Actualités sur les vaccins contre les pneumocoques

Robert Cohen

Coordonateur InfoVac

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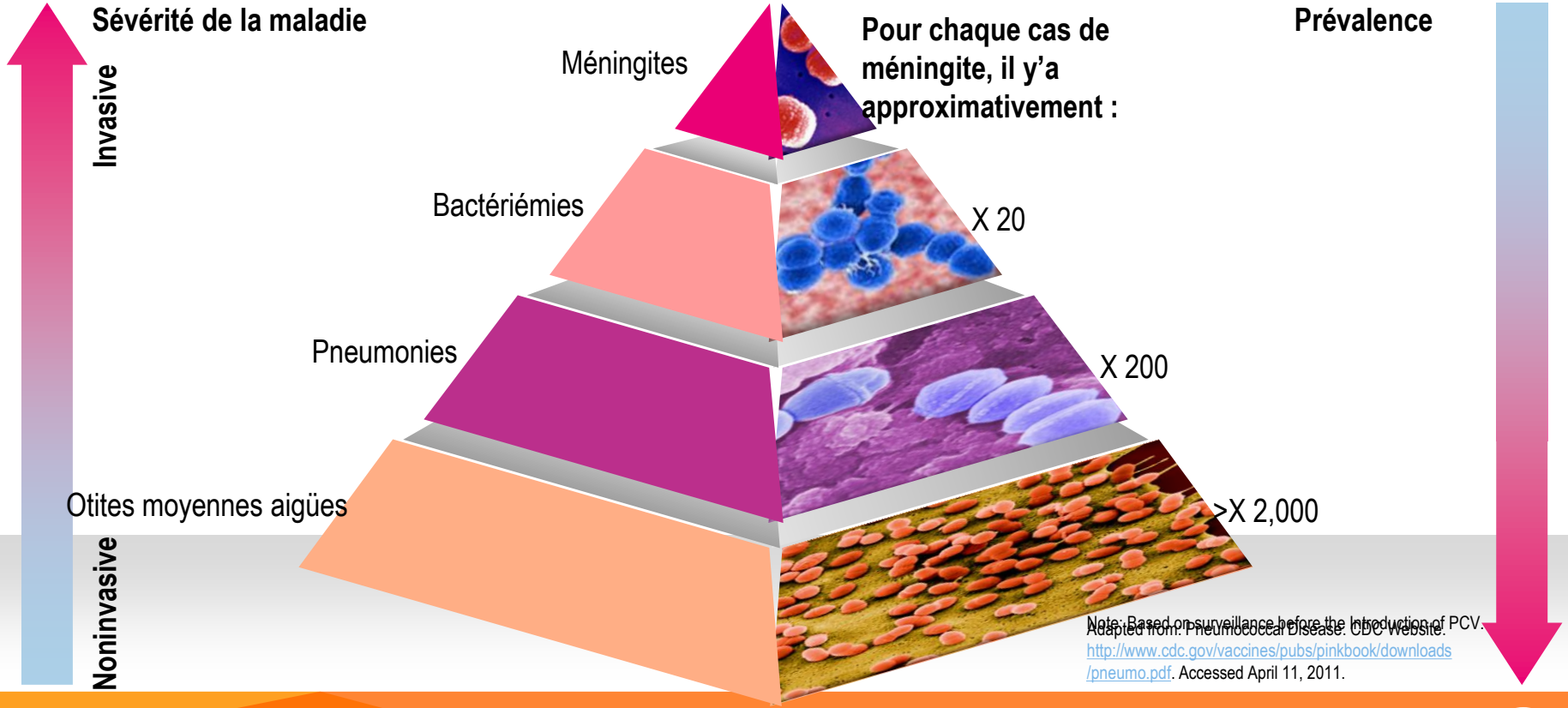
CHI Créteil

AVANT LA VACCINATION

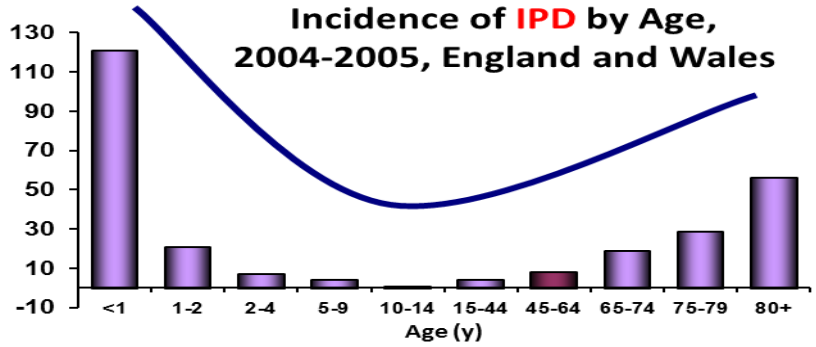
- Incidence des infections pneumococciques
- Spectre des infections pneumococciques
- Sérotypes du pneumocoque
- La résistance aux antibiotiques

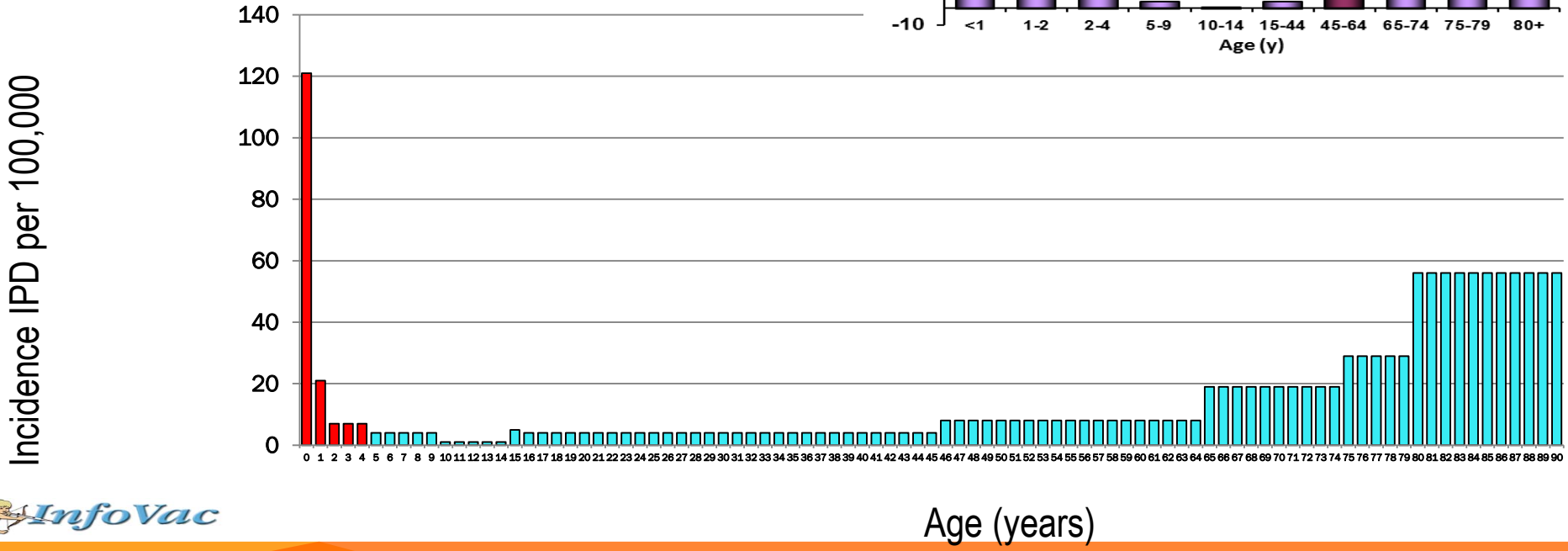
Spectre des infections à pneumocoque de l'enfant



Note: Based on surveillance before the introduction of PCV.
Adapted from: Pneumococcal Disease. CDC Website. http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/pneumo.pdf. Accessed April 11, 2011.

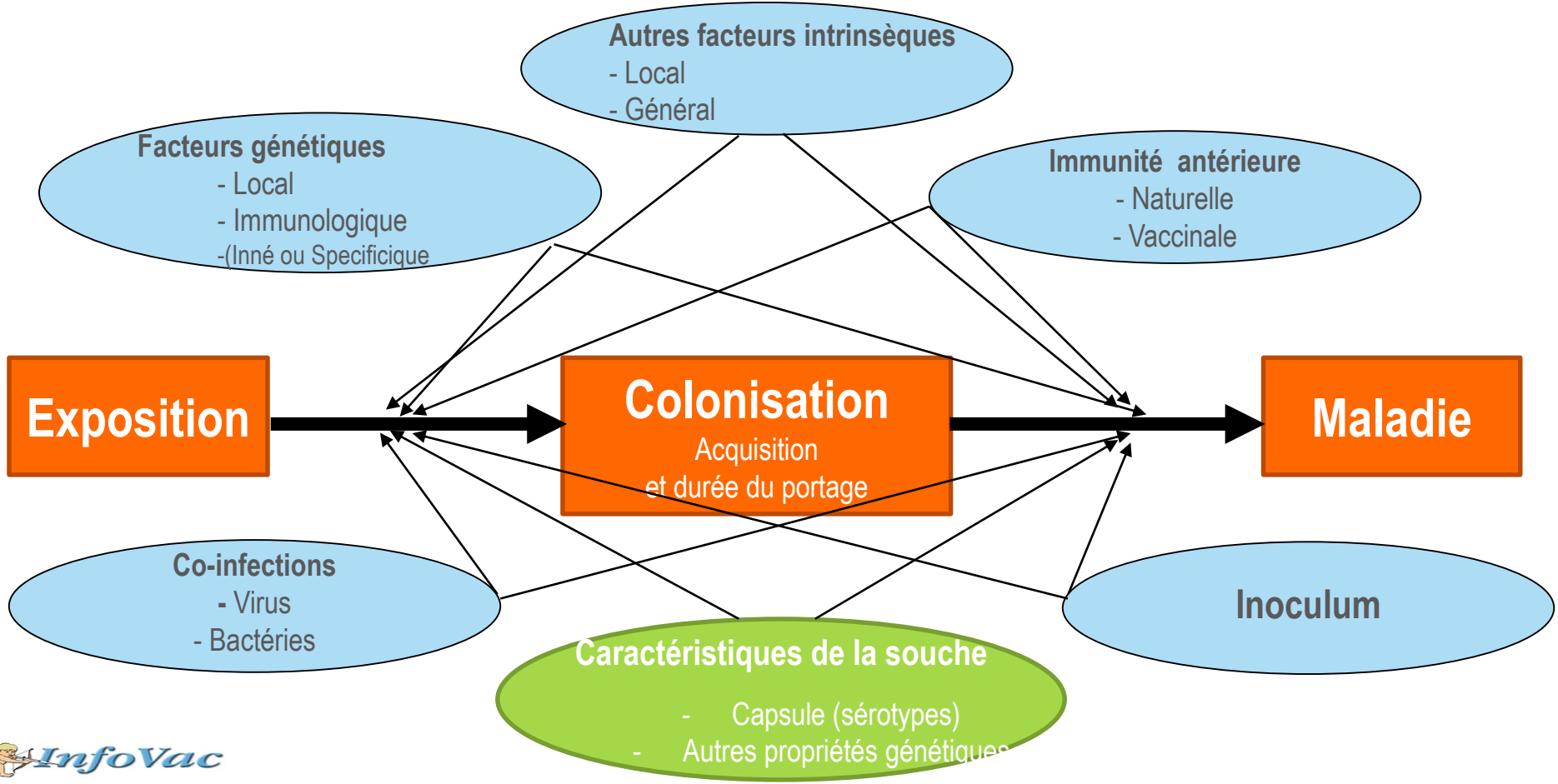
Ron Dagan slide



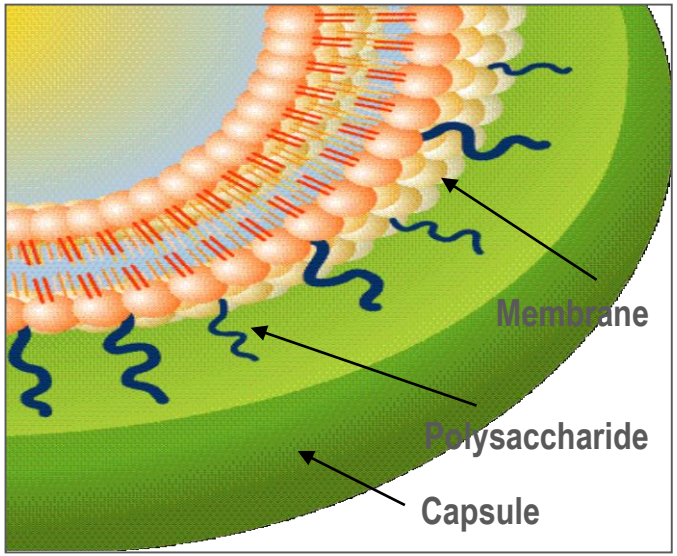


La niche écologique du pneumocoque : le microbiome rhino-pharyngé

- > 700 espèces
- Très peu sont impliquées dans les infections
- La plus importante…**le pneumocoque**


Autres facteurs intrinsèques
- Local
- Général
Facteurs génétiques
- Local
- Immunologique
-(Inné ou Specificique
Immunité antérieure
- Naturelle
- Vaccinale
Exposition
Colonisation
Acquisition
et durée du portage
Maladie
Co-infections
- Virus
- Bactéries
Inoculum
Caractéristiques de la souche
- Capsule (sérotypes)
- Autres propriétés génétiques

Sérotypes



Coupe schématique d'un pneumocoque

- **Capsule polysaccharidique**
  - Protège de la phagocytose
  - Activité anti-complémentaire
  - Support en grande partie de la virulence → action pro-inflammatoire
  - > 94 types capsulaires différents définissant les sérotypes, regroupés en 45 sérogroupes
- **Le PCV7 « couvrait » (4,6B,9V,14,18C,19F, 23F) :**
  - très bien les nourrissons et les jeunes enfants d'Amérique du nord (> 90 %)
  - un peu moins bien les petits Européens
  - Encore moins bien les enfants des pays « moins riches » ou « pauvres »
- **Le PCV13 « couvrait » (1,3,5,6B,7F,19A):**
  - les enfants plus grands
  - les enfants des différents pays « riches », « moins riches » ou « pauvres »

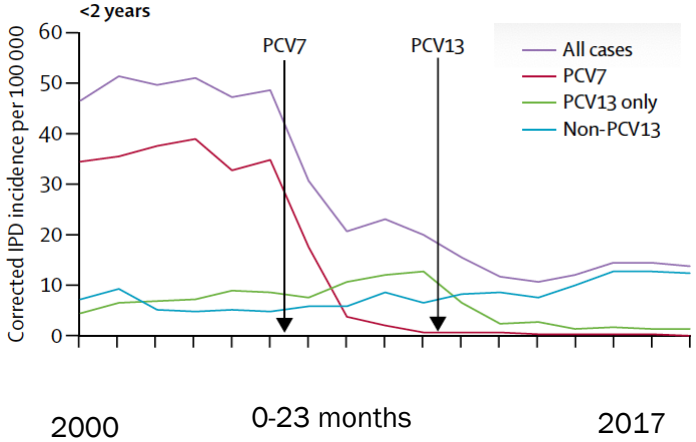
APRÈS LA VACCINATION

- **Incldence a diminuée partout de façon plus ou moins importante**
- **Spectre des infections pneumococciques : il a changé**
  - Répartition des différentes infections
  - Augmentation de la proportion des patients présentant une pathologie sous jacente
- **Sérotypes du pneumocoque**
  - Bouleversement
  - Plus grand chantier écologique depuis l'avènement de l'antibiothérapie
- **La résistance aux antibiotiques ↘ mais…**

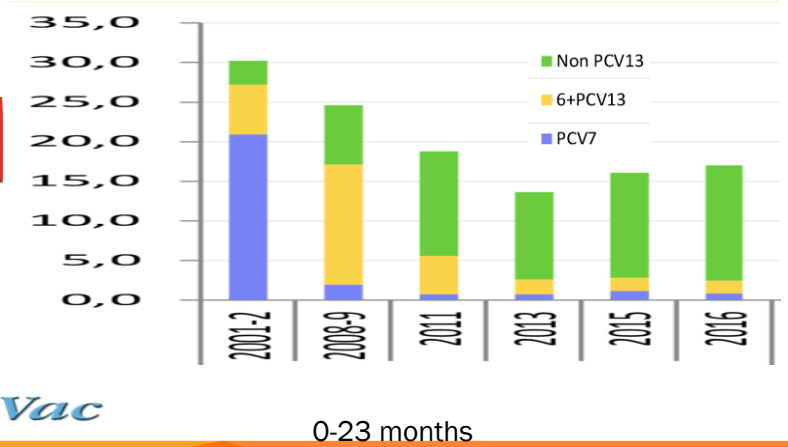
MAIS

Impact of PCVs implementation on incidence of IPD (VT and NVT) in young children

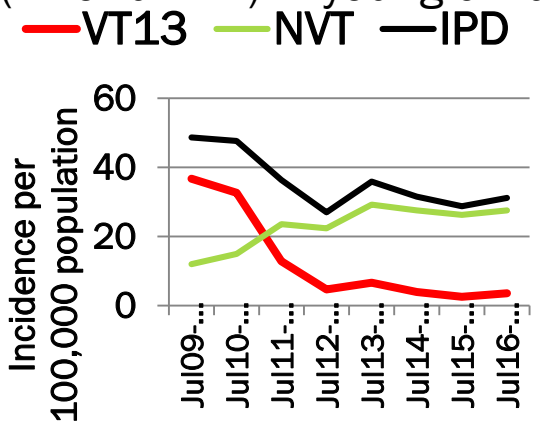
(1)



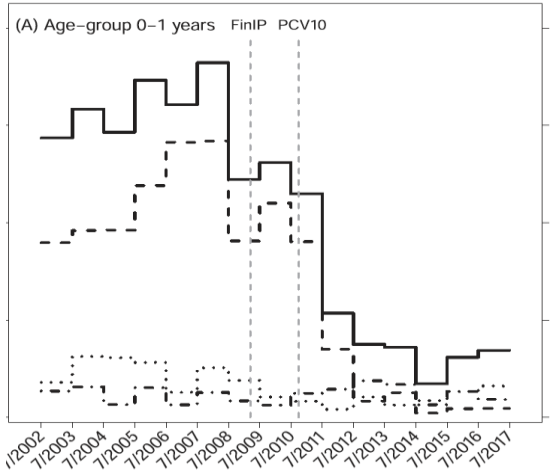
(2)



(3)



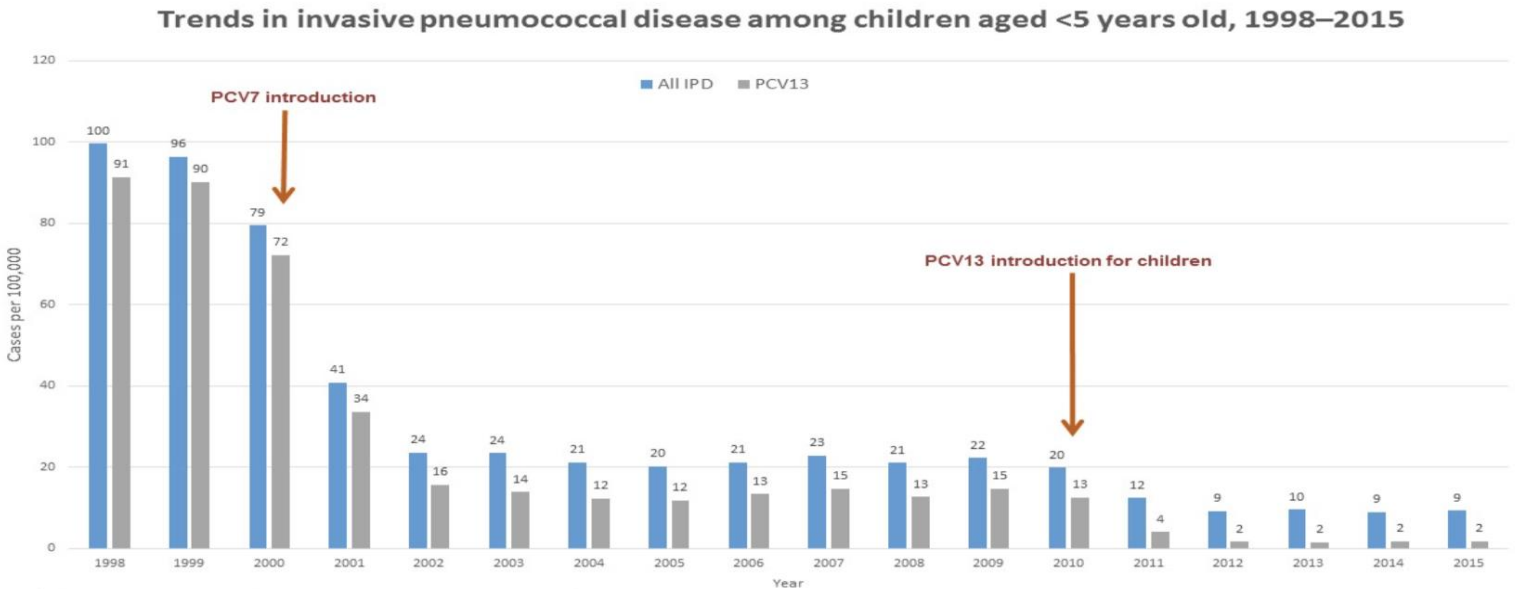
(4)

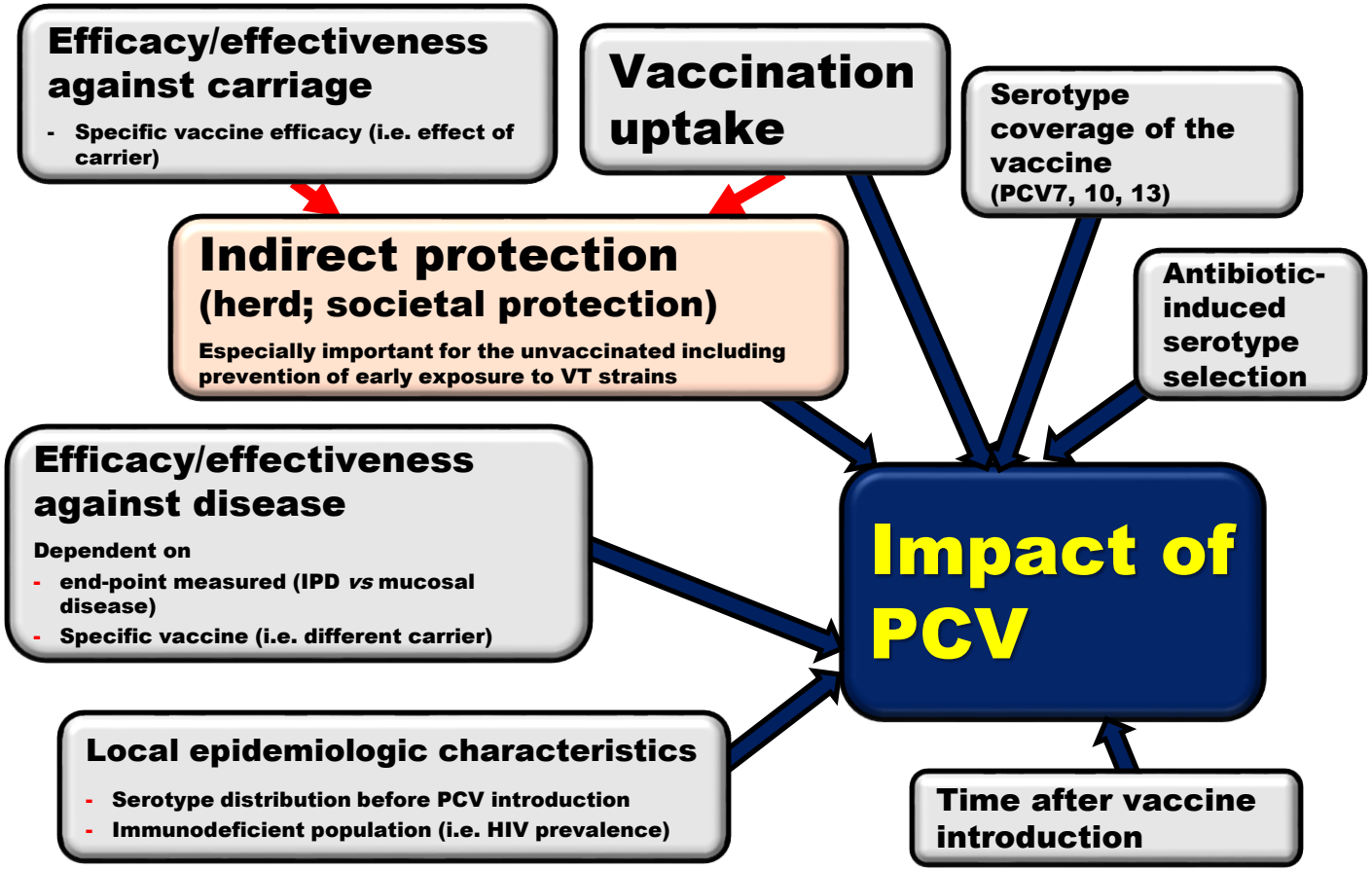


1) Ladhani LID Lancet Infect Dis. 2018 ;18:441
2) French National Reference Center: http://cnr-pneumo.com/docs/rapports/CNRP2017.pdf
3) Benshimol Vaccine. 2014 Jun 5;32(27):3452-9; updated
4) Rinta-Kokko Vaccine. 2018;36:1934

USA 1997 À 2015

Incidence des infections invasives pneumocciques < 5 ans




Efficacy/effectiveness against carriage
- Specific vaccine efficacy (i.e. effect of carrier)
Vaccination uptake
Serotype coverage of the vaccine (PCV7, 10, 13)
Indirect protection (herd; societal protection)
Especially important for the unvaccinated including prevention of early exposure to VT strains
Antibiotic-induced serotype selection
Efficacy/effectiveness against disease
Dependent on
- end-point measured (IPD *vs* mucosal disease)
- Specific vaccine (i.e. different carrier)
Impact of PCV
Local epidemiologic characteristics
- Serotype distribution before PCV introduction
- Immunodeficient population (i.e. HIV prevalence)
Time after vaccine introduction

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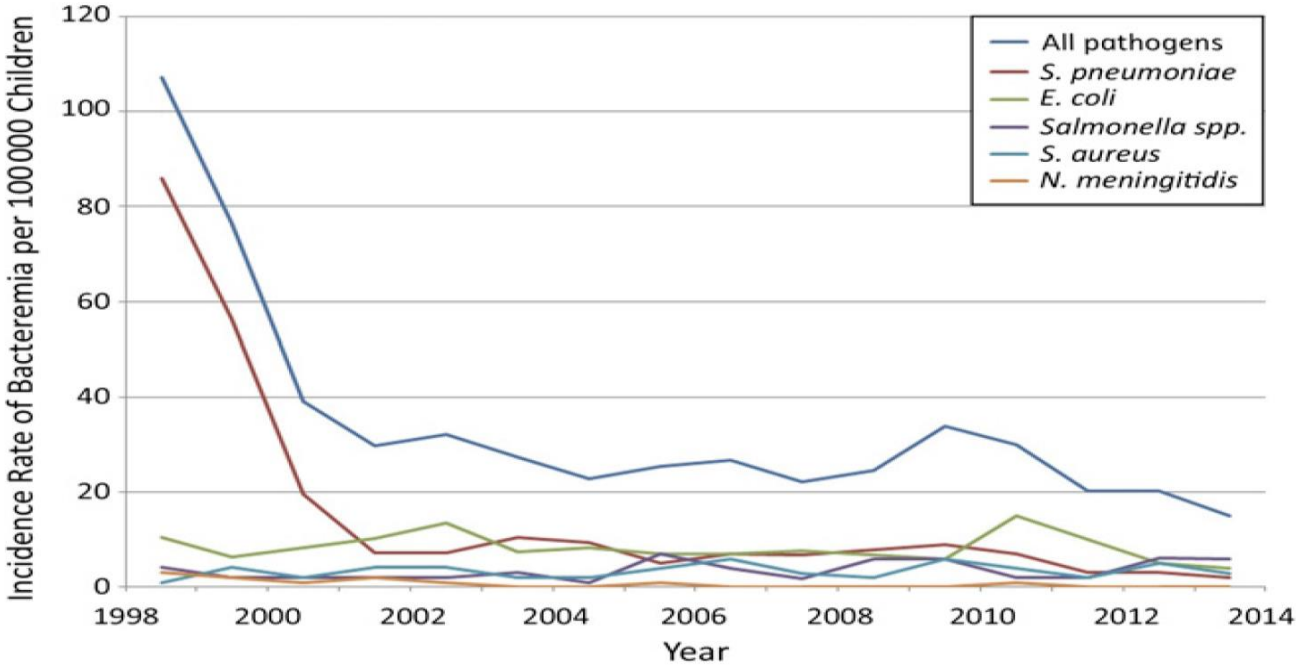
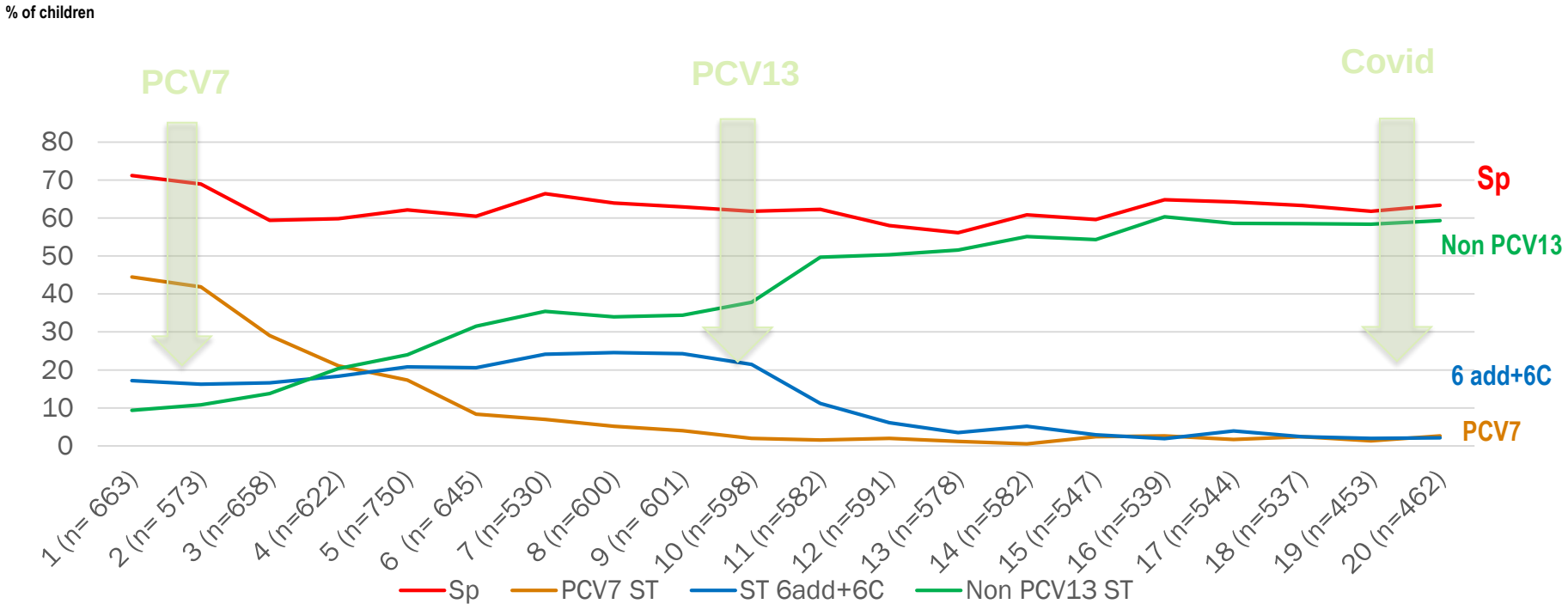
Bacteremia in Children 3 to 36 Months Old After Introduction of Conjugated Pneumococcal Vaccines

Tara L. Greenhow, MD,[a] Yun-Yi Hung, PhD,[b] Arnd Herz, MD[c]

PEDIATRICS Volume 139, number 4, April 2017:



Sp Nasopharyngeal Carriage, AOM fever± otalgia, 11 657 children, 20 years



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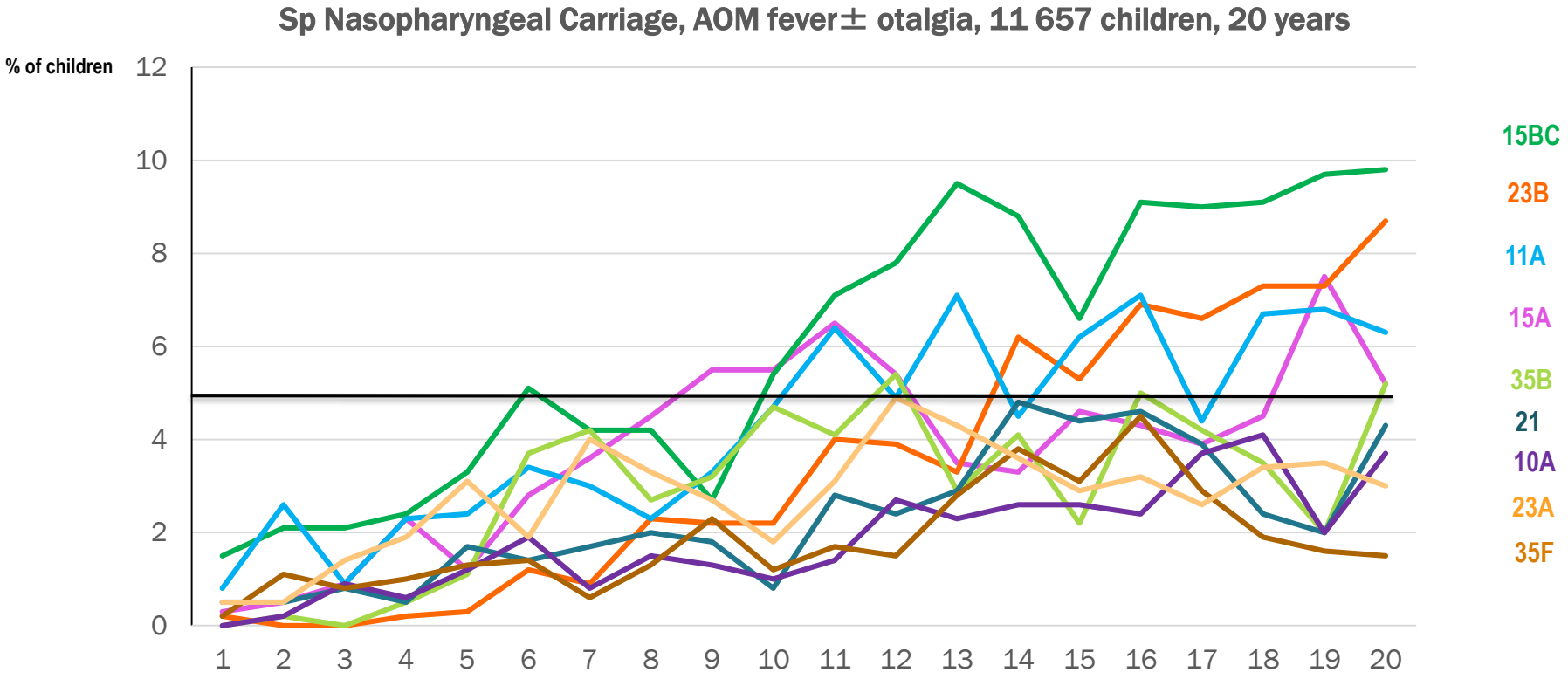
Study Years (Year 1: Oct 2001/June 2002, Year 20: Oct 2020/ June 2021)

Sérotypes non vaccinaux émergents dans le portage



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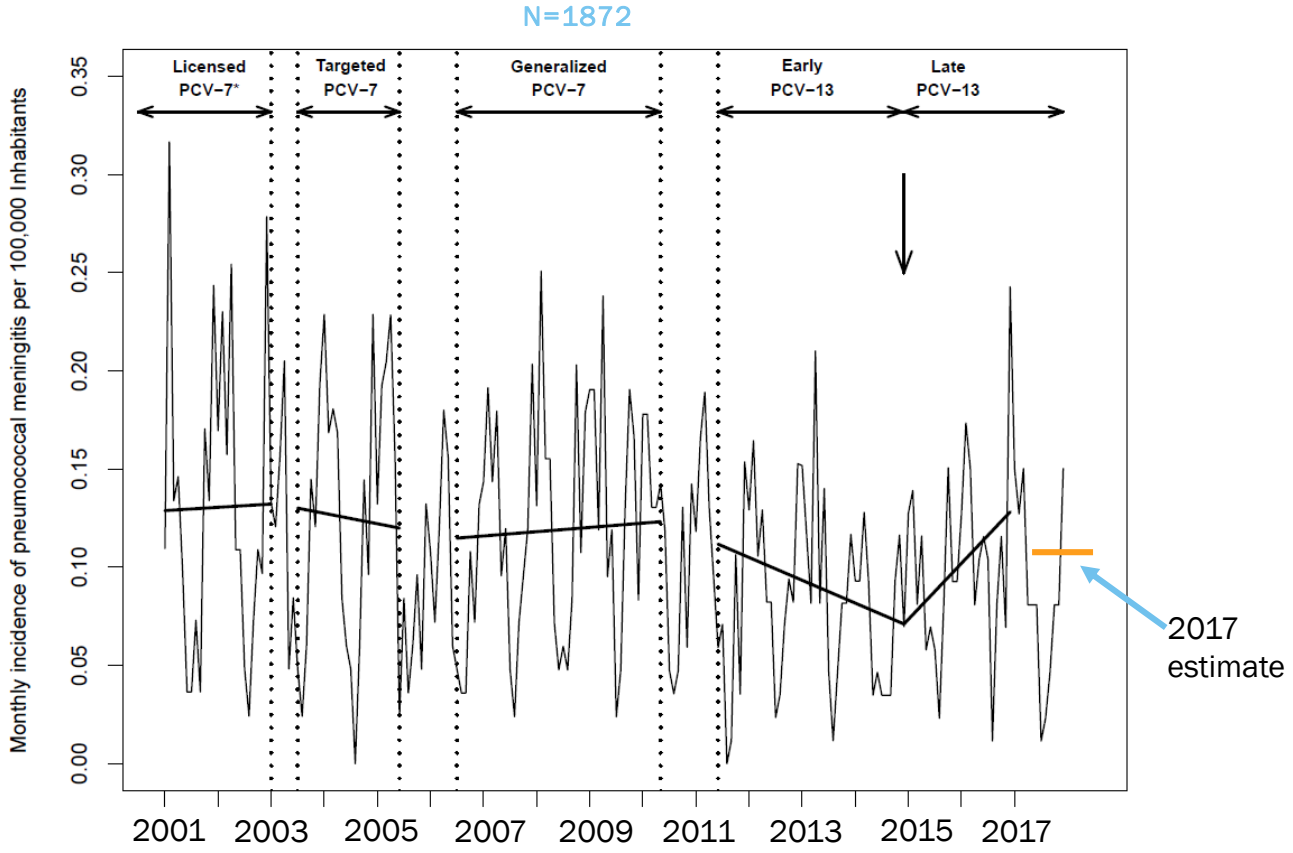
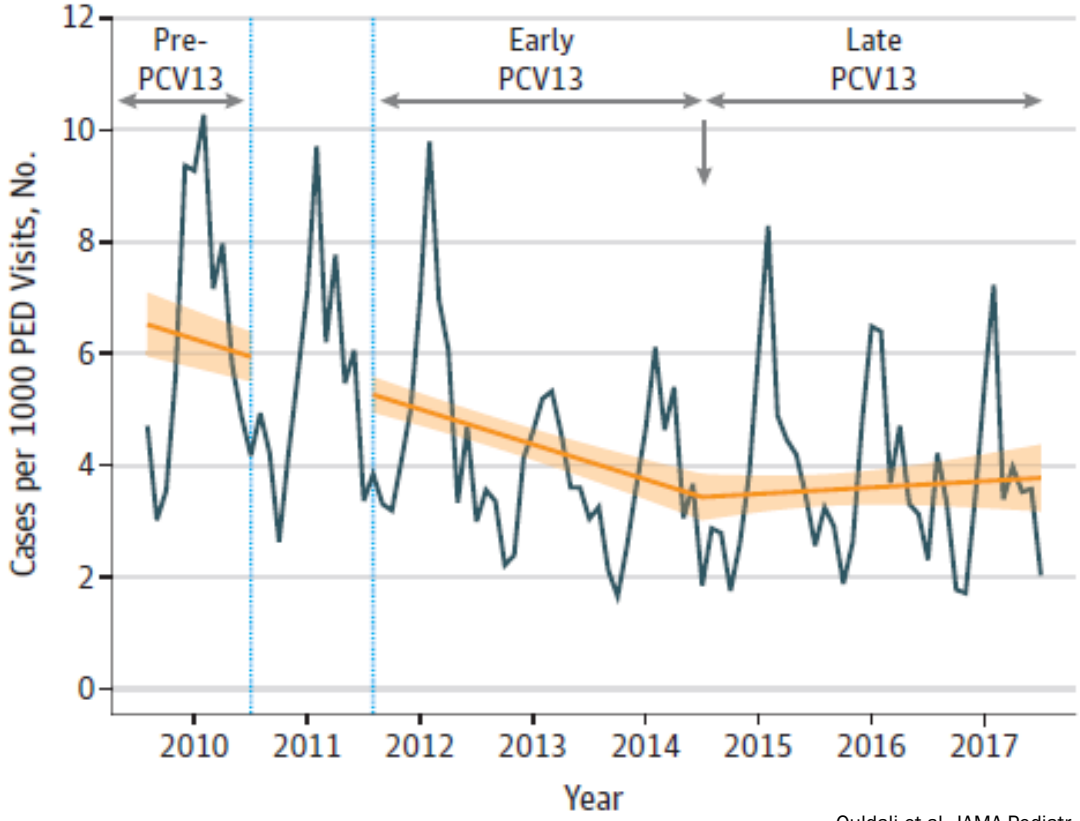
PNEUMOCOCCAL MENINGITIS IN CHILDREN <15 YEARS, FRANCE



ALL CAUSE PNEUMONIA IN CHILDREN <15 YEARS, FRANCE

N=12,567



44% decrease until May 2014

7% increase since June 2014

Ouldali et al. JAMA Pediatr. 2019 Feb 4. doi: 10.1001/jamapediatrics.2018.5273

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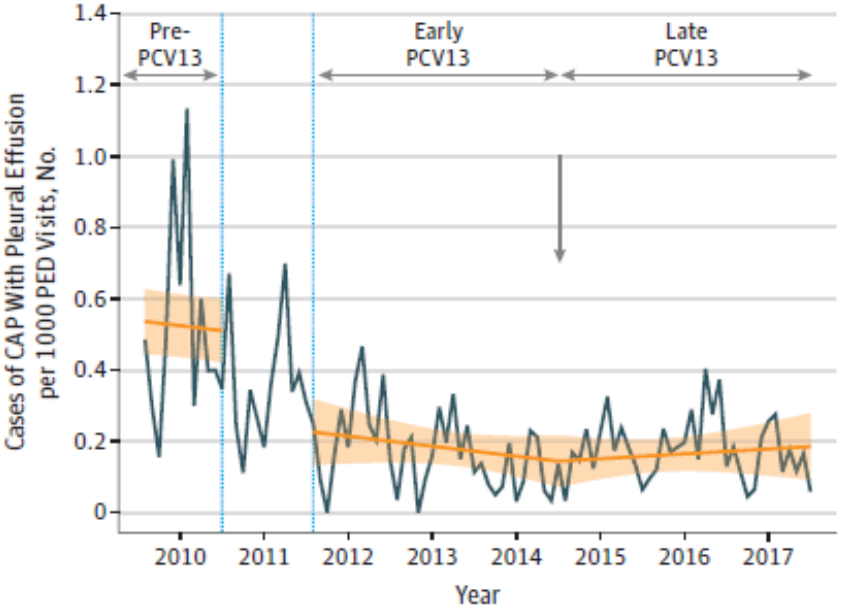
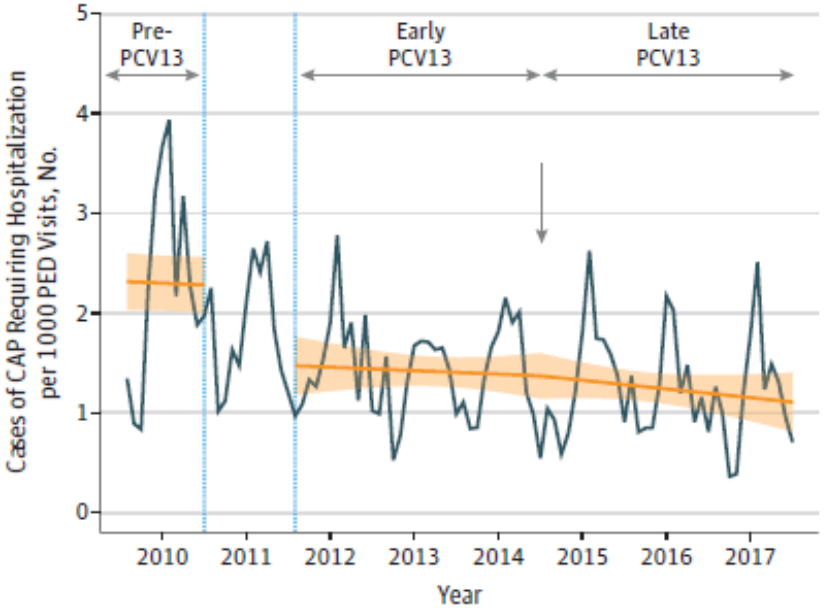
SEVERE PNEUMONIA IN CHILDREN <15 YEARS, FRANCE

Pneumonia with pleural effusion, n=673



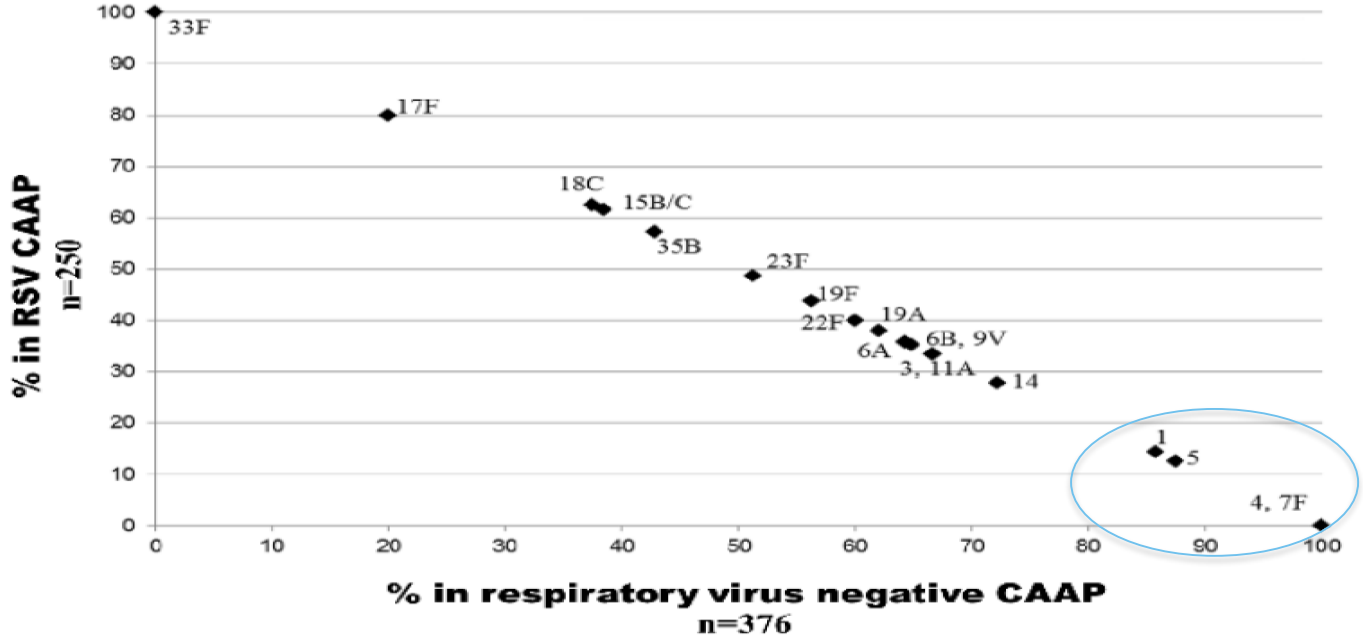
Hospitalized pneumonia, n=4273



InfoVac

Ouldali et al. JAMA Pediatr. 2019 Feb 4. doi: 10.1001/jamapediatrics.2018.5273

Greenberg et al. JID 2016. Nasopharyngeal pneumococcal carriage during childhood community-acquired alveolar pneumonia: Relationship between specific serotypes and co-infecting viruses



MADHI F JOURNAL OF THE PEDIATRIC INFECTIOUS DISEASES SOCIETY 2019

Table 1. Bacterial Causes Identified in Children Hospitalized for Parapneumonic Effusion and Pleural Empyema According to PCV13 Period

			After PCV13			
Bacterial Cause	Total (n = 220)	Before PCV13 (June 2009–May 2011) (n = 110)	First Period (June 2011–May 2013) (n = 48)	Second Period (June 2013–May 2015) (n = 29)	Third Period (June 2015–May 2017) (n = 33)	*P*
Streptococcus pneumoniae (n [%])	146 (66.4)	87 (79.1)	32 (66.7)	15 (51.7)	12 (36.4)	<.001
Positive pleural culture	33	25	4	2	2	
Positive blood culture	31	15	11	1	4	
Positive BinaxNOW/ag	72	40[a]	16[b]	11	5	
Positive PCR	10	7	1	1	1	
GAS (n [%])	38 (17.3)	7 (6.4)	10 (20.8)	6 (20.7)	15 (45.5)	<.001
Positive pleural culture	20	2	6	5	7	
Positive blood culture	2	0	1	0	1	
Positive PCR	16	5	3	1	7	
Staphylococcus aureus (n [%])	34 (15.5)	14 (12.7)	7 (14.6)	7 (24.1)	6 (18.2)	.472
Positive pleural culture	27	10	7	5	5	
Positive blood culture	7	4		2	1	
Others (n [%])	5	3[c]	1[d]	1[e]	—	—

Vaccine 33 (2015) 5072–5079

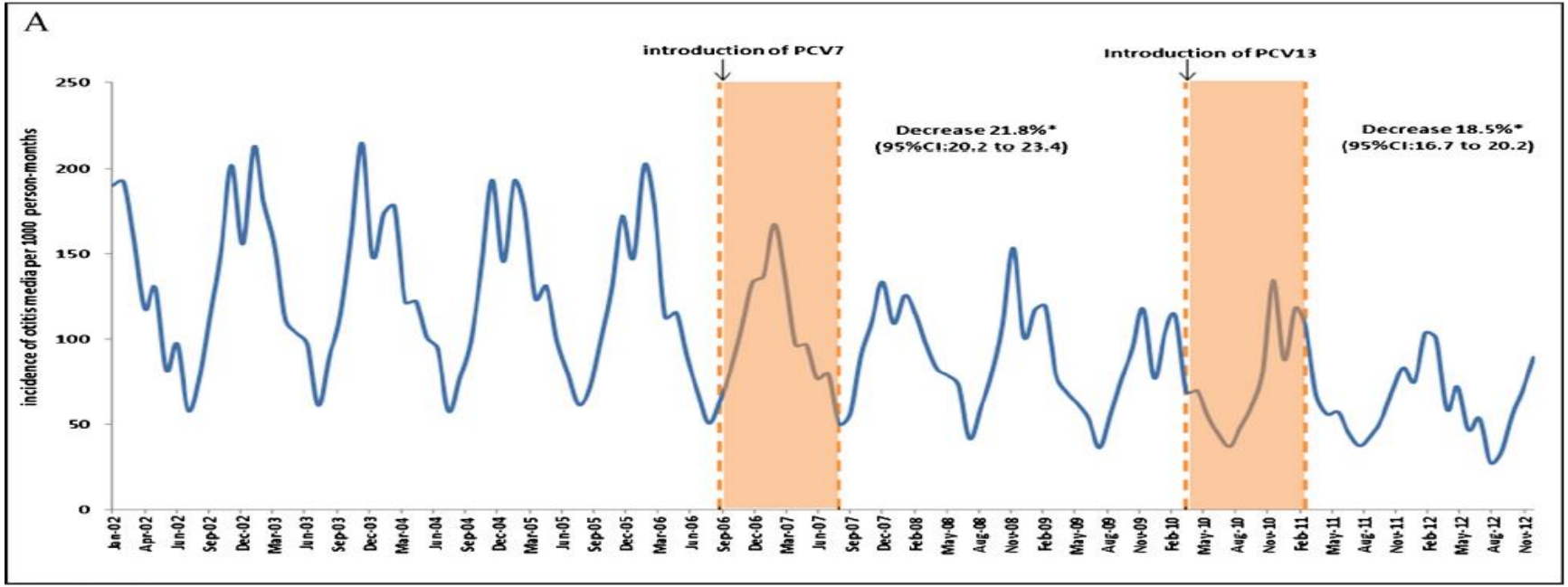
Contents lists available at ScienceDirect

Vaccine

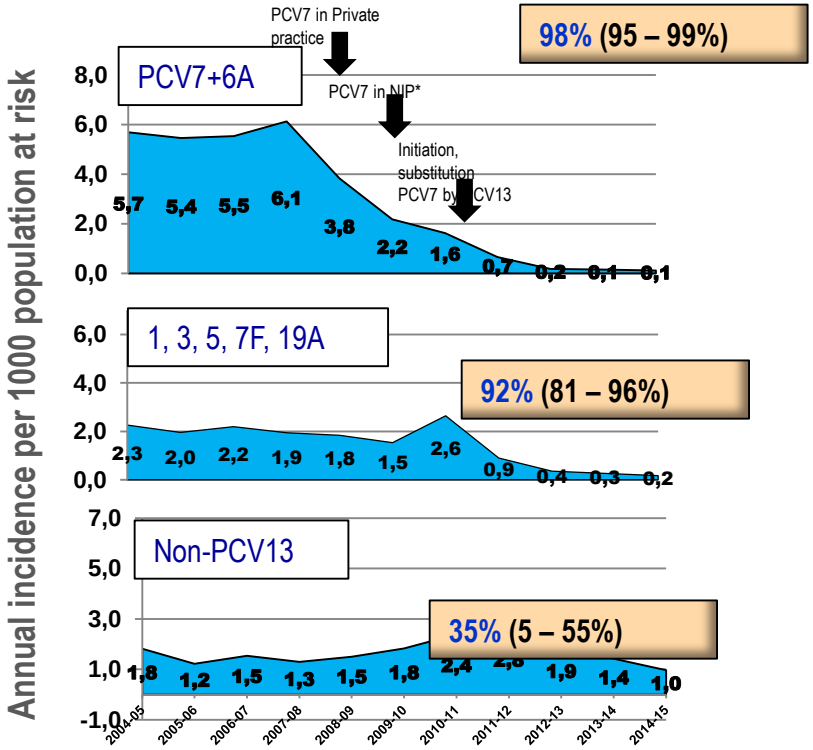
journal homepage: www.elsevier.com/locate/vaccine

Impact of pneumococcal conjugate vaccines on childhood otitis media in the United Kingdom

Wallis C.Y. Lau [a], Macey Murray [b], Aisha El-Turki [b,c], Sonia Saxena [d], Shamez Ladhani [e,g], Paul Long [f], Mike Sharland [g], Ian C.K. Wong [a,b], Yingfen Hsia [g,*]



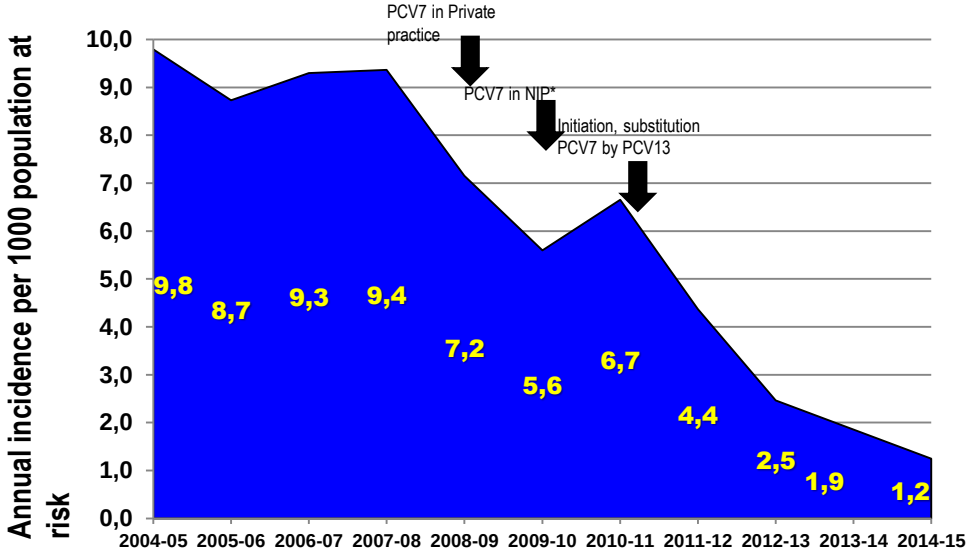
Impact of the Sequential PCV7/PCV13 Introduction to the NIP on Pneumococcal OM, Children < 24m



Ron Dagan slide

Rate Reduction 2014-2015 vs. 2004-2008

87% (82 – 90%)



All Pneumococcal OM

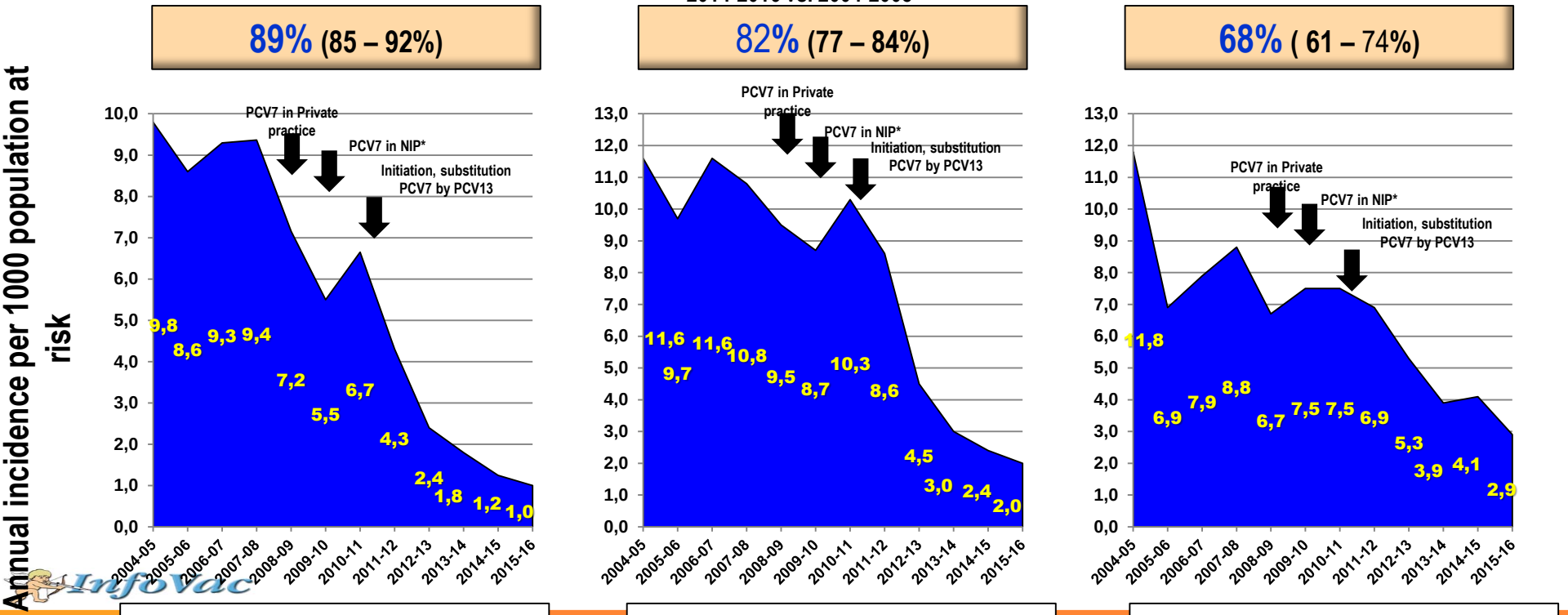
Ben-Shimol et al, CID 59:1724-32 , 2014, updated

Impact of the Sequential PCV7/PCV13 Introduction to the NIP on Pneumococcal OM, Children <24m

Ron Dagan slide

Rate Reduction
2014-2016 vs. 2004-2008

89% (85 – 92%) | **82%** (77 – 84%) | **68%** (61 – 74%)



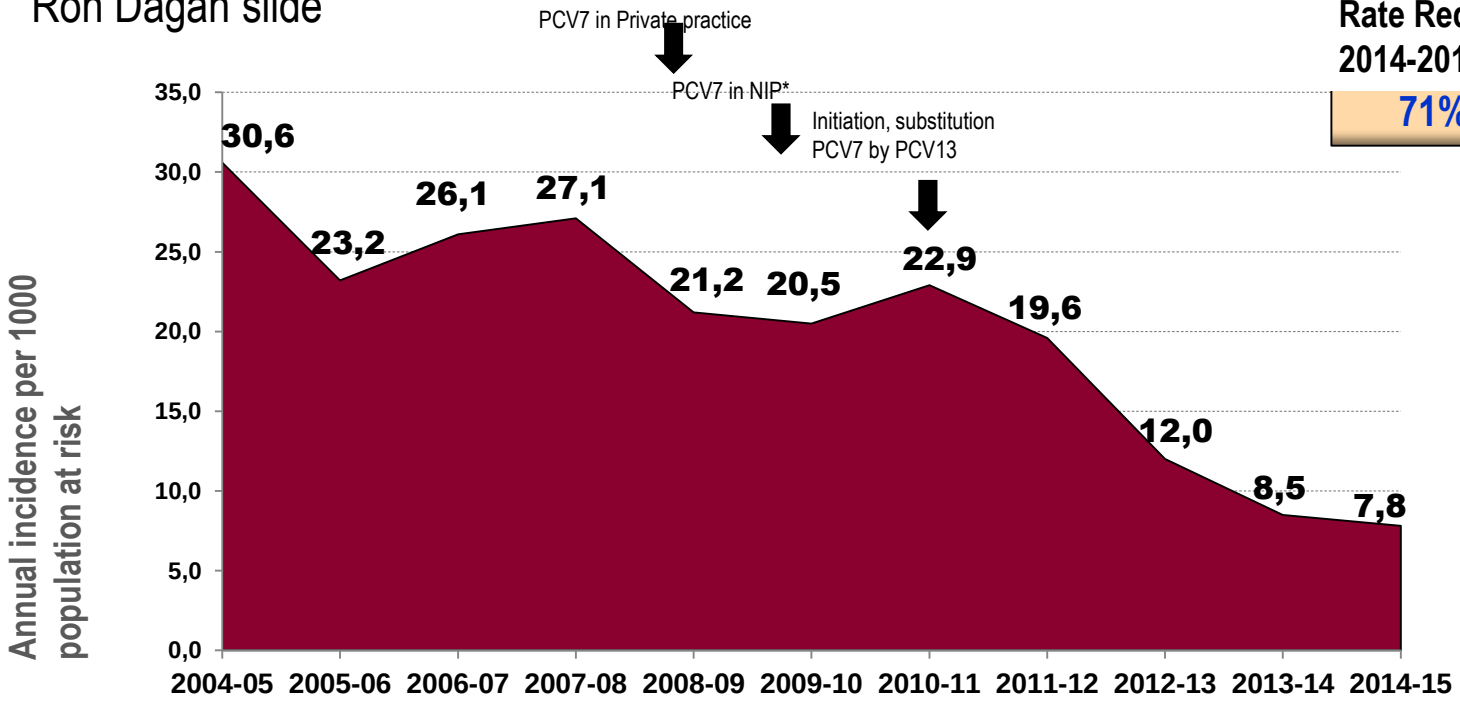
All Pneumococcal OM | NTHi | Culture-negative

Each study year is July 1st through June 30th

Ben-Shimol et al, 63:611-8, 2016, Updated

SOUTHERN ISRAEL, 2004-2015*
Overall OM (pneumococcal and non-pneumococcal) incidence in children < 24m with MEF culture

Ron Dagan slide



Rate Reduction 2014-2015 vs. 2004-2008

71% (59 – 74%)

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* Each study year is July 1st through June 30th

Ben-Shimol et al, CID 59:1724-32 , 2014, updated

Review

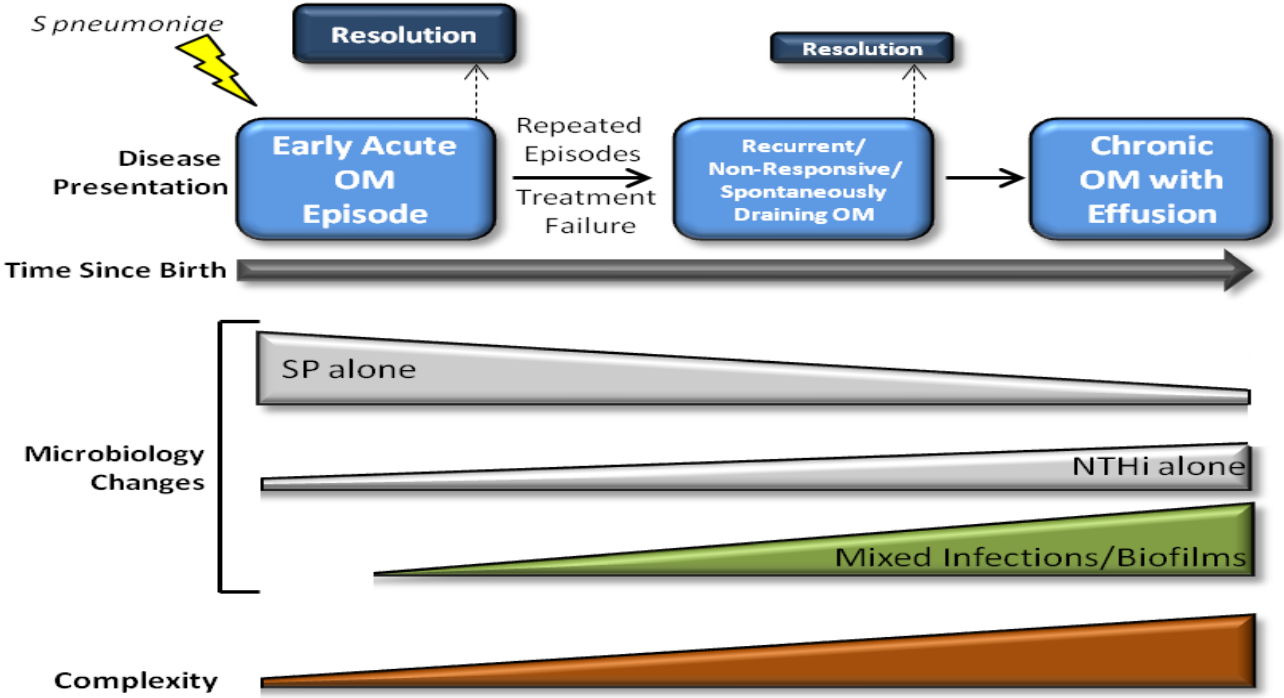
Prevention of early episodes of otitis media by pneumococcal vaccines might reduce progression to complex disease

Ron Dagan, Stephen Pelton, Lauren Bakaletz, Robert Cohen

Lancet Infect Dis 2016; 16: 480–92

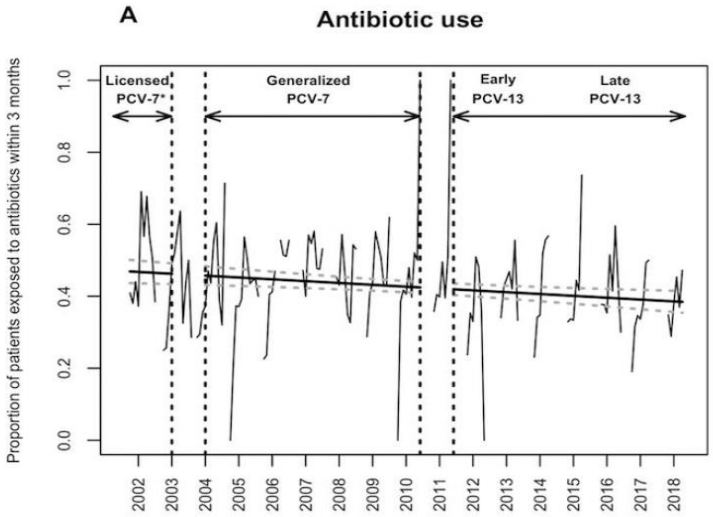
Otitis media is a common childhood infection of the middle ear and a major cause of morbidity. This multifactorial disease manifests as a spectrum of clinical syndromes from uncomplicated acute otitis media to more complex

Involvement of *S pneumoniae* in OM evolution: the disease continuum model of pathogenesis



InfoVac

Dagan et al et al, lancet Infect Dis


A
Antibiotic use
Licensed PCV-7*
Generalized PCV-7
Early PCV-13
Late PCV-13
Proportion of patients exposed to antibiotics within 3 months
0.0
0.2
0.4
0.6
0.8
1.0
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
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2013
2014
2015
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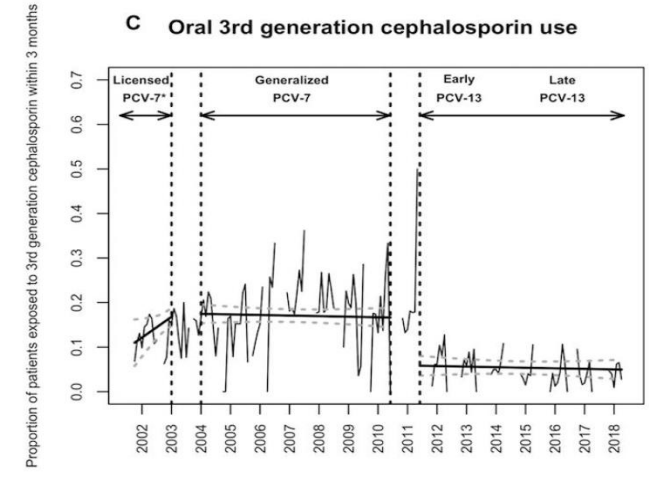
2017
2018


C
Oral 3rd generation cephalosporin use
Licensed PCV-7*
Generalized PCV-7
Early PCV-13
Late PCV-13
Proportion of patients exposed to 3rd generation cephalosporin within 3 months
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
2002
2003
2004
2005
2006
2007
2008
2009
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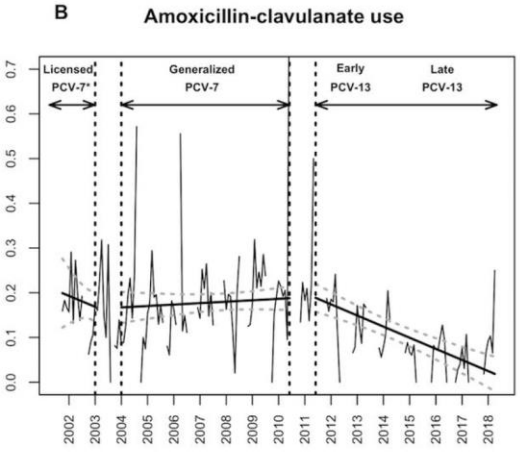
B
Amoxicillin-clavulanate use
Licensed PCV-7*
Generalized PCV-7
Early PCV-13
Late PCV-13
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
2002
2003
2004
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2006
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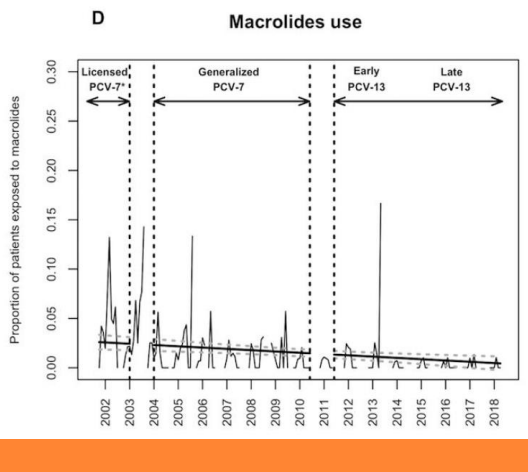
2018


D
Macrolides use
Licensed PCV-7*
Generalized PCV-7
Early PCV-13
Late PCV-13
Proportion of patients exposed to macrolides
0.00
0.05
0.10
0.15
0.20
0.25
0.30
2002
2003
2004
2005
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2007
2008
2009
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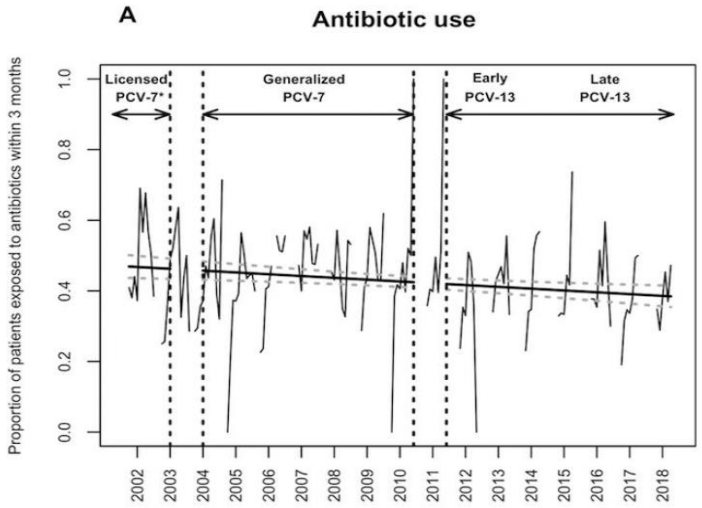
2017
2018


A
Antibiotic use
Proportion of patients exposed to antibiotics within 3 months
Licensed PCV-7*
Generalized PCV-7
Early PCV-13
Late PCV-13
0.0
0.2
0.4
0.6
0.8
1.0
2002
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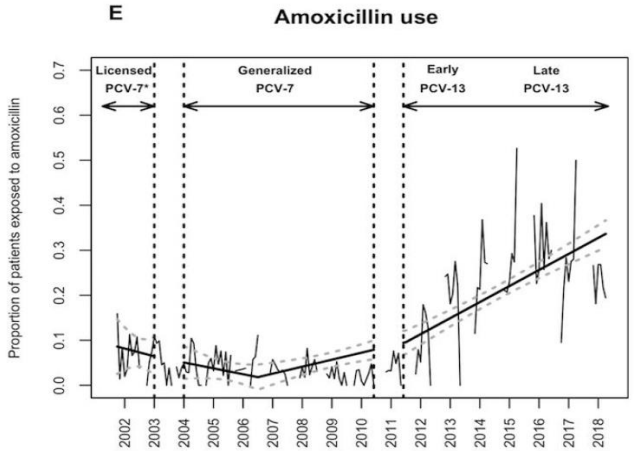
E
Amoxicillin use
Proportion of patients exposed to amoxicillin
Licensed PCV-7*
Generalized PCV-7
Early PCV-13
Late PCV-13
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
2002
2003
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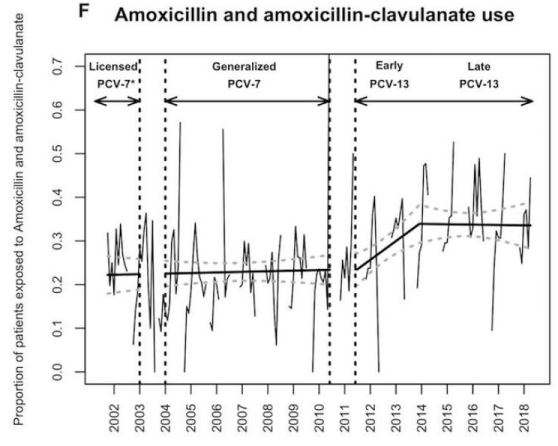
2016
2017
2018


F
Amoxicillin and amoxicillin-clavulanate use
Proportion of patients exposed to Amoxicillin and amoxicillin-clavulanate
Licensed PCV-7*
Generalized PCV-7
Early PCV-13
Late PCV-13
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
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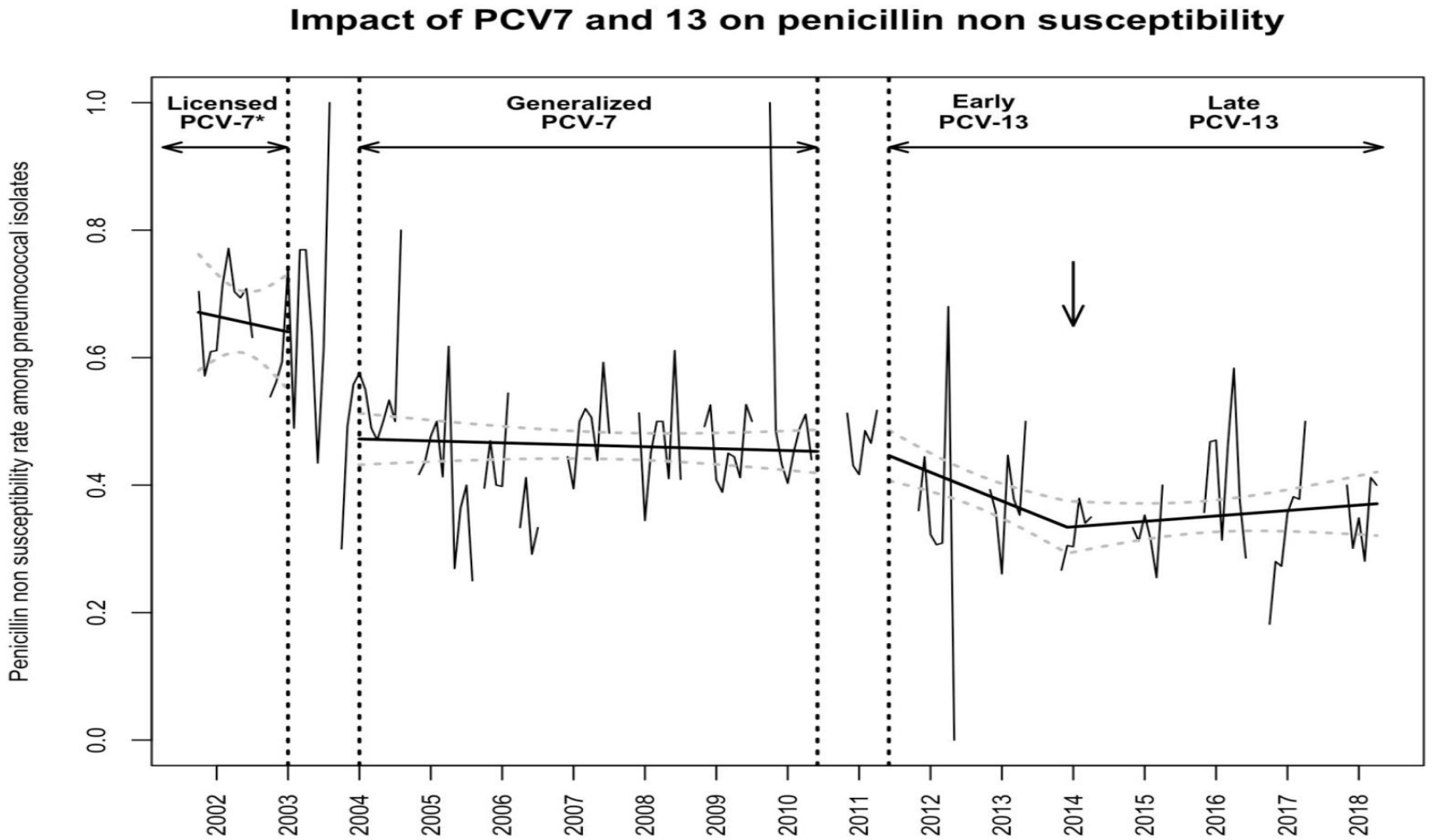
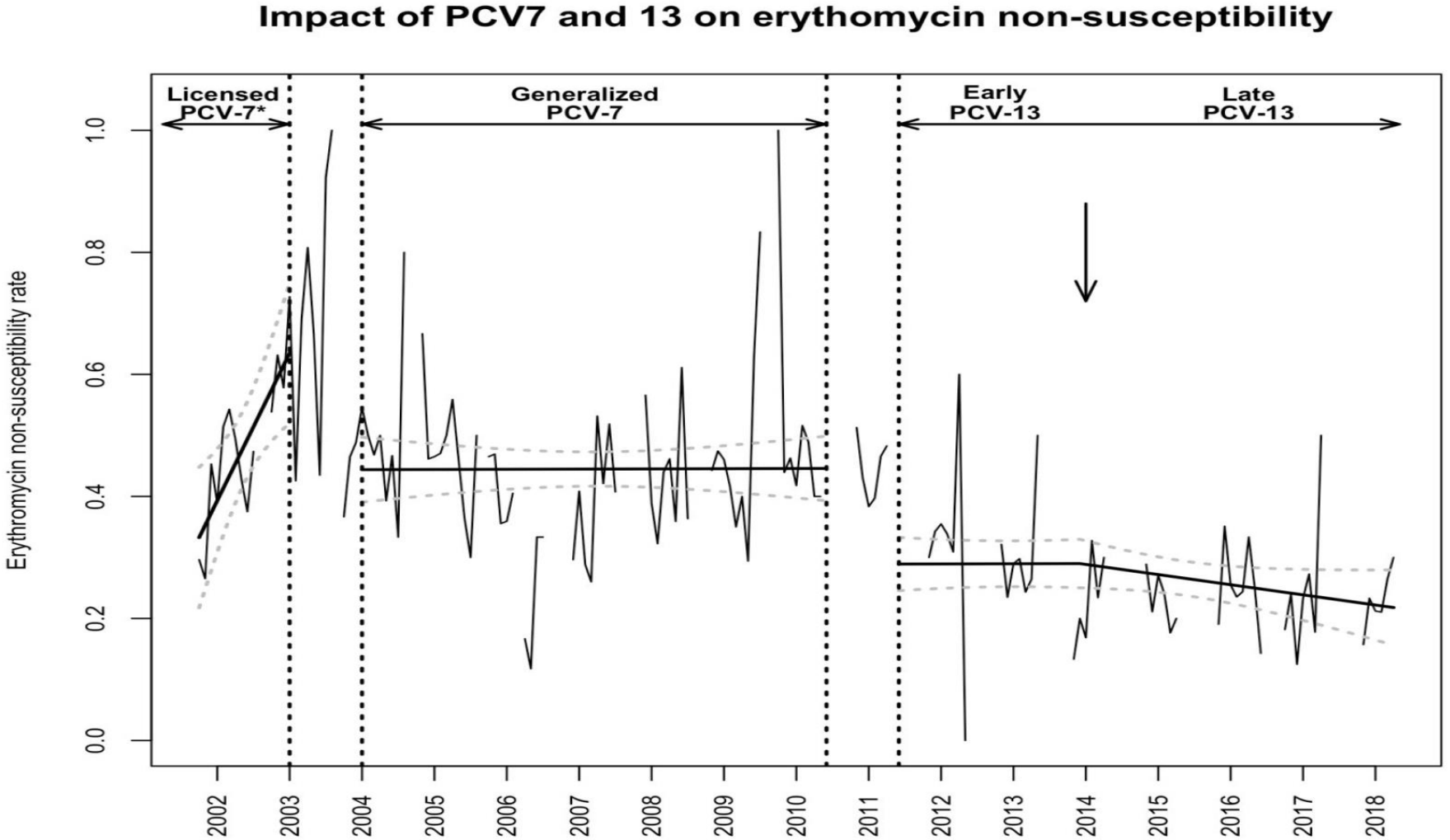
2014
2015
2016
2017
2018

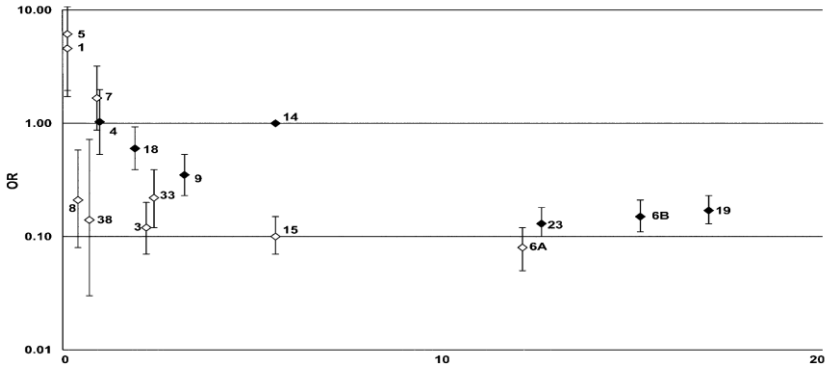

Impact of PCV7 and 13 on penicillin non susceptibility
Licensed PCV-7*
Generalized PCV-7
Early PCV-13
Late PCV-13
Penicillin non susceptibility rate among pneumococcal isolates
0.0
0.2
0.4
0.6
0.8
1.0
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018


Impact of PCV7 and 13 on erythomycin non-susceptibility
Licensed PCV-7*
Generalized PCV-7
Early PCV-13
Late PCV-13
Erythromycin non-susceptibility rate
0.0
0.2
0.4
0.6
0.8
1.0
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018

Brueggeman JID 2003;187: 1427…IPD 150/Ca351

Serotype[a]	Total	Invasive	Carriage	OR (95% CI)[b]
4	6	5	1	**12.1 (1.4–104.2)**
1	5	4	1	**9.6 (1.1–86.5)**
14	75	54	21	**8.8 (5.1–15.4)**
18C	29	20	9	**5.8 (2.6–13.2)**
23F	48	7	41	**0.4 (0.2–0.8)**

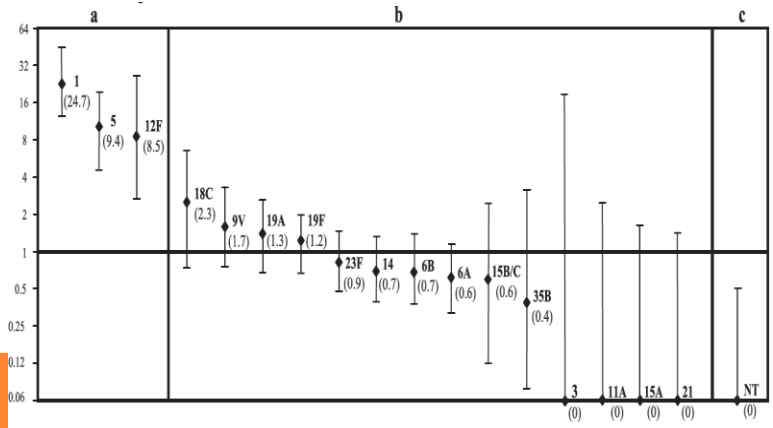
Brueggeman JID 2004;190:1203…IPD 769/Ca 492

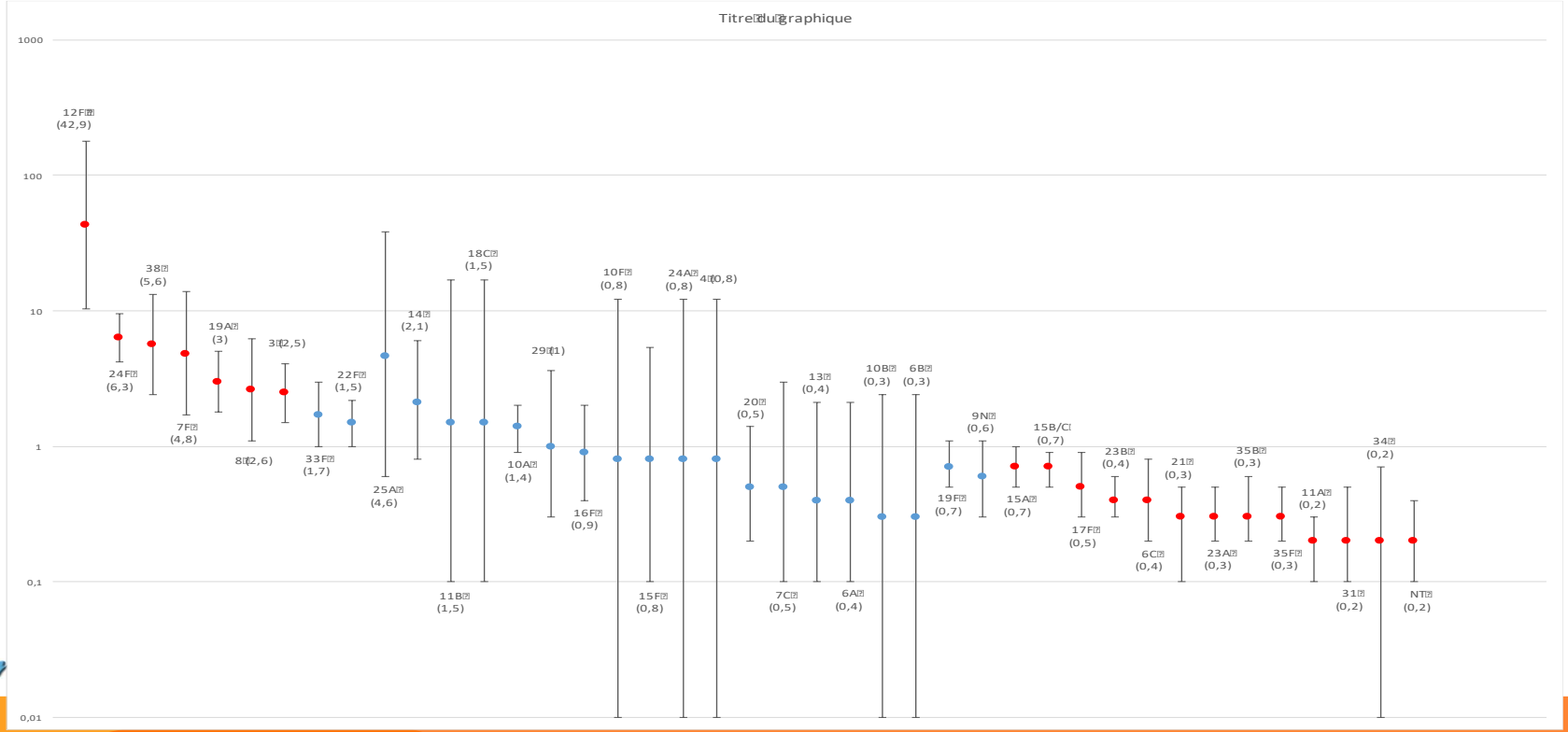


Hannage 2005;73:431…IPD 224

Serogroup or serotype	No. of invasive isolates (No. of carriage isolates)	OR	95% CI
38	6 (1)	5.94	0.71–49.79
14	40 (11)	**4.07**	2.03–8.17
18C	13 (4)	**3.28**	1.05–10.23
19A	17 (6)	**2.89**	1.12–7.47
7F	15 (6)	2.52	0.96–6.63
4	7 (4)	1.72	0.50–5.95
6B	51 (33)	**1.643**	1.01–2.67
9V	8 (5)	1.57	0.51–4.88
19F	22 (30)	0.68	0.38–1.22
23F	20 (29)	0.64	0.35–1.16
3	1 (2)	0.48	0.04–5.36
10	1 (2)	0.48	0.04–5.36
6A	14 (28)	**0.45**	0.23–0.88
15	2 (5)	0.38	0.07–1.99
22	1 (4)	0.23	0.03–2.15
35F	2 (9)	**0.21**	0.04–0.98

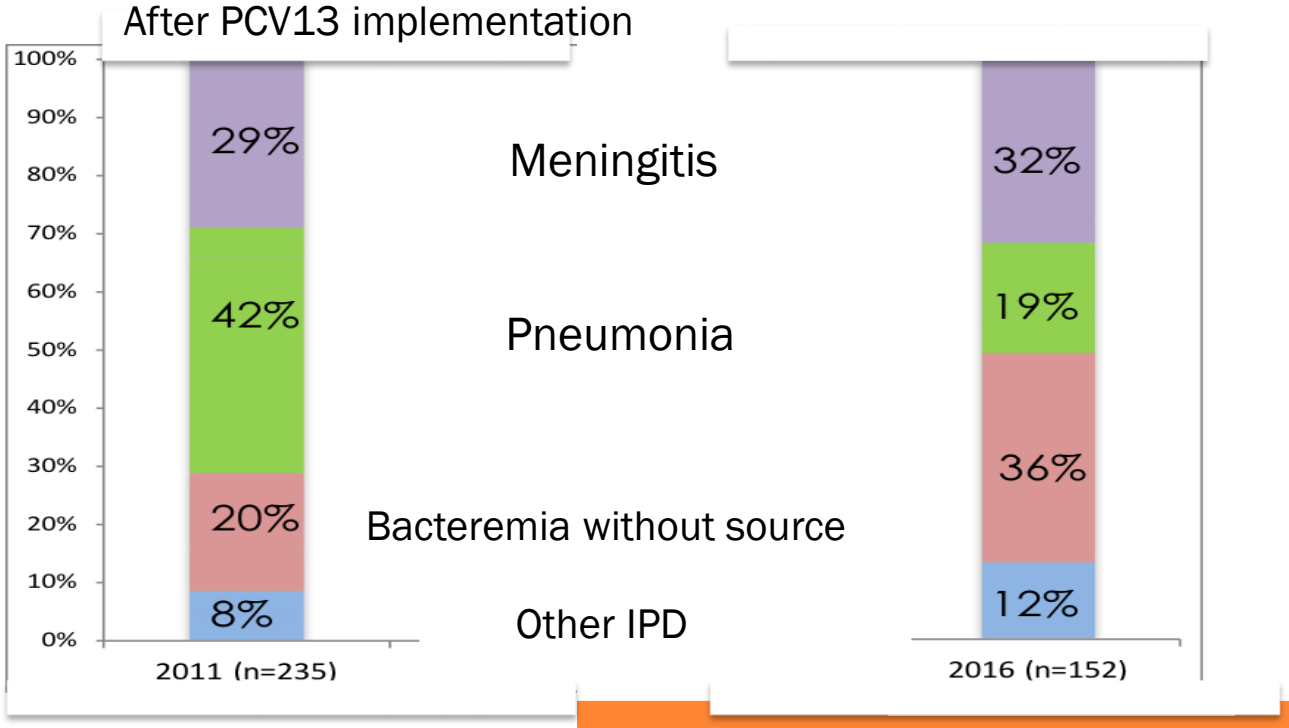
Shouval PIDJ 2006;25:603… IPD189/ Ca176




Titre du graphique
1000
100
10
1
0,1
0,01
12F (42,9)
24F (6,3)
38 (5,6)
7F (4,8)
19A (3)
8 (2,6)
3 (2,5)
33F (1,7)
22F (1,5)
25A (4,6)
14 (2,1)
11B (1,5)
18C (1,5)
10A (1,4)
29 (1)
16F (0,9)
10F (0,8)
15F (0,8)
24A (0,8)
4 (0,8)
20 (0,5)
7C (0,5)
13 (0,4)
6A (0,4)
10B (0,3)
6B (0,3)
19F (0,7)
9N (0,6)
15A (0,7)
15B/C (0,7)
17F (0,5)
23B (0,4)
6C (0,4)
21 (0,3)
23A (0,3)
35B (0,3)
35F (0,3)
11A (0,2)
31 (0,2)
34 (0,2)
NT (0,2)

DISTRIBUTION OF IPD BY CLINICAL ENTITIES

1082 IPD from 2011 to 2016



35% in total IPD cases

ALL SEROTYPES WERE ABLE TO INDUCE ALL CLINICAL PRESENTATIONS, HOWEVER…

PCV type and serotypes	Pneumonia N=340 % [95% CI]	Meningitis N=335 % [95% CI]	Bacteremia without an identified source N=301 % [95% CI]	Other IPD N=106 % [95% CI]
PCV13+6C (n=372)	58.1 [52.9;63.1]	21.5 [17.4;26.0]	13.2 [9.9;17.0]	7.3 [4.8;10.4]
Non-PCV13 (n=710)	17.5 [14.7;20.5]	35.9 [32.4;39.6]	35.5 [32.0;39.1]	11.1 [8.9;13.7]

Levy C CID March 2019

ALL SEROTYPES WERE ABLE TO INDUCE ALL CLINICAL PRESENTATIONS, HOWEVER… FOR NVT WITH HIGH AND LOW DP

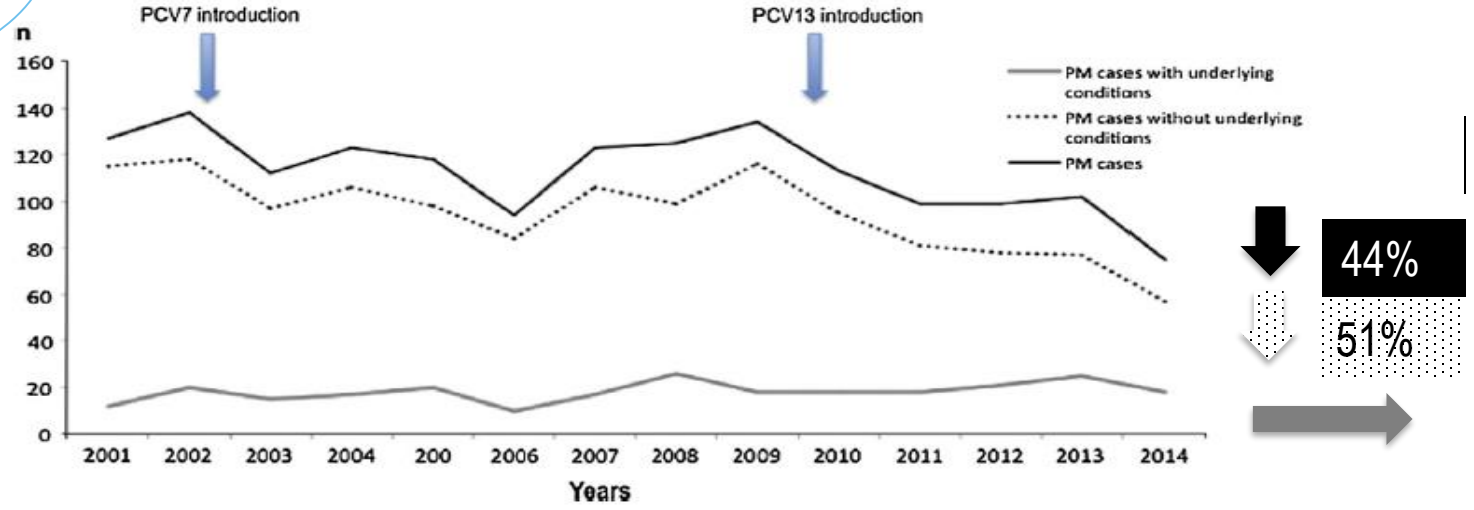
PCV type and serotypes	Pneumonia N=340 % [95% CI]	Meningitis N=335 % [95% CI]	Bacteremia without an identified source N=301 % [95% CI]	Other IPD N=106 % [95% CI]
Non-PCV13 (n=710)	**17.5 [14.7;20.5]**	**35.9 [32.4;39.6]**	**35.5 [32.0;39.1]**	**11.1 [8.9;13.7]**
High disease potential* (including serotypes 8, 12F, 24F, 33F, n=252)	27.8 [22.3;33.7]	31.3 [25.7;37.5]	32.1 [26.4;38.3]	8.7 [5.6;12.9]
Low disease potential* (including serotypes 15A, 15BC, 23B, 16F, n=173)	9.8 [5.8;15.3]	38.7 [31.4;46.4]	39.9 [32.5;47.6]	11.6 [7.2;17.3]

* Using the classification of Balsells et a. Plos One 2017

Levy C CID March 2019

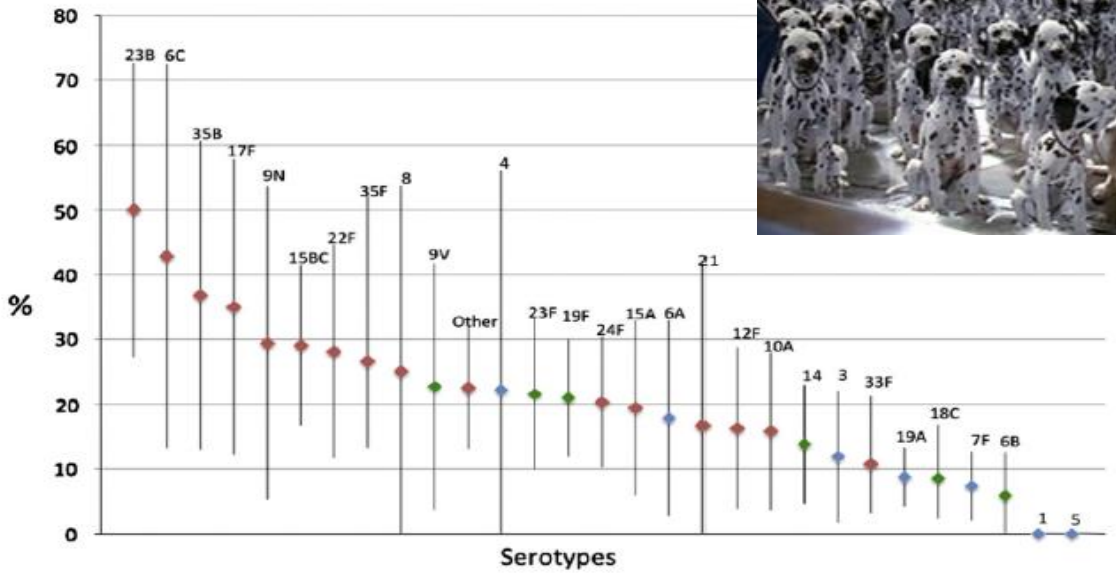
Distribution des méningites à pneumocoque en fonction de la présence de facteurs de risque

Le nombre de patients ayant un FDR et une méningite à pneumocoque est resté stable après l'introduction des PCVs.



Cohen R. Vaccine 2016

Prévalence de méningites à pneumocoque avec facteur de risque par sérotype



Data are percentage (95% CI).

Other = all non vaccine serotypes < 12 cases

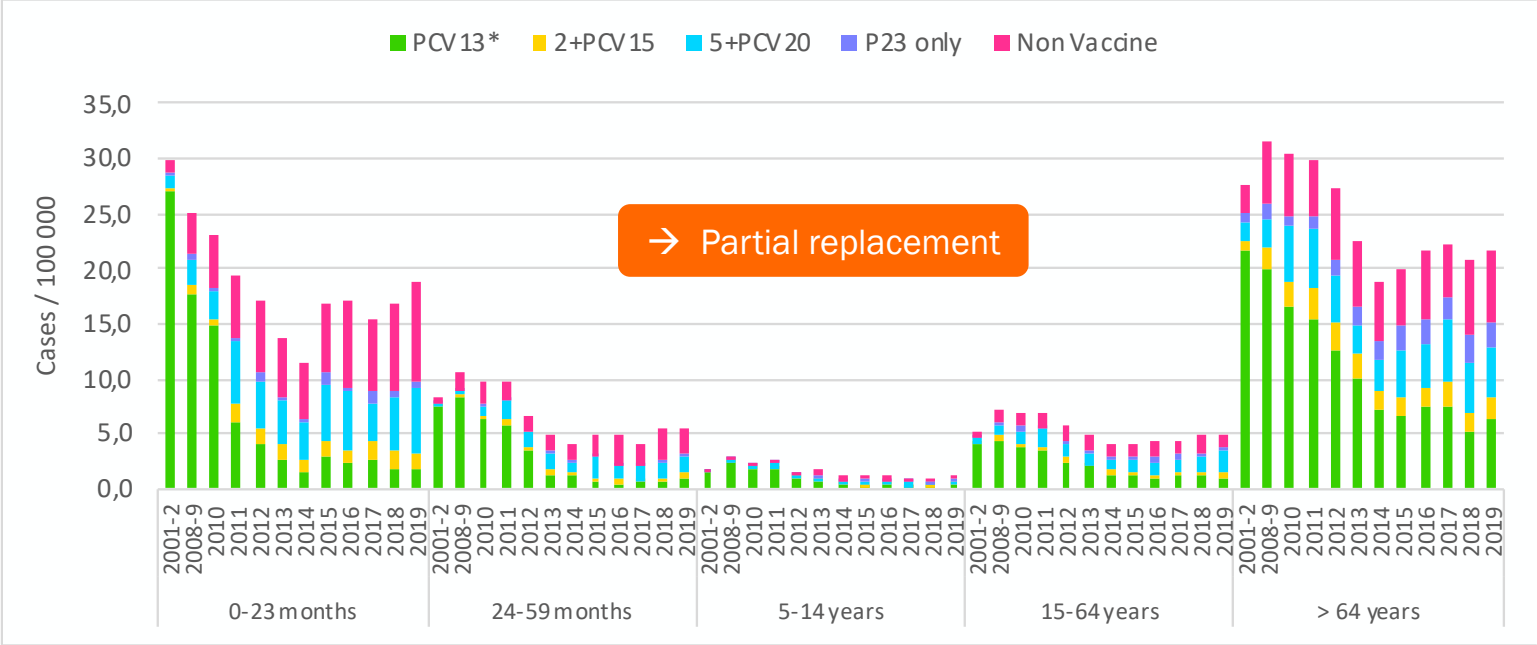
Les sérotypes vaccinaux (PCV13) ont diminué de 68% dans cette population

Vaccins contre les pneumocoques

- **PCV13** : 4, 6B (C), 9V, 14, 18C, 19F, 23F + 1, 3, 5, 6A, 7F, 19A
- **PCV15** : 13v + 22F et 33F
- **PCV20** : 15v + 8, 10A, 11A, 12F et 15B/C
- **Pneumovax :** 2, 9N, 17F, 20

Aucun ne contient : le 24F et le 23B

INCIDENCE RATE OF IPD ACCORDING TO GROUP OF SEROTYPES, FRANCE

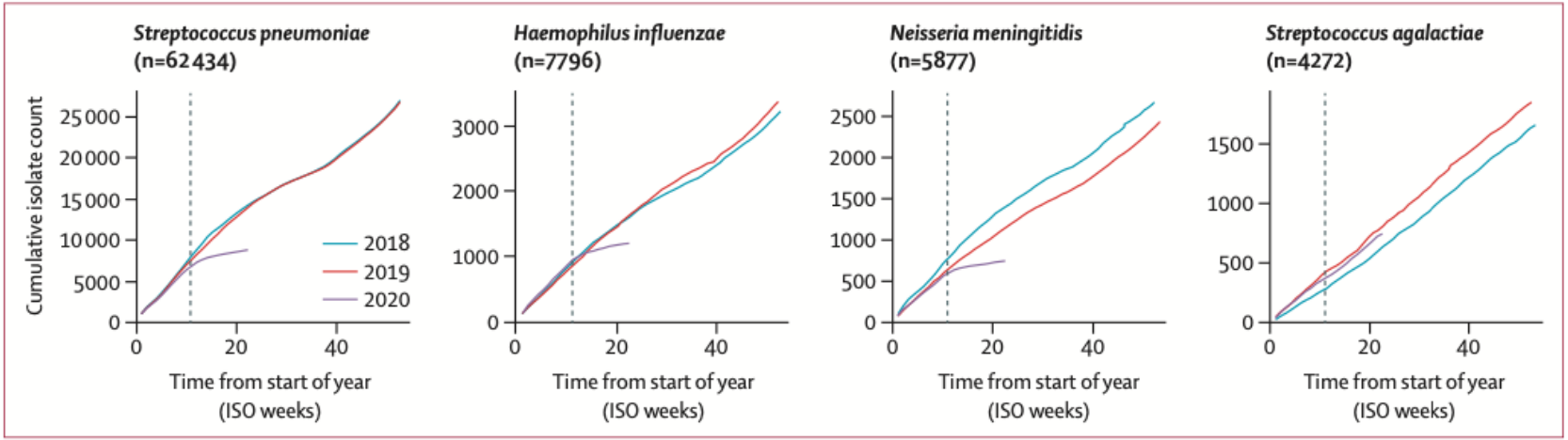


Incidence rate: EPIBAC-Santé Publique France

CNRP-ORP, Rapport d'activité 2020

INVASIVE BACTERIAL DISEASES DURING THE COVID-19 PANDEMIC

Significant reductions

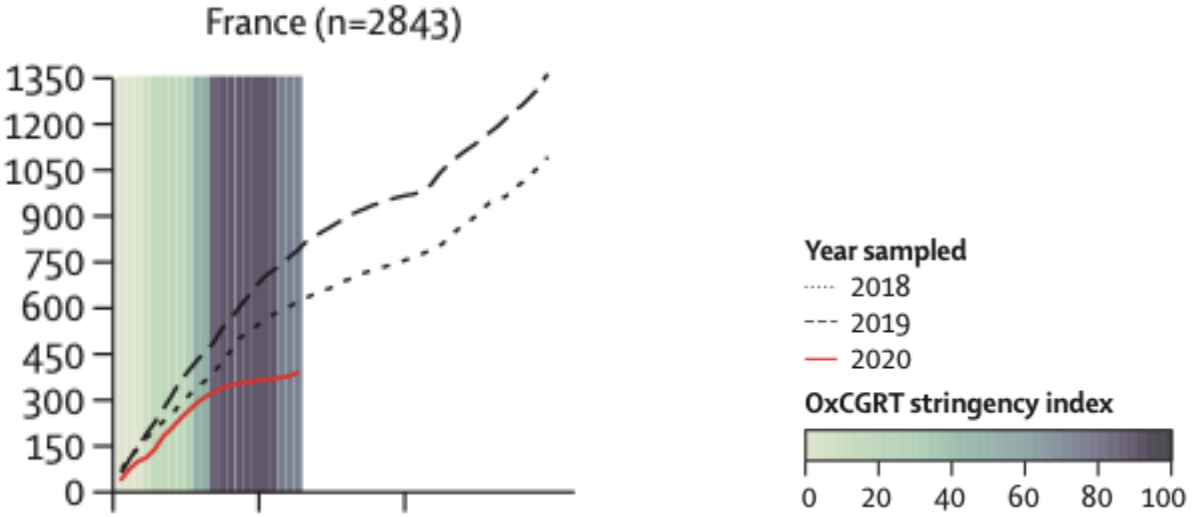


Cumulative number of invasive disease cases collected by Invasive Respiratory Infection Surveillance laboratories in 26 countries and territories each week from Jan 1, 2018 to May 31, 2020.

The World Health Organization (WHO) officially declared the COVID-19 pandemic in week 11 of 2020 (grey dotted line).

Brueggemann *et al*, Lancet Digit Health 2021; 3: e360–70

IPD IN FRANCE DURING THE COVID-19 PANDEMIC



Annual invasive *Streptococcus pneumoniae* cases submitted to Invasive Respiratory Infection Surveillance laboratories from Jan 1, 2018, to May 31, 2020

Brueggemann *et al*, Lancet Digit Health 2021; 3: e360–70

CONCLUSIONS

- **Incidence des infections pneumococciques ↘↘ à ↘↘↘**
  - La surveillance doit se poursuivre
- **Spectre des infections pneumococciques : il a changé**
  - Répartition des différentes infections
  - Augmentation de la proportion des patients présentant une pathologie sous jacente
- **Sérotypes du pneumocoque**
  - Bouleversement
  - Plus grand chantier écologique depuis l'avènement de l'antibiothérapie
- **La résistance aux antibiotiques ↘**

M A I S