Immunosenescence: When our immune system gets old...

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What happens to the immune system in older age?

Immune response after vaccination

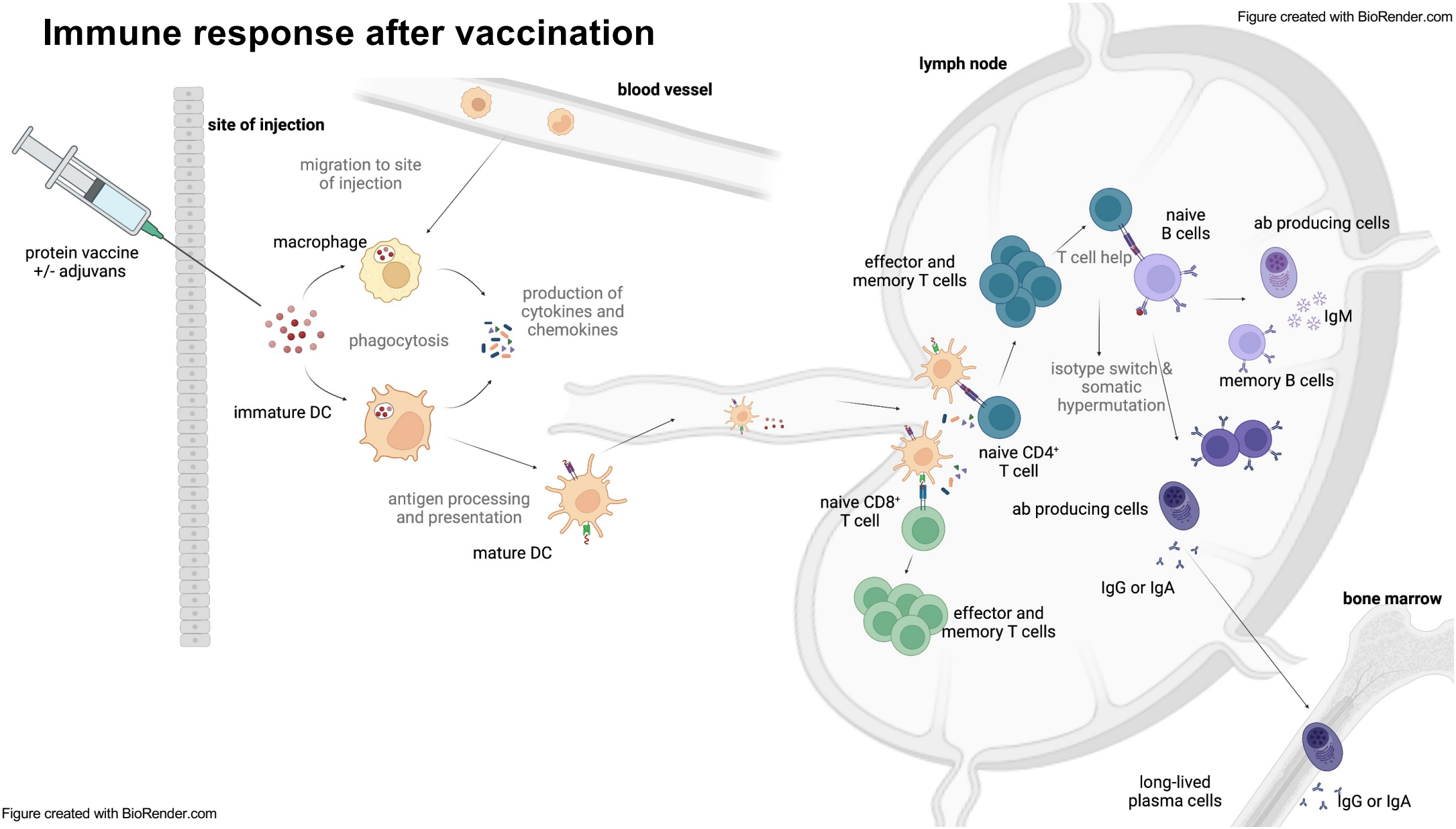
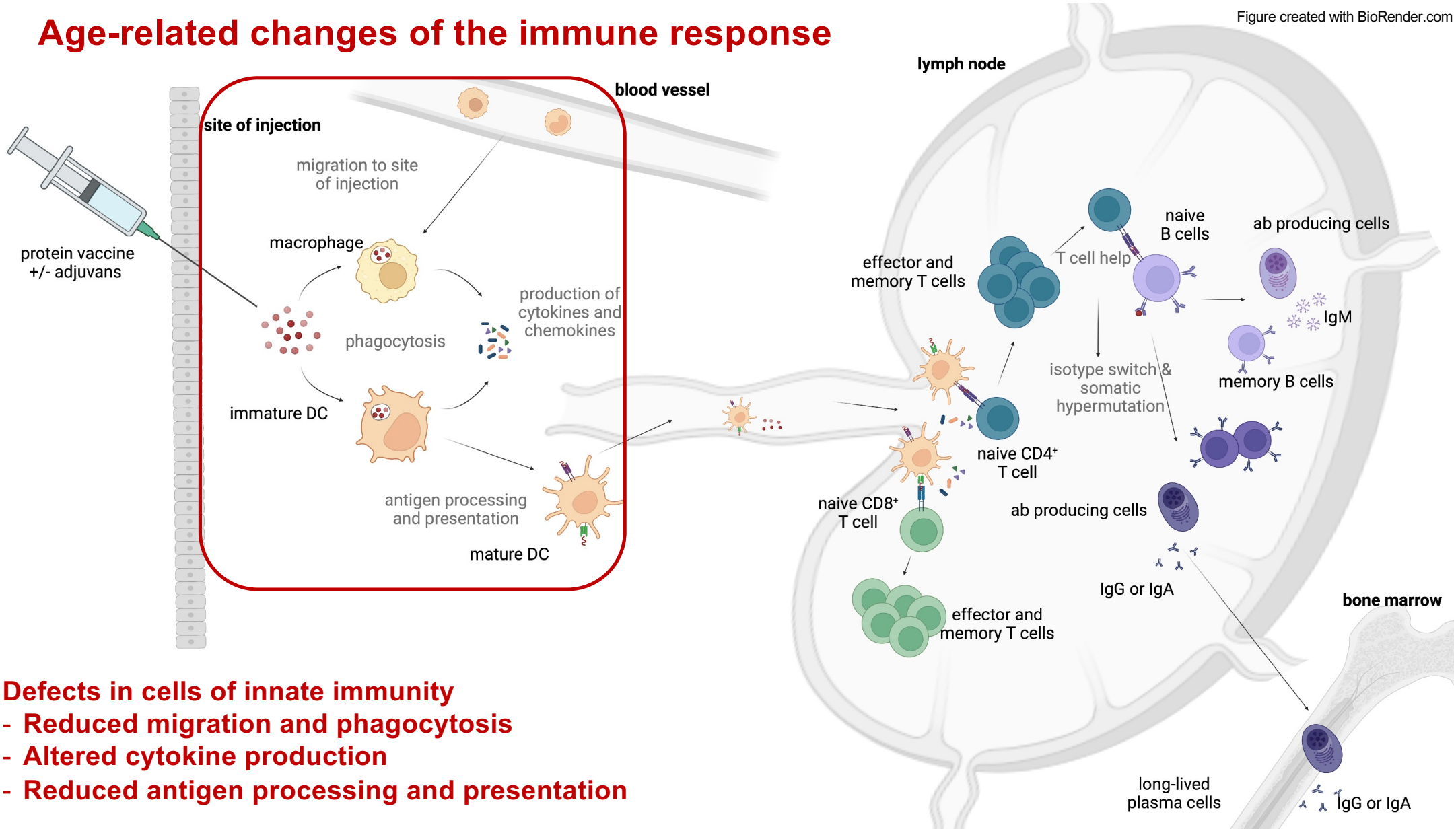


Figure created with BioRender.com

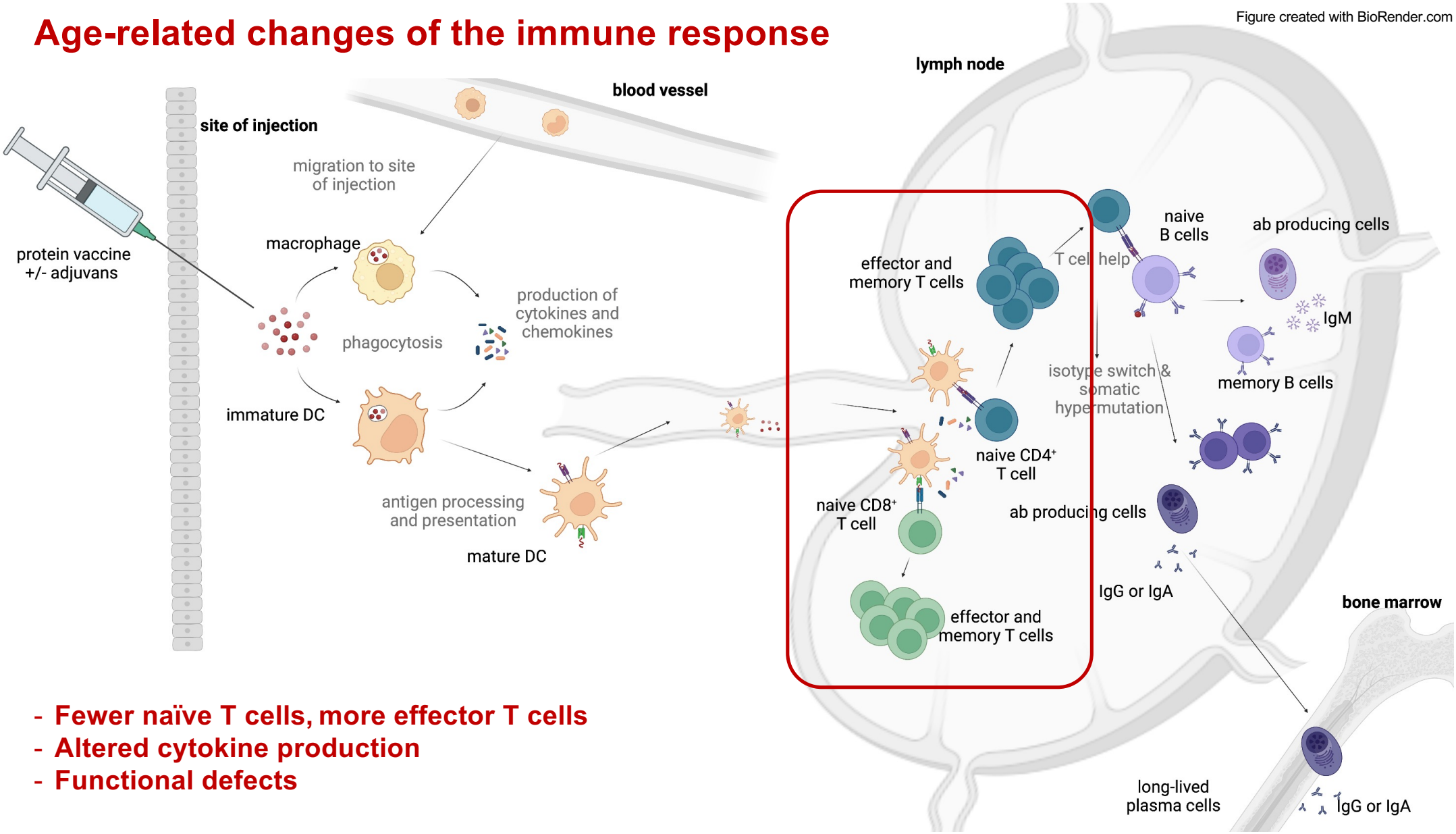
Age-related changes of the immune response



Defects in cells of innate immunity

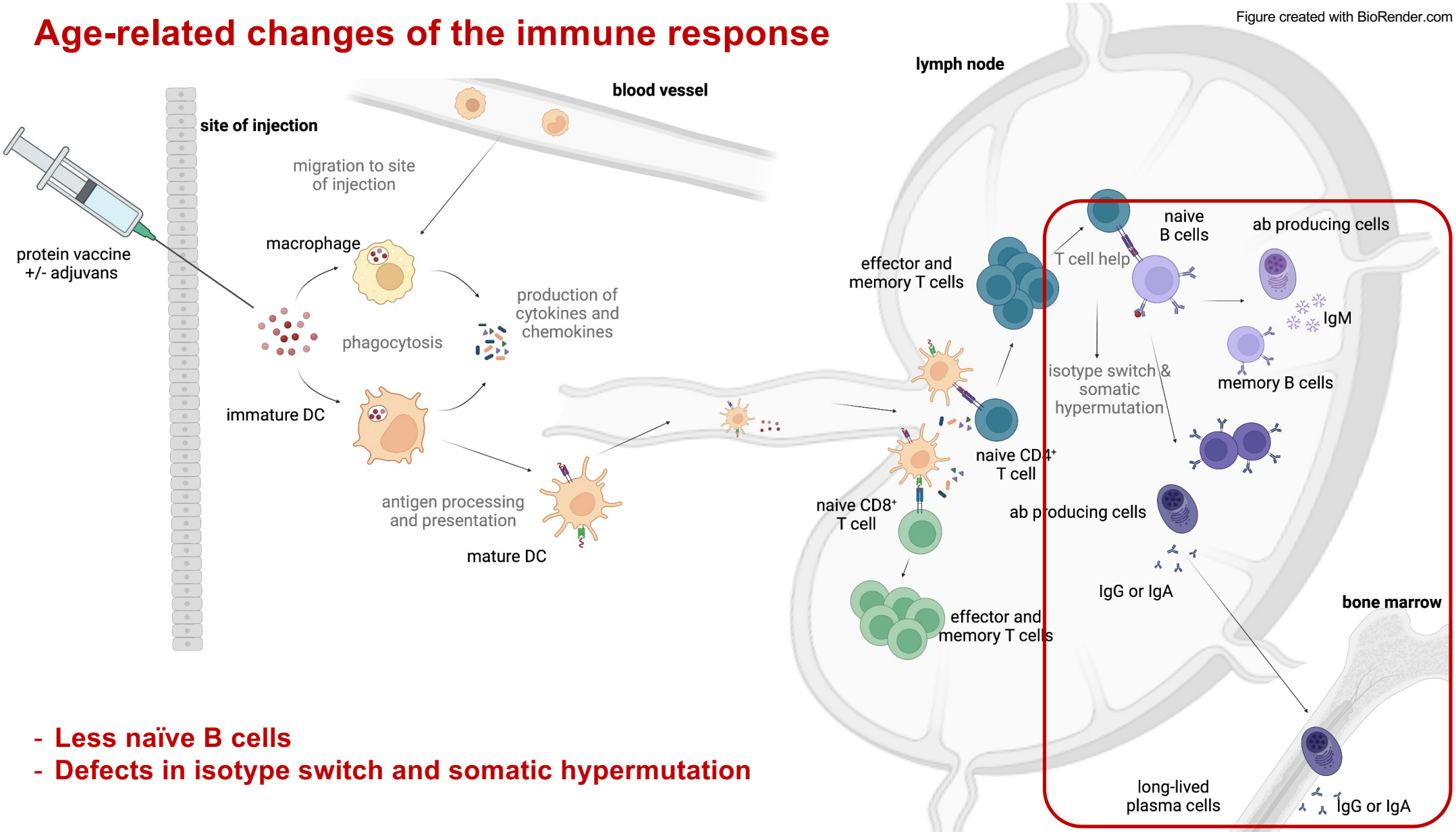
- **Reduced migration and phagocytosis**
- **Altered cytokine production**
- **Reduced antigen processing and presentation**

Age-related changes of the immune response



- **Fewer naïve T cells, more effector T cells**
- **Altered cytokine production**
- **Functional defects**

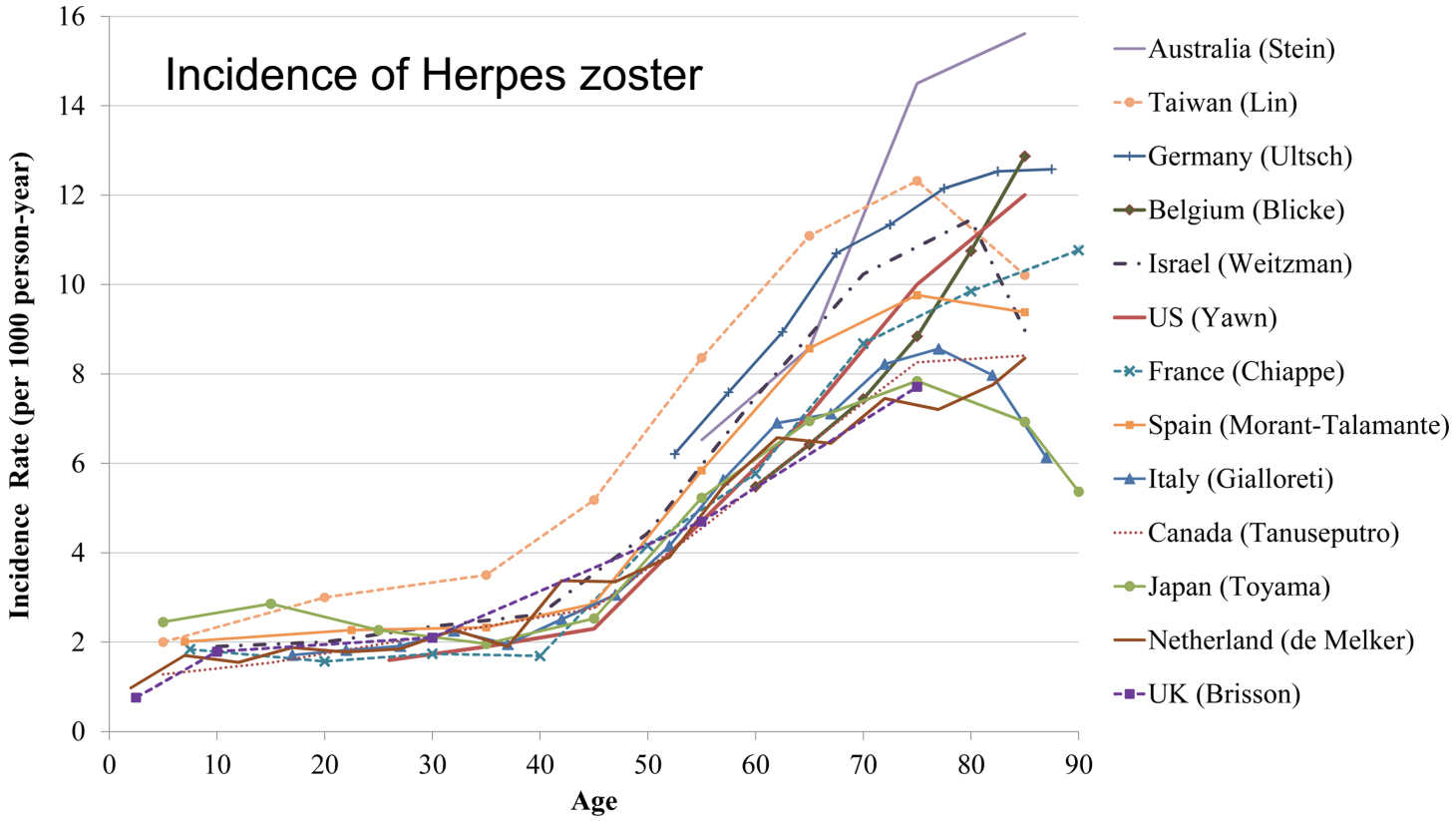
Age-related changes of the immune response



- Less naïve B cells
- Defects in isotype switch and somatic hypermutation

Why are we interested in the aging immune system?

High incidence, morbidity and mortality of infectious disease



Kawai et al., BMJ Open, 2014

High incidence, morbidity and mortality of infectious disease

Risk for COVID-19 Infection, Hospitalization, and Death By Age Group

Updated Mar. 28, 2022 Print

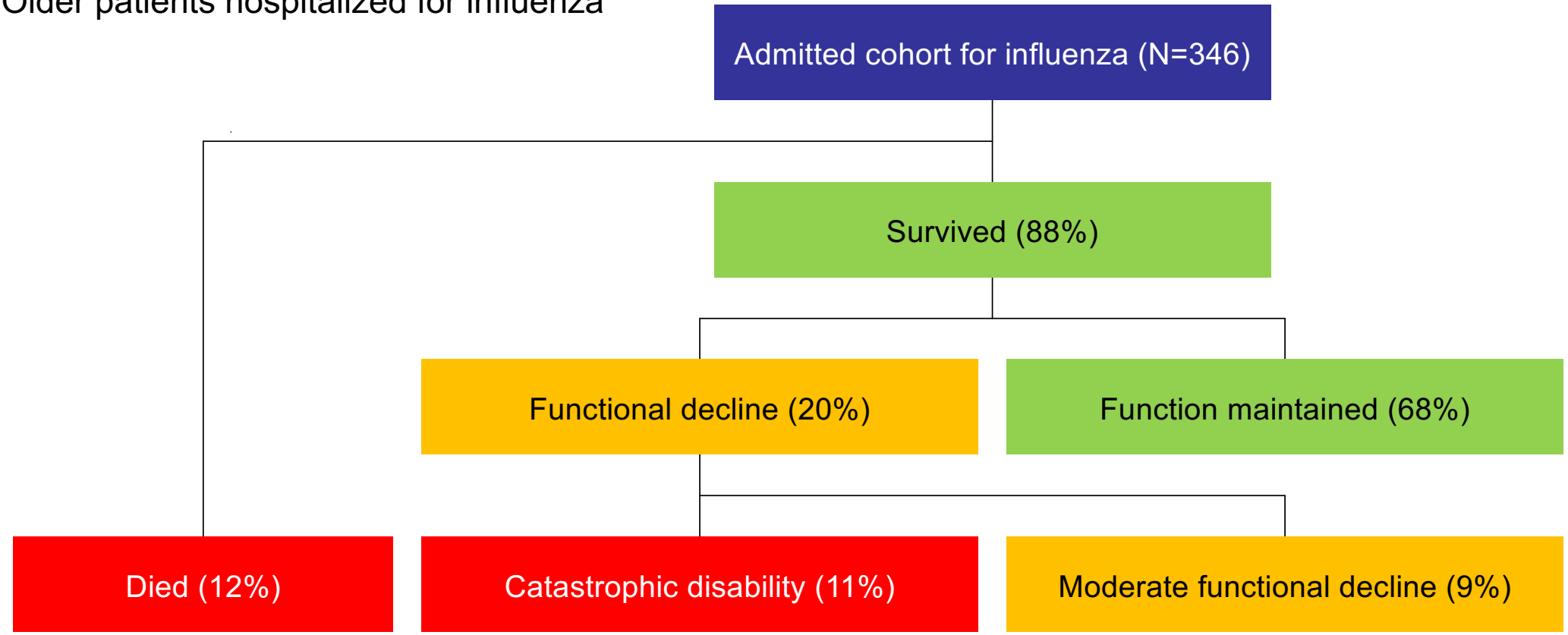
Rate compared to 18-29 years old[1]	0-4 years old	5-17 years old	18-29 years old	30-39 years old	40-49 years old	50-64 years old	65-74 years old	75-84 years old	85+ years old
Cases[2]	<1x	1x	Reference group	1x	1x	1x	1x	1x	1x
Hospitalization[3]	<1x	<1x	Reference group	2x	2x	3x	5x	8x	10x
Death[4]	<1x	<1x	Reference group	4x	10x	25x	65x	140x	340x

… beyond acute illness

- Acute illness, hospitalisation
- Transient increased risk, e.g. for cardiovascular events after infections
- Risk of delir and dementia
- Exacerbation of comorbidities
- Decline of general health status, frailty
- Possible loss of functionality and independence

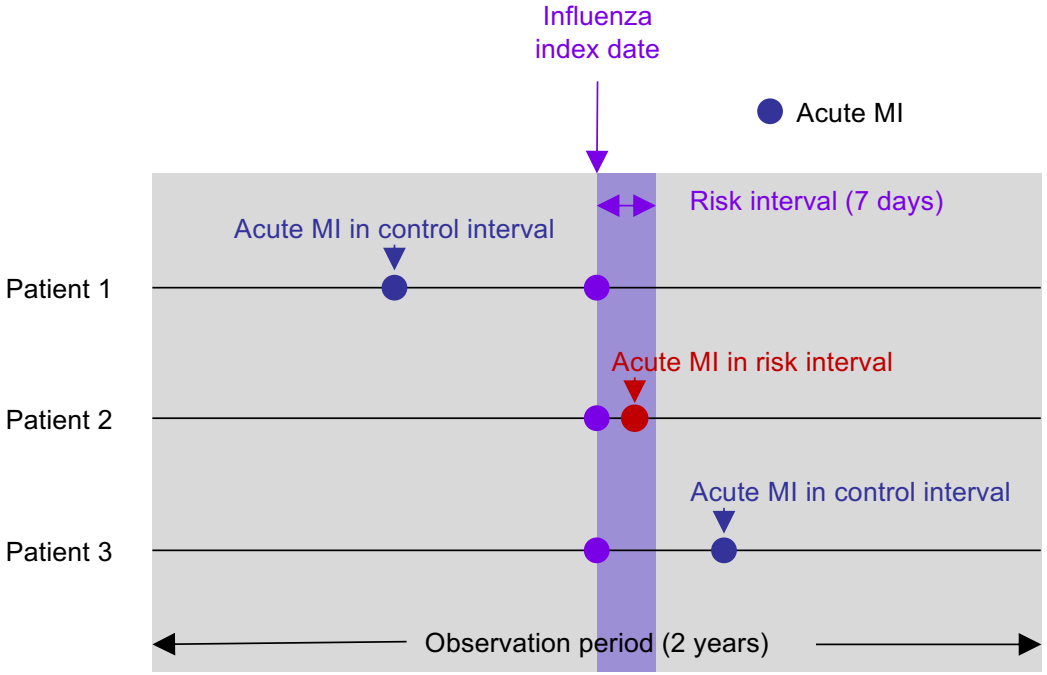
Burden of disease beyond acute infection

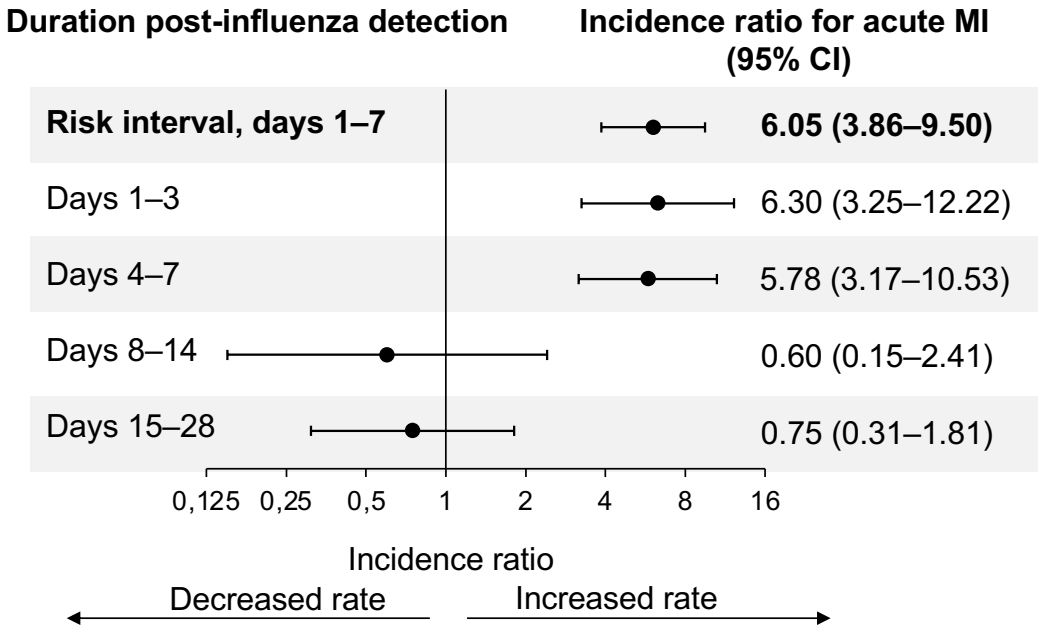
Older patients hospitalized for influenza



The figure was independently created from the original data published by Andrew MK *et al.* 2021
Andrew MK *et al. J Am Geriatr Soc* 2021;69:696–703

Cardiovascular risk





→ **6-fold higher risk for MI** in the first week after influenza diagnosis

332 patients hospitalized with myocardial infarction one year before or after a lab-confirmed infection with influenza

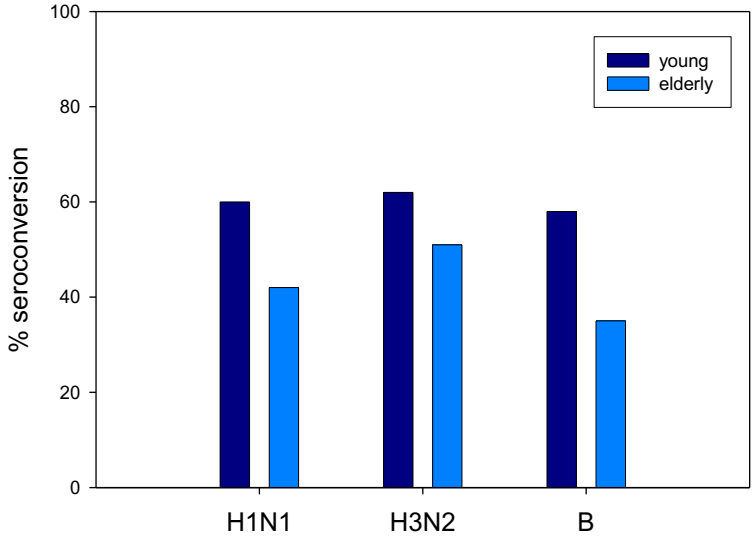
Elevated risk also for stroke and after other infections...

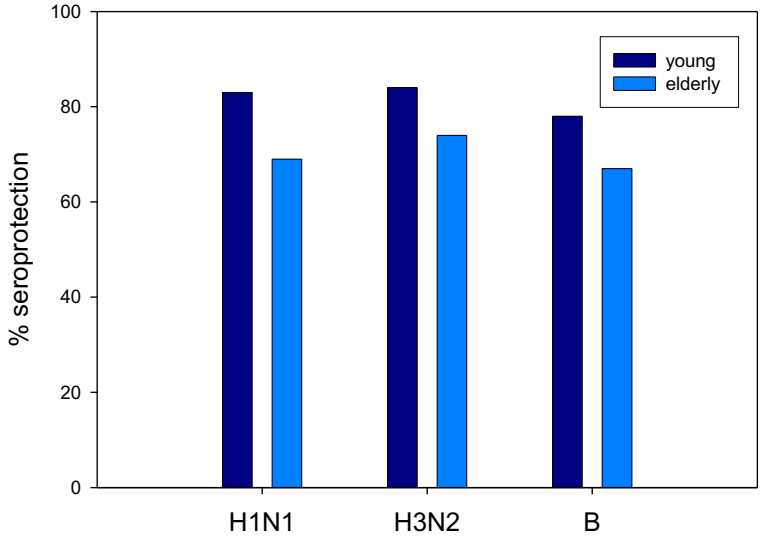
CI, confidence interval; MI, myocardial infarction
Figures generated with data or modified from : Kwong JC *et al. N Engl J Med* 2018;378:345–353

Older adults are an important target group for vaccination

Many vaccines are less immunogenic in older adults

Meta-analysis of 31 studies (1986-2002)





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

Vaccines can be improved for older adults

High-Dose influenza vaccine (trivalent 60µg HA instead of 15µg, approved in the US in 2010/2011)

→ higher antibody levels and seroconversion

→ higher clinical efficacy!

randomized controlled trial: HD-TIV vs SD-TIV

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)‡

Falsey et al., *J Inf Dis,* 2009
Chen et al., *Vaccine,* 2011
DiazGranados et al., *NEJM, 2014*

Vaccines can prevent complications beyond acute infection

Table 1 Efficacy of accepted coronary interventions and influenza vaccine in the prevention of myocardial infarction

Coronary intervention	Prevention	Intervention efficacy/effectiveness against acute myocardial infarction (%)
Smoking cessation[4 23–25]	Secondary	32–43
Statins[38]	Secondary	19–30
Antihypertensive drugs[26–29 32]	Secondary	17–25

MacIntyre et al., *Heart,* 2016

Vaccines can prevent complications beyond acute infection

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Influenza vaccine[5 9 18]	Secondary	15–45

MacIntyre et al., *Heart,* 2016

Varicella-Zoster virus

primary infection

Varicella

Varicella-Zoster virus remains in sensory nerve cells

reactivations immunologically controlled

symptomatic reactivation

Herpes zoster

VZV-specific immune response

Photos: Shutterstock
Figure based on Hope-Simpson, 1965

Varicella-Zoster virus

vaccination of children prevents primary infection

Photos: Shutterstock
Figure based on Hope-Simpson, 1965

Vaccination against Herpes zoster

primary infection

Varicella

Varicella-Zoster virus remains in sensory nerve cells

reactivations immunologically controlled

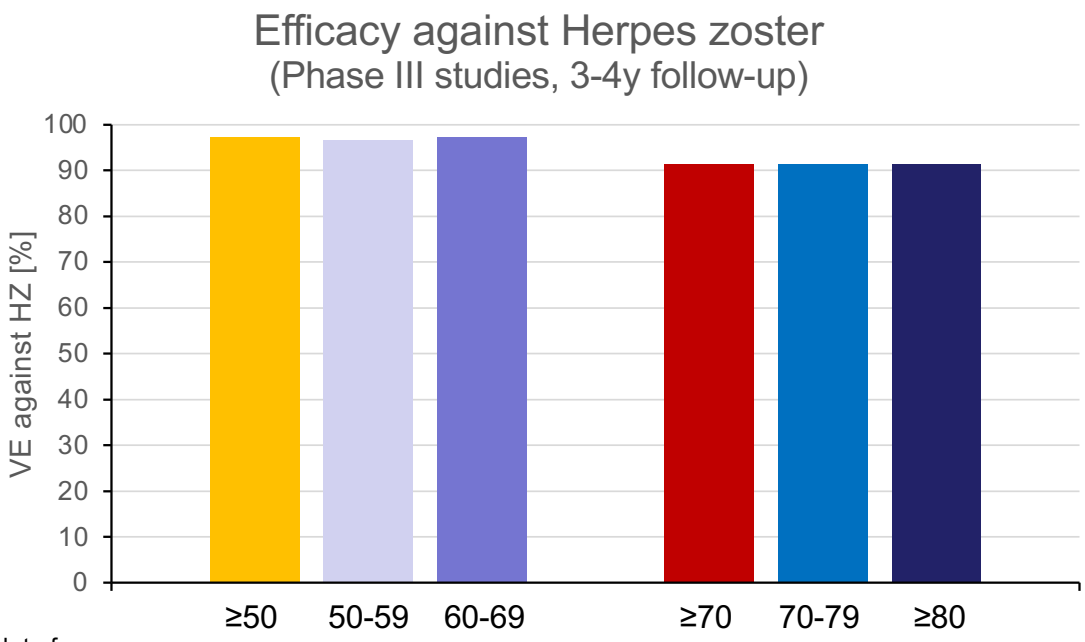
VZV-specific immune response

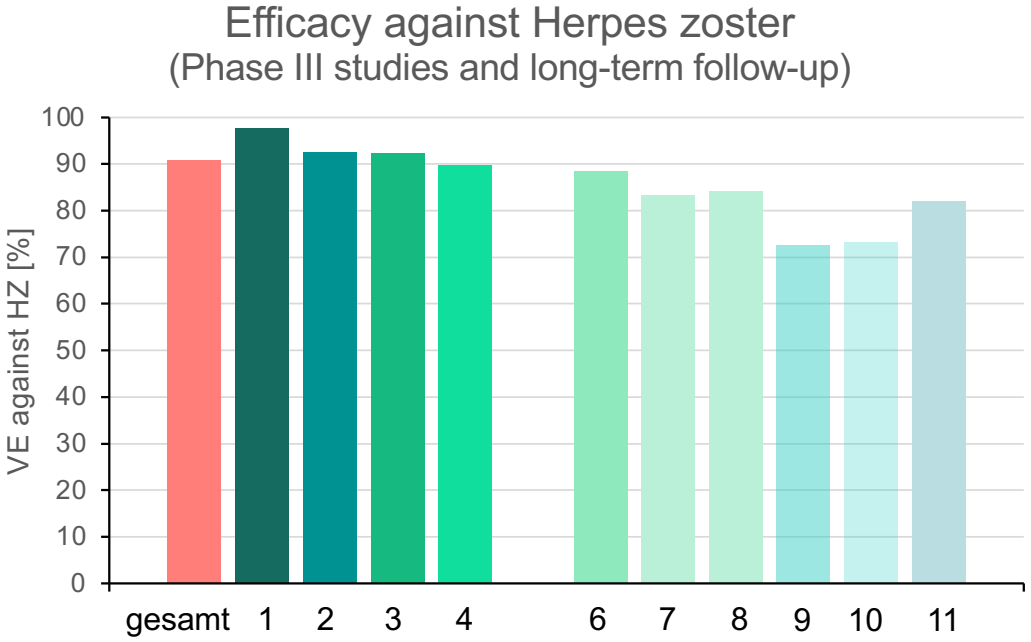
Adult vaccination boosters the existing VZV-specific immune response and restores immunological control

Photos: Shutterstock
Figure based on Hope-Simpson, 1965

Clinical efficacy

Vaccination against herpes zoster
50µg recombinant glycoprotein E plus adjuvant AS01$_\beta$ (MPL, QS21, liposomes)
2 doses, 8-12 weeks apart





data from:
Lal, *NEJM*, 2015
Cunningham, *NEJM*, 2016
Boutry CID, 2021
Strezova, OFID, 2022
Strezova, ECCMID 2024

very high efficacy
→ even in the oldest age group

long-term efficacy shown for 11 years

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