PNEUMOCOCCAL VACCINATION IN OLDER PERSONS

PRESENT AND FUTURE

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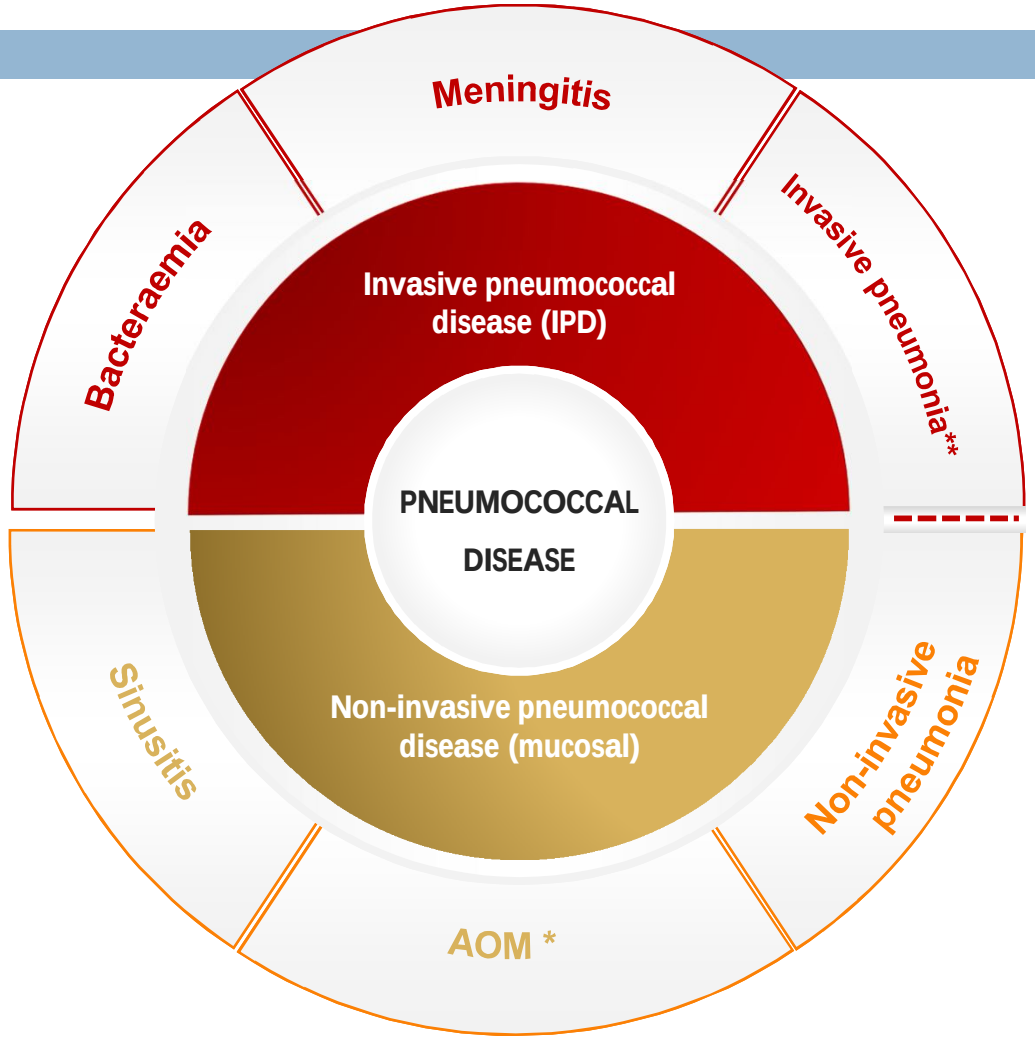
Pneumococcal diseases



* Acute otitis media
** met inbegrip van empyeem

WHO. Acute Respiratory Infections (Update Sept 2009)
Epidemiology and Prevention of Vaccine Preventable Diseases. *The Pink Book* 11th Ed., 2009
Feldman C, Anderson R. *Drugs* 2011; 71(2): 131

Risk groups for Pneumococcal disease

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

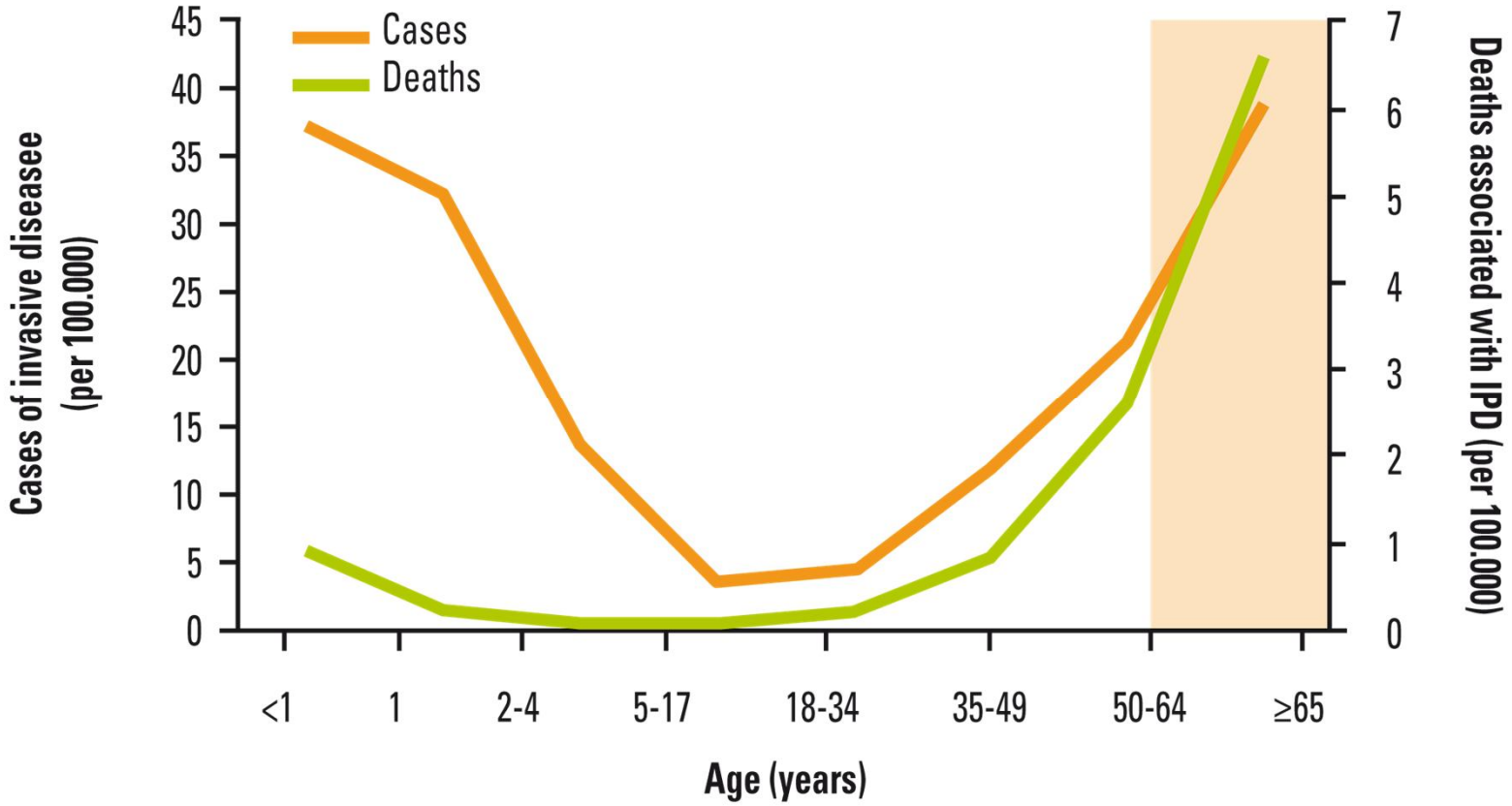
- Chronic heart disease
- Chronic lung disease
- Chronic liver disease or ethylism
- Chronic kidney disease

Healthy adults ≥ 65 Y.

Hoge Gezondheidsraad

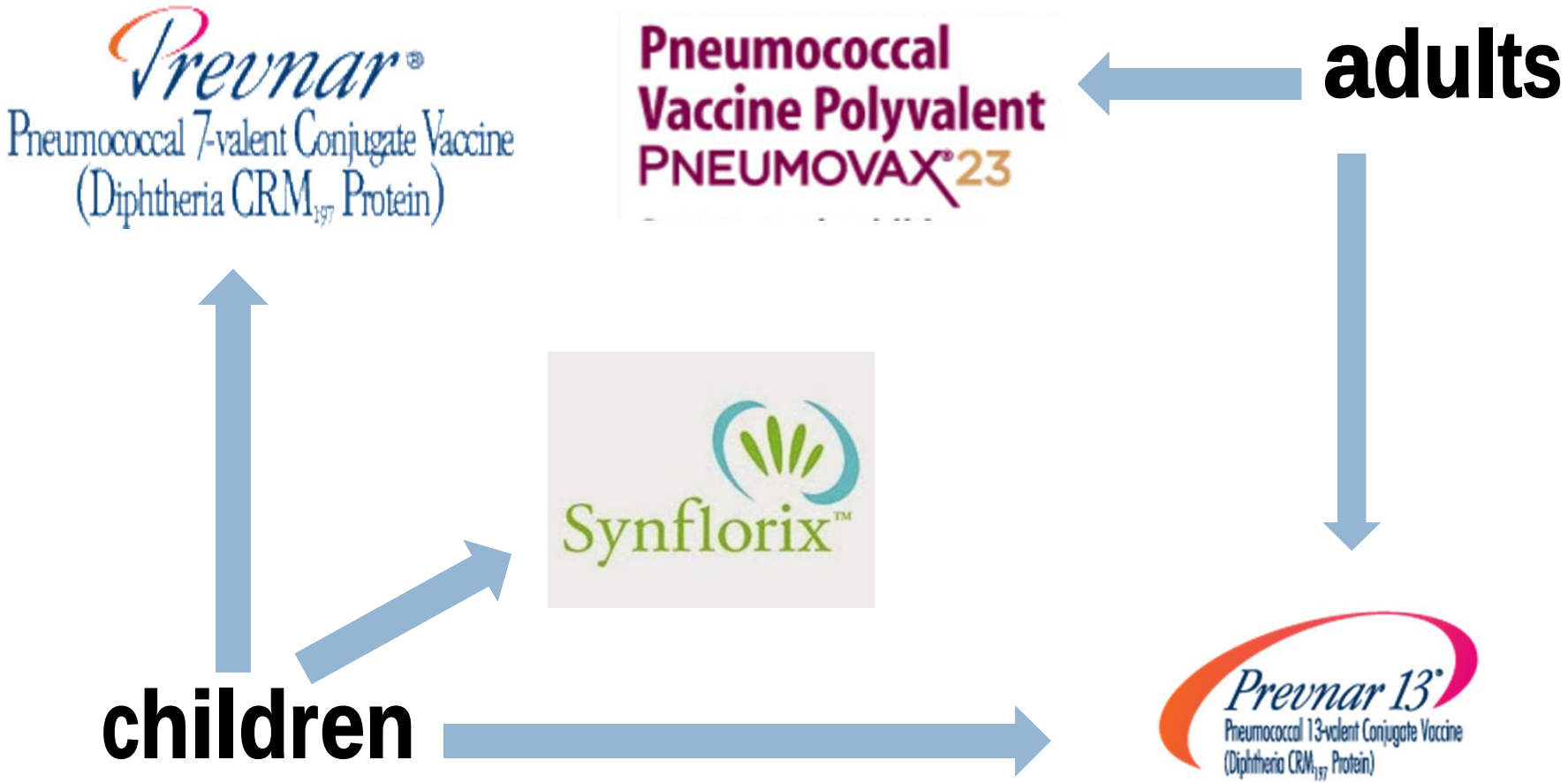
federale overheidsdienst
VOLKSGEZONDHEID, VEILIGHEID VAN DE VOEDSELKETEN EN LEEFMILIEU

Incidence and mortality of IPD

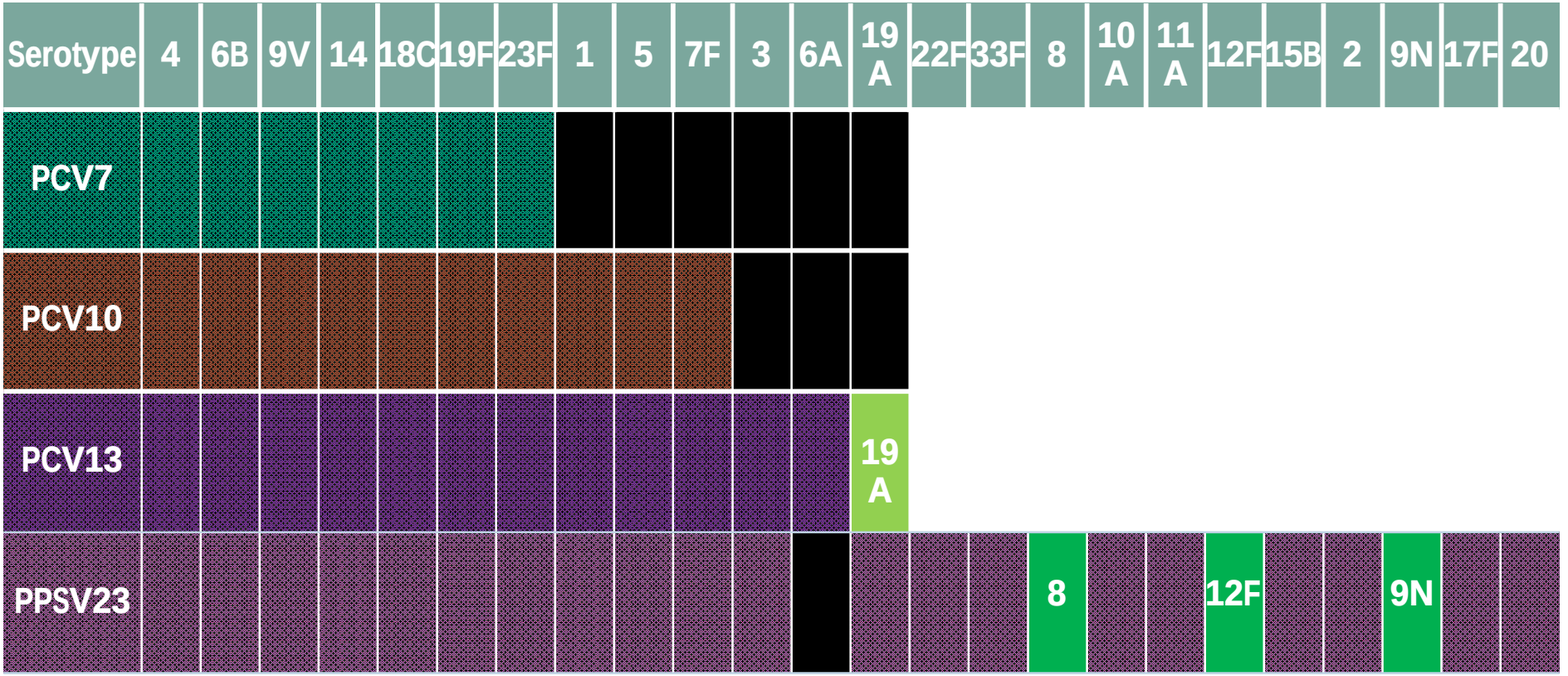


CDC. 2010. ABC Surveillance Report, Emerging Infections Program Network, Streptococcus pneumoniae, 2009.

PCV7, PCV10, PCV13, PPV23



PCV7, PCV10, PCV13, PPV23



Pneumococcal vaccination policies

World Health Organization
Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

6 APRIL 2012, 87th YEAR / 6 AVRIL 2012, 87e ANNÉE
No. 14, 2012, 87, 129–144
http://www.who.int/wer

Contents

Pneumococcal vaccines
WHO position paper – 2012

Vaccins antipneumococciques
Note de synthèse de l'OMS – 2012

WHO position

Currently available PCVs are safe and efficacious and the increased number of serotypes present in these vaccines, compared to the first licensed PCV7, represent significant progress in the fight against pneumococcal morbidity and mortality, in particular from a developing country perspective.[45, 46]

WHO recommends the inclusion of PCVs in childhood immunization programmes worldwide. In particular, countries with high childhood mortality (i.e. under 5 mortality rate of >50 deaths/1000 births) should make the introduction of these multicomponent PCVs a high priority.

Further data are needed from different epidemiological settings on the impact of large-scale PCV vaccination of individuals >50 years of age in order to establish the relative priority of immunization programmes in that age group. However, given the documented effects of herd protection in adult age groups following routine infant immunization with PCV7, higher priority should normally be given to introducing and maintaining high coverage of infants with PCVs.

In resource-limited settings where there are many competing health priorities, evidence does not support routine immunization of the elderly and high-risk populations with PPV23. Also, because of the low level of evidence for benefit, routine PPV23 vaccination of HIV-infected adults is not recommended in such settings. In countries that do not routinely administer PPV23 to high-risk populations, data are insufficient to recommend introducing this vaccine to reduce the morbidity and mortality associated with influenza.[48]

Pneumococcal vaccination policies

Recommended immunization schedules for adults: Clinical practice guidelines by the Escmid Vaccine Study Group (EVASG), European Geriatric Medicine Society (EUGMS) and the World Association for Infectious Diseases and Immunological Disorders (WAidid)

Susanna Esposito, Paolo Bonanni, Stefania Maggi, Litjan Tan, Filippo Ansaldi, Pier Luigi Lopalco, Ron Dagan, Jean-Pierre Michel, Pierre van Damme, Jacques Gaillat, Roman Prymula, Timo Vesikari, Cristina Mussini, Uwe Frank, Albert Osterhaus, Lucia Pastore Celentano, Marta Rossi, Valentina Guercio & Gaetan Gavazzi

Old adults	Influenza vaccination	Routine annual influenza vaccination for all individuals 65 y of age and older
	Pneumococcal vaccination	In the 65 y and older population: • without previous PPV23 vaccination, the use of the PCV13 vaccine first and a second vaccination with PPV23 8 weeks to 6 months after the PCV13 shot; • with previous PPV23 vaccination, a new vaccination with PCV13 at least 12 months after the PPV23 vaccination; • PPV23 or PCV13 may be co-administered with the influenza vaccine; • the use of PPV23 together with or before PCV13 is not recommended.If PCV13 is not available, experts recommend the use of PPV23 for any patients 75 y or older and a risk-based strategy for population between 65 and 75 y

Human Vaccines & Immunotherapeutics

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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Evidence: controversies PPV23

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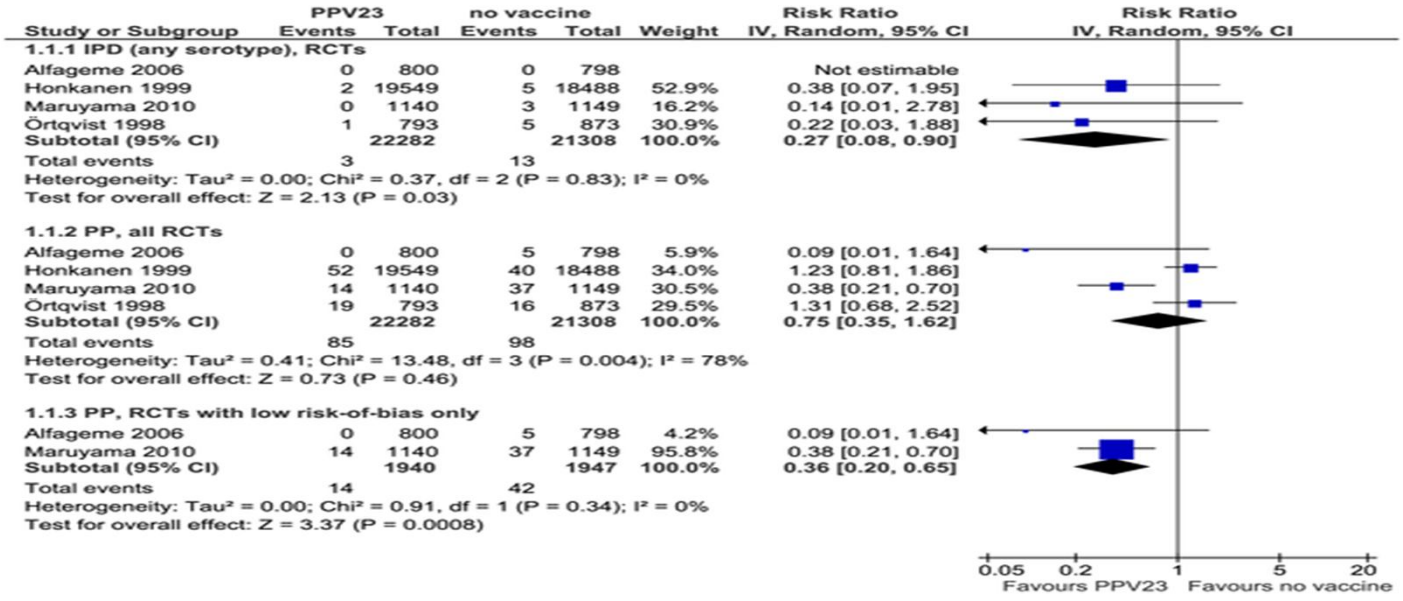
Cochrane Database Syst Rev. 2017 Jan 24;1:CD001390.

PPV23 effect on IPD and PP in elderly RCTs

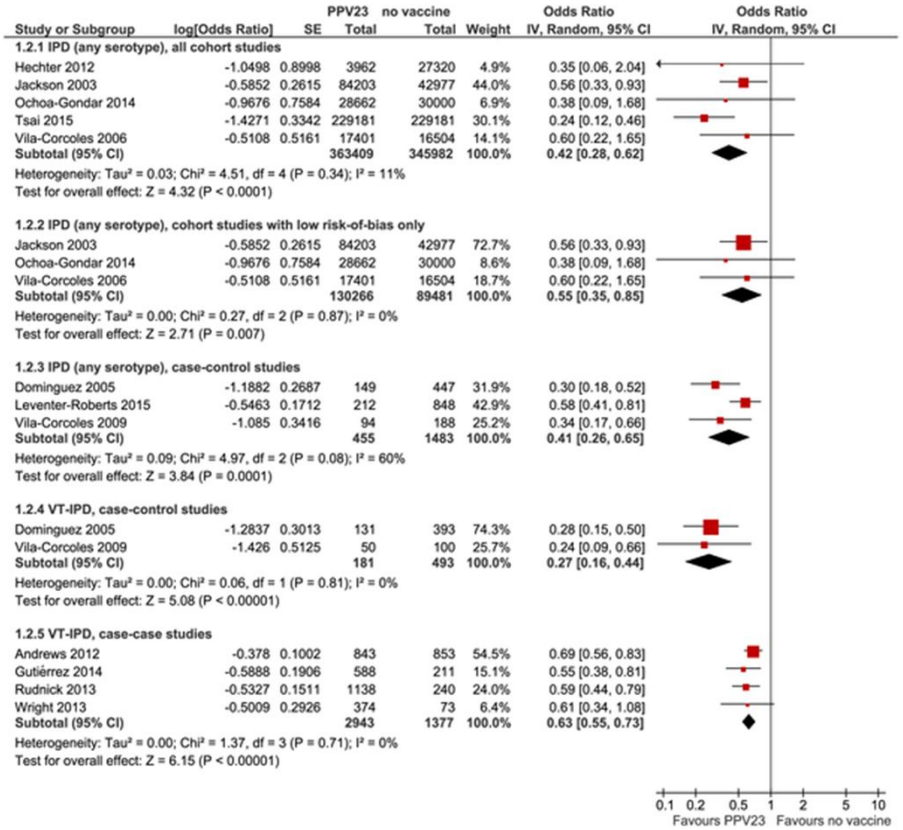
- IPD: 73 % VE
- PP: 64 % VE



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

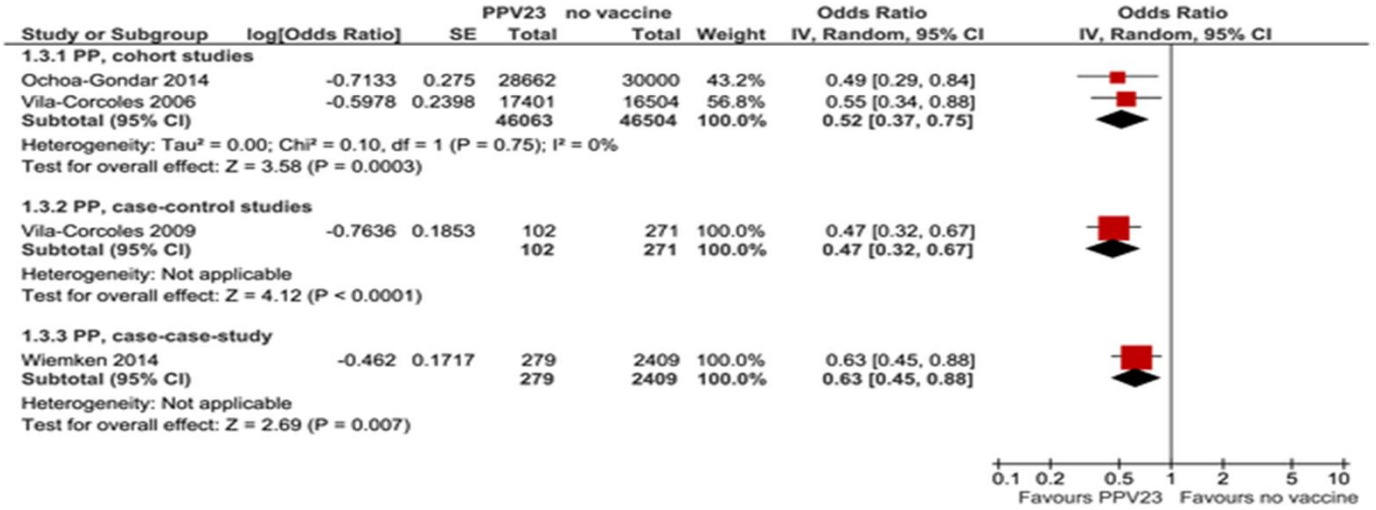
- IPD
  - Cohort studies: VE: 45 %
  - Case control: VE 59 %
- VT-IPD
  - Case control: VE 73 %
  - Case case: VE 37 %



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

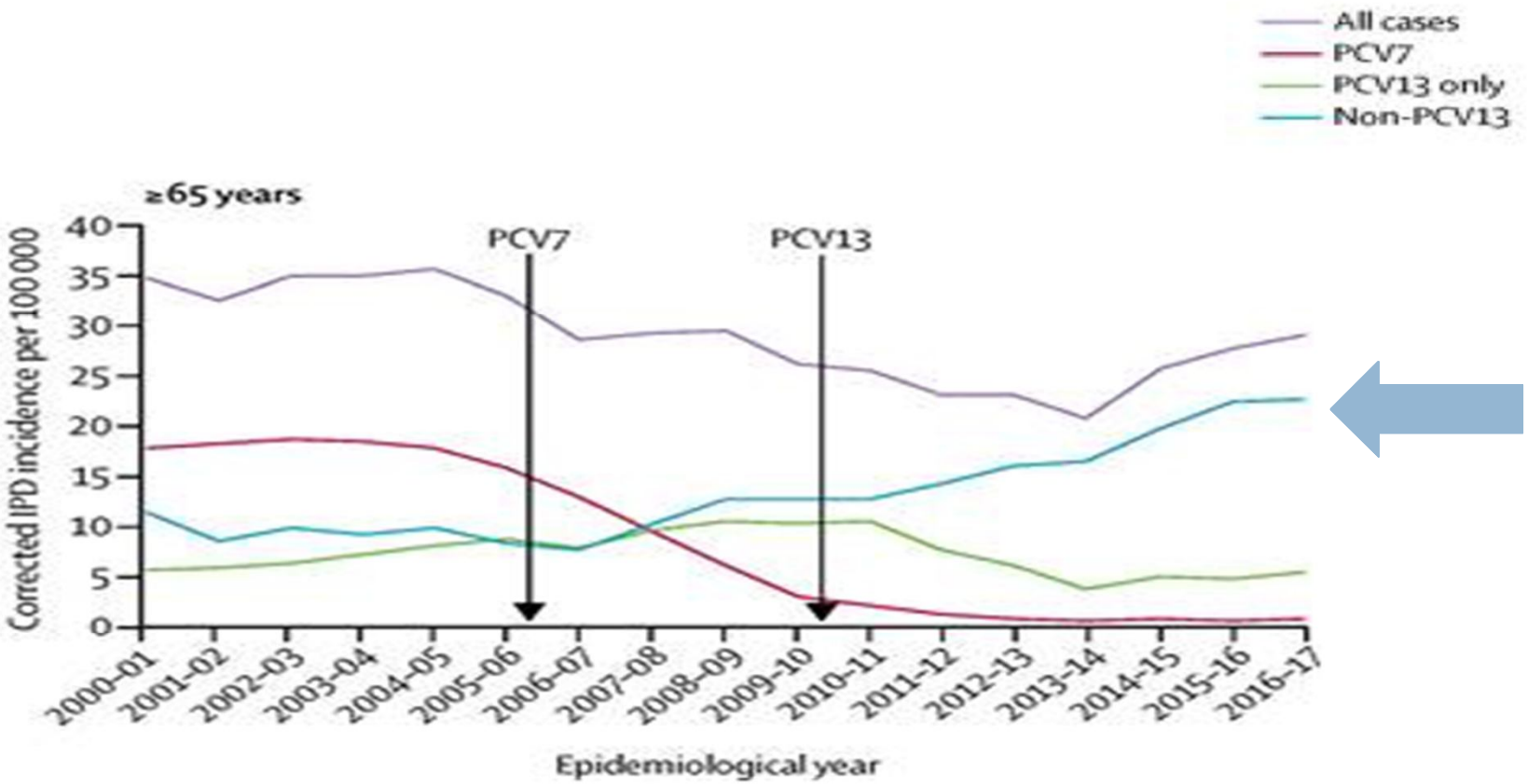
PPV23 effect on PP in elderly Observational studies

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



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

Increase of NON-PCV serotypes England & Wales



Lancet Infect Dis. 2018 Apr;18(4):441-451

PCV13 in adults

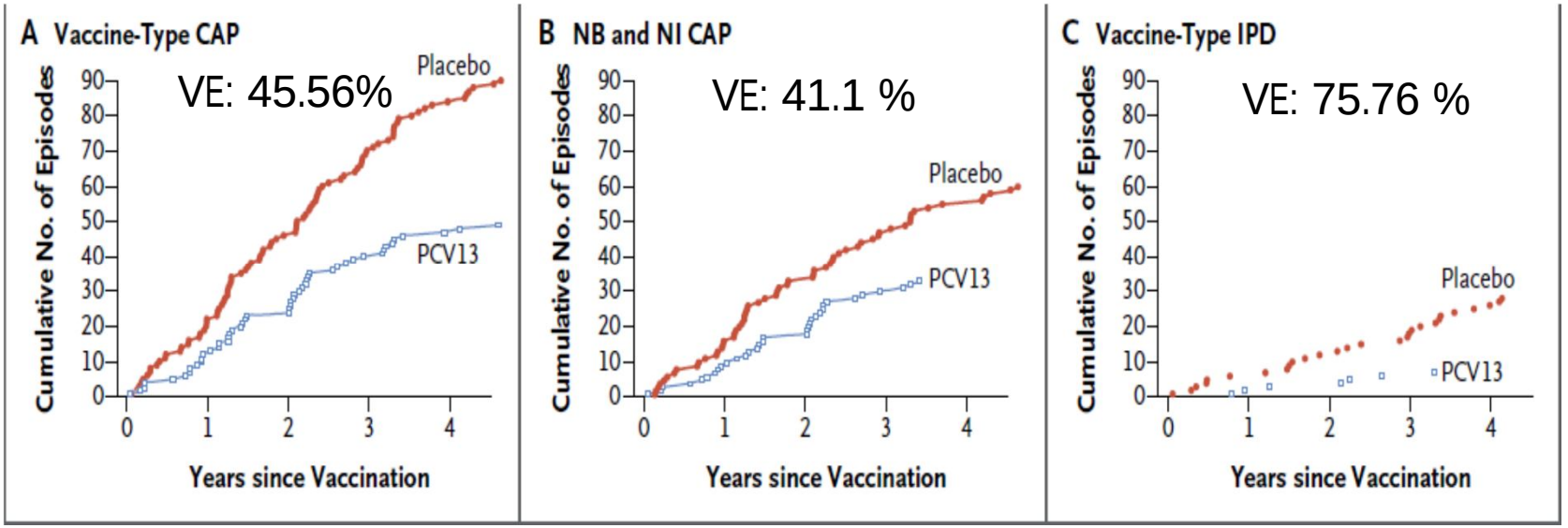
CAPITA

	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.

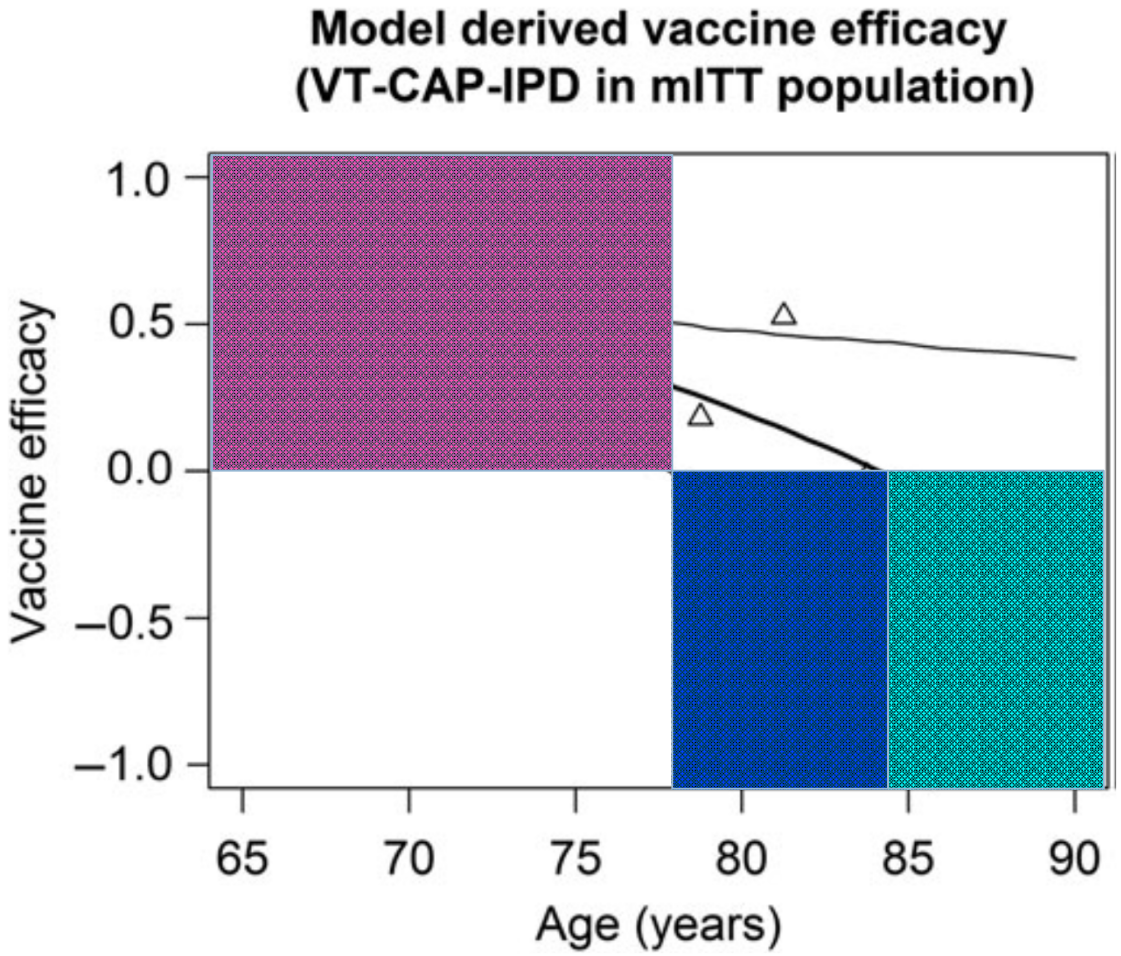
PCV13 in adults: CAPITA



	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



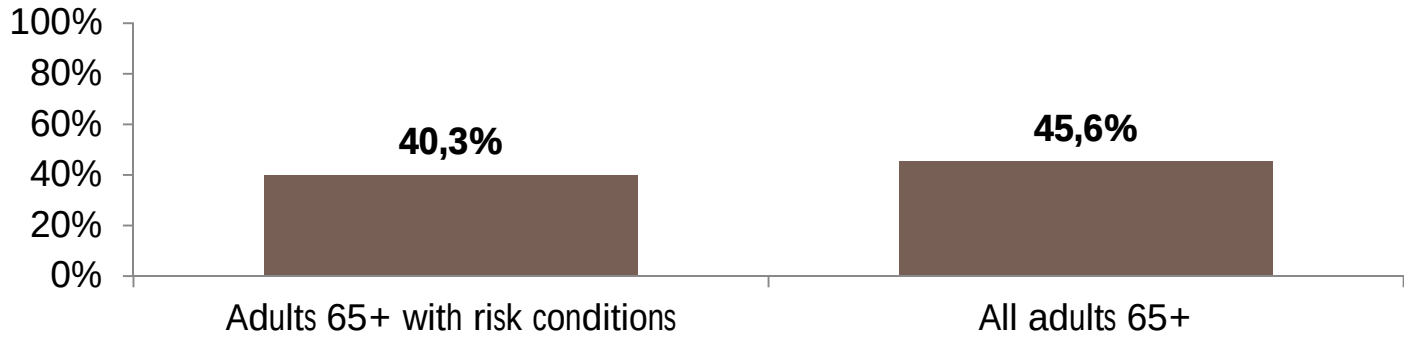
DOI: 10.1093/cid/civ686

Post Hoc Analysis of the Efficacy of PCV13 Against **VT-CAP** in **At-Risk Older Adults**

- Nearly **50%** of the 65+ population in the CAPiTA ≥1 at-risk conditions: **heart, liver, lung diseases, diabetes, asthma, or smoking**

- VT-CAP in at-risk adults 65+ was **4.3 times greater** than adults without known risk

PCV13 Vaccine Efficacy in Preventing a First Episode of VT-CAP



Suaya JA, et al. *Vaccine*. 2018;36(11):1477-1483.

Nested Real-World Effectiveness TND Study Methods: Definition of CAP

Inclusion Criteria

- ≥2 clinical criteria for pneumonia
- Radiographic evidence of pneumonia

To Be Included in the TND Analysis*

- Age ≥65 years
- Provided consent to have pneumococcal vaccination history confirmed by health insurance records

Exclusion Criteria

- HAP (hospitalized within previous 48 hours)
- Did not have a final diagnosis of pneumonia at discharge
- Did not supply a urine sample for laboratory testing

The Following Patients Were Excluded From the TND*

- Health insurer could not be reached
- Received a pneumococcal vaccine ≤30 days prior to urine sample

*In addition to inclusion/exclusion criteria from surveillance study.

CAP=community-acquired pneumonia; HAP=hospital-acquired pneumonia; TND=test-negative design.

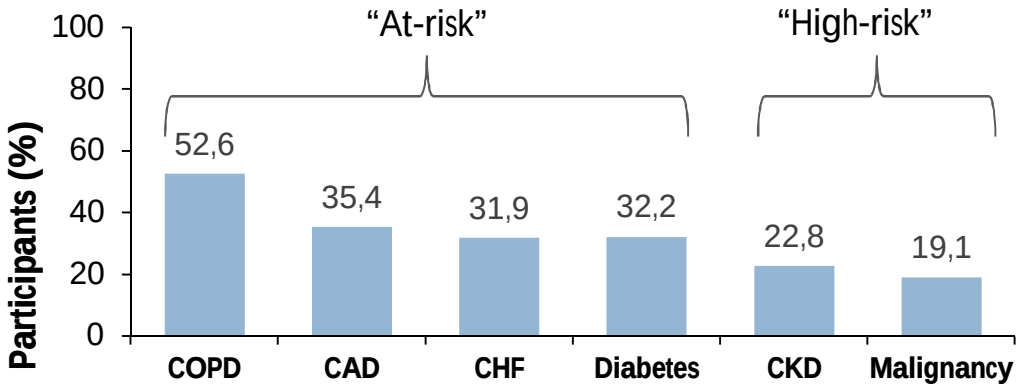
McLaughlin JM, et al. *Clin Infect Dis.* 2018; May 21. doi:10.1093/cid/ciy312.

Nested Real-World Effectiveness TND Study Results

Clinical and Demographic Characteristics of ***CAP Patients Aged ≥65***

Study Population at a Glance (N=2034)	
Age median, years	76 (65–102)
Aged ≥80	35.4%
White Race	88.5%
Non-Hispanic	>99%
"High-risk"	45.8%
"At-risk"	42.1%
BMI median	26.2 (30.2% obese)
PSI median	106 (27.0% PSI=5)
Current Smoker	19.0%

Comorbid Conditions



- **Percentages are of the total study population. Some participants had >1 comorbid condition**

Hospitalization Data

LOS median	6 days
Hosp. Mortality	6.5%
30-day Mortality	12.7%

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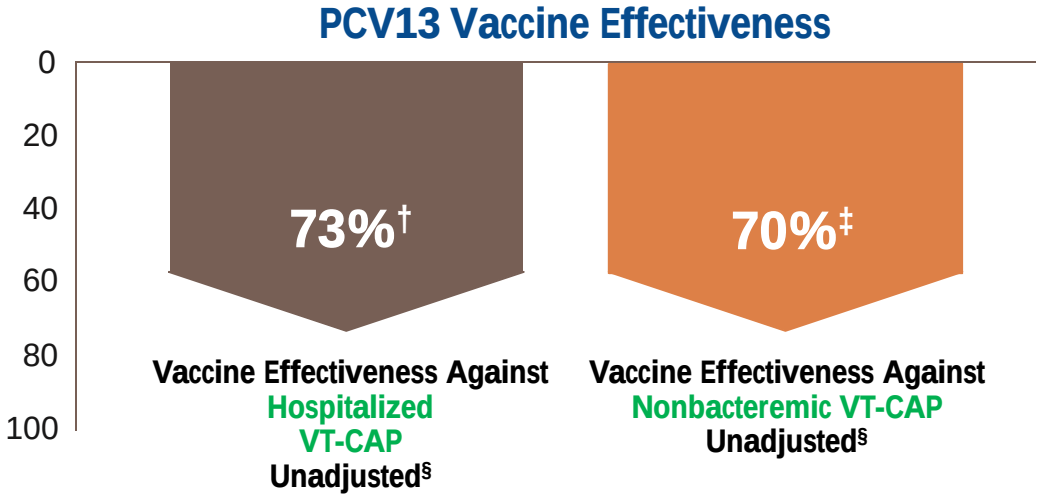
McLaughlin JM, et al. *Clin Infect Dis.* 2018; May 21. doi:10.1093/cid/ciy312.

Nested Real-World Effectiveness TND Study Results

2 × 2 Contingency Table, n (%): Primary Exposure of Interest

	Case PCV13 (+) CAP	Control PCV13 (–) CAP
Ever PCV13	3 (4.4)	285 (14.5)
Never PCV13	65 (95.6)	1681 (85.5)



McLaughlin JM, et al. *Clin Infect Dis.* 2018; May 21. doi:10.1093/cid/ciy312.

Pneumococcal vaccination, Belgium

February 2015

Adults 19-85 y. with high risk for PD

- **Primo-vaccination** : PCV13 → 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 → PPV23 after 8w
- **Previously vaccinated** with PPV23: PCV13 once ≥ 1 j. after last PPV23
- **(Booster: ?** Depends on epidmiologie over 5 y. and additional data)

Adults >85 y.

- No data on effect > 85 j.
- On individual basis as 2.

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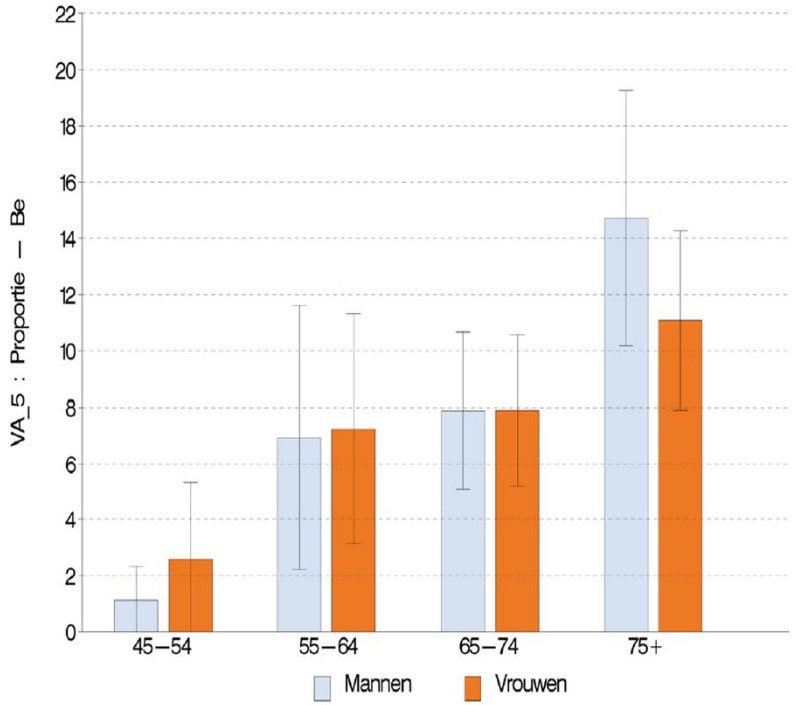
VOLKSGEZONDHEID, VEILIGHEID VAN DE VOEDSELKETEN EN LEEFMILIEU

Pneumococcal vaccination coverage in older persons, EU



Belgium, 2013

PPV23 vaccination any time

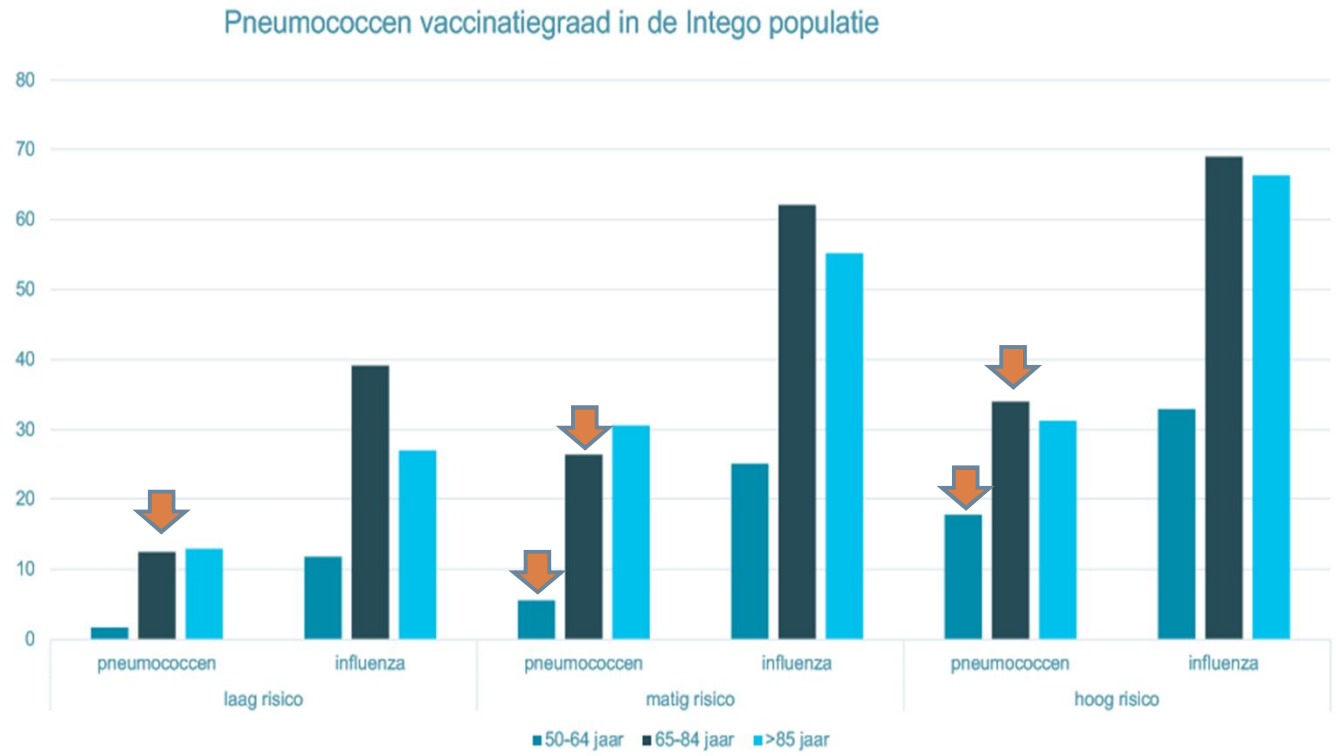
- ≥ 65 y. : 70,1 %
- ≥ 75 y. : 80,2 %

England, 2016

https://www.gov.uk/government/publications/pneumococcal-polysaccharide-vaccine-ppv-vaccine-coverage-estimates
https://his.wiv-isp.be/nl/Gedeelde%20%20documenten/VA_NL_2013.pdf

Pneumococcal vaccination coverage

- Intego database: n = 100 484 (2015)
- 6 – 35 % vaccine coverage



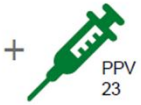
: HCPH recommended

Prof. C. Matheï, intego.be

Pneumococcal vaccine uptake

East Flanders

= 2160

+


= 883 (40,9%); PPV-23 within 32 weeks after PCV-13

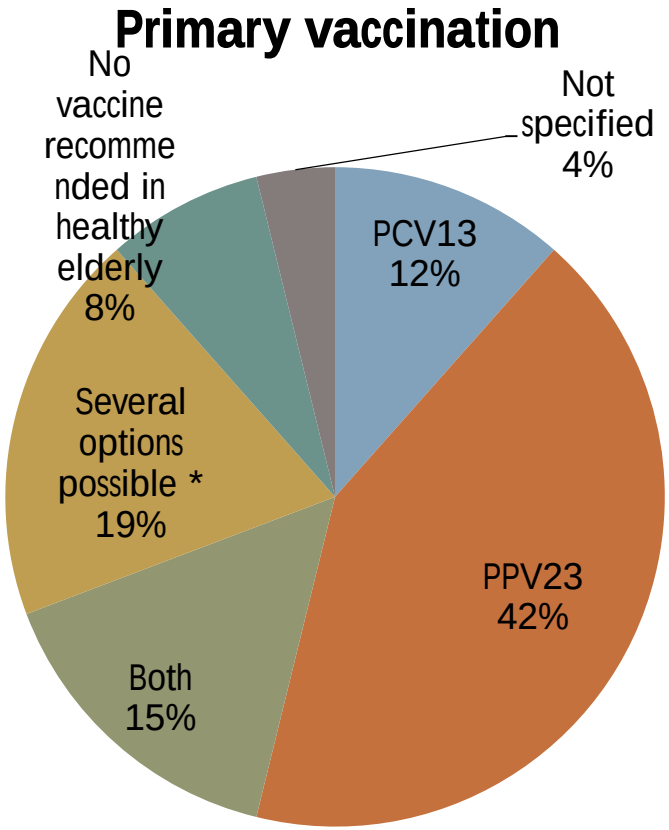
+

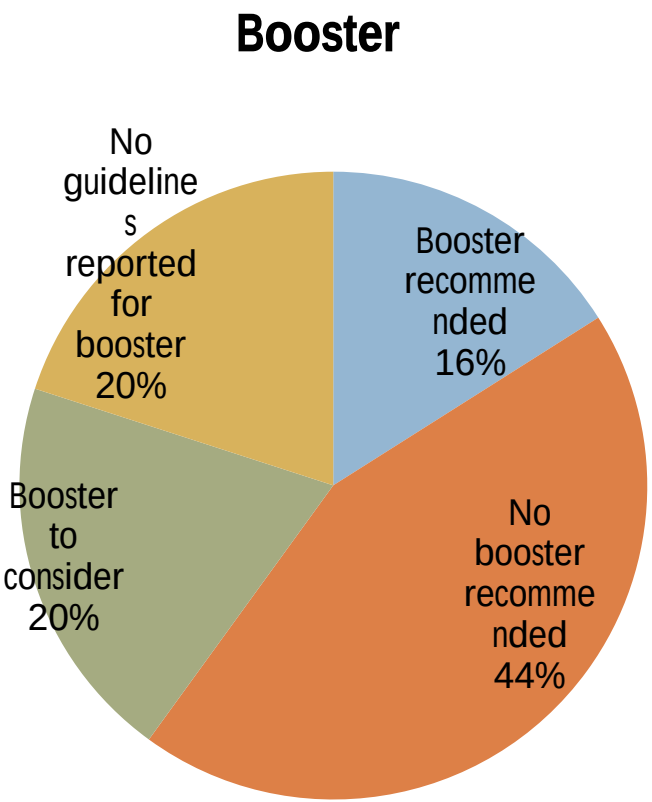

= 7 (0,32%); PPV-23 33 to 52 weeks after PCV-13

Comorbidity	Prevalence in Flemish region (50-64 years old)[3]	Expected # patients 50-64 years in 56 phar-macies	# patients 50-64 years vaccinated with PCV-13 + PPV-23
Chronic lung disease	4.4%	1131	69 (6,17%)
Chronic heart disease (excl. hypertension)	5,8%	1491	98 (6,58%)
Chronic kidney disease (excl. kidney stones)	1,0%	257	26 (10,12%)
Chronic liver disease	1,2%	308	0 (0%)
Total		3187	193 (6,06%)

KOVAG

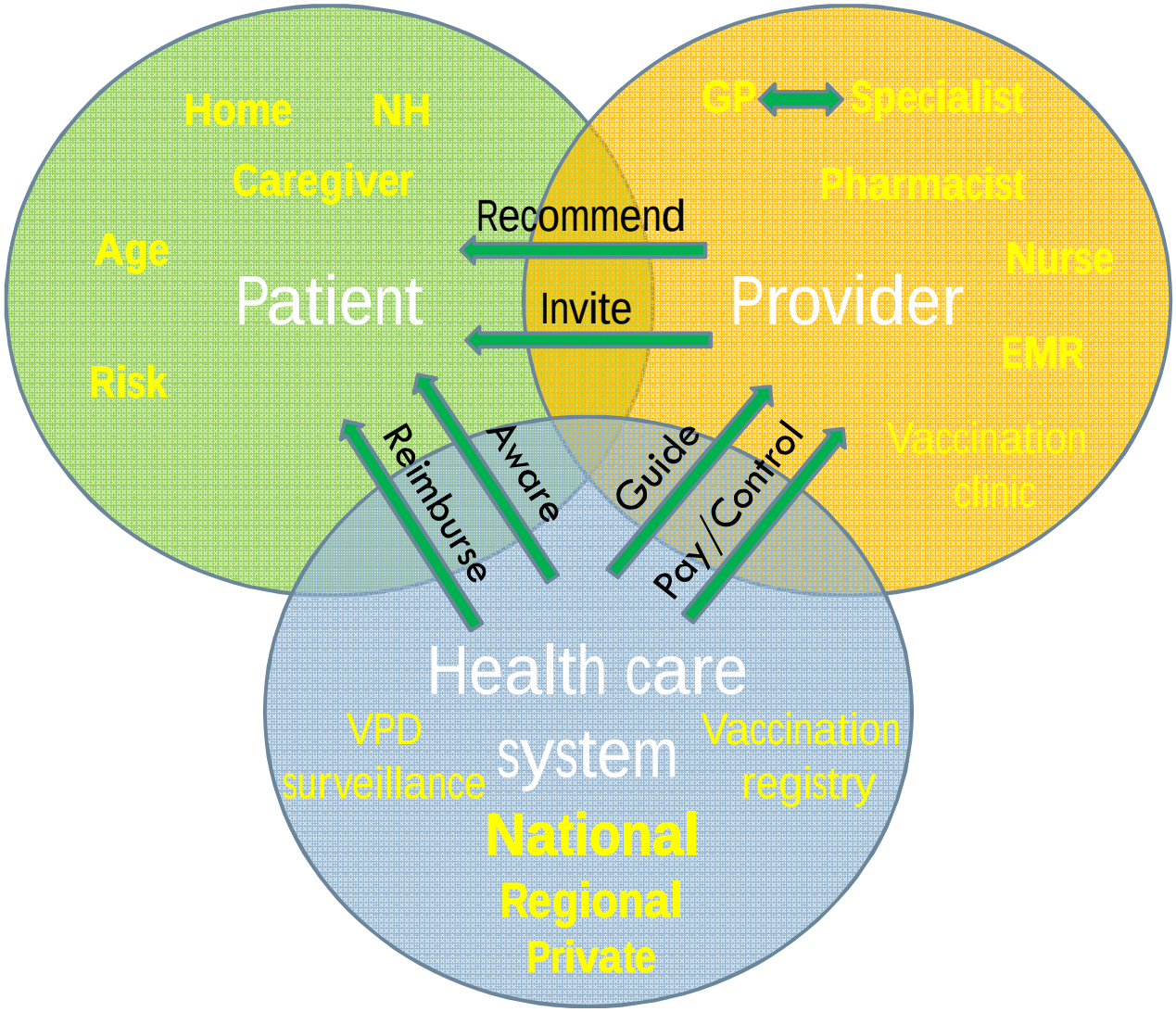
Pneumococcal vaccine recommendations Healthy elderly, EU





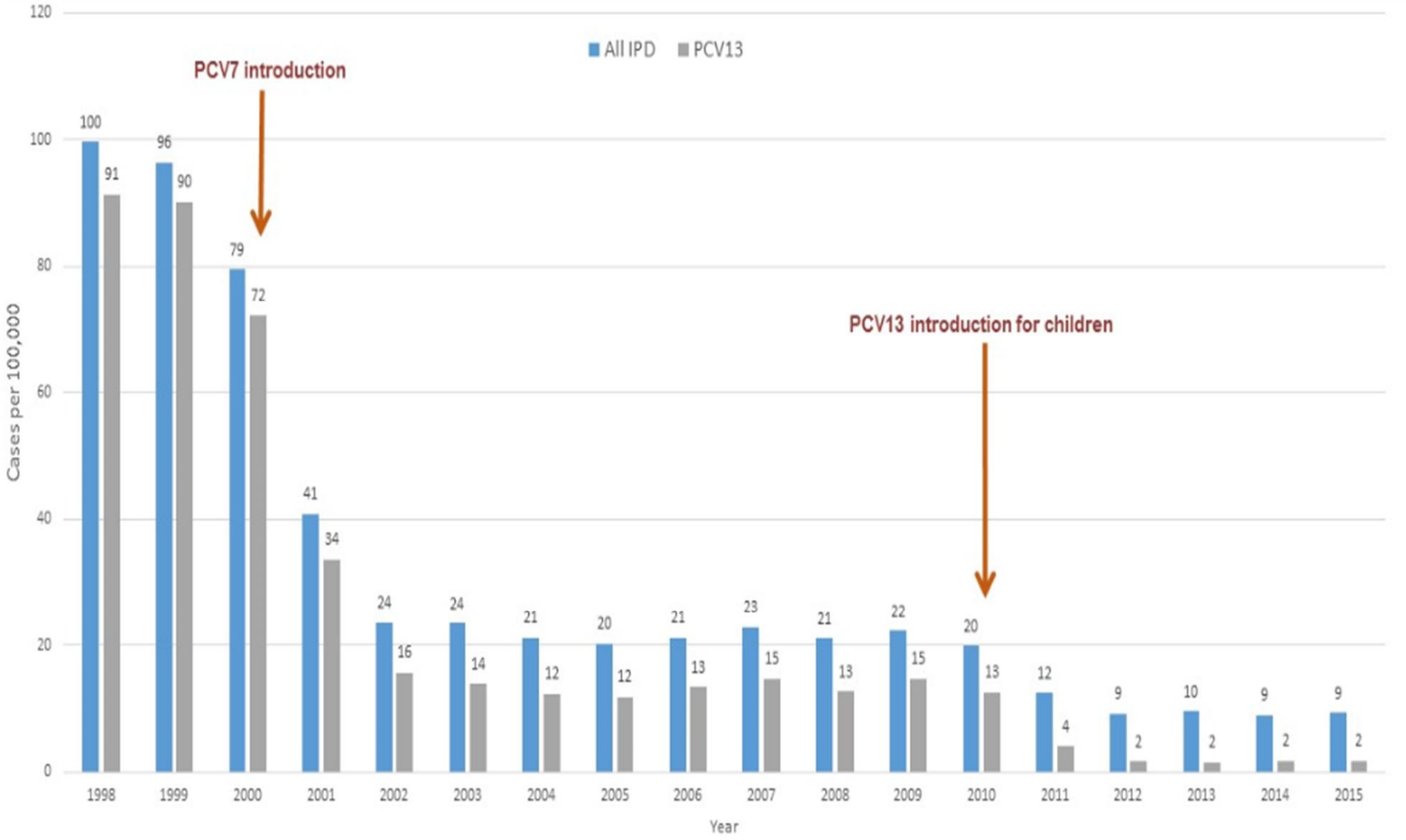
Eur J Clin Microbiol Infect Dis. 2019 Feb 18. doi: 10.1007/s10096-019-03485-3.

Multicomponent interventions to improve vaccine uptake



Herd effect
in pneumococcal vaccination

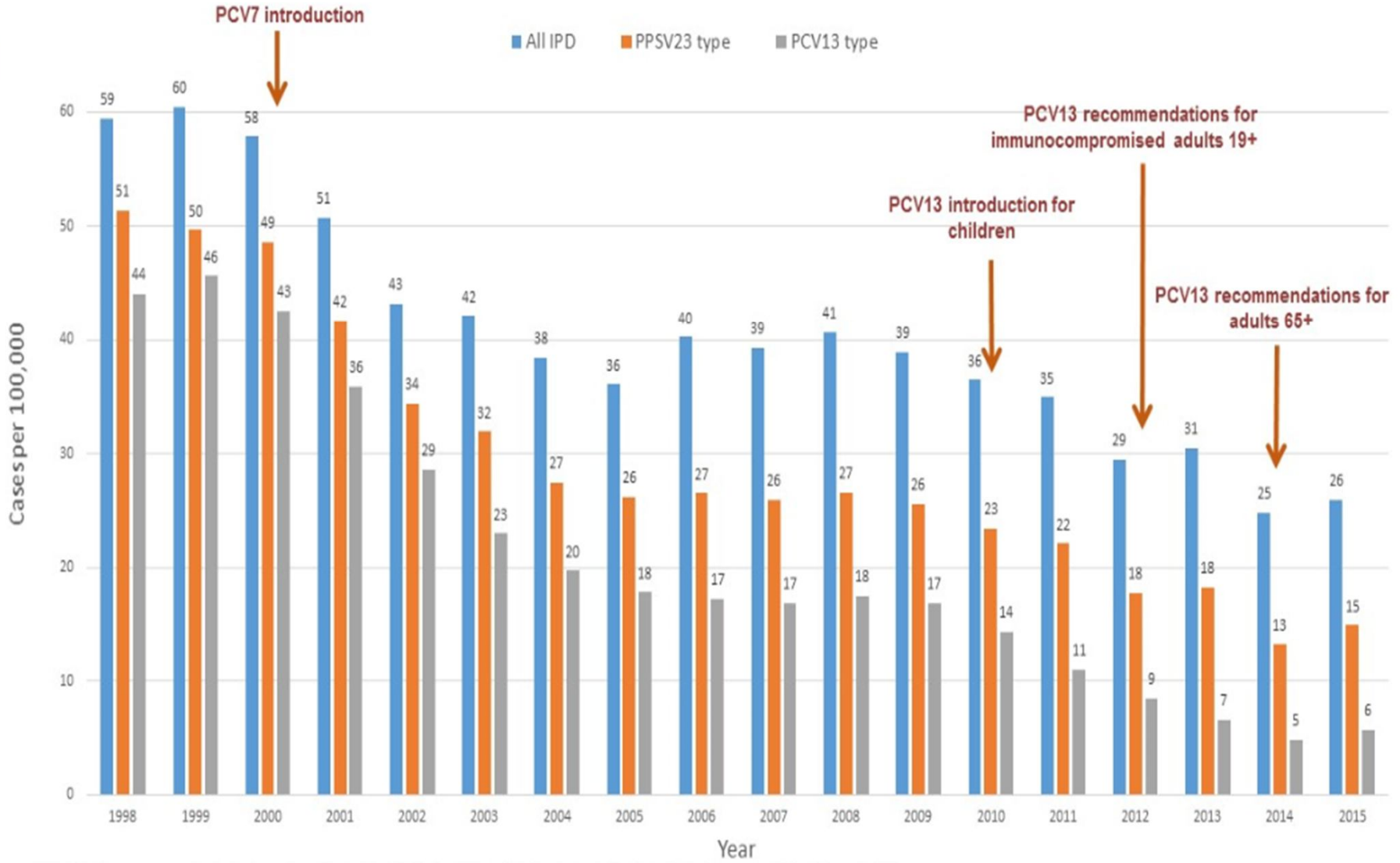
IPD <5 y. USA 1998-2015



*PCV13 serotype: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F

Active Bacterial Core surveillance data, 1998–2015, unpublished

IPD >65 y. USA 1998-2015

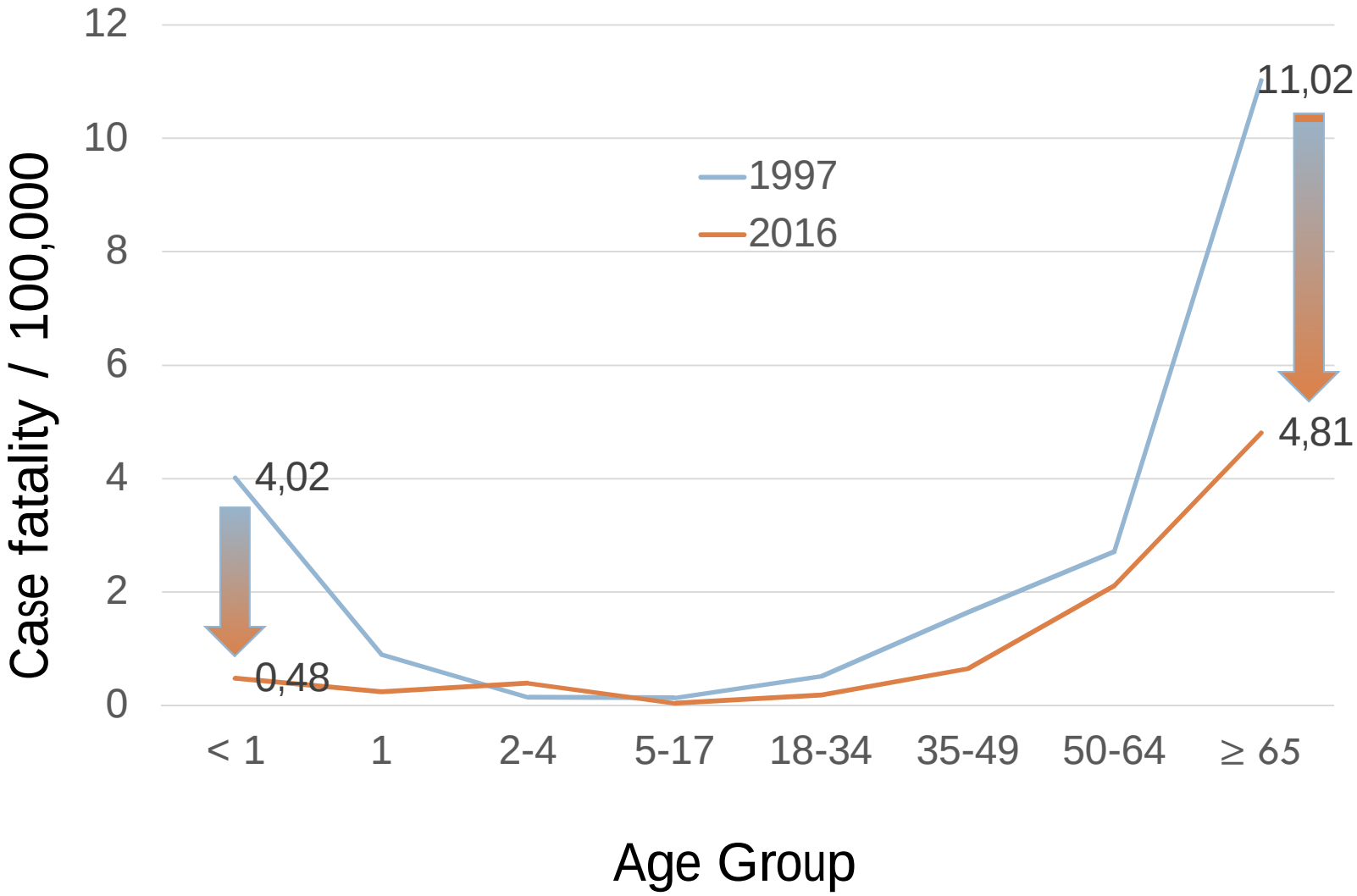


*PPSV23 serotypes: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F

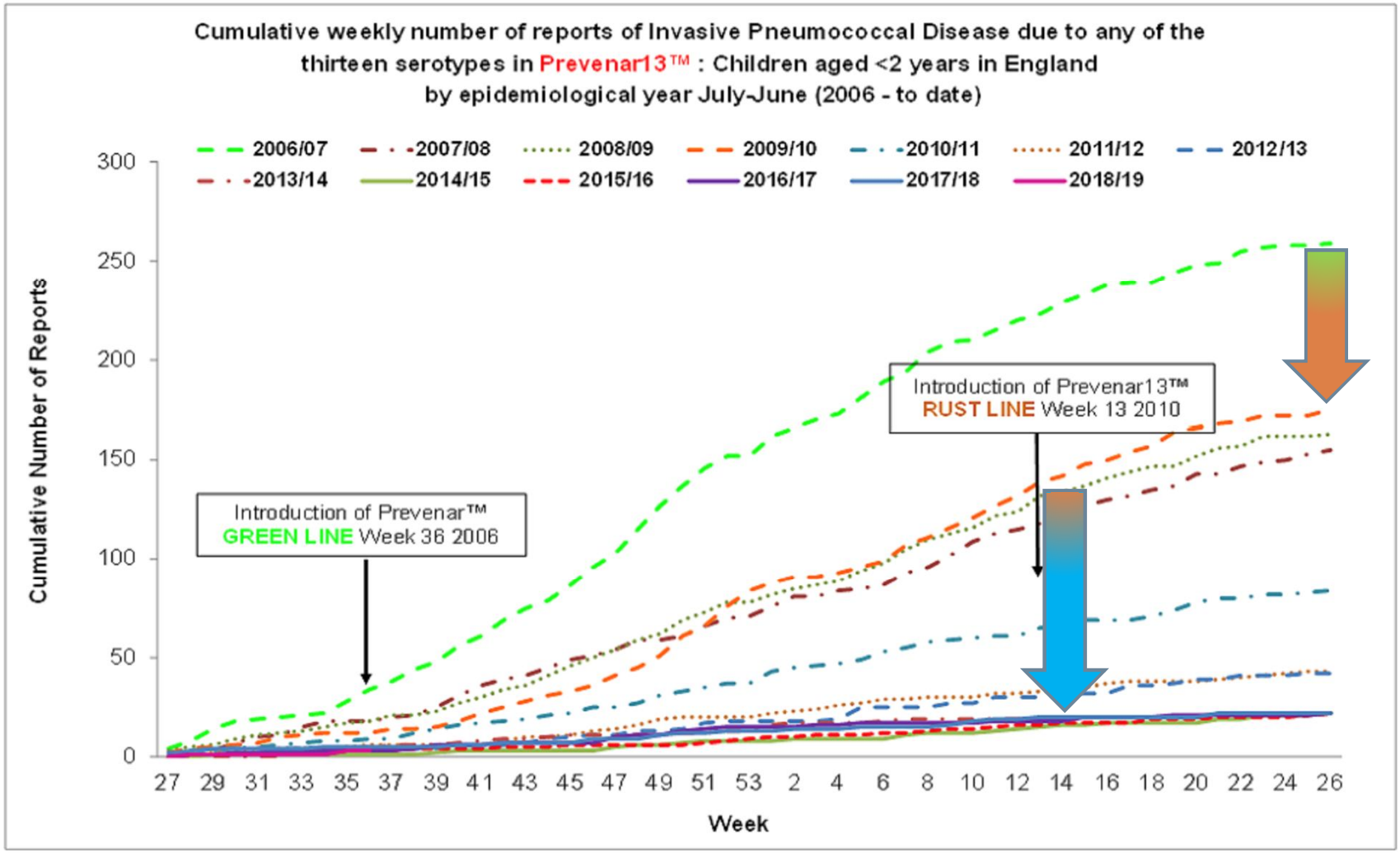
†PCV13 serotype: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F

Active Bacterial Core surveillance data, 1998–2015, unpublished

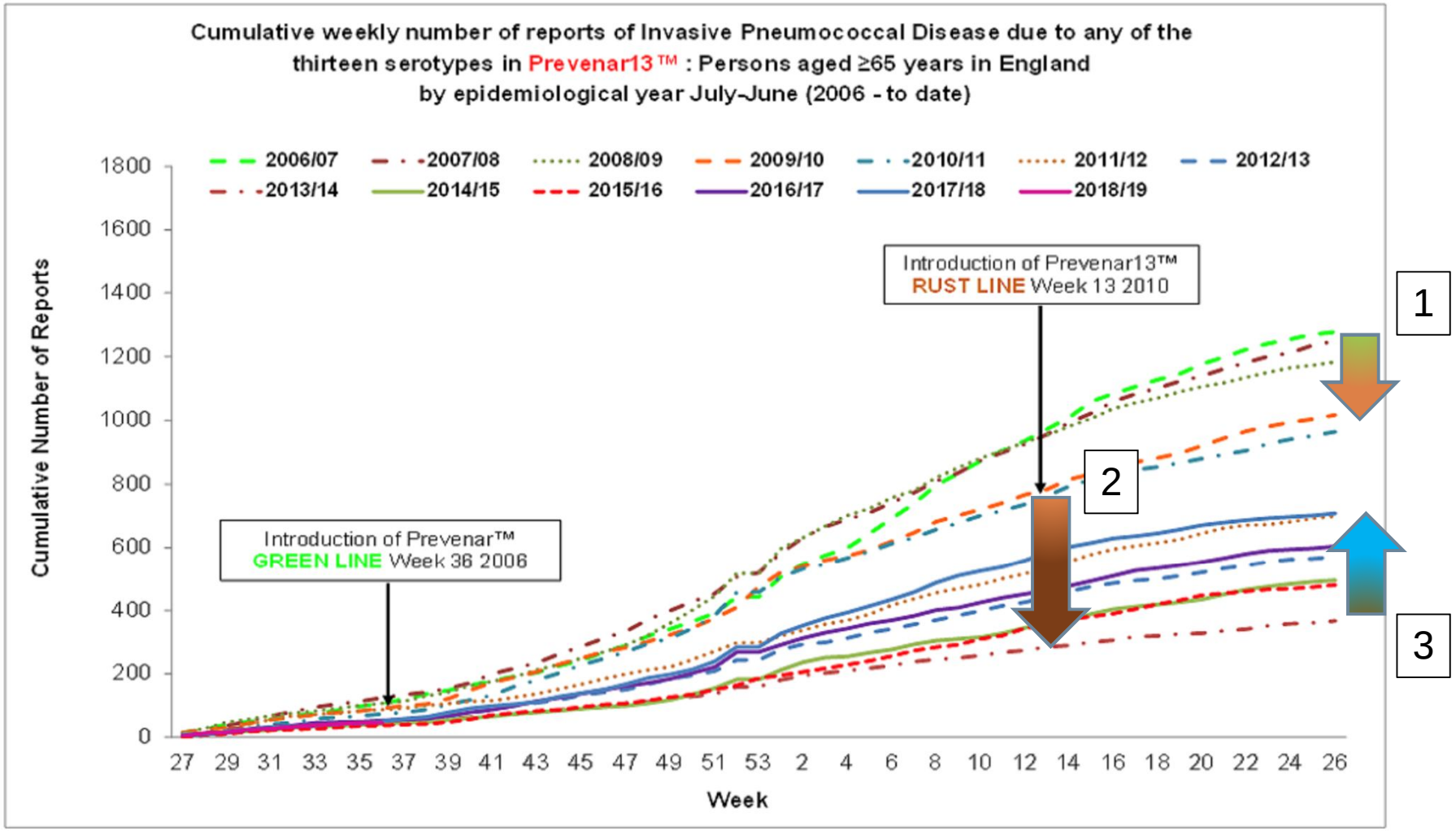
IPD case fatality, USA



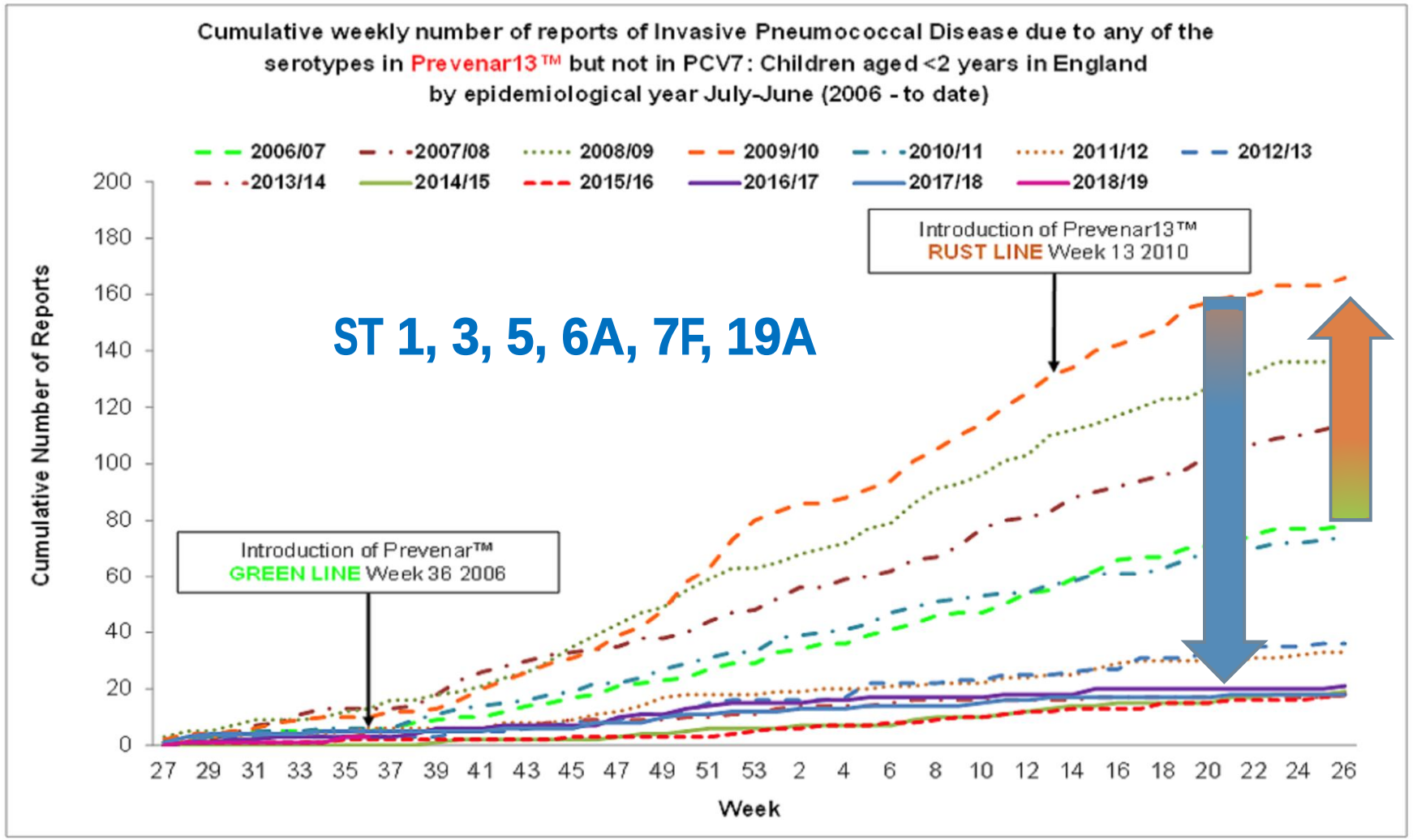
IPD with PCV13 SG <2 y. England & Wales



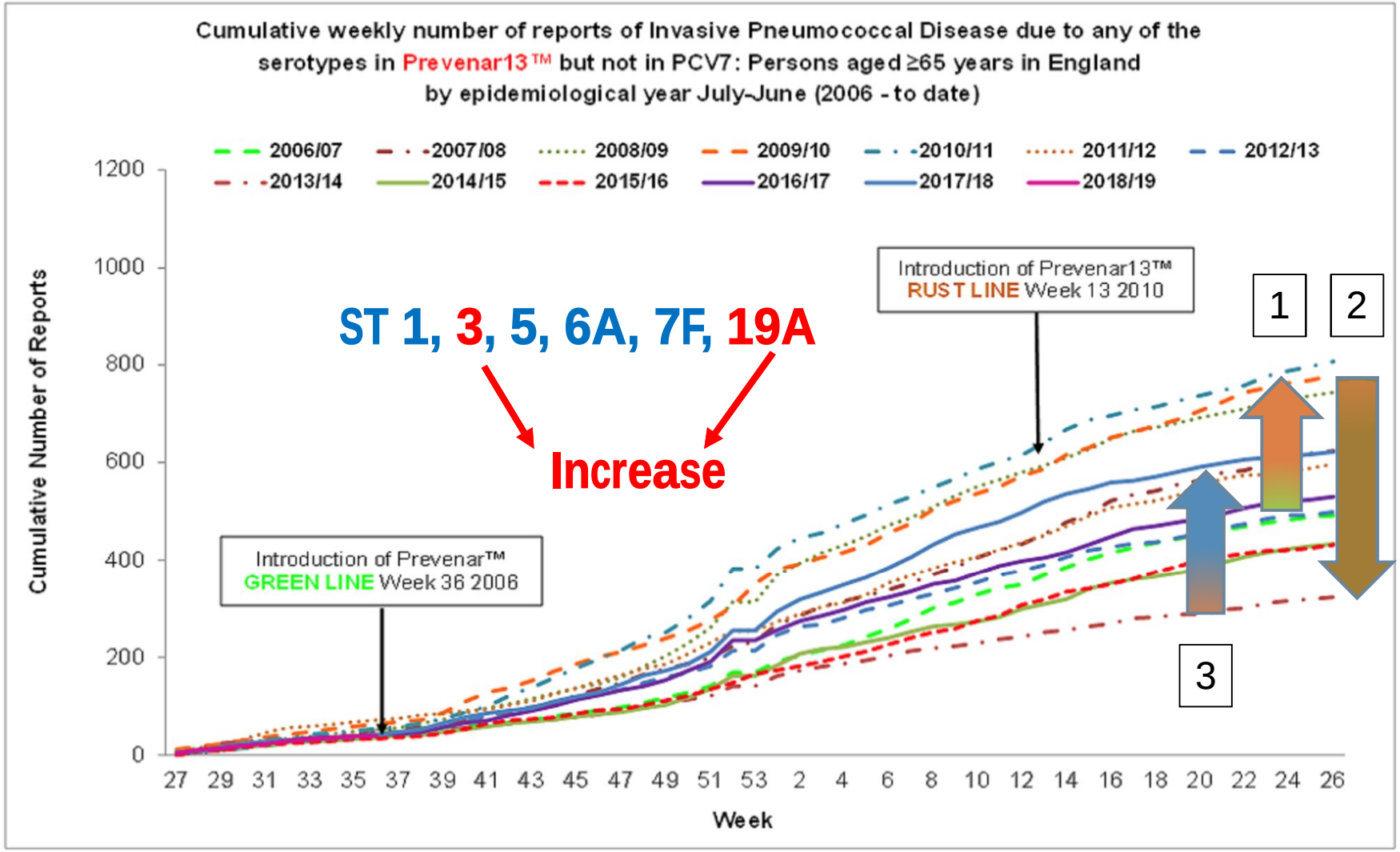
IPD with PCV13 SG ≥65 y. England & Wales



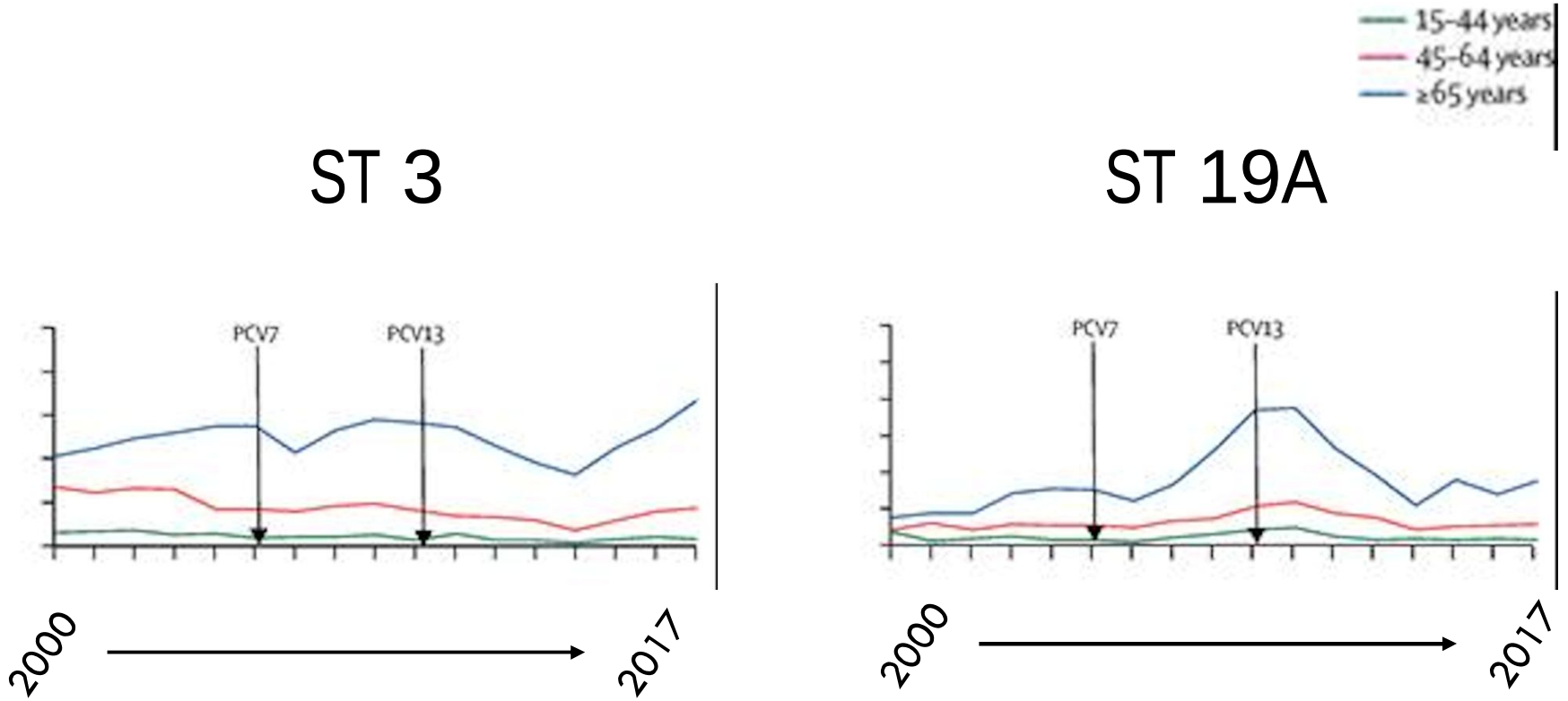
IPD with PCV13 but **NON**-PCV7 SG <2 y. England & Wales



IPD with PCV13 but **NON**-PCV7 SG ≥65 y. England & Wales

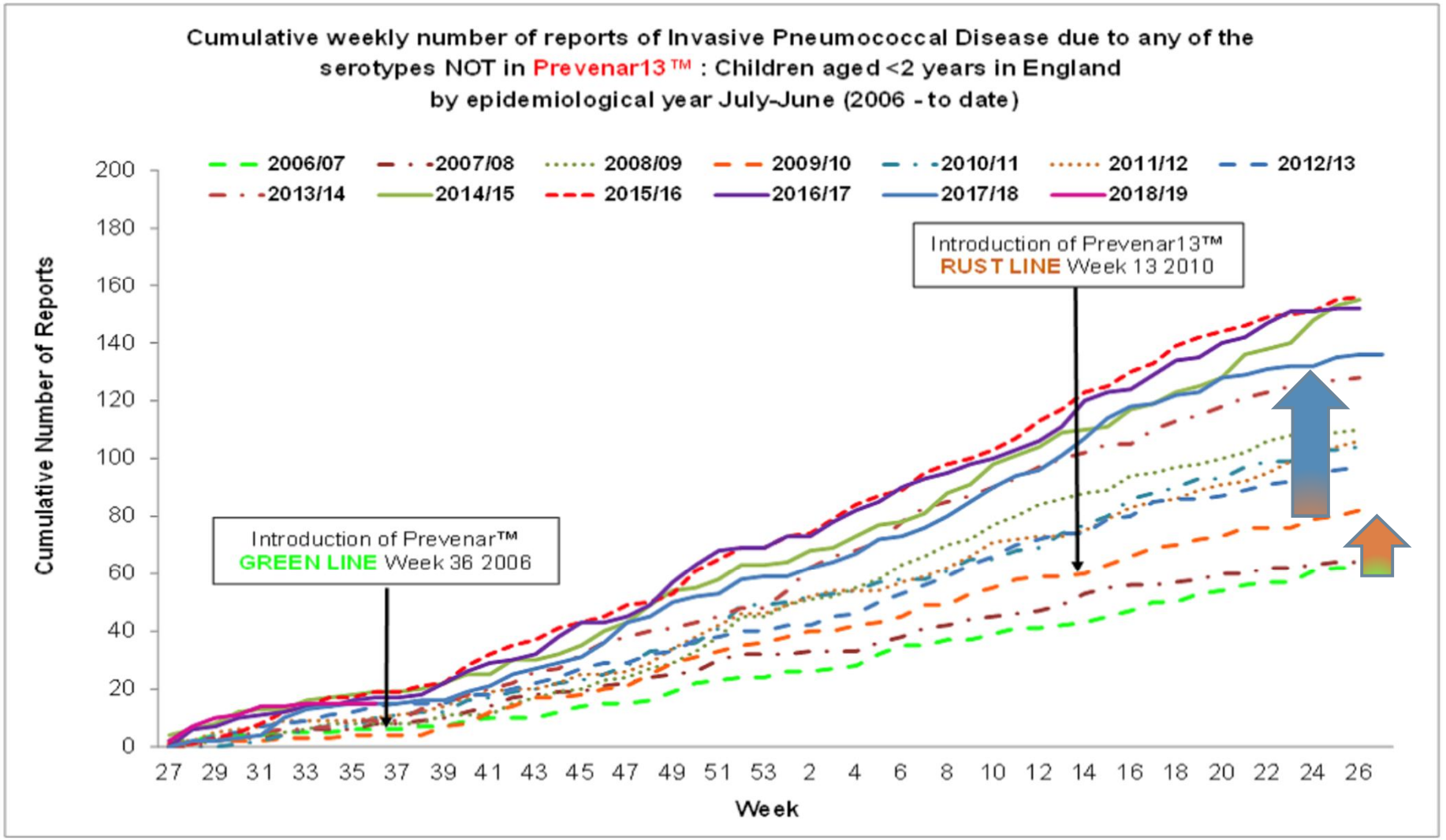


Increase PCV13 ST England & Wales

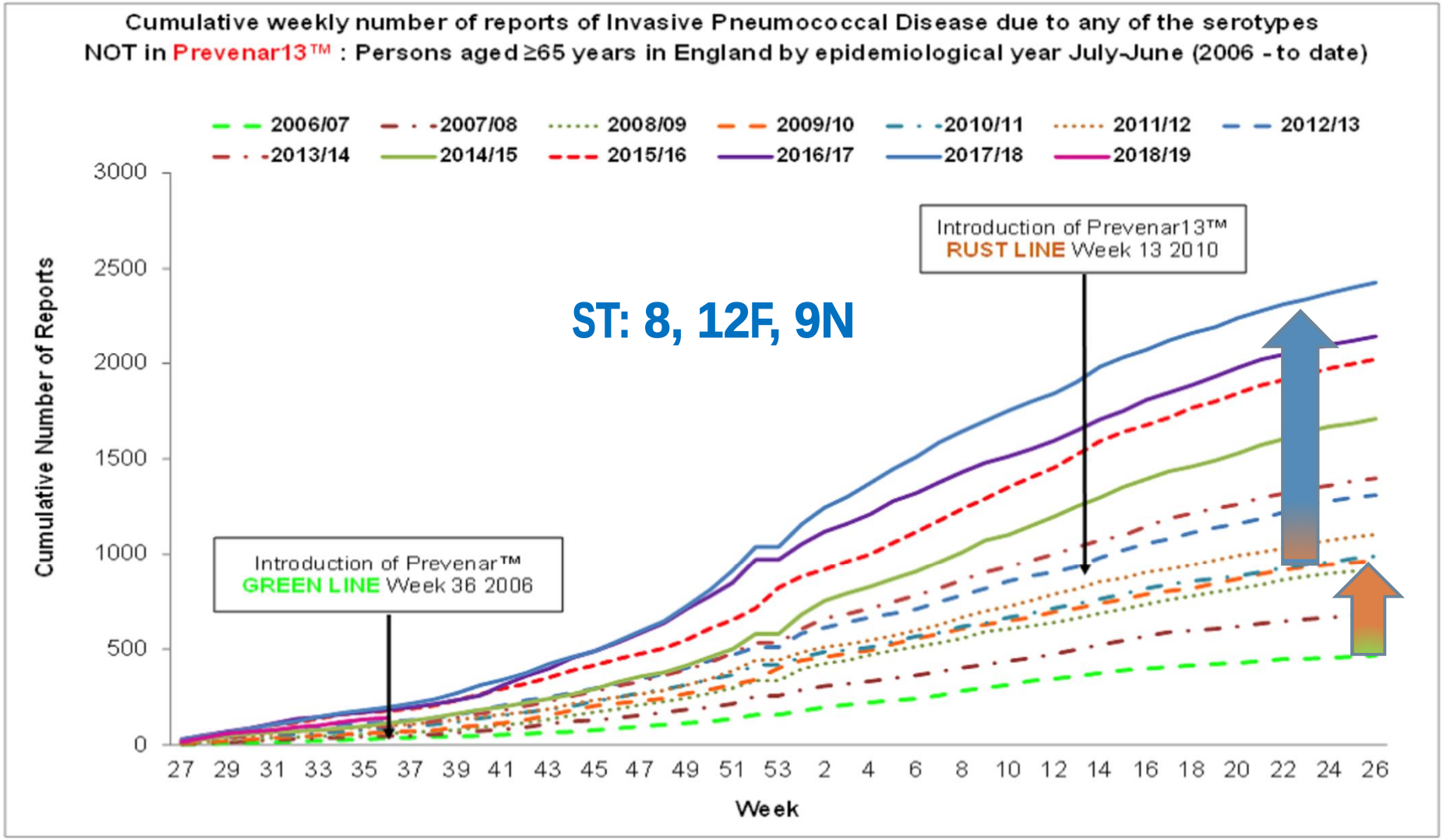


Lancet Infect Dis. 2018 Apr;18(4):441-451

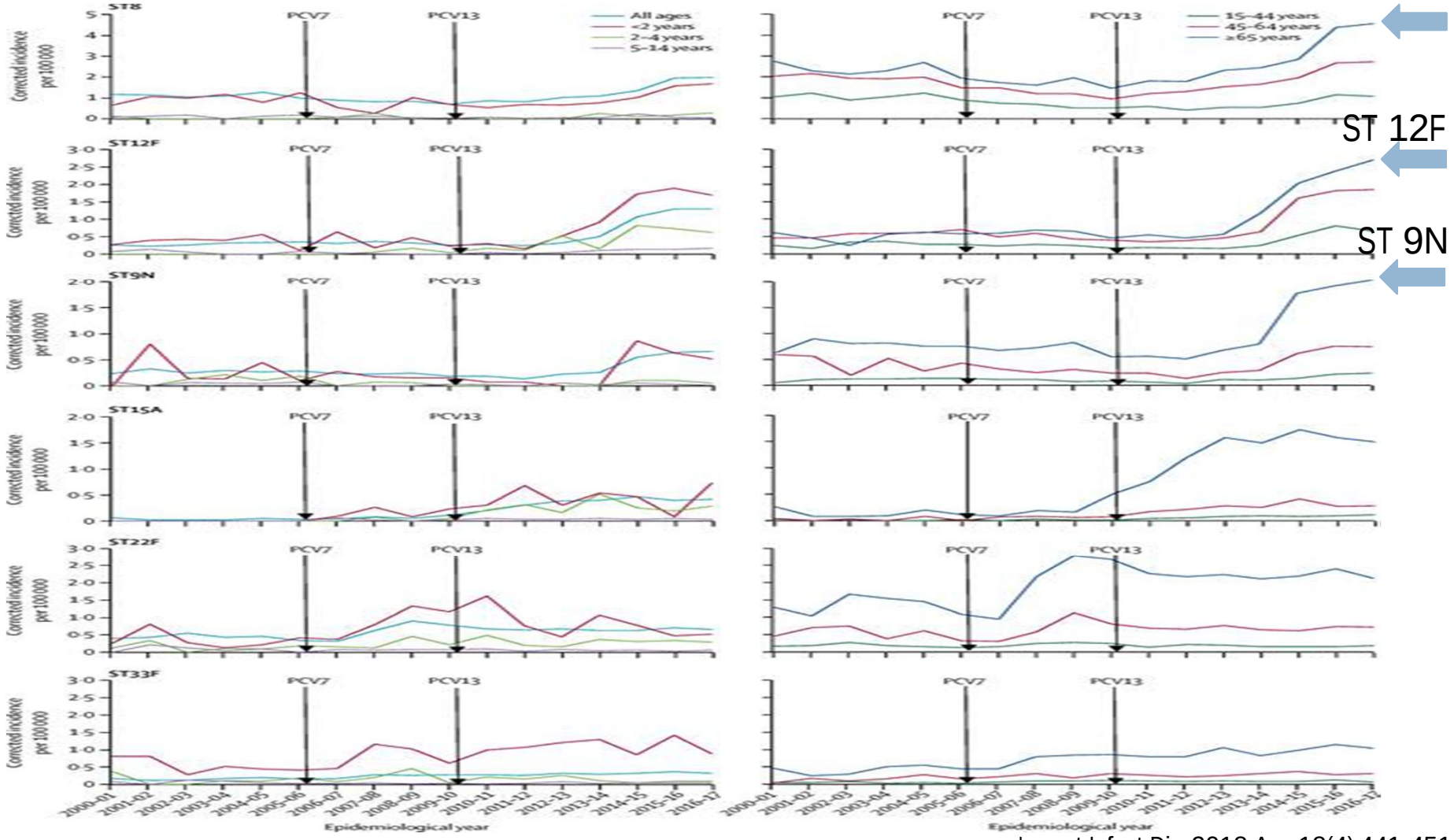
IPD with **NON**-PCV13 SG <2 y. England & Wales



IPD with **NON**-PCV13 SG ≥65 y. England & Wales

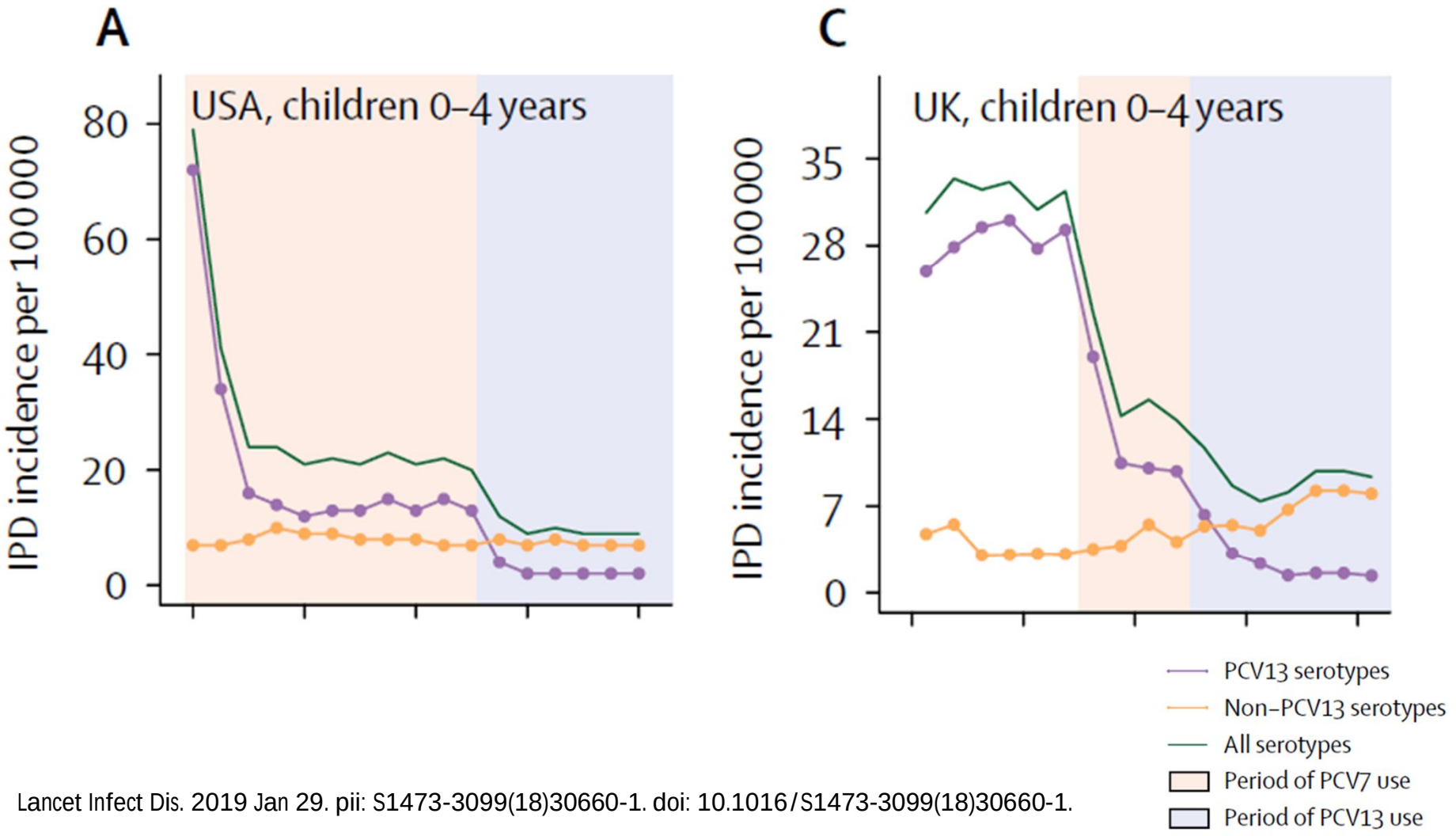


Increase NON-PCV13 ST Enland & Wales



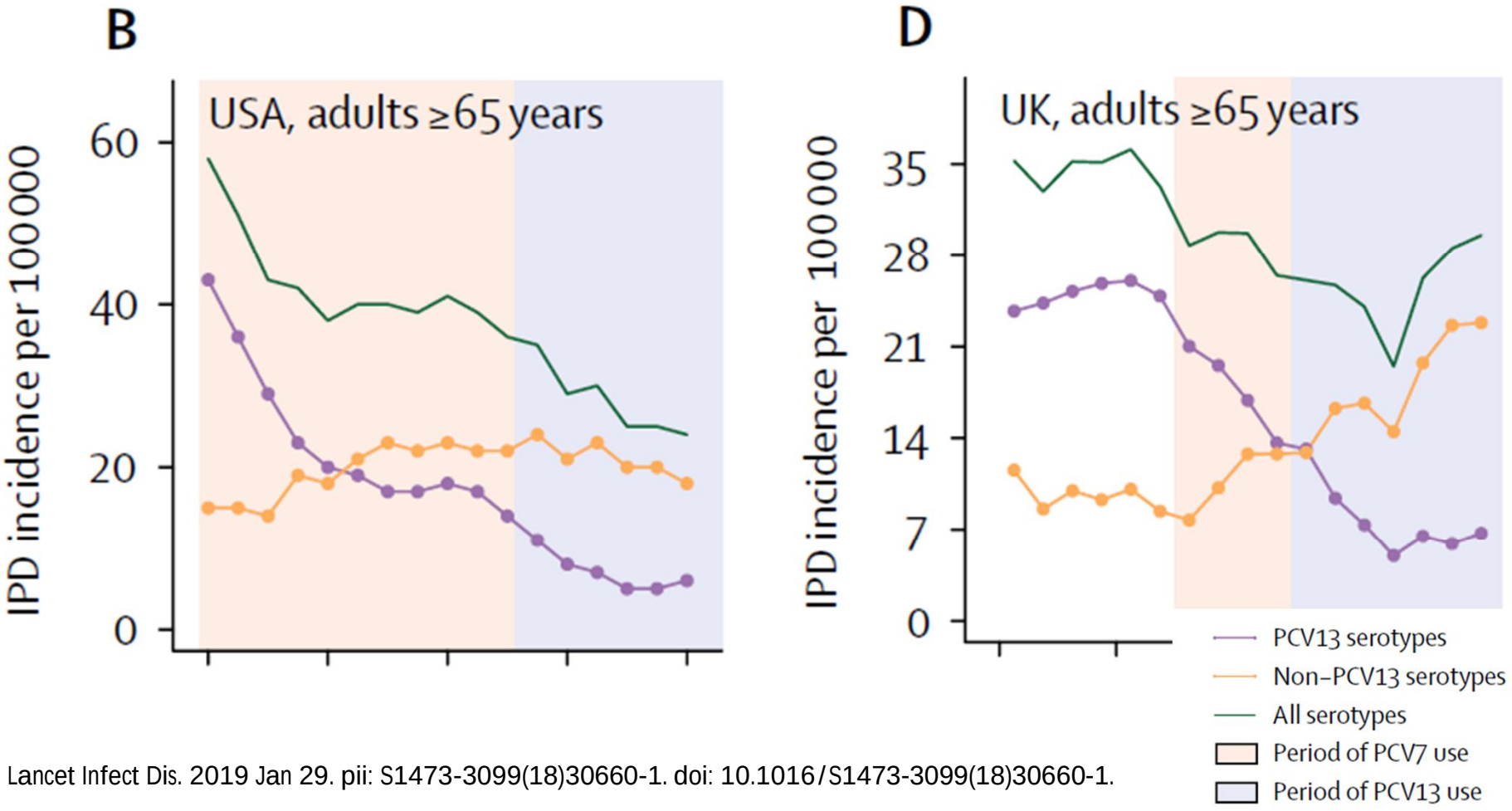
Lancet Infect Dis. 2018 Apr;18(4):441-451

ST epidemiology USA vs UK 0-4 y



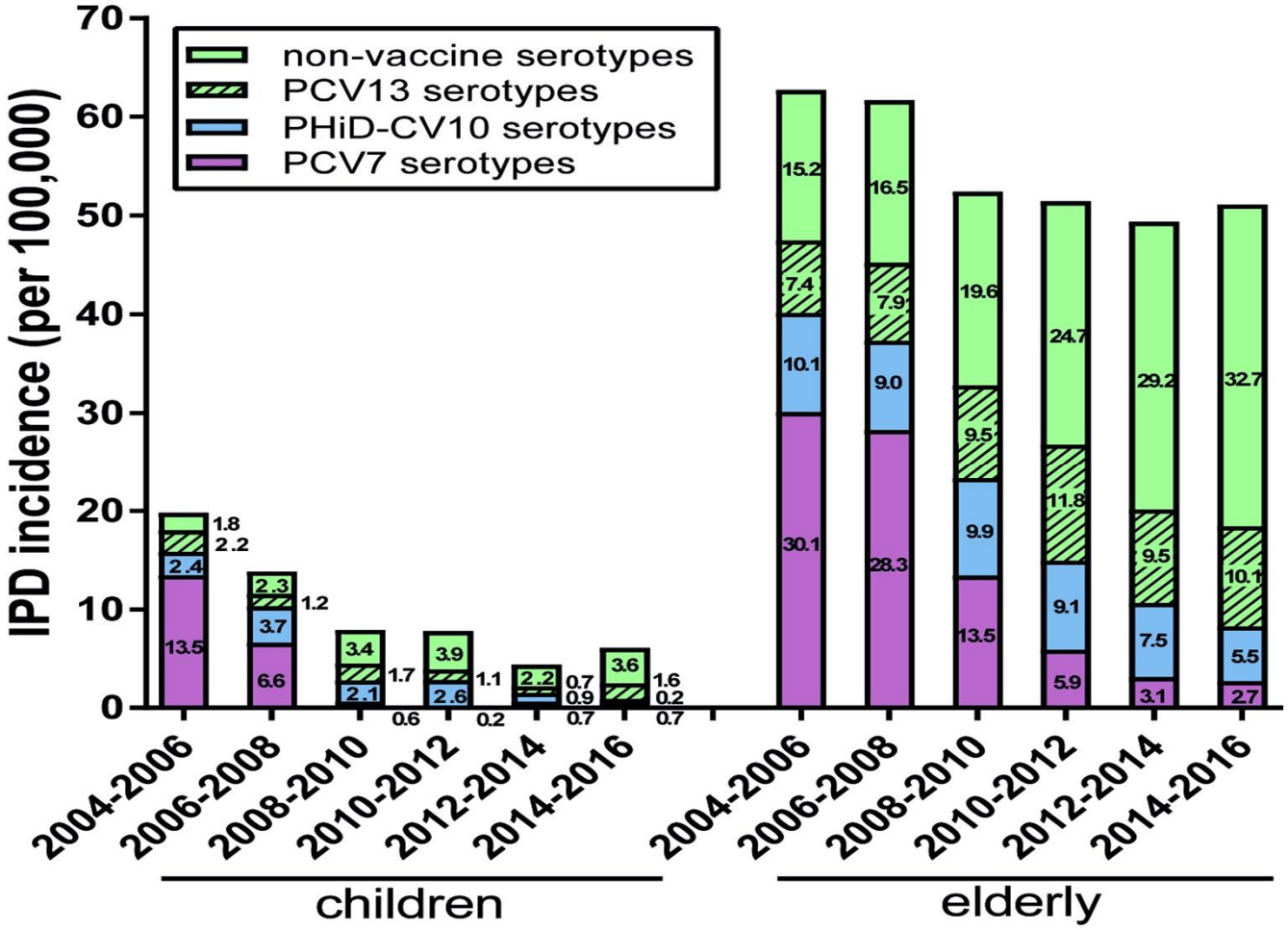
Lancet Infect Dis. 2019 Jan 29. pii: S1473-3099(18)30660-1. doi: 10.1016/S1473-3099(18)30660-1.

ST epidemiology USA vs UK >= 65 y



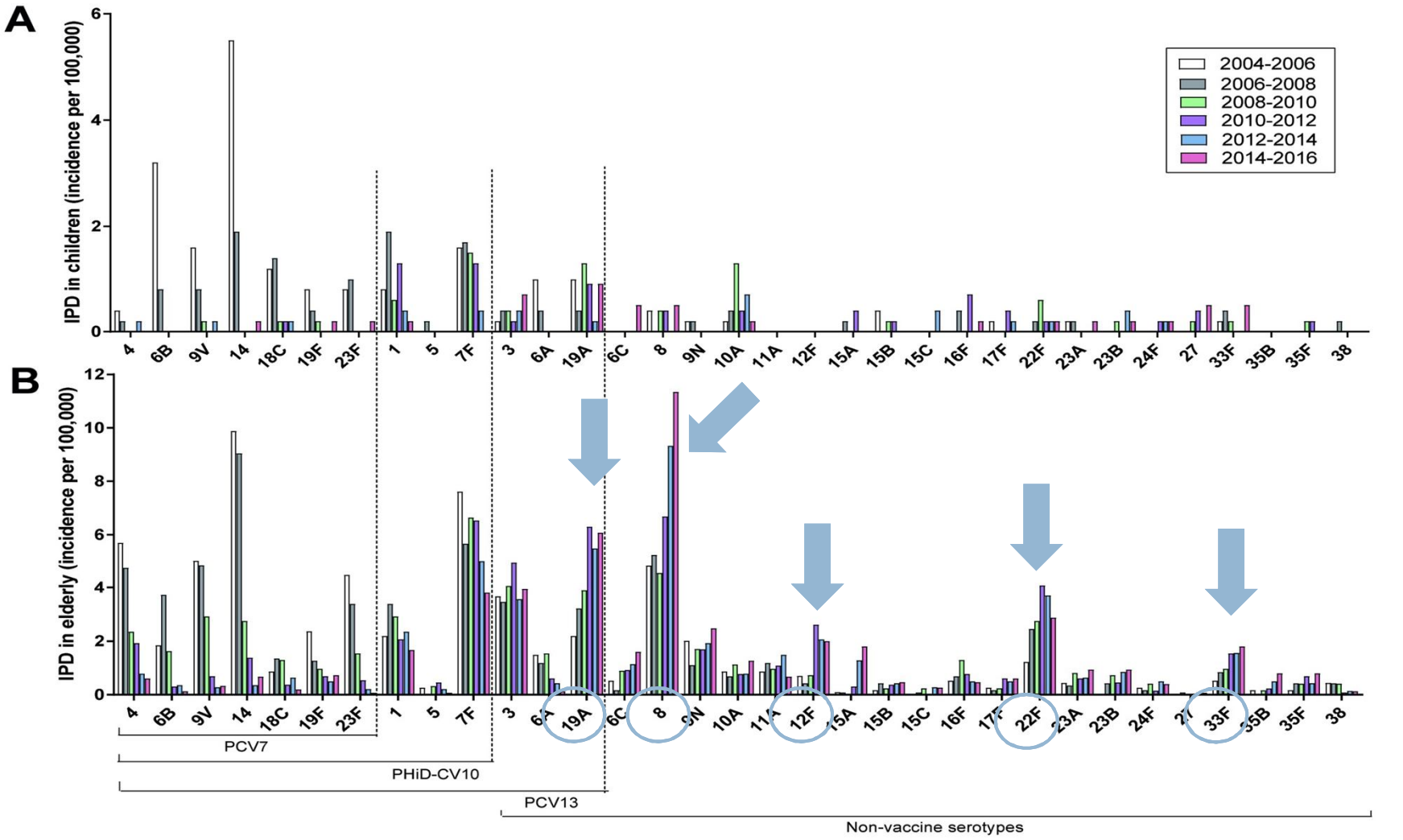
Lancet Infect Dis. 2019 Jan 29. pii: S1473-3099(18)30660-1. doi: 10.1016/S1473-3099(18)30660-1.

PCV10 and IPD
The Netherlands



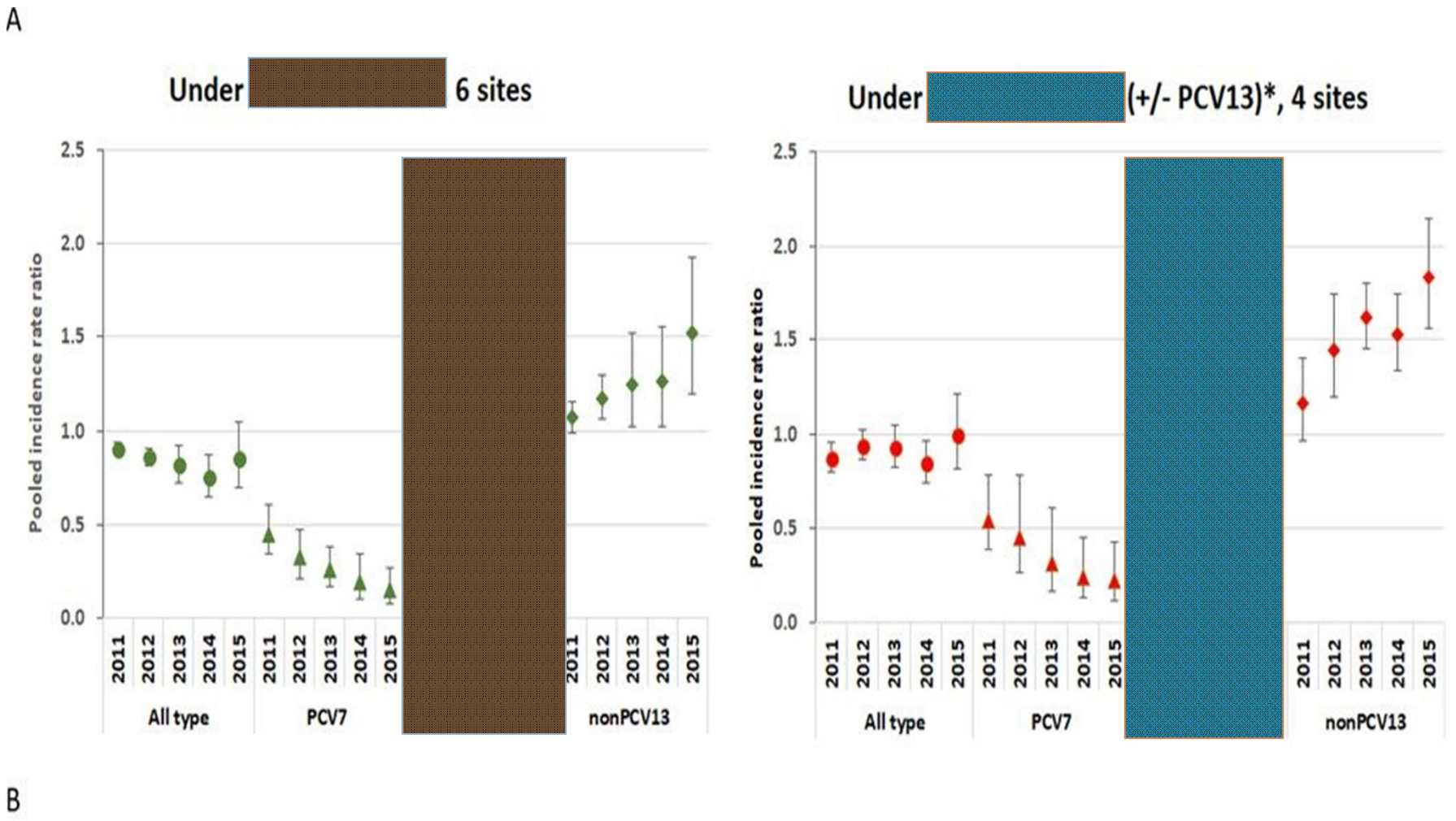
PLoS One. 2018 Mar 30;13(3):e0194823

PCV10 and IPD
The Netherlands



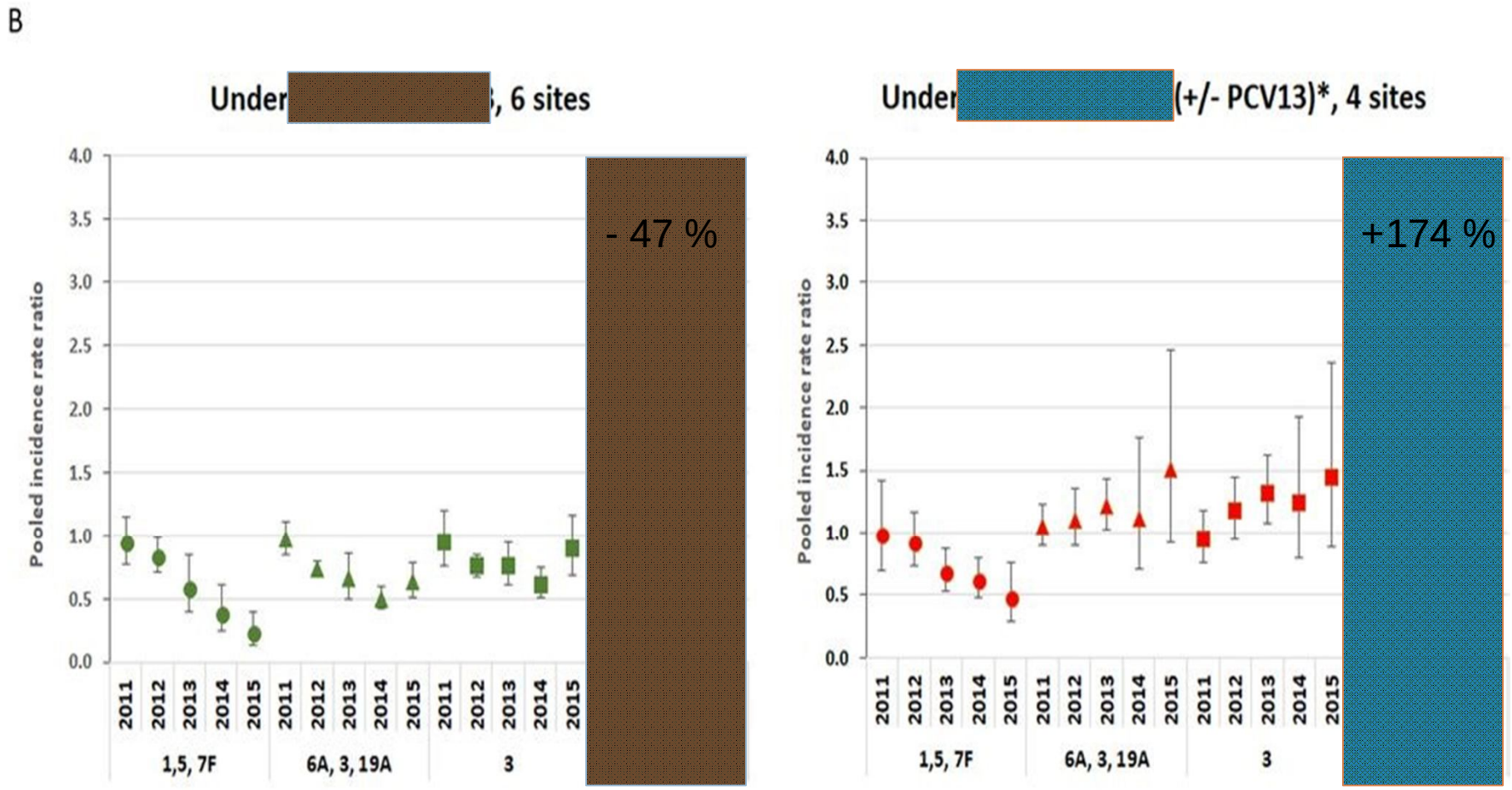
PLoS One. 2018 Mar 30;13(3):e0194823

Indirect effect PCV infant program on IPD in older adults



Hanquet et al Thorax. doi: 10.1136/thoraxjnl-2018-211767

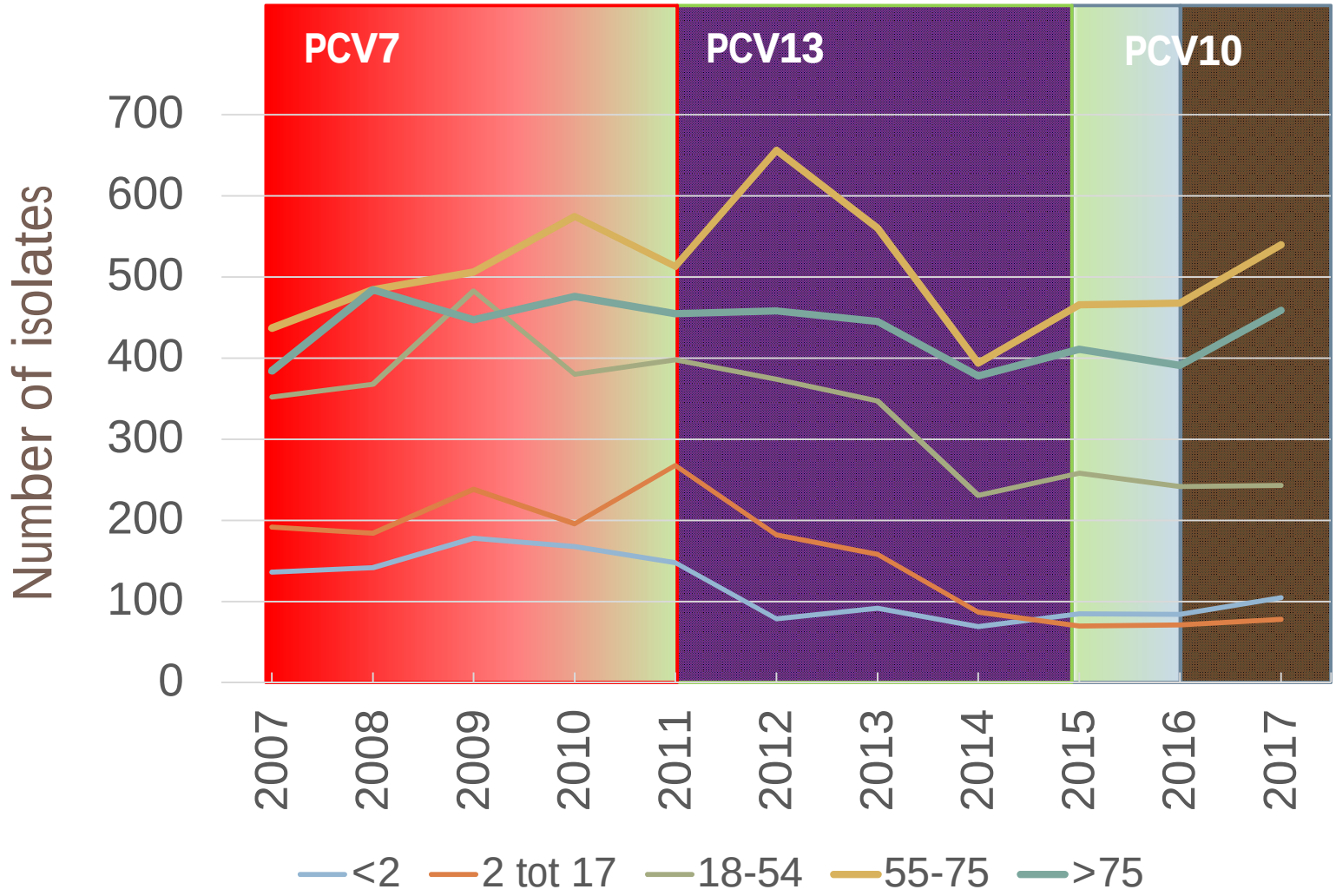
Indirect effect PCV infant program on IPD in older adults



Hanquet et al Thorax. doi: 10.1136/thoraxjnl-2018-211767

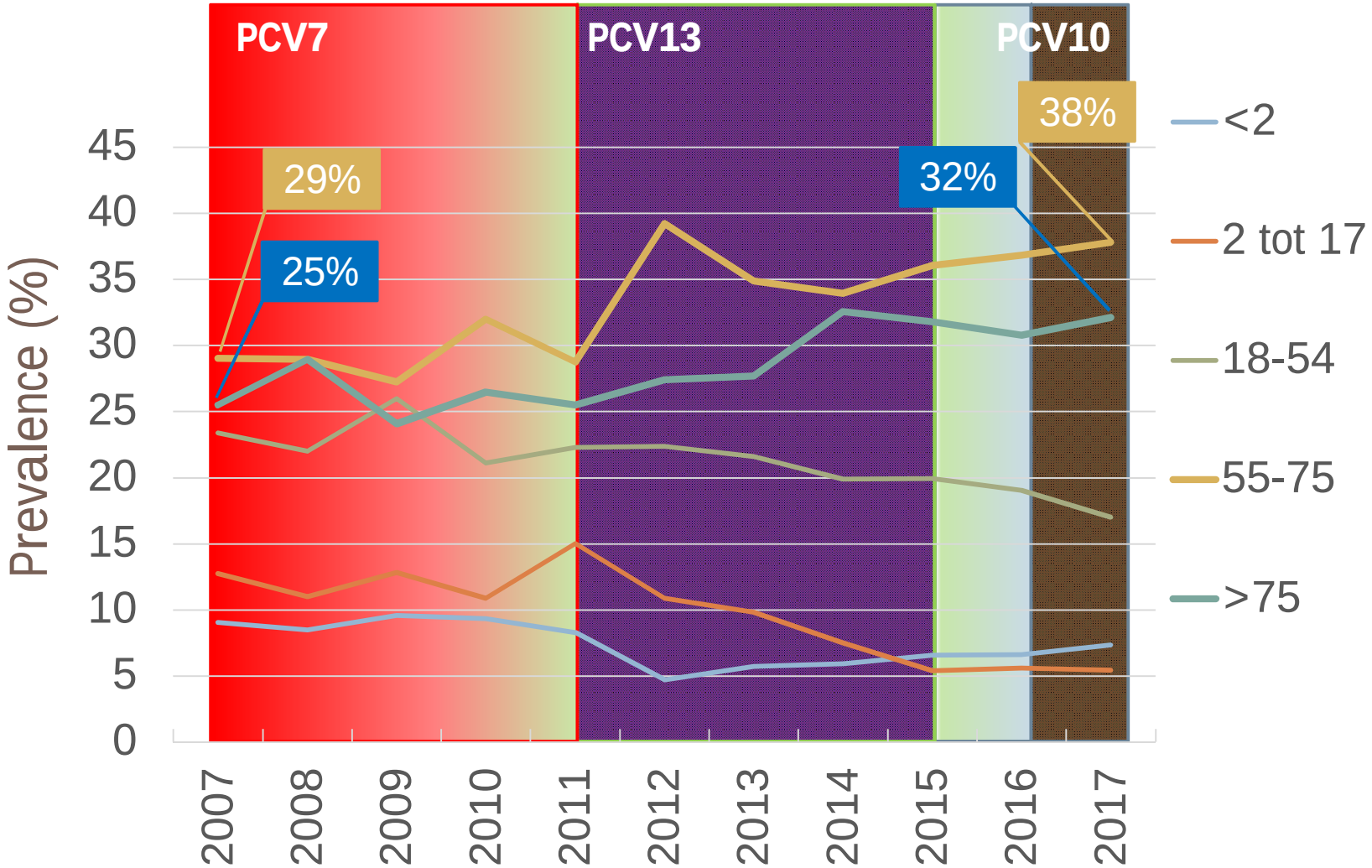
IPD isolates per age group

Belgium 2007-2017

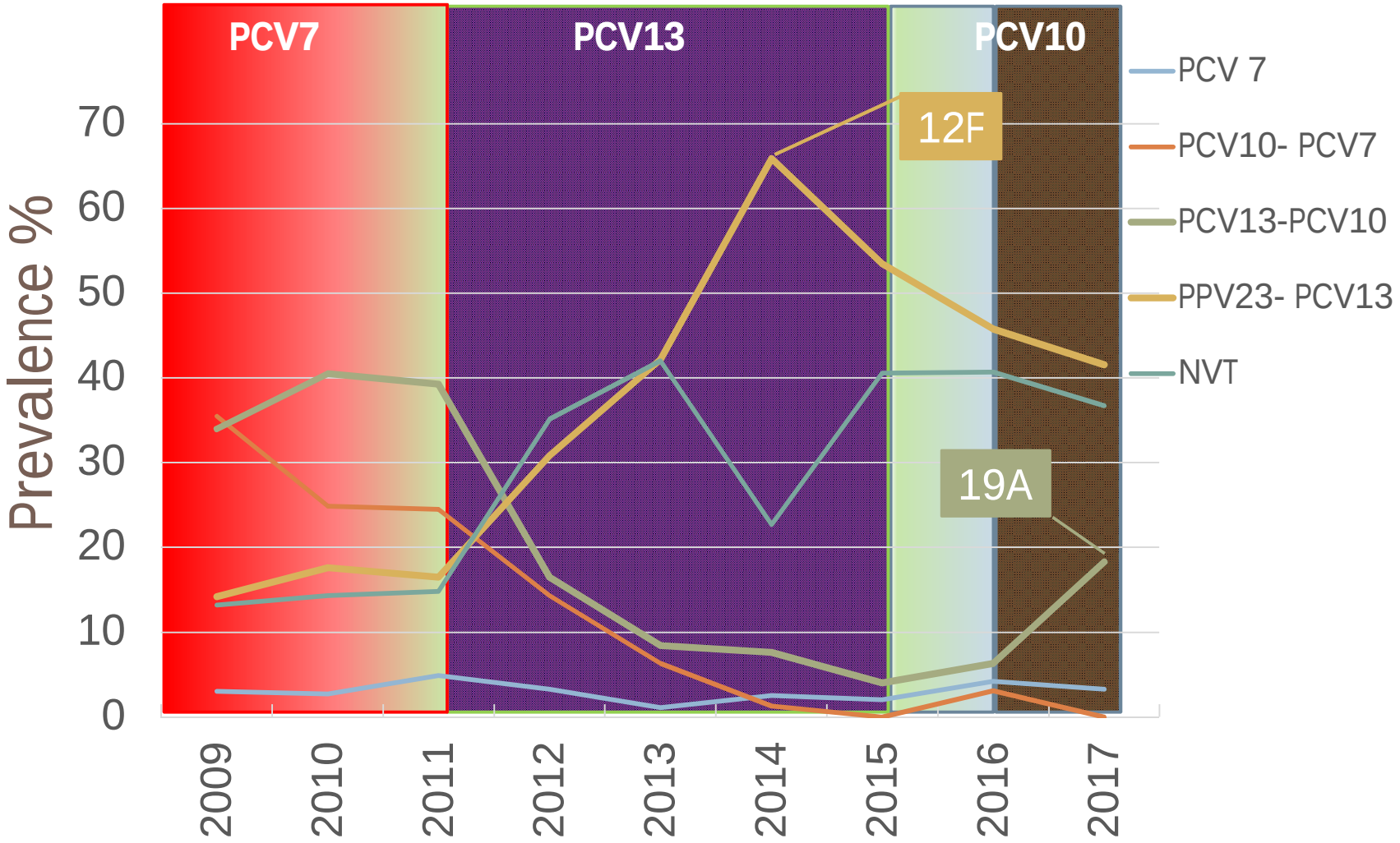


Prevalence of IPD isolates by age

Belgium 2007-17



Prevalence of vaccine and non-vaccine ST Belgium 2009-2017



Switch in a childhood pneumococcal vaccination programme from PCV13 to PCV10: a defendable approach?

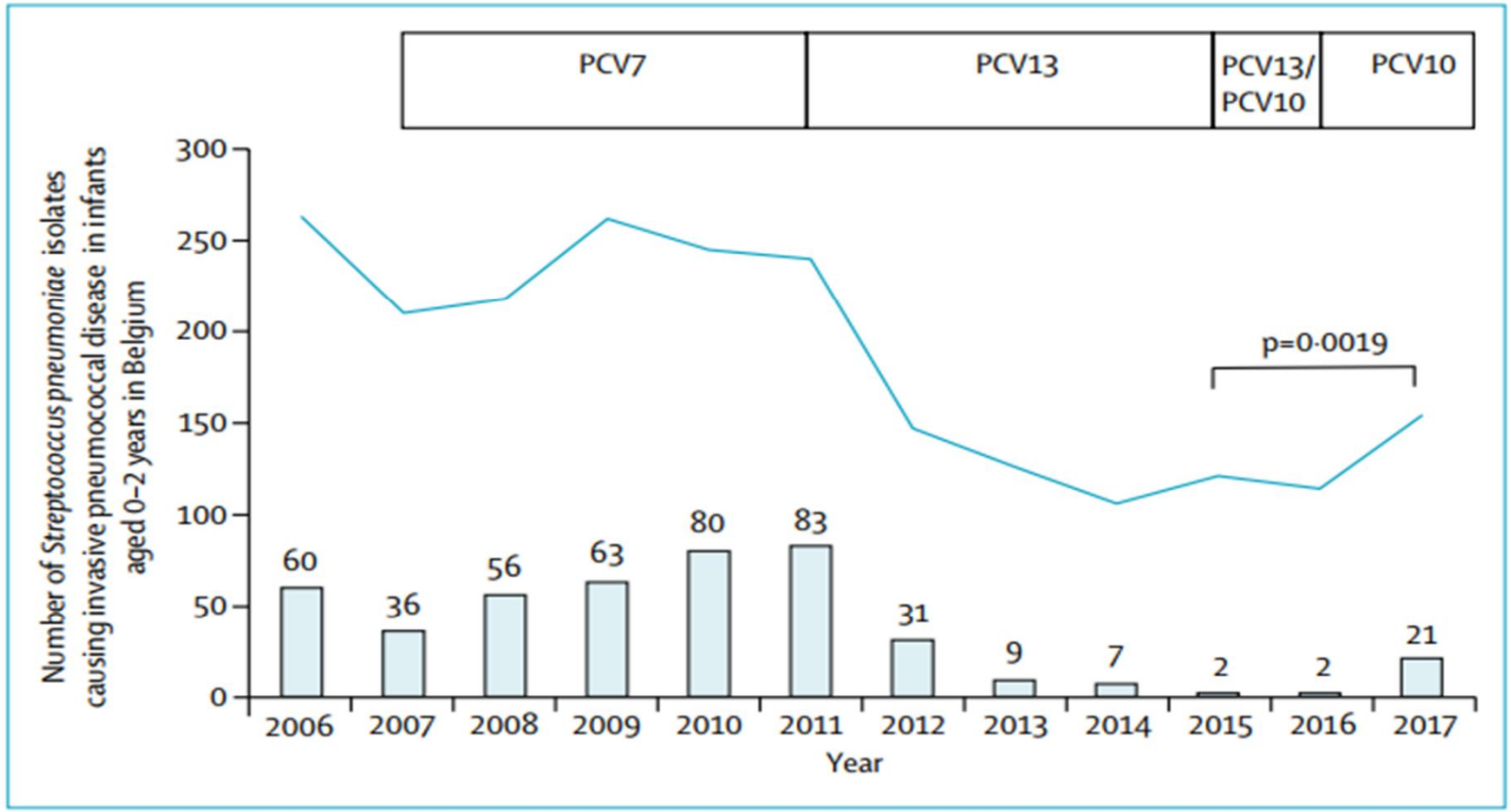
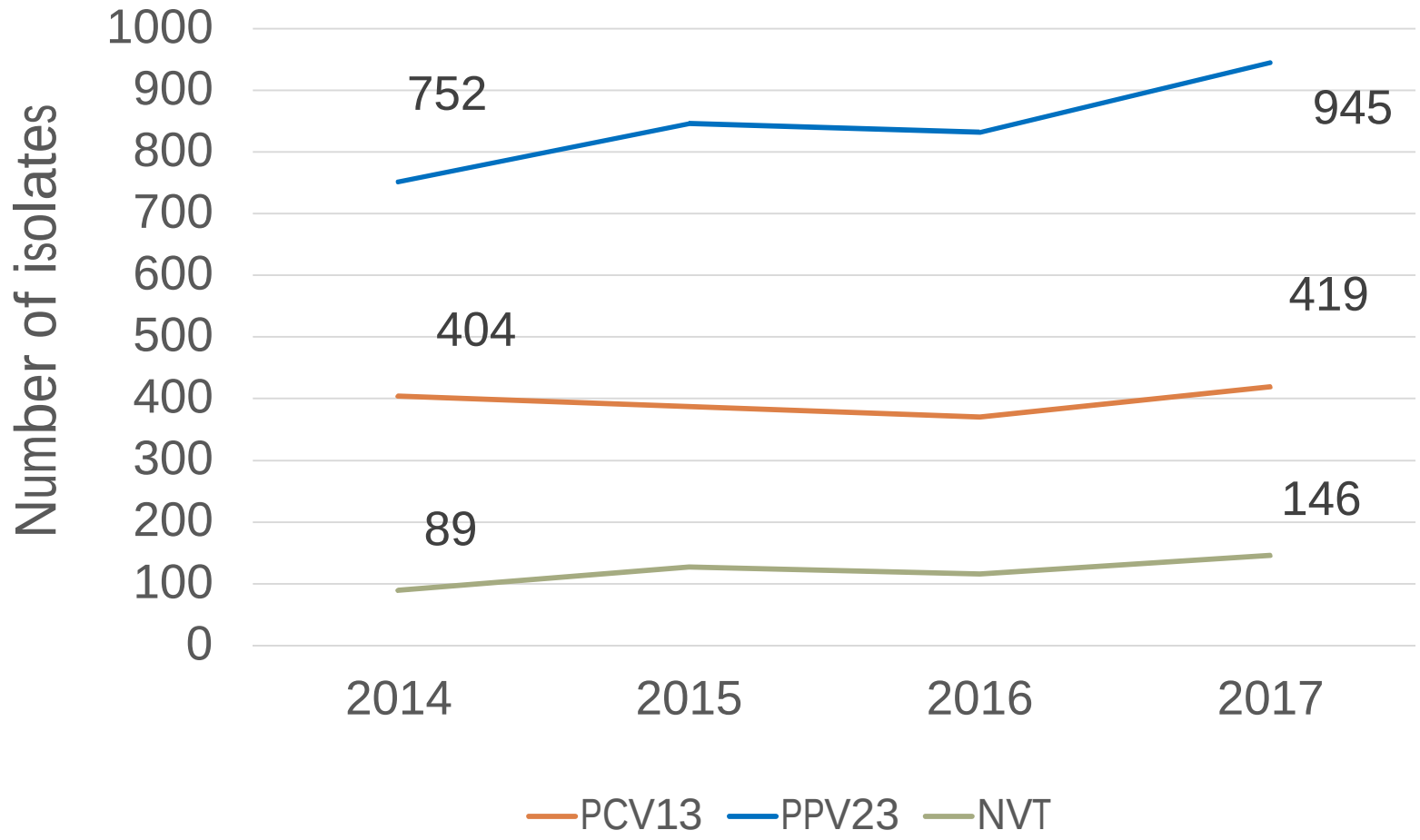


Figure: **Evolution of the number of pneumococcal isolates (line) and serotype 19A isolates (columns) in Belgium causing invasive pneumococcal disease in children aged 0–2 years, 2006–17**

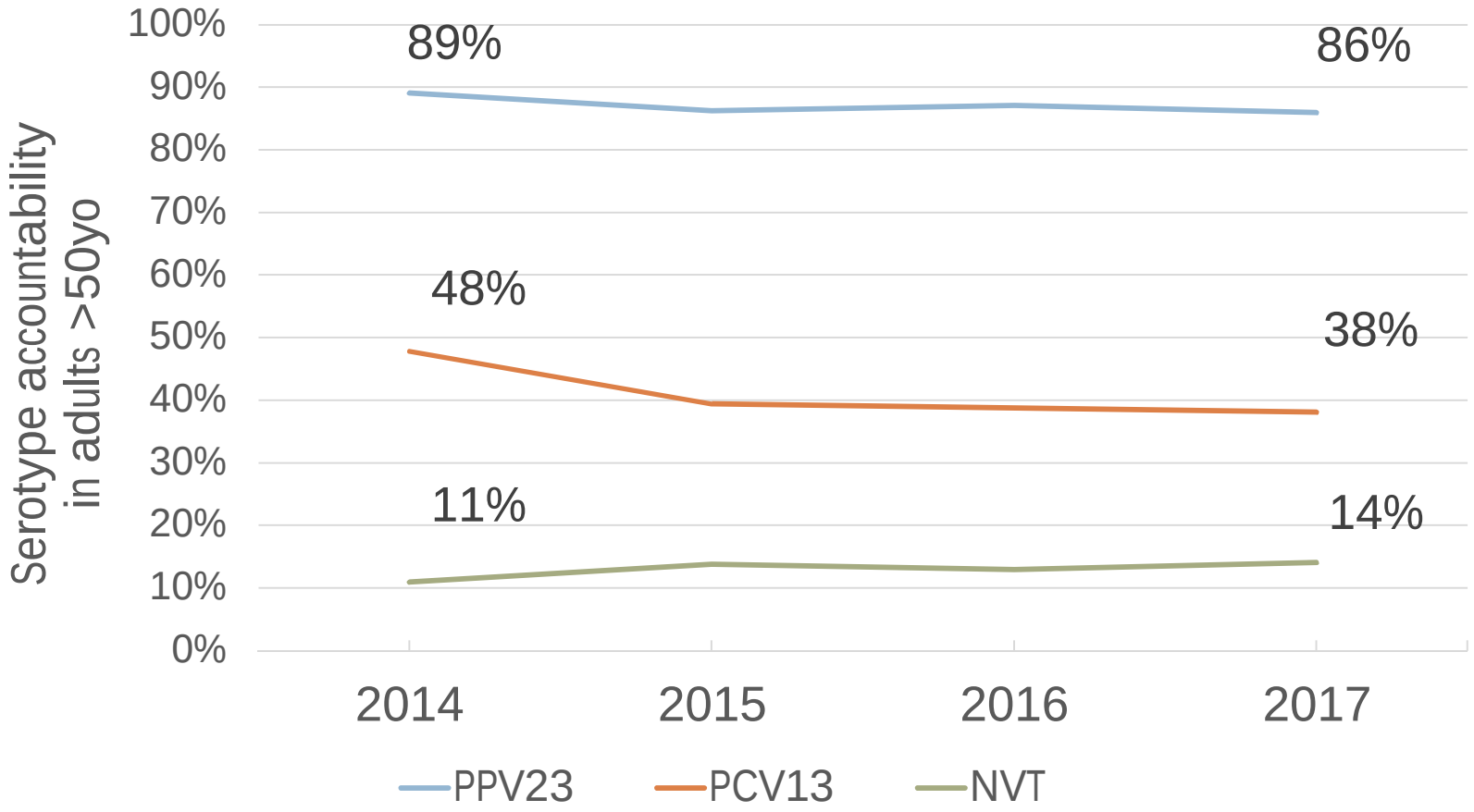
Lancet Infect Dis http://dx.doi.org/10.1016/S1473-3099(18)30346-3

Vaccine and non-vaccine ST evolution adults

> 50 y Belgium 2014-2017



Vaccine and non-vaccine ST evolution adults **> 50 y** Belgium 2014-2017



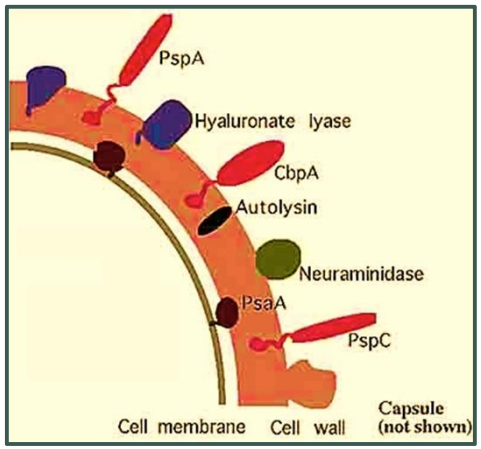
Evolving pneumococcal epidemiology in the EU

- Evidence controversies: oldest old and high risk ?
- Policy heterogeneity
- Impact of childhood pneumococcal vaccination
- Surveillance !!

- **Lifelong pneumococcal vaccination strategy**
  - **child – at risk – old**
- **Uniform EU vaccination policy**

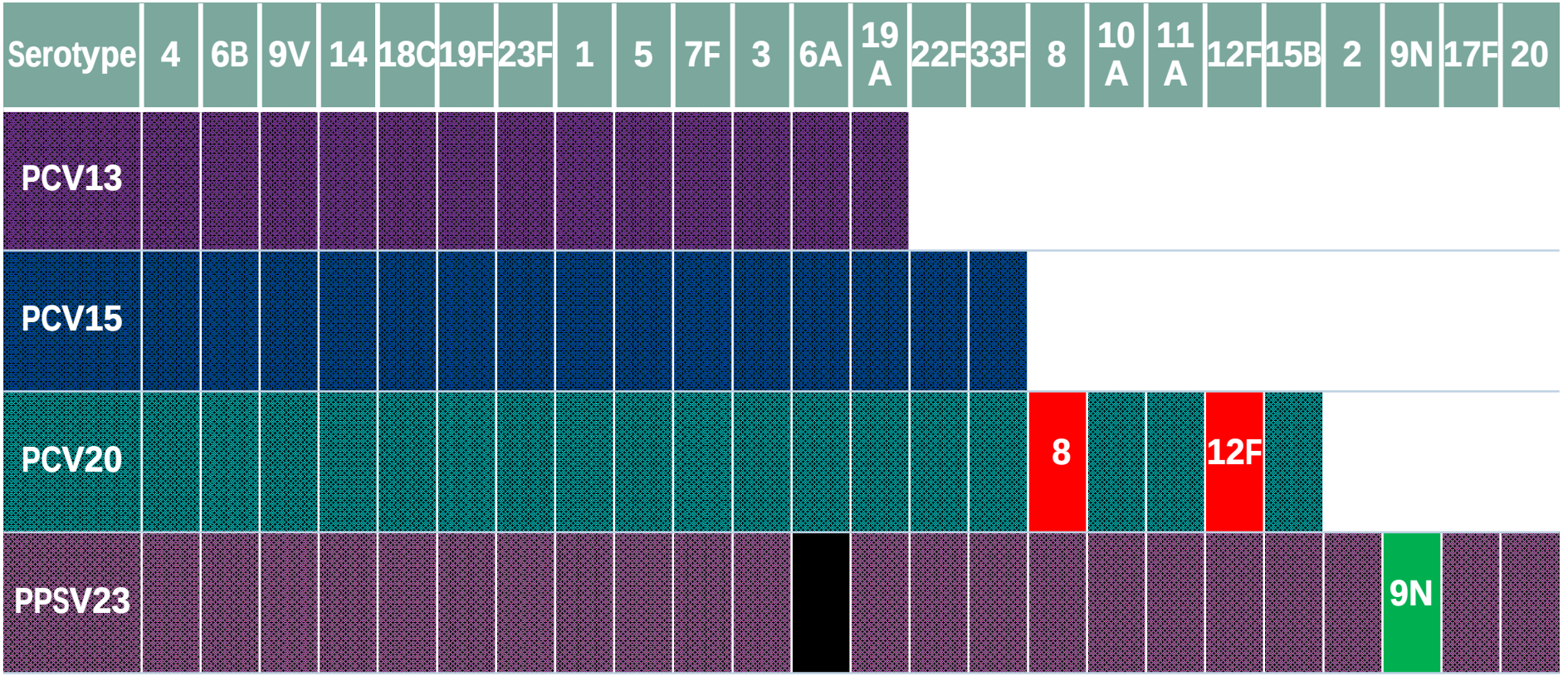
Future

- **Monitoring**
  - Vaccine uptake
  - Pneumococcal disease epidemiology:
    - IPD, non-bactraemic PD, carriage
    - All age groups,
    - Direct and indirect effects
  - Post licensure monitoring of vaccine effectiveness ≥ 65y.
    - Duration of protection ? Vaccination interval sequences?
    - Case – control IPD and Pneumococcal CAP
    - Adult carriage studies
    - UA tests
- **Higher valent vaccines**: PCV15, 20 → ~~PCV93~~
- **Alternative vaccines**
  - Other ST corresponding to ST epidemiology
  - Protein vaccines
  - Combination PCV and protein vaccine
  - Inactivated whole cell vaccine



Rodgers GL, Klugman PP. *Vaccine* 2011; 29: 43
Moffitt KL, Malley R. *Curr Opinion Immunol* 2011; 23: 407-413

Future PCV


Serotype
4
6B
9V
14
18C
19F
23F
1
5
7F
3
6A
19 A
22F
33F
8
10 A
11 A
12F
15B
2
9N
17F
20
PCV13
PCV15
PCV20
8
12F
PPSV23
9N

Conclusion

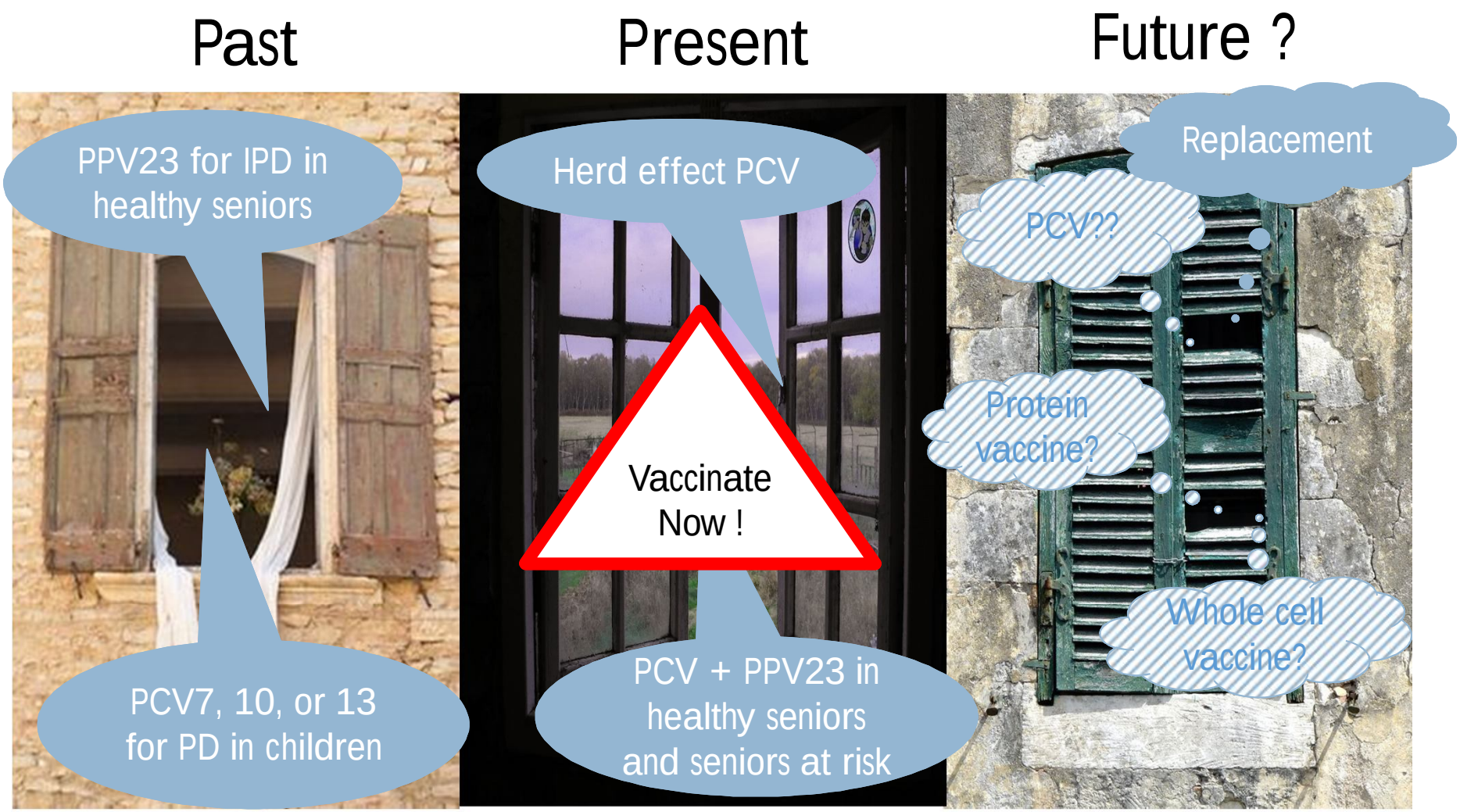

Past
Present
Future ?
PPV23 for IPD in healthy seniors
PCV7, 10, or 13 for PD in children
Herd effect PCV
Vaccinate Now !
PCV + PPV23 in healthy seniors and seniors at risk
Replacement
PCV??
Protein vaccine?
Whole cell vaccine?

Table 1. Estimates of population size, disease rates, case-fatality rates, and associated costs*.

	65–74 Years		75–84 Years		≥85 Years	
	Moderate	High	Moderate	High	Moderate	High
No. of Belgian Adults	420,774	44,181	365,901	30,610	153,348	6,495
Annual Disease Incidence (per 100K)						
Bacteremia	37.4	82.0	48.0	105.2	107.0	234.5
Meningitis	1.69	3.71	2.18	4.78	5.03	11.02
Pneumococcal CAP						
Inpatient	129	439	186	599	546	1,733
Outpatient	89	305	134	433	207	666
Annual Case-Fatality (per 100)						
Bacteremia	14.0	14.0	17.6	17.6	24.2	24.2
Meningitis	12.8	12.8	24.0	24.0	53.9	53.9
Pneumococcal CAP						
Inpatient	3.9	3.9	5.6	5.6	8.6	8.6
Outpatient	1.9	1.9	1.8	1.8	1.8	1.8
Utilities						
General Population Utility	0.7962	0.6001	0.7162	0.5490	0.6238	0.5876
Annual Disutility due to Disease						
Bacteremia	0.1759	0.1320	0.1758	0.1354	0.1741	0.1741
Meningitis	0.1759	0.1320	0.1758	0.1354	0.1741	0.1741
Pneumococcal CAP						
Inpatient	0.0717	0.0537	0.0716	0.0551	0.0709	0.0709
Outpatient	0.0066	0.0049	0.0047	0.0036	0.0027	0.0027
Medical Care Costs (per case)						
Requiring Inpatient Care						
Bacteremia	€ 15,439	€ 12,338	€ 16,658	€ 13,313	€ 16,543	€ 13,221
Meningitis	€ 11,279	€ 9,014	€ 10,932	€ 8,737	€ 10,857	€ 8,676
Pneumococcal CAP	€ 8,501	€ 9,359	€ 16,073	€ 17,695	€ 15,482	€ 17,044
Requiring Outpatient Care Only						
Pneumococcal CAP	€ 867	€ 985	€ 864	€ 982	€ 866	€ 984
Vaccination (per person)						
PCV13	€ 63.64	€ 63.64	€ 63.64	€ 63.64	€ 63.64	€ 63.64
Administration	€ 10.24	€ 10.24	€ 10.24	€ 10.24	€ 10.24	€ 10.24

*Methods and sources used in estimating parameter values set forth in S1 File

https://doi.org/10.1371/journal.pone.0199427.t001

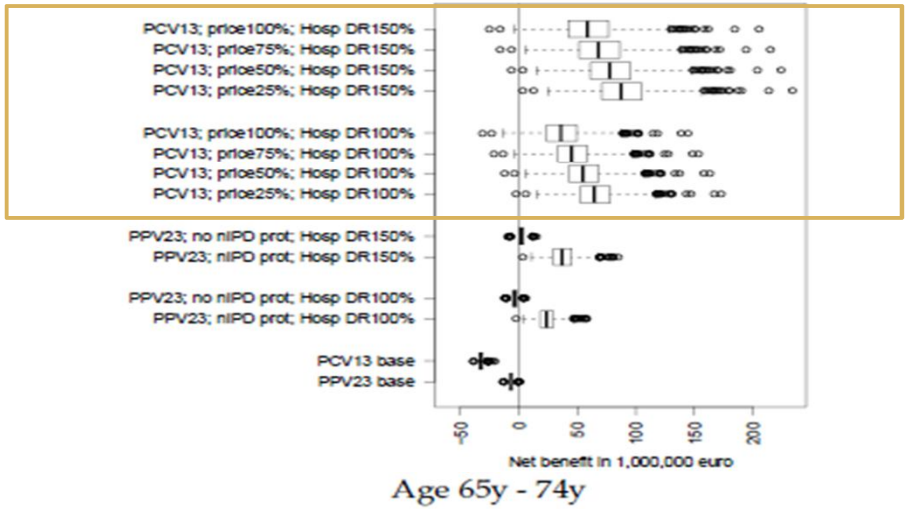
Marbaix S, Peetermans WE, Verhaegen J, Annemans L, Sato R, et al. (2018) Cost-effectiveness of PCV13 vaccination in Belgian adults aged 65-84 years at elevated risk of pneumococcal infection. PLOS ONE 13(7): e0199427. https://doi.org/10.1371/journal.pone.0199427
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0199427

PLOS ONE

KCE cost-effectiveness analysis (Nov 2016)

In persons 65-74 years, with medium risk (sensitivity analysis KCE)

HIGHER BURDEN: Using QALY loss of the medium risk group AND All incidences 200% of baseline AND Quick PCV13 serotype relapse: PCV13 incidence returns to 2015 value within 7 years AND Willingness to pay 35,000 euro per QALY gained



Age 65y - 74y

Vaccination with **PCV13** when used in a **population with medium risk** results in a **net benefit**

Blommaert A, Hanquet G, Willem L, Theeten H, Thiry N, Bilcke J, Verhaegen J, Beutels P. Use of pneumococcal vaccines in the elderly: an economic evaluation. Health Technology Assessment (HTA) Brussels: Belgian Health Care Knowledge Centre (KCE). 2016. KCE Reports 274. D/2016/10.273/79.

Cost-Effectiveness of Introducing PCV13 Vaccination Among the Elderly with comorbidities in Belgium

Results

Table 3. Cost-effectiveness/utility of PCV13 versus no routine vaccination in moderate/high-risk Belgian adults aged 65–84 years.

	No Vaccine	PCV13	Difference
Population-Level Results			
No. of Cases			
IPD	7,352	6,825	-527
Pneumococcal CAP			
Hospitalized	33,662	32,588	-1,074
Outpatient	17,617	16,947	-669
No. of Deaths	4,279	4,104	-176
Total Costs (in million)			
Medical Care	472.13	452.03	-20.10
Vaccination	0.00	36.91	36.91
Total			
Medical + Vaccination	472.13	488.95	16.82
Life-Years (discounted)	9,590,018	9,591,268	1,251
Quality-Adjusted Life-Years (discounted)	6,724,131	6,725,113	982
Cost-Effectiveness			
Cost per Life-Year Gained			€ 13,444
Cost per Quality-Adjusted Life-Year Gained			€ 17,126

Within Willingness To Pay limit

Marbaix S, Peetermans WE, Verhaegen J, Annemans L, Sato R, Mignon A, Atwood M, Weycker D. **Cost-effectiveness of PCV13 vaccination in Belgian adults aged 65-84 years at elevated risk of pneumococcal infection.** PLoS One. 2018 Jul 6;13(7):e0199427. doi: 10.1371/journal.pone.0199427. eCollection 2018.

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https://doi.org/10.1371/journal.pone.0199427.t001

41,5 % van Belgen 65-74j

58 % van Belgen 75-84j

50 % van Belgen >=85j

Marbaix S, Peetermans WE, Verhaegen J, Annemans L, Sato R, et al. (2018) Cost-effectiveness of PCV13 vaccination in Belgian adults aged 65-84 years at elevated risk of pneumococcal infection. PLOS ONE 13(7): e0199427. https://doi.org/10.1371/journal.pone.0199427
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0199427

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