Unexpected beneficial biological effects of vaccines

Dr Stephanie Longet, Professeur junior

Groupe Immunité de Muqueuses et Agents Pathogenes

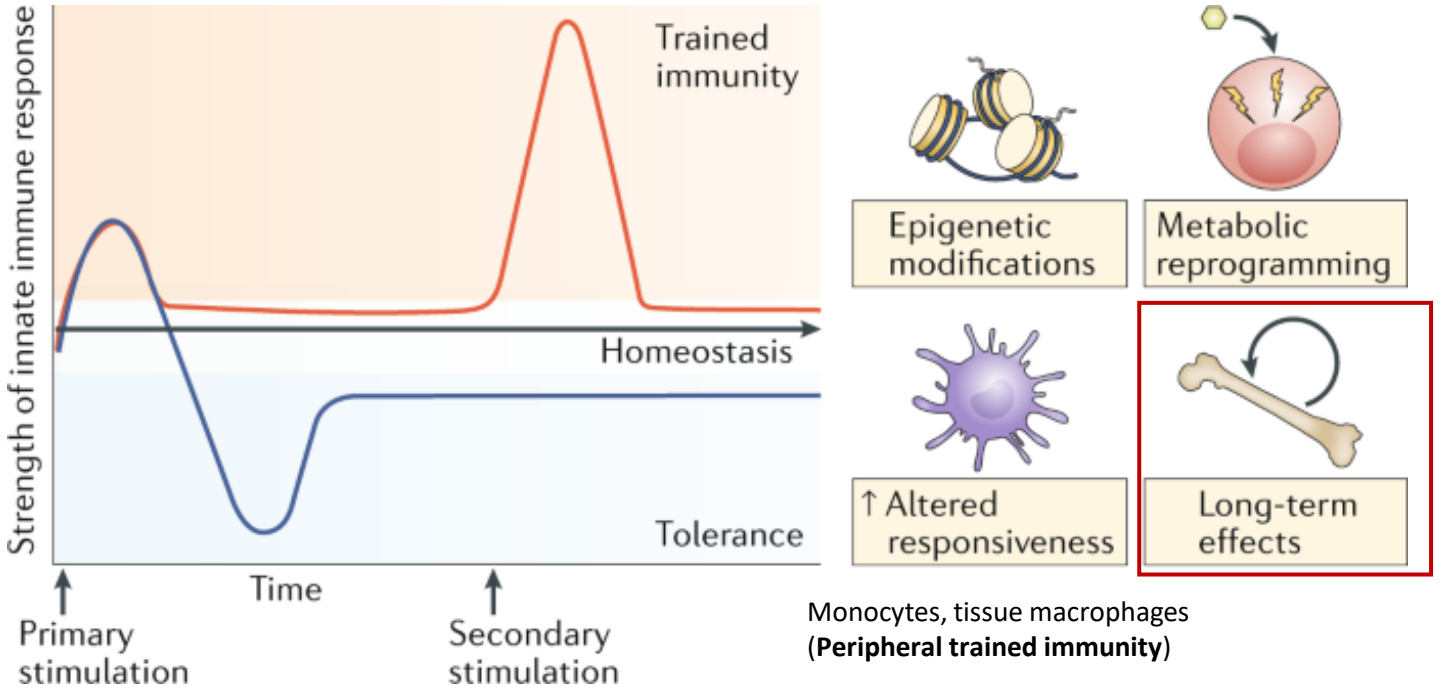
Universite Jean Monnet, Saint-Etienne

Université Jean Monnet Saint-Étienne

Centre International de Recherche en Infectiologie

Trained immunity

Definition: trained immunity is a functional state of the **innate immune system** that is characterized by **long-term epigenetic** and **metabolic reprogramming of cells** associated with potent immune responses.



Monocytes, tissue macrophages (**Peripheral trained immunity**)

Immune progenitor cells in the bone marrow (**Central trained immunity**)

Long-term innate immunity-mediated protective effects of vaccination against heterologous infections

Experimental and clinical studies have demonstrated that **exogenous pathogen-associated molecular patterns** and **endogenous danger-associated molecular patterns** induce trained immunity.

https://www.nature.com/articles/s41581-022-00633-5

https://www.nature.com/articles/s41577-020-0285-6

Differences and similarities between trained and adaptive immunity

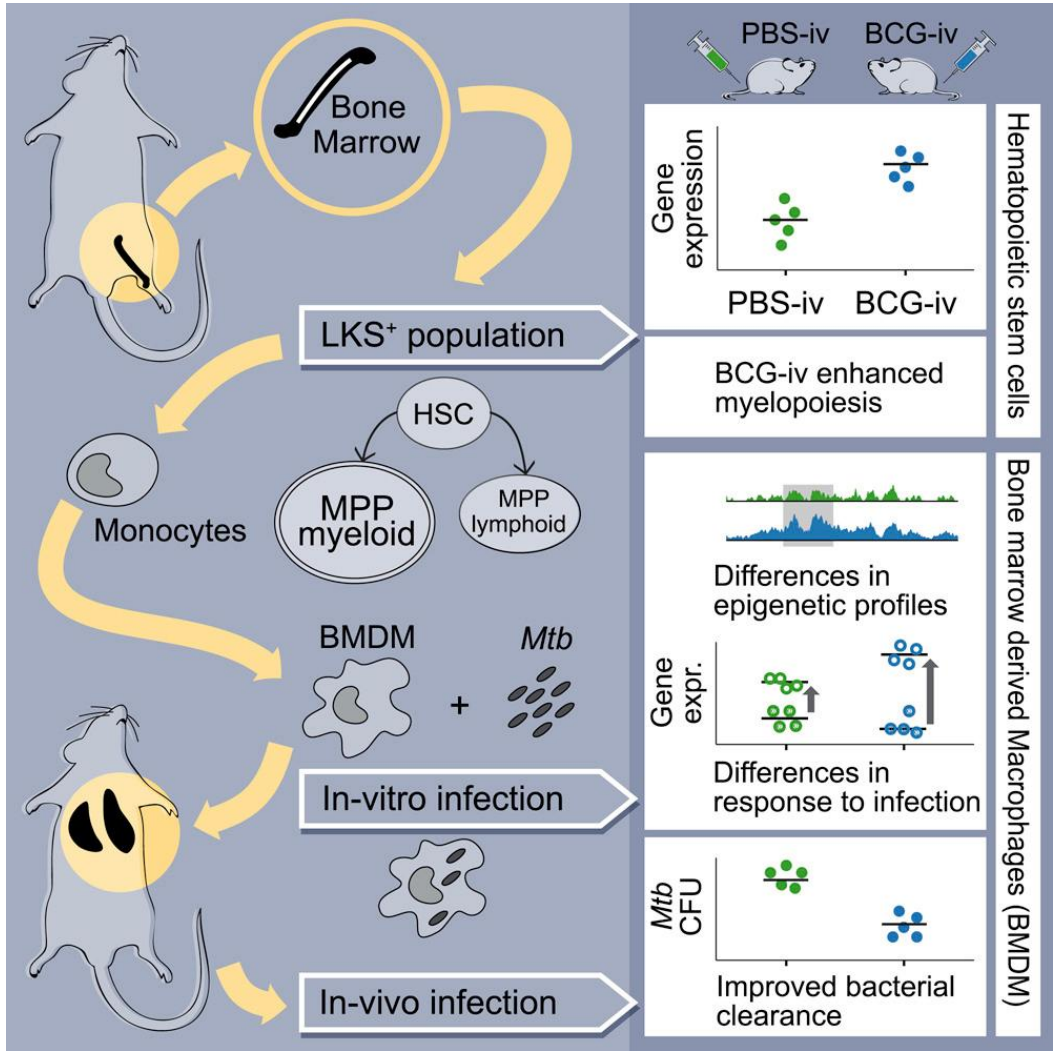
Feature	Trained immunity	Adaptive immunity
Specificity	±	+++
Inducers	Pathogens and derived products (PAMPs)	Antigen presentation plus costimulatory signals and cytokines from DCs
Receptors	PRRs	sIg, TCR, receptors for costimulation and cytokines
Clonality	No	Yes
Cells	Monocytes, Macrophages, NK, DCs, ILCs, and other innate immune cells	B and T lymphocytes
Memory	Months	Years
Memory mechanism	Epigenetic modifications	Clonal expansion and differentiation

It is not based on a clonal expansion of lymphocytes but on reprogramming myeloid cells by stable epigenetic changes

https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2018.02936/full

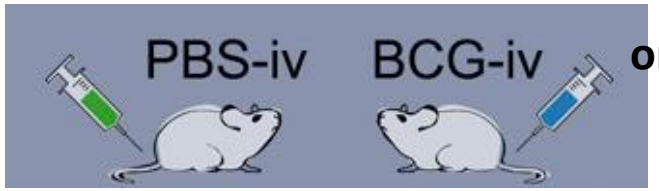
BCG vaccine induces trained immunity – responses to the same pathogen

BCG vaccine: an attenuated, live culture preparation of the Bacillus of Calmette and Guerin (BCG) strain of Mycobacterium bovis



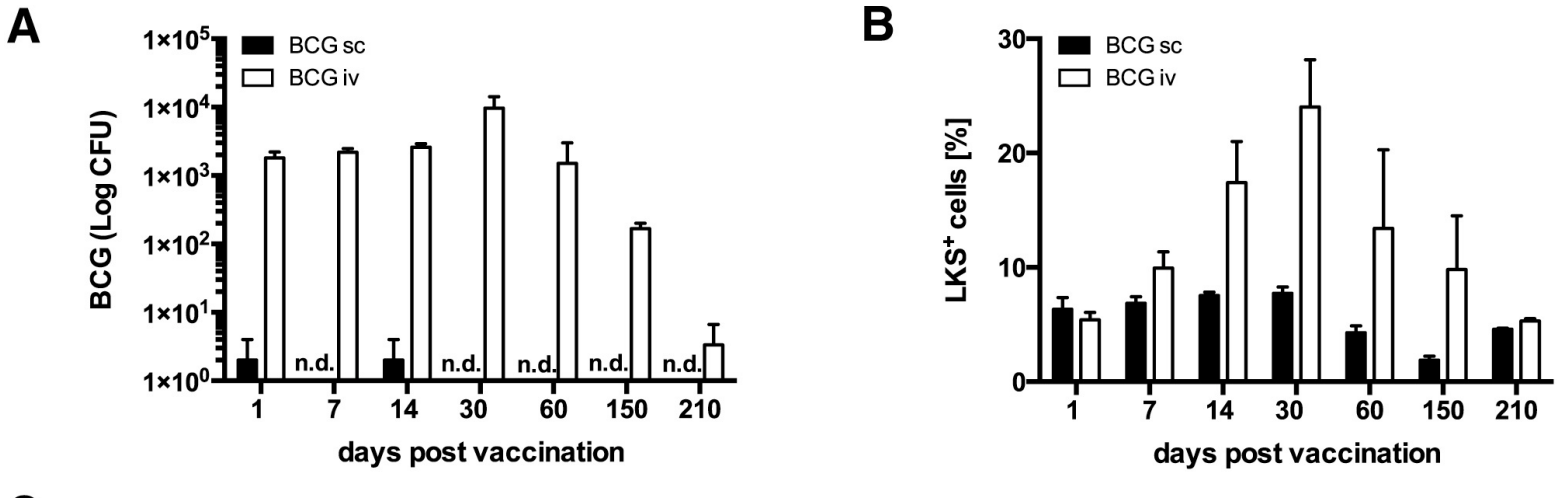
https://www.cell.com/cell/fulltext/S0092-8674(17)31511-8?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867417315118%3Fshowall%3Dtrue

BCG vaccine induces trained immunity – responses to the same pathogen



or sc

Expansion of the **Hematopoietic stem cell progenitor**

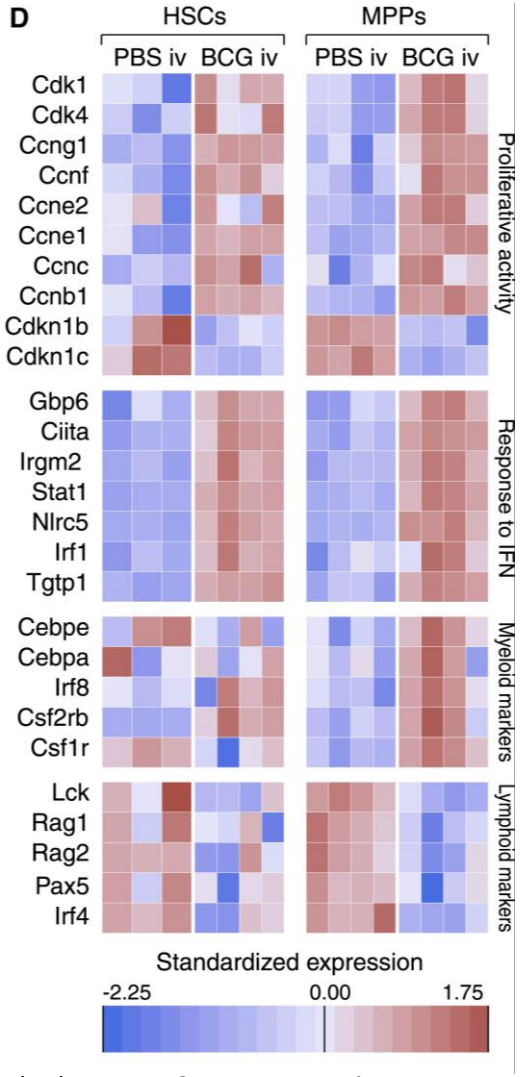


After <u>BCG-iv vaccination</u>, BCG reached the BM, where it was detected up to 7 months post vaccination (A). The number of BCGs in the BM directly correlated with the expansion of the **HSC progenitor** lineage$^-$ c-Kit$^+$ Sca-1$^+$ (LKS$^+$) population (B).

BCG was unable to infect HSCs either in vitro or in vivo, whereas BCG-infected Mo/Mac lineage cells were readily observed . Thus, the expansion of the LKS+ population is not a consequence of direct infection with BCG.

BCG vaccine induces trained immunity – responses to the same pathogen

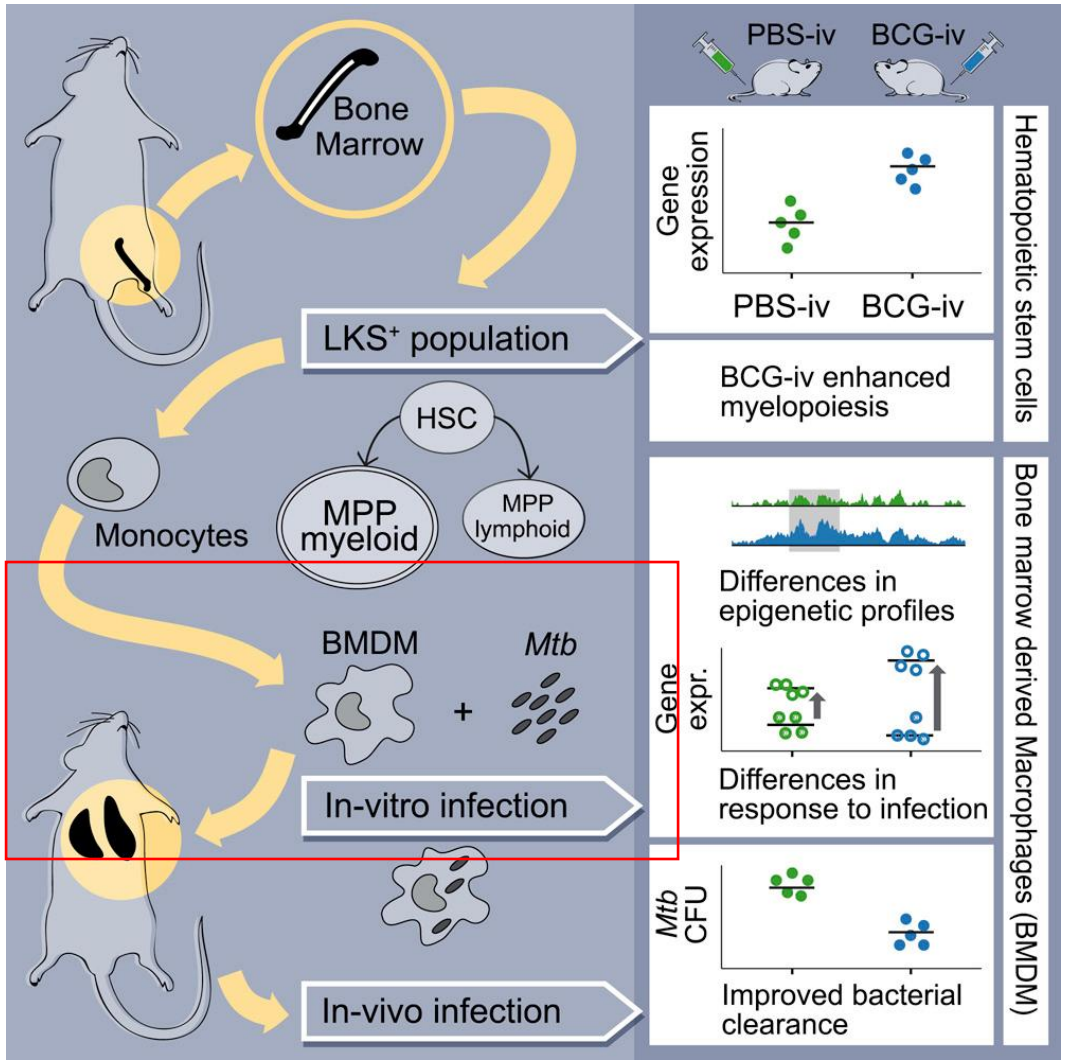
BCG Reprograms HSCs in the Bone Marrow and Enhances Myelopoiesis



https://www.cell.com/cell/fulltext/S0092-8674(17)31511-8?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867417315118%3Fshowall%3Dtrue

BCG vaccine induces trained immunity – responses to the same pathogen

BMDM: monocytes/macrophage generated in vitro from bone marrow cells

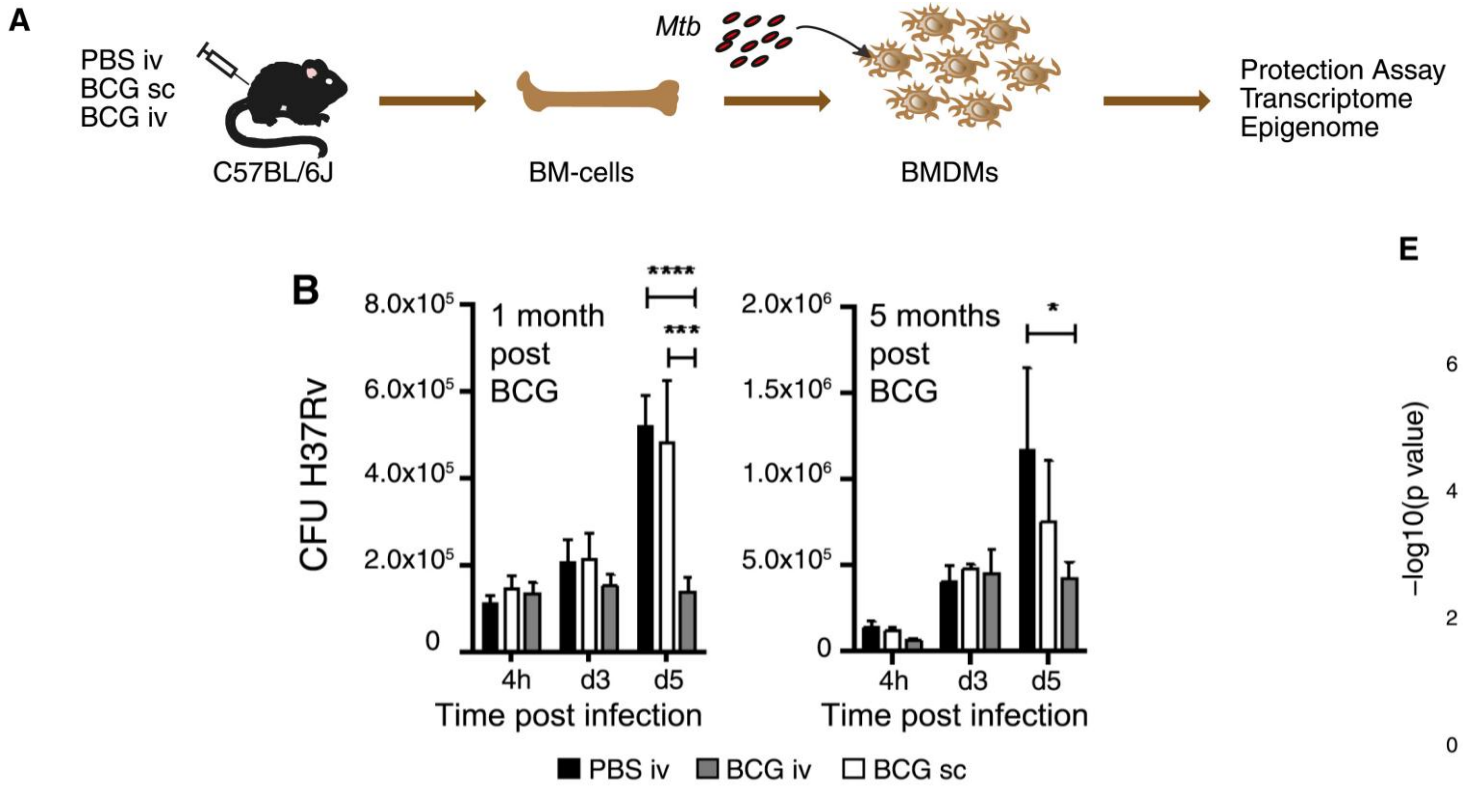


https://www.cell.com/cell/fulltext/S0092-8674(17)31511-8?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867417315118%3Fshowall%3Dtrue

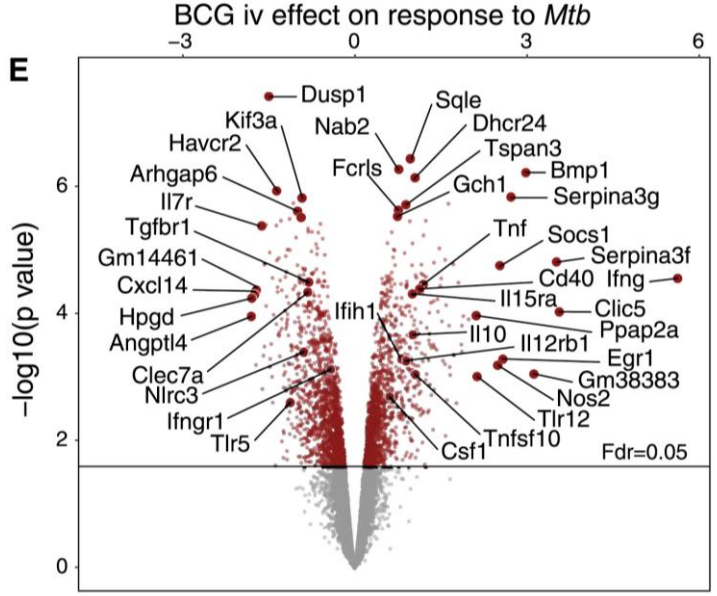
BCG vaccine induces trained immunity – responses to the same pathogen

BMDM from BCG-IV vaccinated mice demonstrate a better protection against Mtb challenge

5 months BCG-iv or BCG-sc vaccinated WT mice



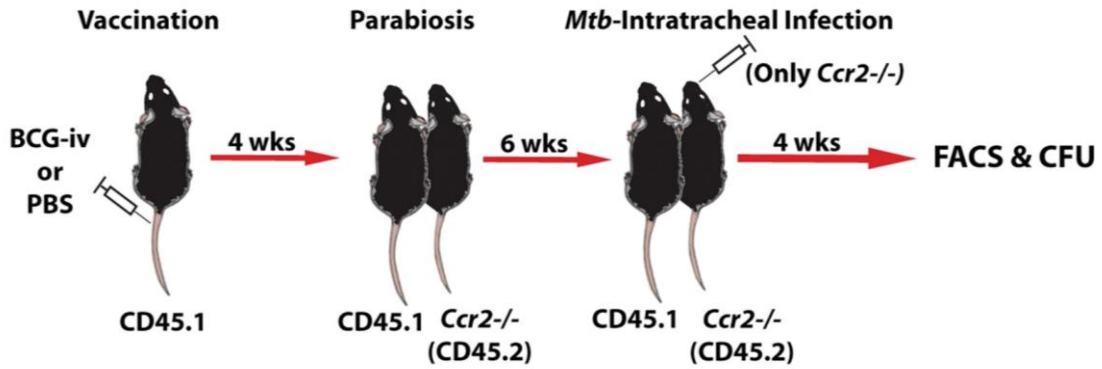
Mice vaccinated with BCG (iv or sc) or control (PBS-iv) were treated with the antimycobacterial drugs isoniazid (INH) and rifampicin (RIF), which eliminated virtually all bacteria from the BM.



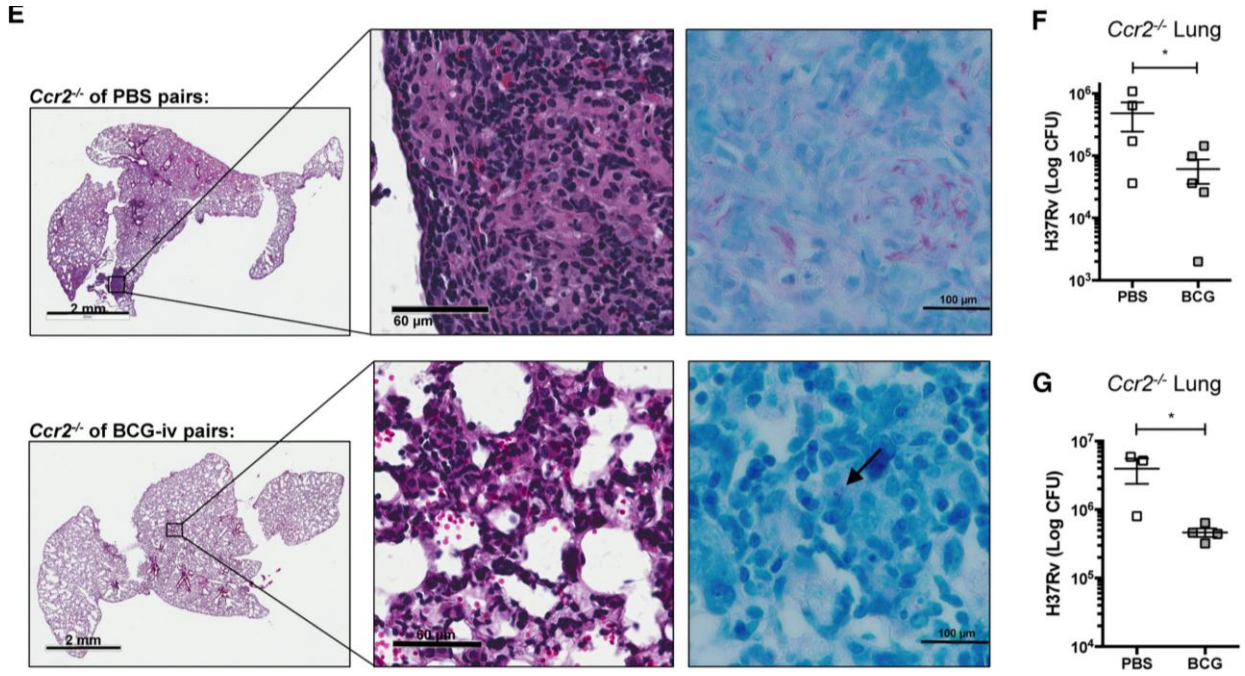
BCG-Trained BMDMs Are Reprogrammed to Provide Protection against Mtb Infection

BCG vaccine induces trained immunity – responses to the same pathogen

CD45.2 mice are partially protected in parabiosis experiment with BCG-iv vaccinated mice



Ccr2-/- mice susceptible to IT Mtb infection



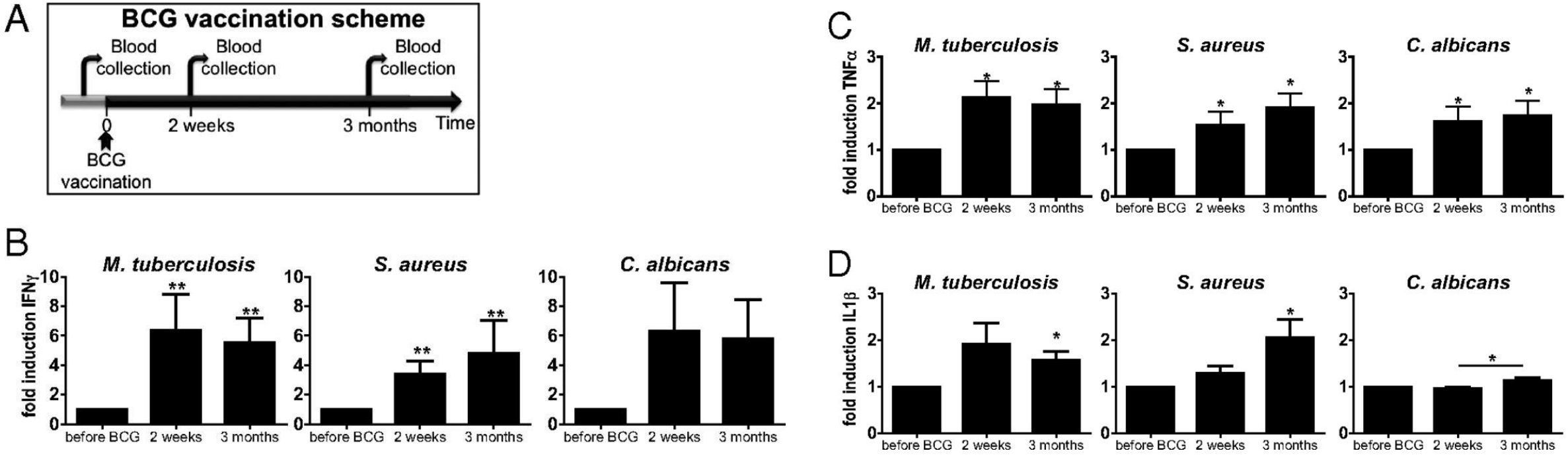
HSC Education is sustainable and does not require persistent exposure to BCG

https://www.cell.com/cell/fulltext/S0092-8674(17)31511-8?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867417315118%3Fshowall%3Dtrue

‘Non-specific immunity’ induced by BCG vaccine

BCG vaccination increased the nonspecific production of proinflammatory cytokines.

Subjects (age range, 20–36 y) who were scheduled to receive a BCG vaccination at the public health service, because of travel or work in TB-endemic countries, were asked to participate in this trial

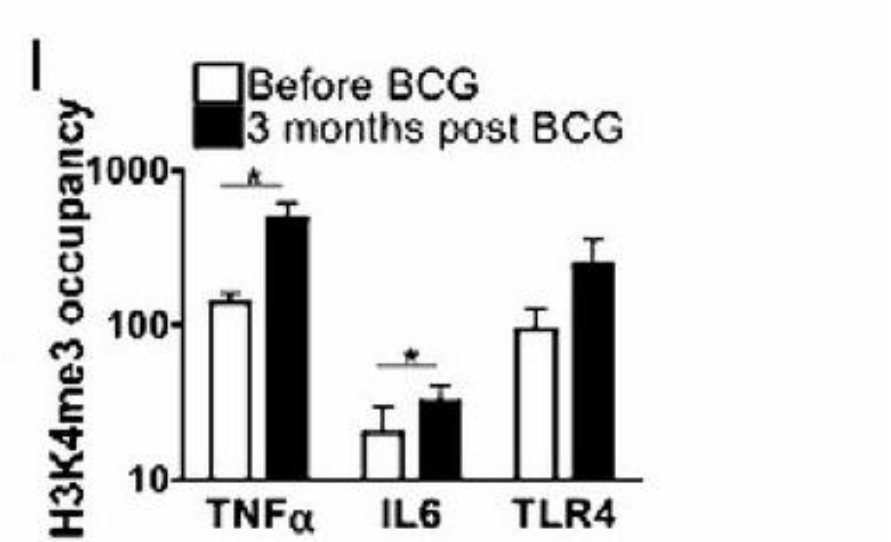


PBMC were stimulated in vitro with sonicated M. tuberculosis, heat-killed S. aureus, and C. albicans.

https://www.pnas.org/doi/10.1073/pnas.1202870109

‘Non-specific immunity’ induced by BCG vaccine

Increased H3K4 Trimethylation in Monocytes After BCG Vaccination



ChIP analysis of the enrichment of H3K4me3 at the promoter of *tnfα*, *il6* and *tlr4* in human monocytes isolated from three subjects before and 3 mo after BCG vaccination.

https://www.pnas.org/doi/10.1073/pnas.1202870109

‘Non-specific immunity’ leading to cross-protection

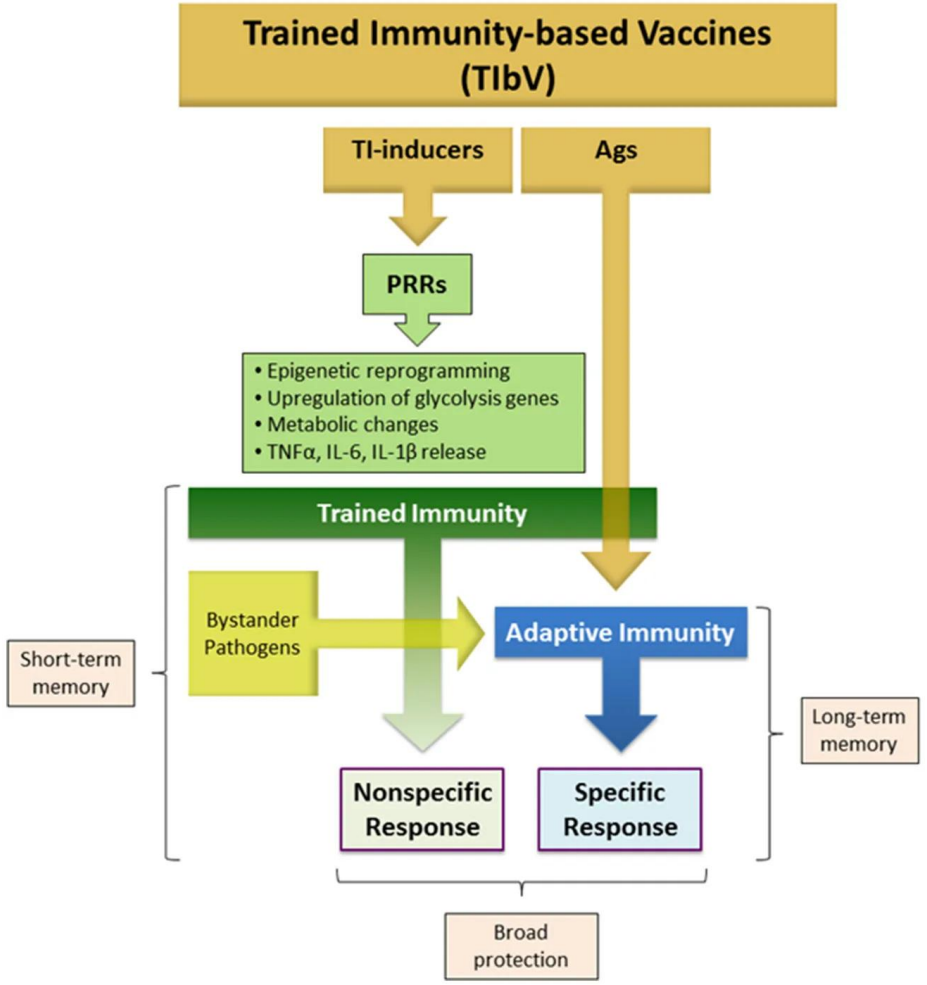
Pathogen recognition receptors (PRRs) expressed on innate immune cells, including long-lived macrophages and their precursors, are involved in the stimulation of trained immunity. Different PRRs have been involved in this task, such as **C-type lectin receptors** (CLRs) and **Nod-like receptors** (NLRs).

Training of the innate immunity is therefore based on **boosting non-specific immunity to re-infection by bacteria, fungi or viruses by certain pathogen's derived components.**

Component	Source	Cross-protection	References
LPS (endotoxin)	Most Gram-negative bacteria, such as *E. coli*	*Staphylococcus aureus*	(29)
Peptidoglycan component muramyl dipeptide	Bacteria	Toxoplasma	(30)
Flagellin	Gram-negative bacteria	Gram-positive bacterium *Streptococcus pneumoniae*	(31)
		Rotavirus	(32)
FimH	*E. coli*	Influenza virus	(33)
β-glucan	Fungi	*Staphylococcus aureus Streptococcus pneumoniae.*	(34)
Chitin	Fungi	*Staphylococcus aureus* or *Escherichia coli*	(35)
CpG oligodeoxynucleotide	Bacteria, synthetic	*E. coli*	(36)
		Influenza virus	(37)
			(38)

https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2018.02936/full

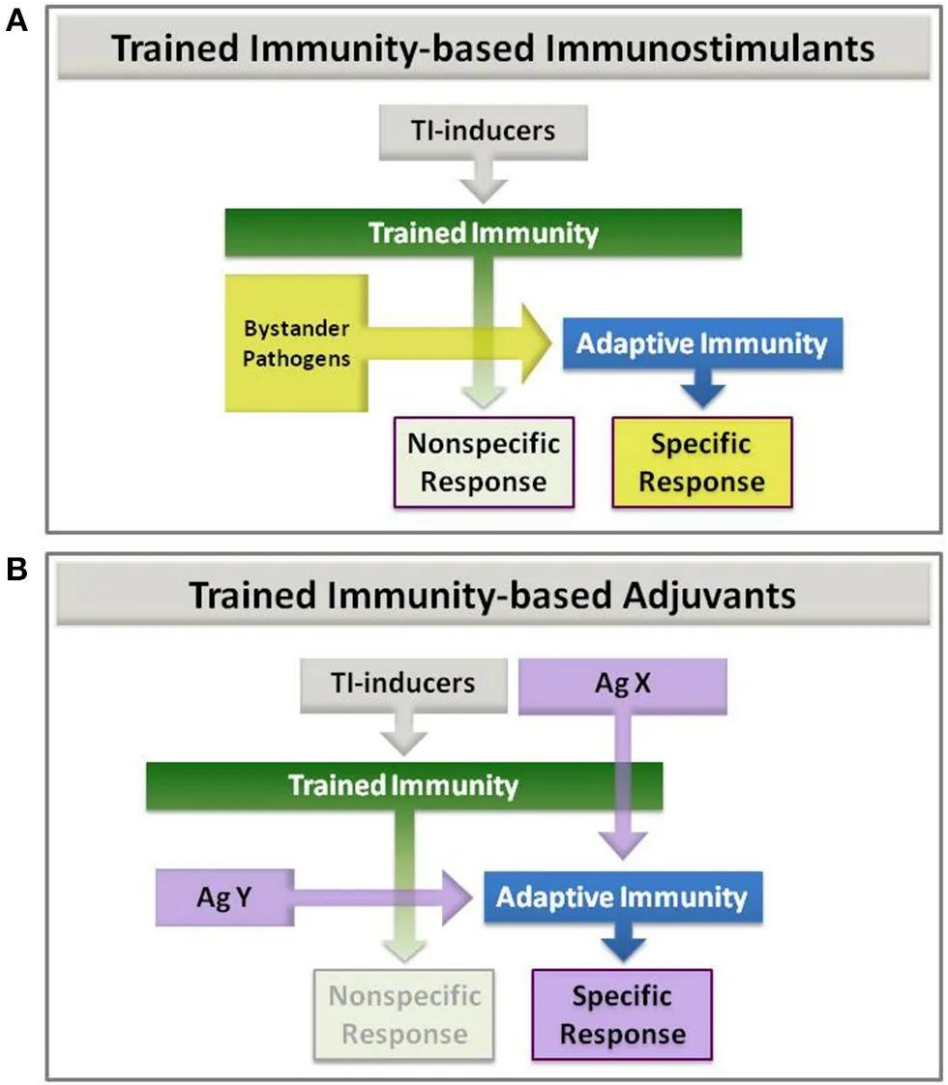
Trained immunity-based vaccines



(A) **Trained immunity (TI) inducers**: a range of PAMPs that target a variety of PRRs triggering different signaling pathways that mediate trained immunity. (B) **TIbV-related Ags**: the antigens associated with the pathogens acting as TI-inducers to which an adaptive immunity is aimed.

https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2018.02936/full

Trained immunity-based vaccines



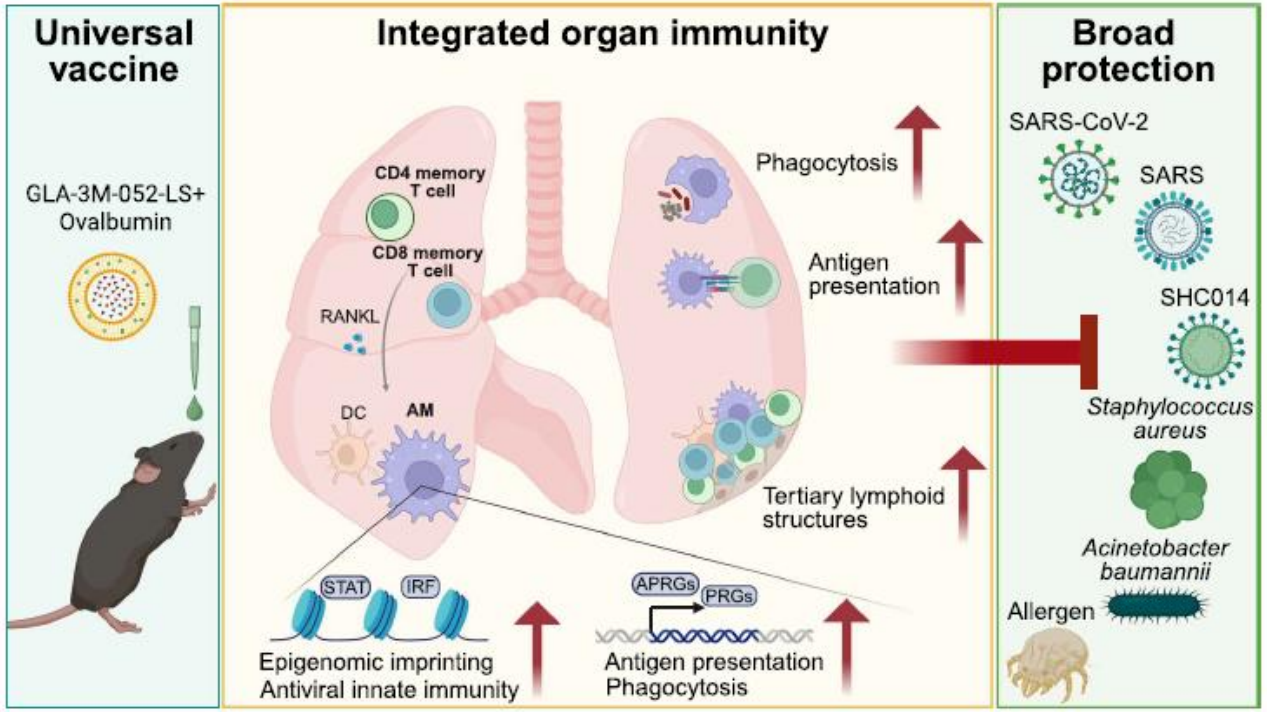
E.g. Candida-derived β-glucan is a paradigmatic example as it is a well-known inducer of trained immunity via dectin-1.

BCG was used as adjuvant for recombinant hepatitis B surface antigen vaccination. Even if the antigen may be administered in a second step once the trained immunity is induced.

https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2018.02936/full

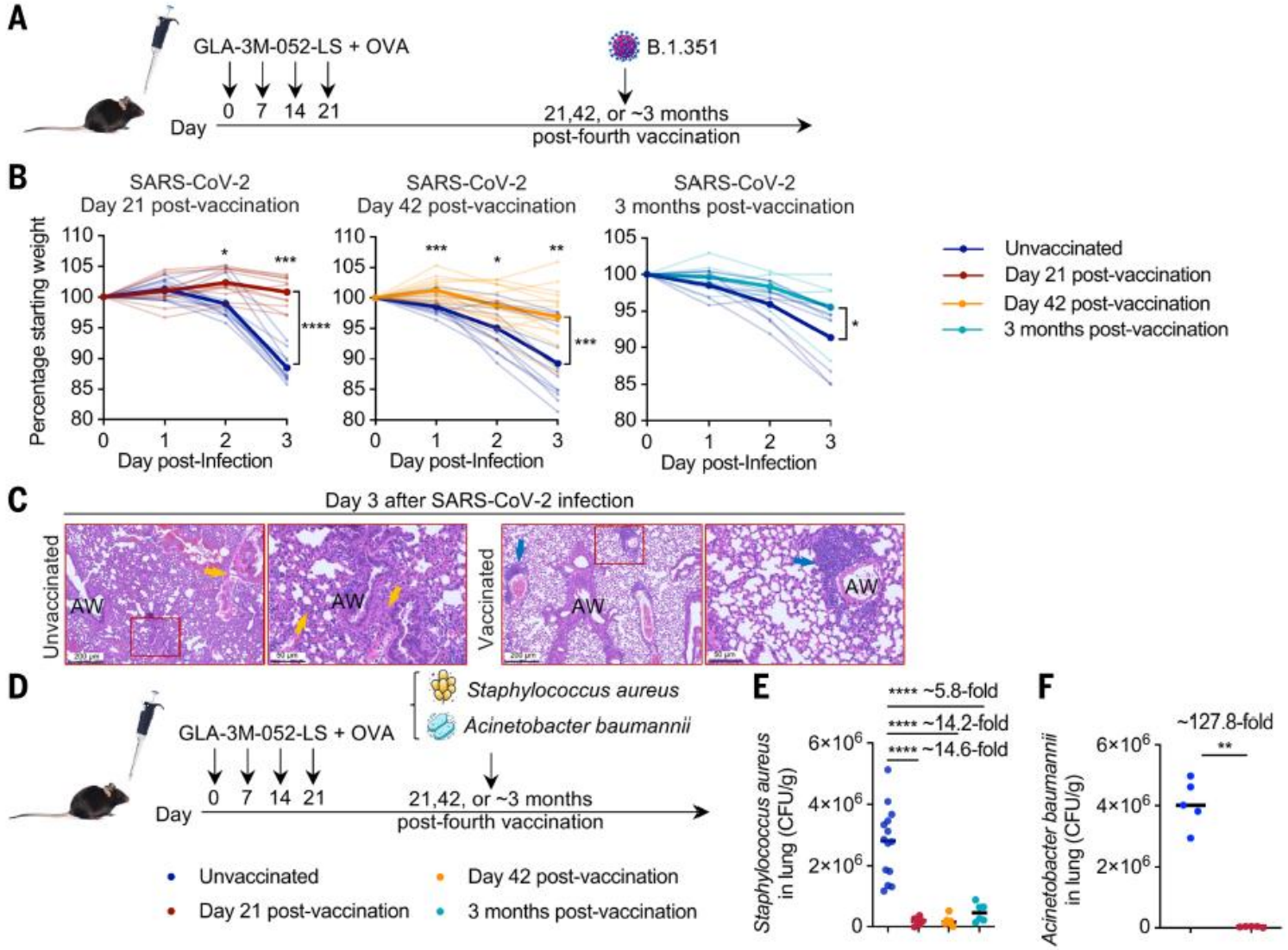
Pathogen-agnostic mucosal vaccine

Design principles of a pathogen-agnostic mucosal vaccine. Intranasal vaccination with a TLR-based liposomal formulation generates tissue-resident and circulating memory T cells which reprogram alveolar macrophages. These trained macrophages exhibit sustained innate activation, stronger antiviral defenses, and enhanced antigen uptake and presentation, underpinned by durable epigenetic remodeling. After vaccination, local immune responses and ectopic lymphoid structures rapidly form in the lung upon pathogen exposure.



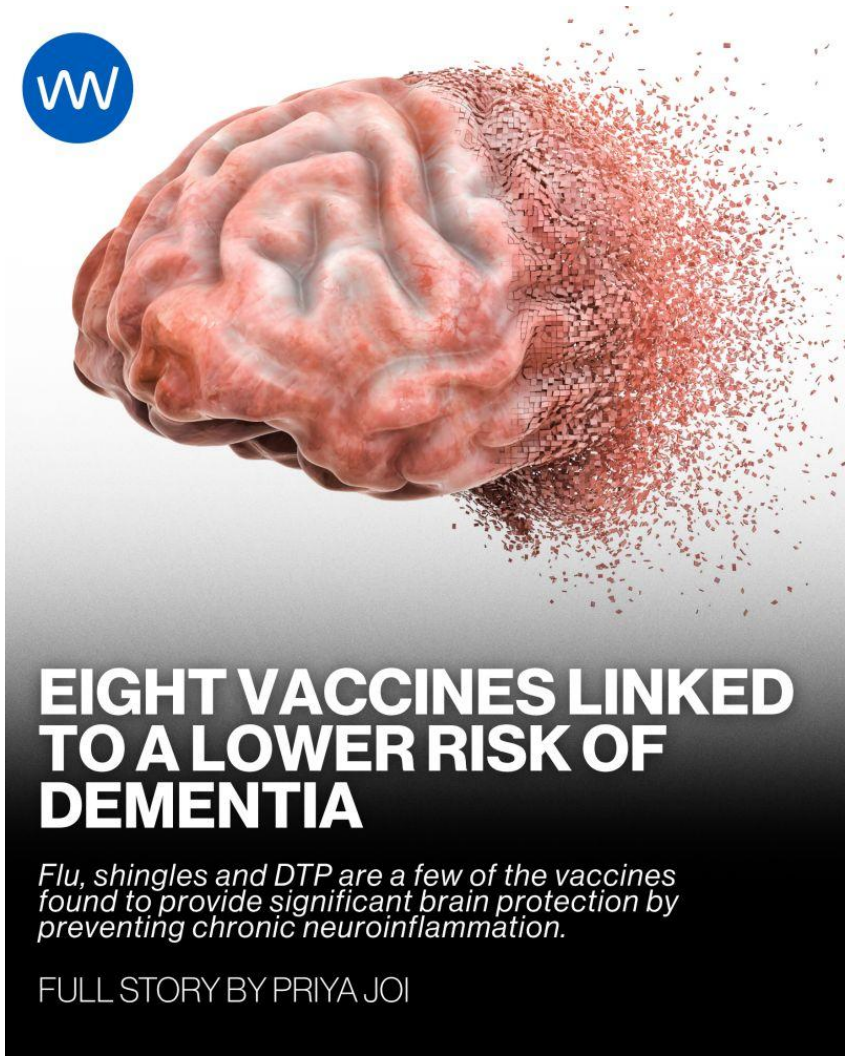
https://www.science.org/doi/10.1126/science.aea1260

Pathogen-agnostic mucosal vaccine



https://www.science.org/doi/10.1126/science.aea1260

Association between vaccinations and decreased risk of dementia



Vaccination against:

Shingles
RSV
Flu
DTP (diphtheria, tetanus and pertussis)
Pneumococcal
Hepatitis A
Hepatitis B
Typhoid

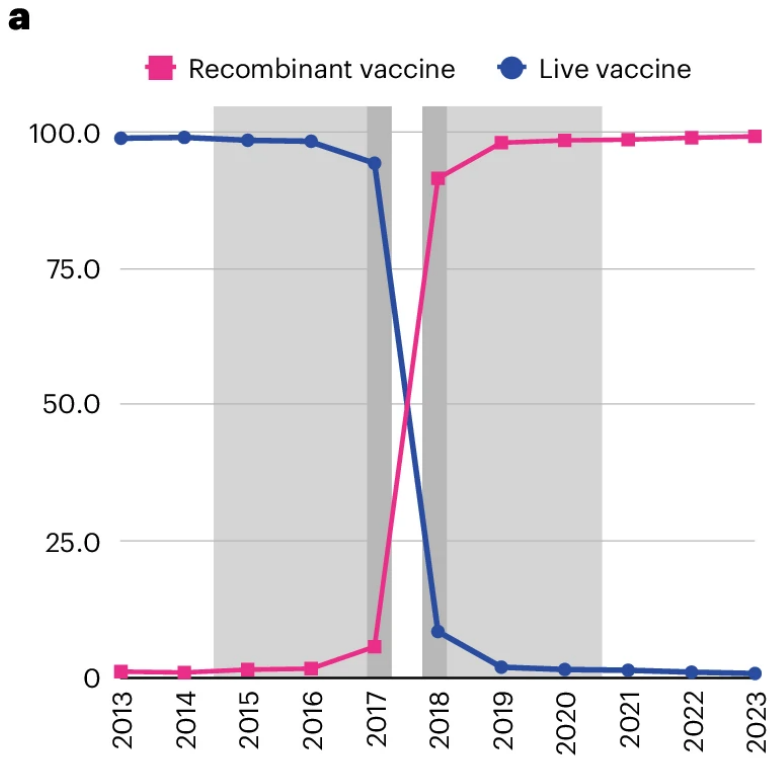
https://www.gavi.org/vaccineswork/eight-vaccines-linked-lower-risk-dementia

The recombinant shingles (Herpes zoster) vaccine is associated with lower risk of dementia

Cohorts included all patients who received their first shingles vaccine dose at the age of 65 or older between 1 November 2017 and 31 October 2020 (primary cohort) and between 1 October 2014 and 30 September 2017 (comparator cohort).

n = 103,837 in each cohort

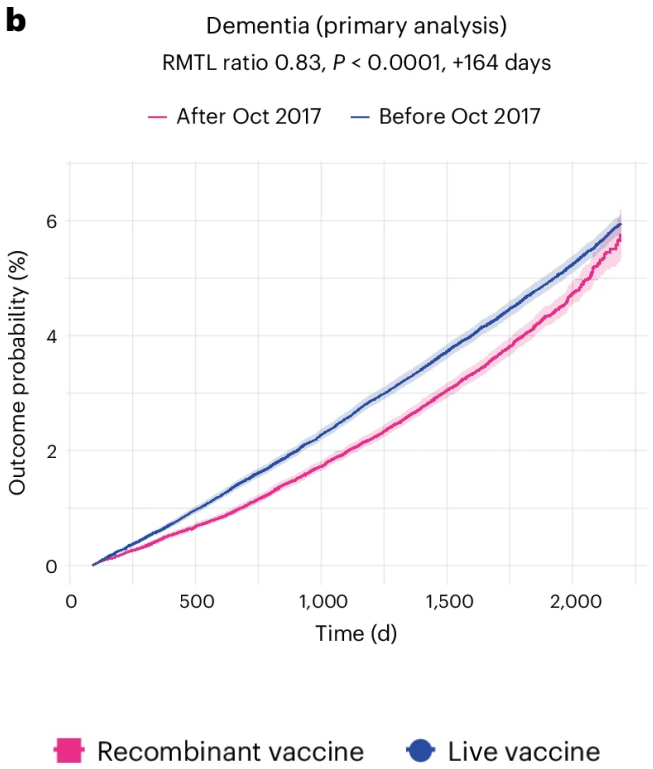
The primary outcome was **a first diagnosis of dementia from 3 months to 6 years post-vaccination** in a time-to-event analysis.

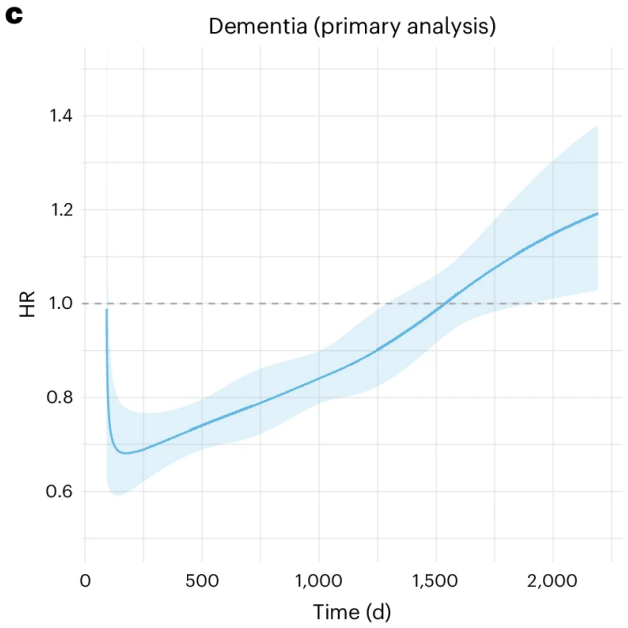


Vascular dementia
Dementia in other diseases classified elsewhere:
Unspecified dementia
Parkinson's disease
Other degenerative diseases of the nervous system, which include all other dementias not mentioned above (for example Alzheimer's disease).

https://www.nature.com/articles/s41591-024-03201-5#Sec3

The recombinant shingles vaccine is associated with lower risk of dementia





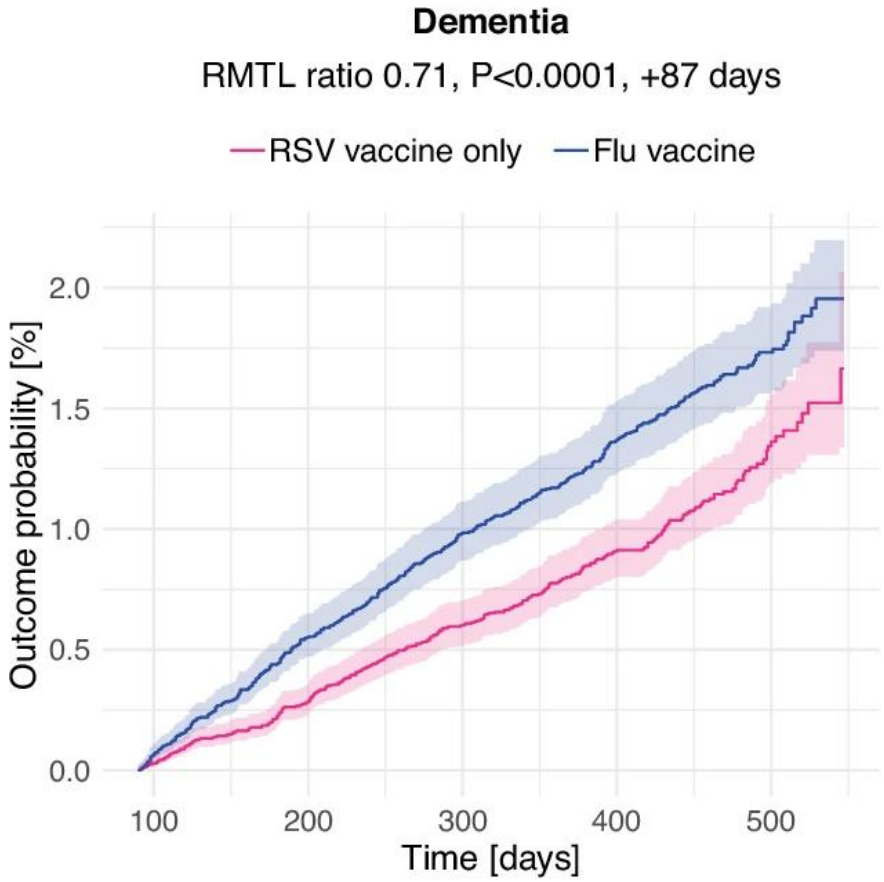
HR: Hazard ratio. HR < 1 indicates a lower risk of dementia

https://www.nature.com/articles/s41591-024-03201-5#Sec3

The AS01 RSV vaccine is associated with lower risk of dementia

Individuals (aged 60 or older) who received only the AS01 RSV vaccine (Arexvy), N= 35,938.

The primary outcome was a first diagnosis of dementia **from 3 months to 18 months post-vaccination in a time-to-event analysis**.



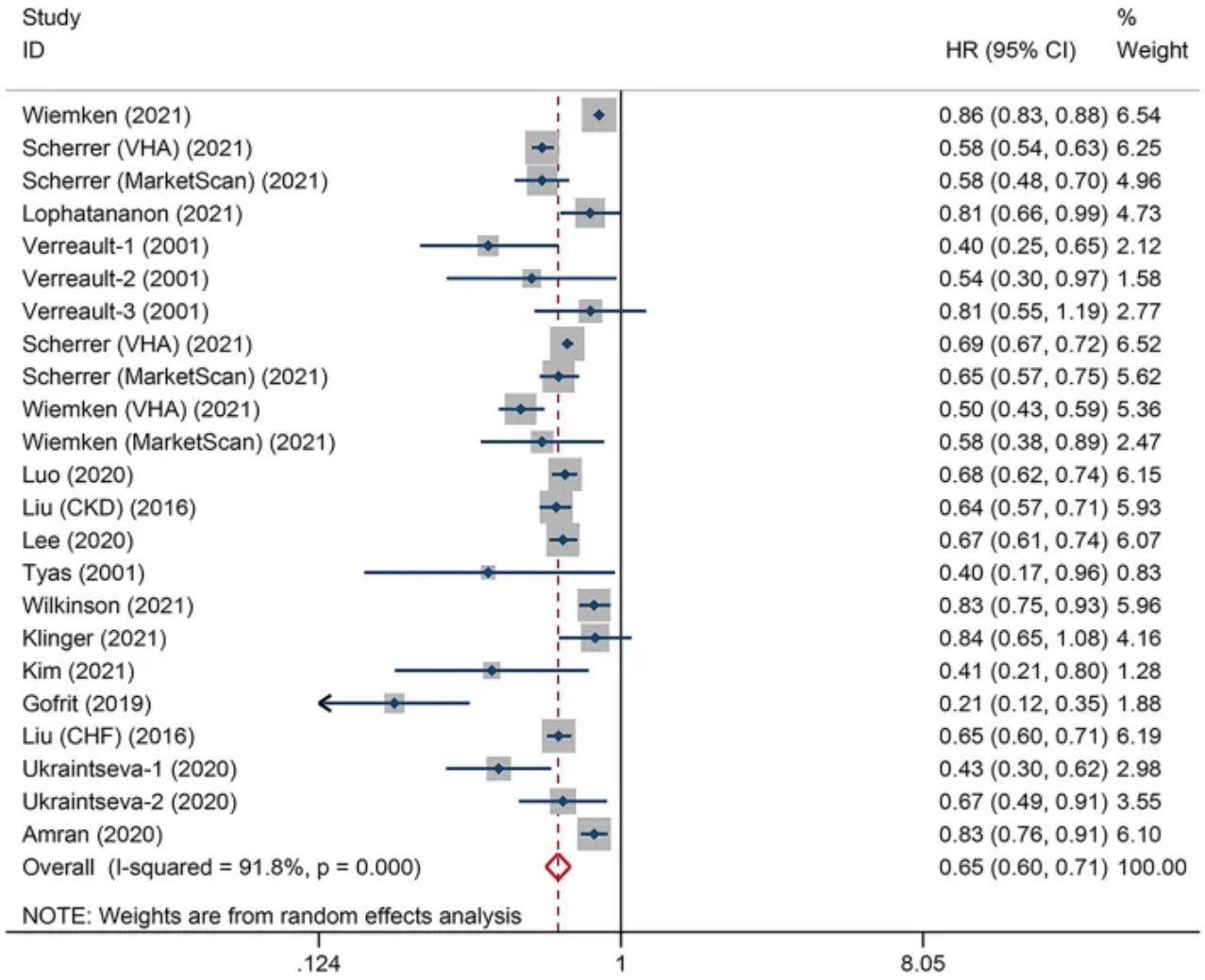
Vascular dementia.

- Dementia in other diseases classified elsewhere.
- Unspecified dementia.
- Parkinson's disease.

Other degenerative diseases of the nervous system, which include all other dementias not mentioned above (e.g. Alzheimer's disease).

https://www.nature.com/articles/s41541-025-01172-3#Sec1

A Meta-Analysis and Systematic Review of Population-Based Observational Studies



https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2022.872542/full

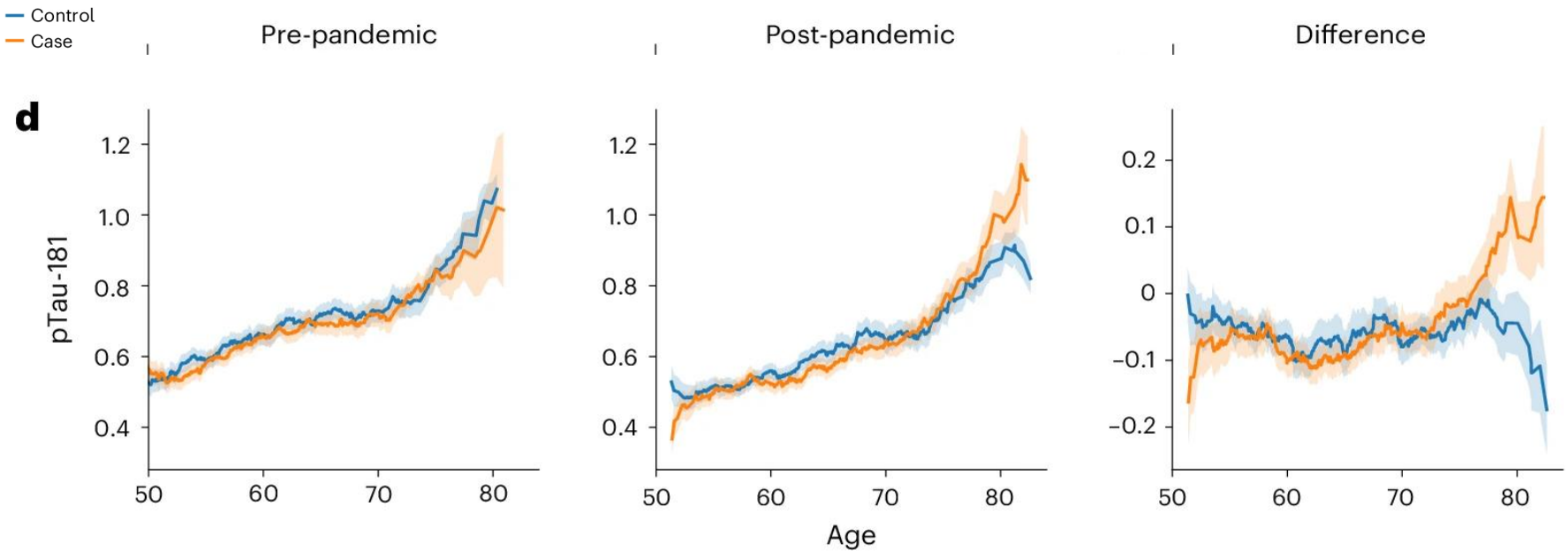
Subgroups	Studies	HR (95%CI)	$P_{overall\ effect}$	Heterogeneity (I^2, P_H)	Effects model
Total	17	0.65 (0.60, 0.71)	<0.001	91.8%, <0.001	Random
Vaccine type					
Influenza	9	0.74 (0.63, 0.87)	<0.001	97.7%, <0.001	Random
Herpes zoster	3	0.69 (0.67, 0.72)	<0.001	10.8%, 0.339	Fixed
Tdap[†]	3	0.69 (0.58, 0.82)	<0.001	97.1%, <0.001	Random
Bacillus Calmette–Guerin	3	0.42 (0.17, 1.07)	0.069	91.5%, <0.001	Random
Pneumonia	2	0.68 (0.41, 1.13)	0.137	92.8%, <0.001	Random
Poliomyelitis	2	0.78 (0.44, 1.40)	0.406	73.6%, 0.052	Random
Other	1	0.78 (0.74, 0.81)	<0.001	21.0%, 0.256	Fixed
Gender					
Male	5	0.66 (0.58, 0.74)	<0.001	56.8%, 0.055	Random
Female	5	0.67 (0.63, 0.72)	<0.001	0.0%, 0.911	Fixed
Age					
<70 years	5	0.74 (0.66, 0.84)	<0.001	72.6%, 0.001	Random
≥70 years	7	0.64 (0.57, 0.72)	<0.001	94.6%, <0.001	Random
Dose[‡]					
1 vaccine	3	1.03 (0.98, 1.08)	0.229	6.9%, 0.342	Fixed
2-3 vaccine	3	0.87 (0.74, 1.02)	0.088	88.9%, <0.001	Random
≥4 vaccine	4	0.51 (0.32, 0.80)	0.003	98.7%, <0.001	Random
Dementia type					
Alzheimer's disease	10	0.63 (0.55, 0.72)	<0.001	87.9%, <0.001	Random
Vascular dementia	1	0.60 (0.45, 0.80)	<0.001	NA	NA
Other dementia	1	0.69 (0.62, 0.75)	<0.001	NA	NA

https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2022.872542/full

Hypothesis 1: vaccines prevent infections, and infections cause inflammation that can damage the brain

Example: people who had previously contracted COVID-19 showed increased levels of blood biomarkers linked to amyloid build-up in the brain, which is linked to Alzheimer's disease

Plasma proteomic evidence for increased β-amyloid pathology after SARS-CoV-2 infection



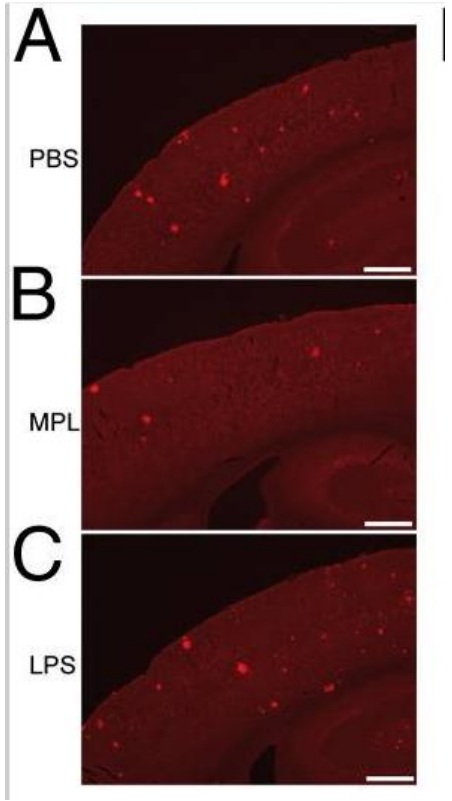
https://www.nature.com/articles/s41591-024-03426-4

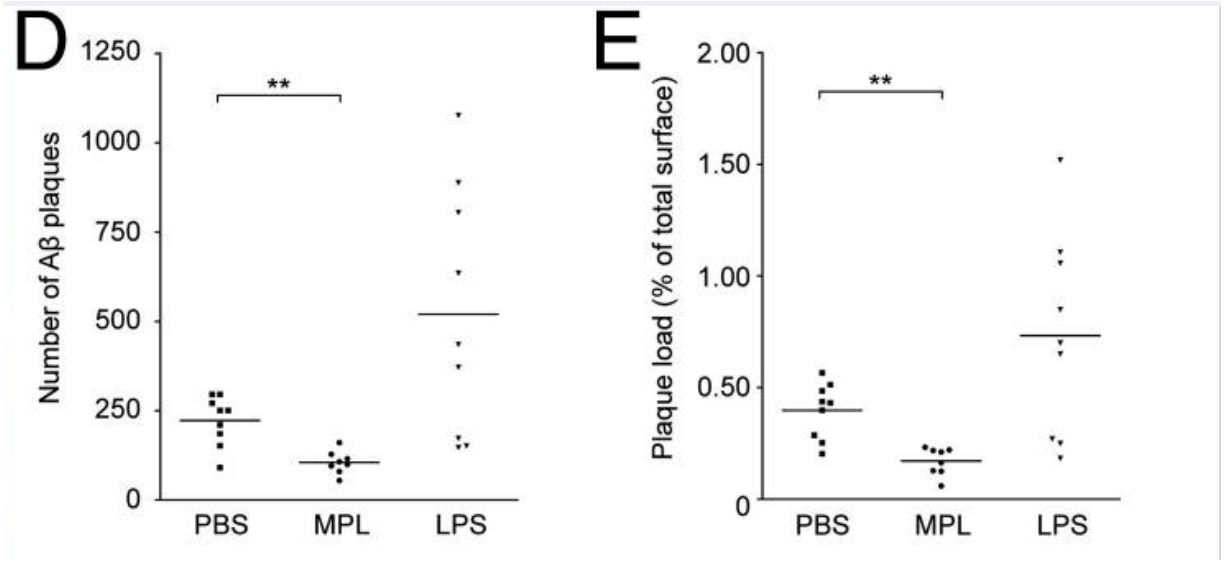
Hypothesis 2: vaccines can have broader effects on the immune system beyond protection against a single pathogen

Example: AS01 might protect against dementia via specific immunological pathways

AS01 is a family of liposome-based vaccine Adjuvant Systems containing two immunostimulants: 3-O-desacyl-4'-monophosphoryl lipid A (MPL, TLR4 activator) and the saponin QS-21 (a purified plant extract derived from Quillaja saponaria)

TLR4 stimulation with MPL has been shown to improve Alzheimer's disease pathology in mice





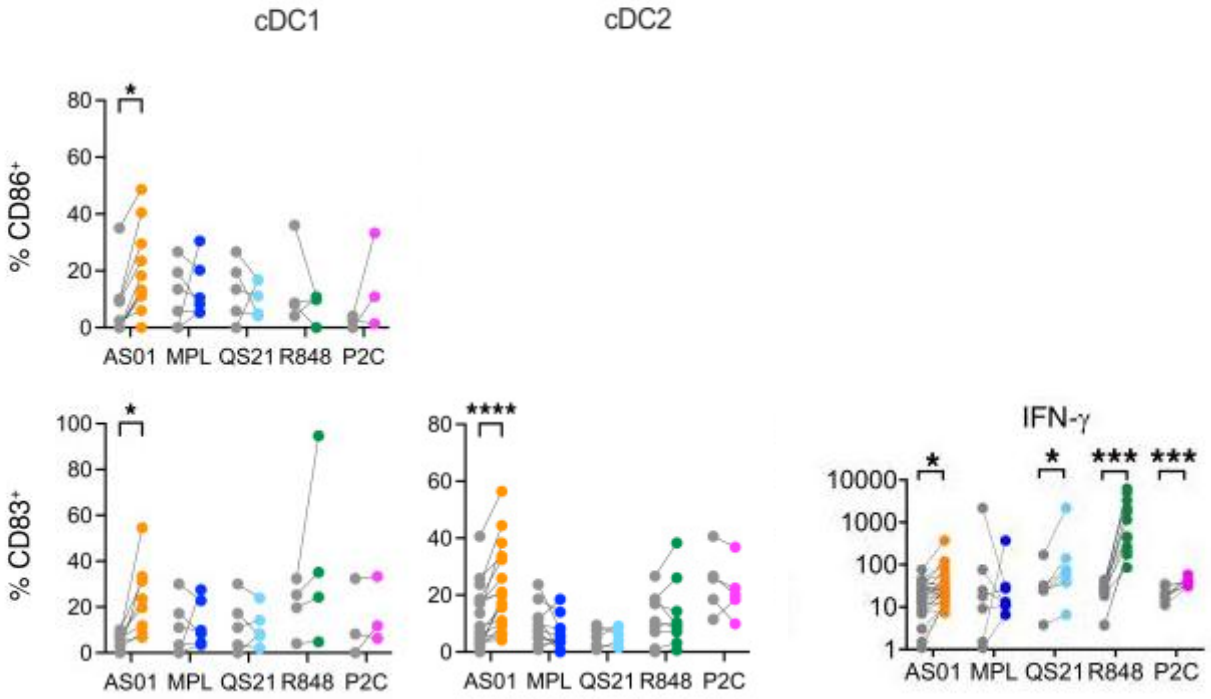
APP/PS1 are double transgenic mice expressing a chimeric mouse/human amyloid precursor protein (Mo/HuAPP695swe) and a mutant human presenilin 1 (PS1-dE9)

Mouse model

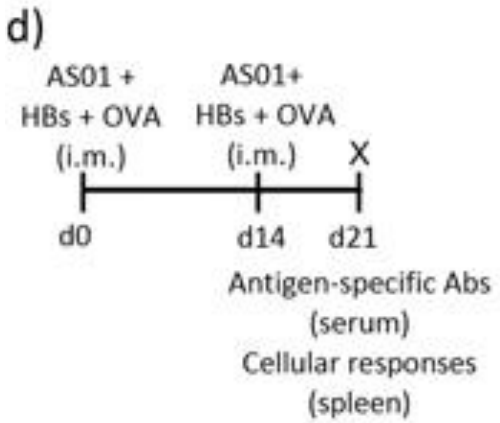
https://pmc.ncbi.nlm.nih.gov/articles/PMC3562771/#s3

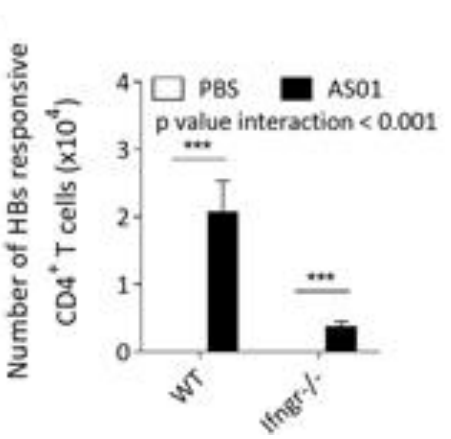
Hypothesis 2: vaccines can have broader effects on the immune system beyond protection against a single pathogen

AS01 activates dendritic cells and trigger an age-independent cytokine cascade that culminates in the production of interferon gamma (IFN-γ). IFN-γ might attenuate amyloid plaque deposition (as seen in mice) and is negatively correlated with cognitive decline in cognitively unimpaired older adults.



Ex vivo human lymph nodes





Mice

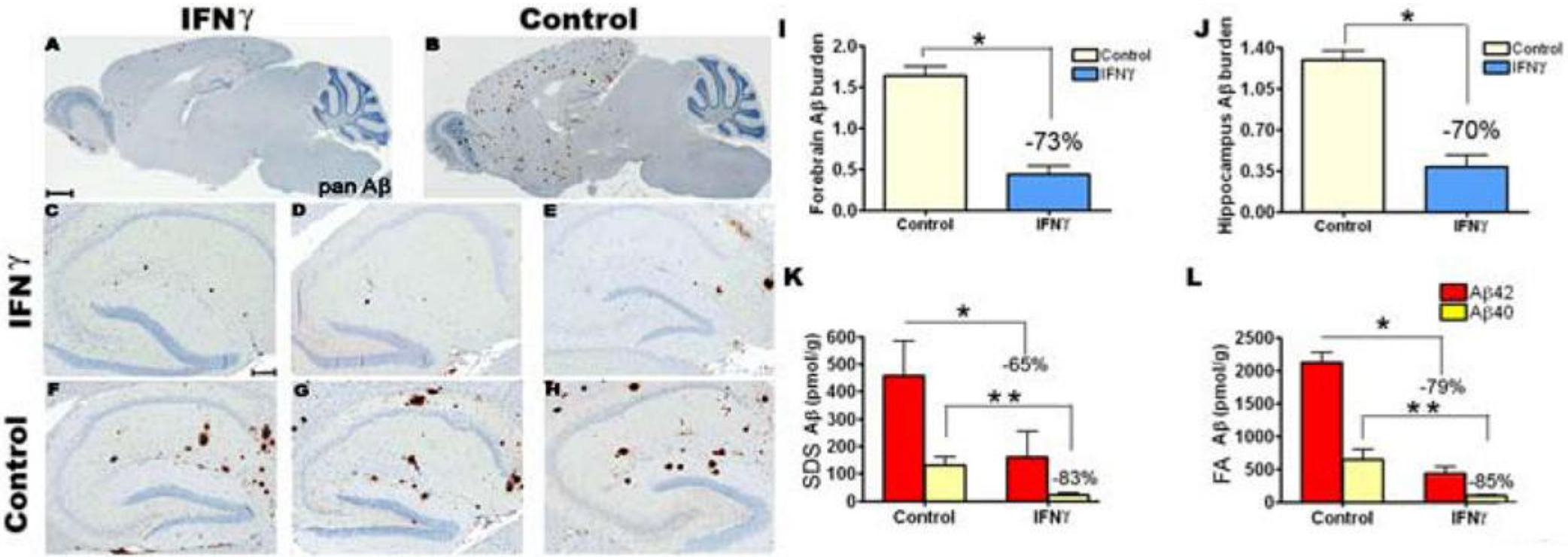
https://pmc.ncbi.nlm.nih.gov/articles/PMC11563676/

https://pmc.ncbi.nlm.nih.gov/articles/PMC5627273/#Sec2

Hypothesis 2: vaccines can have broader effects on the immune system beyond protection against a single pathogen

Recombinant adeno-associated virus serotype 1 to express murine IFNγ in the brains of APP transgenic TgCRND8 mice

Significant attenuation of amyloid deposition in murine IFNγ expressing (P2→5mo) TgCRND8 mice

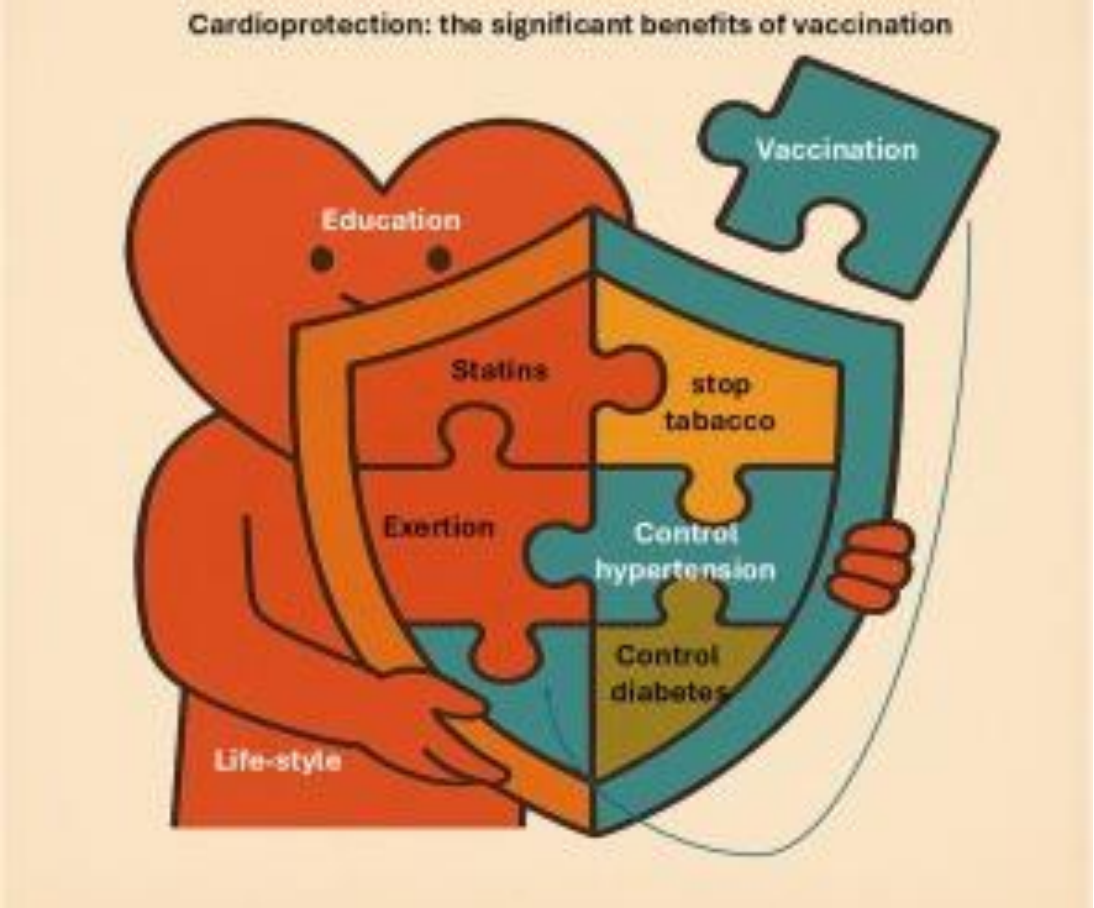


https://pmc.ncbi.nlm.nih.gov/articles/PMC3798002/

Hypothesis 3: people who get vaccinated might be more likely overall to look after their health, and that broader health advantage may explain at least part of the observed risk reduction.

To be evaluated…

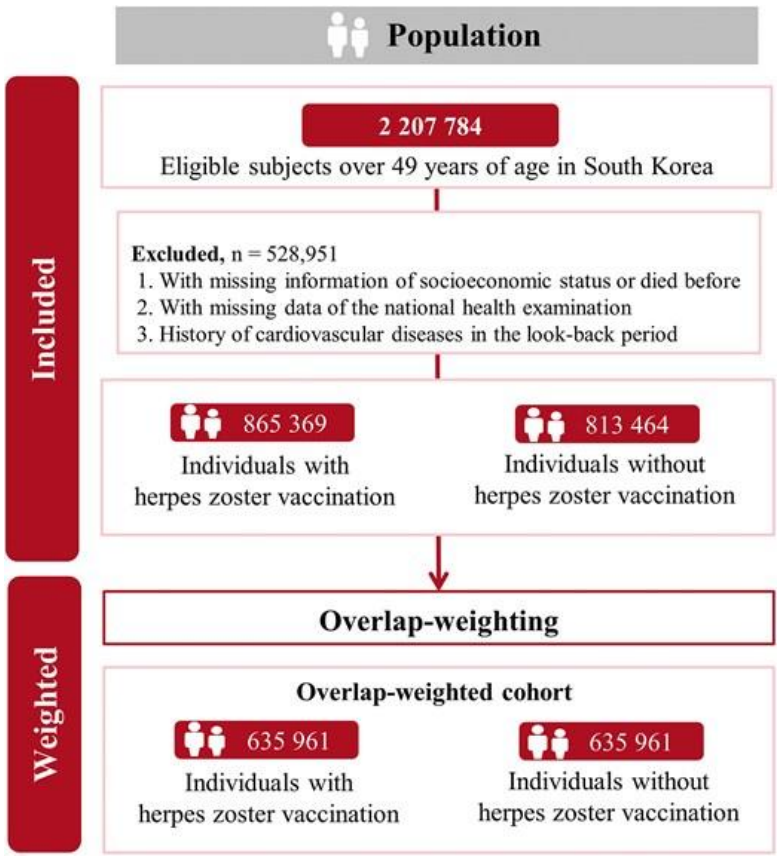
Vaccination reduces the risk of major adverse cardiovascular events



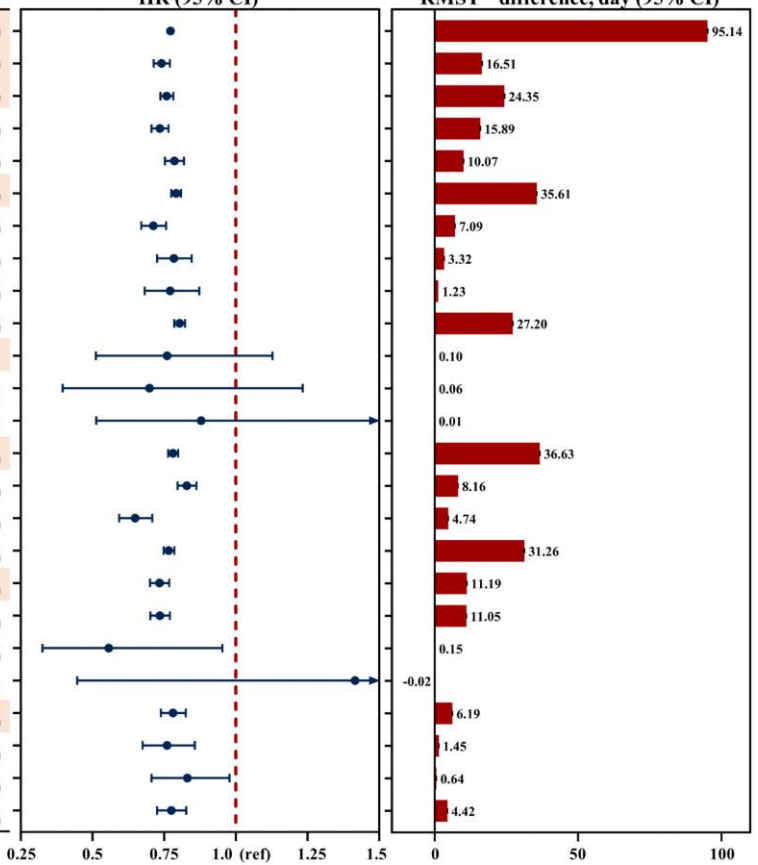
https://www.sciencedirect.com/science/article/pii/S1875213625004620#bib0075

Shingles vaccination reduces the risk of major adverse cardiovascular events

Live zoster vaccination was designated as the exposure variable. The primary outcome was the new onset of any cardiovascular event after at least 30 days following vaccination.



	Events, *n* (%)		
	Unvaccinated	Vaccinated	HR (95% CI)
Any cardiovascular diseases outcome	102,776 (16.16)	78,463 (12.34)	**0.77 (0.76 to 0.78)**
MACE	14,549 (2.29)	10,284 (1.62)	**0.74 (0.71 to 0.77)**
Cerebrovascular disorders	23,249 (3.66)	17,040 (2.68)	**0.76 (0.74 to 0.78)**
Stroke	13,602 (2.14)	9626 (1.51)	**0.74 (0.71 to 0.77)**
Transient ischemic attack	11,022 (1.73)	8364 (1.32)	**0.79 (0.75 to 0.82)**
Dysrhythmia	40,233 (6.33)	30,740 (4.83)	**0.79 (0.77 to 0.81)**
Atrial fibrillation	5825 (0.92)	4025 (0.63)	**0.71 (0.67 to 0.76)**
Sinus tachycardia	3260 (0.51)	2405 (0.38)	**0.78 (0.73 to 0.85)**
Sinus bradycardia	1290 (0.20)	960 (0.15)	**0.77 (0.68 to 0.87)**
Ventricular arrhythmias	32,681 (5.14)	25,274 (3.97)	**0.80 (0.78 to 0.82)**
Inflammatory heart disease	125 (0.020)	96 (0.015)	0.76 (0.51 to 1.13)
Pericarditis	63 (0.010)	45 (0.007)	0.70 (0.40 to 1.23)
Myocarditis	62 (0.010)	54 (0.008)	0.88 (0.51 to 1.51)
Ischaemic heart disease	40,774 (6.41)	31,167 (4.90)	**0.78 (0.76 to 0.80)**
Acute coronary disease	12,610 (1.98)	10,118 (1.59)	**0.83 (0.80 to 0.86)**
Myocardial infarction	2999 (0.47)	1879 (0.30)	**0.65 (0.59 to 0.71)**
Angina	32,109 (5.05)	24,064 (3.78)	**0.77 (0.75 to 0.79)**
Other cardiac disorders	10,084 (1.59)	7177 (1.13)	**0.73 (0.70 to 0.77)**
Heart failure	9995 (1.57)	7122 (1.12)	**0.74 (0.70 to 0.77)**
Cardiac arrest	88 (0.014)	52 (0.008)	**0.56 (0.33 to 0.95)**
Cardiogenic shock	10 (0.0016)	13 (0.0020)	1.42 (0.44 to 4.52)
Thrombotic disorders	6633 (1.04)	4960 (0.78)	**0.78 (0.74 to 0.83)**
Arterial embolism and thrombosis	1441 (0.23)	1058 (0.17)	**0.76 (0.67 to 0.86)**
Pulmonary embolism	758 (0.12)	576 (0.09)	**0.83 (0.71 to 0.98)**
Deep vein thrombosis	4641 (0.73)	3452 (0.54)	**0.78 (0.73 to 0.83)**

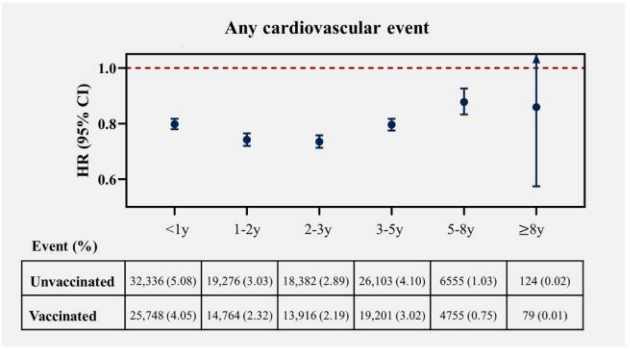


https://academic.oup.com/eurheartj/article/46/30/2991/8124786?login=true

Shingles vaccination reduces the risk of major adverse cardiovascular events

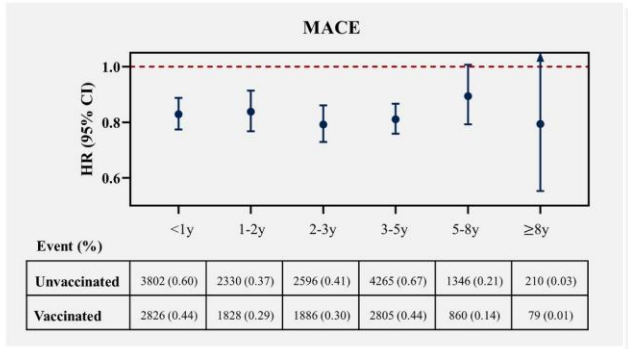
Time persistence association with the development of overall cardiovascular events after zoster vaccination

Major adverse cardiac events



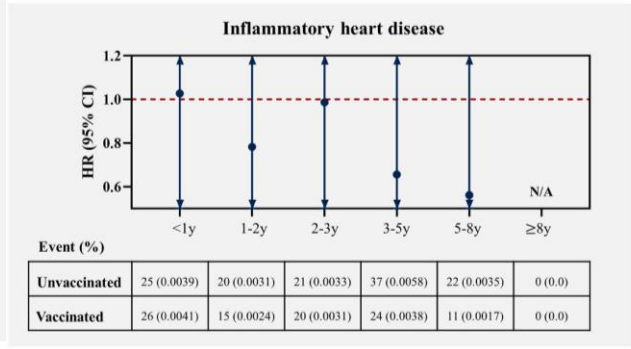
Event (%)

	<1y	1-2y	2-3y	3-5y	5-8y	≥8y
Unvaccinated	32,336 (5.08)	19,276 (3.03)	18,382 (2.89)	26,103 (4.10)	6555 (1.03)	124 (0.02)
Vaccinated	25,748 (4.05)	14,764 (2.32)	13,916 (2.19)	19,201 (3.02)	4755 (0.75)	79 (0.01)



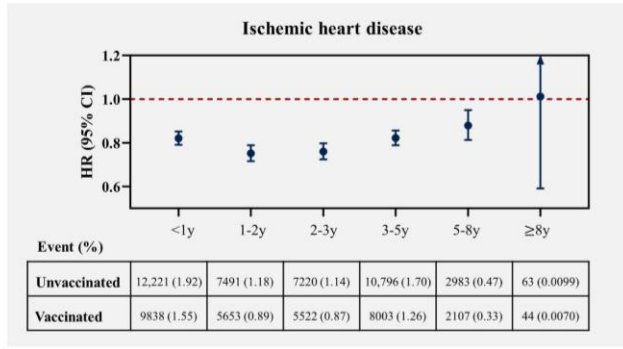
Event (%)

	<1y	1-2y	2-3y	3-5y	5-8y	≥8y
Unvaccinated	3802 (0.60)	2330 (0.37)	2596 (0.41)	4265 (0.67)	1346 (0.21)	210 (0.03)
Vaccinated	2826 (0.44)	1828 (0.29)	1886 (0.30)	2805 (0.44)	860 (0.14)	79 (0.01)



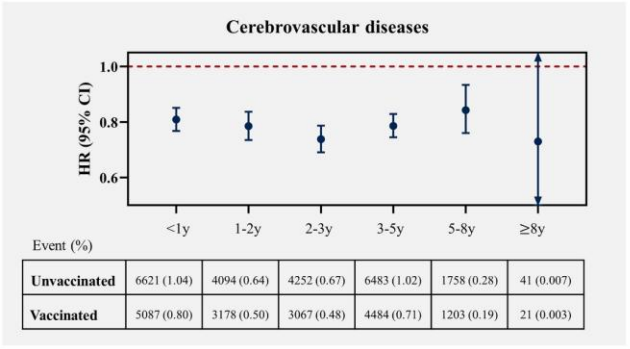
Event (%)

	<1y	1-2y	2-3y	3-5y	5-8y	≥8y
Unvaccinated	25 (0.0039)	20 (0.0031)	21 (0.0033)	37 (0.0058)	22 (0.0035)	0 (0.0)
Vaccinated	26 (0.0041)	15 (0.0024)	20 (0.0031)	24 (0.0038)	11 (0.0017)	0 (0.0)



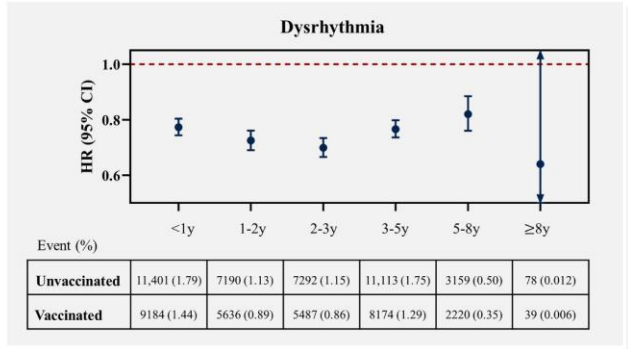
Event (%)

	<1y	1-2y	2-3y	3-5y	5-8y	≥8y
Unvaccinated	12,221 (1.92)	7491 (1.18)	7220 (1.14)	10,796 (1.70)	2983 (0.47)	63 (0.0099)
Vaccinated	9838 (1.55)	5653 (0.89)	5522 (0.87)	8003 (1.26)	2107 (0.33)	44 (0.0070)



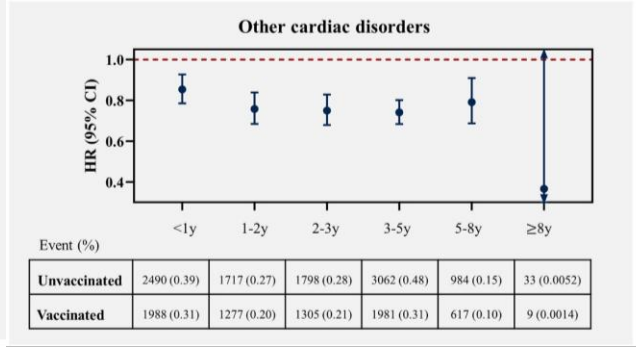
Event (%)

	<1y	1-2y	2-3y	3-5y	5-8y	≥8y
Unvaccinated	6621 (1.04)	4094 (0.64)	4252 (0.67)	6483 (1.02)	1758 (0.28)	41 (0.007)
Vaccinated	5087 (0.80)	3178 (0.50)	3067 (0.48)	4484 (0.71)	1203 (0.19)	21 (0.003)



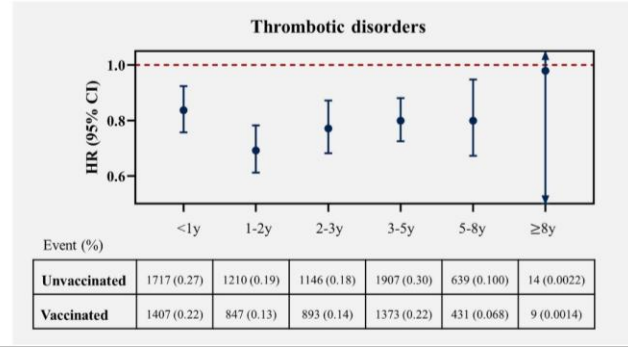
Event (%)

	<1y	1-2y	2-3y	3-5y	5-8y	≥8y
Unvaccinated	11,401 (1.79)	7190 (1.13)	7292 (1.15)	11,113 (1.75)	3159 (0.50)	78 (0.012)
Vaccinated	9184 (1.44)	5636 (0.89)	5487 (0.86)	8174 (1.29)	2220 (0.35)	39 (0.006)



Event (%)

	<1y	1-2y	2-3y	3-5y	5-8y	≥8y
Unvaccinated	2490 (0.39)	1717 (0.27)	1798 (0.28)	3062 (0.48)	984 (0.15)	33 (0.0052)
Vaccinated	1988 (0.31)	1277 (0.20)	1305 (0.21)	1981 (0.31)	617 (0.10)	9 (0.0014)



Event (%)

	<1y	1-2y	2-3y	3-5y	5-8y	≥8y
Unvaccinated	1717 (0.27)	1210 (0.19)	1146 (0.18)	1907 (0.30)	639 (0.100)	14 (0.0022)
Vaccinated	1407 (0.22)	847 (0.13)	893 (0.14)	1373 (0.22)	431 (0.068)	9 (0.0014)

https://academic.oup.com/eurheartj/article/46/30/2991/8124786?login=true

Meta-analysis: polysaccharide pneumococcal vaccination decreases the risk of a cardiovascular events

18 studies were included, with a total of 716,108 participants. Vaccination with PPV23 was associated with decreased risk of **any cardiovascular event** (RR: 0.91;95% CI: 0.84-0.99), and **MI** (RR of 0.88; 95% CI:0.79-0.98) in all age groups, **with a significant effect in those 65 years** and older, but not in the younger age group.

Similarly, PPV23 vaccine was associated with significant risk reduction in all-cause mortality in all ages (RR: 0.78; 95%CI: 0.68-0.88), specifically in those aged 65 years and older (RR: 0.71; 95%CI: 0.60-0.84).

A significant risk reduction in cerebrovascular disease was not observed following pneumococcal vaccination.

https://pmc.ncbi.nlm.nih.gov/articles/PMC7776373/

Inconsistent results…

Double-blind, placebo-controlled, parallel-arm randomized clinical trial conducted at 6 centers across Australia.

Participants were **community-dwelling adults 55 to 60 years of age** at baseline in 2016 to 2017, with at least **2 risk factors (obesity, hypertension, or hypercholesterolemia) for cardiovascular disease** but no prior CVD event or indication for early pneumococcal vaccination. N= 4725.

-> 23-valent PPV (PPV23) or placebo (saline)

The primary outcome was a composite of fatal and nonfatal myocardial infarction or ischemic stroke

No significant difference in the primary outcome (58 of 2366 events in the active PPV23 group compared with 64 of 2357 events in the control group, hazard ratio, 0.90; 95% CI, 0.63-1.28; *P* = .57) !

https://jamanetwork.com/journals/jamacardiology/article-abstract/2839121

Meta-analysis: pre-infection COVID-19 vaccination is associated with lower risks of cardiovascular, cerebrovascular, and venous thromboembolism events following SARS-CoV-2 infection in the pre- and post-Omicron eras

23 studies

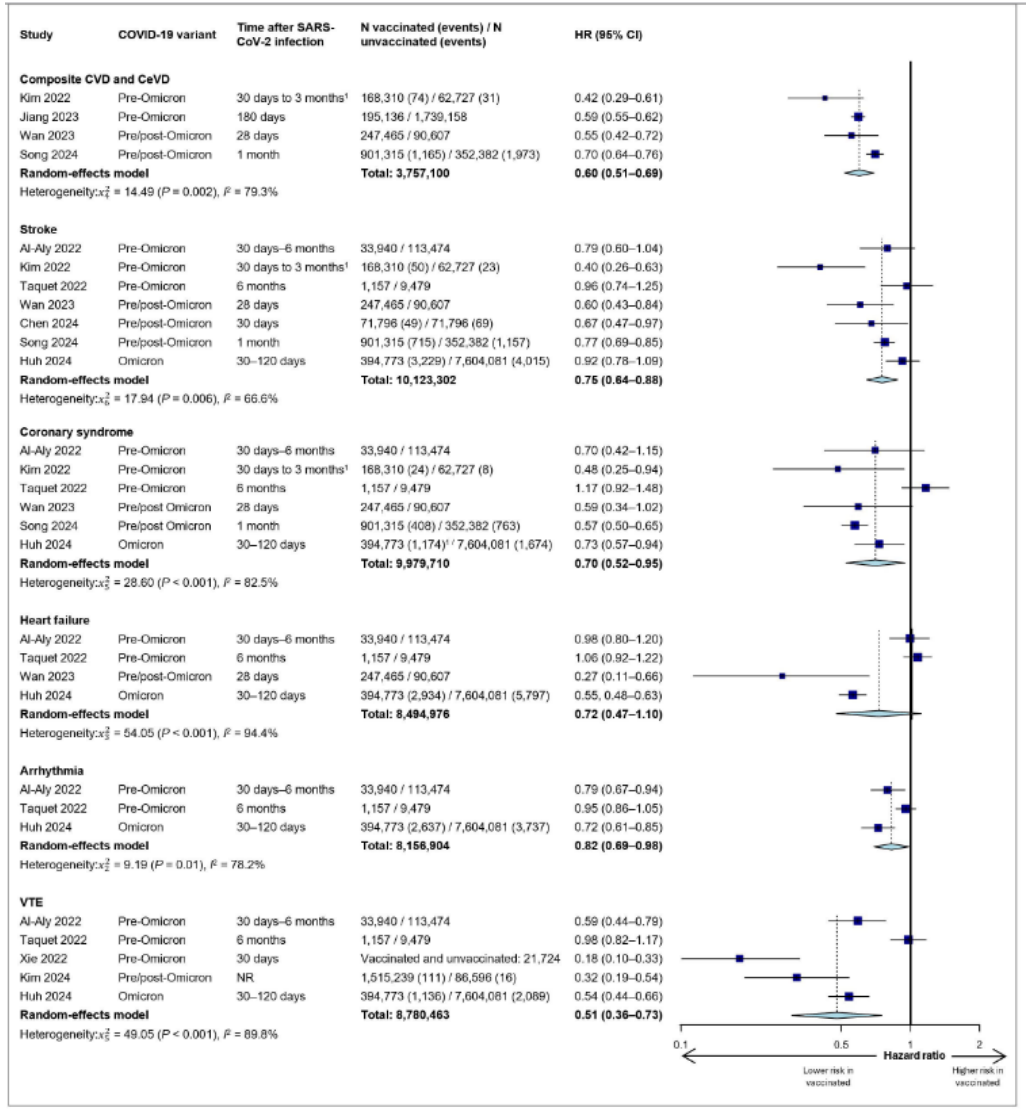
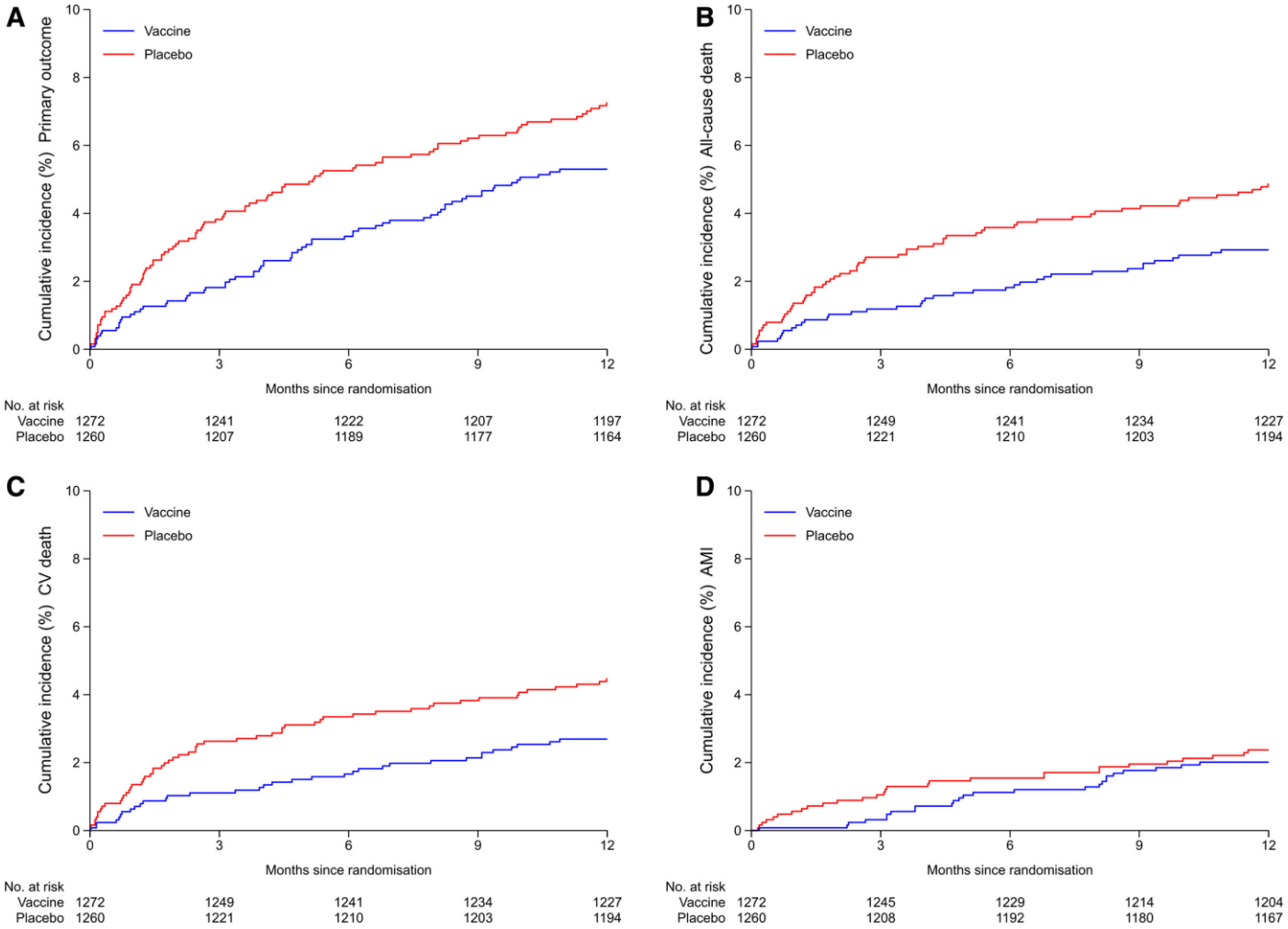


Figure 2 Pooled HRs (random-effects) of the risks of CVD/CeVD/VTE events after SARS-CoV-2 infection in COVID-19-vaccinated individuals compared with unvaccinated individuals.

https://www.medrxiv.org/content/10.64898/2026.05.21.26353568v1.full

Influenza Vaccination After Myocardial Infarction

1290 vaccine versus 1281 placebo

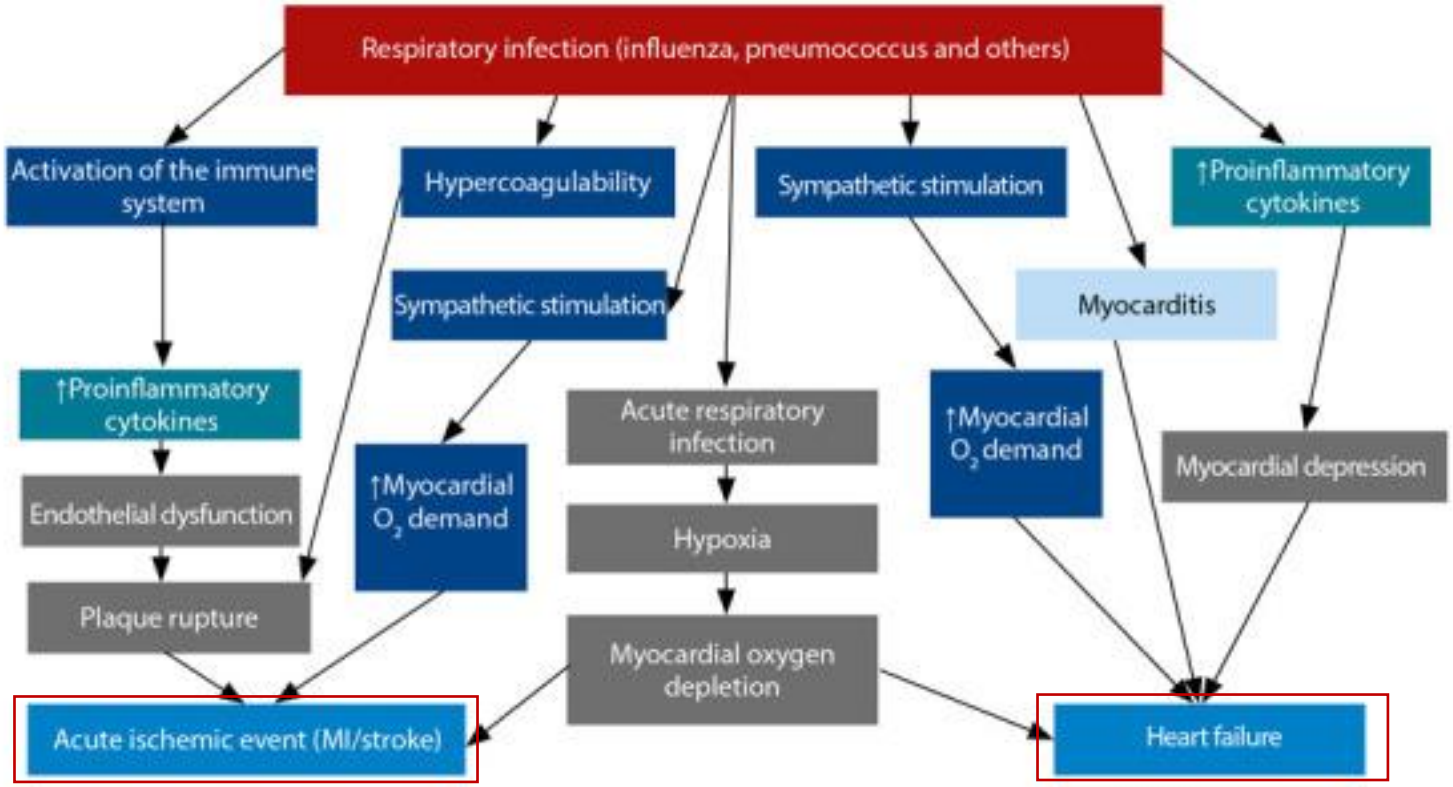


AMI indicates acute myocardial infarction; and CV, cardiovascular.

Influenza vaccination early after an MI or in high-risk coronary heart disease resulted in a lower risk of a composite of all-cause death, MI, or stent thrombosis, and a lower risk of all-cause death and cardiovascular death, as well, at 12 months compared with placebo.

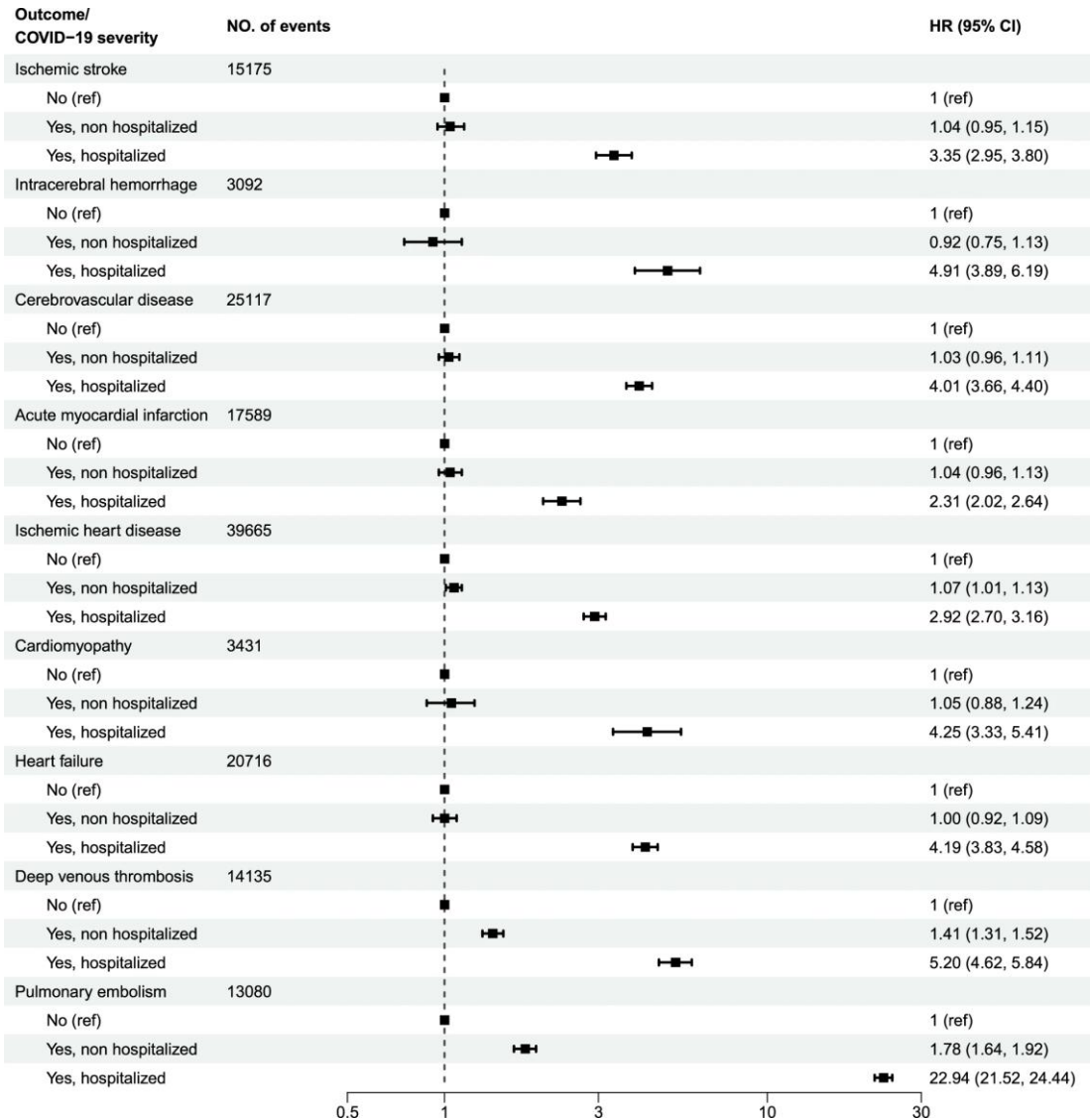
https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.121.057042?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

Indirect roles of vaccines



https://pmc.ncbi.nlm.nih.gov/articles/PMC10999318/

Indirect effects of vaccines by reducing the risks linked to infections



https://www.nature.com/articles/s41467-025-66270-1

Conclusion

- Induction of antigen-specific responses -> protection

- Indirect biological effects
  - ➢ Trained immunity
  - ➢ Impact on the development of dementia
  - ➢ Influence on the risk of cardiovascular events