

Impfungen und Demenz Doppelter Nutzen?

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Übersicht

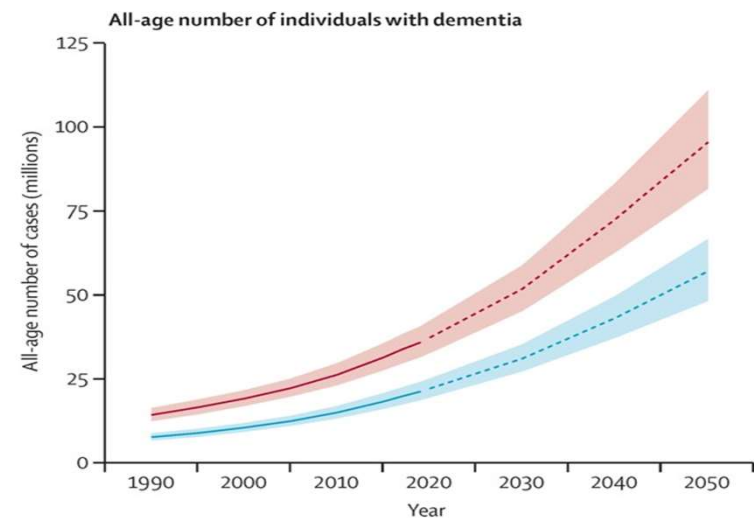
- Kurzer Refresher: Demenz
 - Epidemiologie
 - Prävention
 - Behandlung
- Infektion und Neurodegeneration
- Herpes Zoster Impfung
 - Beobachtungsstudien
 - Natural experiments
- Zusammenfassung

Demenz

- Chronisch progrediente Erkrankung mit Einfluss auf
 - Gedächtnis
 - Aufmerksamkeit/Konzentration
 - Sprache
 - Emotionaler Kontrolle
 - Sozialverhalten
- Mindestens 6 Monate
- Keine Störung des Bewusstseins
- Beeinträchtigung der Alltagsfunktionen

Epidemiologie

- Schätzung in Österreich
 - ca. 150-175.000 Menschen Leben mit Demenz (Wurm et al, 2022)
 - Verdoppelung bis 2050
- Weltweit ca. 55 Millionen erkrankt
 - Verdreifachung bis 2050

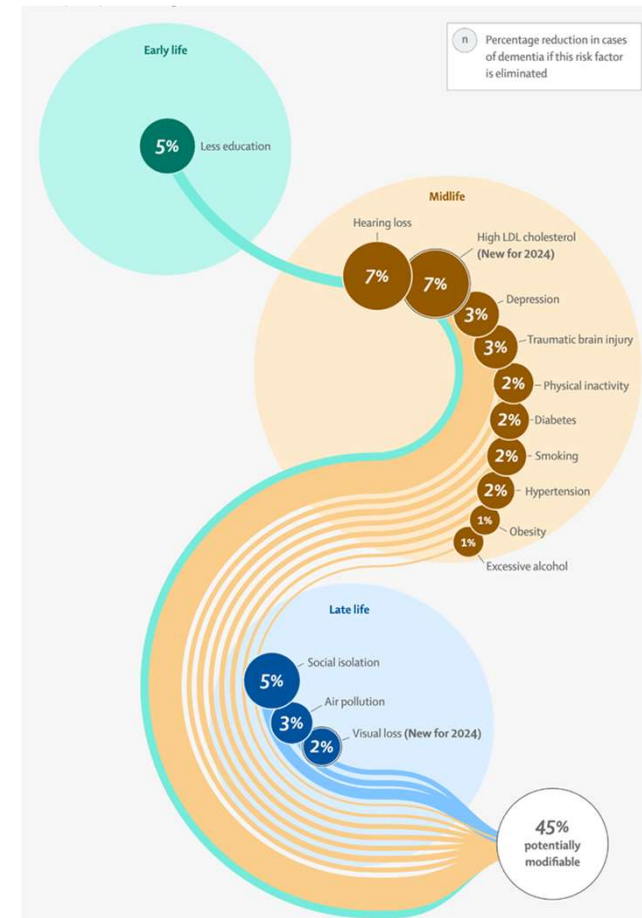


Nichols et al. Lancet Public Health 2022

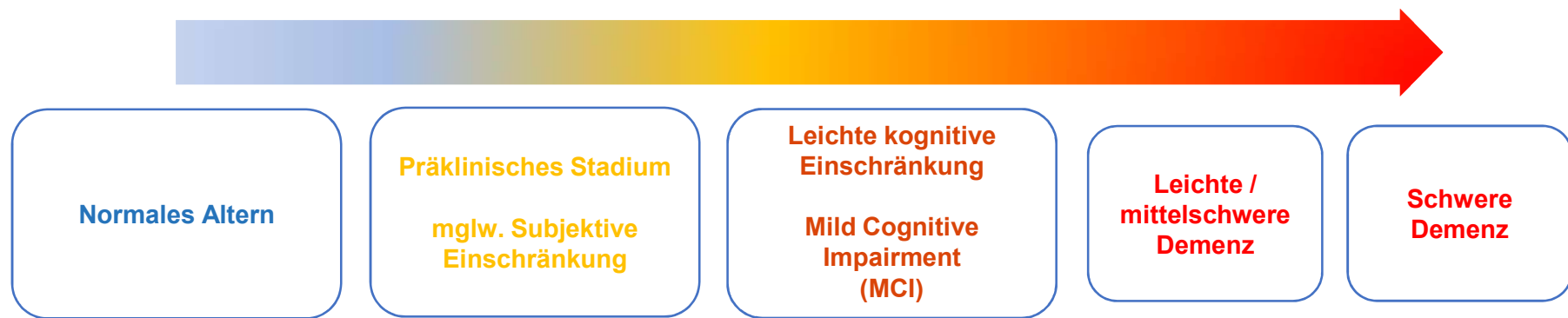
Risikofaktoren

- 45% aller Demenzerkrankungen sind vermeidbar
- Größte Hebel im mittleren Leben

- ☐ Hörstörungen
- ☐ Hohes LDL
- ☐ Depression
- ☐ Soziale Isolation
- ☐ Luftverschmutzung

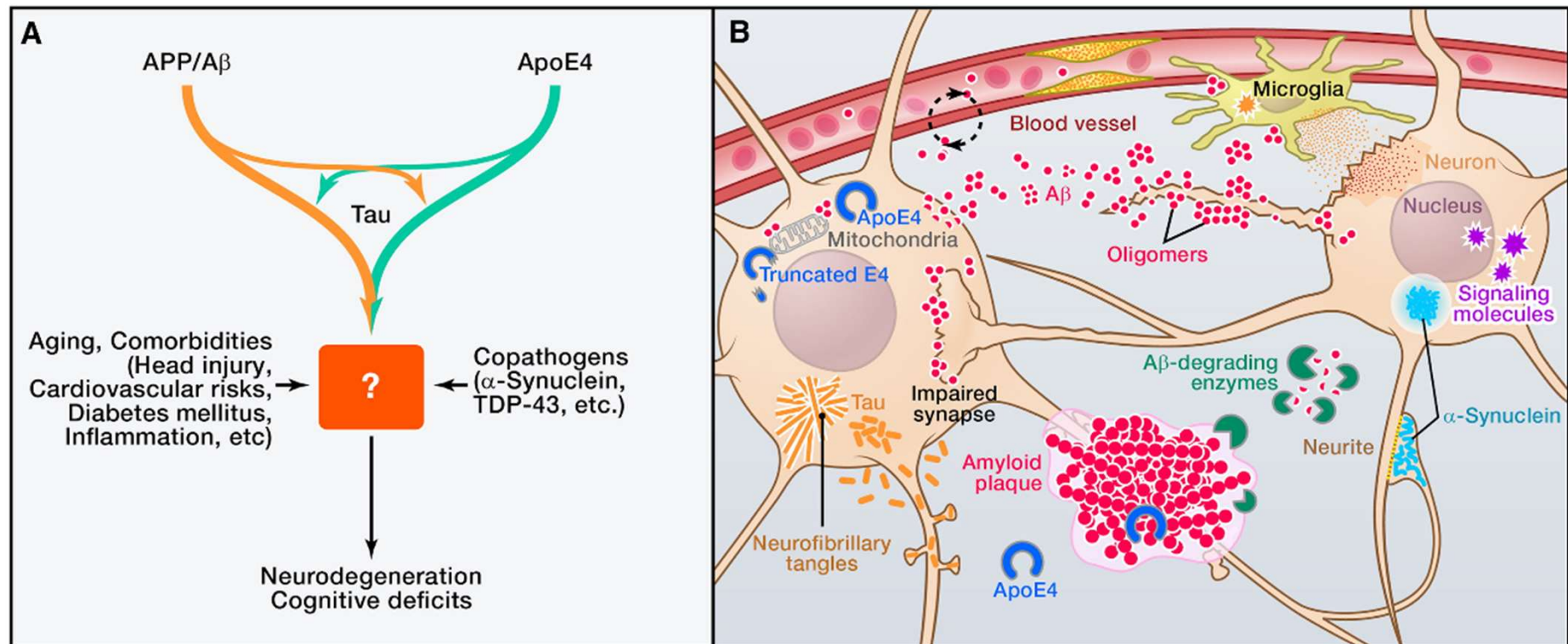


Kontinuum

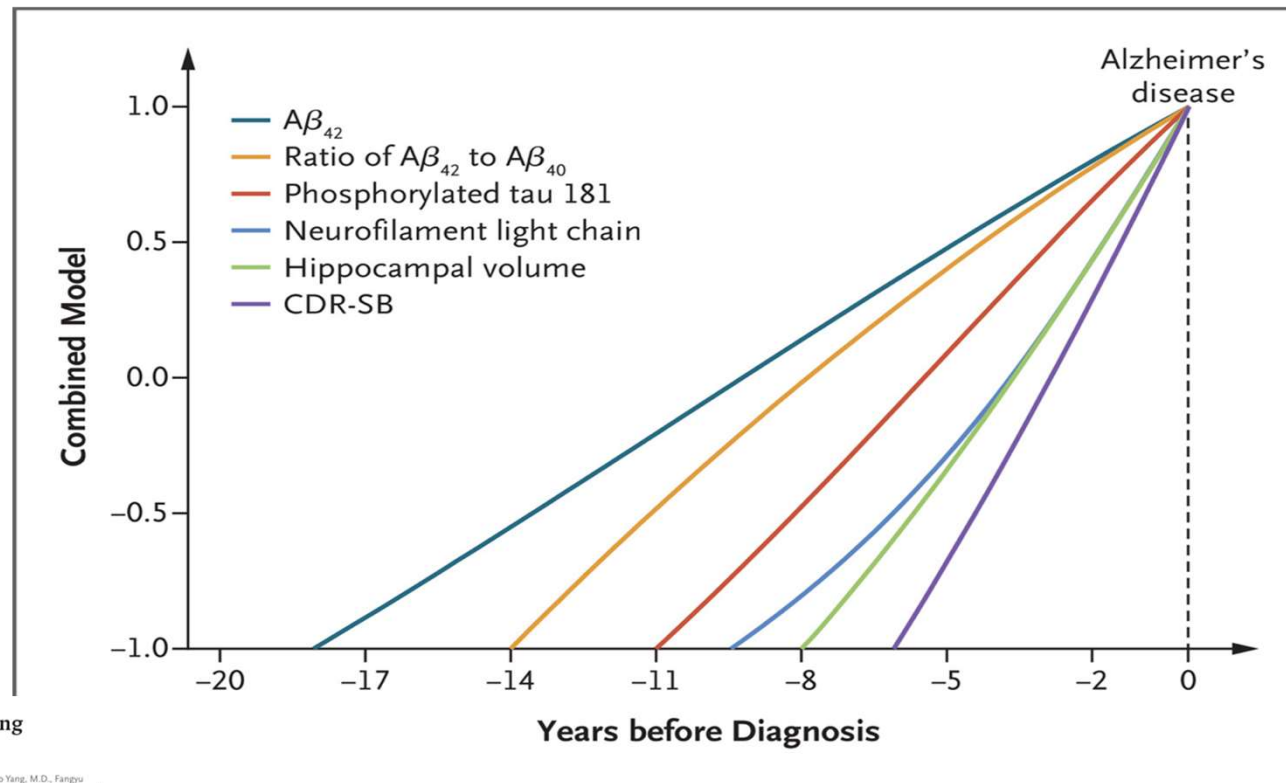


Dubois B et al, Alz&Dem 2016; Aisen PS et al, Alzheimers Res Ther 2017

Alzheimer Erkrankung (AD)



Neuropathologische Kaskade der AD

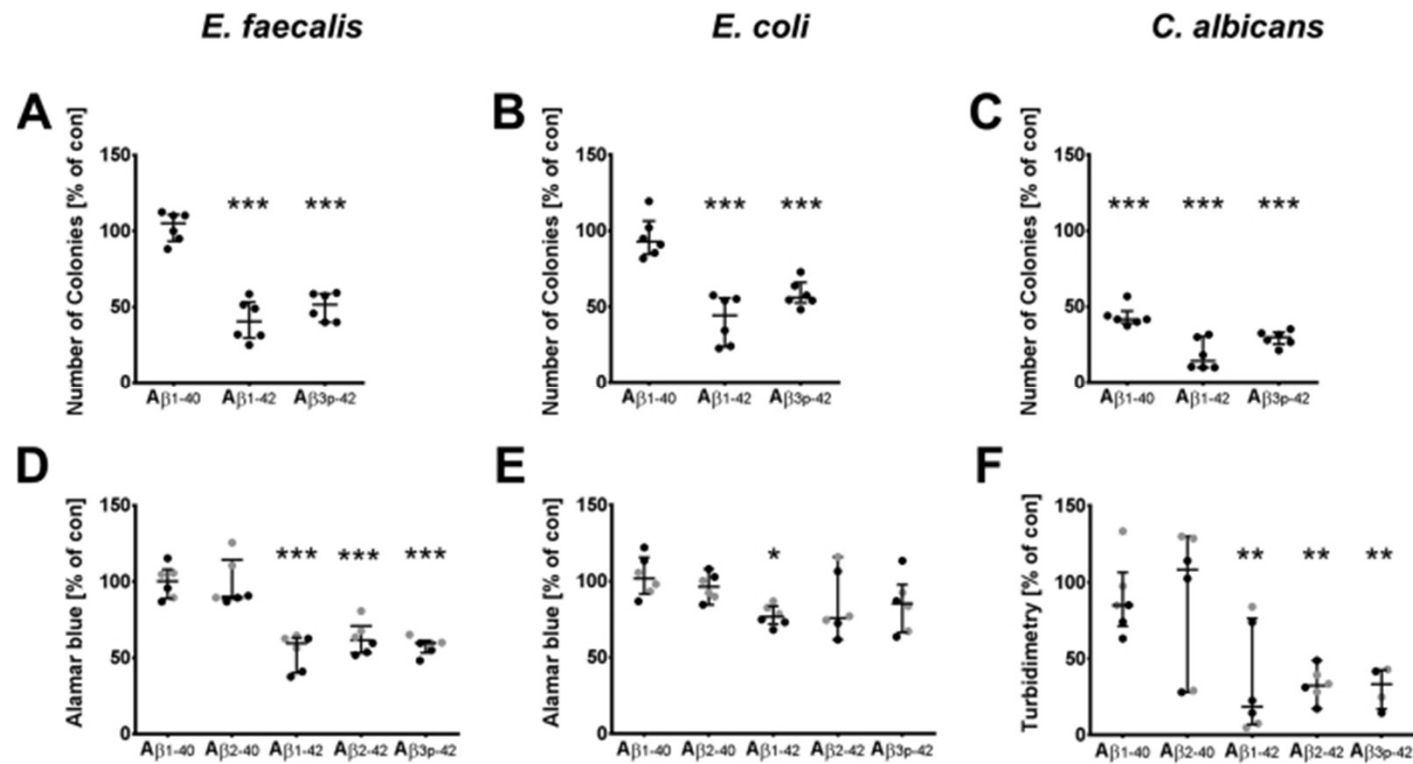


Biomarker Changes during 20 Years Preceding Alzheimer's Disease

Authors: Jianping Jia, M.D., Ph.D., Yuyi Ning, M.D., Meilin Chen, M.D., Shuheng Wang, M.D., Hao Yang, M.D., Fangyu Li, M.D., Jiyi Ding, M.D., and Shan Wang, M.D. [Author Info & Affiliations](#)

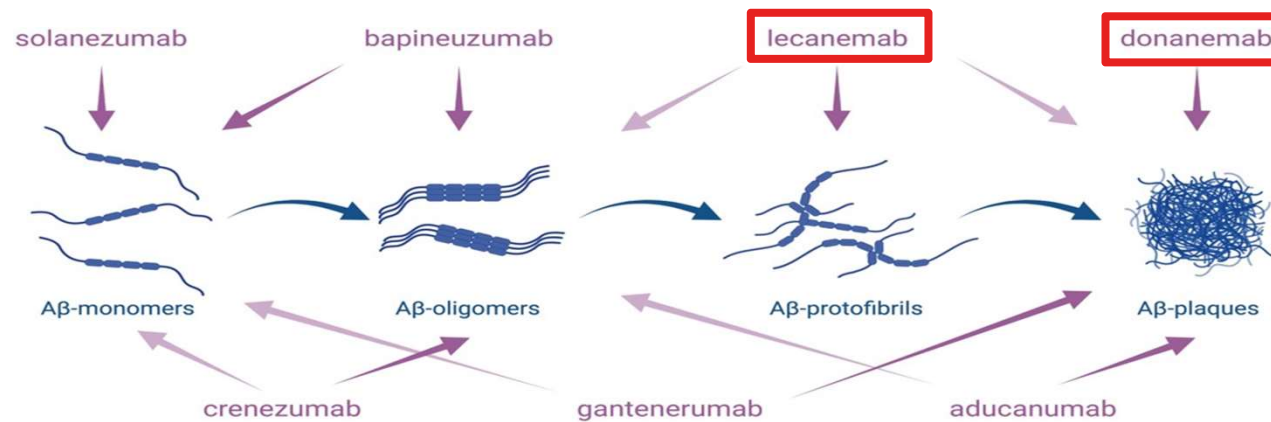
Published February 21, 2024 | N Engl J Med 2024;390:712-722 | DOI: 10.1056/NEJMoa2310168 | VOL. 390 NO. 8

Was macht Amyloid Beta?



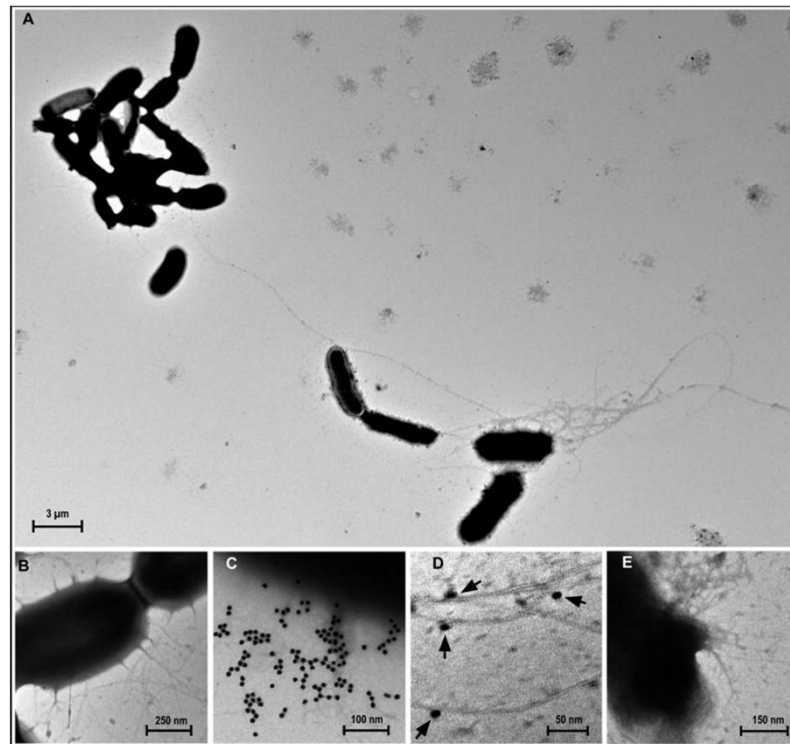
Spitzer et. al, [Sci Rep](https://doi.org/10.1038/srep32222). 2016 Sep 14;6:32228. doi: 10.1038/srep32222

Angriffspunkte Anti-Amyloid Antikörper



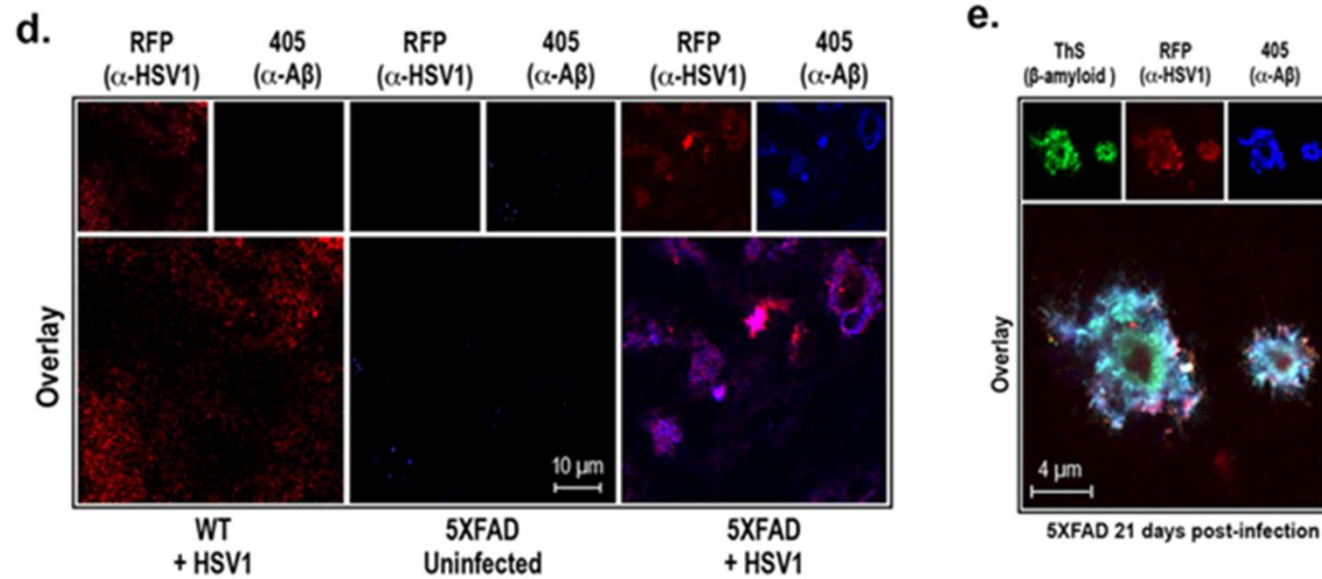
Perneckzy et al., Brain 2023

Amyloid Oligomere fangen Würmer



Sci Transl Med. 2016 May 25;8(340):340ra72.
doi: 10.1126/scitranslmed.aaf1059

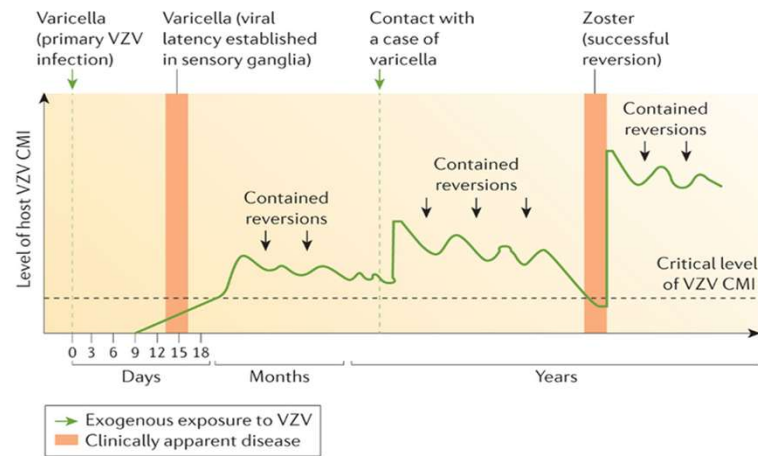
... und auch Viren



Neuron. 2018 Jul 11;99(1):56–63.e3. doi: 10.1016/j.neuron.2018.06.030

Latente Infektionen...

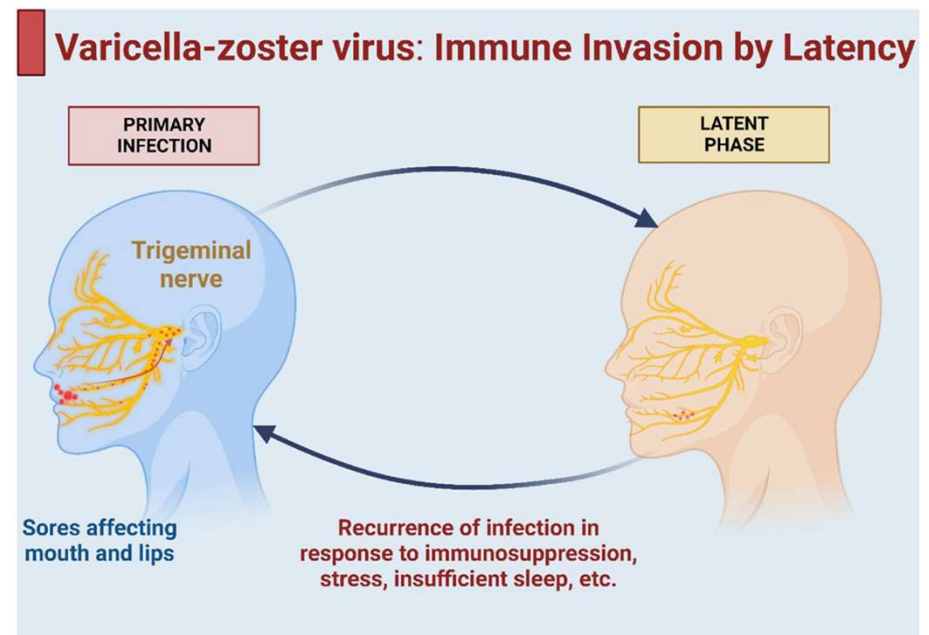
Figure 5 Natural history and pathogenesis of zoster



Nature Reviews | **Disease Primers**

Adapted from Hope-Simpson, R. E. The nature of herpes zoster: a long-term study and a new hypothesis
Proc. R. Soc. Med. **58**, 9–20 (1965), with permission from The Royal Society of Medicine

Gershon, A. A. *et al.* (2015) Varicella zoster virus infection
Nat. Rev. Dis. Primers doi:10.1038/nrdp.2015.16



... könnten zu einem chronischen Problem werden

PLATZHALTER HSV-1 Hypothese

Hugo Lövhem;
ADPD 2025; Vienna

Hinein in die Klinik

Herpesviren und AD

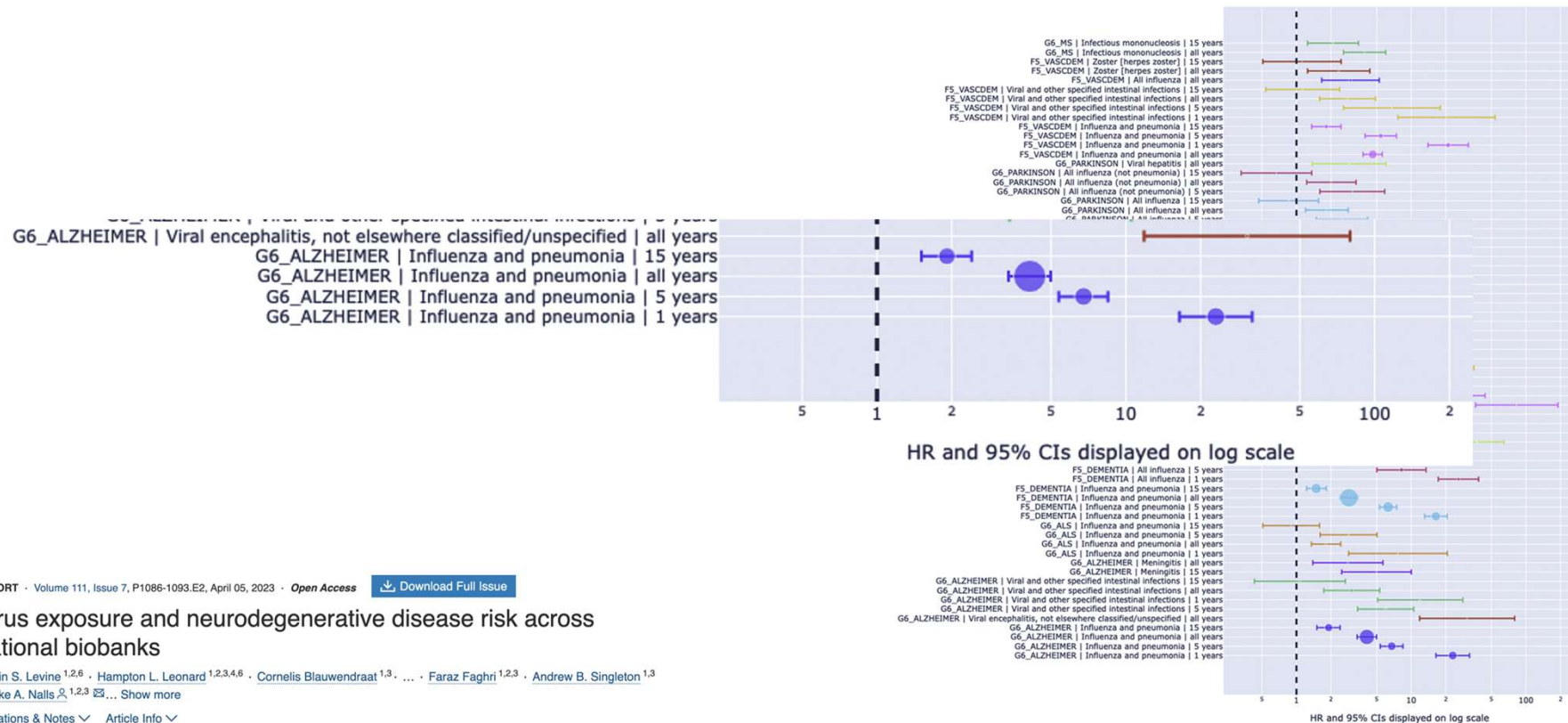
Journal of Medical Virology 33:224–227 (1991)

Latent Herpes Simplex Virus Type 1 in Normal and Alzheimer's Disease Brains

Gordon A. Jamieson, Norman J. Maitland, Gordon K. Wilcock, John Craske, and Ruth F. Itzhaki

Molecular Neurobiology Laboratory, Department of Optometry and Vision Sciences, UMIST, Manchester, England (G.A.J., R.F.I.); Department of Pathology, University of Bristol, Bristol, England (N.J.M.); Department of Care of the Elderly, Frenchay Hospital, Bristol, BS16 1LE, England (G.K.W.); Public Health Laboratory, Withington Hospital, Manchester, England (J.C.)

Infektion und Neurodegeneration



REPORT · Volume 111, Issue 7, P1086-1093.E2, April 05, 2023 · [Open Access](#)

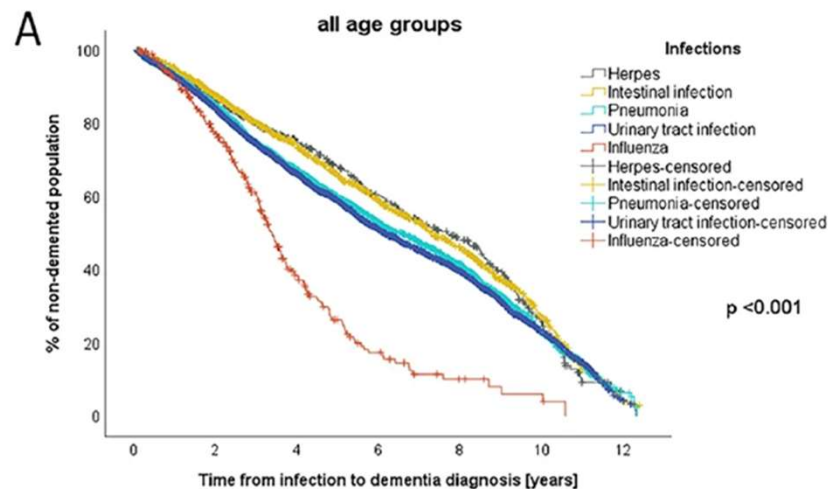
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Virus exposure and neurodegenerative disease risk across national biobanks

Kristin S. Levine^{1,2,6} · Hampton L. Leonard^{1,2,3,4,6} · Cornelis Blauwendraat^{1,3} · ... · Faraz Faghri^{1,2,3} · Andrew B. Singleton^{1,3}
 · Mike A. Nalls^{1,2,3} [Show more](#)

[Affiliations & Notes](#) [Article Info](#)

Klinische Daten



[Home](#) > [The Journal of Prevention of Alzheimer's Disease](#) > [Article](#)

Heightened Prevalence of Common Hospital-Treated Infections Preceding Dementia Diagnosis with Accelerated Dementia Onset after Influenza

Original Research | [Open access](#) | Published: 28 May 2024

Volume 11, pages 1445–1454, (2024) | [Cite this article](#)

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[H. Untersteiner](#), [R. Wurm](#), [B. Reichardt](#), [S. Goeschl](#), [E. Berger-Sieczkowski](#), [T. König](#), [T. Parvizi](#), [S. Silvaiah](#) & [Elisabeth Stögmänn](#) ✉

Angeborene Immunität und AD

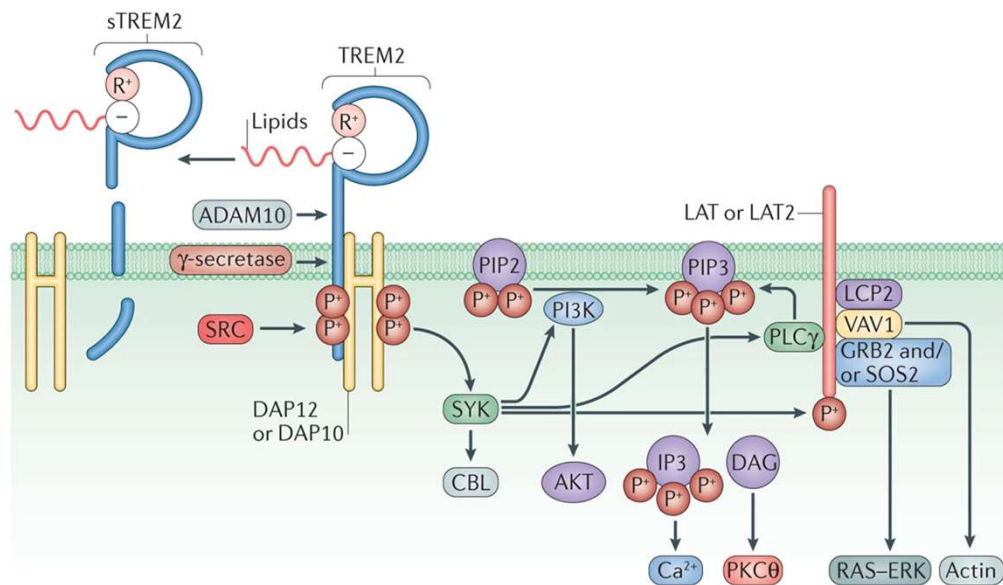
Progress | Published: 25 February 2016

TREM2 variants: new keys to decipher Alzheimer disease pathogenesis

Marco Colonna  & Yaming Wang

Nature Reviews Neuroscience 17, 201–207 (2016) | [Cite this article](#)

21k Accesses | 285 Citations | 26 Altmetric | [Metrics](#)



Nature Reviews | Neuroscience

VZV Infektionen und Demenz

Table 2. Characteristics of Herpes Zoster Case Subjects and Their Matched Controls^a

Characteristic	Herpes Zoster (n = 39,205)	Non-Herpes Zoster (n = 39,205)	χ^2 Test P Value
Sex			
Female	21,422 (54.64)	21,422 (54.64)	1.000
Male	17,783 (45.36)	17,783 (45.36)	
Age at entry, mean (SD), y	63.54 (10.00)	63.5 (10.00)	
50–59	16,702 (42.60)	16,702 (42.60)	1.000
60–69	11,284 (28.78)	11,284 (28.78)	
70–79	8,354 (21.31)	8,354 (21.31)	
80–89	2,617 (6.68)	2,617 (6.68)	
≥ 90	248 (0.63)	248 (0.63)	
Residence			
1 (most urbanized)	11,627 (29.66)	11,627 (29.66)	1.000
2	17,381 (44.33)	17,381 (44.33)	
3	6,646 (16.95)	6,646 (16.95)	
4 (most rural)	3,551 (9.06)	3,551 (9.06)	
Depression ^b			
No	34,768 (88.68)	35,537 (90.64)	<.0001
Yes	4,437 (11.32)	3,668 (9.36)	
Autoimmune disease ^b			
No	36,506 (93.12)	37,337 (95.24)	<.0001
Yes	2,699 (6.88)	1,868 (4.76)	
Ischemic stroke ^b			
No	33,460 (85.35)	33,825 (86.28)	<.0001
Yes	5,745 (14.65)	5,380 (13.72)	
Traumatic brain injury ^b			
No	36,266 (92.50)	36,498 (93.10)	.001
Yes	2,939 (7.50)	2,707 (6.90)	
Alcohol use disorder ^b			
No	36,106 (92.10)	36,326 (92.66)	.003
Yes	3,099 (7.90)	2,879 (7.34)	
Herpes simplex virus infection ^b			
No	38,882 (99.18)	39,069 (99.65)	<.0001
Yes	323 (0.82)	136 (0.35)	
Herpes zoster drug ^c			
No	37,074 (94.56)	38,998 (99.47)	<.0001
Yes	2,131 (5.44)	207 (0.53)	
Dementia ^d			
No	37,031 (94.45)	37,175 (94.82)	.022
Yes	2,174 (5.55)	2,030 (5.18)	
Follow-up, mean (SD), y	6.08 (4.05)	6.35 (4.04)	<.0001

^aValues shown as n (%) unless otherwise noted.

^bWhole period.

^cHerpes zoster drug prescribed on or after the index date.

^dDementia diagnosed after the index date.

Table 4. Cox Regression Analysis of Dementia Incidence Among Case Subjects With Herpes Zoster

Variable	n	Unadjusted			Adjusted ^a		
		HR	95% CI	P Value	HR	95% CI	P Value
Herpes zoster drug ^b							
No	37,074	1.00			1.00		
Yes	2,131	0.47	0.34–0.65	<.0001	0.55	0.40–0.77	.0004
Sex							
Female	21,422	1.00			1.00		
Male	17,783	0.95	0.87–1.03	.209	0.82	0.75–0.89	<.0001
Age at entry, y							
50–59	16,702	1.00			1.00		
60–69	11,284	5.09	4.20–6.17	<.0001	4.54	3.74–5.50	<.0001
70–79	8,354	14.06	11.72–16.85	<.0001	10.66	8.87–12.81	<.0001
80–89	2,617	27.79	22.99–33.58	<.0001	18.32	15.10–22.23	<.0001
≥ 90	248	37.05	27.22–50.44	<.0001			
Residence							
1 (most urbanized)	11,627	0.70	0.60–0.81	<.0001	0.91	0.79–1.06	.2371
2	17,381	0.75	0.65–0.86	<.0001	0.94	0.81–1.08	.362
3	6,646	0.92	0.79–1.08	.317	0.98	0.84–1.14	.7729
4 (most rural)	3,551	1.00			1.00		
Depression ^c							
No	34,768	1.00			1.00		
Yes	4,437	2.76	2.51–3.04	<.0001	1.20	1.08–1.34	.0008
Autoimmune disease ^c							
No	36,506	1.00			1.00		
Yes	2,699	1.41	1.22–1.63	<.0001	1.16	1.00–1.34	.0459
Ischemic stroke ^c							
No	33,460	1.00			1.00		
Yes	5,745	4.28	3.94–4.67	<.0001	2.01	1.84–2.20	<.0001
Traumatic brain injury ^c							
No	36,266	1.00			1.00		
Yes	2,939	1.87	1.66–2.11	<.0001	1.13	1.00–1.28	.0499
Alcohol use disorders ^c							
No	36,106	1.00			1.00		
Yes	3,099	7.25	6.65–7.91	<.0001	4.76	4.31–5.26	<.0001
Herpes simplex virus ^c							
No	38,882	1.00			1.00		
Yes	323	0.67	0.40–1.13	.1346	0.91	0.60–1.38	.6533

^aAdjusted for sex, age, residence, depression, autoimmune disease, ischemic stroke, traumatic brain injury, alcohol use disorder, antiviral treatments, herpes zoster drug, and herpes simplex virus infections.

^bHerpes zoster drug prescribed on or after the index date.

^cWhole period.

Abbreviation: HR = hazard ratio.

ORIGINAL RESEARCH

Herpes Zoster and Dementia: A Nationwide Population-Based Cohort Study

Vincent Chin-Hung Chen, MD, PhD^{a,b}; Shu-I Wu, MD, PhD^{c,d,e}; Kuo-You Huang, PhD^f; Yao-Hsu Yang, MD^{g,h,i,j,k}; Ting-Yu Kuo, MS^h; Hsin-Yi Liang, MD^{h,k}; Kuan-Lun Huang, MD^{k,l}; and Michael Gossop, PhD^m

Published: December 12, 2017

- Demenzzinzidenz nach H. Zoster erhöht
- Antivirale Therapie modifiziert diese Assoziation dtl.

Mehr Herpes, mehr Demenz

Research | [Open access](#) | Published: 12 March 2024

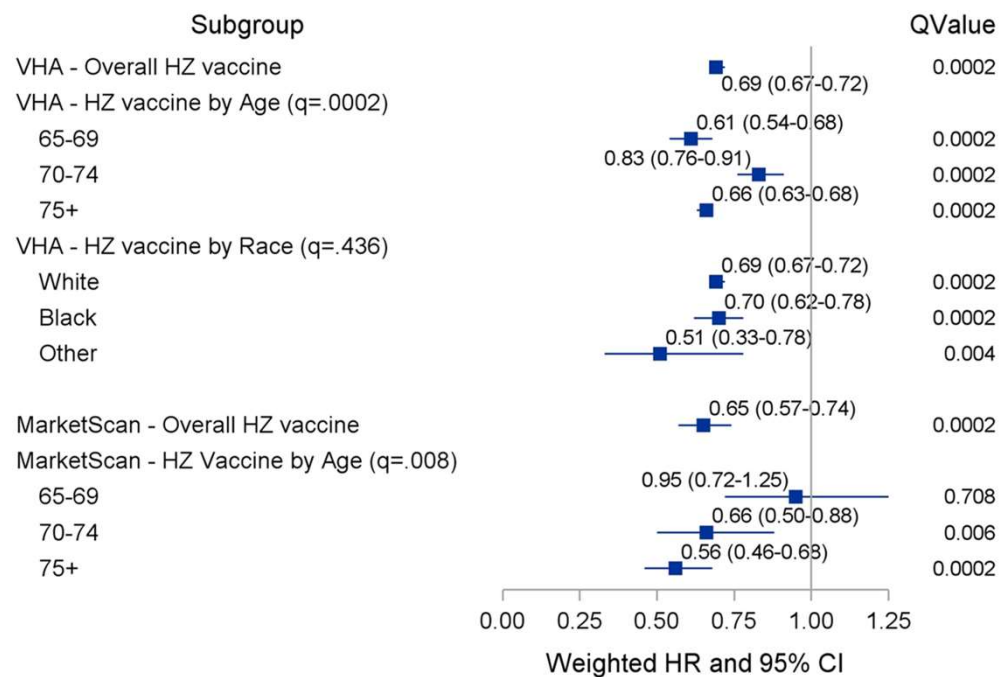
The associations of herpes simplex virus and varicella zoster virus infection with dementia: a nationwide

Variables		Cohort (N = 752,205)	All dementia		Alzheimer's disease		Vascular dementia	
			Hazard ratio (95% CI)	p-value†	Hazard ratio (95% CI)	p-value†	Hazard ratio (95% CI)	p-value†
HSV or VZV infection	No	475,884 (63.3%)	1 (ref)	< 0.0001	1 (ref)	< 0.0001	1 (ref)	< 0.0001
	HSV only	91,990 (12.2%)	1.38 (1.33–1.43)		1.49 (1.42–1.56)		1.46 (1.24–1.72)	0.0001
	VZV only	113,645 (15.1%)	1.41 (1.37–1.46)		1.52 (1.46–1.57)		1.34 (1.16–1.54)	0.0001
	Co-infection	70,686 (9.4%)	1.57 (1.50–1.63)		1.75 (1.66–1.85)		1.52 (1.24–1.87)	
Age (years)	< 65	537,743 (71.5%)	1 (ref)	< 0.0001	1 (ref)	< 0.0001	1 (ref)	< 0.0001
	≥ 65	214,462 (28.5%)	14.03 (13.64–14.44)		14.70 (14.18–15.24)		8.26 (7.37–9.26)	
Sex	Male	348,125 (46.3%)	1 (ref)	< 0.0001	1 (ref)	< 0.0001	1 (ref)	0.0002
	Female	404,080 (53.7%)	1.49 (1.46–1.53)		1.61 (1.57–1.66)		1.21 (1.10–1.34)	
Depression		58,961 (7.8%)	1.40 (1.36–1.44)	< 0.0001	1.41 (1.36–1.46)	< 0.0001	1.30 (1.12–1.51)	0.0005
Dyslipidaemia		137,800 (18.3%)	0.94 (0.91–0.96)	< 0.0001	0.93 (0.90–0.96)	< 0.0001	0.89 (0.79–1.01)	0.07
Ischaemic stroke		30,950 (4.1%)	1.54 (1.49–1.59)	< 0.0001	1.44 (1.38–1.51)	< 0.0001	2.16 (1.86–2.52)	< 0.0001
Coronary heart disease		86,082 (11.4%)	1.10 (1.07–1.13)	< 0.0001	1.11 (1.07–1.15)	< 0.0001	1.02 (0.89–1.17)	0.77
Hypertension		239,976 (31.9%)	1.39 (1.35–1.42)	< 0.0001	1.37 (1.33–1.41)	< 0.0001	1.76 (1.57–1.97)	< 0.0001
Diabetes mellitus		157,642 (21%)	1.31 (1.28–1.34)	< 0.0001	1.30 (1.26–1.34)	< 0.0001	1.34 (1.20–1.49)	< 0.0001
Chronic kidney disease		3,287 (0.4%)	1.10 (0.96–1.25)	0.16	1.05 (0.89–1.25)	0.55	0.92 (0.48–1.78)	0.80
Body mass index	Underweight	15,993 (2.1%)	1 (ref)	< 0.0001	1 (ref)	< 0.0001	1 (ref)	< 0.0001
	Normal	220,444 (29.3%)	0.66 (0.63–0.69)		0.62 (0.58–0.66)		0.59 (0.47–0.74)	
	Overweight	169,660 (22.6%)	0.54 (0.51–0.56)		0.50 (0.47–0.53)		0.45 (0.36–0.57)	
	Obese	226,268 (30.1%)	0.46 (0.44–0.49)		0.42 (0.40–0.45)		0.45 (0.36–0.57)	
Household income level	Low	138,623 (18.4%)	1 (ref)	< 0.0001	1 (ref)		1 (ref)	
	Lower middle	136,824 (18.2%)	0.96 (0.93–0.99)		0.97 (0.93–1.01)	0.13	0.95 (0.81–1.11)	0.52
	Higher middle	181,648 (24.1%)	0.88 (0.86–0.91)		0.89 (0.85–0.92)	< 0.0001	0.83 (0.72–0.96)	0.01
	High	255,307 (33.9%)	0.88 (0.86–0.91)		0.90 (0.86–0.93)	< 0.0001	0.77 (0.68–0.89)	0.0002

[im & Dong Hui Lim](#) 

[a this article](#)

Impfungen schützen...



PLOS ONE

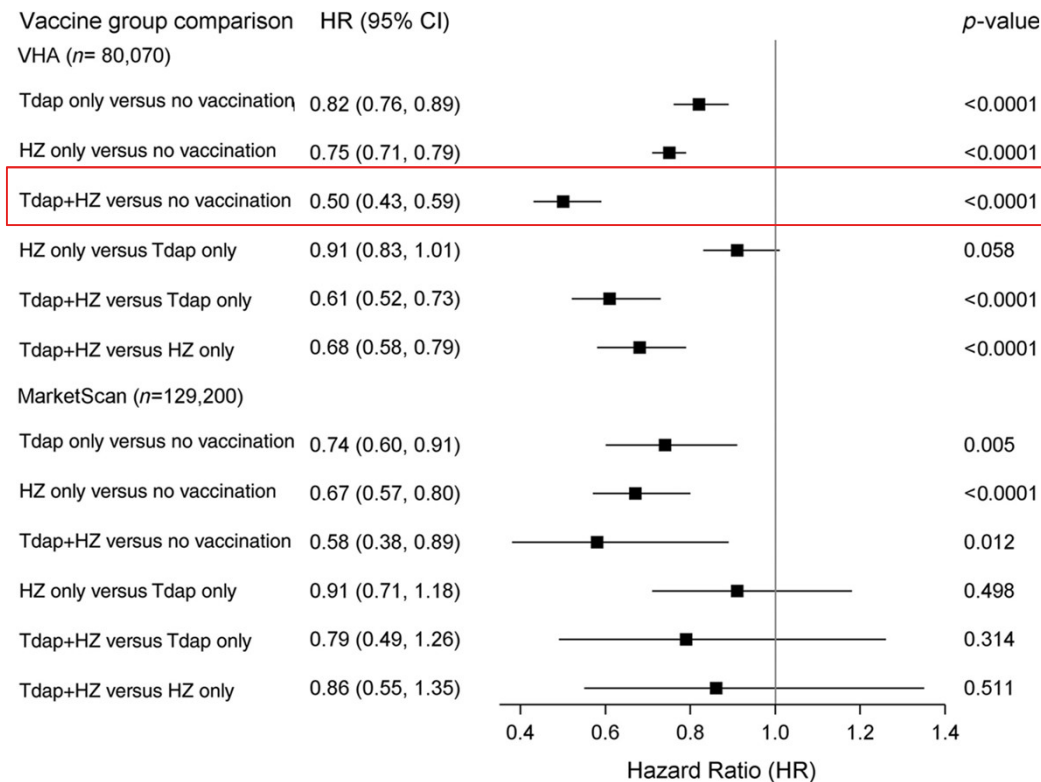
OPEN ACCESS PEER-REVIEWED
RESEARCH ARTICLE

Impact of herpes zoster vaccination on incident dementia: A retrospective study in two patient cohorts

Jeffrey F. Scherrer Joanne Salas Timothy L. Wiemken Daniel F. Hoft Christine Jacobs John E. Morley

Published: November 17, 2021 • <https://doi.org/10.1371/journal.pone.0257405>

... egal welche?



Comparison of rates of dementia among older adult recipients of two, one, or no vaccinations

Timothy L. Wiemken PhD, MPH, Joanne Salas MPH, John E. Morley MBBCh, Daniel F. Hoft MD, PhD, Christine Jacobs MD, Jeffrey F. Scherrer PhD [✉](#)

First published: 12 December 2021 | <https://doi.org/10.1111/jgs.17606> | Citations: 22

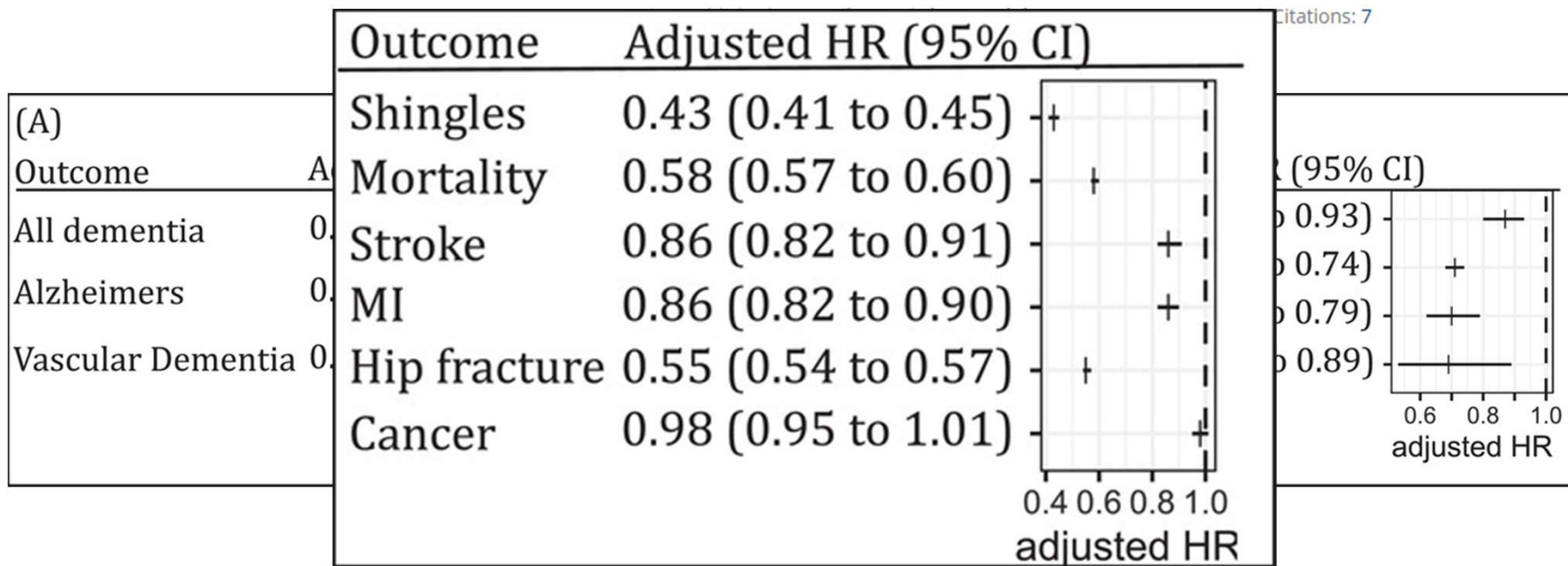
- Dipht/Pertussis/Polio + VZV reduziert Risiko mehr als eine alleine
- Biases?

Biases?

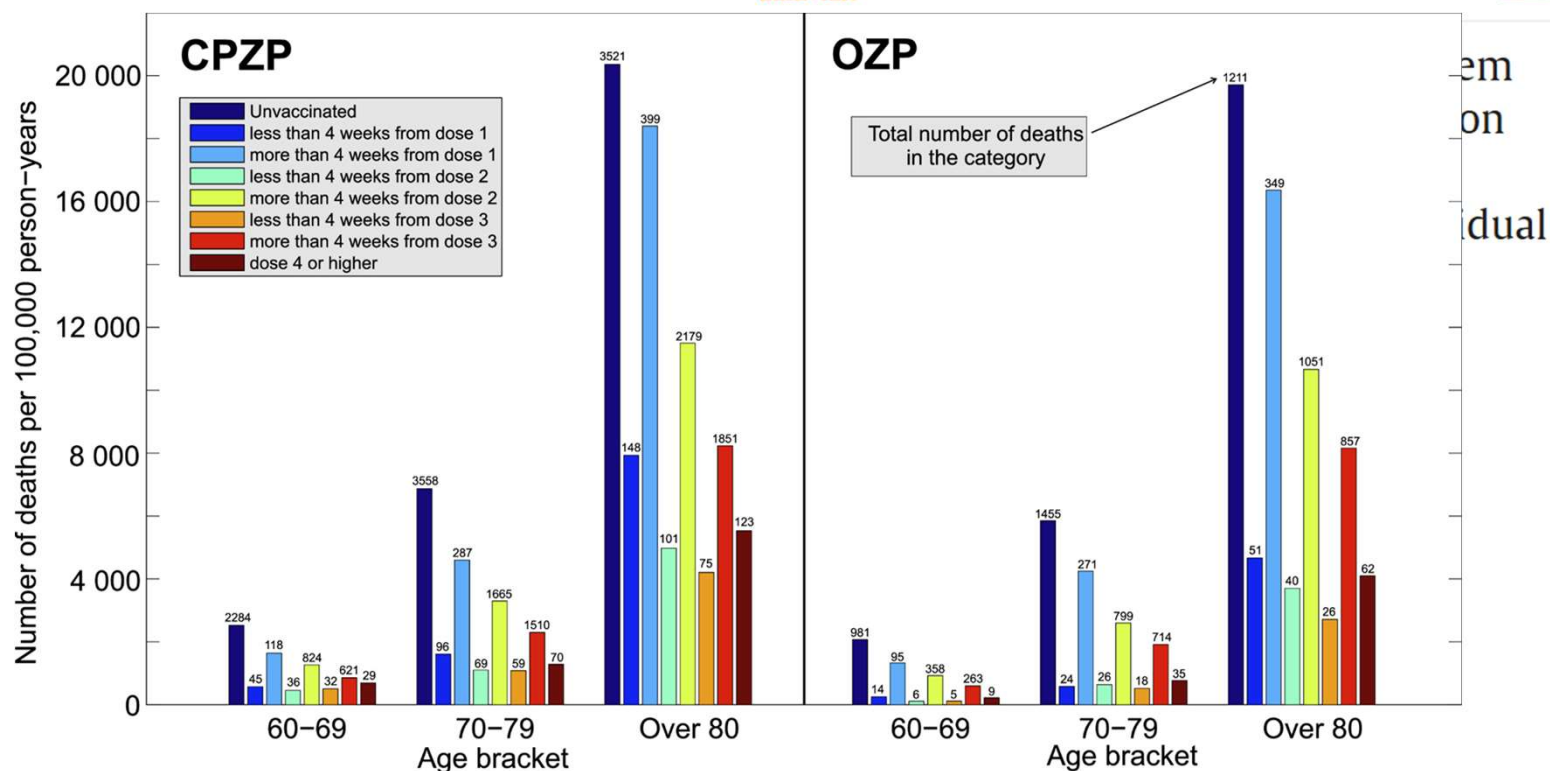
RESEARCH ARTICLE | [Open Access](#) | 

Reduced dementia incidence after varicella zoster vaccination in Wales 2013–2020

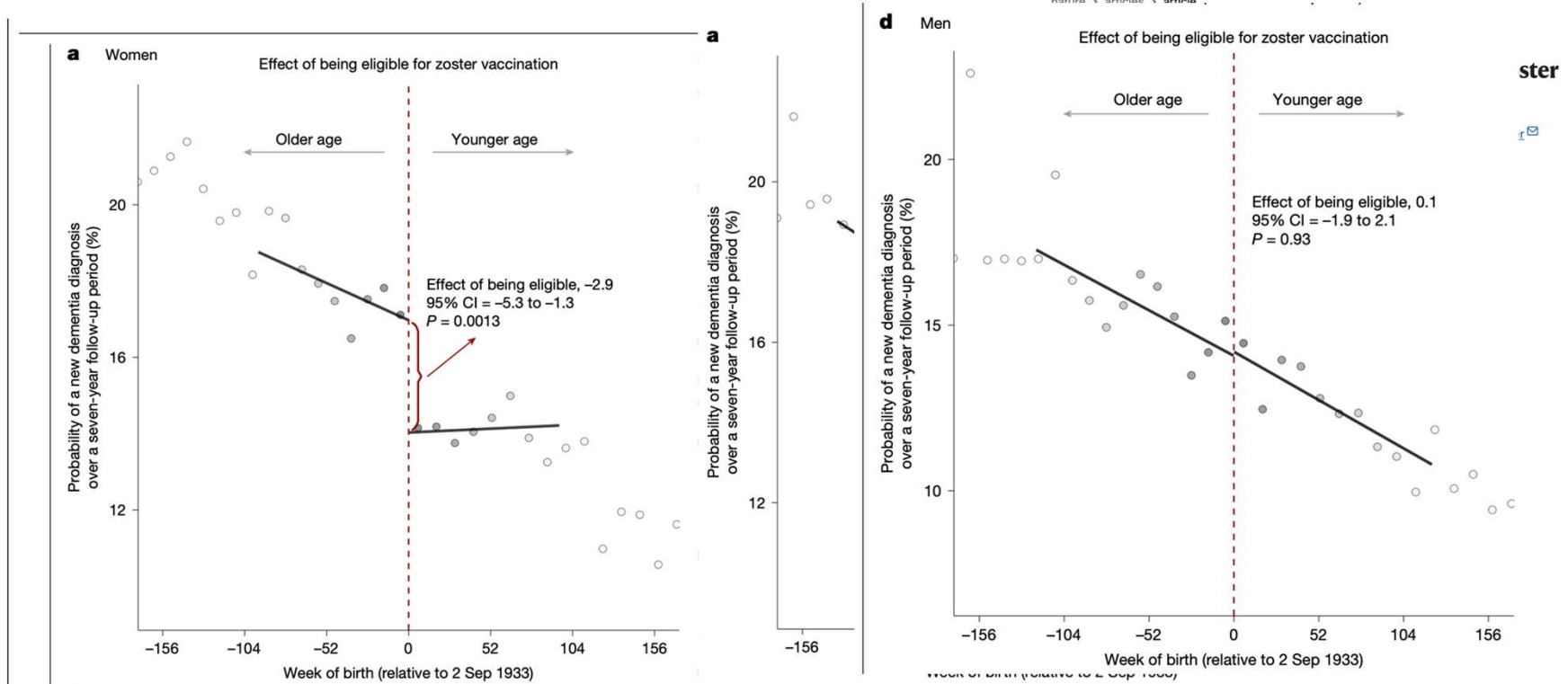
Christian Schnier  Janet Janbek, Richard Lathe, Jürgen Haas



Healthy vaccinee bias



Natural experiments

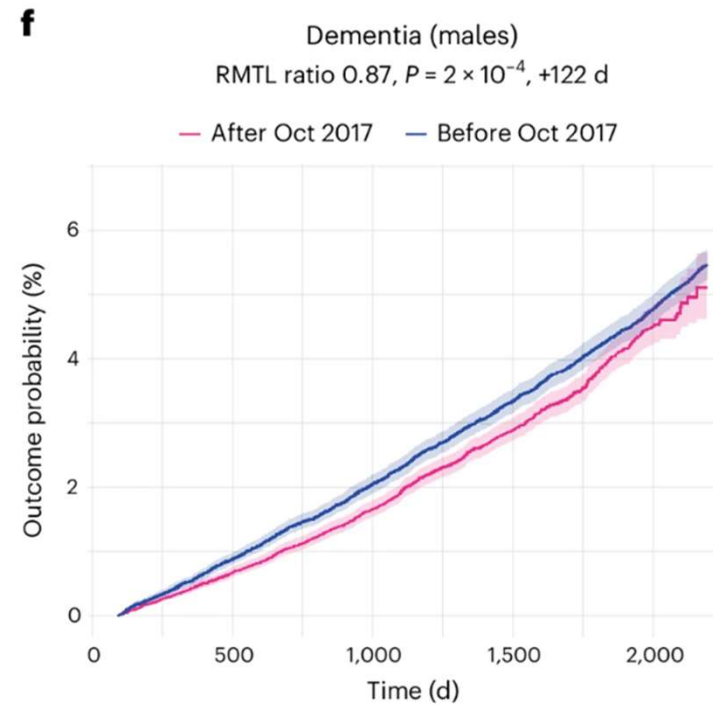
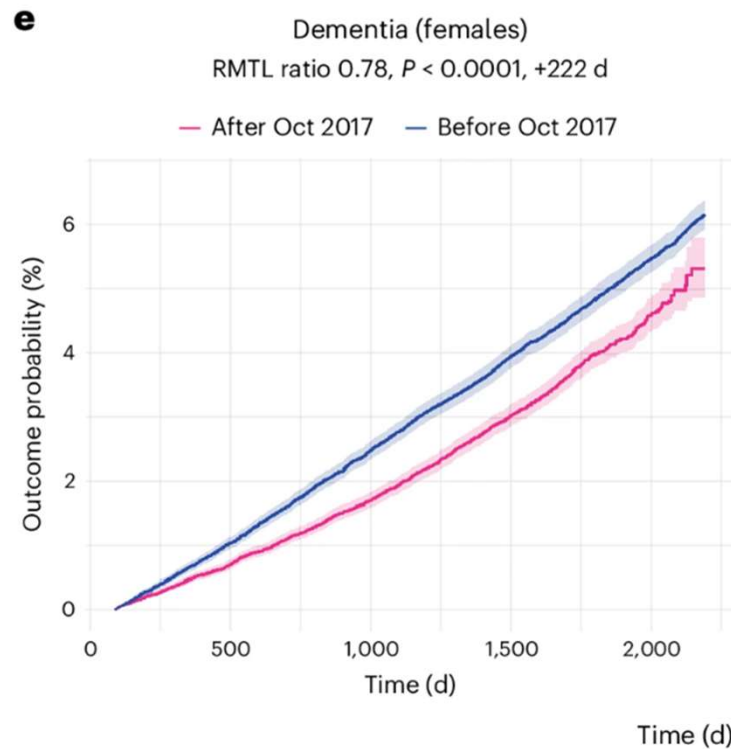


Natural experiment #2

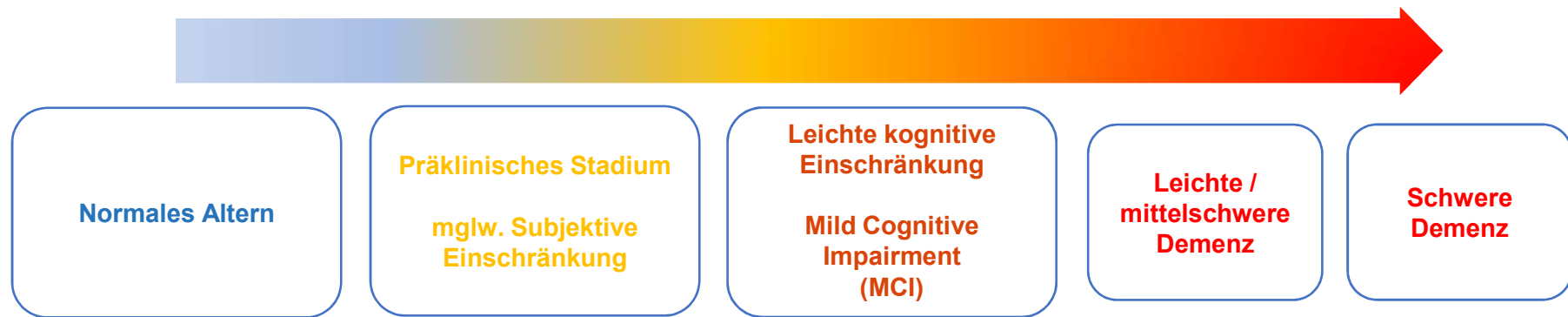
nature medicine



41591-024-03201-5



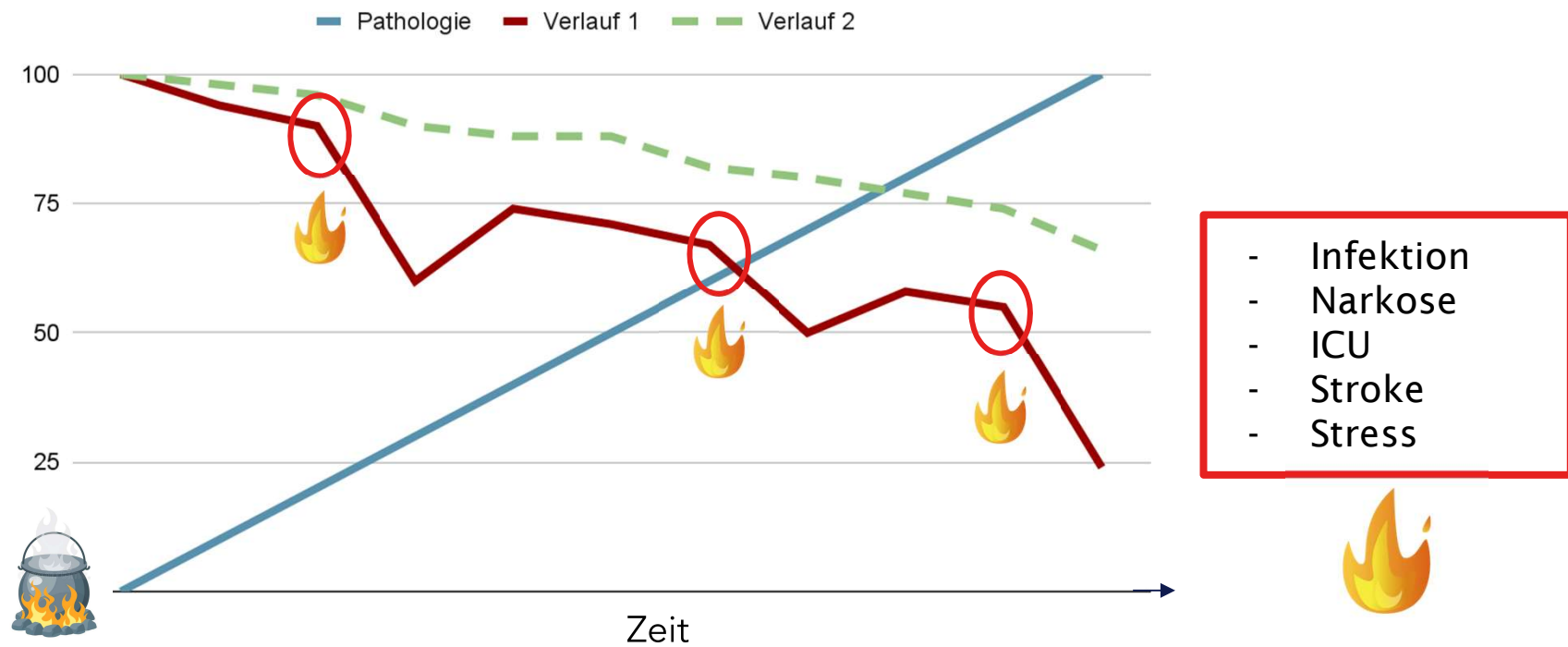
Ist ein Kontinuum kontinuierlich?



Dubois B et al, Alz&Dem 2016; Aisen PS et al, Alzheimers Res Ther 2017

Boost Hypothese

Klinik vs Pathologie



Zusammenfassung

- Infektionen sind ein Risiko für die Entwicklung von Demenz
 - neurotrope Viren könnten eine besondere Rolle spielen
- Ursachen nicht sicher geklärt
 - angeborene Immunität, Vaskulopathie oder spezifische Rolle von Beta-Amyloid möglich
- Impfungen in Beobachtungsstudien mit niedriger Inzidenz von Demenz assoziiert
 - sowohl bei Impfungen als auch bei Infektionen additive Effekte
- Natürliche Experimente legen eine Wirksamkeit abseits von Biases nahe
 - effektivere Impfungen sind auch effektiver gegen Demenz

Einordnung

- Vorhandene Evidenz zeigt eindeutig in die Richtung von Nutzen
- Antivirale Therapien in Erprobung, unklar ob jemals randomisierte Evidenz für Impfungen vorliegen wird
- Bei ohnehin klarer Indikation für VZV Impfung ist der Effekt auf Demenz die Kirsche obenauf

Vielen Dank für Ihre Aufmerksamkeit

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