Unità di Pediatria ad Alta Intensità di Cura
Università degli Studi di Milano
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico

34 Congresso Nazionale di
ANTIBIOTICOTERAPIA
in età pediatrica

Impatto dei vaccini pneumococcici coniugati nei diversi continenti

N. Principi, Milano

Impatto dei vaccini pneumococcici coniugati nei diversi continenti

Nicola Principi

Vaccini pneumococcici coniugati autorizzati

PCV7	**4**	**6B**	**9V**	**14**	**18C**	**19F**	**23F**
	CRM_{197}						

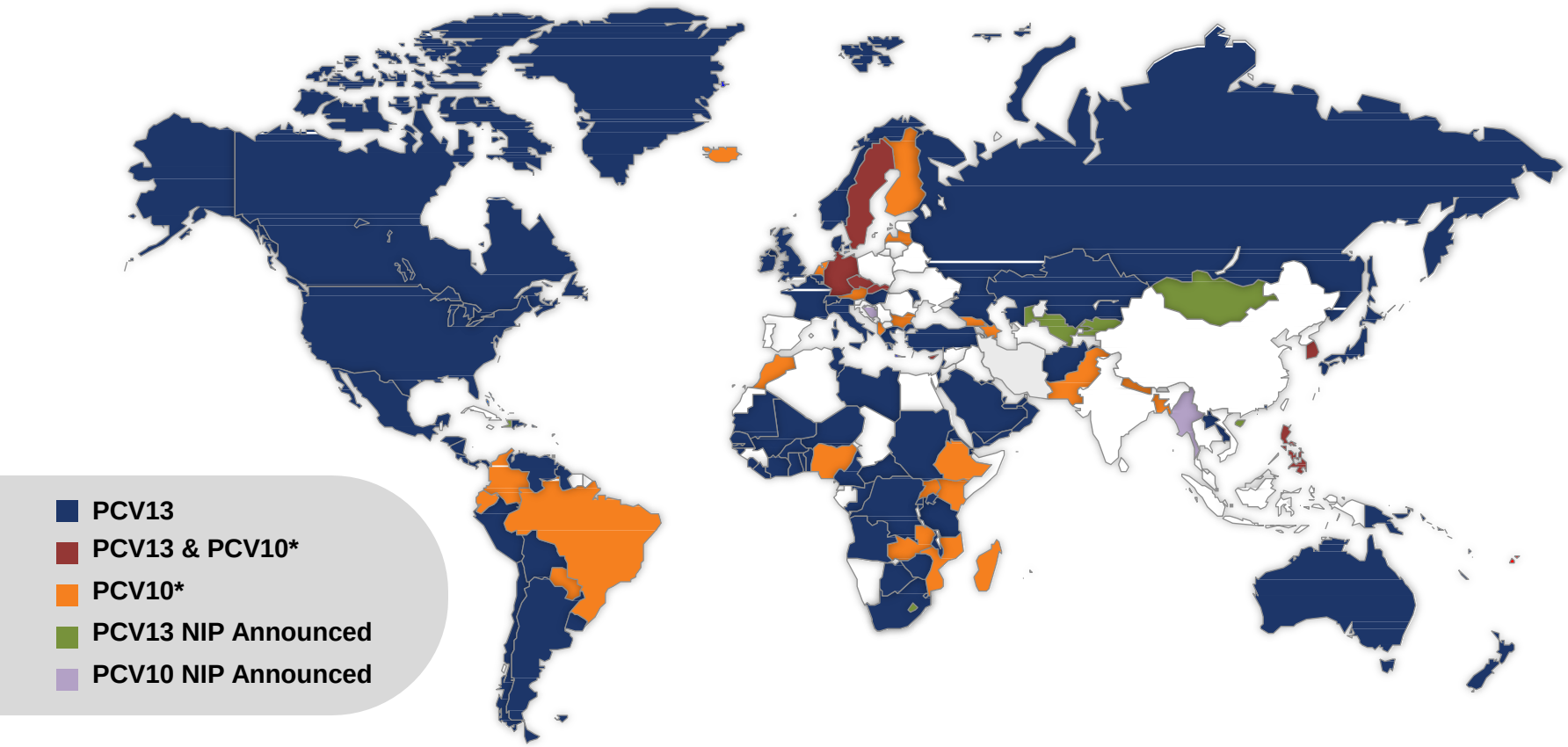
PCV10	**4**	**6B**	**9V**	**14**	**18C**	**19F**	**23F**	**1**	**5**	**7F**
	Protein D				TT	D	Protein D			

PCV13	**4**	**6B**	**9V**	**14**	**18C**	**19F**	**23F**	**1**	**5**	**7F**	**3**	**6A**	**19A**
	CRM_{197}												

Quantità di Antigene per Polisaccaride
PCV7, PCV13: 2.2 µg, eccetto sierotipo 6B (4.4 µg) PCV10: 1 µg, eccetto sierotipo 4, 18C, 19F (3 µg)

1. Prevenar 13. Summary of Product Characteristics. Pfizer, Inc.; 2. CDC. *MMWR* 1988;37:13-16; 3. Vesikari T et al. *Pediatr Infect Dis J. 2009;28:S66 –S76.*

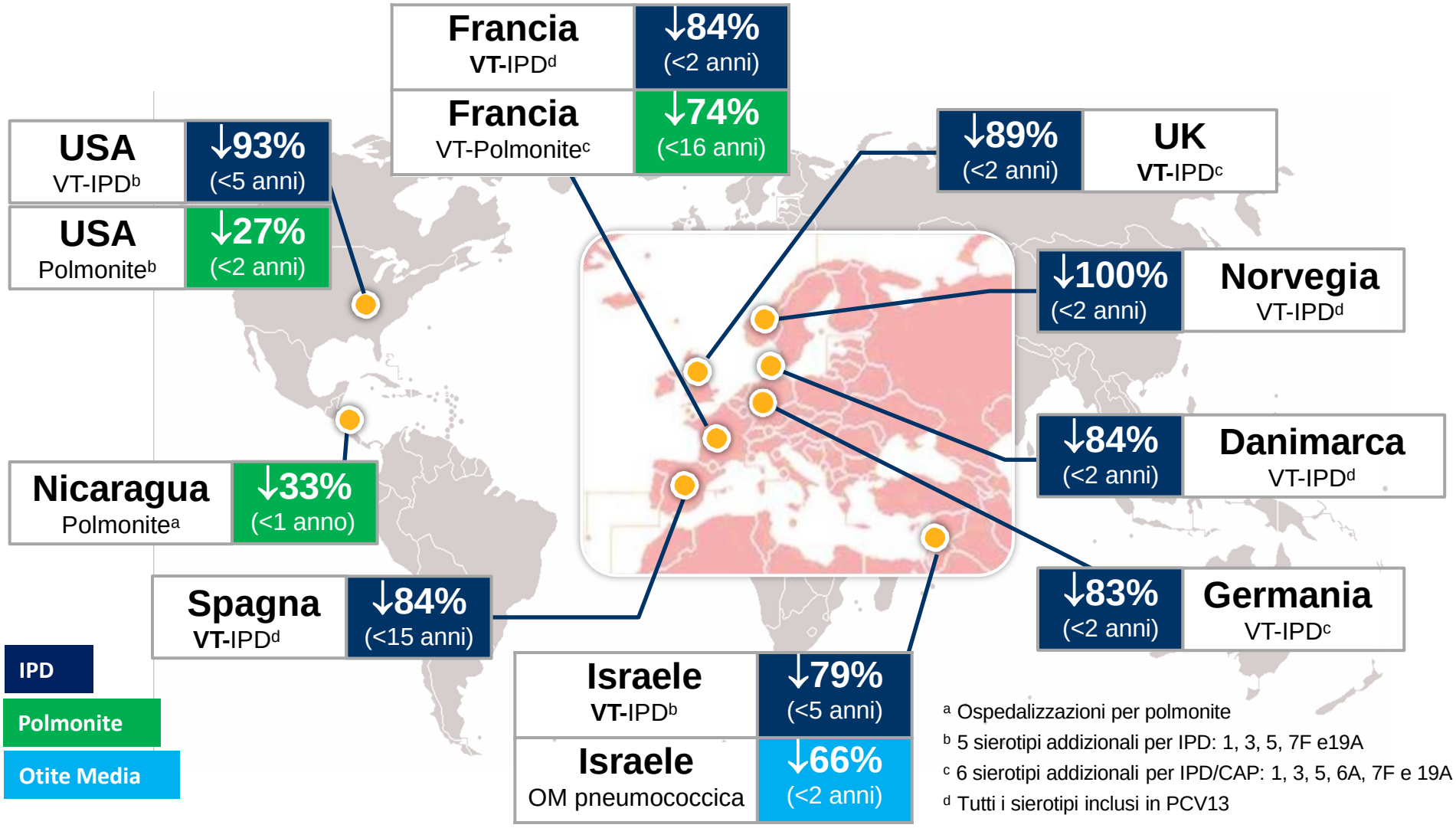
PCV13 È APPROVATO IN ~150 PAESI NEL MONDO E INCLUSO IN OLTRE 90 PROGRAMMI DI IMMUNIZZAZIONE NAZIONALI CON UNA COORTE DI NUOVI NATI, COPERTA DALLA VACCINAZIONE, CHE AMMONTA COMPLESSIVAMENTE A 41 MILIONI DI SOGGETTI



*Entrambi i vaccini sono disponibili/rimborsati nel NIP oppure diverse regioni usano vaccini differenti nell'ambito del NIP.
Both PCVs are available/reimbursed in the NIP or the NIP consists of different PCVs by region

1. Gavi Alliance Progress Report 2013. http://www.gavialliance.org/results/gavi-progress-reports/.

Impatto del PCV13 sulla malattia pneumococcica invasiva e non invasiva[1]



[a] Ospedalizzazioni per polmonite
[b] 5 sierotipi addizionali per IPD: 1, 3, 5, 7F e19A
[c] 6 sierotipi addizionali per IPD/CAP: 1, 3, 5, 6A, 7F e 19A
[d] Tutti i sierotipi inclusi in PCV13

1. References su richiesta.

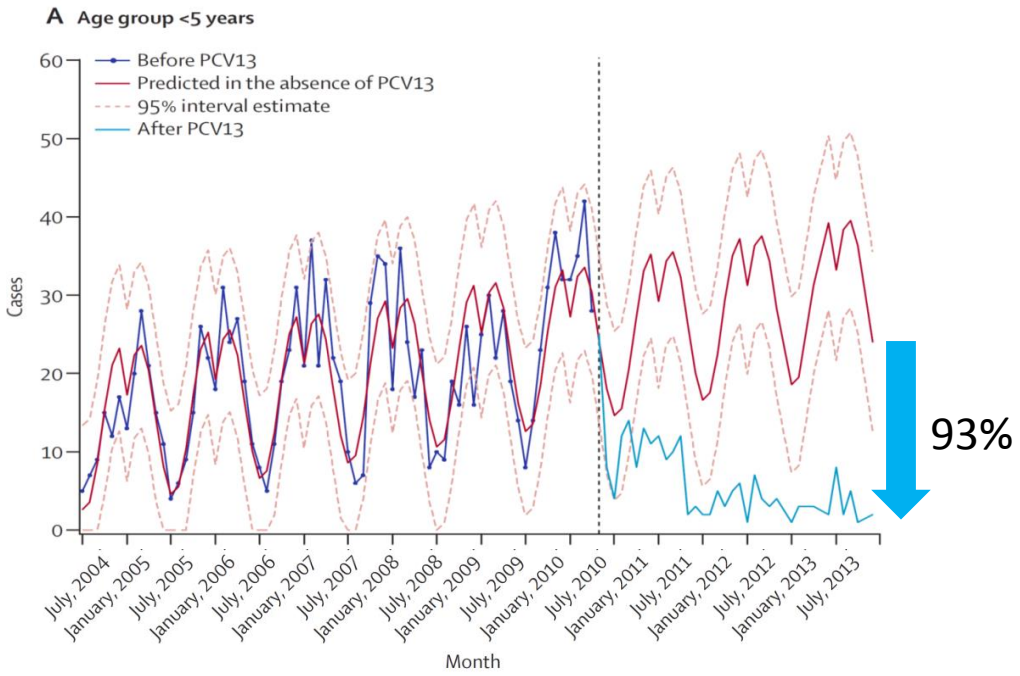
US

NIP 3 + 1

PCV13 in Apr 2010

Sorveglianza ABC : IPD in bambini <5 anni

Casi Osservati vs. Attesi di 5 sierotipi aggiuntivi del PCV13 (1,3,5,7F e 19A) Bambini <5 Anni (2004–2012)



Vaccine coverage: 96% in 2013 (≥1 doses, 2–59 months old).

Reproduced from[1]

National data; CDC population-based IPD surveillance conducted in 10 ABC areas across US. Cumulative count of IPD evaluated and modelled vs. expected. Case – control study of VE in children aged 2–59 months residing in ABC areas; 765 cases and 4/case matched controls based on age (±2 weeks) & zip code (May 2010–2013). ABC, Active Bacterial Core; CDC, Centers for Disease Control and Prevention; IPD, invasive pneumococcal disease; NIP, national immunization programme; PCV13, 13-valent pneumococcal conjugate vaccine; VE, vaccine programme effectiveness.

* Serotypes: 1, 3, 5, 7F, 19A.

1. Moore M *et al.* Lancet Feb 2015. http://dx.doi.org/10.1016/S1473-3099(14)71081-3

Active Bacterial Core surveillance: Impatto del vaccino pneumococcico coniugato 13-valente sulla malattia pneumococcica invasiva negli Stati Uniti

USA
NIP 3 + 1
PCV13, Apr 2010

IDSA

PCV5-IPD*:
Casi osservati vs attesi in assenza di PCV13 per età

Età (anni)	Diminuzione % dal confronto incidenza attesa vs osservata per PCV5-IPD*, (95% CI)		
	2010–2011	2011–2012	2012-2013
<5	- 66 (- 61-70)	- 88 (- 86 -89)	**- 93 (-91 -94)**
5–17	- 35 (- 21-45)	- 59 (48 -66)	**- 75 (-67 -80)**
18–49	- 33 (- 26 -38)	- 64 (60 -68)	**- 72 (-69 -75)**
50–64	- 23 (- 18 -28)	- 54 (50 -57)	**- 62 (-59 -65)**
≥65	- 23 (- 13 -31)	- 46 (39 -52)	**- 58 (-52 -64)**

***Serotypes: 1, 3, 5, 7F, 19A.**

- **RIDUZIONI STATISTICAMENTE SIGNIFICATIVE NELL'INCIDENZA DI IPD DOVUTA AI 5 SIEROTIPI ADDIZIONALI DI PCV13 IN TUTTI I GRUPPI DI ETÀ ENTRO 3 ANNI DALL'INTRODUZIONE DEL PCV13 NEI NIP PEDIATRICI**

National data; CDC population-based IPD surveillance conducted in 10 ABC areas across USA. Cumulative count of IPD evaluated and modelled vs expected. Case–control study of VE in children aged 2–59 months residing in ABC areas; 765 cases and 4/case matched controls based on age (±2 weeks) & zip code (May 2010–2013)

Kim et al. IDWeek October 8-12, 2014, Philadelphia, PA.

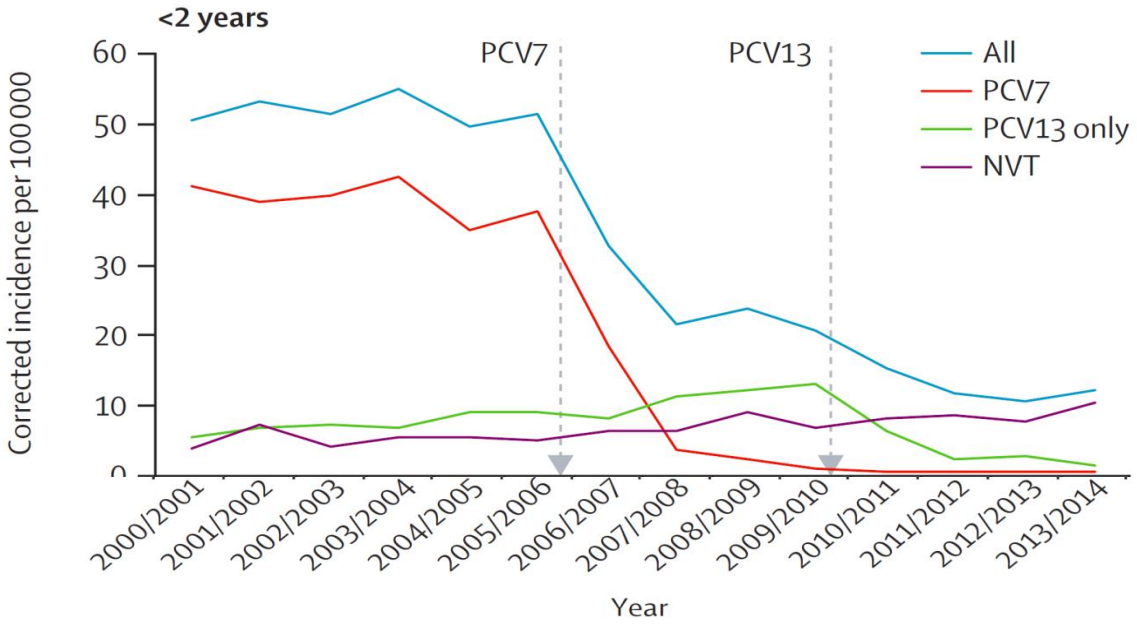
UK

NIP 2 + 1

PCV7 NIP Sep 2006
PCV13 NIP, Apr 2010

Incidenza di Casi di IPD in bambini <2 Anni

Corrected* IPD Incidence in Children <2 Years



Reproduced from[1]

Vaccine coverage: 94% in 2012–2013, at 1 year of age[2]

2013–2014 vs. 2008–2010

- **89% reduction in incidence of IPD due to six additional PCV13 serotypes***
- **46% reduction in incidence of all type IPD**

IPD, invasive pneumococcal disease; NIP, national immunization programme; PCV7, 7-valent pneumococcal conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine.

* Corrected for proportion of samples serotyped, missing age, denominator compared with 2009–2010 and for trend in total IPD upto 2009–2010.

1. Waight et al. Lancet Infect Dis. Published online 20 March 2015; 2. NHS Immunisation Statistics England 2012–13;

UK

NIP 2 + 1

PCV7 NIP Sep 2006
PCV13 NIP, Apr 2010

Casi di IPD Sierotipo-Specifici in Bambini <5 Anni

Serotype Specific Number of Cases and Rate Reduction for Additional Serotypes Included in PCV13

	Cases¤ 2008–2010	Cases¤ 2013–2014	Rate Reduction	95% CI
Serotype 1	59	5	91%	68–98*
Serotype 3	26	8	68%	6–89
Serotype 6A	10	0	100%	62–100*
Serotype 7F	90	8	91%	74–97*
Serotype 19A	85	7	91%	75–97*

Reproduced from[1]

Vaccine coverage: 94% in 2012–2013, at 1 year of age[2]

2013–2014 vs. 2008–2010

- **89% reduction in incidence of IPD due to six additional PCV13 serotypes***
- **46% reduction in incidence of all type IPD**
- **Significant increase of 24F IPD**

IPD, invasive pneumococcal disease; NIP, national immunization programme; PCV7, 7-valent pneumococcal conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine.

¤ Corrected for proportion of samples serotyped, missing age, denominator compared with 2009–2010 and for trend in total IPD upto 2009–2010.

* Statistically significant ($p<0.01$). Null hypothesis of IRR=1 was set at 1% for serotype specific analysis. Insufficient cases of serotype 5 to merit analysis.

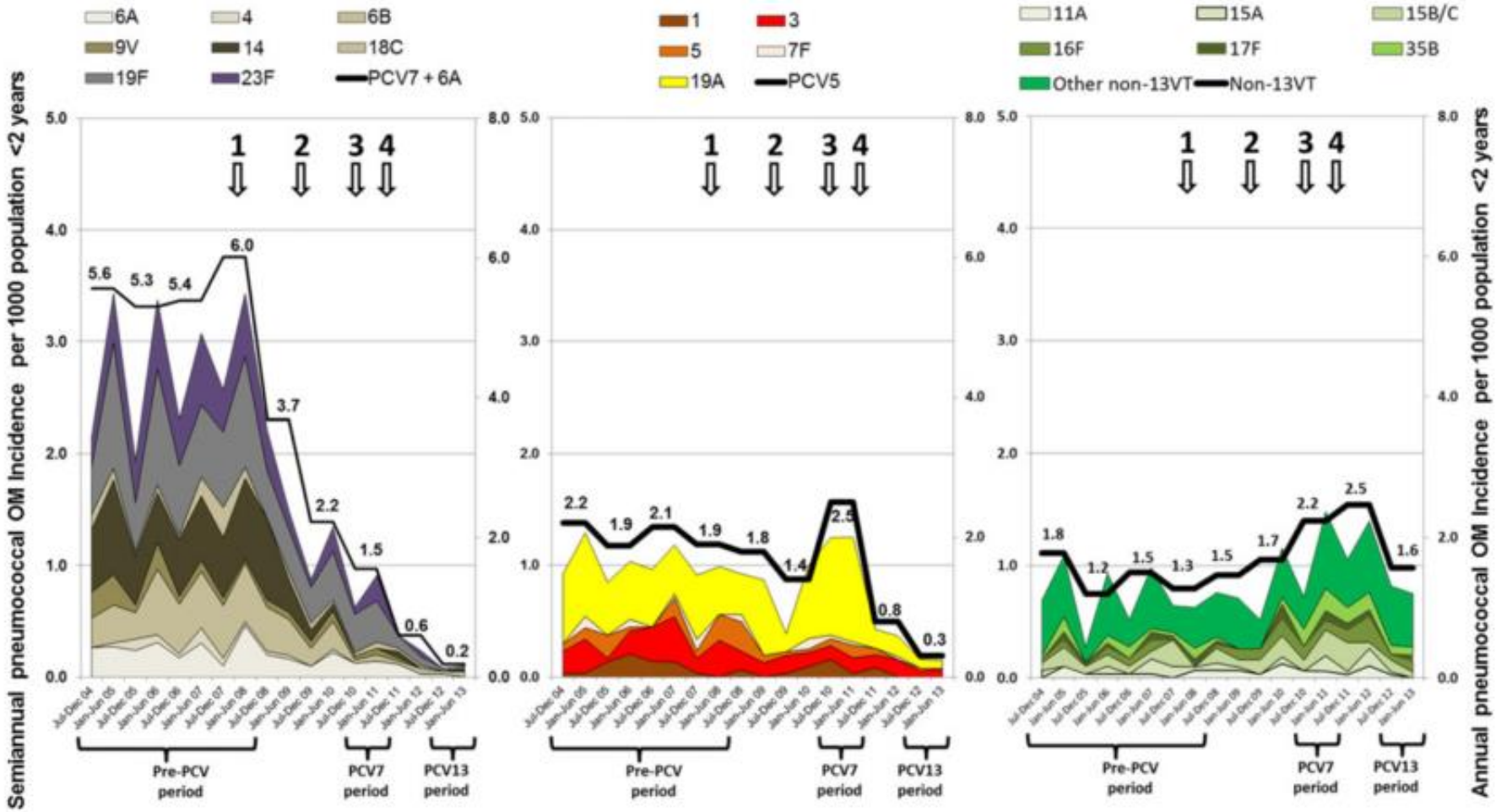
1. Waight et al. Lancet Infect Dis. Published online 20 March 2015.
2. NHS Immunisation Statistics England 2012–13.

Studio Prospettico sulle Polmoniti - Francia, 2014

Outcome	Periods			*P*	Decrease Post-PCV13 / Pre-PCV13
	Pre-PCV13	Transitional	Post-PCV13		
All Cause CAP Age <2 years	747 (36.6)*	642 (34.6)	513 (29.9)	<0.001	↓ **31%**
CAP+ Pleural Effusion	164 (8.0)	119 (6.4)	80 (4.7)	0.001	↓ **51%**
Pneumococcal CAP	63 (3.1)	47 (2.5)	24 (1.4)	0.001	↓ **62%**

Angoulvant et al., CID 2014: 58;918-24

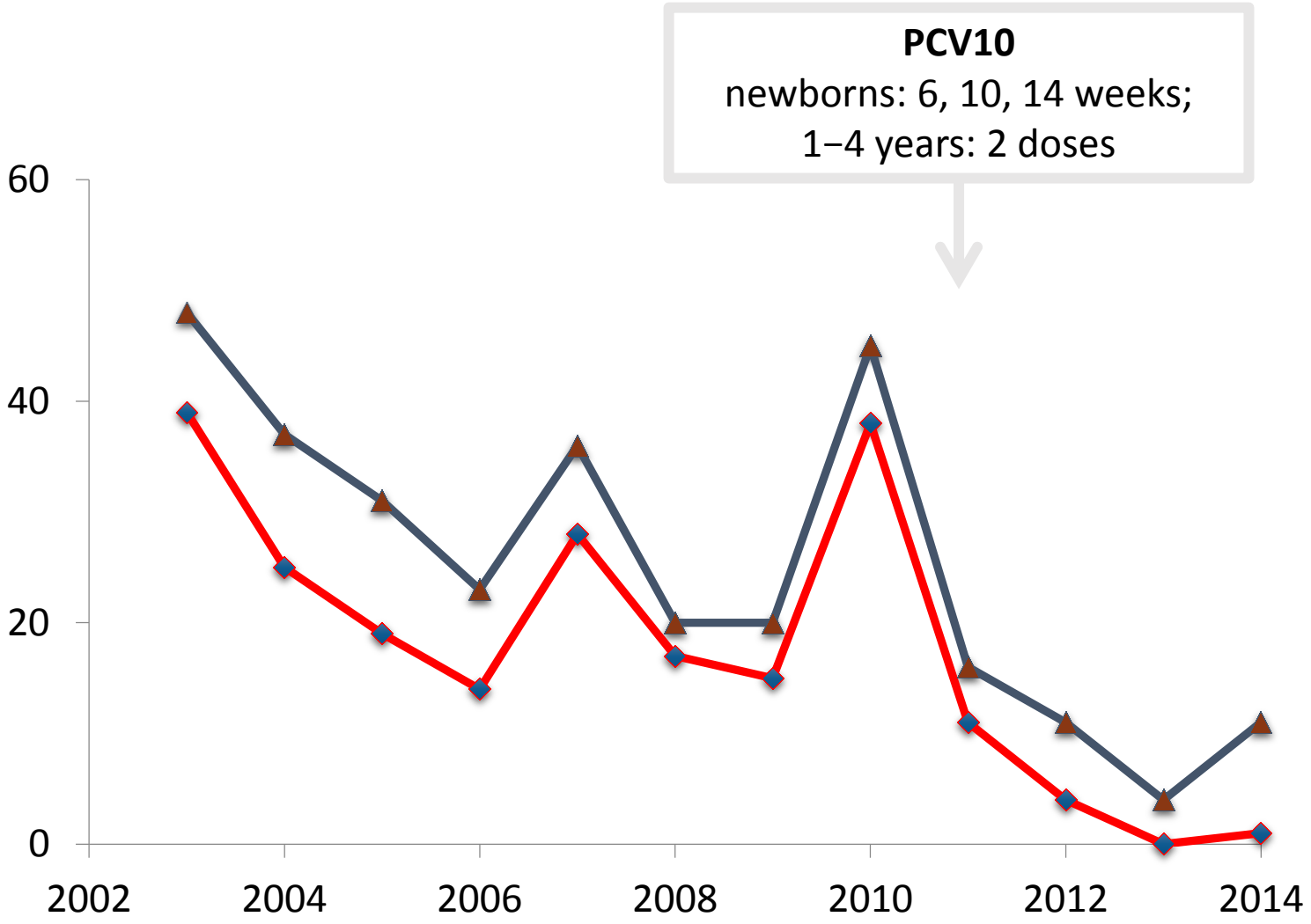
“La quasi eliminazione dei Sierotipi Vaccinali nell‘Otite Media Acuta” in Israele



Ben-Shimol et al., Clin Infect Dis 2014.

Kenya

Early impact of PCV10 on IPD in Kilifi, Kenya



Total number of IPD cases

Number of IPD cases due to vaccine serotypes

http://www.kemri-wellcome.org/index.php/en/studies_inner/75

Finland

Relative rate reduction of IPD after PCV10 introduction

Vaccinated cohort (children aged 3–38 months, 2010-2013; N=272 049) compared to 2 age and season matched cohorts (2003-2006; N=260 308 and 2005-2008; N=265 712). Data from national registries

	incidence/100,000 person-years (number of cases)		Relative rate reduction (95%CI)
	Reference cohort combined	Target cohort	
Vaccine-types	**49.1** (162+157)	**4.2** (14)	**-92** (-86, -95)
Overall IPD	**62.9** (216+193)	**12.9** (43)	**-80** (-72, -85)

Jokinen, *et al*. PLoS ONE 10(3): e0120290. doi:10.1371/journal.pone.0120290)

AOM and pneumonia in Iceland: early reduction after PCV10 introduction

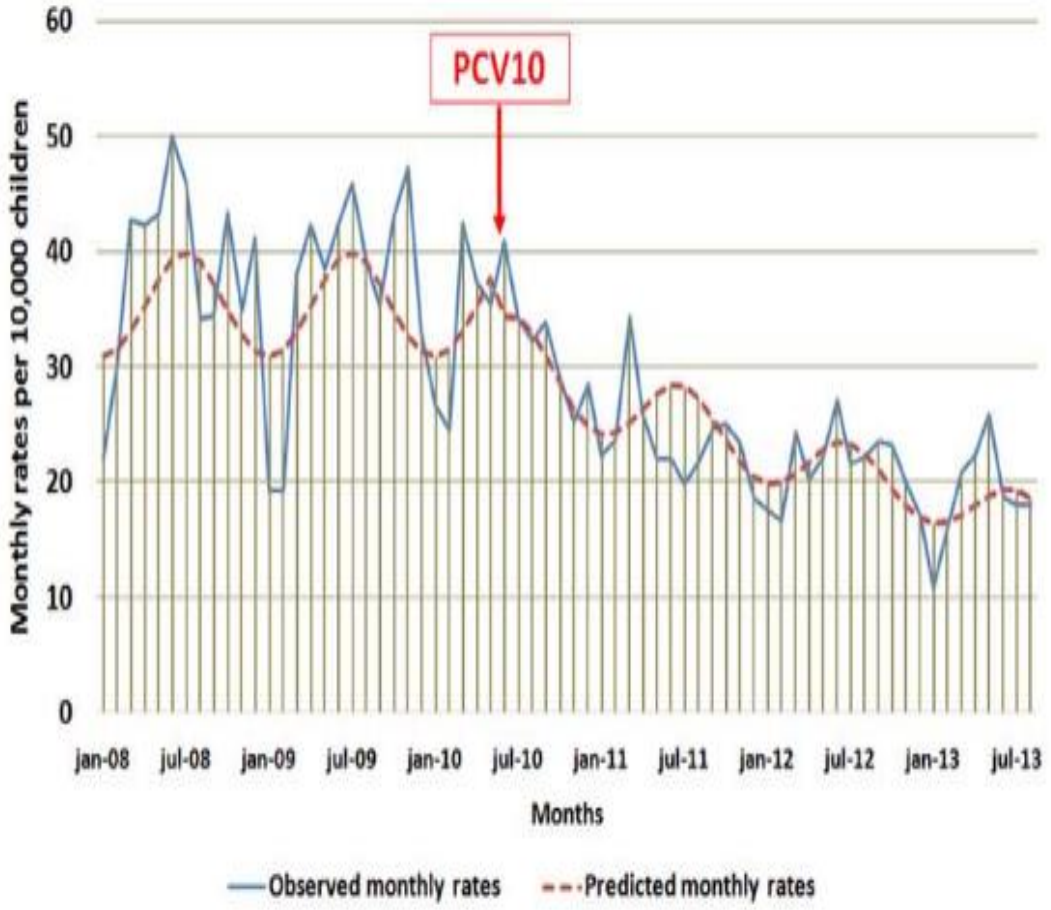
Comparison of cohorts of children <2 years of age
Children born in 2011: vaccinated cohort
Children born in 2008 – 2010: reference cohort, no

	Mean Annual Incidence/1000			
	2008-10 (UnVacc)	2011 Vacc	OR (95%CI)	P-value
OM	**108**	**87**	**0.76** (0.67, 0.85)	P=0.001
Pneumonia	**39**	**29**	**0.74** (0.61,0.88)	P<0.001

Siggurdson, *et al*. ESPID 2014

Brazil

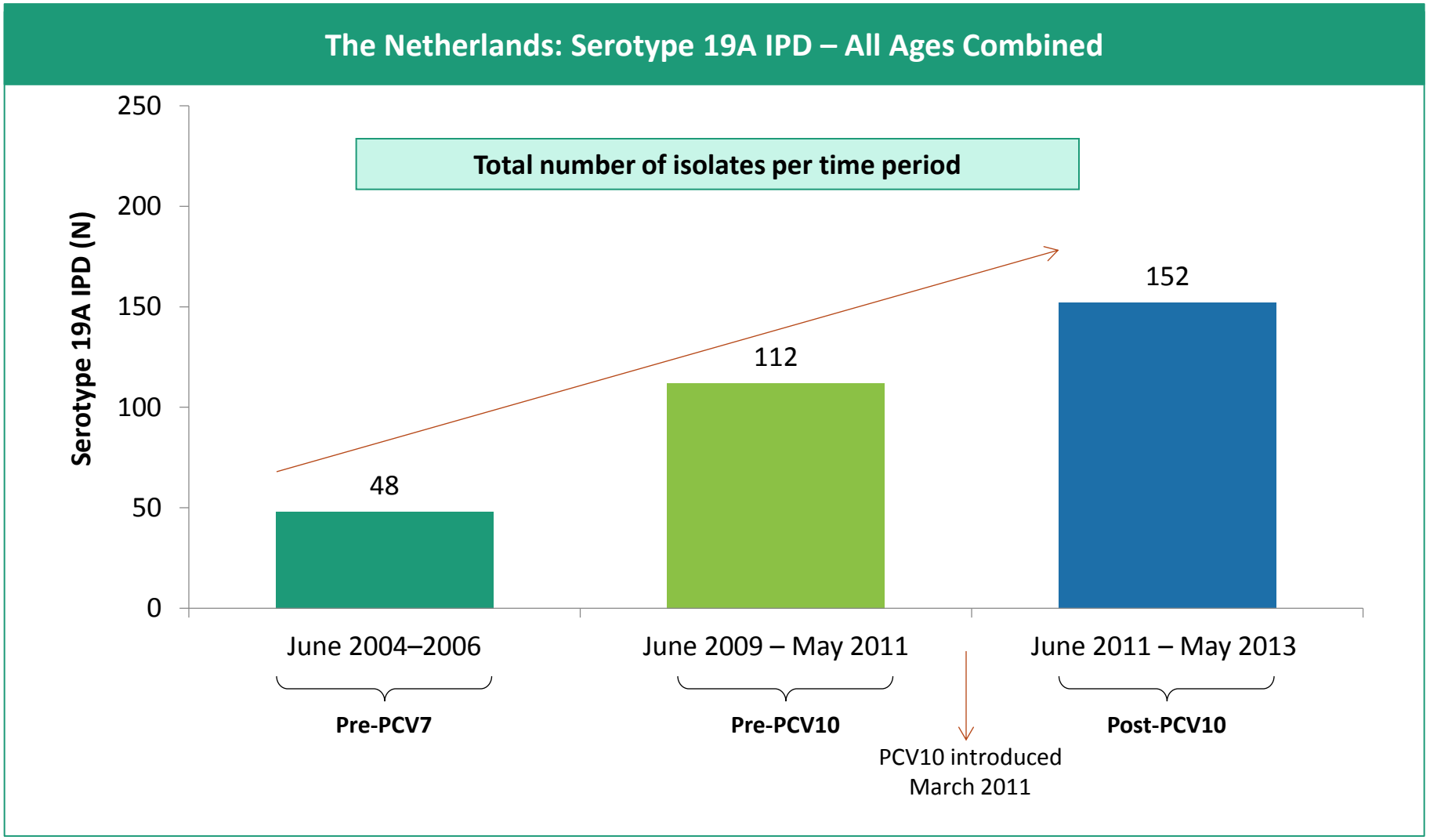
Reduction in all cause otitis media related visits after PCV10 introduction children 2-23 moa in Brazil, Goiana



Reduction of **44.5%** in rates of all-cause otitis in the postvaccination period

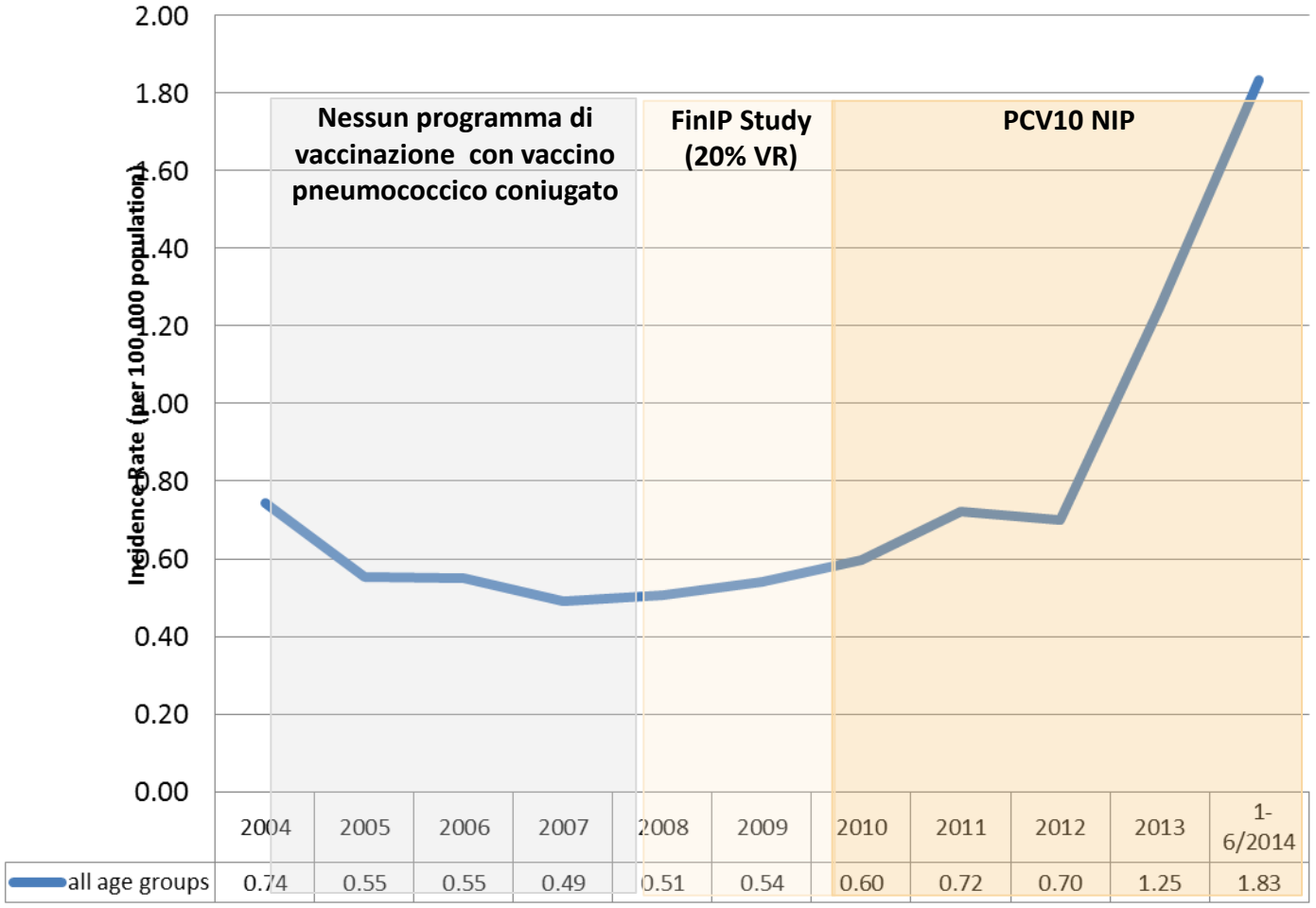
Sartori, et al. ISPPD, Hyderabad, India, 10-14 March 2013 (poster)

The Netherlands Serotype 19A IPD Sentinel Surveillance



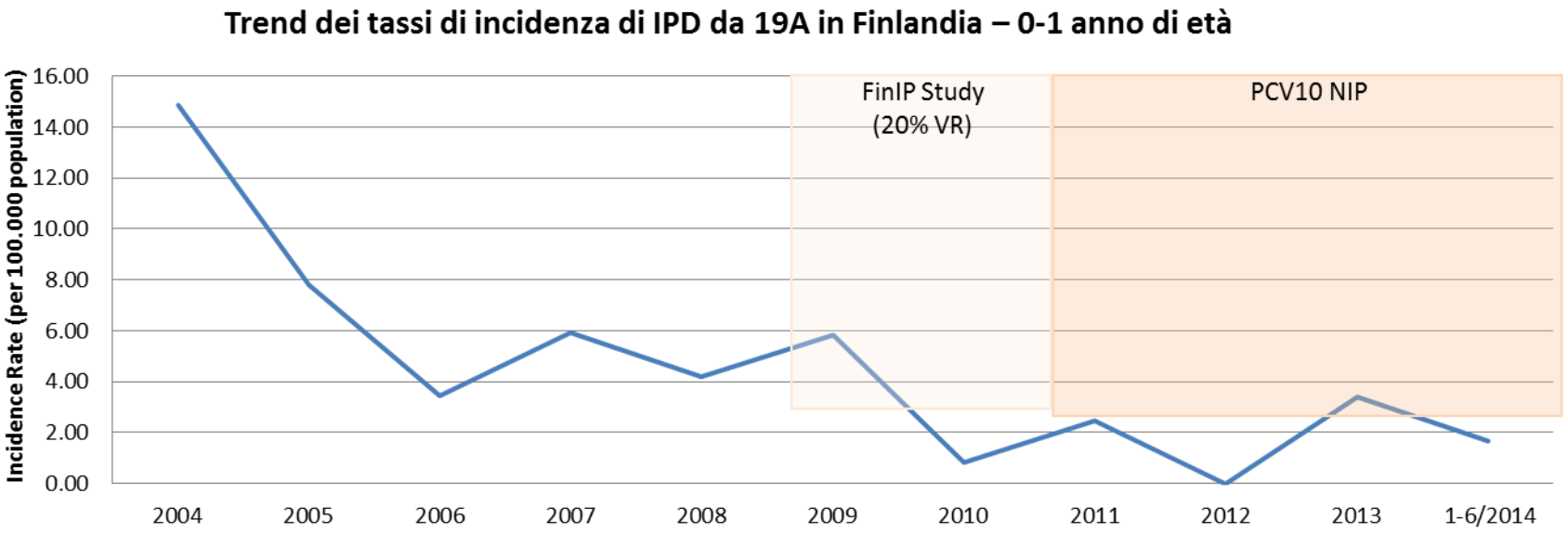
Knol M, et al.; 2014; Adapted from Poster P-294; ISPPD 2014; 9-13 Mar 2014; Hyderabad, India.

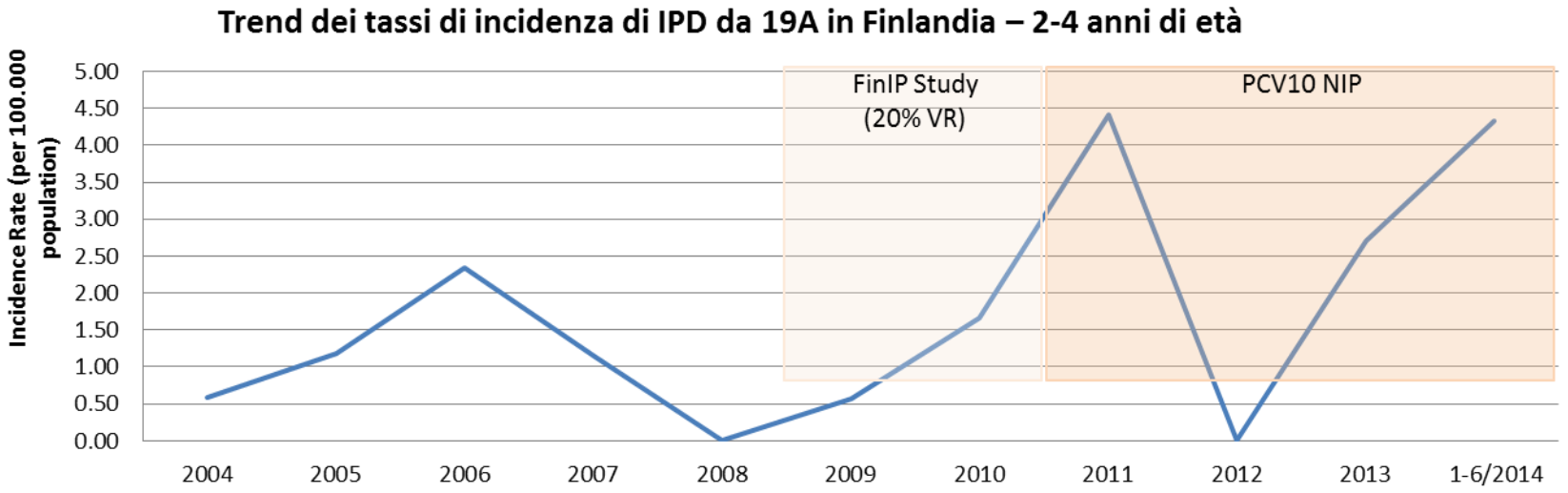
Finlandia: IPD da ST19A – *Vaccine Effectiveness* per tutte le età



1. Rinta-Kokko, et al. ISPPD 2014, Abstract 0560. 2. National Institute for Health and Welfare - Incidence of Invasive Pneumococcal Disease in Finland (Available at https://www.thl.fi/en/web/thlfi-en/topics/information-packages/incidence-of-invasive-pneumococcal-disease-in-finland, Accesses May 2015)

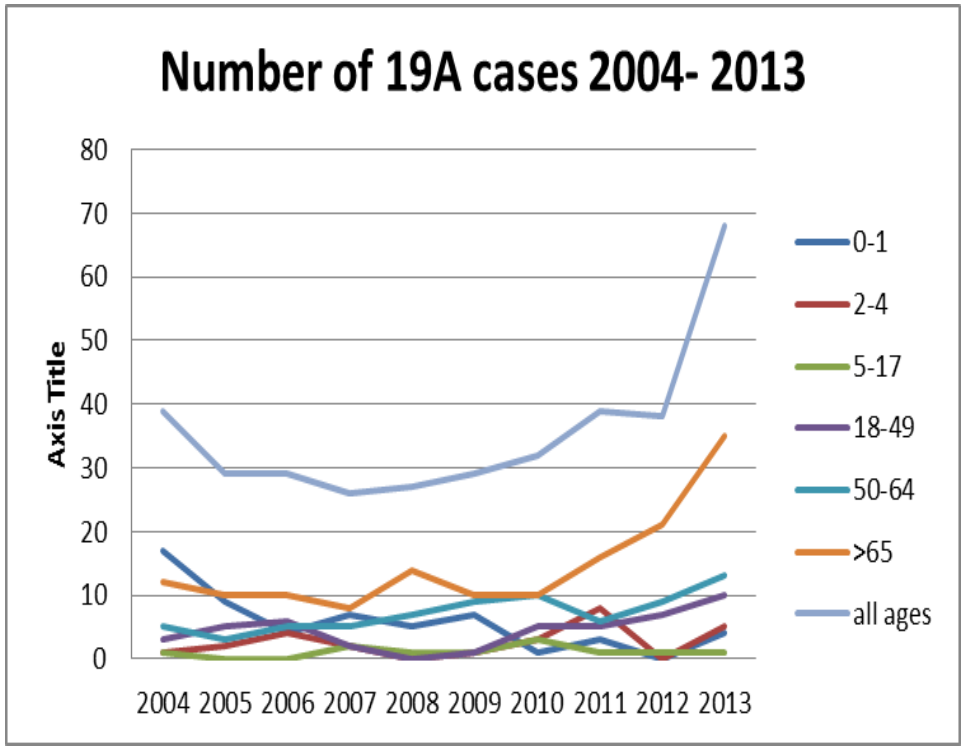
Finlandia: IPD da sierotipo 19A nei bambini per coorte di età





1. National Institute for Health and Welfare - Incidence of Invasive Pneumococcal Disease in Finland (Available at https://www.thl.fi/en/web/thlfi-en/topics/information-packages/incidence-of-invasive-pneumococcal-disease-in-finland, Accesses May 2015). 2. Jokinen, et al. PLoS One. 2015 Mar 17;10(3):e0120290. 3. Rinta-Kokko, et al. ESPID 2015, Abstract 0735

19A cases in Finland

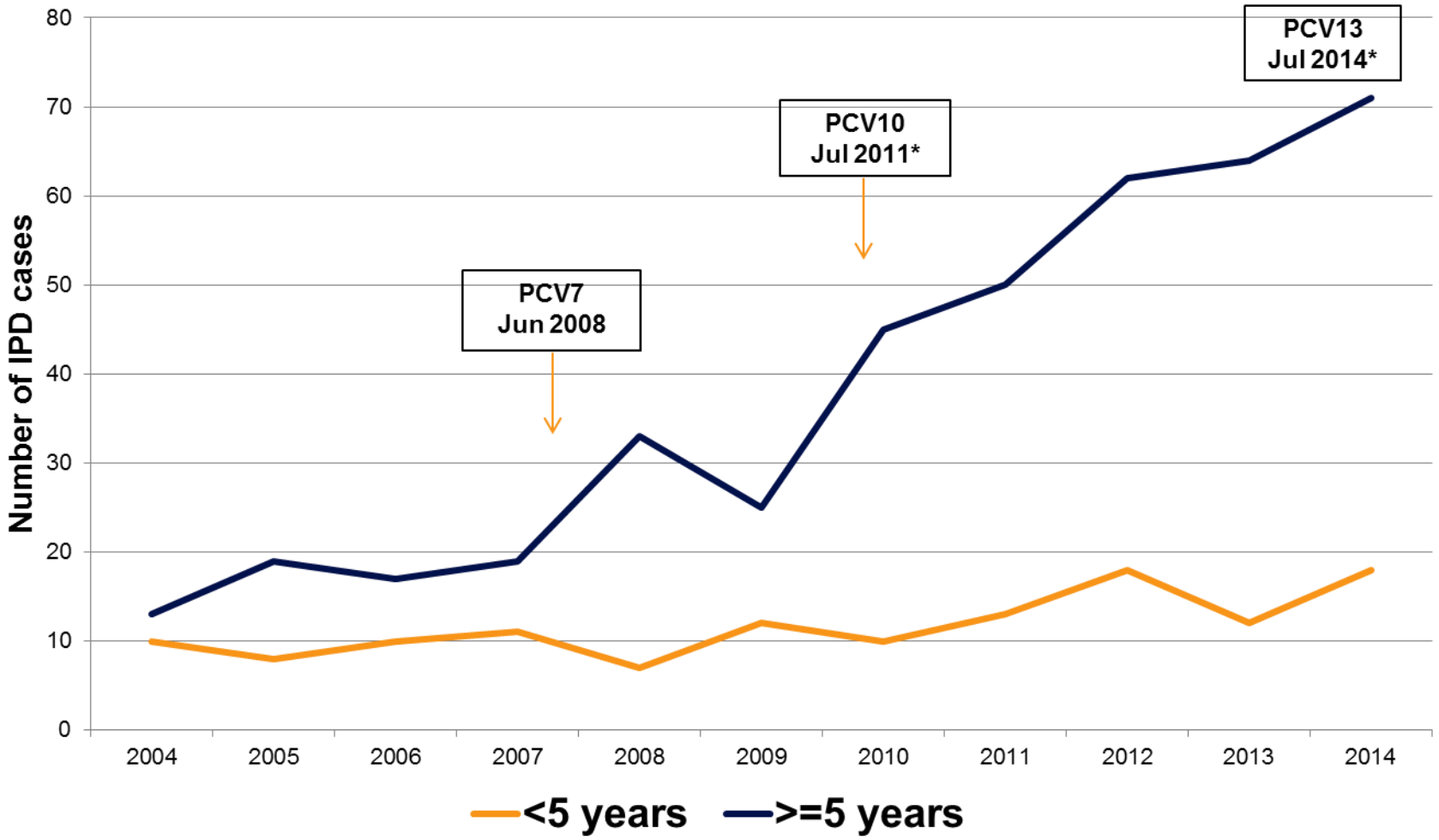


	19A (nb)			
	2010	2011	2012	2013
<1 year	1	3	0	4
2-4 years	3	8	0	5
5-17 years	3	1	1	1
18-49 years	5	5	7	10
50-64 years	10	6	9	13
>65 years	10	16	21	35

Link to the data:
http://www.thl.fi/fi/tutkimus-ja-asiantuntijatyo/hankkeet-ja-ohjelmat/pneumokokkikonjugaattirokotteen-vaikuttavuuden-arviointi/vakavan-pneumokokkitaudin-ipd-ilmaantuvuus-suomessa-serotyyppi-ja-ikaryhmittain

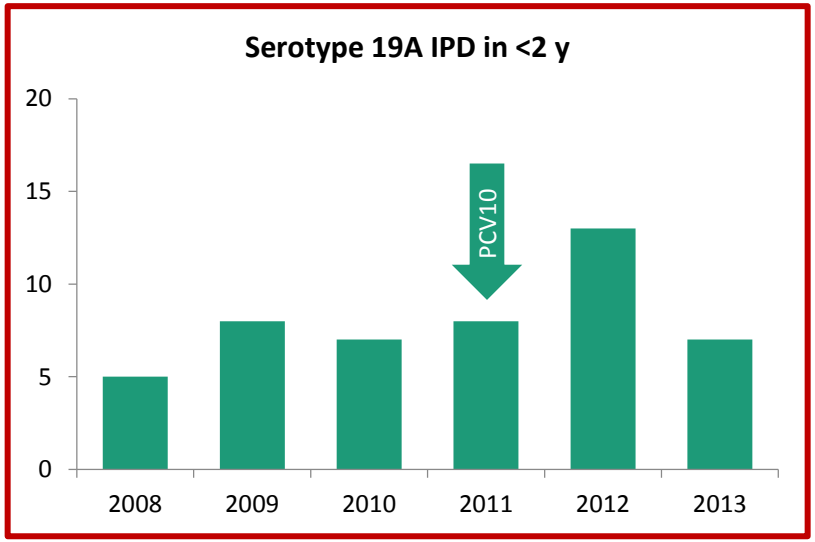
Look at this: Liitetaulukot serotyypeittäin (xls 80 kt, päivitetty 14.10.2014)

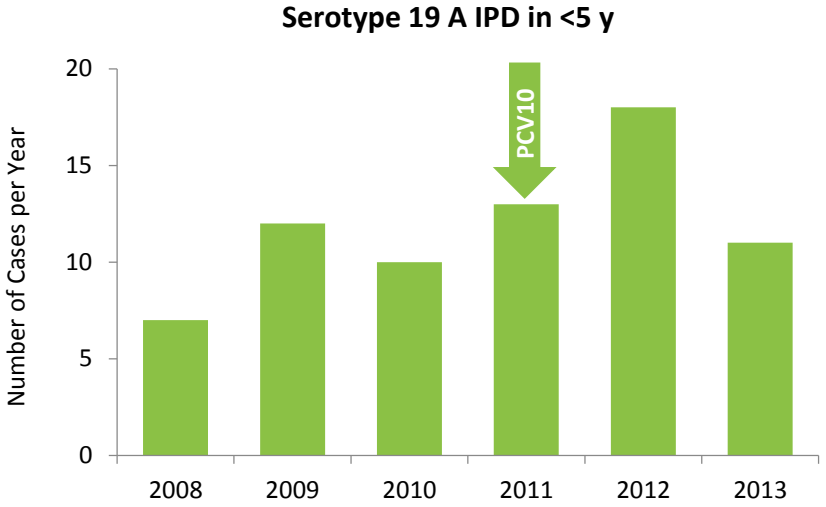
19A IPD cases in New Zealand

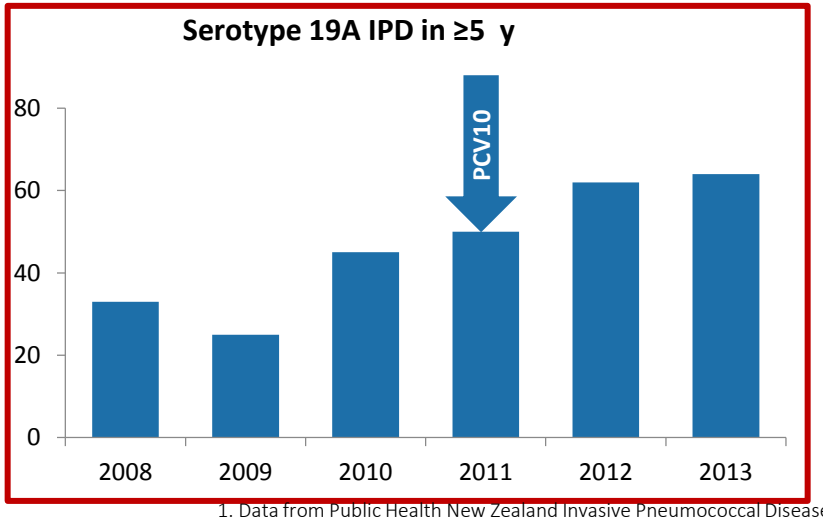


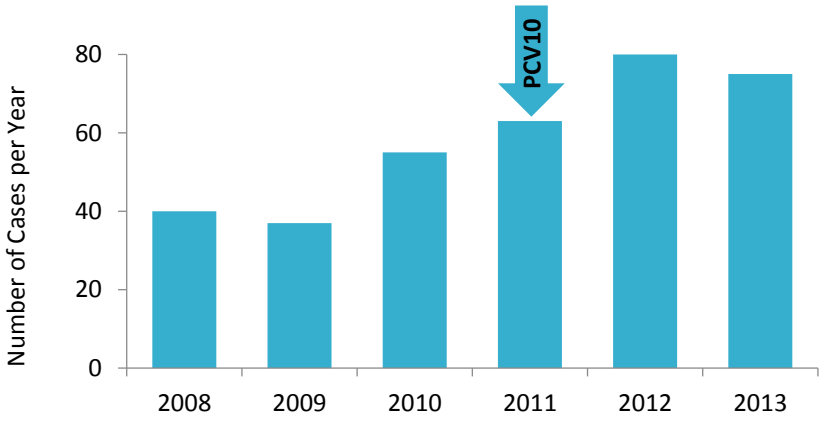
Source: New Zealand Public Health Surveillance: institute of Environmental Science and Research Ltd (ESR); Accessed 13Feb2015 from https://surv.esr.cri.nz/surveillance/IPD.php

19A New Zealand



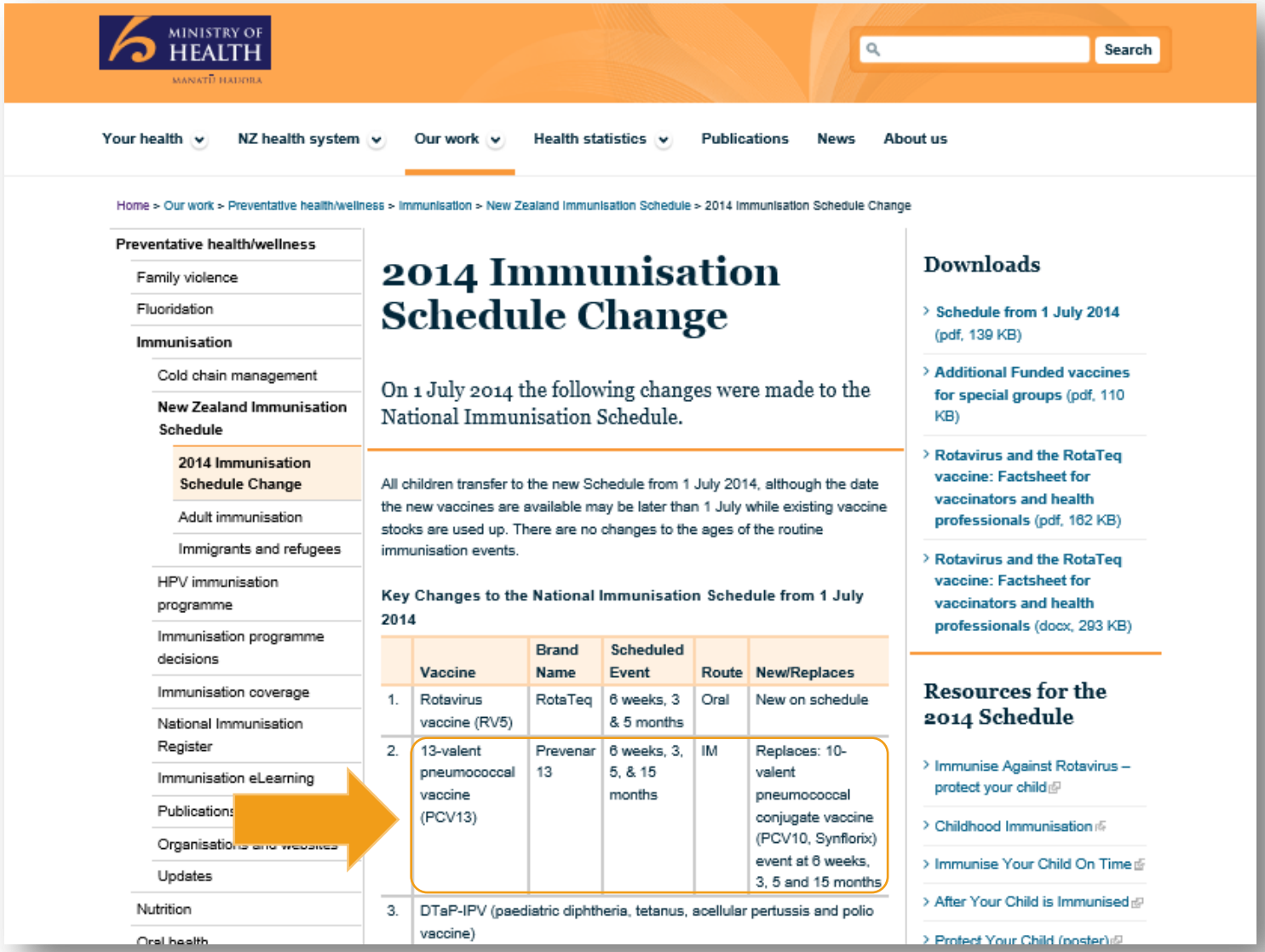






1. Data from Public Health New Zealand Invasive Pneumococcal Disease. ESR 2012 Annual Report and ESR 2013 Quarterly Reports (Quarters 1-4). Accessed 21 April 21, 2014 from https://surv.esr.cri.nz/surveillance/IPD.php.

New Zealand: Immunisation Schedule Change **PCV7 → PCV10 → PCV13**



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2014 Immunisation Schedule Change

On 1 July 2014 the following changes were made to the National Immunisation Schedule.

All children transfer to the new Schedule from 1 July 2014, although the date the new vaccines are available may be later than 1 July while existing vaccine stocks are used up. There are no changes to the ages of the routine immunisation events.

Key Changes to the National Immunisation Schedule from 1 July 2014

	Vaccine	Brand Name	Scheduled Event	Route	New/Replaces
1.	Rotavirus vaccine (RV5)	RotaTeq	6 weeks, 3 & 5 months	Oral	New on schedule
2.	13-valent pneumococcal vaccine (PCV13)	Prevenar 13	6 weeks, 3, 5, & 15 months	IM	Replaces: 10-valent pneumococcal conjugate vaccine (PCV10, Synflorix) event at 6 weeks, 3, 5 and 15 months
3.	DTaP-IPV (paediatric diphtheria, tetanus, acellular pertussis and polio vaccine)				

Downloads

- Schedule from 1 July 2014 (pdf, 139 KB)
- Additional Funded vaccines for special groups (pdf, 110 KB)
- Rotavirus and the RotaTeq vaccine: Factsheet for vaccinators and health professionals (pdf, 162 KB)
- Rotavirus and the RotaTeq vaccine: Factsheet for vaccinators and health professionals (docx, 293 KB)

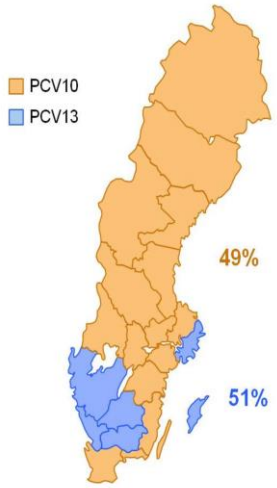
Resources for the 2014 Schedule

- Immunise Against Rotavirus – protect your child
- Childhood Immunisation
- Immunise Your Child On Time
- After Your Child is Immunised
- Protect Your Child (poster)

Fonte: http://www.health.govt.nz/our-work/preventative-health-wellness/immunisation/new-zealand-immunisation-schedule/2014-immunisation-schedule-change

Impatto della Vaccinazione con PCV10 e PCV13 sui casi di CAP ospedalizzata nei bambini <2 anni in Svezia (1998-2012)

PCV7 nel 2007 (nel NIP nel 2009)
PCV10 e PCV13 nel 2010



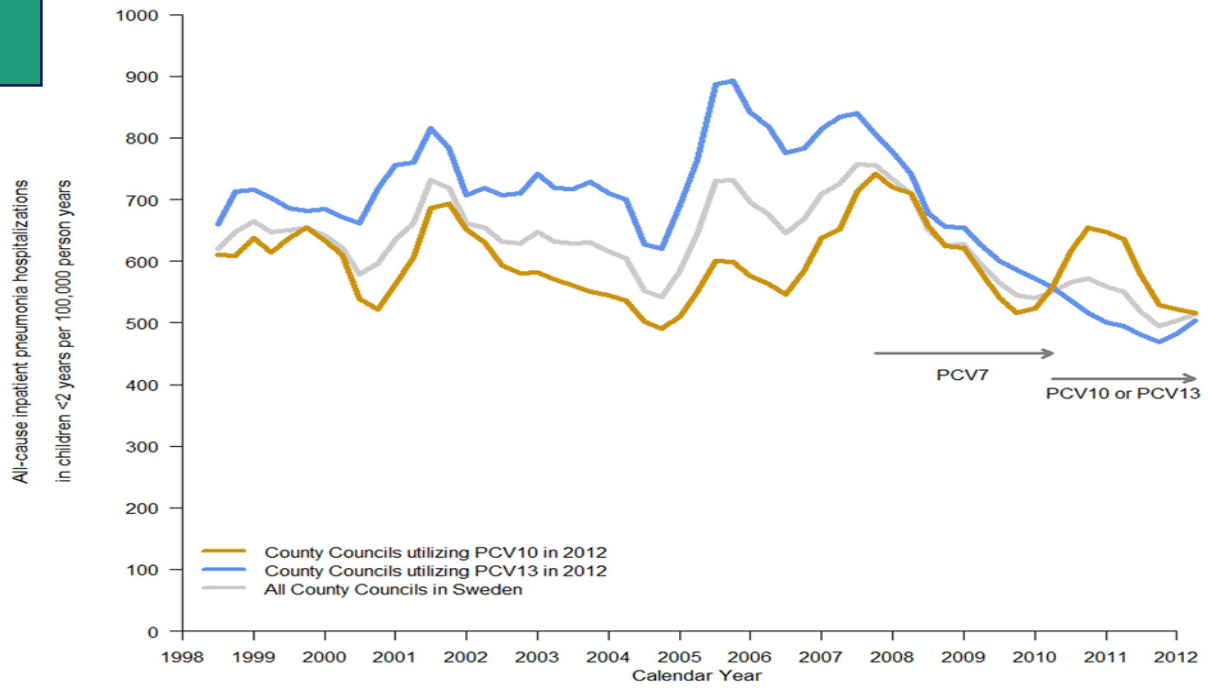
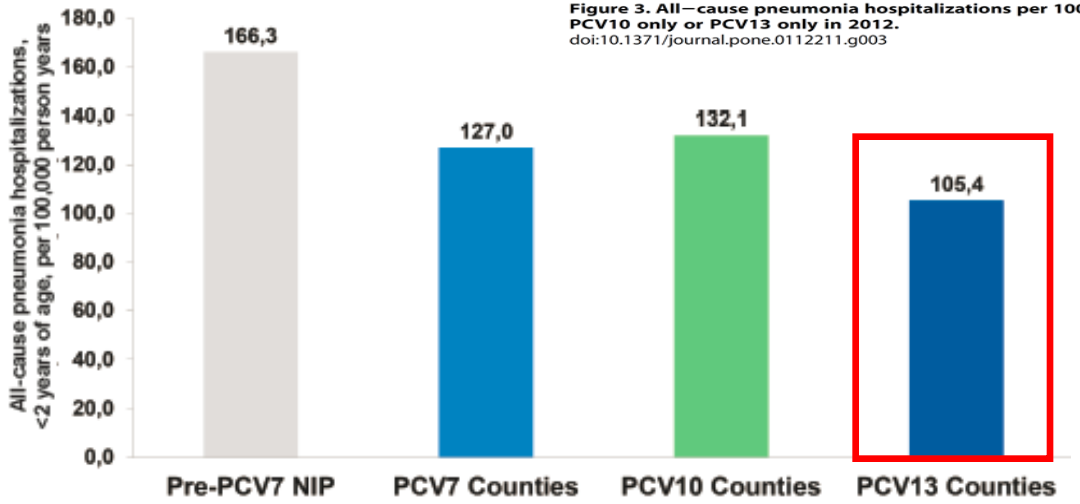


Figure 3. All−cause pneumonia hospitalizations per 100,000 person-years by all County Councils and by County Councils utilizing PCV10 only or PCV13 only in 2012.
doi:10.1371/journal.pone.0112211.g003



Le Regioni con PCV13 hanno ottenuto una riduzione di CAP da tutte le cause, nei bambini di 2 anni di età

Berglund A. Et al, PLOS One, 2014;9 (11).

Titoli OPA per i sierotipi 19F / 19A dopo la terza dose del ciclo primario

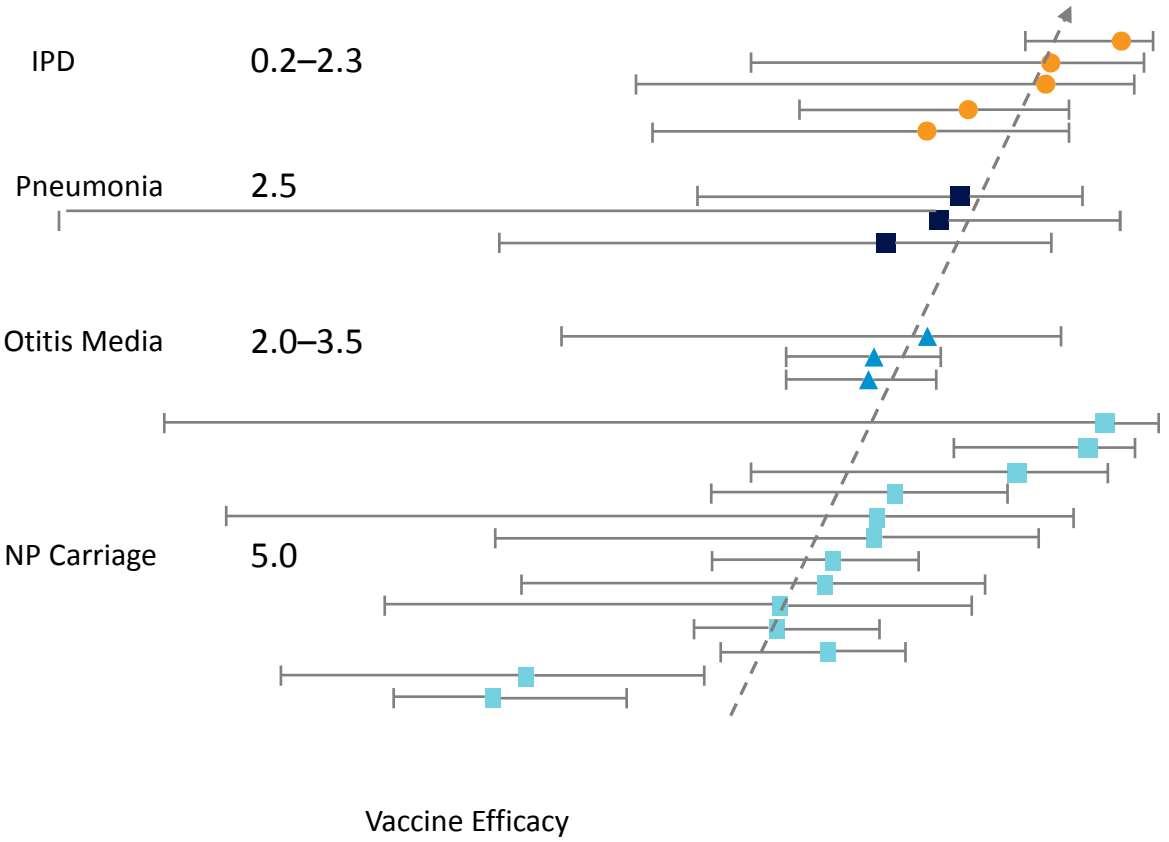
TITOLI GMT OPA PER SIEROTIPO				
Sierotipo	**PCV7[1]**	**PCV10[1]**	**PCV10[2]**	**PCV13[3]**
19F	52	148,6	125,4	150
19A	4,5	8,6	34	442

Confronto di studi con vaccini diversi, con test immunologici fatti in laboratori differenti.

1. Vesikari T, et al. *Pediatr Infect Dis J* 2009;28:S66-76.
2. Iwata et al. HVI 2015 Volume 11 Issue 4
3. Keinenger DM et al. *Vaccine* 2010;28:4192-4203.

GMC necessarie per la protezione da IPD – Polmoniti – OMA - Carriage

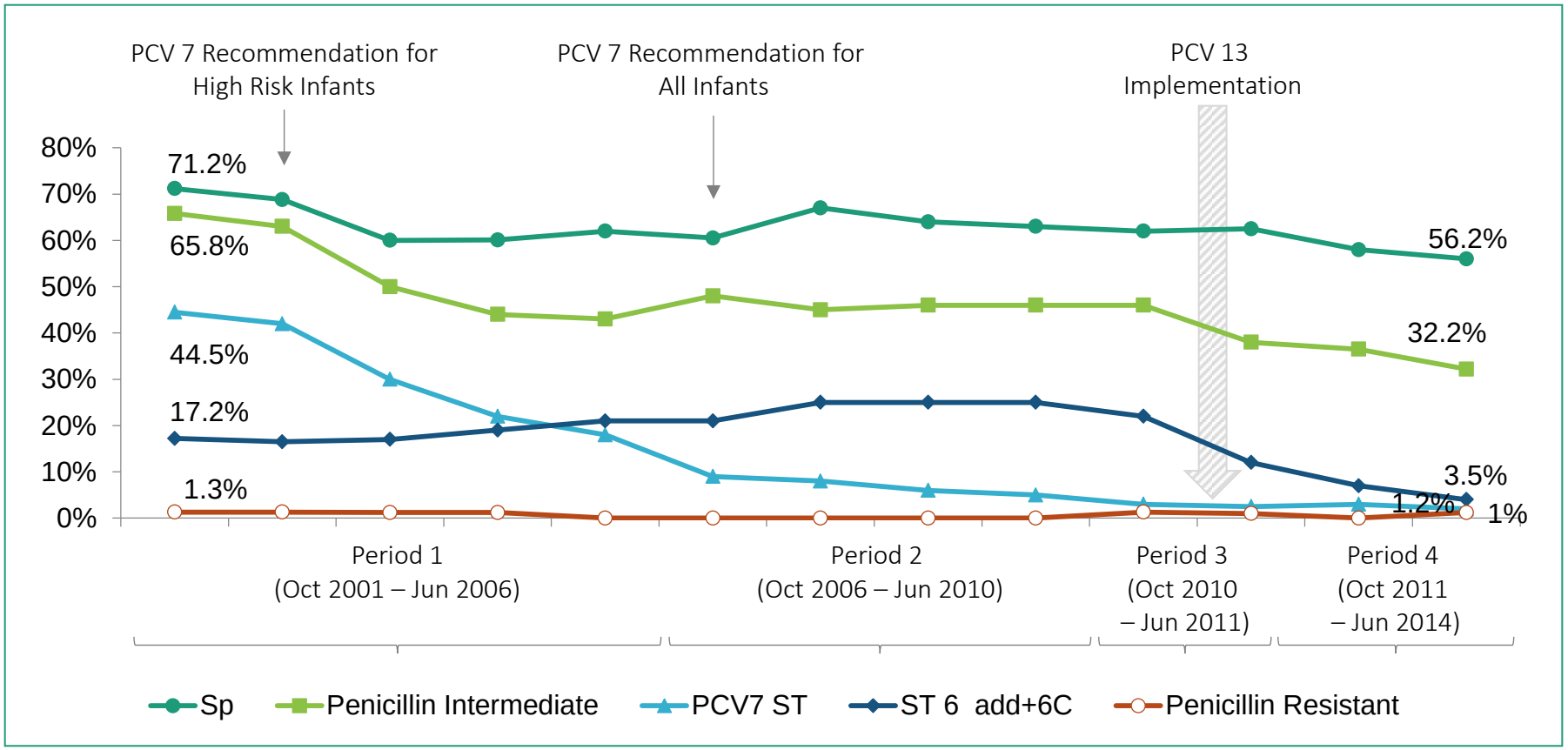
Pneumococcal Conjugate Vaccine Efficacy against Various Endpoints (µg/ml)



Proceedings of the Ninth Global Vaccine Research Forum and Parallel Satellite Symposia, WHO. Bamako, Mali, 6–9 December 2009.

(D Goldblatt GVRF 2009)

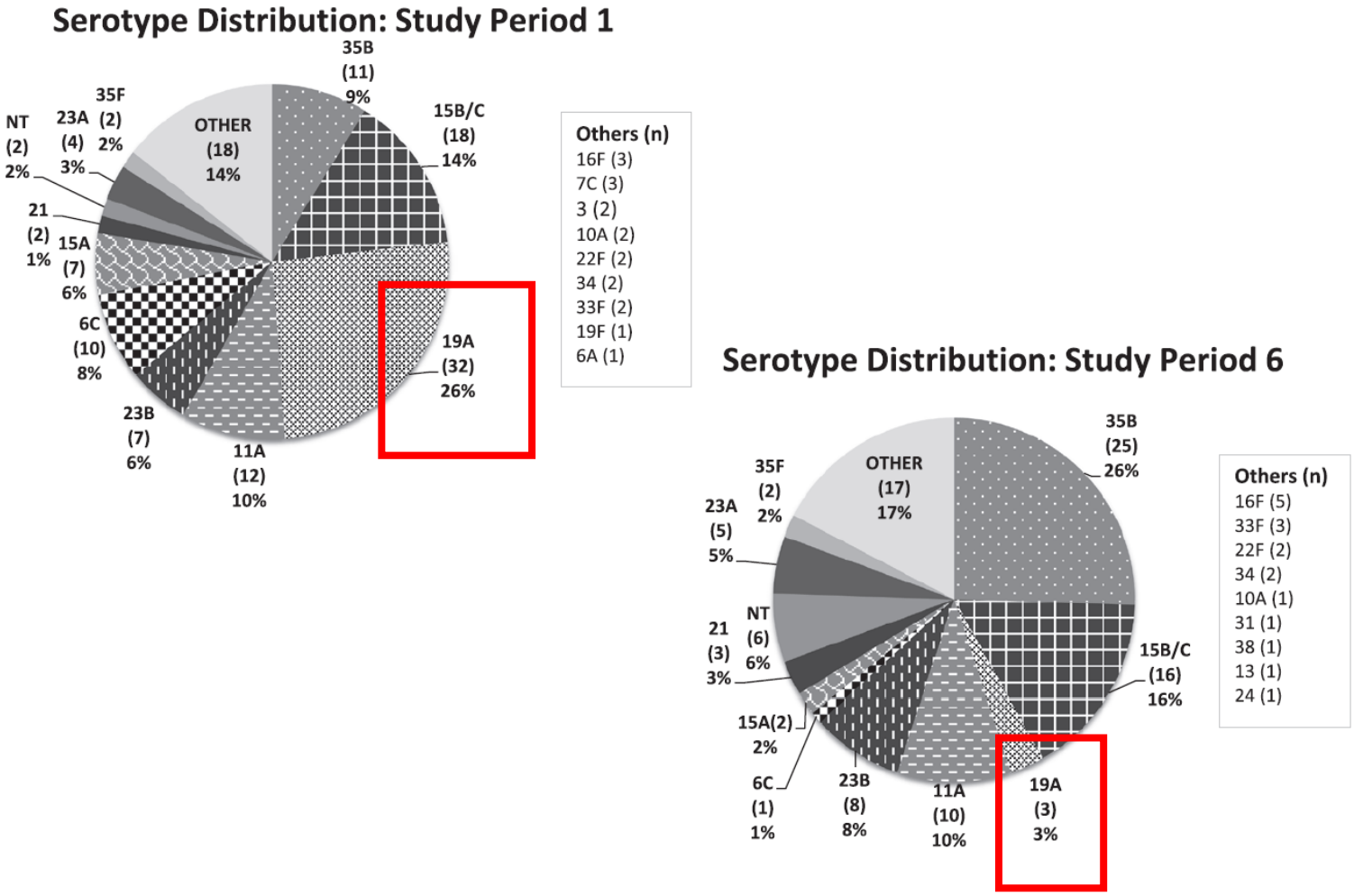
Carriage pneumococcico 2001 - 2014 in Francia prima e dopo PCV13. *Cohen et al. Vaccine 2015*



- NPC surveillance study requested by EMA as post-licensing commitment
- Determine if PCVs (PCV7, PCV13) cause serotype shift in AOM and/or changes in antibiotic resistance

Distribution of pneumococcal nasopharyngral carriage serotypes before and after PCV13 introduction in Atlanta, Georgia

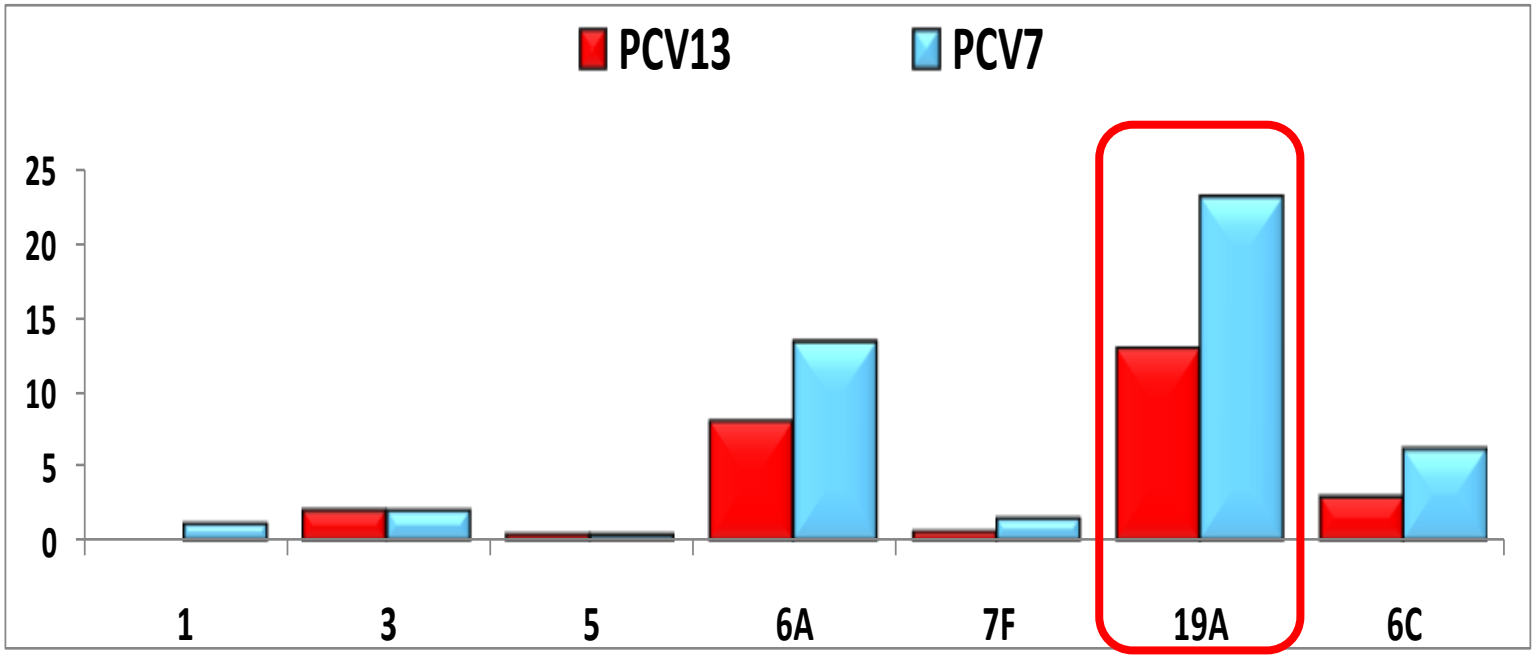
(from Desai AP. Et al. Pediatr Infect Dis J 2015)



PCV13: Effectiveness for Serotype 19A (NPC)

Nasopharyngeal Carriage

Randomized study in Israel of the effect on NPC of PCV13 vs. PCV7 administered at 2, 4, 6 and 12 months



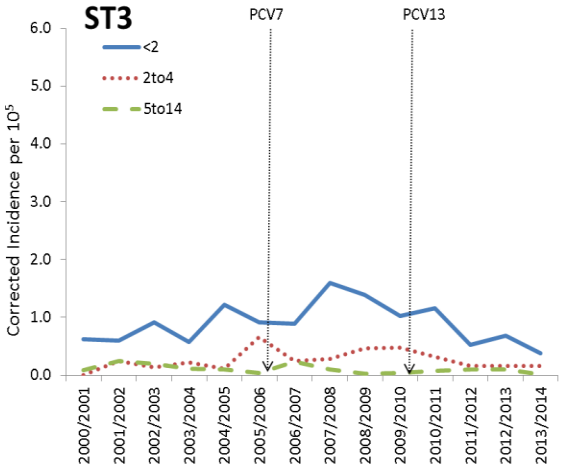
Dagan R et al. Presented at ISPPD, March 11-15, 2012, Iguazu, Brazil.

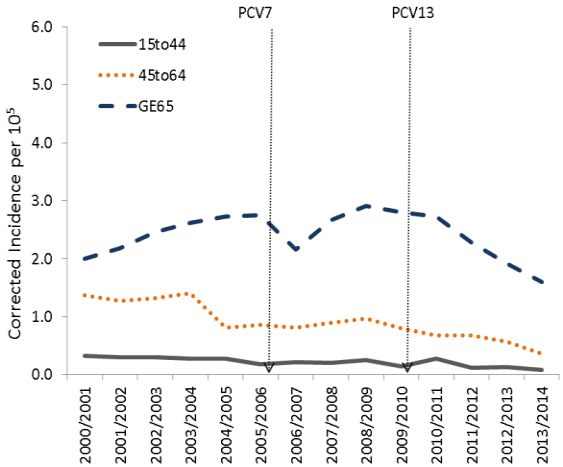
Nasopharyngeal *Streptococcus pneumoniae* colonization after PCV10 and PCV7

(from van den Bergh RM, et al. Clin Infect Dis 2013)

	PHiD-CV Group			7vCRM Group		
	n	N	% (95% CI)	n	N	% (95% CI)
Any *S. pneumoniae*[a]						
Age 5 months	211	519	40.7 (36.4 to 45.0)	100	259	38.6 (32.6 to 44.8)
Age 11–13 months	249	514	48.4 (44.0 to 52.9)	119	258	46.1 (39.9 to 52.4)
Age 14–16 months	252	514	49.0 (44.6 to 53.4)	126	257	49.0 (42.8 to 55.3)
Age 18–20 months	286	514	55.6 (51.2 to 60.0)	148	258	57.4 (51.1 to 63.5)
Age 23–25 months	293	512	57.2 (52.8 to 61.6)	131	257	51.0 (44.7 to 57.2)
Across all visits	477	520	91.7 (89.0 to 94.0)	233	260	89.6 (85.3 to 93.0)
Serotypes common to both vaccines[b]						
Age 5 months	42	519	8.1 (5.9 to 10.8)	18	259	6.9 (4.2 to 10.8)
Age 11–13 months	36	514	7.0 (5.0 to 9.6)	15	257	5.8 (3.3 to 9.4)
Age 14–16 months	27	514	5.3 (3.5 to 7.6)	12	257	4.7 (2.4 to 8.0)
Age 18–20 months	26	514	5.1 (3.3 to 7.3)	9	258	3.5 (1.6 to 6.5)
Age 23–25 months	14	512	2.7 (1.5 to 4.5)	7	257	2.7 (1.1 to 5.5)
Across all visits	90	520	17.3 (14.2 to 20.8)	43	260	16.5 (12.2 to 21.6)
Serotype 19A						
Age 5 months	41	519	7.9 (5.7 to 10.6)	17	259	6.6 (3.9 to 10.3)
Age 11–13 months	33	514	6.4 (4.5 to 8.9)	19	257	7.4 (4.5 to 11.3)
Age 14–16 months	42	514	8.2 (6.0 to 10.9)	22	257	8.6 (5.4 to 12.7)
Age 18–20 months	56	514	10.9 (8.3 to 13.9)	28	258	10.9 (7.3 to 15.3)
Age 23–25 months	31	512	6.1 (4.2 to 8.5)	20	257	7.8 (4.8 to 11.8)
Across all visits	146	520	28.1 (24.3 to 32.2)	80	260	30.8 (25.2 to 36.8)

UK: Impatto anche sul sierotipo 3 nelle IPD, tutte le età





SEROTYPE	2002/2003	2003/2004	2004/2005	2005/2006	2006/2007	2007/2008	2008/2009	2009/2010	2010/2011	2011/2012	2012/2013	2013/2014
Over 65	90	109	148	170	141	187	222	225	226	192	167	146
5 to 64	58	68	60	70	90	113	149	129	146	118	108	65
2 to 4	1	2	1	7	3	4	8	9	6	3	3	3
Under 2	6	4	10	8	9	17	17	13	15	7	9	5

Waight P. et al, Lancet Infect Dis 2015; 15:535-543