INFECTION PREVENTION IN OLDER PERSONS

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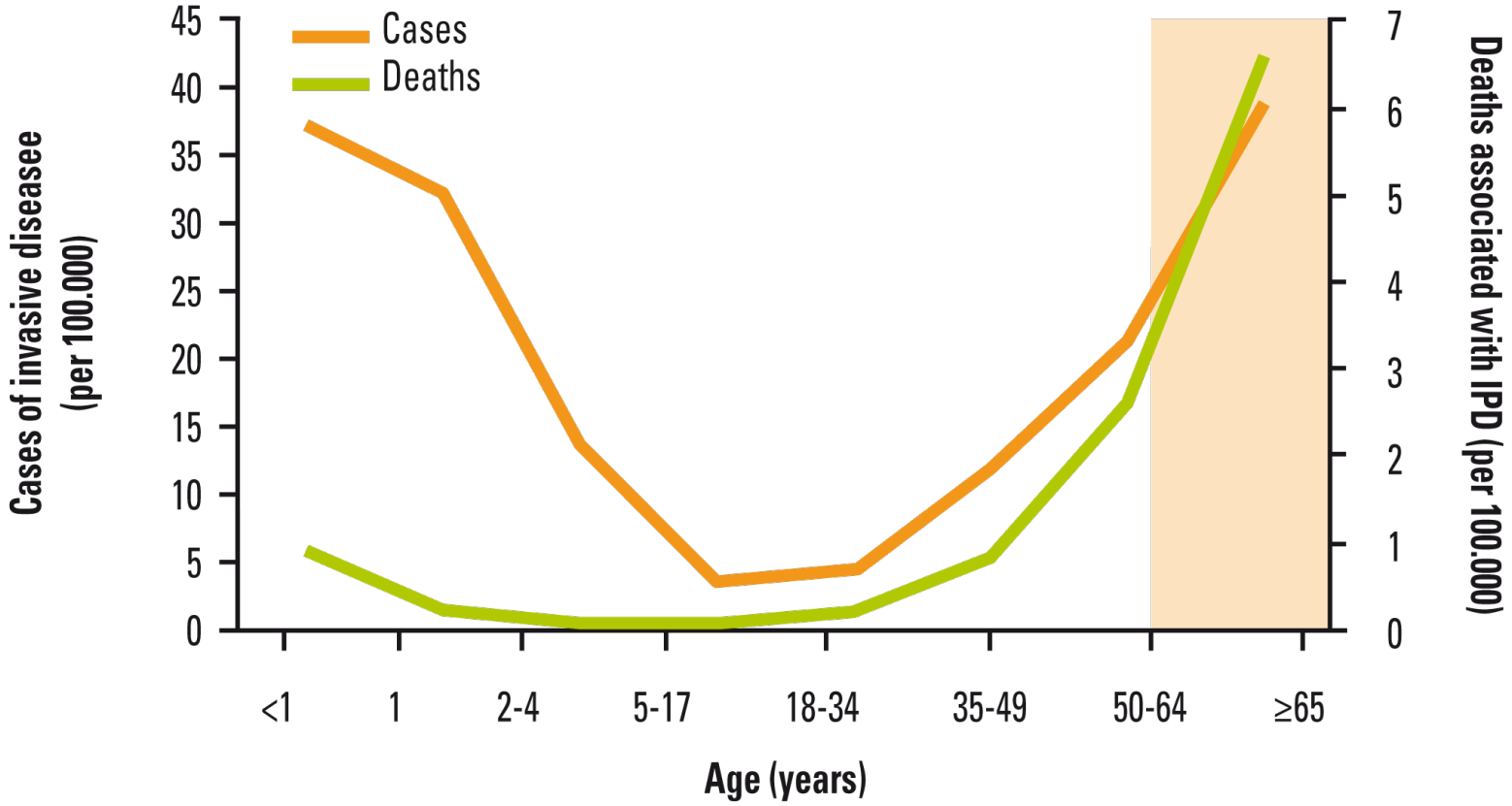
Incidence and mortality of infectious diseases

WHO?



CDC. 2010. ABC Surveillance Report, Emerging Infections Program Network, Streptococcus pneumoniae, 2009.

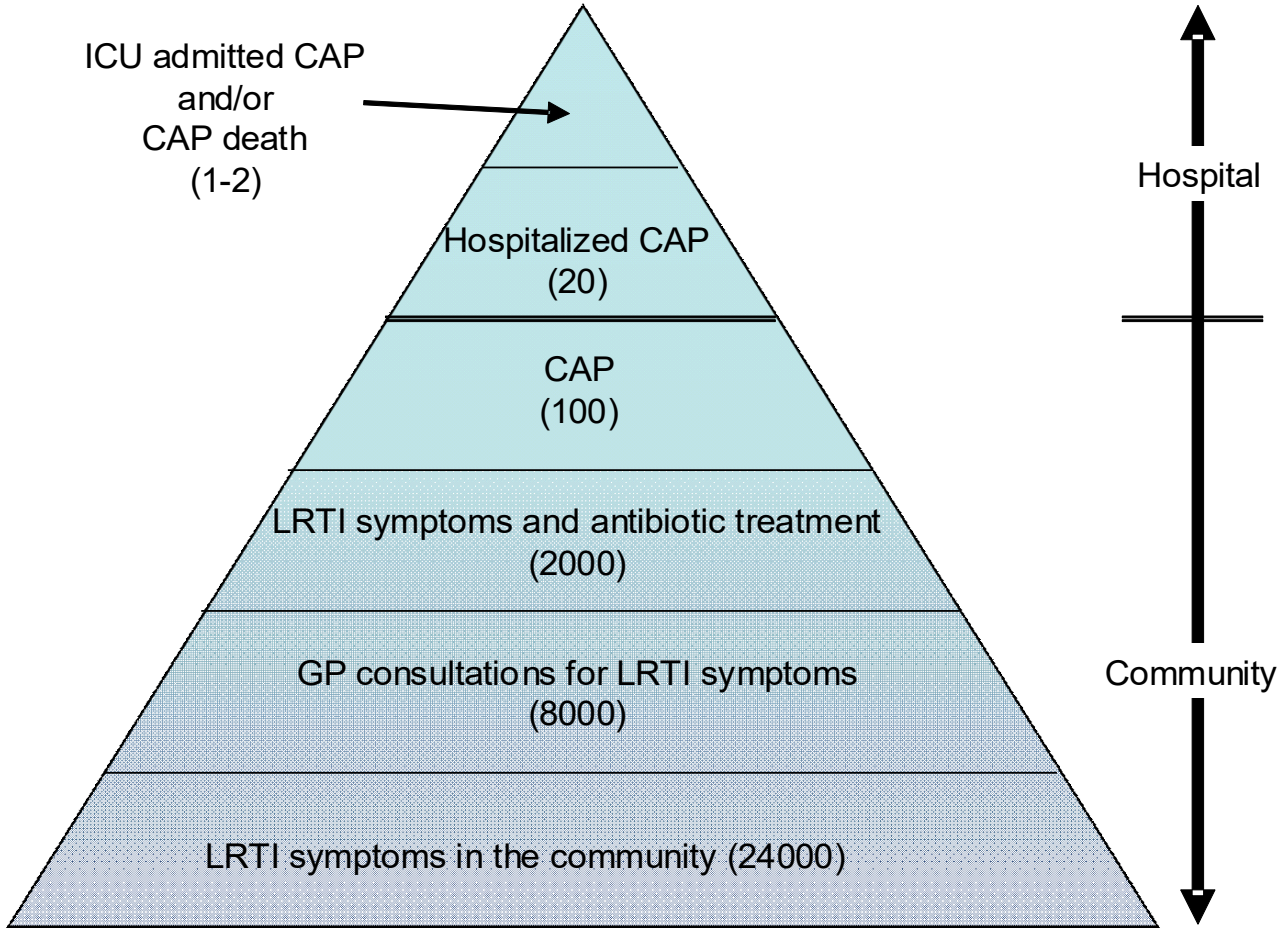
België

Top ten causes of death, all ages Belgium, 2002			
	Deaths		Years of Life Lost
Causes	(000)	(%)	(%)
All causes	102	100	100
Ischaemic heart disease	14	15	13
Cerebrovascular disease	9	9	6
Trachea, bronchus, lung cancers	7	7	8
Lower respiratory infections	5	5	3
Chronic obstructive pulmonary disease	4	5	4
Alzheimer and other dementias*	4	4	2
Colon and rectum cancers	3	3	3
Breast cancer	2	3	4
Self-inflicted injuries	2	2	6
Prostate cancer	2	2	1

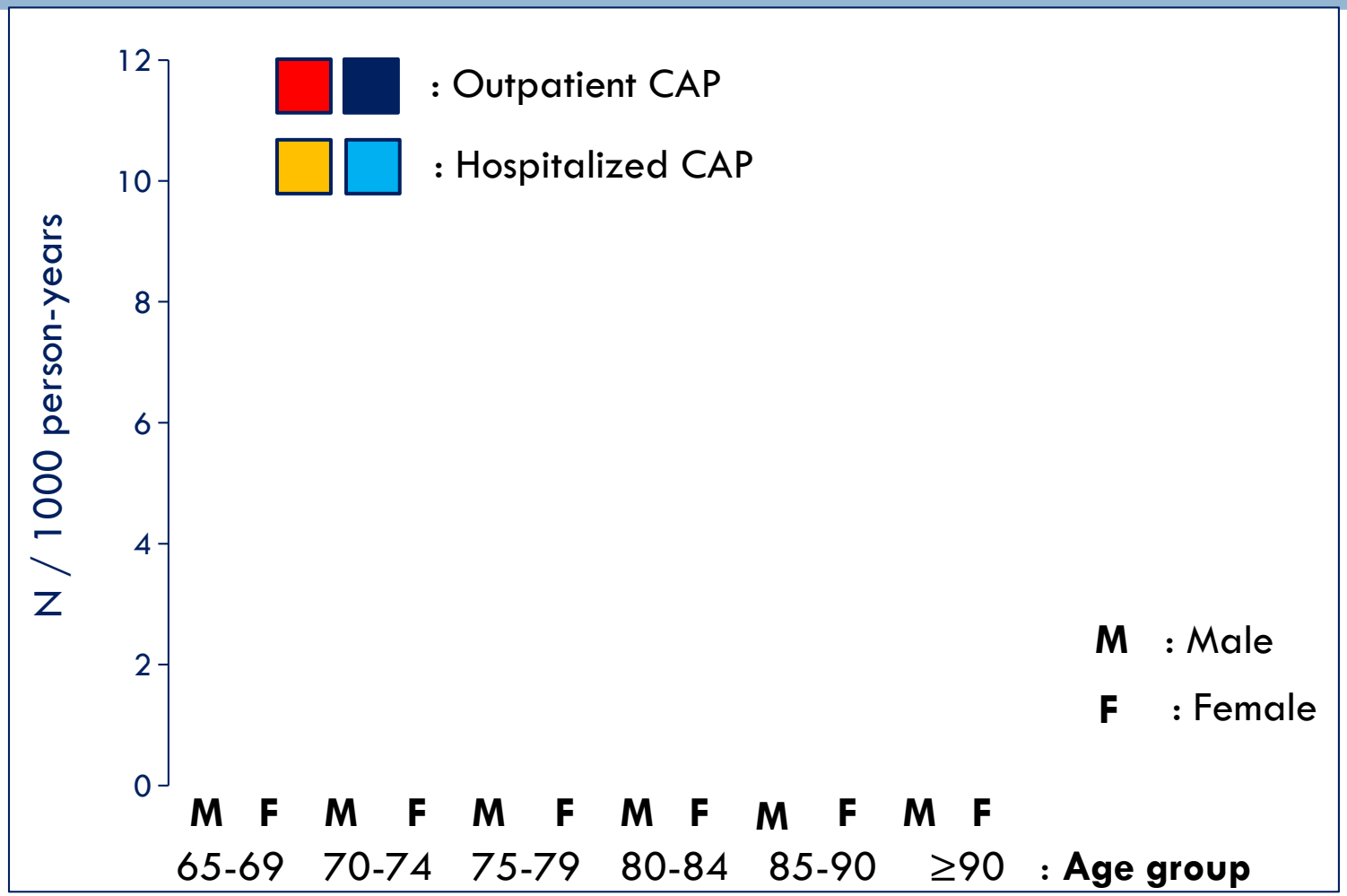
Source: Death and DALY estimates by cause, 2002
http://www.who.int/entity/healthinfo/statistics/bodgbddeathdalyestimates.xls

http://www.who.int/healthinfo/statistics/bodgbddeathdalyestimates.xls

Incidence of Lower Respiratory Tract Infections

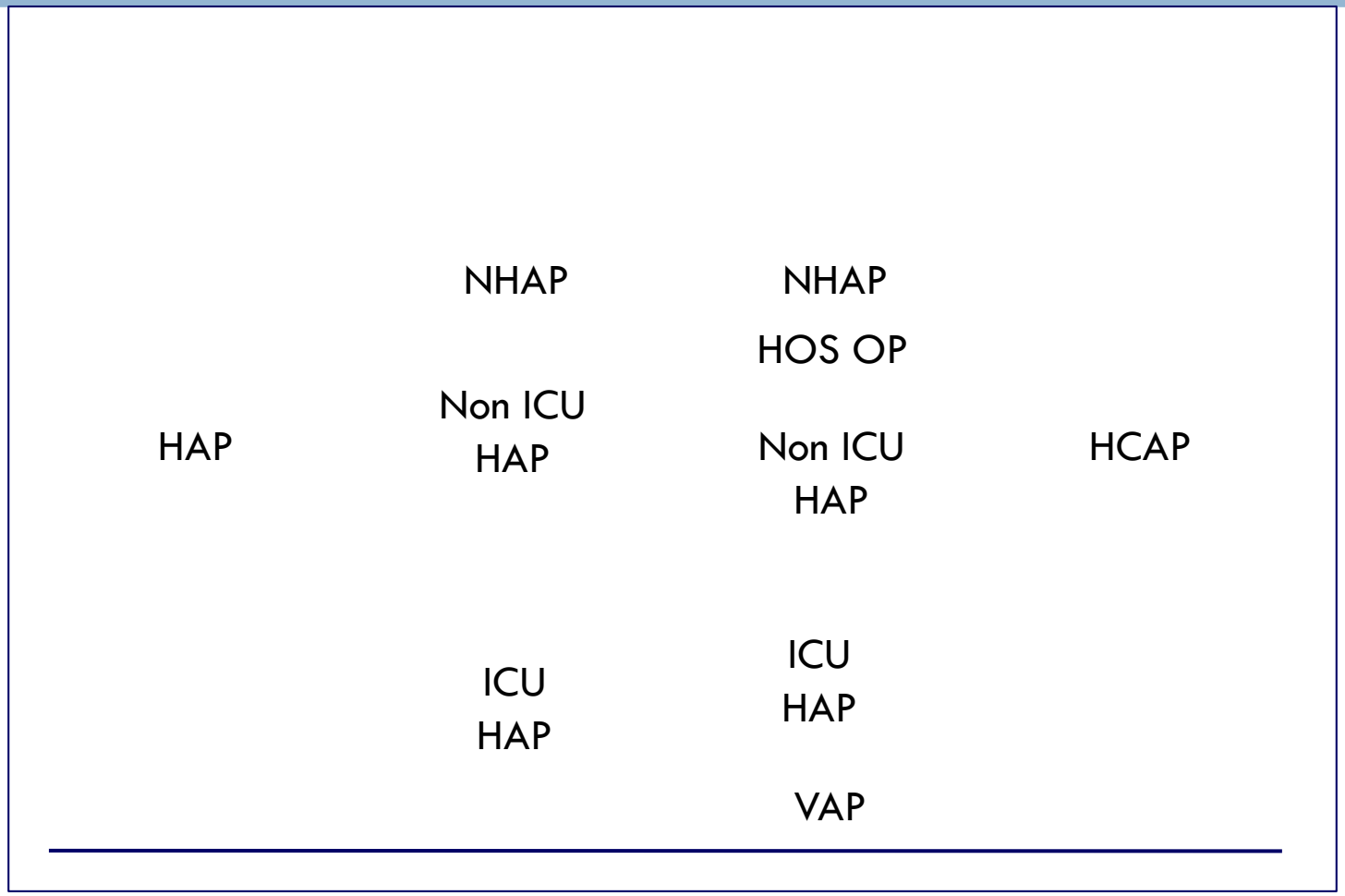


Incidence of Lower Respiratory Tract Infections

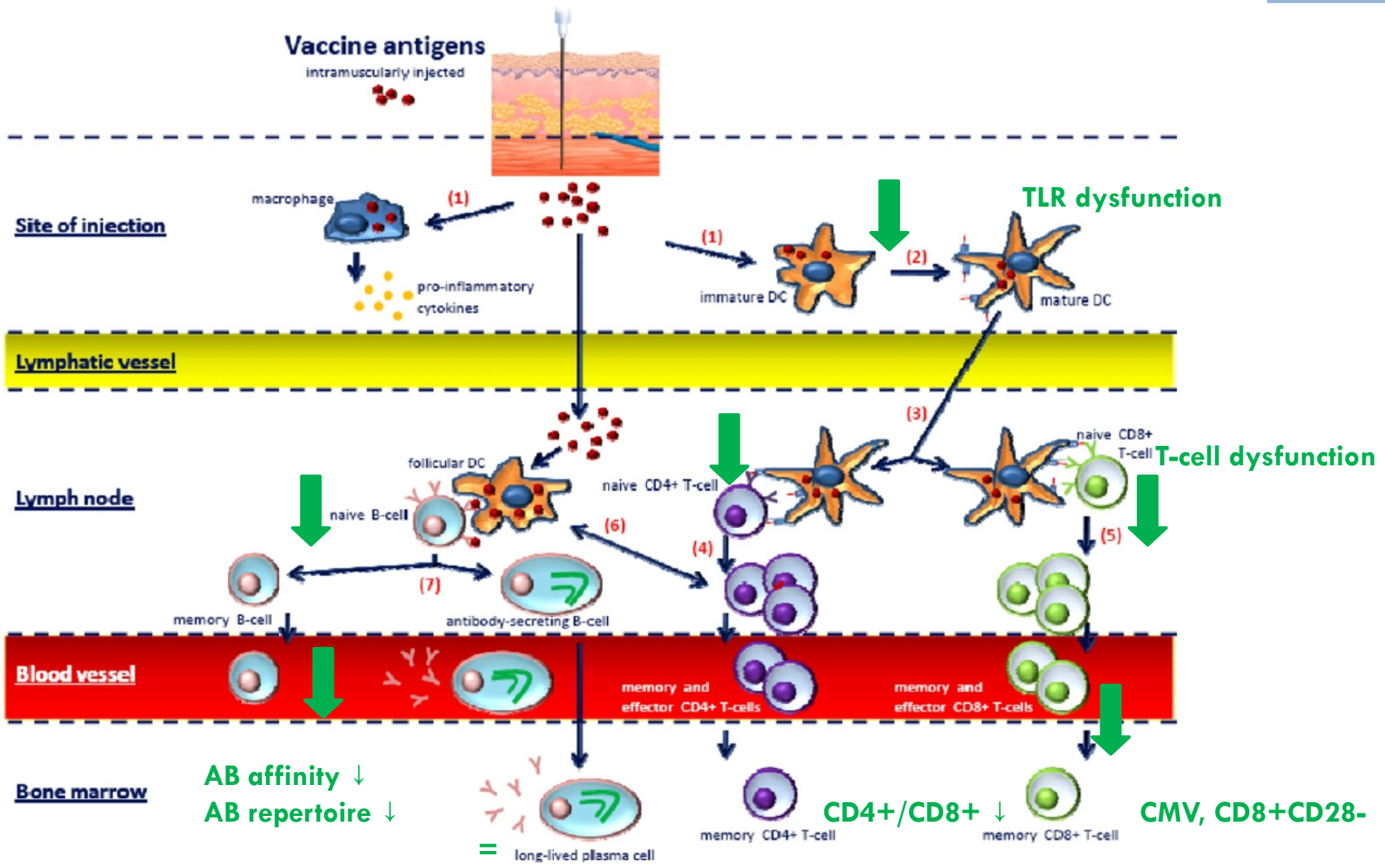


Clin Infect Dis 2004;39: 1642-50

Pneumonia and Health Care Setting

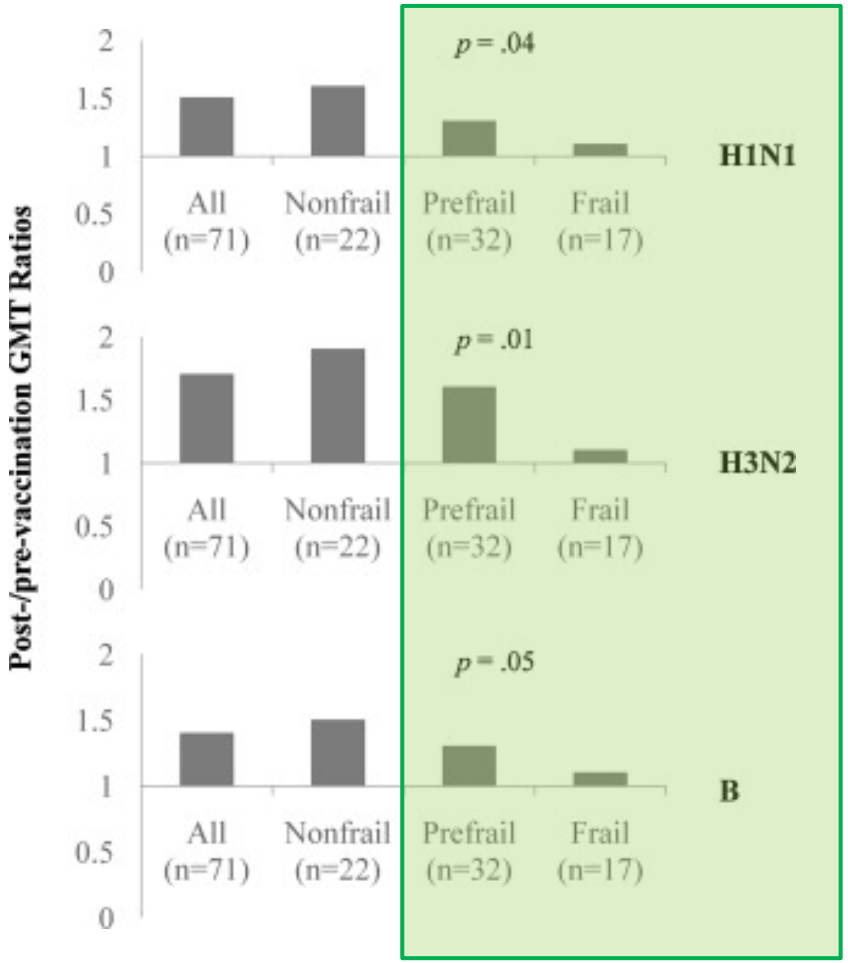


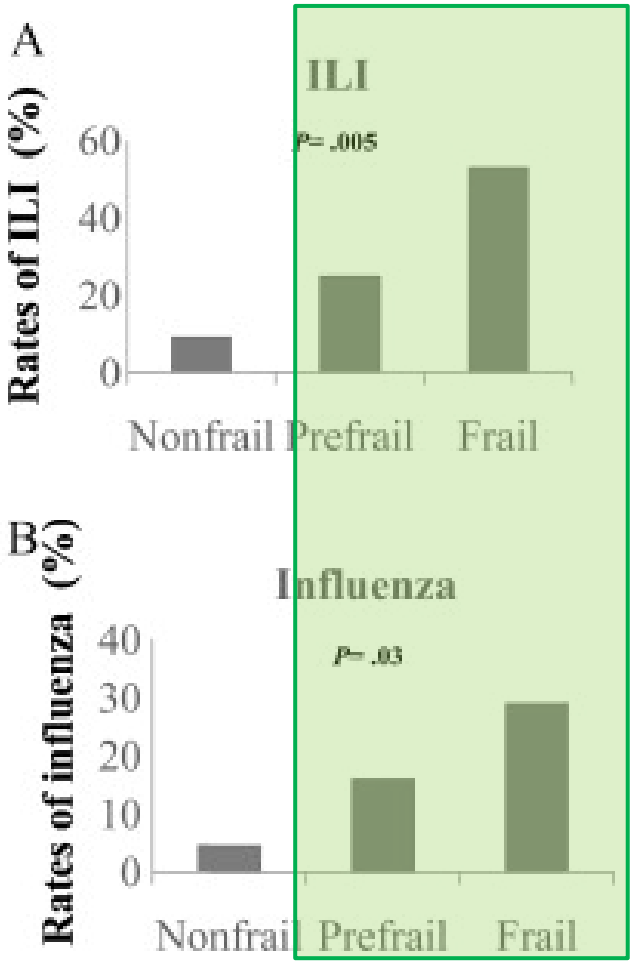
Immunosenescence



Immunosenescence

Frailty and immune response TIV

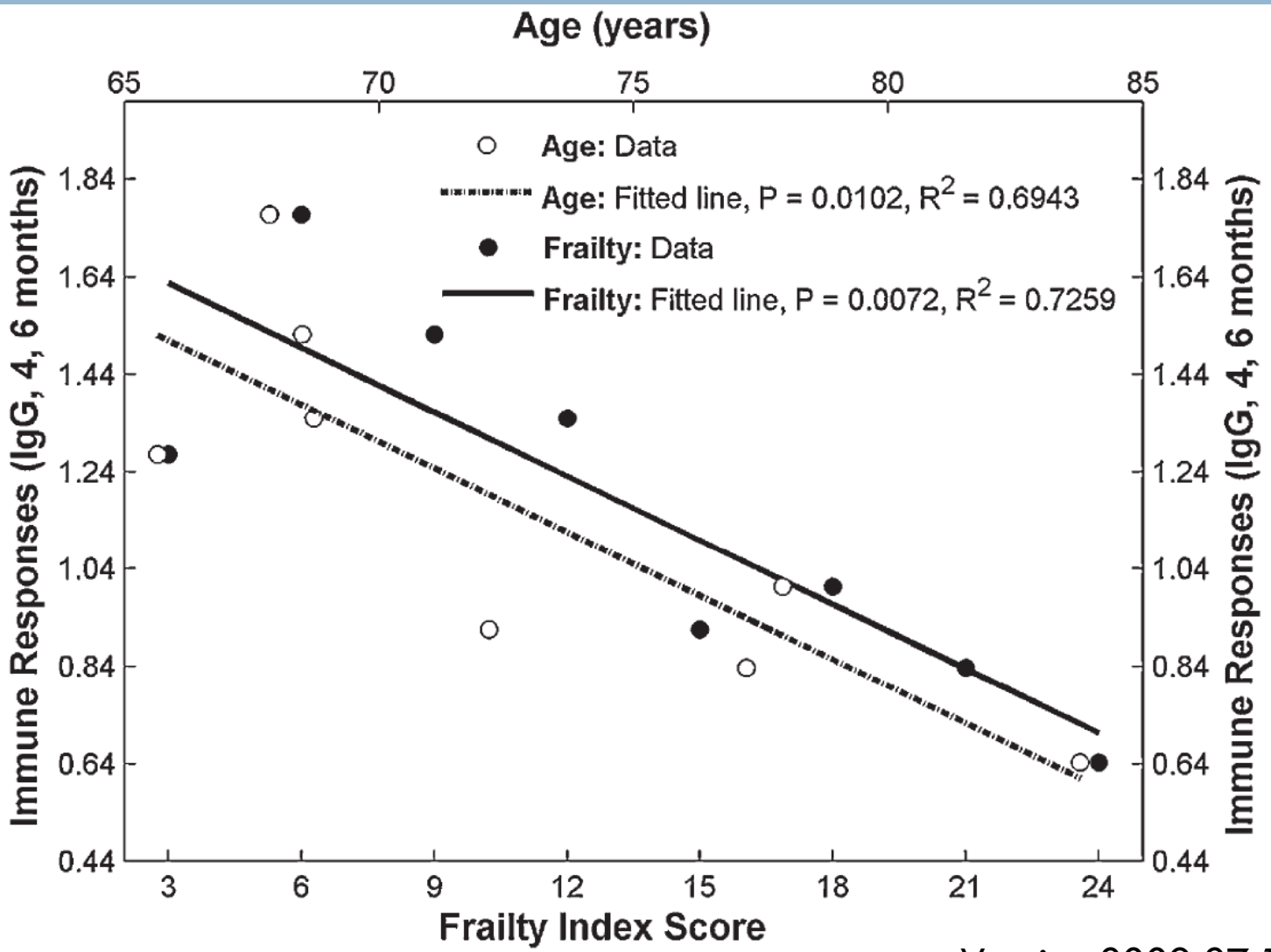




Vaccine 2011; 29: 5015-5021

Immunosenescence

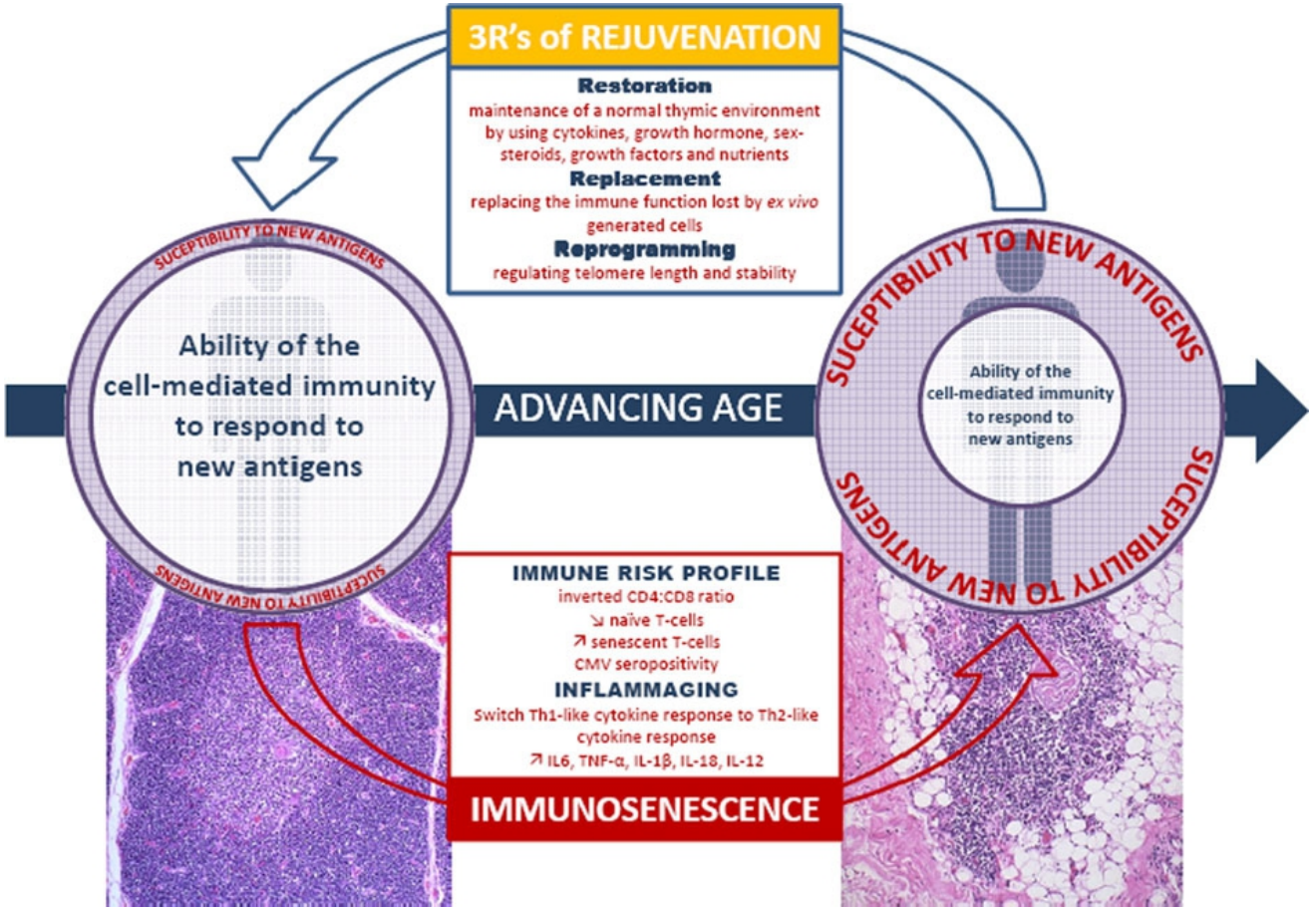
Frailty and immune response PCV7 & PPV23



Vaccine 2009;27:1628-36

Tackling immunosenescence

- Immune – rejuvenation



AGE (2013) 35:609–620

Tackling immunosenescence

Enhancing vaccine effect

- Vaccine coverage (epidemiology, valency)
- High dose vaccines
- Adjuvated vaccines
- Vaccine formulations (virosome, ID, IN + SC/IM,…)
- Booster vaccines

- Higher postvaccination Ab titers

Influenza vaccination Belgium

A. **Group 1:**

- Pregnant women (2nd & 3th trimester)
- > 6 m. + chronic heart, lung, kidney, liver, metabolic, neuromuscular, immunological disease
- $^{24}_{12}$ **65 y.**
- **Institutionalized persons**
- 6m – 18 y. + chronic aspirine use

Group 2:

- Health care workers

Evidence: controversies TIV

- **Authors' conclusions**
  - The available evidence is of **poor quality** and provides **no guidance regarding the safety, efficacy or effectiveness** **of influenza vaccines for people aged 65 years or older.**
  - DOI: 10.1002/14651858.CD004876.pub3

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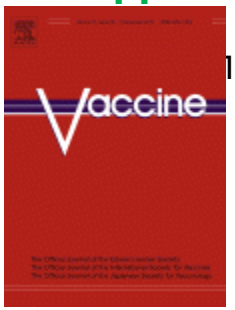
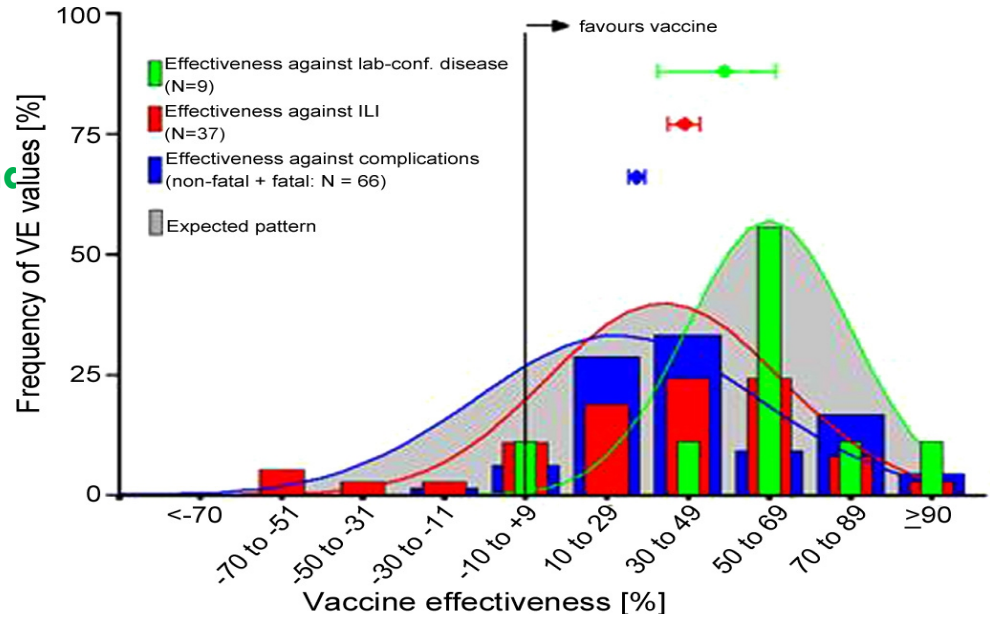
- **Cochrane re-arranged:**
  - **Support** for policies **to vaccin**

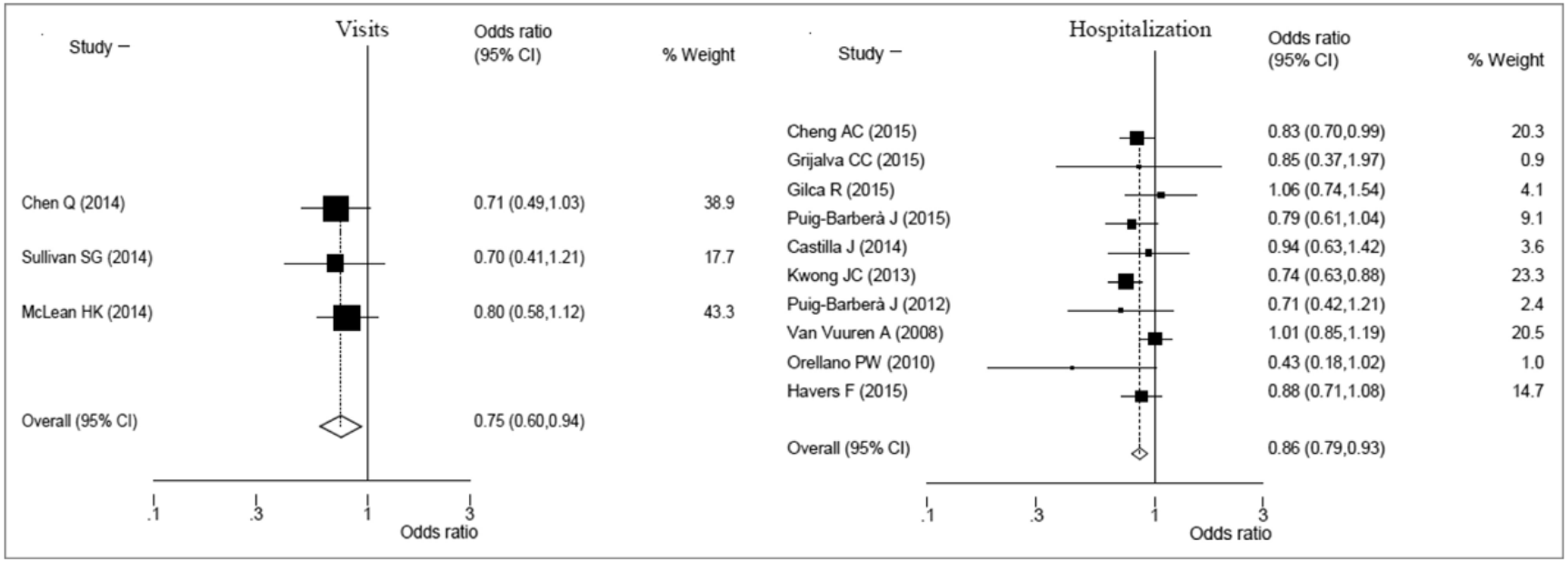


1 (2013) 6030– 6033



TIV vaccination in the elderly

- Influenza vaccination effect elderly
  - VE visits: 25 %
  - VE hospitalization 14 %



Hum Vaccin Immunother. 2017 May 8; :0. Epub 2017 May 8.

Effectiveness of seasonal influenza vaccine in community dwelling elderly people: a meta-analysis of test-negative design case-control studies

- Influenza activity

	Vaccine match		Vaccine mismatch	
	OR (95% CI)	p value	OR (95% CI)	p value
Non-epidemic seasons	0·65 (0·41–1·03)	0·0656	0·87 (0·57–1·32)	0·5043
Sporadic activity	0·69 (0·48–0·99)	0·0489	0·92 (0·68–1·25)	0·5945
Local activity	0·62 (0·28–1·36)	0·2126	0·83 (0·38–1·79)	0·6079
Epidemic seasons	0·48 (0·39–0·59)	<0·0001	0·64 (0·52–0·78)	0·0004
Regional outbreaks	0·42 (0·30–0·60)	0·0002	0·57 (0·41–0·79)	0·0029
Widespread outbreaks	0·54 (0·46–0·62)	<0·0001	0·72 (0·60–0·85)	0·0015

OR=odds ratio.

Table 2: Results from the mixed-effects meta-regression model

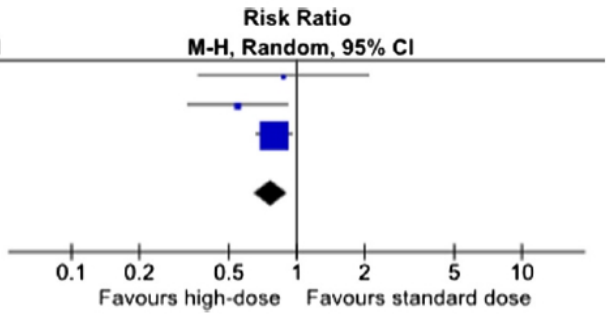
Lancet Infect Dis 2014;14: 1228–39

High dose vs low dose TIV (>65 y.)
Effect against laboratory proven influenza

- HD VE + 25 % vs LD TIV

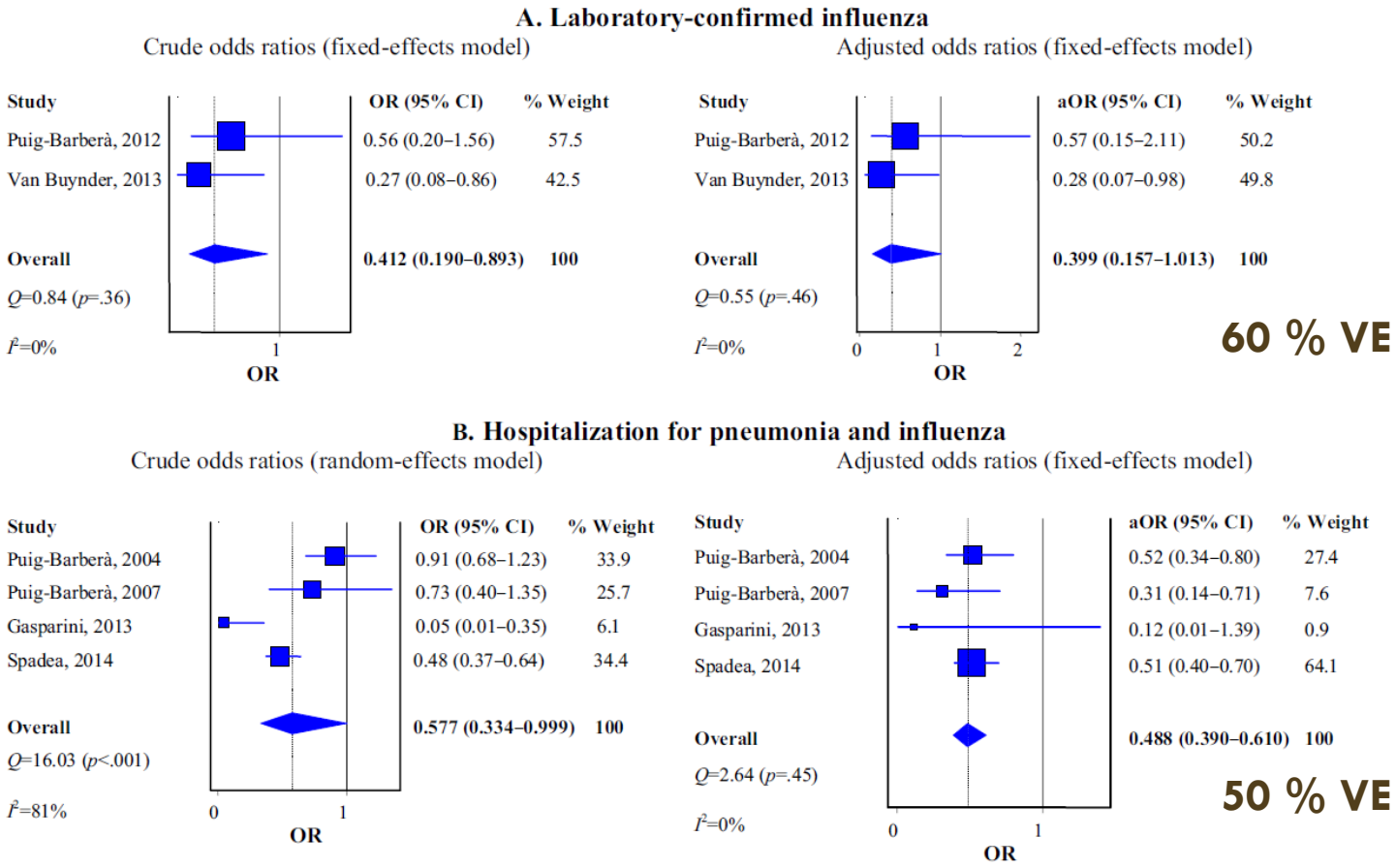
Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
DiazGranados 2013	14	6107	8	3051	3.7%	0.87 [0.37, 2.08]
DiazGranados 2014, Y1	23	7253	42	7244	10.9%	0.55 [0.33, 0.91]
DiazGranados 2014, Y2	205	8737	259	8749	85.4%	0.79 [0.66, 0.95]
Total (95% CI)		**22097**		**19044**	**100.0%**	**0.76 [0.65, 0.90]**
Total events	242		309			

Heterogeneity: Tau² = 0.00; Chi² = 1.92, df = 2 (P = 0.38); I² = 0%
Test for overall effect: Z = 3.16 (P = 0.002)



Vaccine. 2017 May 15;35(21):2775-2780.

MF-59 udjuvated TIV vaccine effect



Vaccine. 2017 Jan 23;35(4):513-520

Pneumococcal vaccination, Belgium

TARGET GROUPS:

February 2015

Adults with high risk for PD

- Immunocompromise
- Asplenia (anatomic or functional)
- Sickle-cell disease and hemoglobinopathia
- CSF leakage or cochlear implant

Adults with comorbidity

- Chronic heart disease
- Chronic lung disease
- Chronic liver disease or ethylism
- Chronic kidney disease

Hoge Gezondheidsraad

federale overheidsdienst
VOLKSGEZONDHEID, VEILIGHEID VAN DE VOEDSELKETEN EN LEEFMILIEU

Pneumococcal vaccination, Belgium

February 2015

Adults 19-85 y. with high risk for PD

- **Primo-vaccination** : PCV13 $^{23}_{11}$ PPV23 after 8w
- **Previously vaccinated** with PPV23: PCV13 once ≥ 1 j. after last PPV23
- **Revaccination**: PPV23 every 5 y.

Adults 50-85 y. with comorbidity
Healthy adults 65-85 y.

- **Primo-vaccination**: PCV13 $^{23}_{11}$ PPV23 after 8w
- **Previously vaccinated** with PPV23: PCV13 once ≥
- **(Booster: ?** Depends on epidmiologie over 5 y. and

Hoge Gezondheidsraad

Adults >85 y.

- No data on effect > 85 j.

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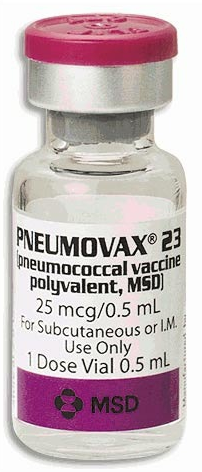
VOLKSGEZONDHEID, VEILIGHEID VAN DE VOEDSELKETEN EN LEEFMILIEU

Evidence: controversies PPV23



- **Authors' conclusions**
  - This meta-analysis provides evidence supporting the recommendation for PPV to prevent **IPD in adults**. The evidence from RCTs is less clear with respect to adults with **chronic illness**. This might be because of lack of effect or lack of power in the studies. The meta-analysis does not provide evidence to support the routine use of PPV to prevent **all-cause pneumonia** or **mortality**.
  - DOI: 10.1002/14651858.CD000422.pub3

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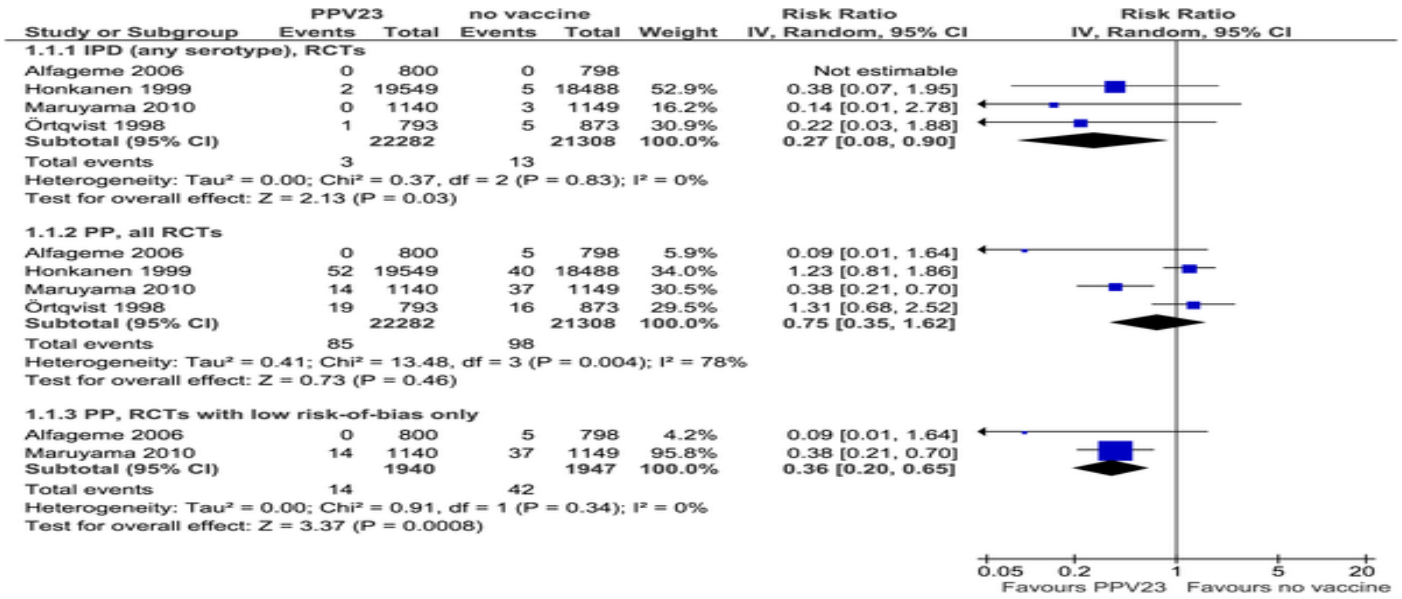
PPV23 vaccination in COPD patients

- Effect of pneumococcal vaccination
  - COPD exacerbation prevention: 47% VE (CI:19-56%)
  - CAP prevention: 48% VE (CI:11-57%)
  - No effect
    - Mortality
    - Hospital admission

Cochrane Database Syst Rev. 2017 Jan 24;1:CD001390.

PPV23 effect on IPD and PP in elderly RCTs

- IPD: 73 % VE
- PP: 64 % VE

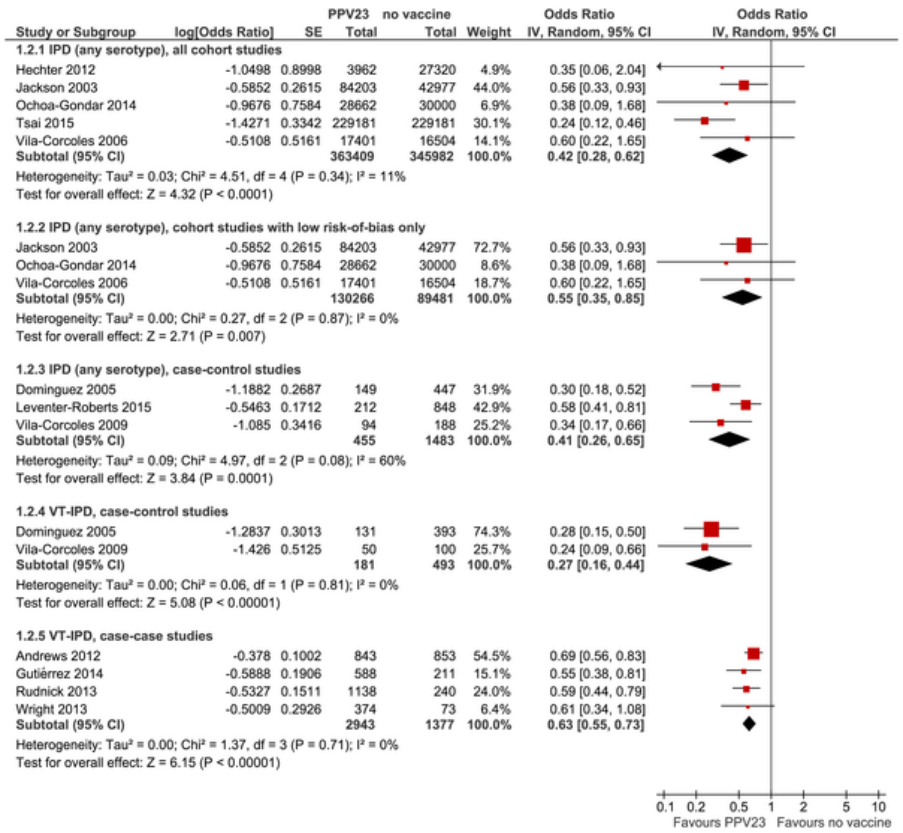


Study or Subgroup	PPV23 Events	PPV23 Total	no vaccine Events	no vaccine Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 IPD (any serotype), RCTs						
Alfageme 2006	0	800	0	798		Not estimable
Honkanen 1999	2	19549	5	18488	52.9%	0.38 [0.07, 1.95]
Maruyama 2010	0	1140	3	1149	16.2%	0.14 [0.01, 2.78]
Örtqvist 1998	1	793	5	873	30.9%	0.22 [0.03, 1.88]
Subtotal (95% CI)		**22282**		**21308**	**100.0%**	**0.27 [0.08, 0.90]**
Total events	3		13			
Heterogeneity: Tau² = 0.00; Chi² = 0.37, df = 2 (P = 0.83); I² = 0%						
Test for overall effect: Z = 2.13 (P = 0.03)						
1.1.2 PP, all RCTs						
Alfageme 2006	0	800	5	798	5.9%	0.09 [0.01, 1.64]
Honkanen 1999	52	19549	40	18488	34.0%	1.23 [0.81, 1.86]
Maruyama 2010	14	1140	37	1149	30.5%	0.38 [0.21, 0.70]
Örtqvist 1998	19	793	16	873	29.5%	1.31 [0.68, 2.52]
Subtotal (95% CI)		**22282**		**21308**	**100.0%**	**0.75 [0.35, 1.62]**
Total events	85		98			
Heterogeneity: Tau² = 0.41; Chi² = 13.48, df = 3 (P = 0.004); I² = 78%						
Test for overall effect: Z = 0.73 (P = 0.46)						
1.1.3 PP, RCTs with low risk-of-bias only						
Alfageme 2006	0	800	5	798	4.2%	0.09 [0.01, 1.64]
Maruyama 2010	14	1140	37	1149	95.8%	0.38 [0.21, 0.70]
Subtotal (95% CI)		**1940**		**1947**	**100.0%**	**0.36 [0.20, 0.65]**
Total events	14		42			
Heterogeneity: Tau² = 0.00; Chi² = 0.91, df = 1 (P = 0.34); I² = 0%						
Test for overall effect: Z = 3.37 (P = 0.0008)						

Falkenhorst G, Remschmidt C, Harder T, Hummers-Pradier E, Wichmann O, et al. (2017) Effectiveness of the 23-Valent Pneumococcal Polysaccharide Vaccine (PPV23) against Pneumococcal Disease in the Elderly: Systematic Review and Meta-Analysis. PLOS ONE 12(1): e0169368. https://doi.org/10.1371/journal.pone.0169368
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0169368

PPV23 effect on IPD in elderly
Observational studies

- IPD
  - Cohort studies: VE: 45 %
  - Case control: VE 59 %
- VT-IPD
  - Case control: VE 73 %
  - Case case: VE 37 %



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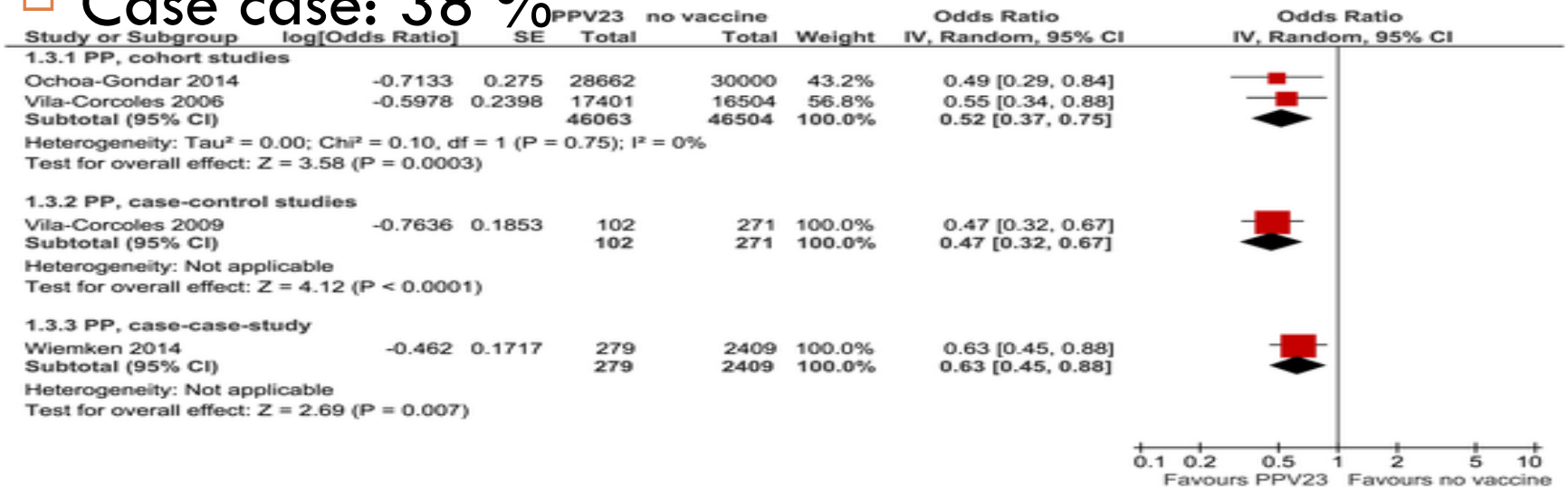
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0169368

PPV23 effect on PP in elderly Observational studies

- Cohort studies: VE: 48 %
- Case control: VE 53 %
- Case case: 38 %



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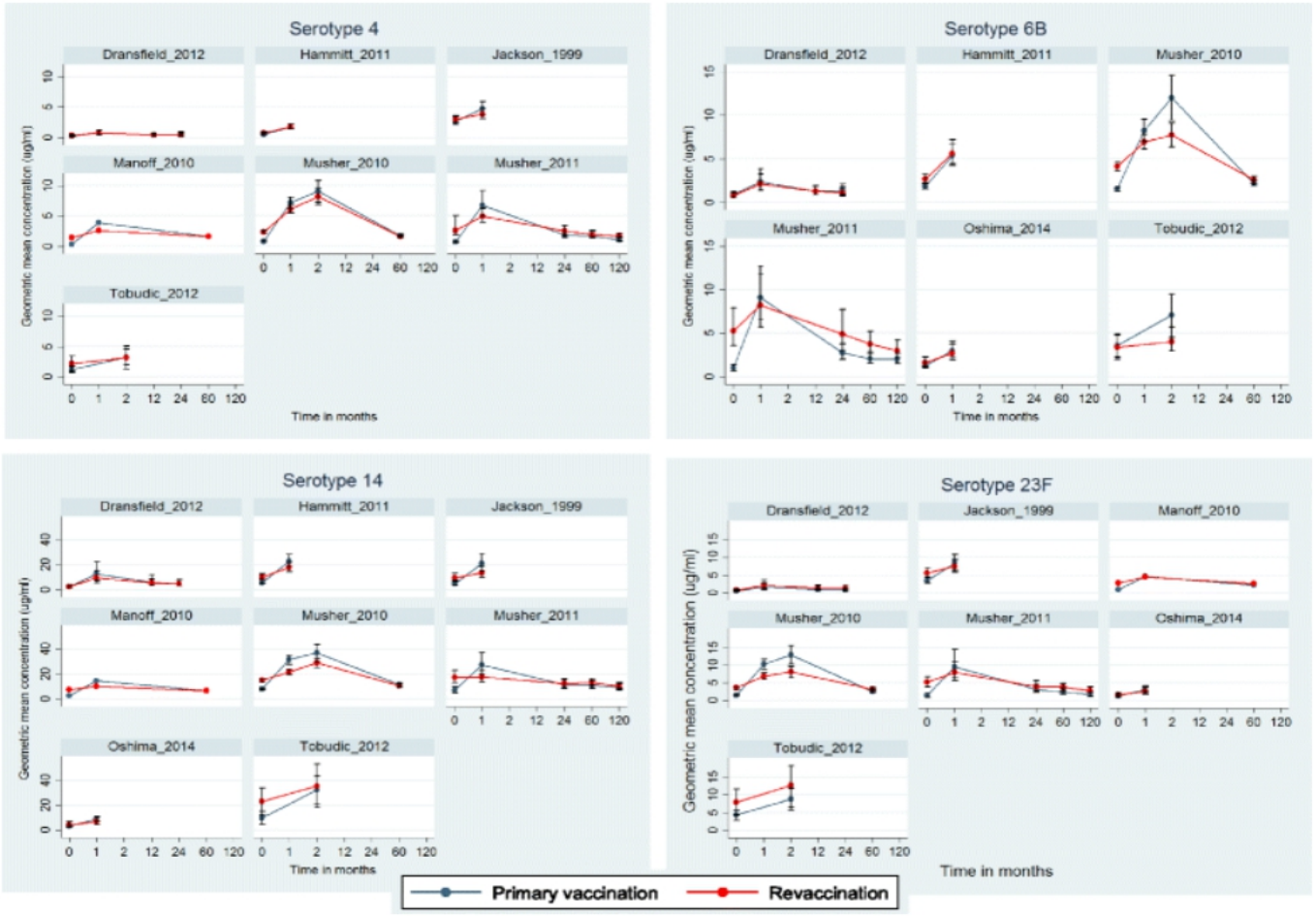
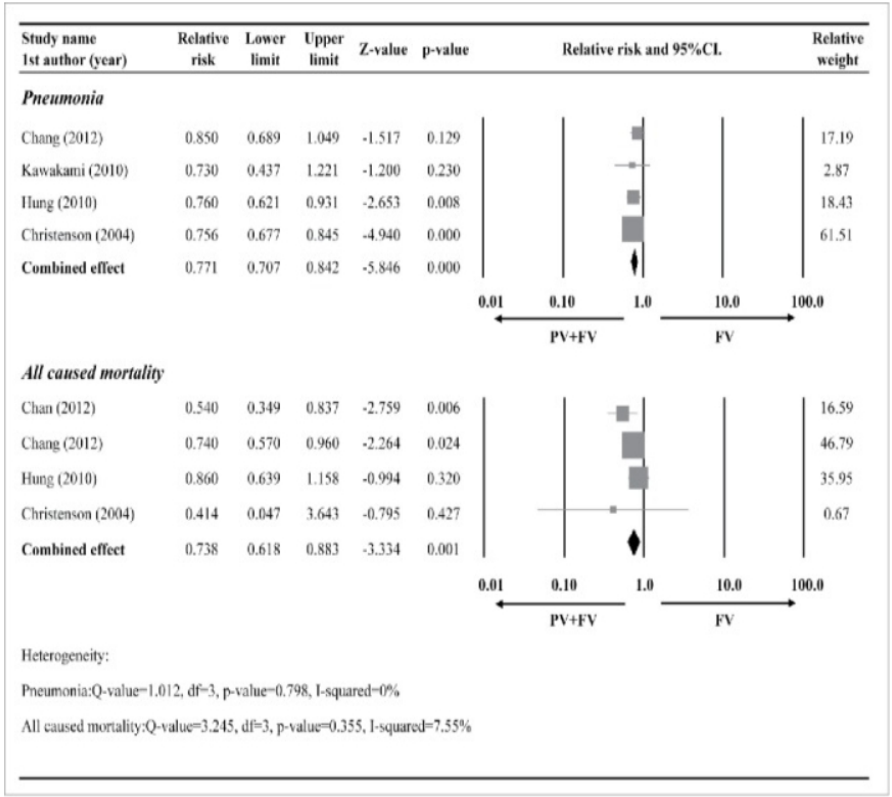
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0169368

Effectiveness, immunogenicity and safety of PPV23 revaccinations in the elderly: a systematic review.



BMC Infect Dis. 2016 Nov 25;16(1):711

Effect TIV + PPV vaccination



Study name 1st author (year)	Relative risk	Lower limit	Upper limit	Z-value	p-value	Relative risk and 95%CI.	Relative weight
Pneumonia							
Chang (2012)	0.850	0.689	1.049	-1.517	0.129		17.19
Kawakami (2010)	0.730	0.437	1.221	-1.200	0.230		2.87
Hung (2010)	0.760	0.621	0.931	-2.653	0.008		18.43
Christenson (2004)	0.756	0.677	0.845	-4.940	0.000		61.51
Combined effect	0.771	0.707	0.842	-5.846	0.000		
						0.01 0.10 1.0 10.0 100.0	
						PV+FV FV	
All caused mortality							
Chan (2012)	0.540	0.349	0.837	-2.759	0.006		16.59
Chang (2012)	0.740	0.570	0.960	-2.264	0.024		46.79
Hung (2010)	0.860	0.639	1.158	-0.994	0.320		35.95
Christenson (2004)	0.414	0.047	3.643	-0.795	0.427		0.67
Combined effect	0.738	0.618	0.883	-3.334	0.001		
						0.01 0.10 1.0 10.0 100.0	
						PV+FV FV	

Heterogeneity:

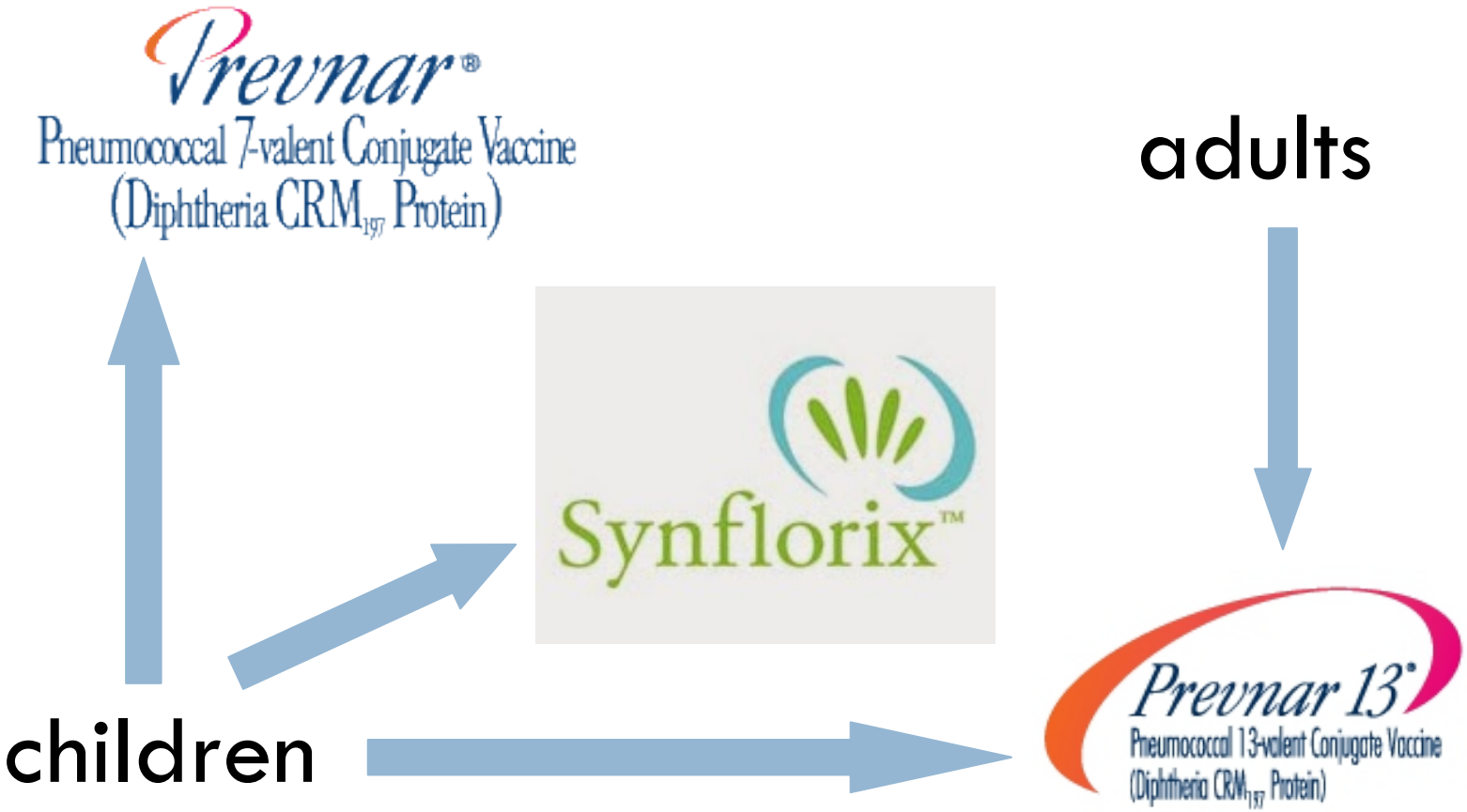
Pneumonia:Q-value=1.012, df=3, p-value=0.798, I-squared=0%

All caused mortality:Q-value=3.245, df=3, p-value=0.355, I-squared=7.55%

- TIV + PPV23
  - Pneumonia VE: + 23 %
  - Mortality VE: + 26 %

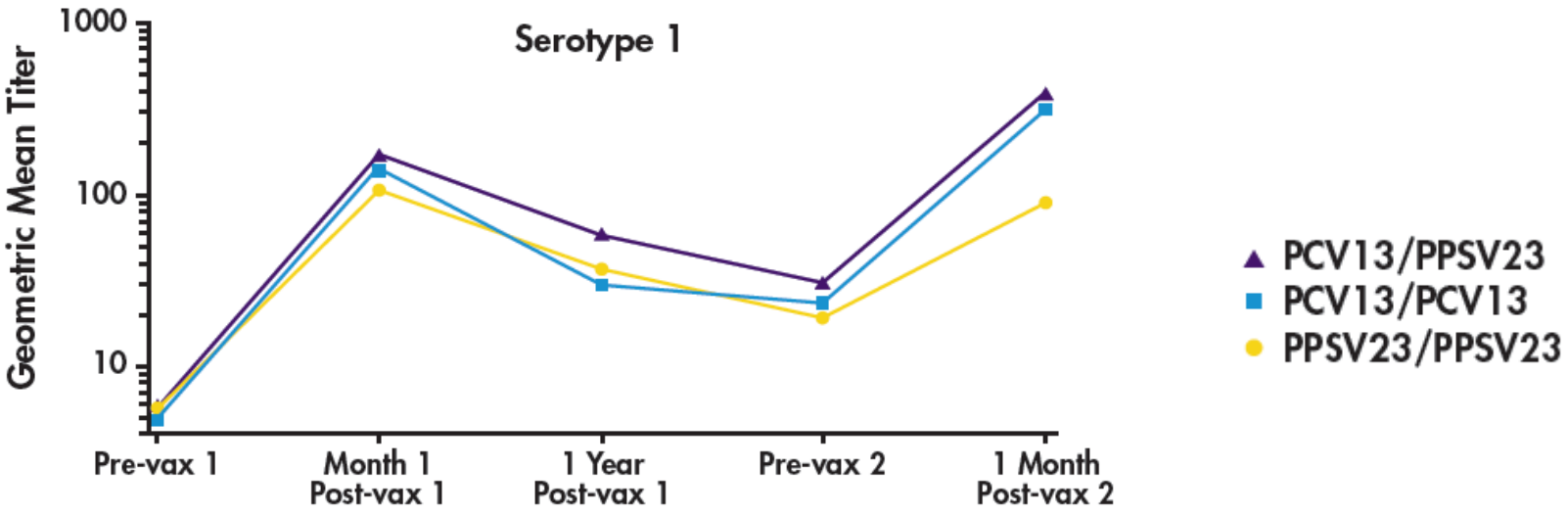
Hum Vaccin Immunother. 2016 Dec;12(12):3056-3064

PCV7, PCV10, PCV13



PCV13 in adults

- Immunogenicity PCV13
  - ≥ PPV23 in PPV naive 60-65 y.
  - ≥ PPV23 in PPV prevaccinated ≥ 70 y.
  - No immunotolerane boosting



PCV13 in adults

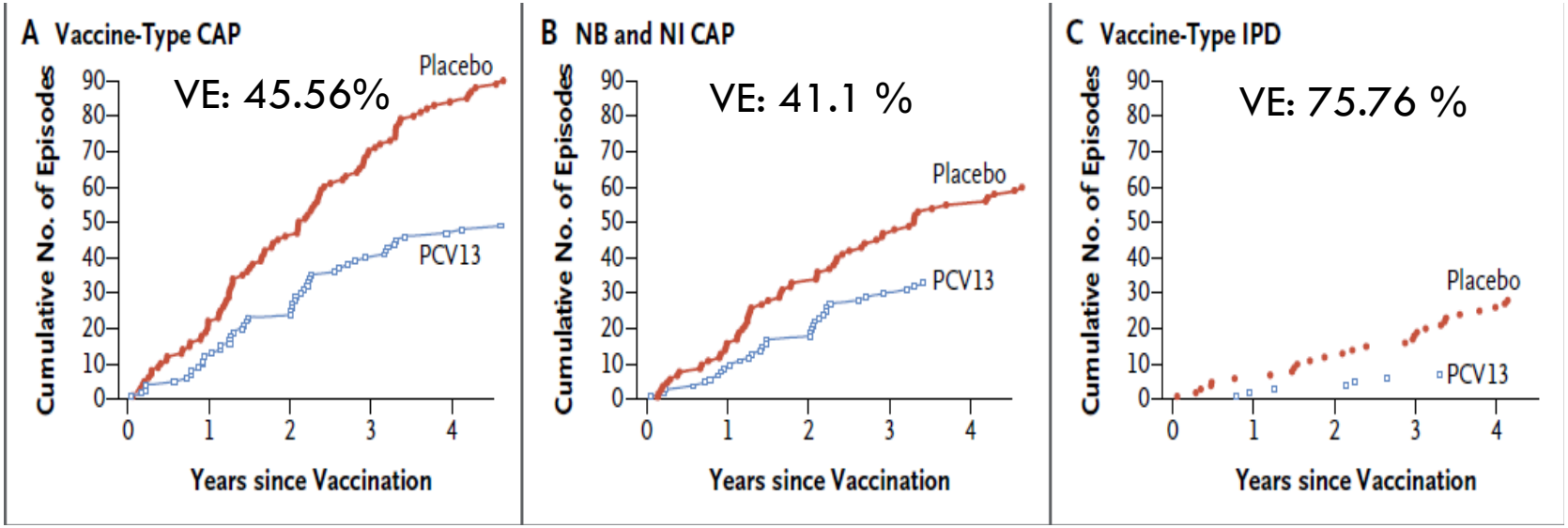
CAPITA

	PCV13	Placebo	Total
Number	42,237	42,255	84,492
Male	55.5 %	56.3 %	55.9 %
Age, mean (SD)	72.8	72.8	72.8
Age groups			
< 75 y	68.7 %	68.8 %	68.7 %
75 – 84 y	27.8 %	27.8 %	27.8 %
≥ 85 y	3.6 %	3.4 %	3.5 %
Comorbid disease*	42.3 %	42.4 %	42.3 %

*: asthma, Diabetes, Splenectomy Heart, Lung, or Liver disease.

N Engl J Med 2015;372:1114-25.

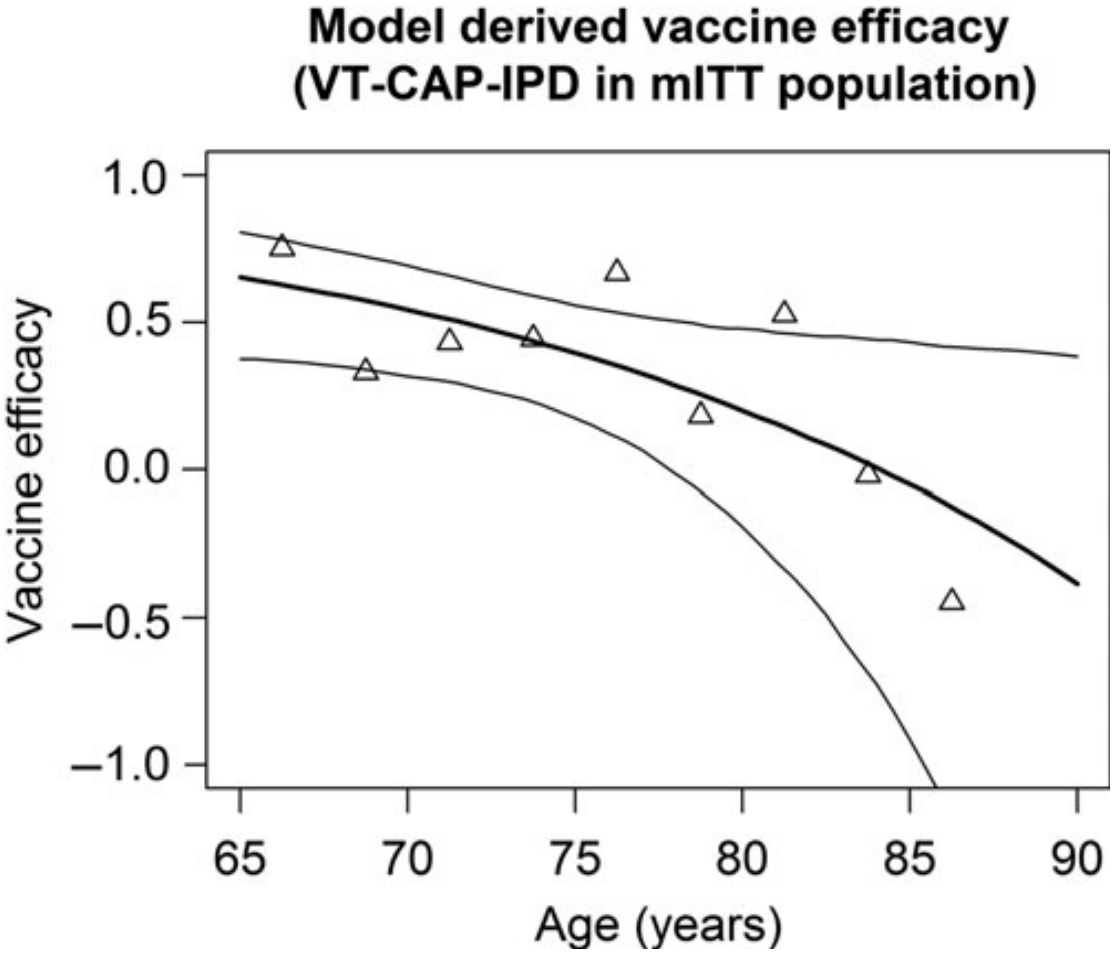
PCV13 in adults: CAPITA



	VE %	95 % CI	*P*
VT CAP (PP)			
Total	45.56	21.82 – 62.49	< 0.001
Age groups			
< 75 y	52.54	24.09 – 70.99	0.001
75 – 84 y	46.43	-4.33 – 73.57	0.07
≥ 85 y	-100	-1156.63 – 57.78	0.51

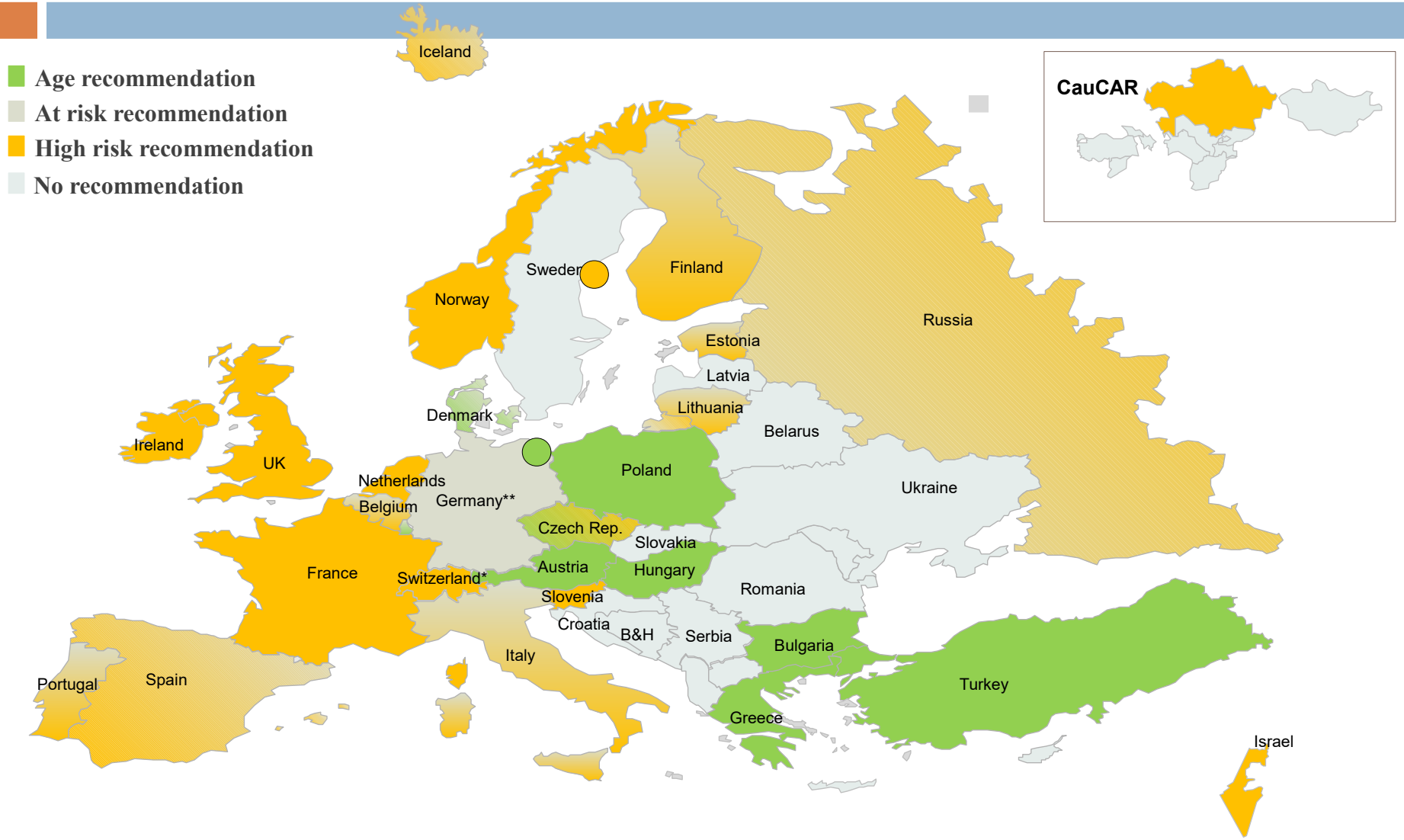
N Engl J Med 2015;372:1114-25.

PCV13 vaccine efficacy and age



DOI: 10.1093/cid/civ686

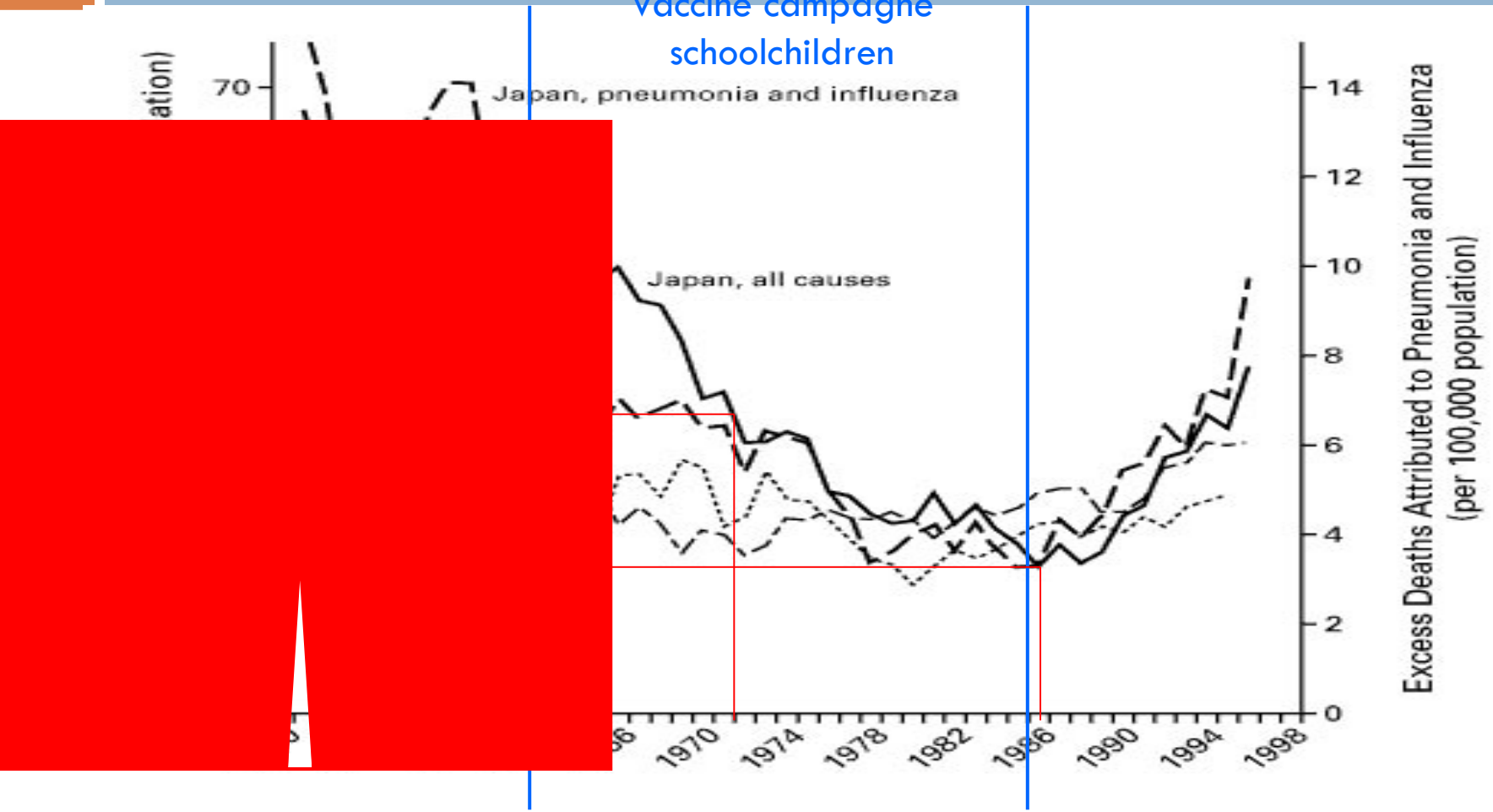
European National Recommendations for Prevenar13 in Adults



* Recommended At Risk >5 years but not approved by Health Authority. ** National Age based funded but not recommended.
Last update 2015-09-09. References are available on request.

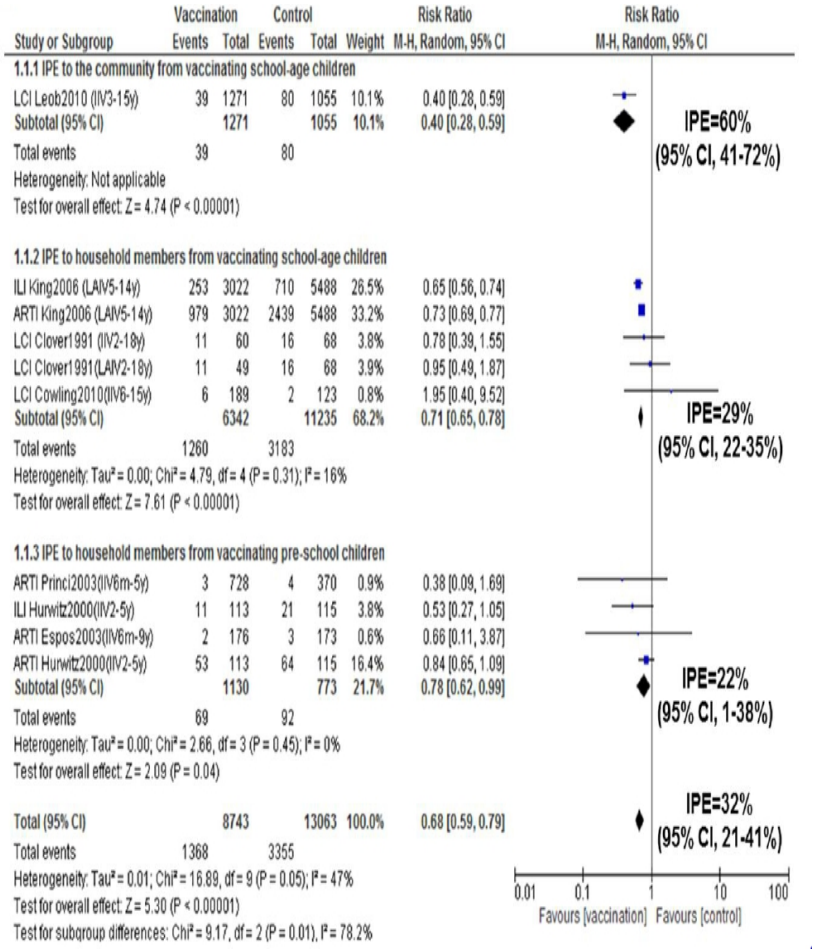
Herd vaccination strategy

Herd vaccination strategy: Children and Influenza



N Engl J Med 2001;344:889-96

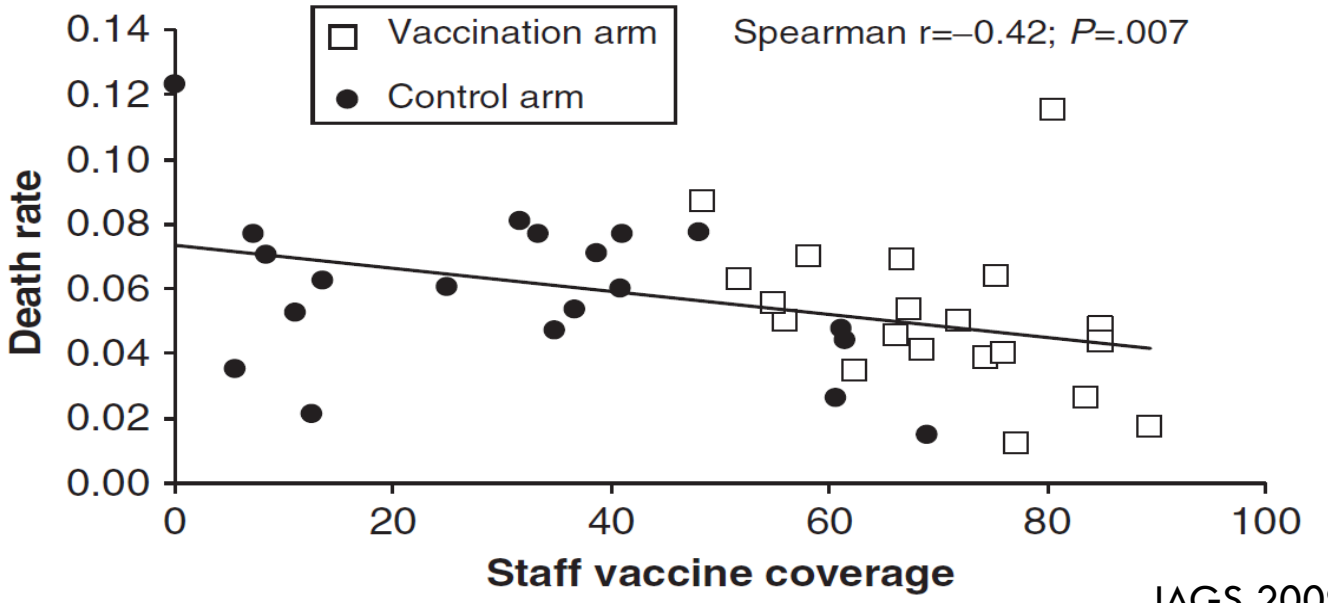
Indirect protective effect TIV



- School-age children
  - Community: VE 60 %
  - Household: VE 32 %
- Preschool children
  - Household: VE 22 %
- Total: VE 32 %

Clin Infect Dis. 2017 May 5. doi: 10.1093/cid/cix420.

Herd vaccination strategy: HCW and Influenza



JAGS 2009;57:1580-86

TIV vaccinated Health Care Workers Belgium

38.6 % (95 % CI: 26,4 – 44,4)

Gezondheidsenquete 2008

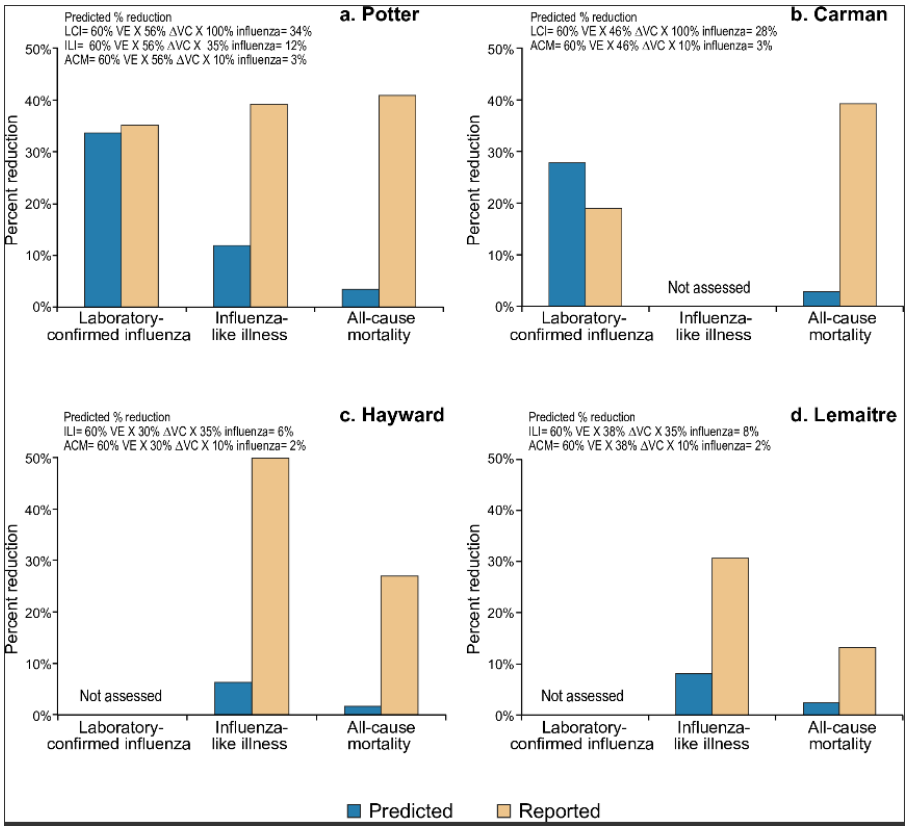
Controversies: Herd vaccination strategy for HCW and Influenza

	HCW TIV	Residents	Remark
Carman 2000	50.9 vs 4.9 %	Mortality ↓ Influenza =	Necropsy PCR influenza ↓
Hayward 2006	48.2 vs 5.9 %	Mortality ↓ ILI ↓ Physician visits ↓ Hospialisation ↓	In moderate, not in low influenza season
Oshitani 2000	Vaccine coverage ↑	ILI attack rate ↓	Resident coverage ↑ (80 %)
Potter 1997	61 %	Mortality ↓ ILI ↓	No mortality ↓ by resident vaccination
Lemaitre 2000	69.9 vs 31.8 %	Mortality ↓ ILI ↓ Hospitalisation =	Sick leave HCW ↓

Influenza and complications in residents =

DOI: 10.1002/14651858.CD005187.pub4

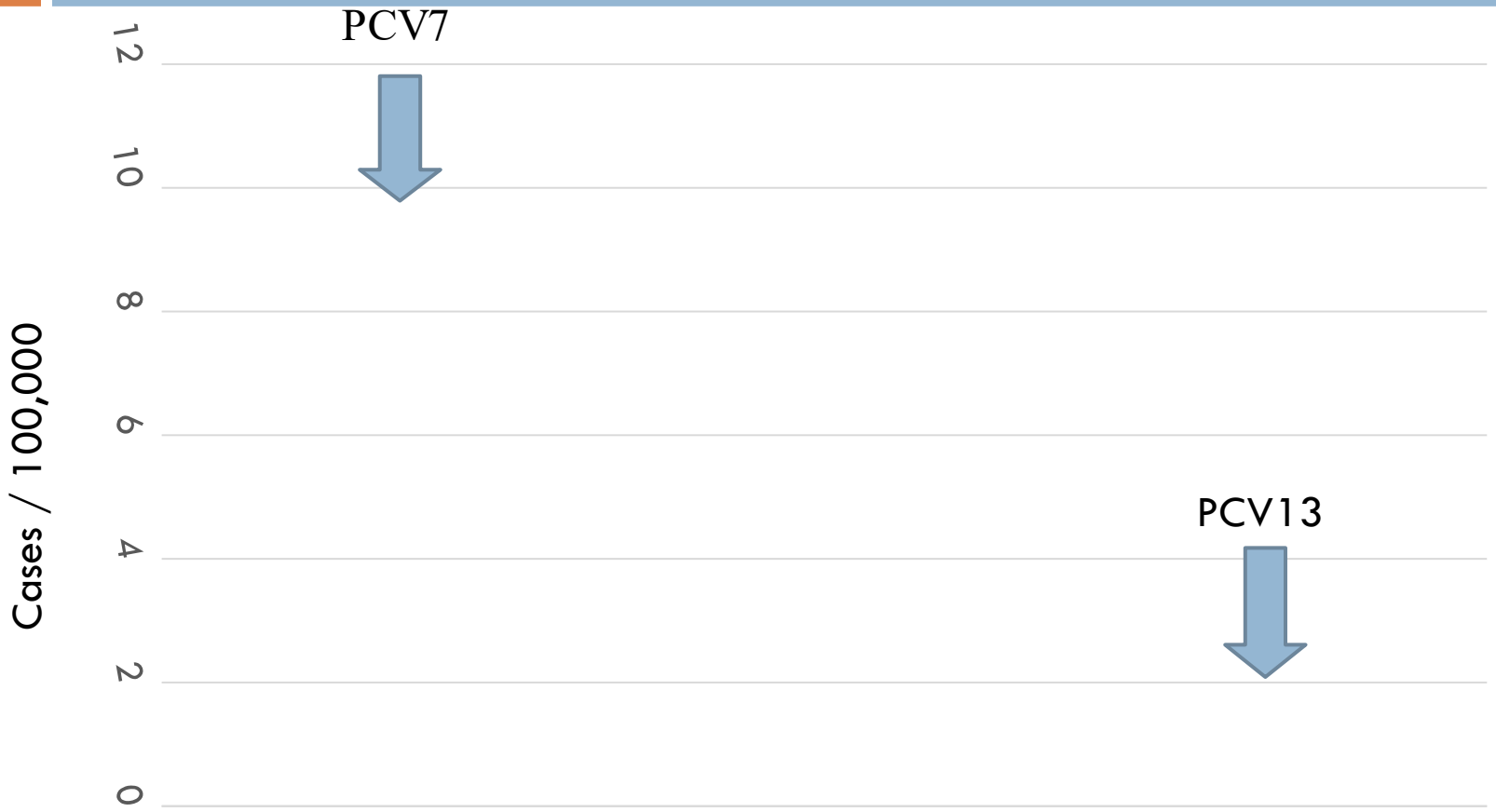
Influenza Vaccination of Healthcare Workers: Critical Analysis of the Evidence for Patient Benefit Underpinning Policies of Enforcement.



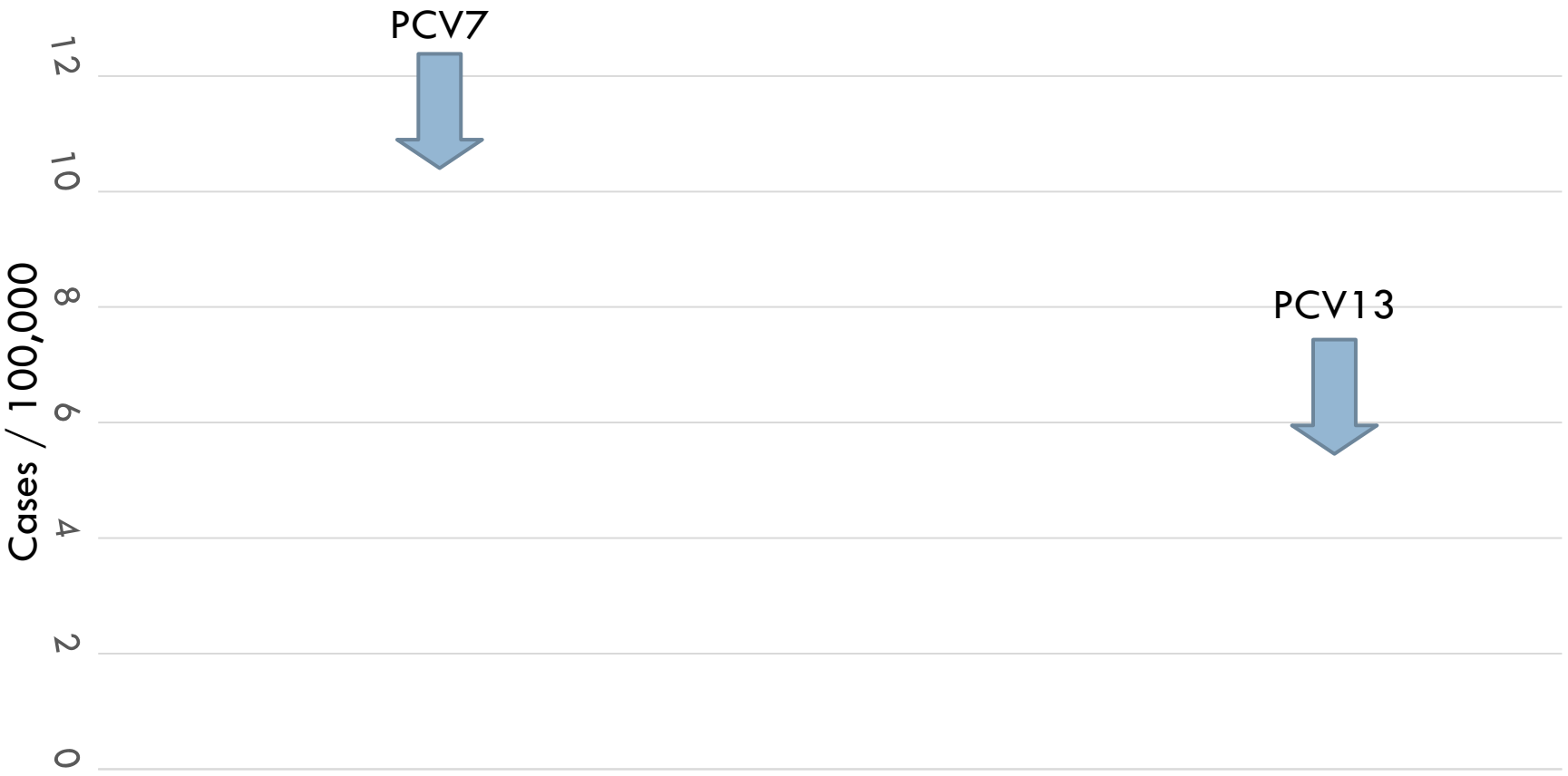
- Overreporting of reduction of influenza and mortality
- Persisting low evidence
- Voluntary TIV HCW

PLoS One. 2017 Jan 27;12(1):e0163586.

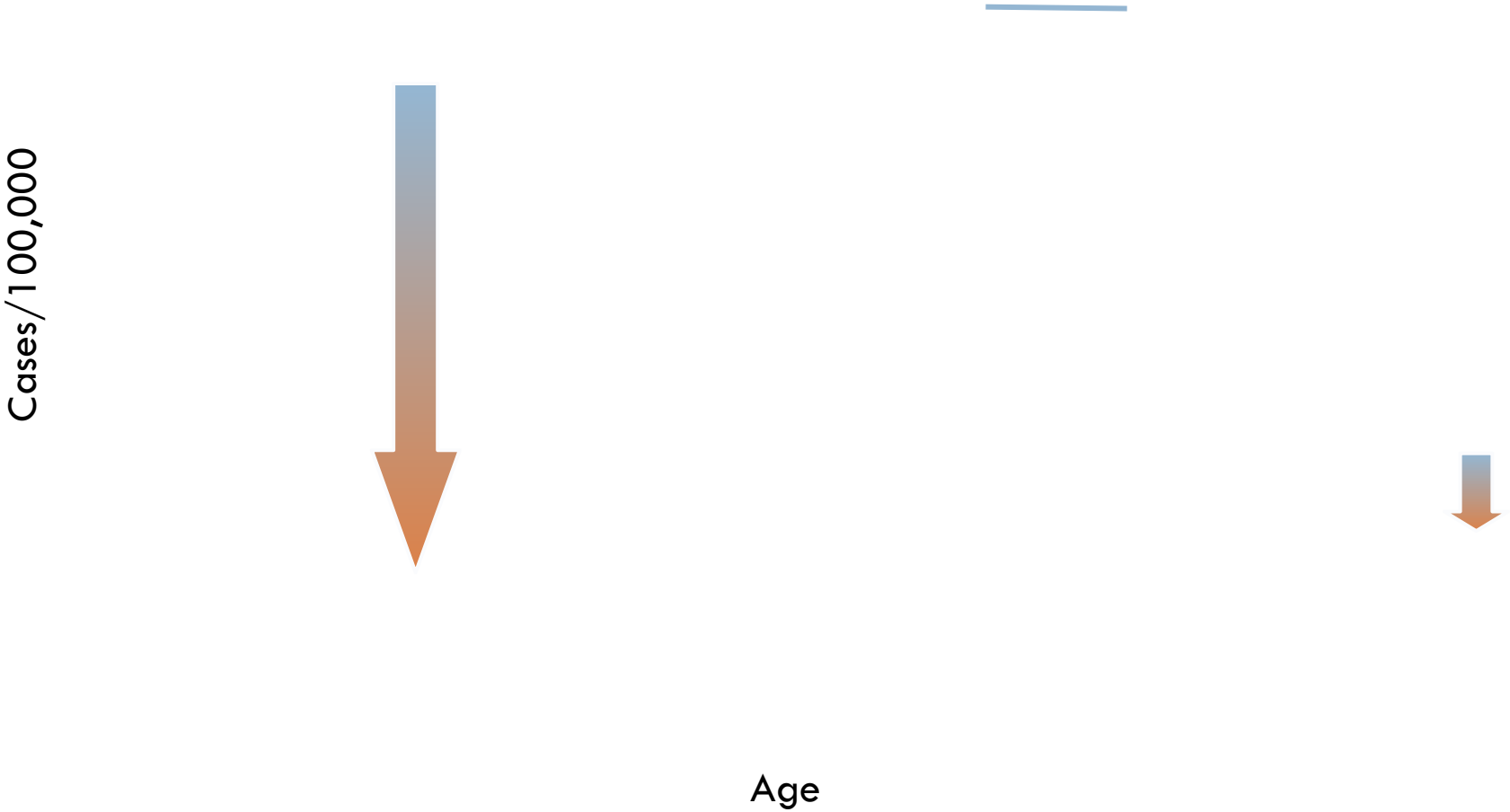
IPD cases USA 1997 - 2013



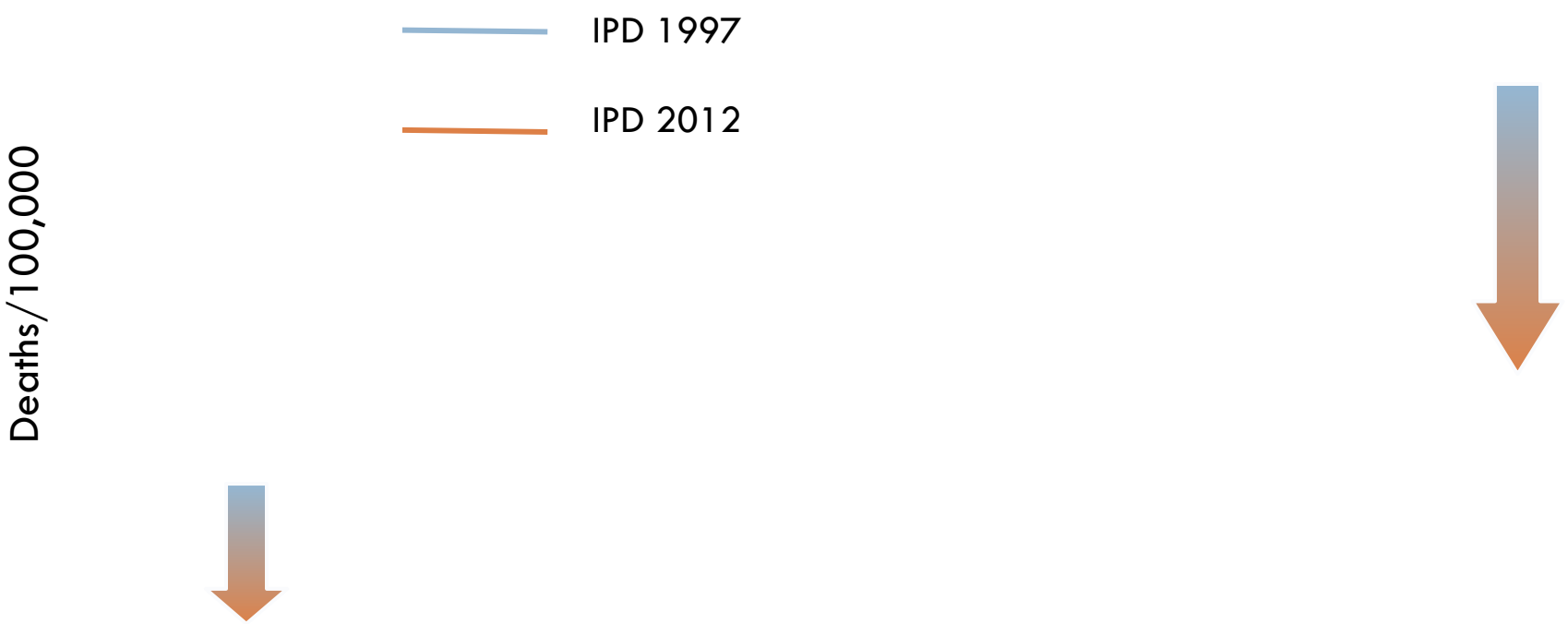
IPD mortality USA 1997 - 2013



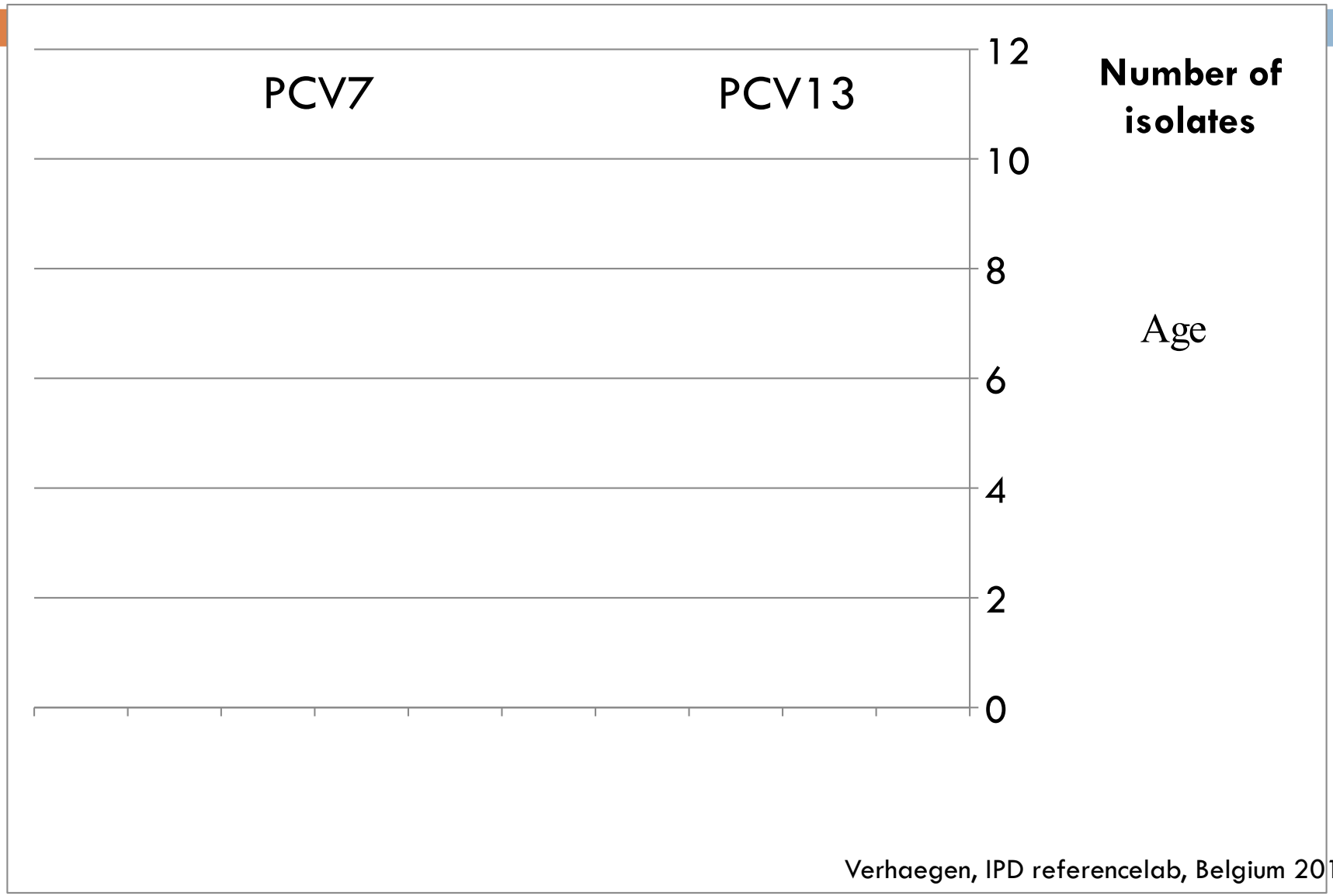
IPD cases USA



IPD mortality USA

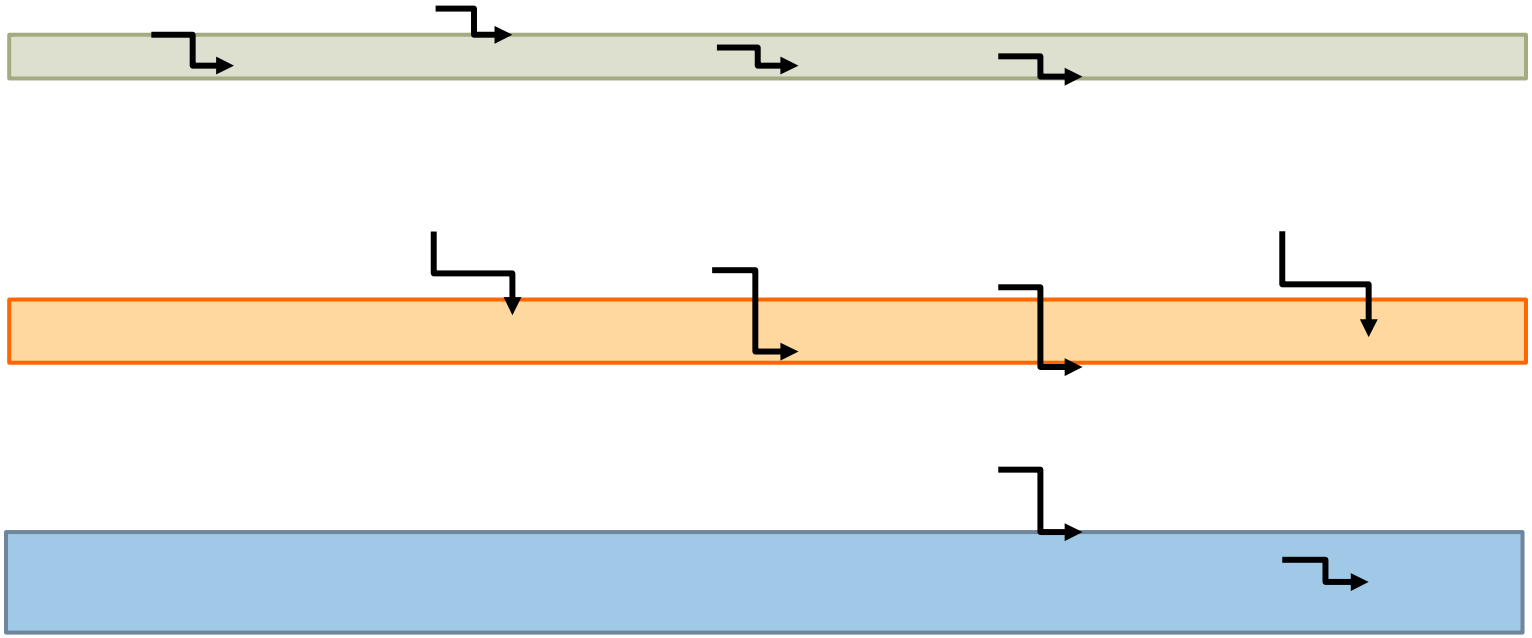


Herd protection against IPD



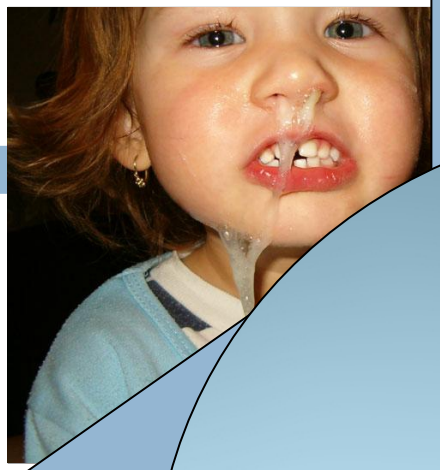
Verhaegen, IPD referencelab, Belgium 2014

SG coverage pneumococcal vaccines, Belgium 2008-2014



65 – 84 y. ≥ 85 y. Total

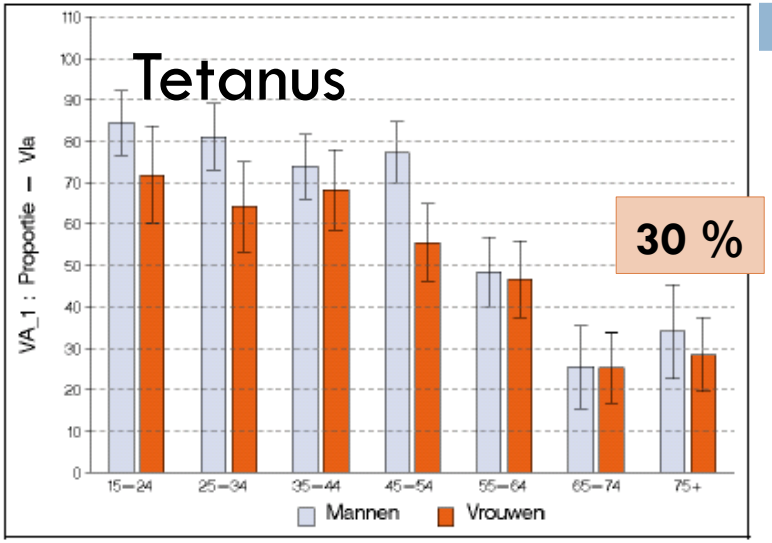
Poster EUGMS 2015, Oslo

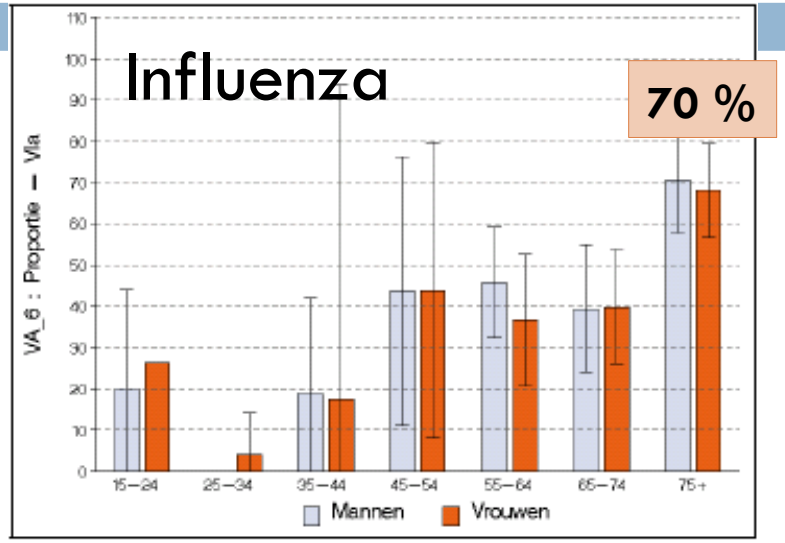


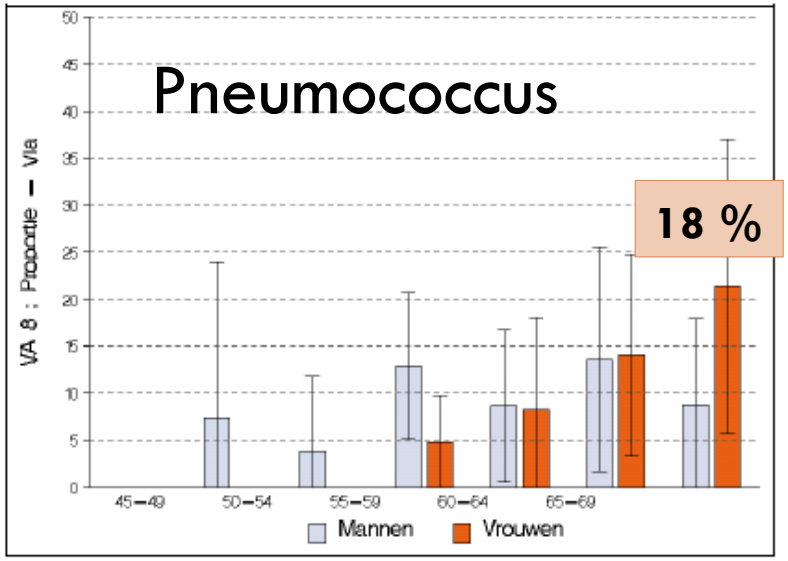
Vaccination strategies in older persons

- Prevent/treat (pre)-frailty and comorbidities
- Vaccinate with most immunogenic vaccines
- Boost
- Vaccinate older (fit) adults
- Vaccinate (grand)(grand)children and contacts
- Vaccinate HCW

Vaccine uptake in Belgium



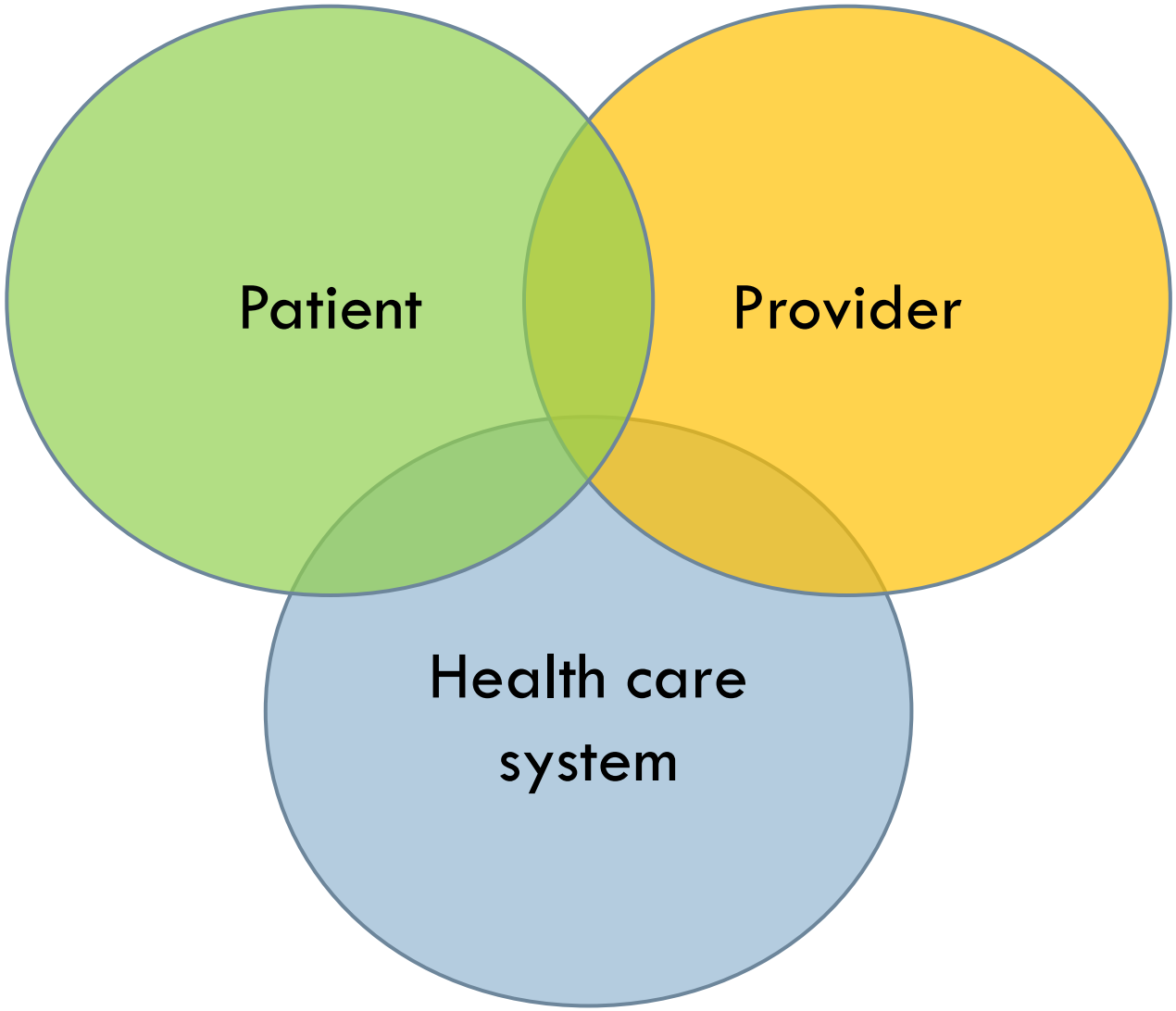




Gezondheidsenquête 2008

How to reach older persons?

HOW?



Vaccine preferences and acceptance of older adults

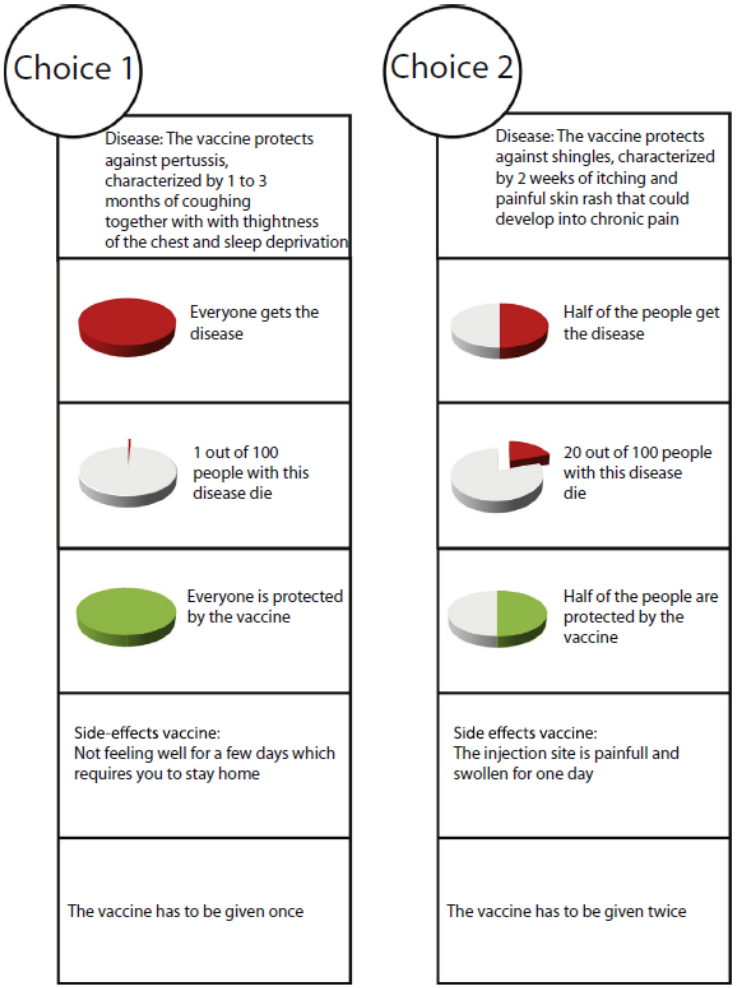


Fig. 1. Example of two scenarios from which respondents had to choose the preferred one.

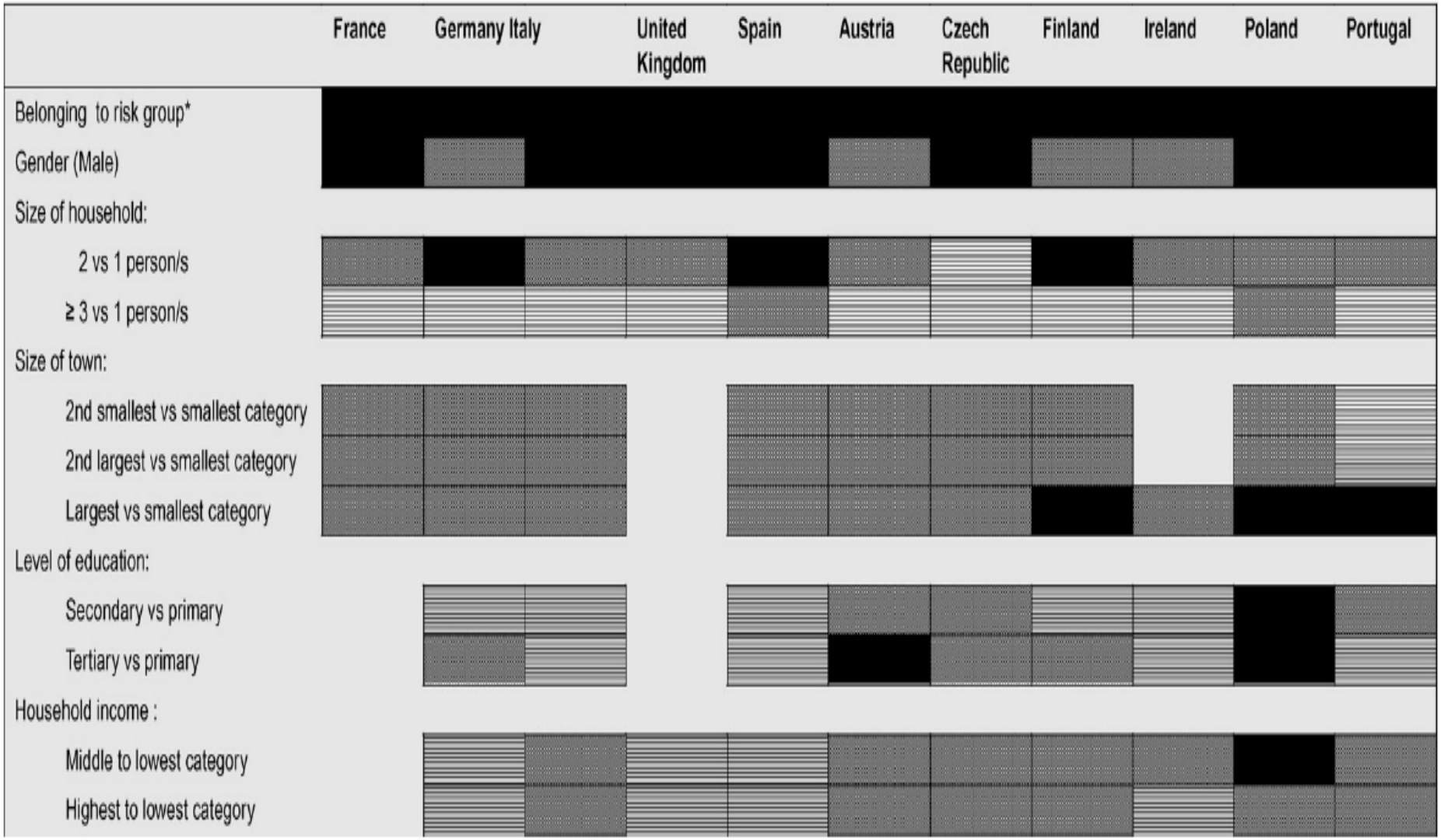
- 11 % opt out (no vaccination)
- **Factors influencing choice**
  - Mortality of disease
  - Susceptibility to disease

Table 5.
The value and estimated vaccination rates for the influenza, pneumococcal disease, herpes zoster and pertussis vaccine.

Vaccine[a]	Study population groups		
	50 years and older (n = 610)	50–65 years (n = 290)	65 years and older (n = 320)
	Estimated vaccination rate (%)	Estimated vaccination rate (%)	Estimated vaccination rate (%)
Pneumococcal disease	68.1	58.1	76.2
Herpes Zoster	58.1	49.5	67.5
Pertussis	53.9	43.8	57.5
Influenza	54.3	42.2	65.5

Vaccine. 2017 May 15;35(21):2823-2830.

Socioeconomic factors and TIV

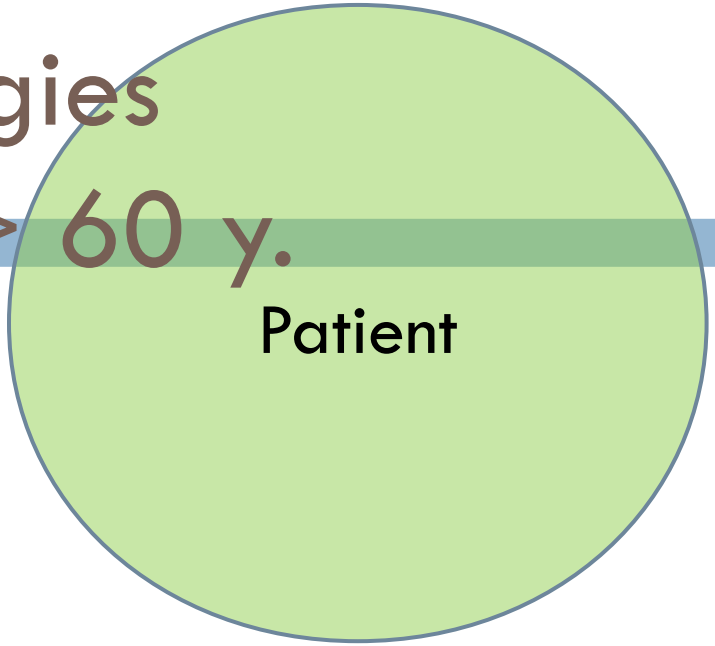


*Includes persons aged ≥65 years, or suffering of chronic illness, or working in medical field

■ Positive predictor; ▤ negative predictor; ▩ factor with no significant odds ratio; □ not applicable.

M.M. Endrich et al. / Vaccine 27 (2009) 4018–4024

TIV vaccination strategies
Community dwelling > 60 y.



- **Demand** ↑
  - *Reminders to patients*
    - Reminder postcard/letter
    - **Personalised** postcard/letter
    - Leaflet + letter > leaflet
    - Phone call (senior) > invitation in clinic
  - *Education of patients*
    - **Risk appraisal**
    - Nurse/Pharmacist education

DOI: 10.1002/14651858.CD005188.pub3

Not vaccinated?

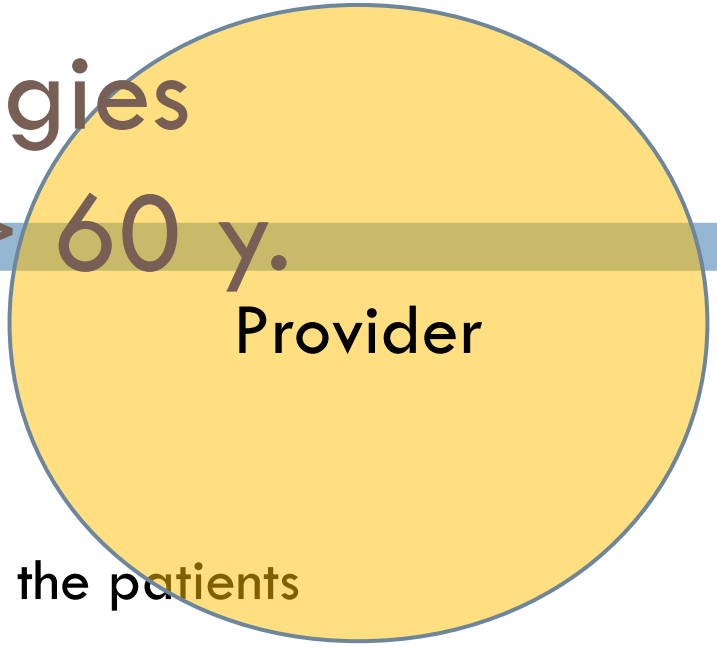
Table 4 Main reasons for not being vaccinated.

Study		Lack of recommendation	Absence of risk perception (%)	Disbelief in efficacy (%)	Fear of side effects (%)	Costs (%)
1	IV		16	17.5	17.5	11
2	IV	2.3%	19.6	19.3	11.2	
3	PV			21	18	8
6	IV	41%	66	13	21	
7	IV	14.7%	19.9	12.5	8.1	
8	PV	55.2%	14.5	4.8	1.6	
9 ('00)	IV		15.4	13.1	26.9	
9 ('01)	IV		12.1	12.9	23.8	
10	IV	36.6%	43.6	27.7		
11	IV/PV			20/19		
12[a]	IV	52%/63% W/E	79			
13	IV/PV	34%	22		14	
14	IV	56.2%	37.6	59.8		

IV = influenza vaccination, PV = pneumococcal vaccination, W = former West Germany, E = former East Germany.
[a]Target groups: including the elderly (⩾60), chronically ill, health care professionals.

Public Health (2007) **121**, 742–751

TIV Vaccination Strategies Community dwelling > 60 y.



- **Provider**
  - **Reminders** to Dr.
    - Reminder of all patients > half of the patients
    - (Competitive uptake poster + postcards)
  - **Facillitators** of vaccination in practice
  - Number of providers: vaccination clinics
  - **Facility**: prompts, computerized reminder system

DOI: 10.1002/14651858.CD005188.pub3

TIV vaccination strategies Community dwelling > 60 y.

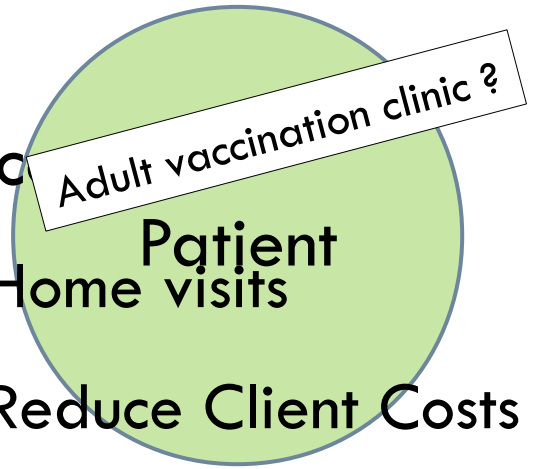
Health care system

- **Societal interventions**
  - No RCTs
  - **Recommendations**
    - **Age based** > risk based strategy
    - Quality and Outcome framework (UK): physician payment for targeted quality care
    - Clinical governance (NHS) contract + payment
    - **Health insurance coverage**

DOI: 10.1002/14651858.CD005188.pub3

Enhancing Access to Vaccination Services

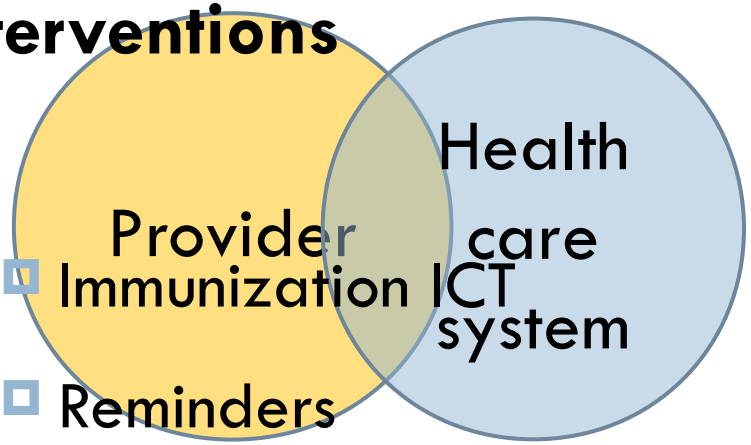
Client-based interventions



- Acc
  - Home visits
  - Reduce Client Costs
  - Vaccination programs
  - d care
  - Vaccination programs

The Guide to Community Preventive Services
THE COMMUNITY GUIDE
What Works to Promote Health

Provider & HCS-based interventions



- Reminders
- Assessment and feedback (+ incentives, benchmarking
- Standing orders
  - Clinics

Multicomponent interventions to improve vaccine uptake