Impact of vaccination on epidemiology in adults

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1. Data on prospective study on IPD in Belgium (2009-2011)
2. Evolution of capsular types of invasive isolates from adults after introduction of PCV7 and PCV13 in Belgium
3. Evolution of capsular types of invasive isolates from adults after introduction of PCV7 and PCV13 in Europe

Epidemiology and outcome of invasive pneumococcal disease (2009-2011)

- collaboration of 50 hospitals, 1332 patients

		age group n(%)		
Type of IPD	Total (n=1332)	18-49y (n=220)	50-64y (n=370)	≥65y (n=742)
bacteraemic pneumonia	1049(79%)	170(77,3)	276 (74,6)	603 (81,3)
empyema	94 (7%)	21 (9,5)	32 (8,6)	41 (5,5)
meningitis	73 (5,5%)	8 (3,6)	32 (8,6)	33 (4,4)
bacteraemia without focus	73 (5,5%)	8 (3,6)	17 (4,6)	48 (6,5)
other	43 (3,2 %)	13 (5,9)	13 (3,5)	17 (2,3)

J. Verhaegen et al., Eurosurveillance, 2014,19:14-22

Epidemiology and outcome of invasive pneumococcal disease (2009-2011)

Comorbidities	age group (n) 18-49y (n=220)	50-64y (n=370)	≥65y (n=742)	P-value
any	118 (54%)	274	627 (85%)	<0,0001
COPD	15	89	231	<0,0001
cancer	13	81	203	<0,0001
heart failure	3	40	206	<0,0001
diabetes	11	47	146	<0,0001
renal insufficiency	3	32	144	<0,0001
immunosuppression	21	51	100	0,32
≥2 comorbidities	50	154	399	≤0,001

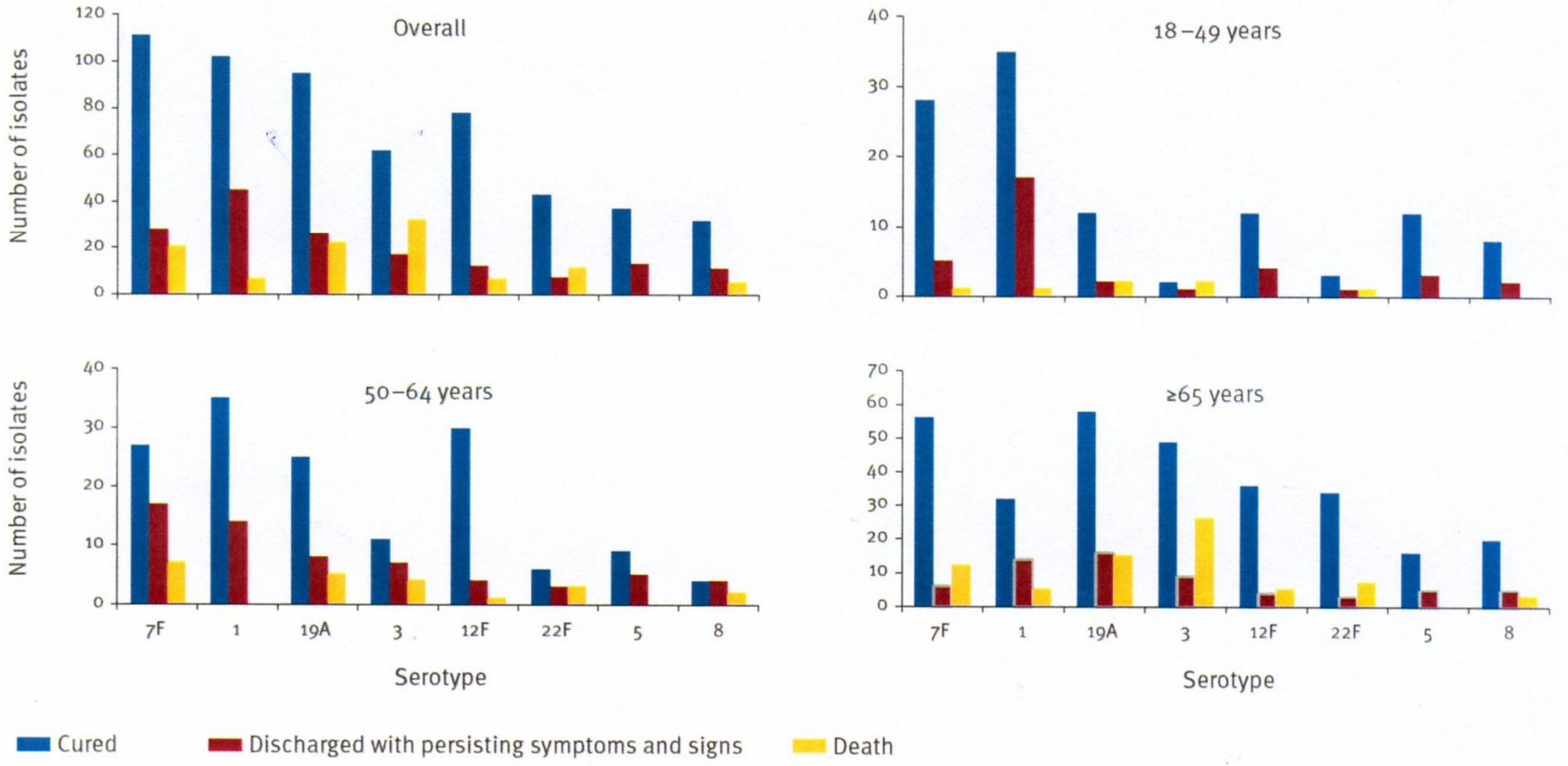
J. Verhaegen et al., Eurosurveillance, 2014,19:14-22

Disease outcome at discharge by age and type of IPD

category	n	admission ICU n(%)	Outcome at discharge			P-value overall
			cured n(%)	with symptoms n (%)	death n (%)	
total	1329	434 (32,7)	884 (66,5)	237 (17,8)	208 (15,7)	
age						0,044
18-49y	219	54 (24,5)	157 (71,7)	49 (22,4)	13 (5,9)	
50-64y	370	154 (41,6)	240 (64,9)	83 (22,4)	47 (12,7)	
≥65y	740	226 (30,6)	487 (65,8)	105 (14,2)	148 (20,0)	
type of IPD						
bacteraemia pneumonia	1049	303 (28,9)	722 (69,0)	169 (16,2)	155 (14,8)	0,0049
empyema	94	49 (52,1)	49 (52,1)	35 (37,2)	10 (10,6)	
meningitis	73	59 (80,8)	38 (52,1)	16 (21,9)	19 (26)	
bacteraemia without focus	73	12 (16,4)	51 (69,9)	4 (5,5)	18 (24,7)	
other	43	11 (25,6)	24 (55,8)	13 (30,2)	6 (14,0)	

J. Verhaegen et al., Eurosurveillance, 2014,19:14-22

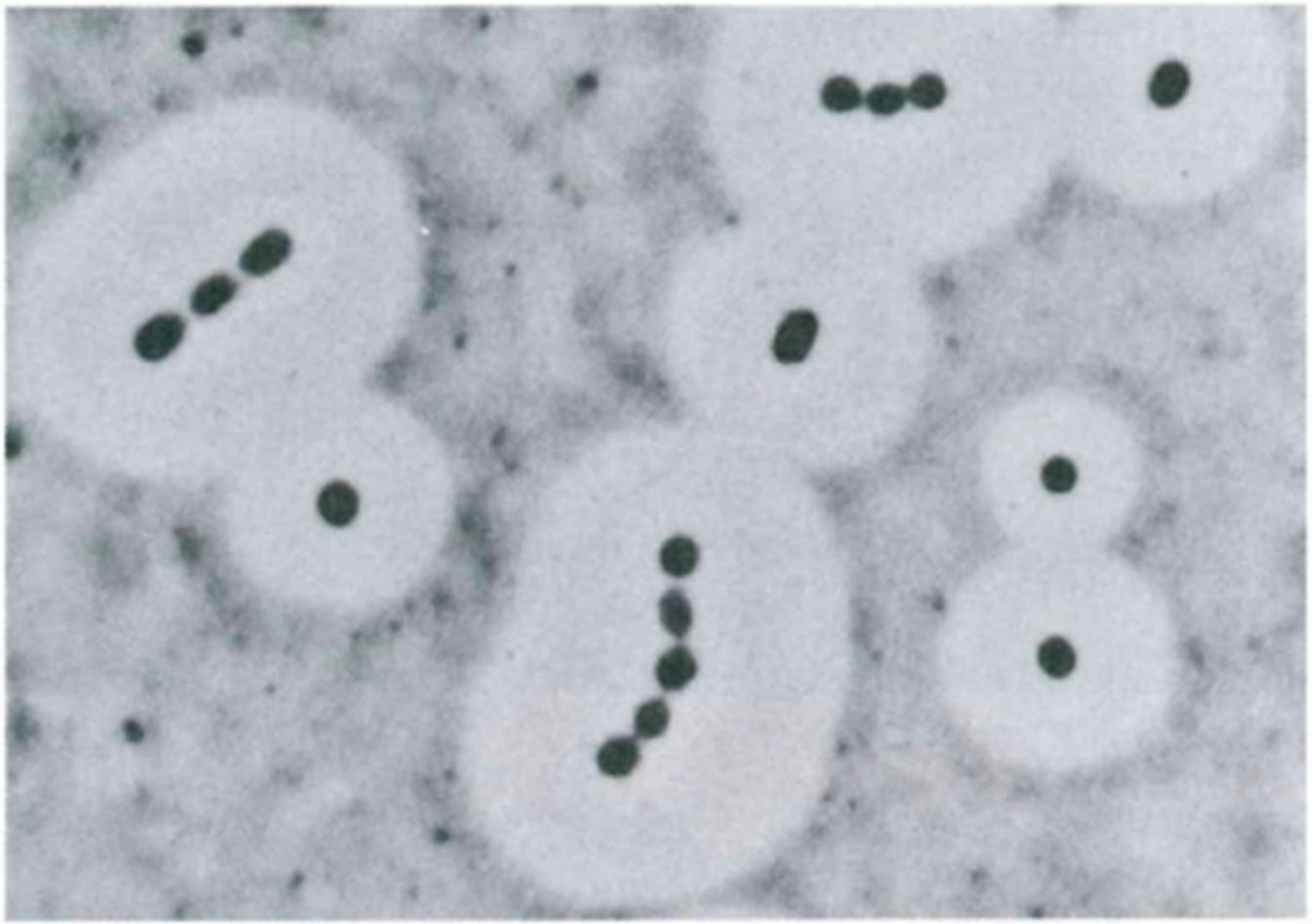
Disease outcome at discharge by age and serotype



Pneumococcus capsular typing

- Danish nomenclature (Kauffman und Lund, 1954)
  - Nine pooled sera = A-I
  - 93 serovars
    - 26 sera of a single serotype
    - 20 group sera = 2 to 4 cross-reacting serovars (e.g. serogroup 7 = 7F, 7A, 7B, 7C)

Since 2006 all IPD isolates from subjects aged <18 years belonging to serogroups were further serotyped with factor sera (Statens Seruminstitut Copenhagen)



Isaac Shechmeister

Figure 29.11 ***Streptococcus pneumoniae.*** India ink negative stain of cells of *Streptococcus pneumoniae.* An extensive capsule surrounds the cells, which are 1.0–1.2 µm in diameter.

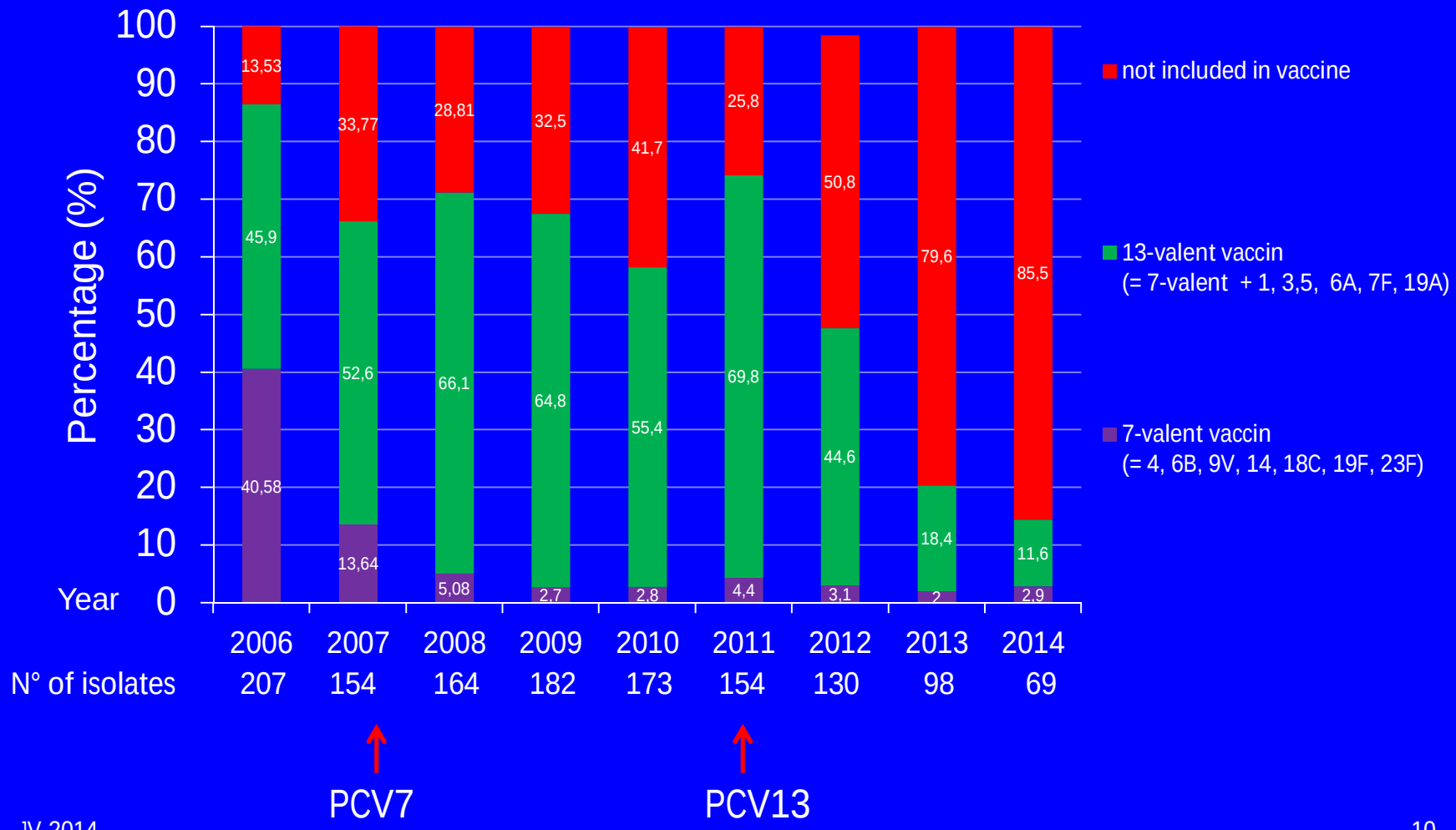
Pneumococcal polysaccharide vaccine

- 23-valent vaccine (Pneumo 23)
  - 0,5 ml single dose vial containing purified capsular polysaccharide from each of the 23 types of S. pneumoniae (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20 22F, 23F)
  - This vaccine induces B-cell type-specific protective antibody without a contribution of helper T-cells
  - Low antibody titers, particularly in children less than 18 months of age

Pneumococcal conjugate vaccines

- 7-valent vaccine (PREVENAR)
  - 2 µg of 6 capsular polysaccharides: 4, 9V, 14, 18C, 19F, 23F
    4 µg of polysaccharide 6B
  - conjugated to 20 µg *C. diphtheriae* CRM_{197} protein
- 10-valent vaccine (SYNFLORIX)
  - 1 µg of 7 capsular polysaccharides: **1**, **5**, 6B, **7F**, 9V, 14, 23F
  - 3 µg of 3 capsular polysaccharides: 4, 18C, 19F
  - conjugated to 9-16 µg Protein D *Haemophilus influenzae* or 10 µg (Tetanus anatoxine (18C) or 6 µg *C. diphtheriae* anatoxine (19F)
- 13-valent vaccine (PREVENAR 13)
  - 13 capsular polysaccharides: 1, **3**, 4, 5, **6A**, 6B, 7F, 9V, 14, 18C, **19A**, 19F, 23F
  - conjugated to 20 µg *C. diphtheriae* CRM_{197} protein
- Conjugate vaccines induce a T-cell dependent immune response resulting in the production of more differentiated high affinity antibodies and also in the development of memory B-cells.

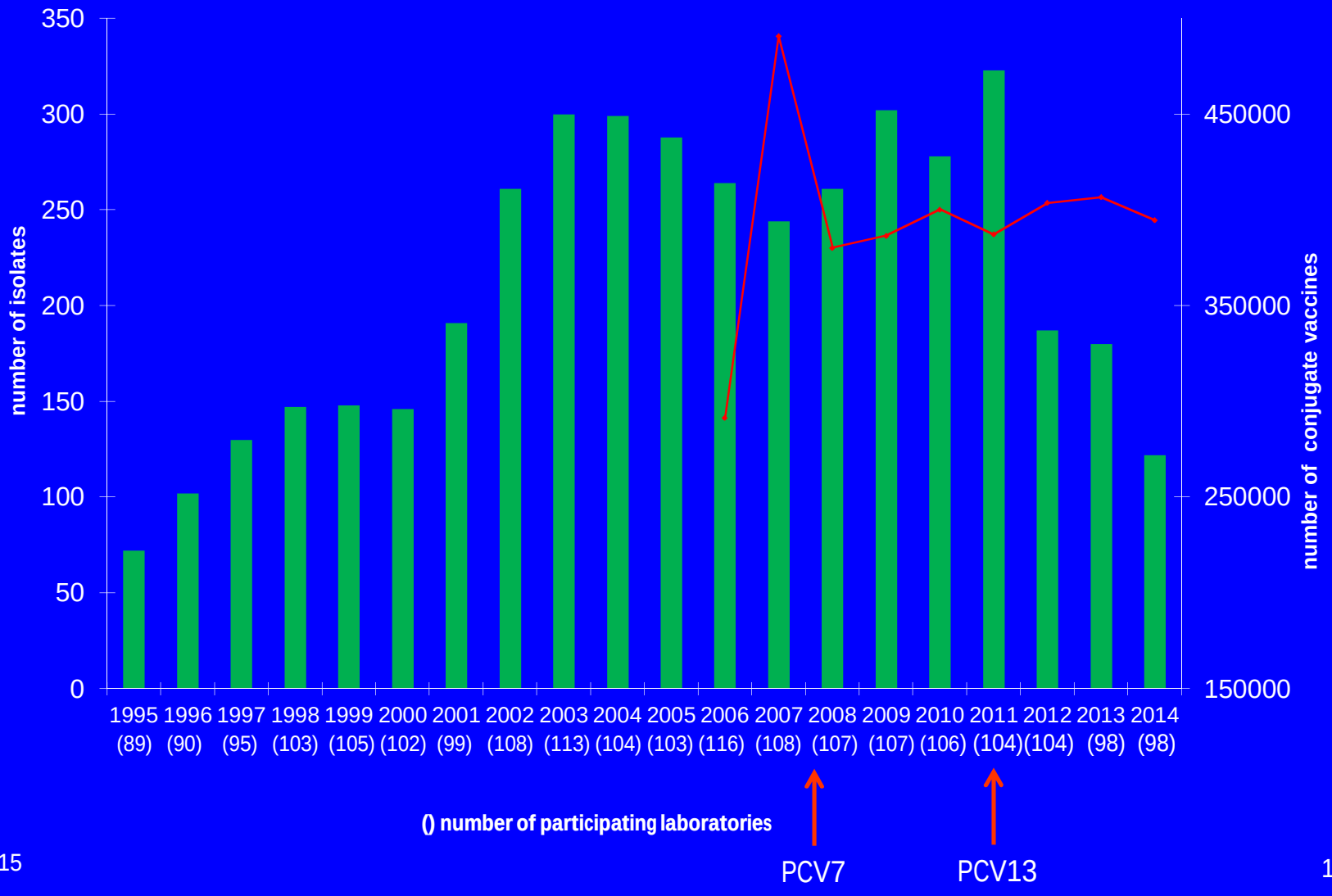
Evolution of number of invasive infections and percentage of capsular types included in the two different conjugate vaccines in children <2 years in Belgium (2006-2014)



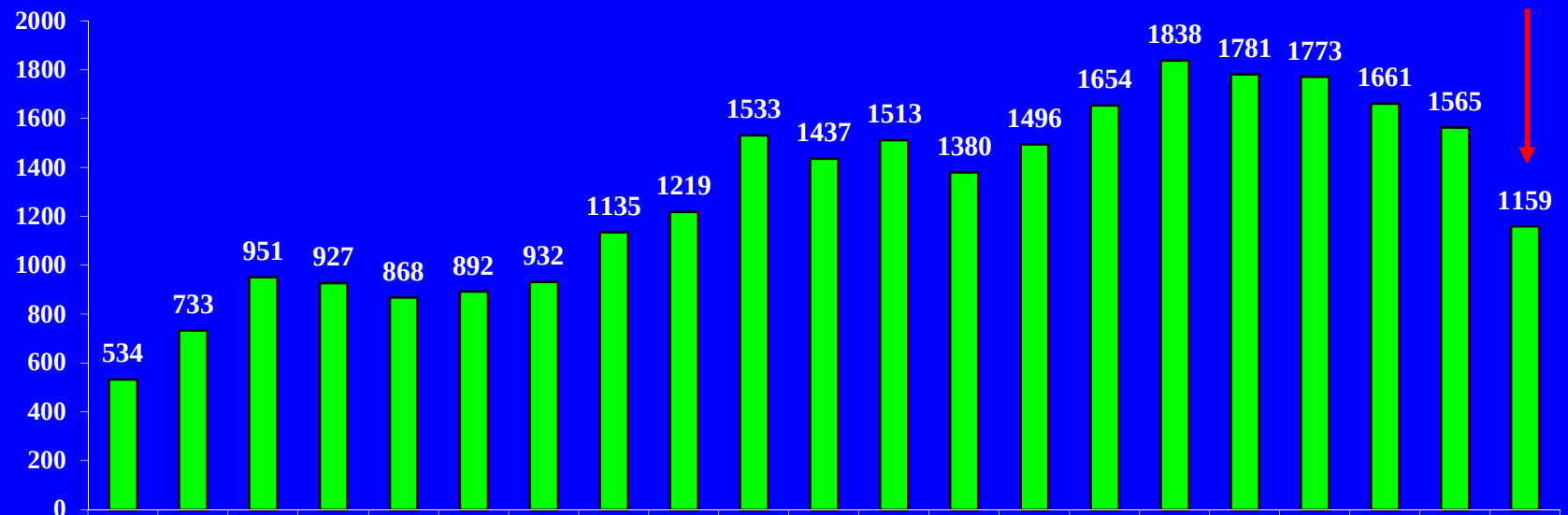
Evolution of some capsular types in invasive pneumococcal infections not included in the 13-valent conjugate vaccine in children ≤2y (Belgium 2009-2014)

capsular type	2009 (N=183)	2010 (N=173)	2011 (N=154)	2012 (**N=130**)	2013 (**N=98**)	2014 (**N=69**)
10A	3,8	1,7	2,6	1,5	8	**11,6**
12F	4,9	5,2	7,8	13,8	10	**20,3**
15B	0,5	1,7	0,6	1,5	0	**7,3**
22F	2,7	0,6	0,6	3	3,1	8,7
33F	5,5	6,4	1,9	3,9	12,2	8,7

Evolution of number of pneumococci isolated from blood and pleural fluid cultures in young children (≤4 years) (1995-2014)

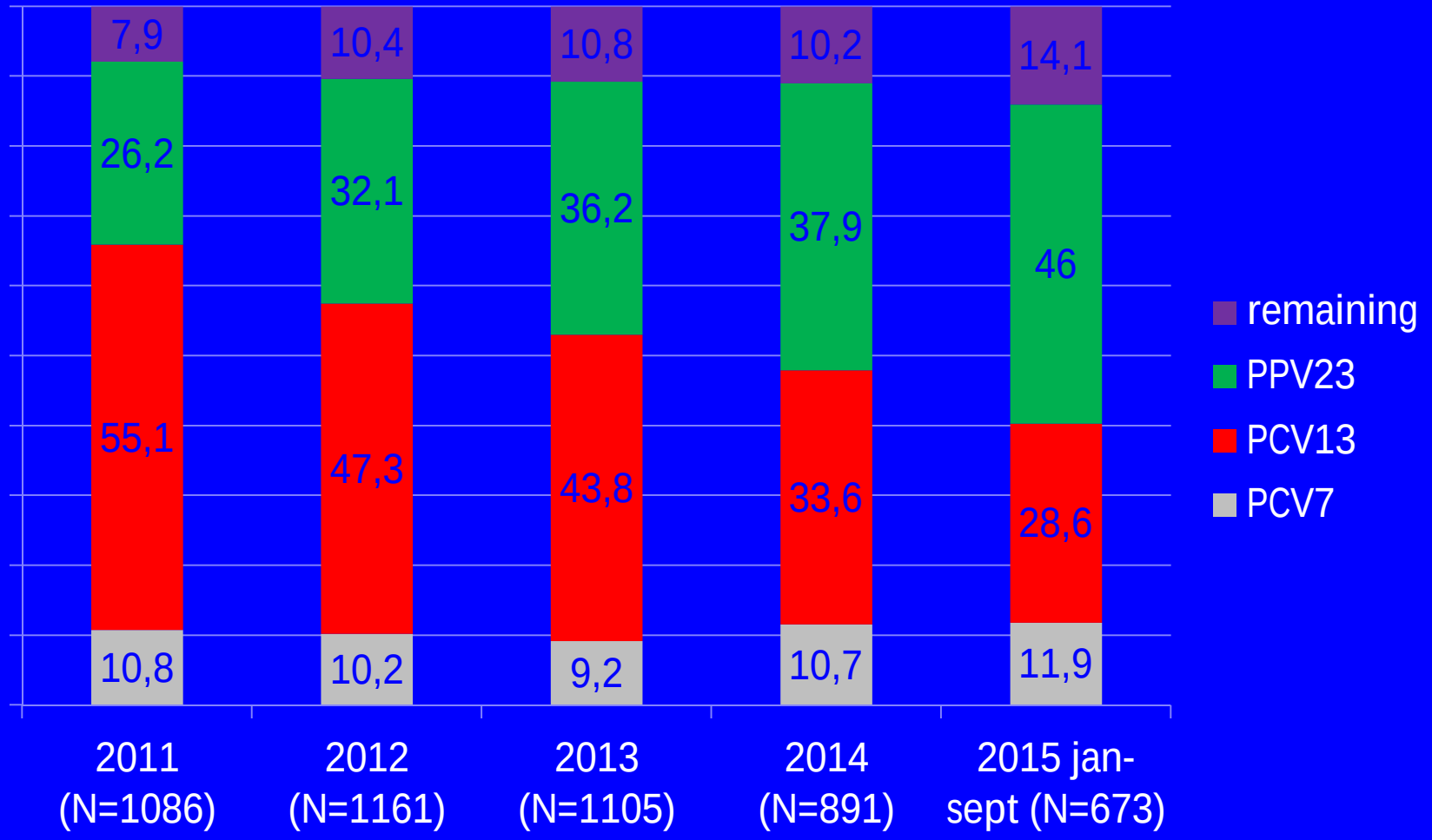


Evolution number of blood culture isolates in Belgium (1994-2014) and number of vaccine doses



	1994	1995 (89)	1996 (90)	1997 (95)	1998 (103)	1999 (105)	2000 (102)	2001 (99)	2002 (108)	2003 (113)	2004 (104)	2005 (103)	2006 (116)	2007 (108)	2008 (107)	2009 (107)	2010 (106)	2011 (104)	2012 (104)	2013 (98)	2014 (98)
Pneumo 23		15.000	136.000	220.000	154.000	91.740	77.000	123.485	171.836	141.655	99.019	115.302	103.748	129.490	127.510	139.338	96.870	111.066	108.236	94.957	86.779
Prevenar 7													291.555	490.725	380.268	386.572	400.255	223.737	0	0	0
Prevenar 13																		163.481	403.691	406.704	394.637

Evolution of relative percentage of vaccine serogroups among invasive pneumococcal infections (≥ 50 years, 2011-2015)



Evolution of capsular types in patients 50+ for number bloodculture and pleural fluid isolates since 2011

Capsular type	2011	2012	2013	2014	2015	Trend
PCV7	104	117	103	96	75	stable
1	110	115	100	49	19	↓
3	102	96	119	80	60	↓
5	43	23	15	4	0	↓
6	50	48	58	38	23	↓
7	128	90	78	51	26	↓
19	161	159	118	78	65	↓
8	24	47	61	63	70	↑
10	14	21	19	22	19	stable
11	28	43	24	23	24	stable
12	85	115	131	108	88	↓
15	33	44	42	39	43	↑
17	11	10	17	6	11	stable
20	3	7	8	11	5	stable
22	57	60	68	45	32	↓
33	20	24	30	21	18	stable
others	120	108	107	91	95	stable
TOTAL	1093	1127	1098	**891**	**673**	↓

red = additional capsular types in PCV13/green = additional capsular types PPV23

Conclusions prevention invasive pneumococcal infections in Belgium

- In 1110 patients (>50y) hospitalized with IPD we observed a mortality rate of 17.5%
- Three years after the introduction of PCV13 in infants we notice a decrease of IPD isolates in the overall population but also in the 50+ population; with significant reduction of isolates belonging to capsular types included in the PCV13.
- Stabilisation or increase of the number of isolates belonging to PPV23

Recommendation of the Belgian Superior Health Council

- Use of PCV13 (1 dose) in combination with PPV23 (with a minimum of 2 months after PCV13) for
  - Adults aged 18 to 85y with high risk of IPD (immunocompromising conditions, asplenia, CSF leak, cochlear implant)
  - Adults aged 50 to 85 y with co-morbidity (chronic cardiac disease, lung disease, diabetes mellitus, alcoholism …)
  - All adults aged ≥65y to 85y

Effect of PCV13 on IPD in England and Wales 4 years after its introduction

Introduction of PCV13 in infants (2+1 schedule) since 2010 (between 2006-2010 PCV7)

Incidence of IPD in 2013/2014 compared with 2008-2010

	2008-2010	2013-2014	Incidence rate ratio 2013-2014 versus 2008-2010
Age<2y			
PCV13	12,67	1,43	0,11
non-vaccine type	7,97	10,23	1,28
all	22,2	12,03	0,54
Age 45-64y			
PCV13	4,55	1,65	0,36
non-vaccine type	4,49	5,7	1,27
all	10,59	7,6	0,72
Age ≥65y			
PCV13	10,33	3,72	0,36
non-vaccine type	12,67	16,33	1,29
all	27,58	20,58	0,75
All age groups			
PCV7	1,46	0,2	0,14
PCV13 (6 additional serotypes)	4,48	1,4	0,31
non-vaccine type	4,19	5,25	1,25
all	10,14	6,85	0,68

Conclusion

- The herd protection induced by PCV7 is continuing and simular indirect protection is occuring from the additional serotypes covered by PCV13
- Evidence of increasing IPD due to non-PCV13 serotypes (8, 10A, 12F, 15A and 24F)

P. Waight et al, Lancet Infect Dis 2015:15:535-43

Evolution of IPD incidence in Norway

- PCV13 implemented in April 2011 (2+1 schedule) in childhood immunization programme

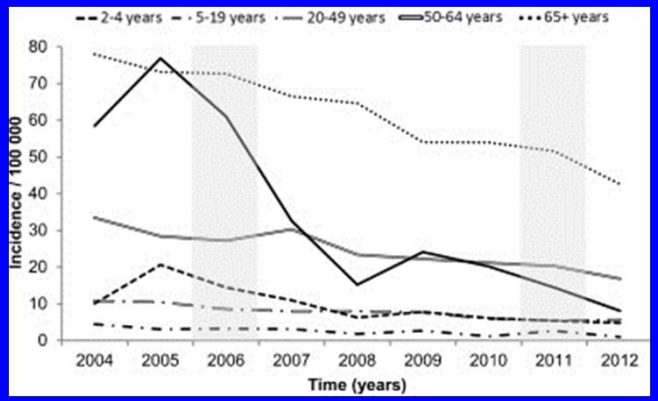


Fig 1:
Age-specific annual incidence of IPD for all serotypes combined: Note that PCV7 vaccination was introduced in July 2006, and PCV13 replaced PCV7 in April 2011 (grey bars).

- Vaccinetype-incidence/100.000 in ≥65y

2005	PCV7	2010	PCV13	2012
46		7,5		
		27		18

- Conclusion:
  - Incidence of IPD caused by vaccine types decreased significantly after the introduction of PCV7 and PCV13 in both the targeted and non-targeted age groups
  - Lag-phase for the indirect effects: 2-3 years
  - 79% of all IPD cases in Norway in 2012 were caused by serotype covered by PPV23

Steens A. et al., Vaccine 2013,31;6232-6238

Effects of infant pneumococcal conjugate vaccination on IPD in children and adults in Germany (1992-2014)

- 24.535 isolates: 3.583 (children <16y) and 20.382 (adults ≥16y)
- 3 periods: no vaccination (before 2006), PCV7: 2007-2010, PCV10/13:2010-2014 (PCV10: 1.9%-19.8% of prescriptions)

	Serotype distribution		
	Before 2006 no vaccination	2007-2010 PCV7	2010-2014 PCV10/13
Children			
PCV7 serot	61,8%	23,5%	5,2%
PCV13 minus PCV7 serot	22,6%	46,8%	35,6%
non PCV13 serot (10A, 12F, 23B, 24F, 38)	15,6%	29,7%	59,2%
Adults			
PCV7 serot	43,4%	24,7%	8,2%
PCV13 minus PCV7 serot	28,9%	41,9%	39,1%
non PCV13 serot (6C, 12F, 15A, 22F, 23B)	27,7%	33,4%	52,7%

- Conclusions
  - The non PCV7 serotypes 1, 3, 7F and 19A increased significantly in 2007-2010 among children and adults
  - After the switch from PCV7 to PCV10/13 serotypes 1, 6A and 7F significantly decreased (decrease of 19A only in 2013-2014)
  - Proportion of non-PCV13 serotypes increased over the whole study period

M. van der Linden et al., Plos One July 2015, 1-17

Effects of use of PCV13 in children on IPD in children and adults in the USA

- Between July 2004-June 2013: 33,688 IPD cases (introduction PCV7 in 2000 and PCV13 in 2010)
- 2004-2010: PCV7 (23,858 isolates)
- 2010-2013: PCV13 (9,830 isolates)
- Difference between incidence expected in absence of PCV13 and that noted after introduction

	2010-11	2011-12	2012-13
All serotypes			
<5y	-45%	-58%	-64%
50-64y	-8%	-28%	-18%
≥65y	-6%	-19%	-12%
PCV13 minus PCV7			
<5y	-66%	-88%	-93%
50-64y	-23%	-54%	-62%
≥65y	-23%	-46%	-58%
non PCV13			
<5y	-4%	+7%	-2%
50-64y	+8%	0%	+26%
≥65y	+1%	-7%	+7%

- Conclusion

  The use of PCV13 in childhood vaccination program resulted in an overall reduction of IPD of 12 – 32%

Moore MR et al., Lancet Infect Dis 2015:15:301-9