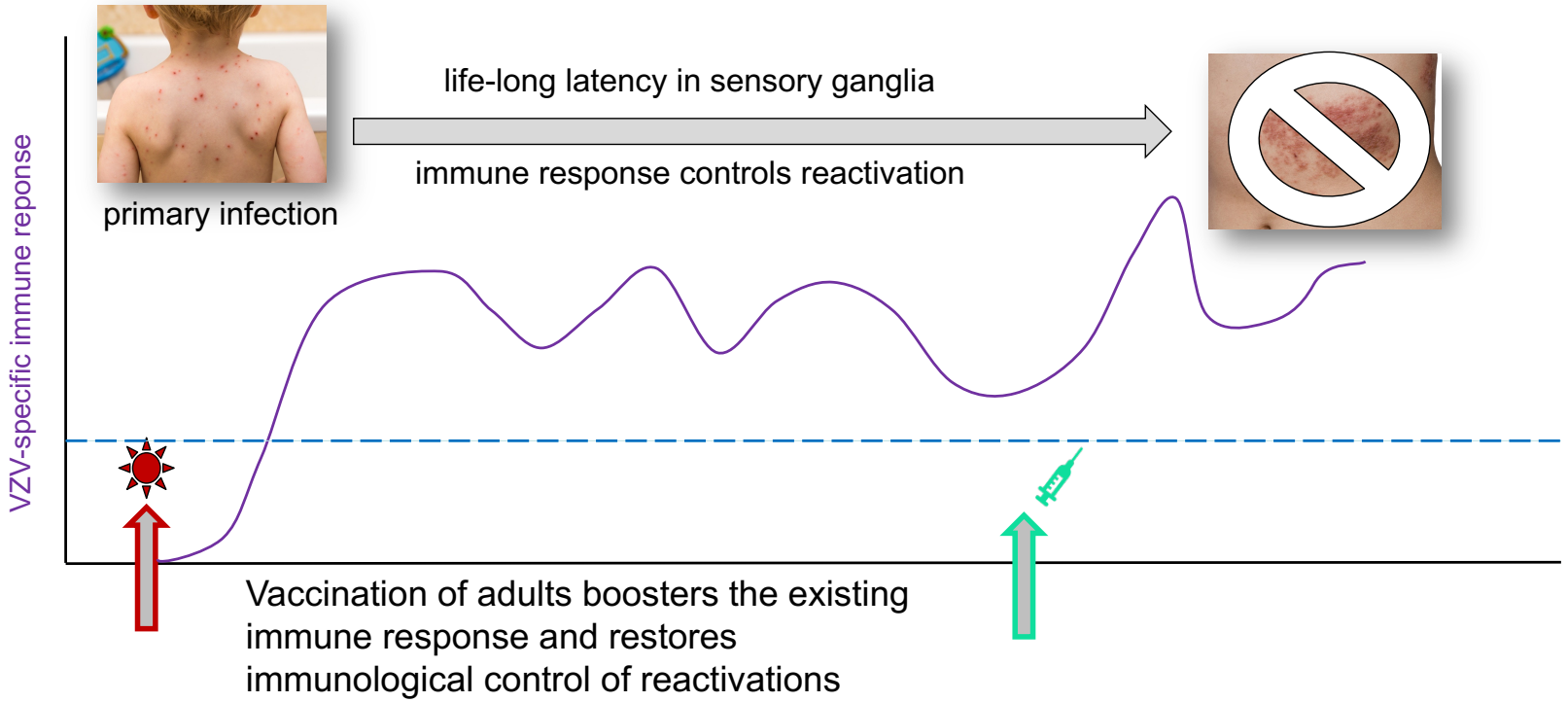
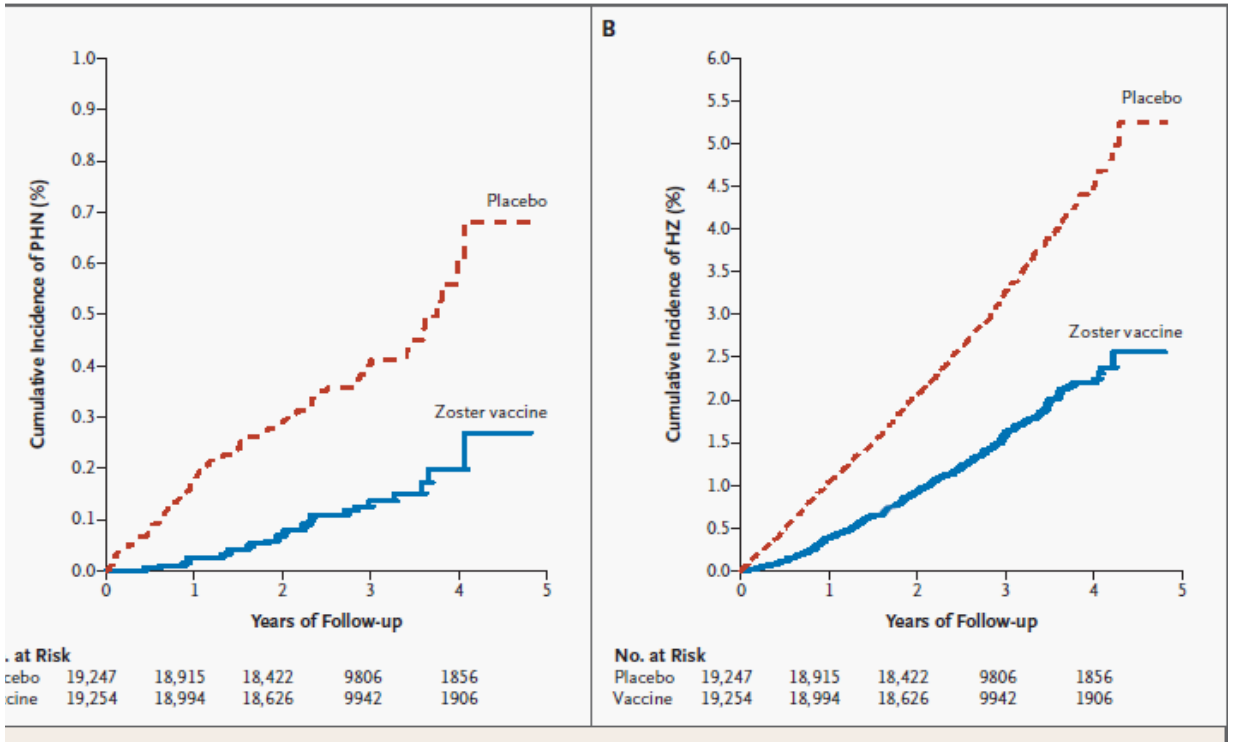
Vaccine
childhood vaccine prevents chickenpox
vaccination of adults boosters the existing immune response and restores immunological control of reactivations



Photos: Shutterstock
Figure freely adapted from Hope-Simpson, 1965

Vaccination against herpes zoster

Live-attenuated vaccine; single dose



Efficacy for HZ

60-69 years	**63.9%**
>70 years	**37.6%**
year 1	**62.0%**
year 5	**43.1%**
year 10	**14.1%**

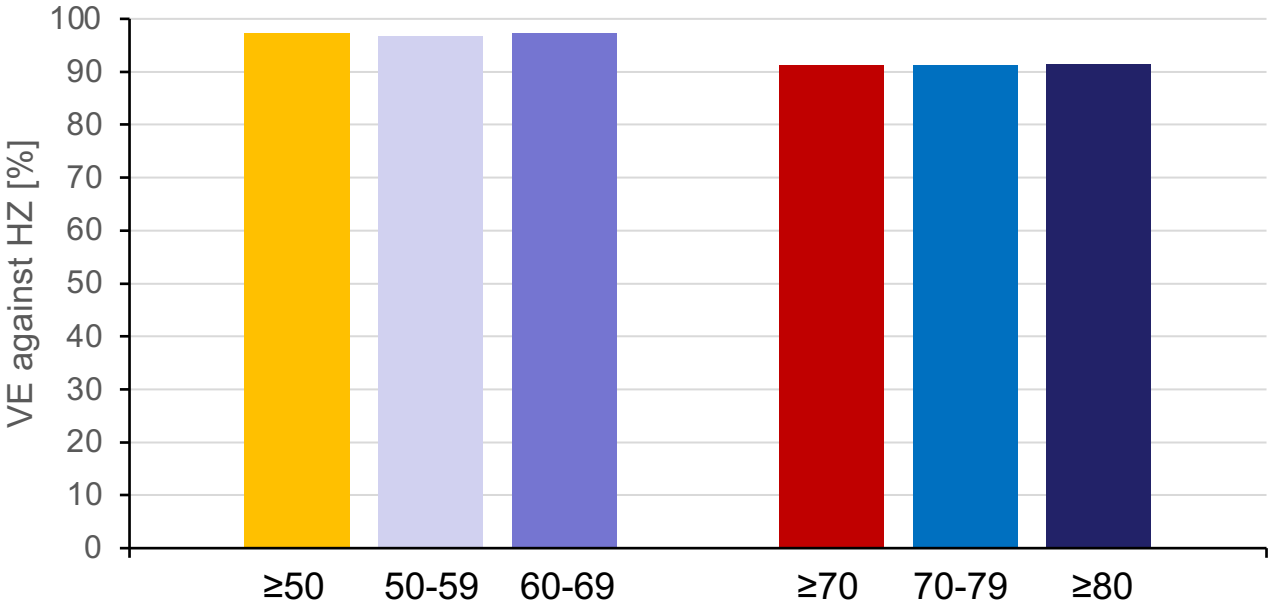
Overall efficacy for herpes zoster	**51.3%**
Overall efficacy for PHN	**66.5%**

Oxman, *NEJM*, 2005
Morrison, *Clin Inf Dis*, 2015
Levine, *J Inf Dis*, 2016
Weinberg, *J Inf Dis*, 2018

Vaccination against herpes zoster

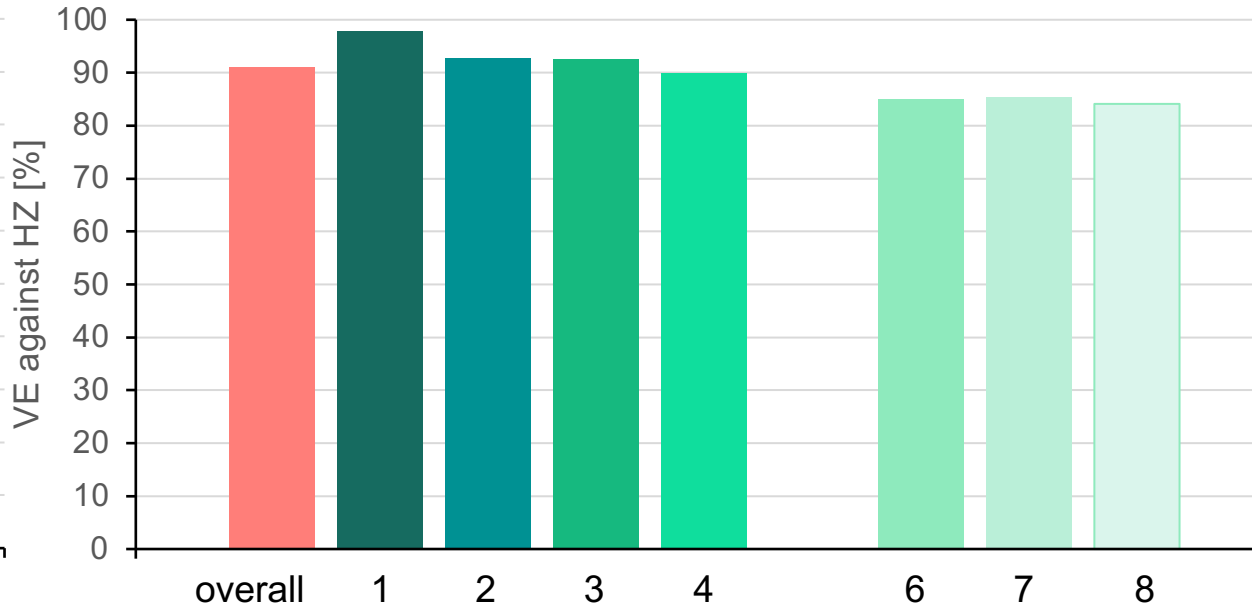
50µg recombinant glycoprotein E plus adjvuvant AS01$_\beta$ (MPL, QS21, liposomes)
2 doses, 8 weeks apart

Efficacy against Herpes zoster
(Phase III studies, 3-4 years follow-up)



very high efficacy
→ even in the oldest age groups

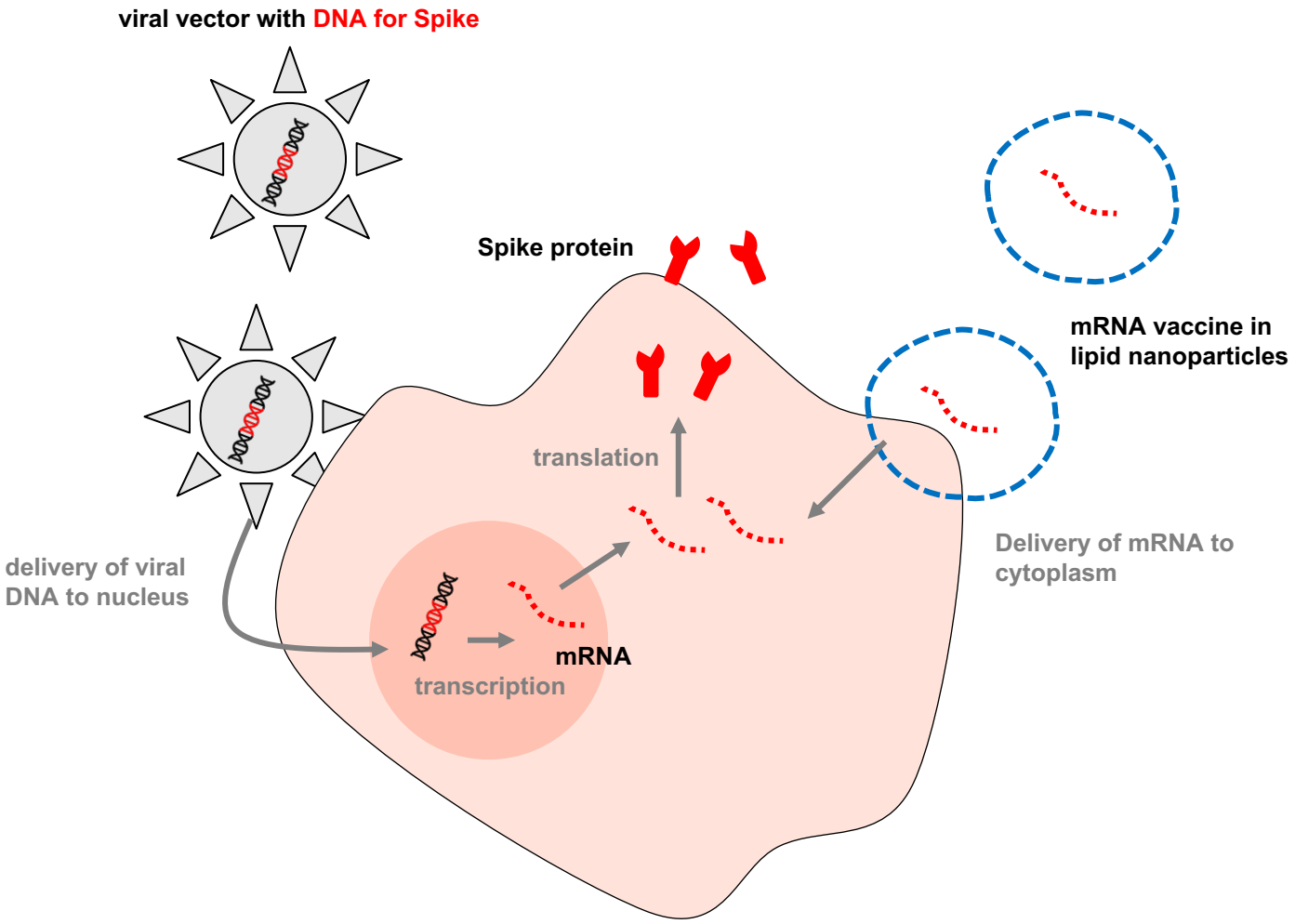
Efficacy against Herpes zoster
(Phase III studies + longer follow-up)



very high efficacy
→ even after 8 years

data from: Lal, *NEJM*, 2015
Cunningham, *NEJM*, 2016
Boutry, CID, 2021

Licensed vaccines against COVID-19 (Europe)



viral vactors
non-replicating “harmless” virus, carrying genetic information of SARS-CoV-2 spike protein
Chimp-Adenovirus: AstraZeneca
Adenovirus 26: Johnson&Johnson/ Janssen

mRNA vaccines
mRNA in Lipid-Nanopartikeln
BioNTech/Pfizer, Moderna

Protein vaccine
Spike protein + adjuvant (Matrix M)
Novavax

Whole virus inactivated vaccine
inactivated virus + adjuvant (Alum+CpG)
only <50 years!
Valneva

Efficacy short term after vaccination

Phase 3 study, BioNTech/Pfizer
clinical efficacy against symptomatic infection (up to 2 months after vaccination)

Table 3. Vaccine Efficacy Overall and by Subgroup in Participants without Evidence of Infection before 7 Days after Dose 2.

Efficacy End-Point Subgroup	BNT162b2 (N=18,198)		Placebo (N=18,325)		Vaccine Efficacy, % (95% CI)†
	No. of Cases	Surveillance Time (No. at Risk)*	No. of Cases	Surveillance Time (No. at Risk)*	
Overall	8	2.214 (17,411)	162	2.222 (17,511)	95.0 (90.0–97.9)
Age group					
16 to 55 yr	5	1.234 (9,897)	114	1.239 (9,955)	95.6 (89.4–98.6)
>55 yr	3	0.980 (7,500)	48	0.983 (7,543)	93.7 (80.6–98.8)
≥65 yr	1	0.508 (3,848)	19	0.511 (3,880)	94.7 (66.7–99.9)
≥75 yr	0	0.102 (774)	5	0.106 (785)	100.0 (–13.1–100.0)

Polack et al., *NEJM*, 2020

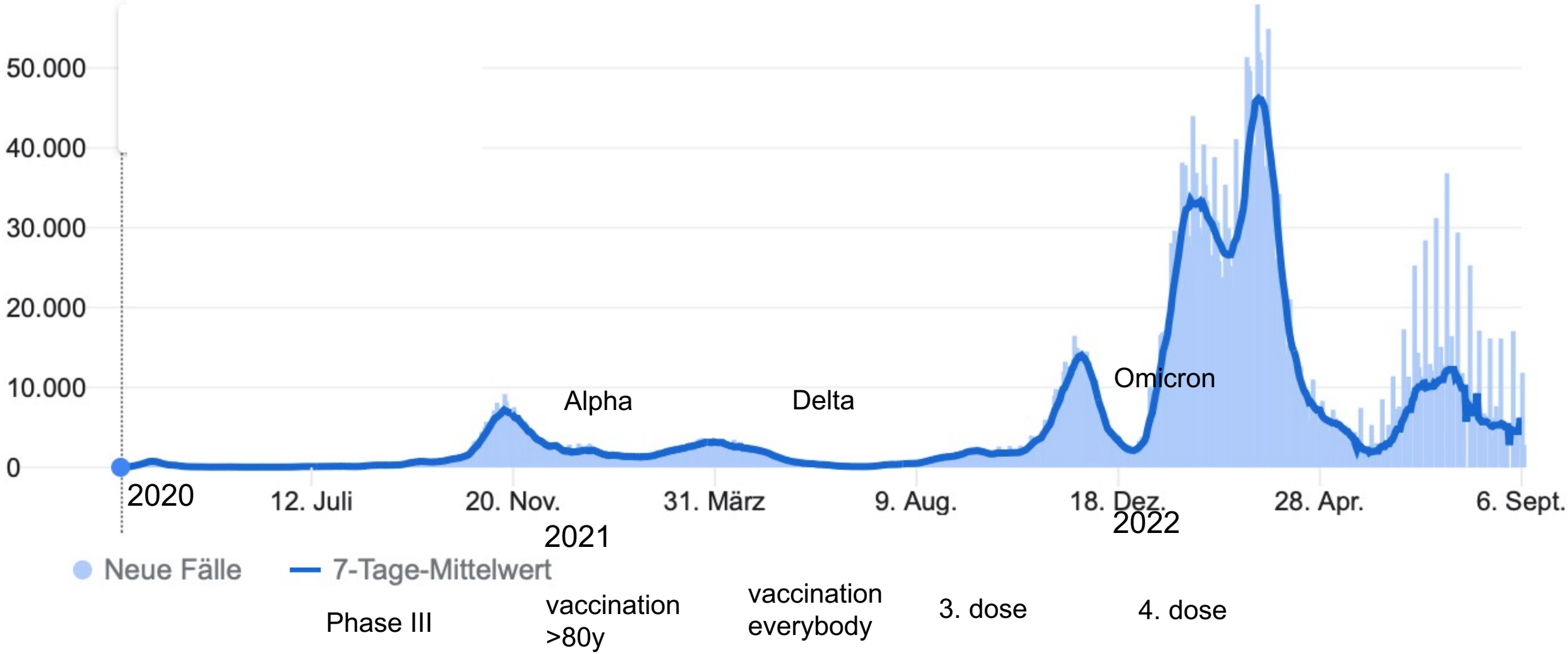
Effectiveness short term after vaccination

	Vaccine effectiveness*		
	Age ≥65 years	Age ≥75 years	Age ≥85 years
SARS-CoV-2 infection†	94·8% (93·9–95·5)	95·1% (93·9–96·0)	94·1% (91·9–95·7)
Asymptomatic SARS-CoV-2 infection	88·5% (86·4–90·3)	87·5% (84·2–90·1)	83·2% (76·3–88·1)
Symptomatic COVID-19	96·4% (95·9–97·0)	96·7% (95·9–97·4)	96·6% (95·2–97·6)
COVID-19-related hospitalisation	96·8% (96·2–97·3)	97·0% (96·2–97·7)	96·9% (95·5 –97·9)
Severe or critical COVID-19-related hospitalisation	97·3% (96·8–97·8)	97·6% (96·8–98·1)	97·4% (95·9 –98·3)
COVID-19-related death	96·9% (96·0–97·6)	97·1% (96·0–97·9)	97·0% (94·9–98·3)

Israel: April 03 2021
>7 days after 2nd dose of BioNTech/Pfizer

Haas et al., *Lancet*, 2021

… a lot of change is happening



Phase III

vaccination >80y

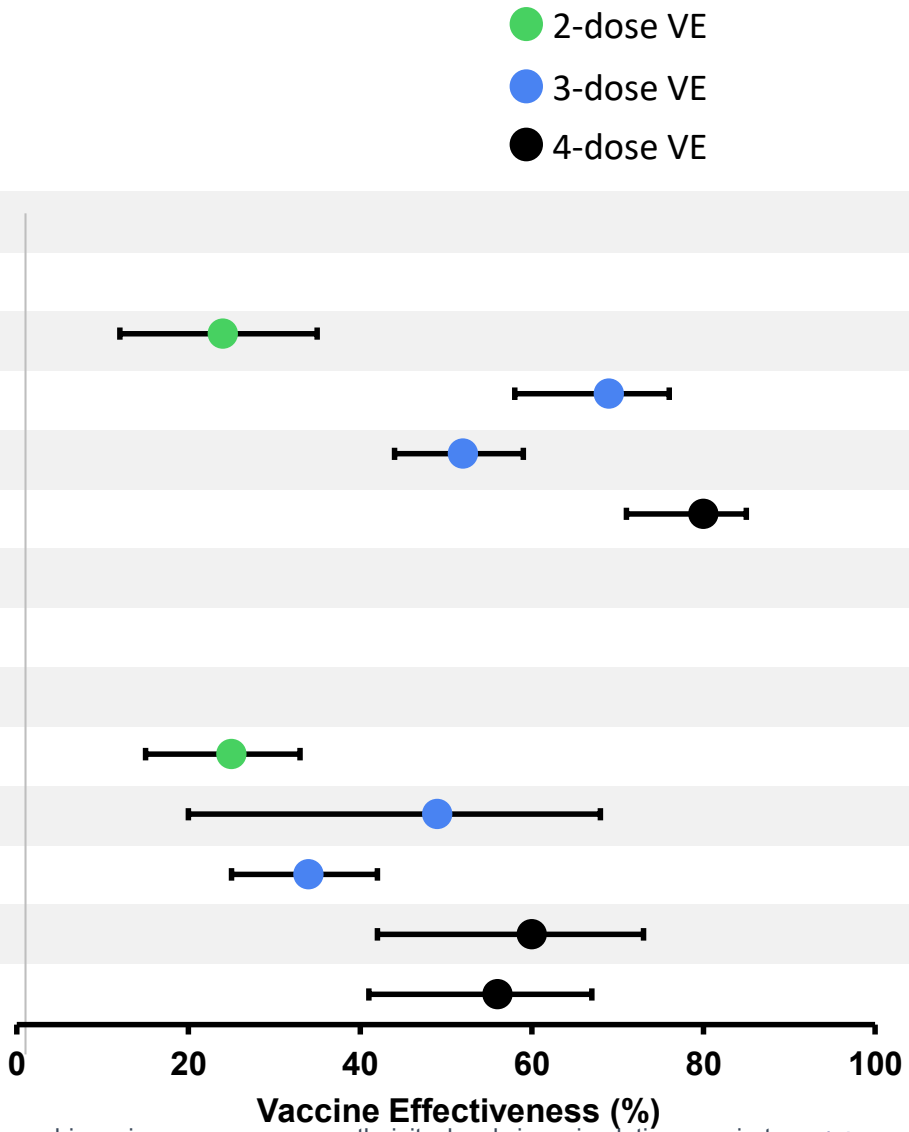
vaccination everybody

3. dose

4. dose

VISION: mRNA VE for hospitalizations among immunocompetent adults ≥18 years by number of doses and time since last dose receipt, late-Mar–late-Jul 2022

Vaccination status (days since most recent dose)	Total	CLI cases	Days since most recent dose, median (IQR)	Adjusted VE % (95% CI)
BA.2/BA.2.12.1 period				
Unvaccinated	6,682	494		Ref.
2 doses (14-149)	*	*	*	*
2 doses (≥150)	5,118	393	371 (308, 413)	24 (12 - 35)
3 doses (7-119)	2,350	72	94 (74, 108)	69 (58 - 76)
3 doses (≥120)	7,686	519	168 (146, 191)	52 (44 - 59)
4 doses (7-59)**	1,204	74	27 (17, 41)	80 (71 - 85)
BA.4/BA.5 period				
Unvaccinated	4,578	913		Ref.
2 doses (14-149)	*	*	*	*
2 doses (≥150)	3,592	619	445 (369, 484)	25 (15 - 33)
3 doses (7-119)	335	32	76 (46, 100)	49 (20 - 68)
3 doses (≥120)	5,030	869	229 (199, 256)	34 (25 - 42)
4 doses (7-59)**	717	81	38 (23, 49)	60 (42 - 73)
4 doses (60-119)**	1,146	157	84 (73, 97)	56 (41 - 67)



* Estimates with confidence intervals >50 percentage points are not shown.

** Only estimated among adults ≥50 years of age

BA.2/BA.2.12.1 estimates: Link-Gelles et al. MMWR: https://www.cdc.gov/mmwr/volumes/71/wr/mm7129e1.htm

BA.4/BA.5 estimates: CDC, preliminary unpublished data. Individuals with prior infections excluded. Adjusted for calendar time, geographic region, age, sex, race, ethnicity, local virus circulation, respiratory or non-respiratory underlying medical conditions, and propensity to be vaccinated.

Vaccines for new variants

BioNTech/Pfizer and Moderna developed mRNA vaccines adapted to Omicron

→ first studies (immunogenicity, safety) with Omicron BA.1
→ Omicron only or bivalent (ancestral mRNA + Omicron)

→ decision was made for bivalent formulation
→ but in the meantime BA.4/5 showed up….

USA:
Licensure of bivalent vaccines (ancestral + BA.4/5)
→ used as booster (3rd and 4th dose)

Europe:
Licensure of bivalent vaccines (ancestral + BA.4/5) → early September
→ distribution has started
→ used as booster (3rd and 4th dose)

→ Licensure of bivalent vaccines (ancestral + BA.4/5) → middle of September

Summary

- **Age-related changes occur in all parts of the immune system**
- **Higher incidence and severity of infections**
- **Reduced immunogenicity and efficacy of many, but not all vaccines**
- **Vaccines specifically recommended for older adults**
  - Influenza → high-dose and adjuvanted vaccines
  - S. pneumoniae → polysaccharide and conjugate vaccines
  - Herpes zoster → adjuvanted subunit vaccine
- **Vaccines for all adults are also relevant in seniors**
  - SARS-CoV-2
  - regular booster vaccinations (tetanus, diphtheria, pertussis)
  - Hepatitis B, travel vaccines…

Challenges with older populations….

- **Heterogeneity of populations: healthy, frail, co-morbidities, medications, community-dwelling, long-term care…**
- **Higher person-to-person variability**
- **Chronolgical age vs. biological age vs. immunological age?**
- **Impact of latent CMV-infection?**
- **Things we know from other age groups might not apply**
  Example: correlation of ELISA and OPA titers for pneumococcal polysaccharicde-specific antibodies in children, but not in older adults
- **Impact of ”antigenic history” → previous vaccination and/or natural exposure**


Thank you!