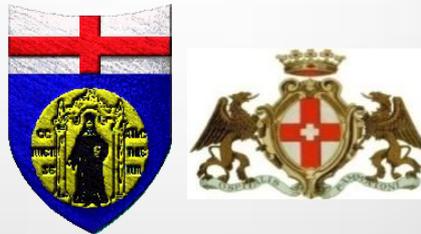


Workshop: Sorveglianza delle Malattie Batteriche Invasive
Istituto Superiore di Sanità
Roma, CNEPS, 28-29 Febbraio 2012

L'esperienza della regione Liguria



Filippo Ansaldi

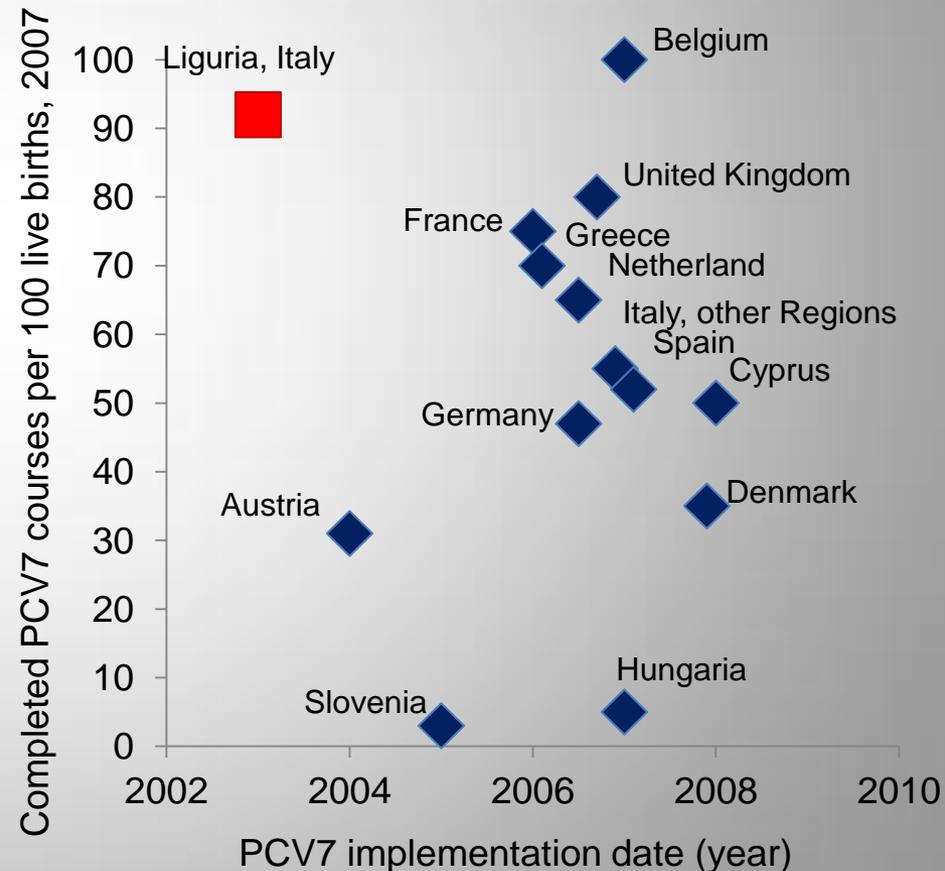
DiSSal, University of Genoa

IRCCS “San Martino” University Hospital, Genoa

A Pilot-Project, on a Regional Basis, on behalf of the Ministry of Health: Introduction of the 7-PCV into the Routine Children Immunization Schedule in Liguria - Italy (2003)



- Population: 1,700,000 inhabitants, birth cohort about 12,500
- Vaccination schedule: 3-5-11 month since May 2003
- PCV7 uptake >80% and >90% in every districts since 2004 and 2007, respectively
- Immunogenicity evaluation
Vaccine 2009
- Effectiveness evaluation
Vaccine 2009
J Int Med Res. 2008
- IPD and non-IPD Surveillance system implementation
Hum Vaccin 2011
Clin Vaccine Immunol 2011
- Carriage evaluation
Vaccine 2012



Protocollo per la sorveglianza delle MIB ed implementazione del sistema di sorveglianza in Liguria, 2006-10



Ospedale
[Sepsi, polmonite, cellulite artrite, etc.
con conferma di laboratorio]

Ospedale
[non -IPD]

Flusso dei dati

Flusso dei
campioni

ASL

Lab di riferimento
Regionale [DiSSal, UO
Igiene IRCCS San Martino]

Regione

18 casi

27 casi

Flusso dei ceppi
da bambino < 5 anni

Database nazionale
(ISS e Ministero)

Lab di riferimento
Nazionale

Passive surveillance of meningitis and IPD, Liguria, 2000-11



Liguria

2007-2010 IPD inc.
(mean /100,000 year)

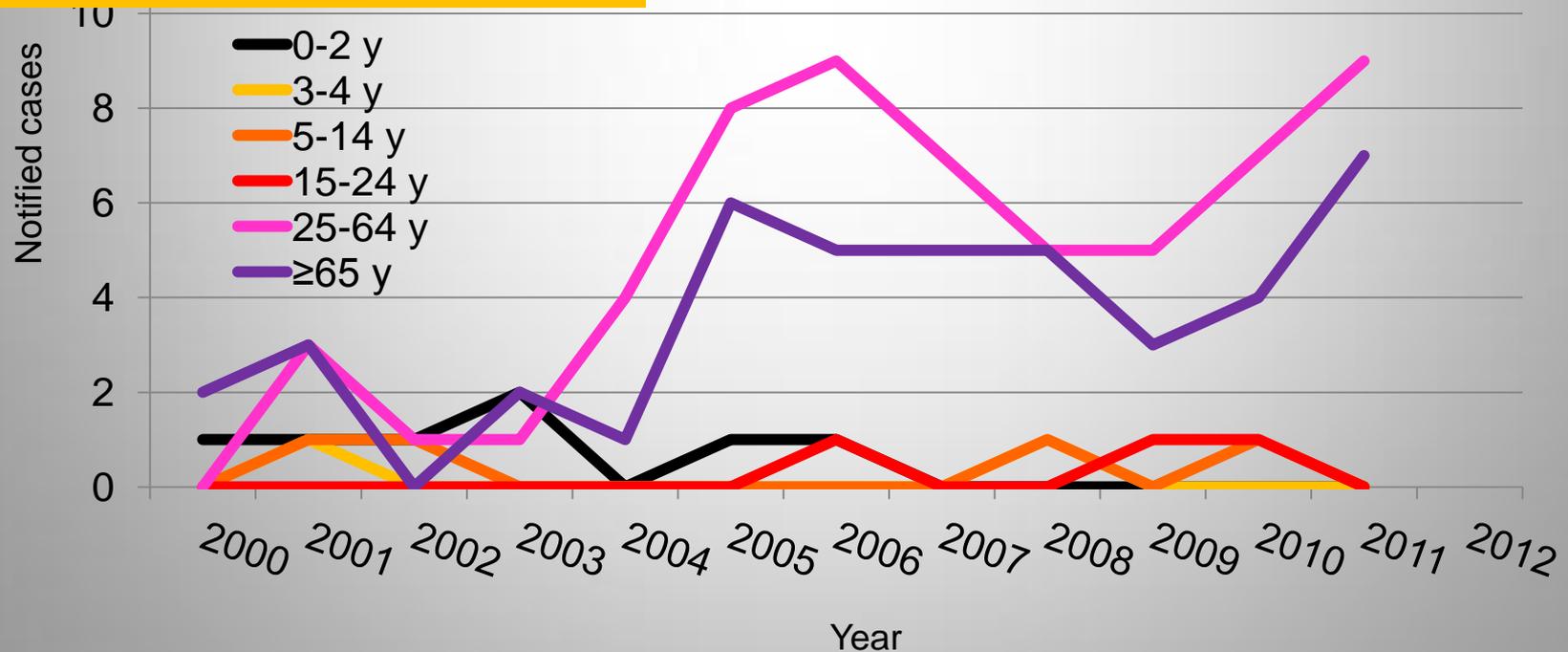
	Passive	Implem.	
0-2 y	0		
0-5 y	0.4	0-5 y	4.1
6-17 y	0.2	6-17 y	0.7
18-64 y	0.7	18-64 y	0.8
≥65 y	1	≥65 y	1.6
All age	0.7		1.1 [0.7-1.8]

Florence¹

2005-2006 IPD inc.
(/100,000 year)

	Cultural methods	Molec. Assays
0-5 y	4.7	35.1

“... pneumococcal vaccination is not included in the vaccination schedule ...”



Passive surveillance of meningitis and IPD, Liguria, 2000-11



Liguria
2007-2010 IPD inc.
 (mean /100,000 year)

	Passive	Implem.	
0-2 y	0		
0-5 y	0.4	0-5 y	4.1
6-17 y	0.2	6-17 y	0.7
18-64 y	0.7	18-64 y	0.8
≥65 y	1	≥65 y	1.6
All age	0.7		1.1 [0.7-1.8]

The Netherlands¹
2006-2008 IPD inc.
 (/100,000 year)

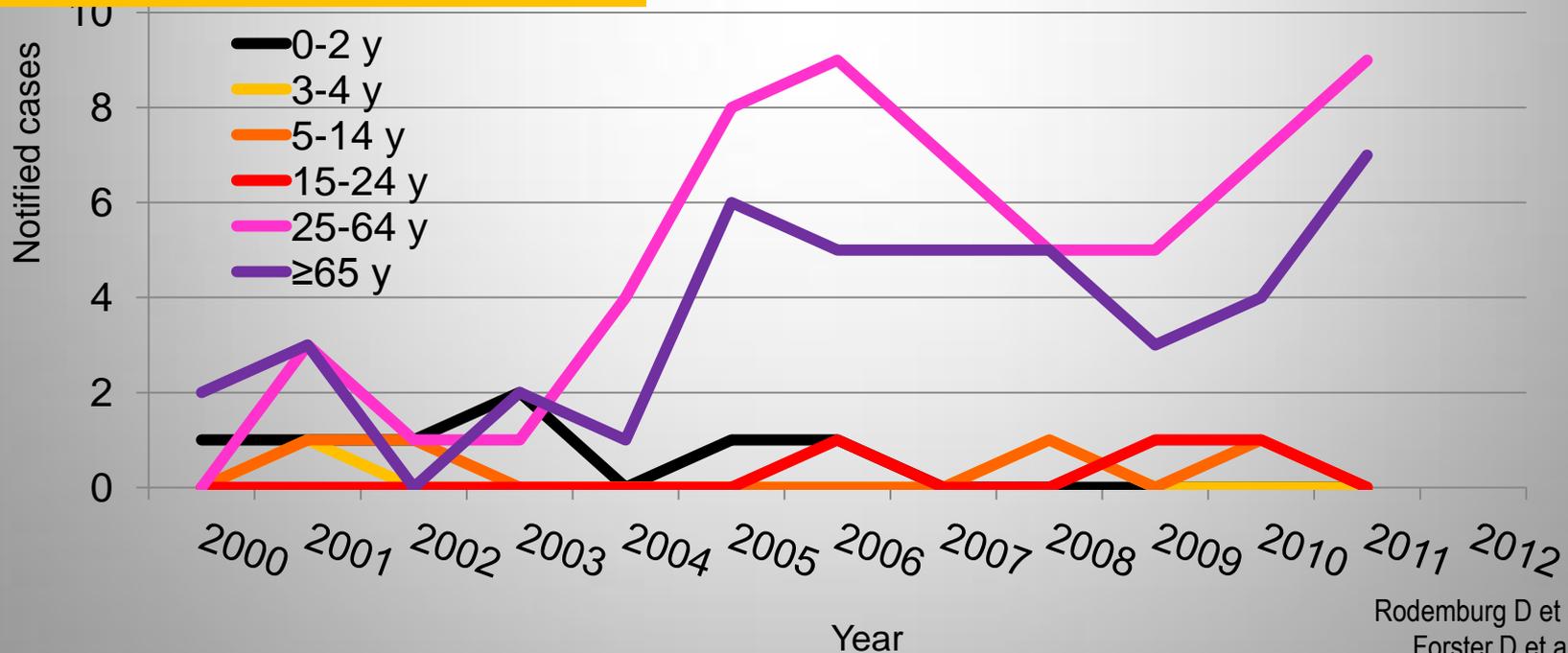
0-2 y	23
3-4 y	9
50-64 y	19
≥65 y	60
All age	16

UK²
2007-2009 IPD inc.
 (/100,000 year)

0-2 y	14-24
All age	7-8

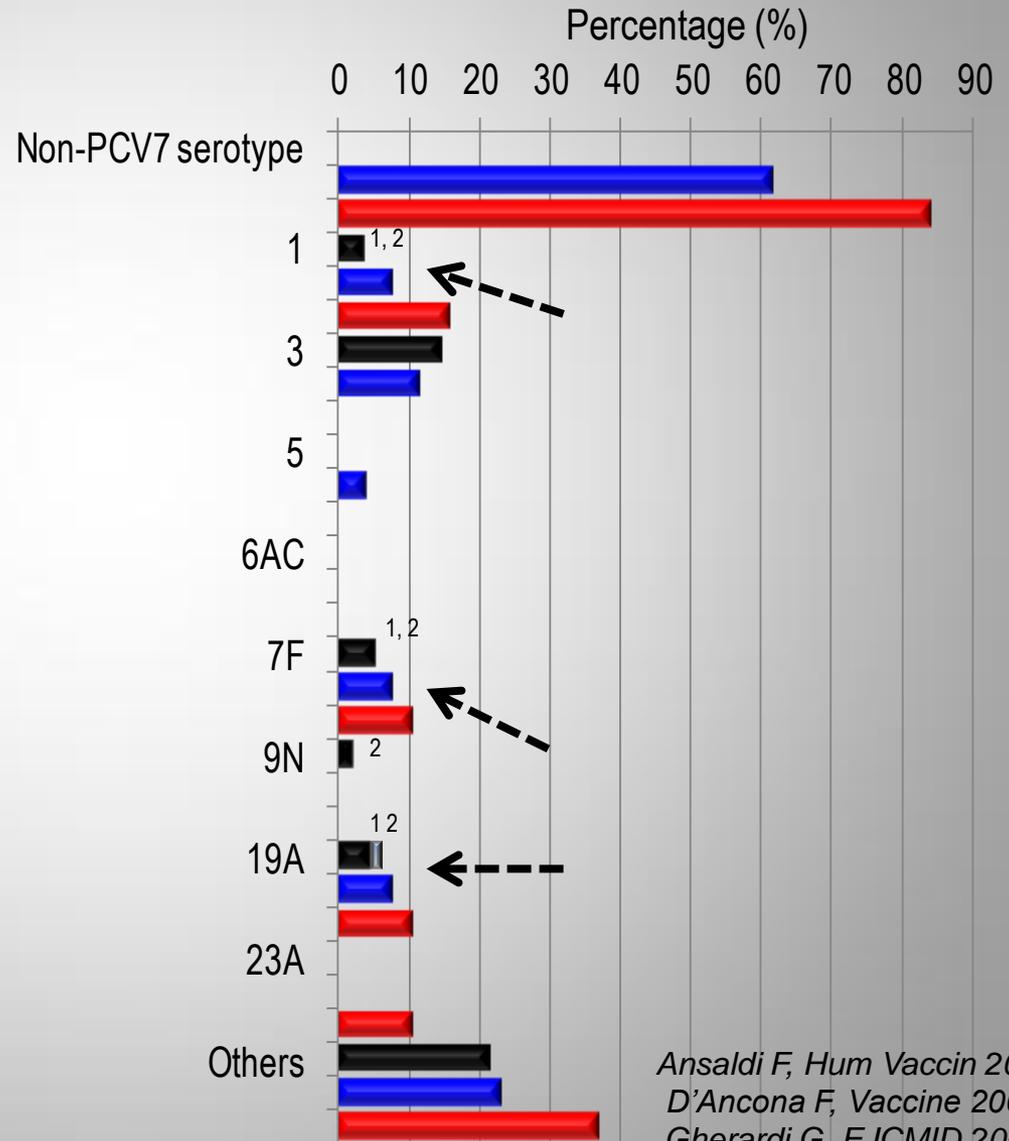
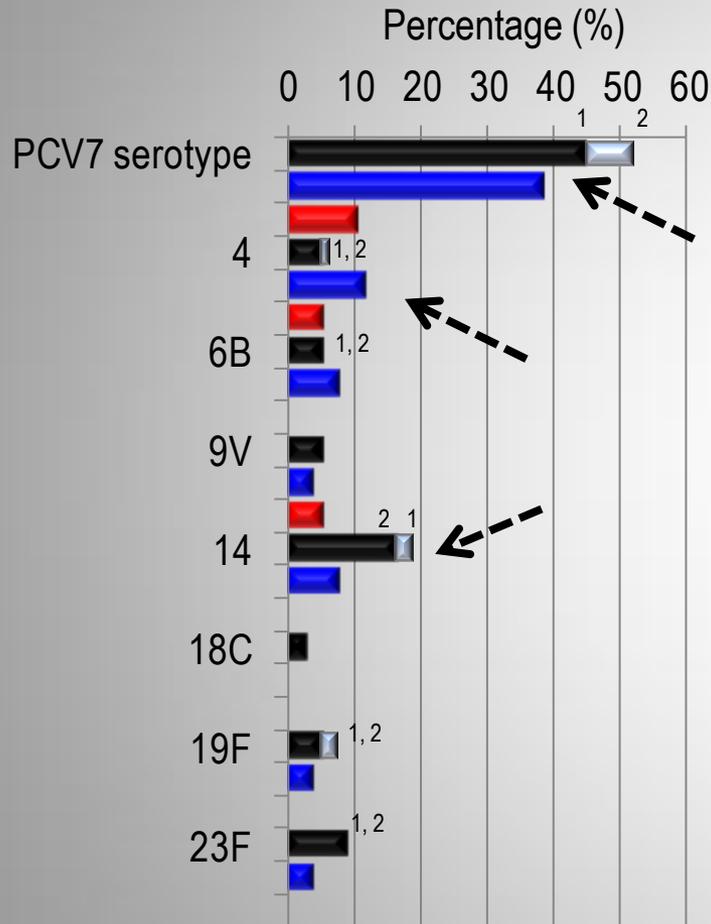
USA³
2007 IPD inc.
 (/100,000 year)

0-5 y	24
5-17 y	2
18-49 y	8
50-64 y	20
≥65 y	38
All age	14



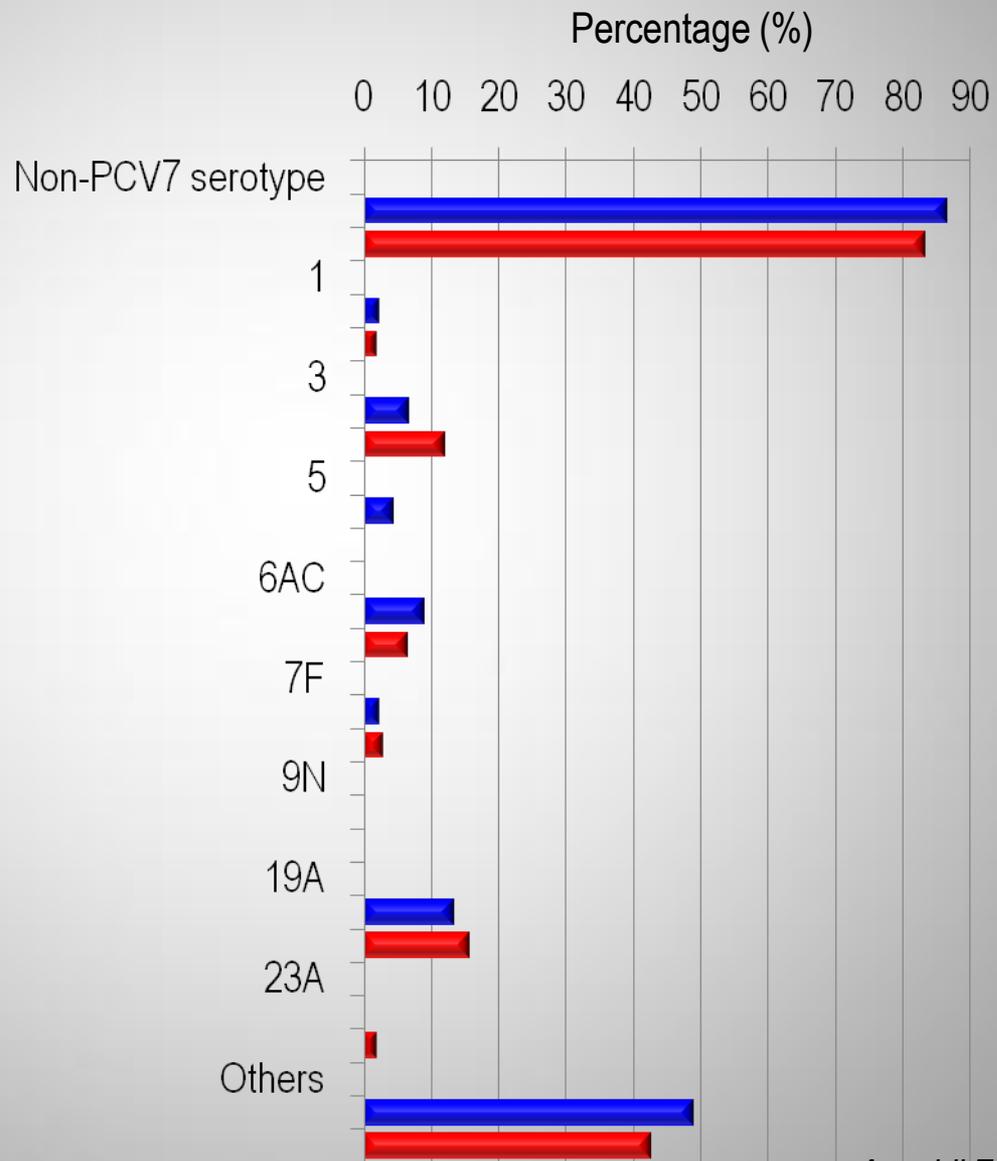
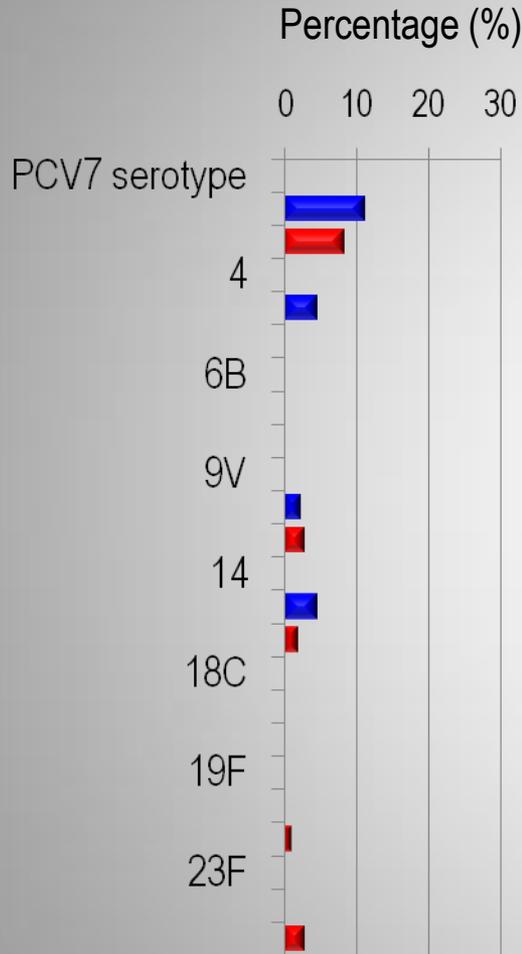
Rodenburg D et al., EID 2011¹
 Forster D et al., JMM 2011²
 Pilishvili T, J Infect Dis 2010³

Serotype distribution in patients with IPD before and after PCV7 implementation in Italy and in Liguria



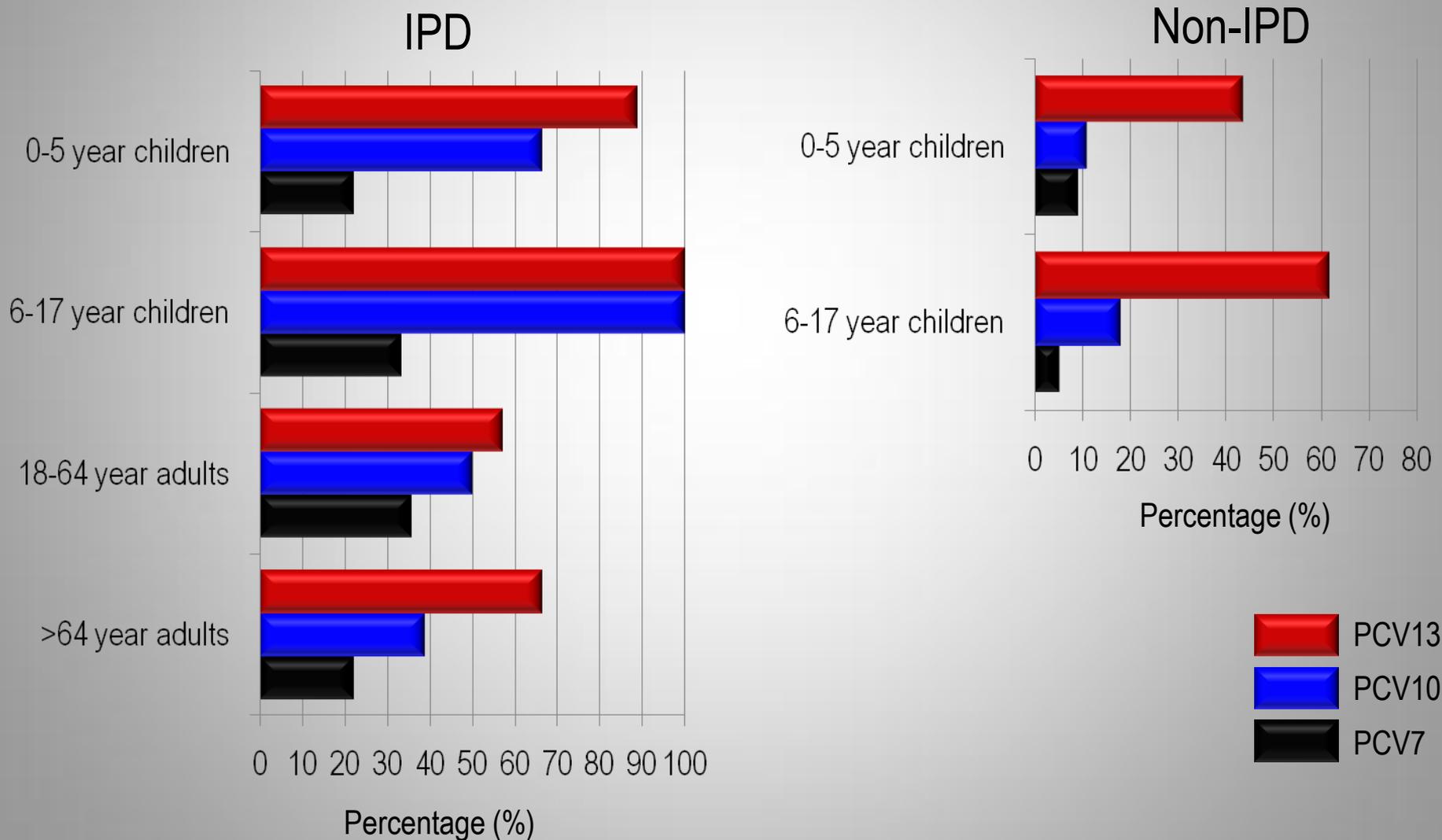

 1999-2003, Italy
 2006-08, Liguria
 2009-10, Liguria

Serotype distribution in patients with non-IPD after PCV7 implementation in Liguria



 2006-08, Liguria
 2009-10, Liguria

Serotype coverage offered by PCV7, PCV10 and PCV13 in preventing IPD and non-IPD, according age groups, in Liguria after PCV7 implementation, 2006-2010

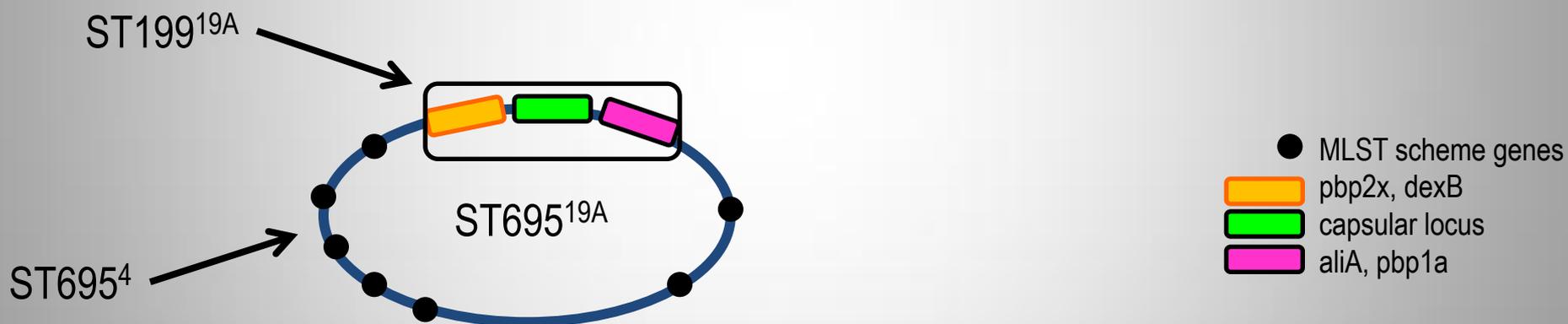




Emergence of non-vaccine serotype: mechanisms of escape

1. Serotype selection
2. Capsular switching
3. Antibiotic resistance

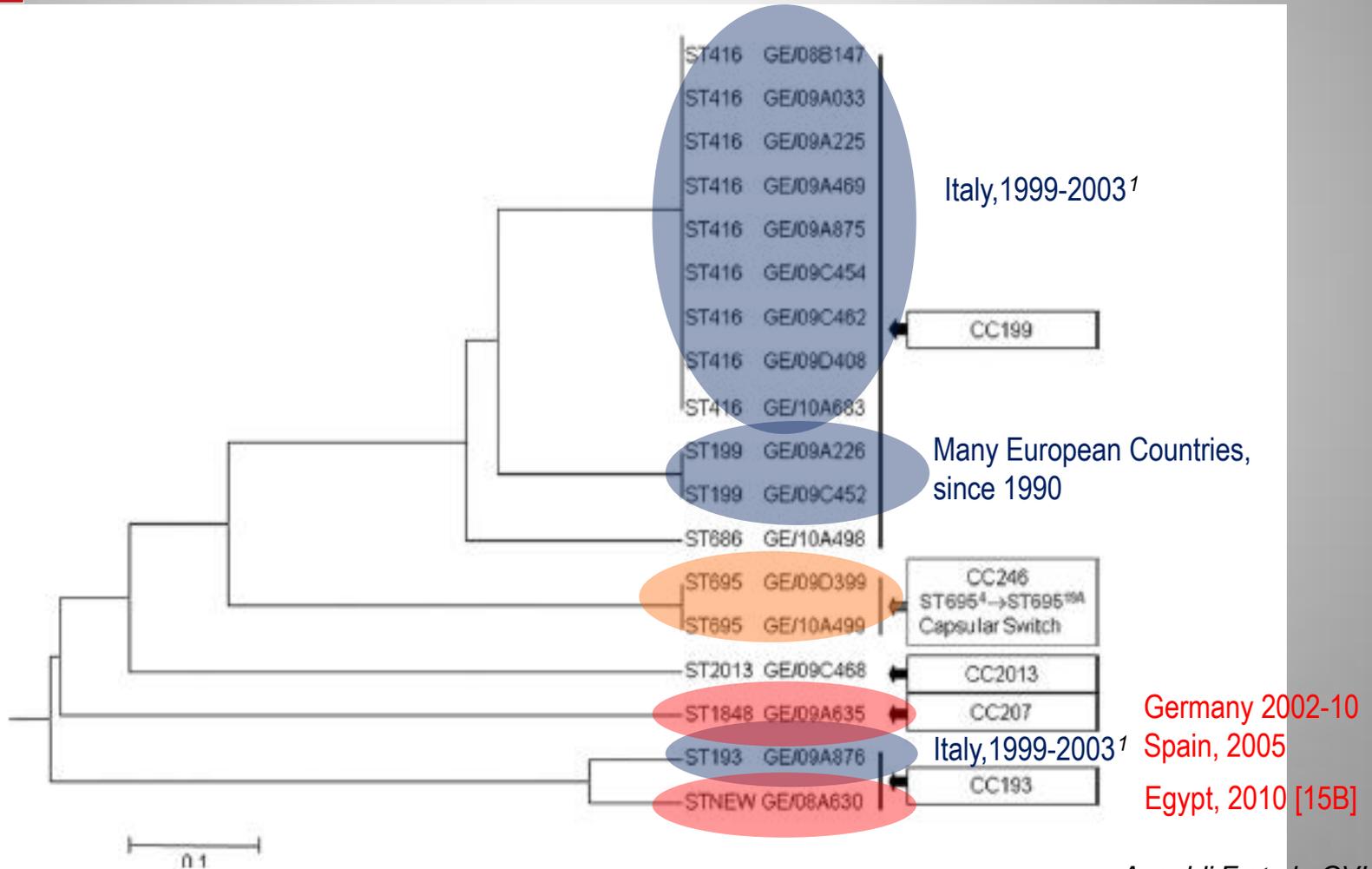
Mechanism of capsular switching



Two serotype 19A (ST695) vaccine escape recombinant in December 2009 and March 2010
Patient A with OMA, who was 4 months old, received only one dose of PCV7
Patient B with OMA, who was 4 years old, completed the vaccination course.
The two recombinants strains belonged to P1 progeny previously identified as the major group of vaccine escape strains circulating in United States.
There is no epidemiological link between the two cases.



UPMGA tree generated from MLST allelic profiles for 18 invasive and noninvasive serotype 19A *S. pneumoniae* isolates



Carriage of St pn 7 years after implementation of vaccination program in a population with very high and long-lasting coverage, Italy.



The primary objectives

- To determine the prevalence of carriage of Streptococcus pn, 7 years after the introduction of the vaccine and 4 years after reaching over 90% coverage
- To study the serotype and strain [ST] distribution in the pediatric age group (first year of life, second year of life, 3-5 years old)
- To explore the correlation between carriage, risk factors and vaccination
- To evaluate the emergence of new serotypes or ST

Study Design

- Prevalence study
- 2 collection periods (fall-winter 2010 and 2011)
- Cluster sampling on Family Paeditrician basis

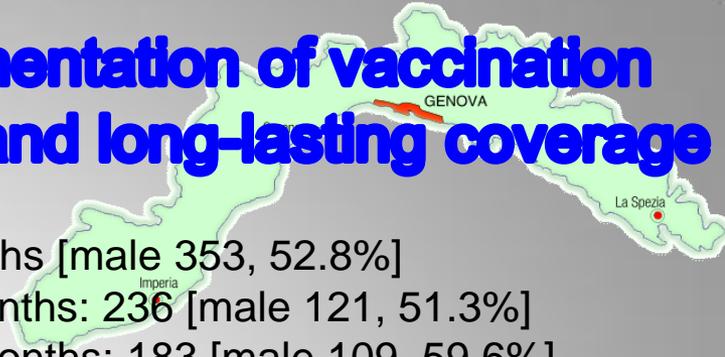
Study population

750 children under 5 years/year.
Enrollment was stratified by age: 0-12 months, 13-24 months and 25-59 months

Lab assays

Broth enrichment and real-time PCR, as recently recommended by CDC
8 multiplex PCR (CDC)
MLST

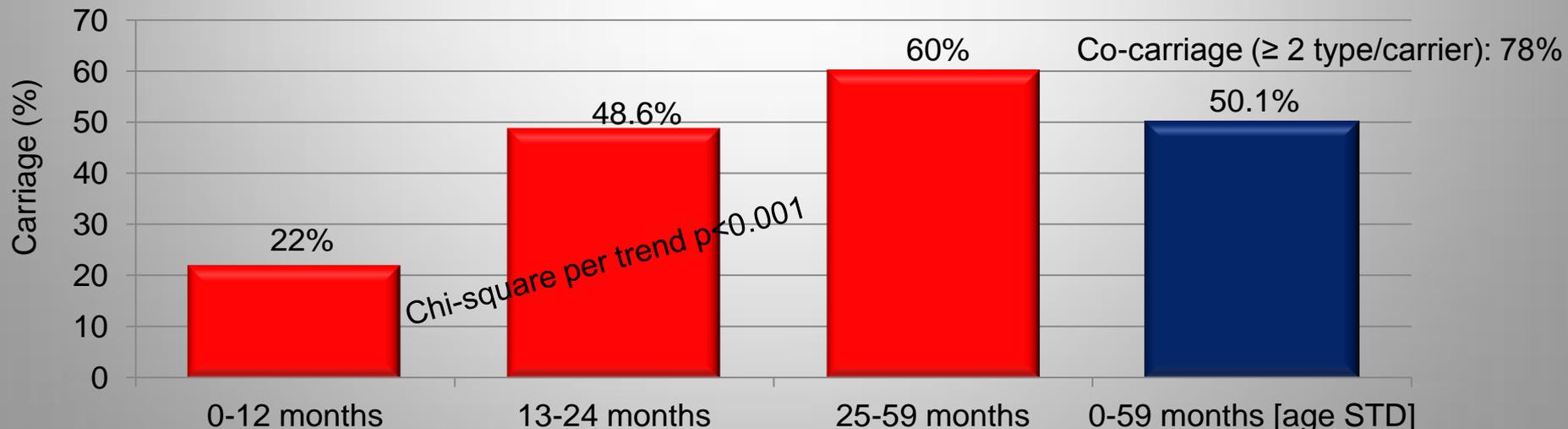
Carriage of St pn 7 years after implementation of vaccination program in a population with very high and long-lasting coverage



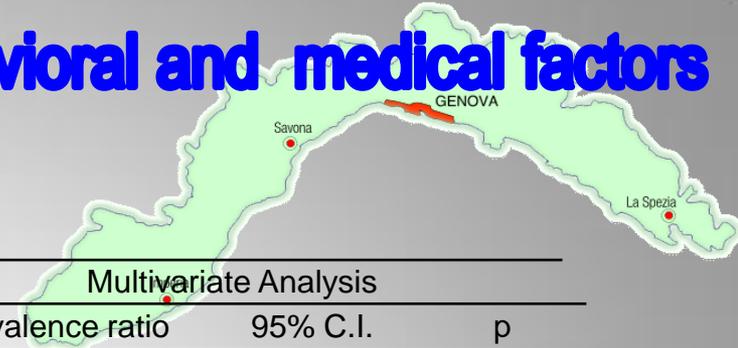
Study population: 669 children aged 0-59 months [male 353, 52.8%]
0-12 months: 236 [male 121, 51.3%]
13-24 months: 183 [male 109, 59.6%]
25-59 months: 250 [male 123, 49.2%]

Questionnaire and sample collection: Oct 18-Dec 18, 2010

PCV7 Vaccination: ≥ 4 months, 1 dose: 572/576 [99.3%]
 ≥ 6 months, 2 doses: 532/540 [98.5%]
 ≥ 13 months, 3 doses: 405/414 [97.8%]

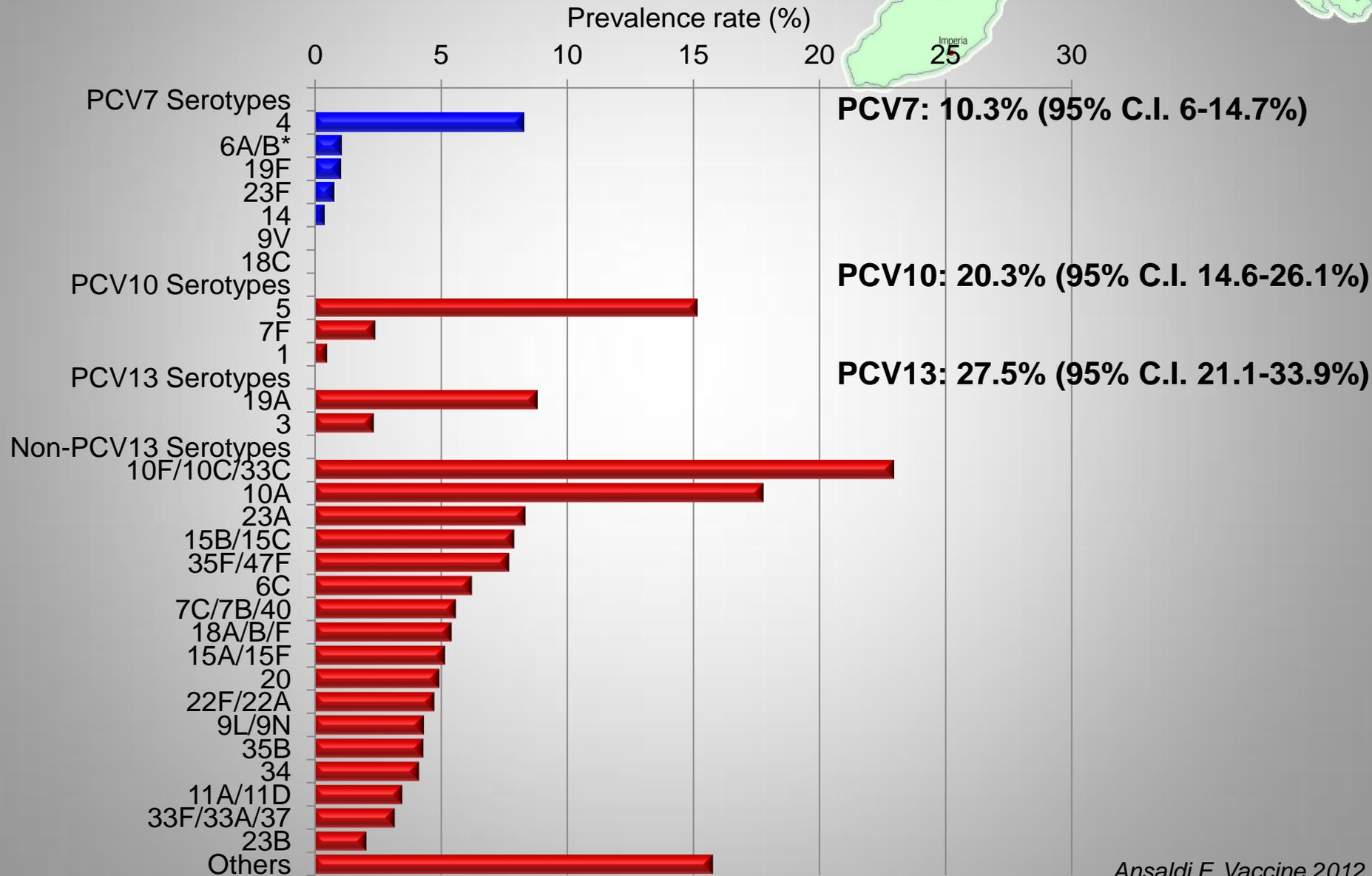


Carriage according demographic, behavioral and medical factors



Characteristic		Univariate Analysis		Multivariate Analysis		
		Carriage (%)	p	Prevalence ratio	95% C.I.	p
Age	0-12. months	22	<0.001	1.02 (per unit)	1.01-1.03	0.006
	13-24 months	18.6				
	25-59 months	60				
Gender	Male vs.	43.7	NS			
	Female	43.4				
Ethnic group	Caucasian	43.9	NS			
	Other	40				
Sibling	No	33.3	<0.001	1.55 (per unit)	1.19-2.01	0.001
	1 sister or br.	55.7				
	≥2 sisters or br.	63.3				
Sleep with siblings	No	47.4	0.005			
	Yes	65.5				
Child day care attendance	No	31	<0.001	1.51	1.16-1.97	0.002
	Yes	59.3				
Smoke among households	No	42.9	NS			
	1 smoker	41.2				
	2 smokers	54.7				
Respiratory infections	No	39.3	0.004			
	Yes	50.8				
Antimicrobial drug	No vs.	43.1	NS			
	Yes	47.4				
PCV7 vaccination	0	9.6	0.001			
	1 dose	17.1				
	2 doses	31.2				

Distribution of PCV7, PCV10, PCV13 and non-PCV13 serotypes, as proportion of colonized subjects



Main Points



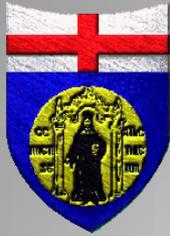
IPD and non-IPD Surveillance: “Since the beginning of PCV7 implementation, the proportion of PCV7 serotype has declined and in 2009–10 it accounted for about 10% of all *Streptococcus pn* responsible for IPD and non-IPD.

The new 13-valent pneumococcal conjugate vaccine, available since July 2010, will offer a significant added benefit covering about 90%, 100% of IPD and more than 40% and 60% of non-IPD detected in pre-school and school children, respectively, after PCV7 introduction.”
... capsular switching in two non.invasive strains ...

Carriage evaluation: 7 years after PCV7 implementation and 6 and 3 after PCV7 uptake reached coverage of >80% and >90% in every districts

- Prevalence of *Streptococcus pn* carriage was similar (crude rate 34.5%, age-std rate 50.1%) respect with carriage rates observed in Southeastern France (50%)¹ and the Netherlands (47-49%)², and higher respect with data from the UK (30%)³, during post-PCV7 hera
- High prevalence of more-than-one serotypes carriage
- Among predictors of carriage, multivariate analysis highlighted the role of “age”, “number of brothers or sisters” “group child care”
- PCV7-serotype carriage was 10.3%: almost complete replacement of vaccine serotypes
- PCV13-serotype coverage reached 27.5%
- Wide heterogeneity of non-PCV13 serotypes and high proportion of low-invasive serotypes, i.e. 11, 15, 23, 35, ...

Acknowledgements



**Di.S.Sal., University of Genoa
I.R.C.C.S. "San Martino" University
Hospital, Genoa**

Giancarlo Icardi
Paolo Durando
Paola Canepa
Antonella Ceravolo
Martina Coppelli
Daniela de Florentiis
Rocco Iudici
Andrea Orsi
Valentina Parodi
Rappazzo Emanuela
Laura Valle
Marta Zancolli

I.R.C.C.S. "G. Gaslini", Genoa

Roberto Bandettini
Maria Cristina Diana
Pasquale Di Pietro
Giovanni Melioli

... and many others