

# Vaccins anti-pneumococciques conjugués de nouvelle génération : quel impact, quels schémas ?

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*Journée du groupe Vaccination-Prévention de la SPILF*

*12 mai 2023*



# Liens d'intérêt 2020-2022

- **Liens durables ou permanents : Néant**
- **Interventions ponctuelles : Pfizer, MSD**
- **Intérêts indirects : Pfizer, MSD**

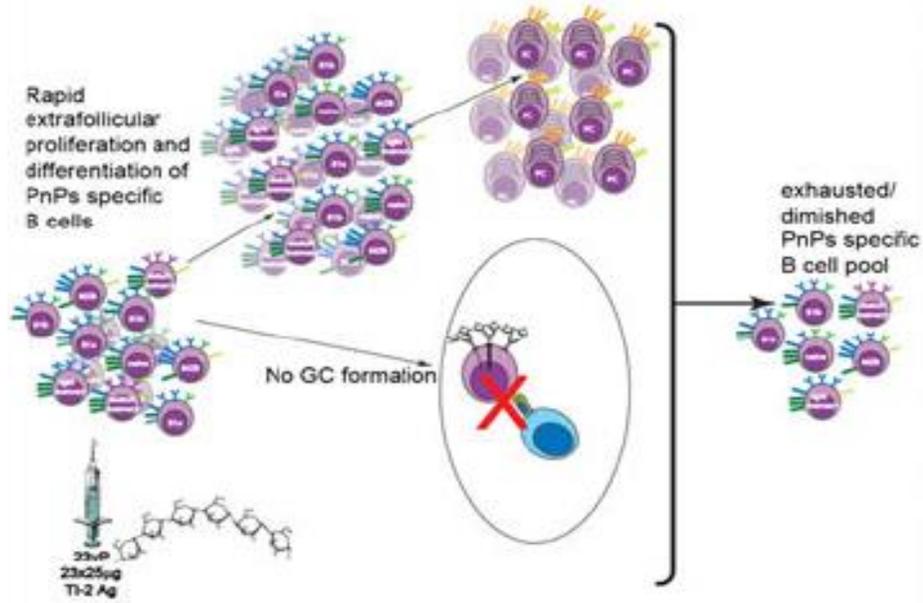
- Vaccins

- Polyosidique 23-valent : **sujets > 2 ans à risque**
- Depuis 2002 : Vaccin conjugué recommandé pour les enfants < 2 ans en France
  - 7-valent Prevenar : 4, 6B, 9V, 14, 18C, 19F, 23F
  - 13-valent Prevenar13 : 7-valent + 1, 3, 5, 6A, 7F, 19A

- De nouveaux vaccins en cours d'essais cliniques

- 15-valent MSD : 13-valent + 22F et 33F
  - Vaxneuvance
- 20-valent Pfizer : 13-valent + 8, 10A, 11A, 12F, 15B/C, 22F et 33F
  - APEXXNAR (EU) - PREVNAR 20™ (USA)
- 24-valent MSD, Affinivax (23-valent + 6A)

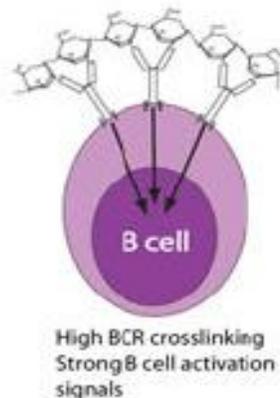
# Immunogénicité du vaccin polysidique 23-valent



Ag = Polyosides capsulaires

## Immunogénicité

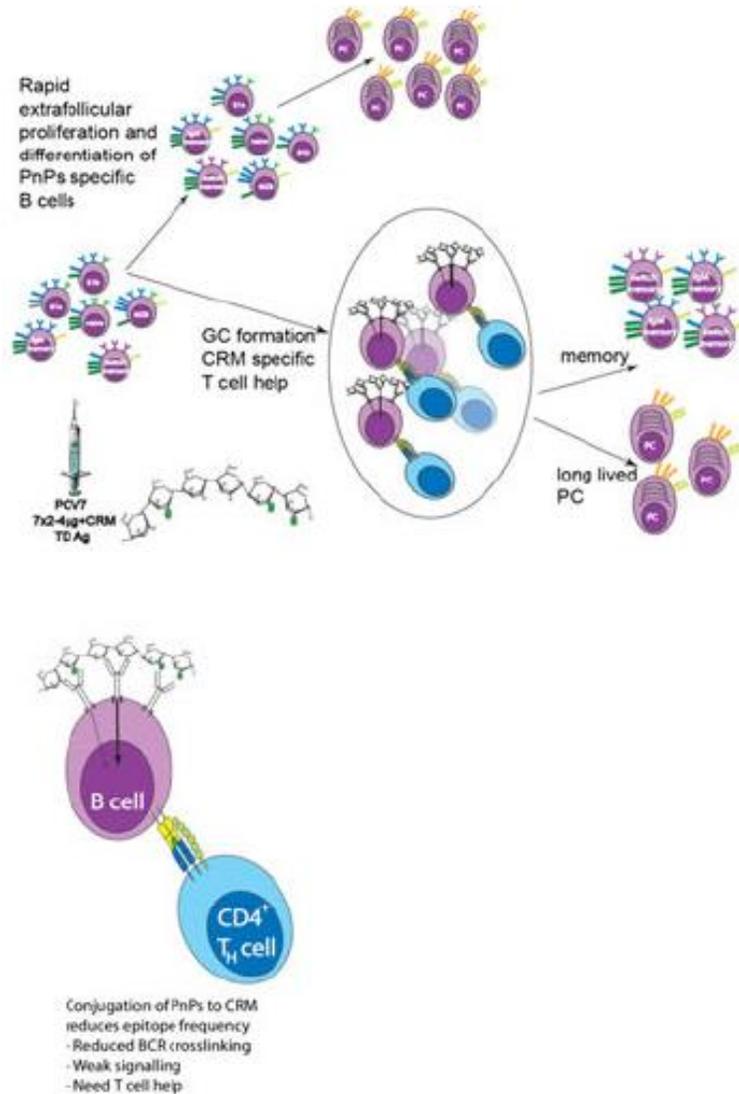
- Ag thymo-**in**dépendant → prolifération des LB spécifiques et différenciation en cellules productrices d'anticorps **sans le concours des LT auxiliaires**
- Pas de mise en place de la mémoire immunitaire
- Stimulation +++ → **déplétion en LB**
- Réponse AC insuffisante avant l'âge de 2 ans



Pas de mémoire immunitaire :  
→ **revaccination** au bout de 5 ans compte-tenu de la durée de vie des Ac

D'après Clutterbuck *et al.*, JID 2012

# Immunogénicité des vaccins conjugués



- Réponse Ac précoce, dès l'âge de 6-8 semaines
- Réponse mémoire
- Meilleure activité fonctionnelle et avidité
- Réponse immune au niveau des muqueuses du rhinopharynx ++
  - Réduction du portage rhinopharyngé

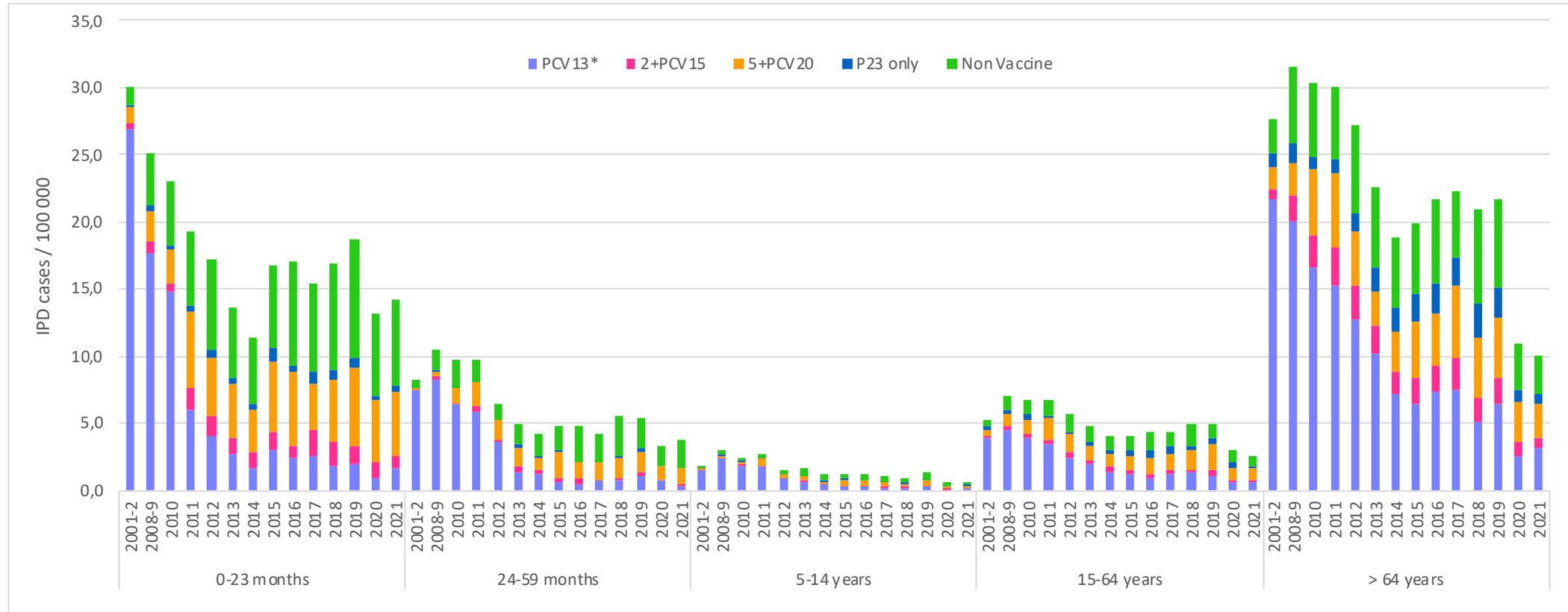
→ Immunité de groupe

D'après Clutterbuck *et al.*, JID 2012

# Incidence rate of IPD according to group of serotypes, France

**PCV13** : 4, 6B, 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    **P23 only** : 2, 9N, 17F, 20

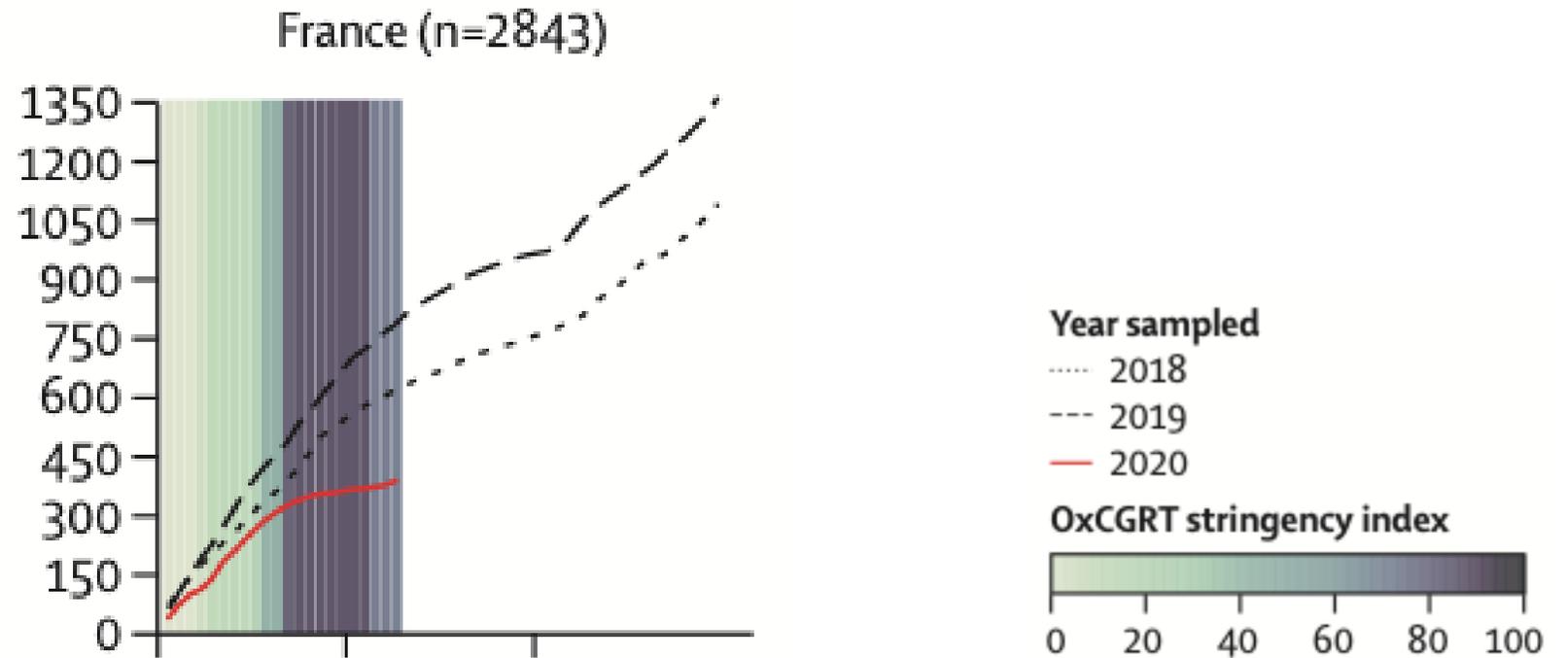


Significant decrease in all age groups

→ Partial replacement

Incidence rate: EPIBAC-SantéPublique France  
CNRP-ORP 2021, unpublished data

# IPD in France during the COVID-19 pandemic

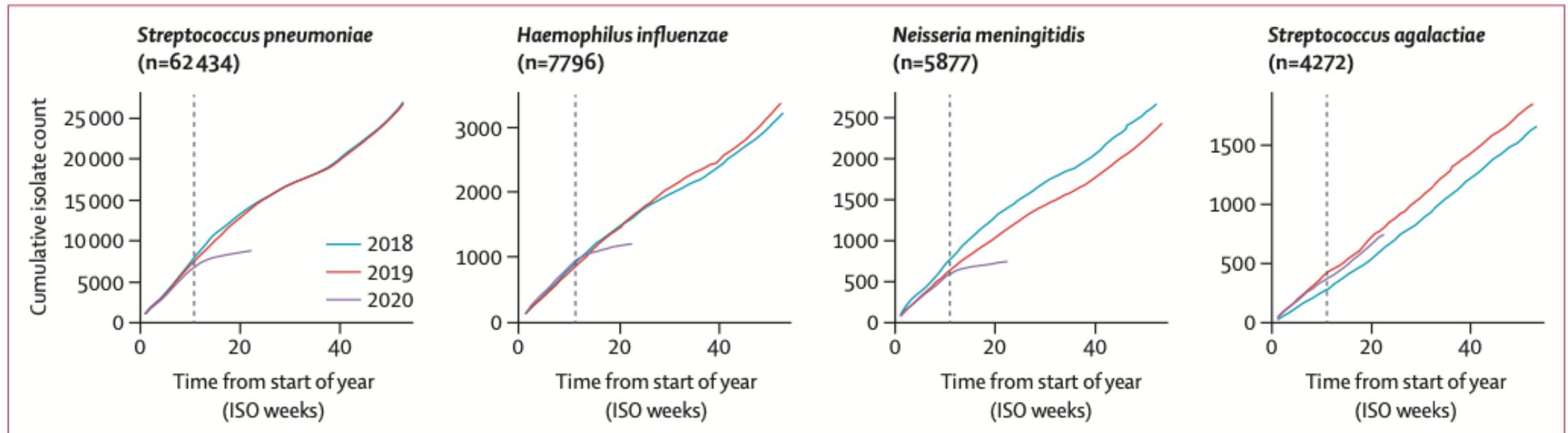


Annual invasive *Streptococcus pneumoniae* cases submitted to Invasive Respiratory Infection Surveillance laboratories from Jan 1, 2018, to May 31, 2020

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

# Incidence of 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.

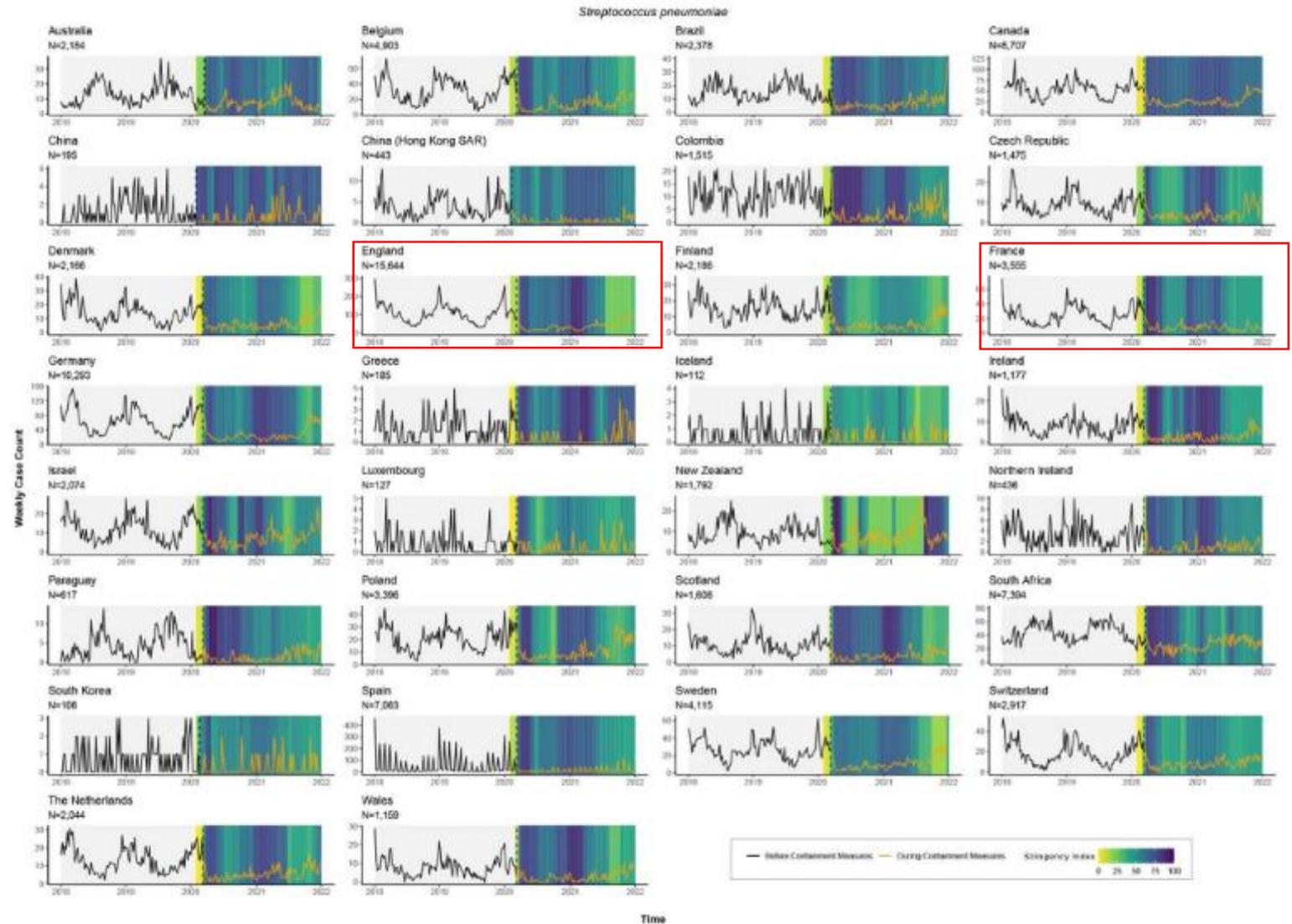
*The World Health Organization (WHO) officially declared the COVID-19 pandemic in week 11 of 2020 (grey dotted line).*

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

# Sustained reductions in life-threatening invasive bacterial diseases during the first two years of the COVID-19 pandemic: analyses of prospective surveillance data from 30 countries participating in the IRIS Consortium

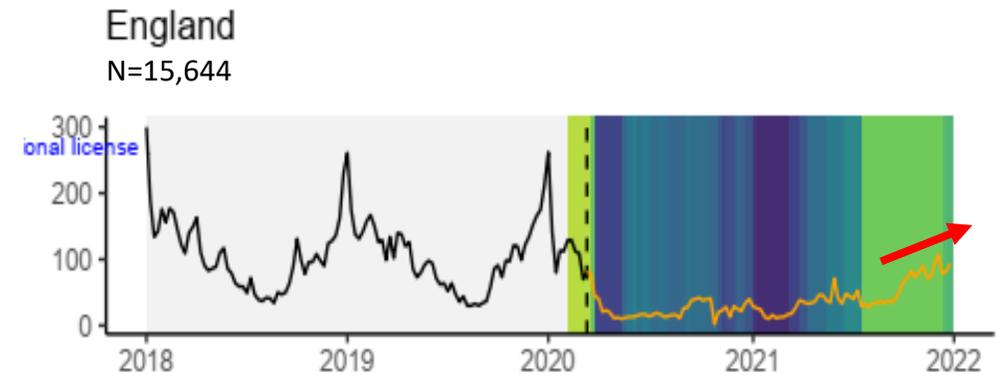
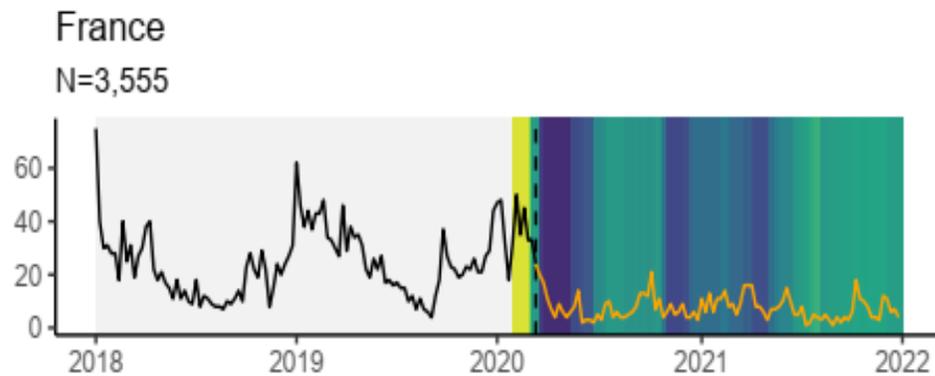
Shaw D *et al.* medRxiv 2022.12.16.22283251

IPD cases / week

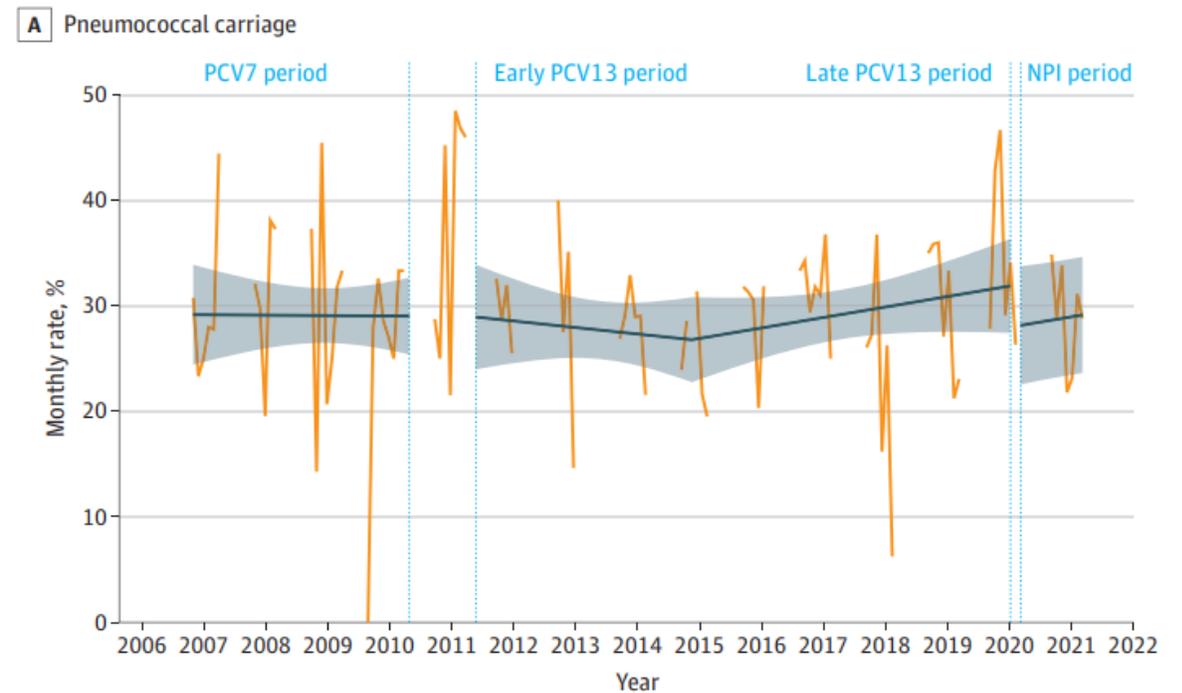
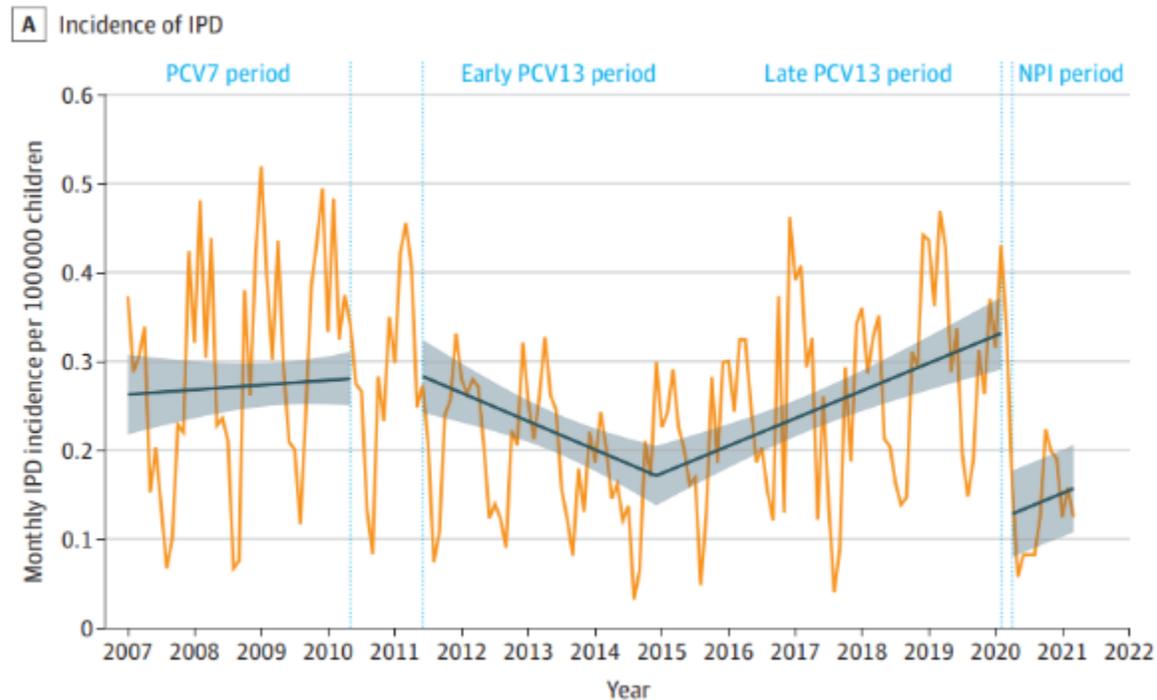


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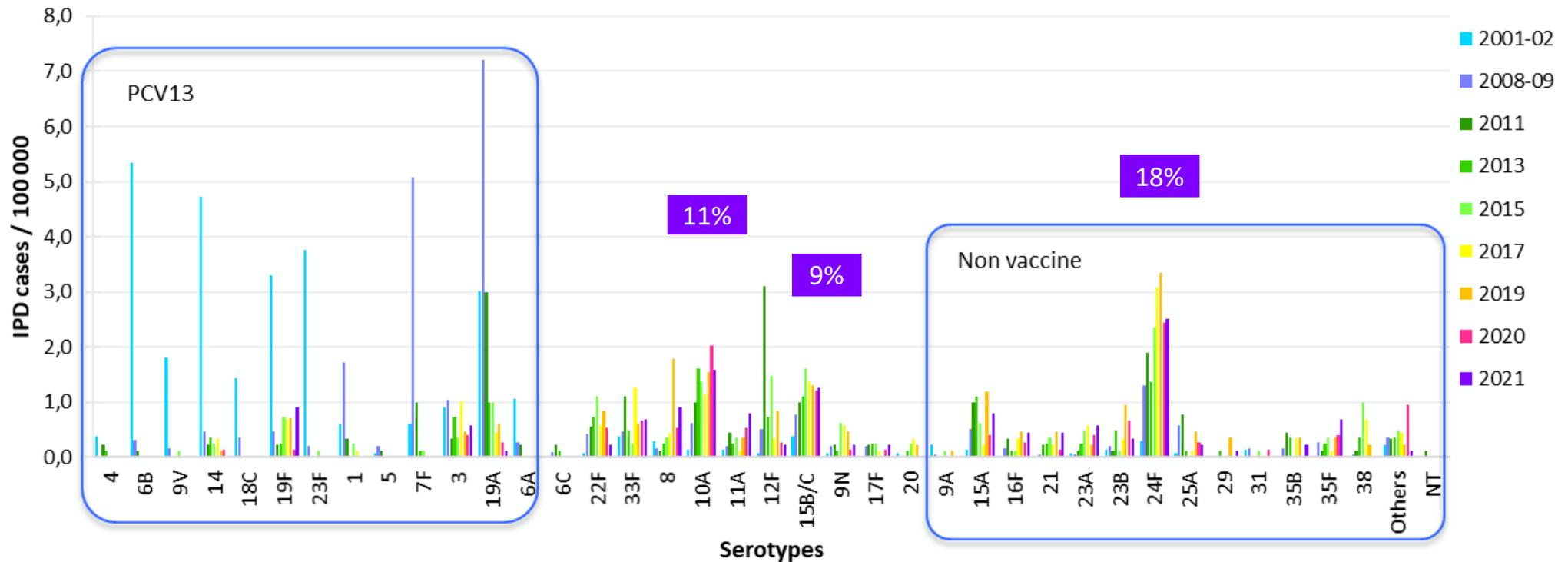
# NPI during the COVID-19 Pandemic, IPD, Pneumococcal Carriage, and Respiratory Viral Infections Among Children in France



Rybak A. *et al.* JAMA Network Open. 2022;5(6):e2218959

# Serotype specific incidence rate of IPD, children < 2 years

Direct effect : quasi-eradication of PCV13 IPD (except 19F and 3)  
 Emerging non PCV13 serotypes: **24F**, 10A, 15B/C

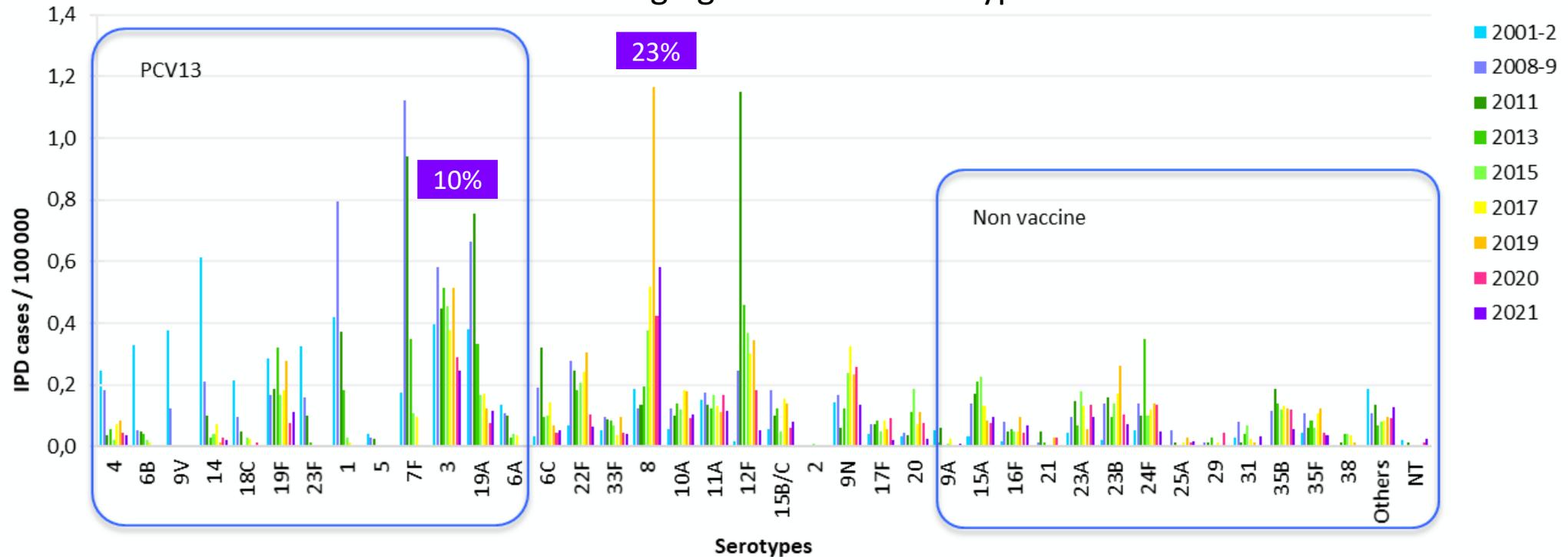


IPD < 2 years	2001-02	2008-09	2011	2013	2015	2017	2019	2020	2021
Number of cases	399	481	174	110	136	135	157	97	125

Incidence rate: EPIBAC-SantéPublique France  
 CNRP-ORP, 2021 unpublished data

# Serotype specific incidence rate of IPD, adults 15-64 years

Indirect effect : quasi-eradication of PCV13 IPD (except **3**, 19F and 19A)  
Emerging non PCV13 serotype: **8**

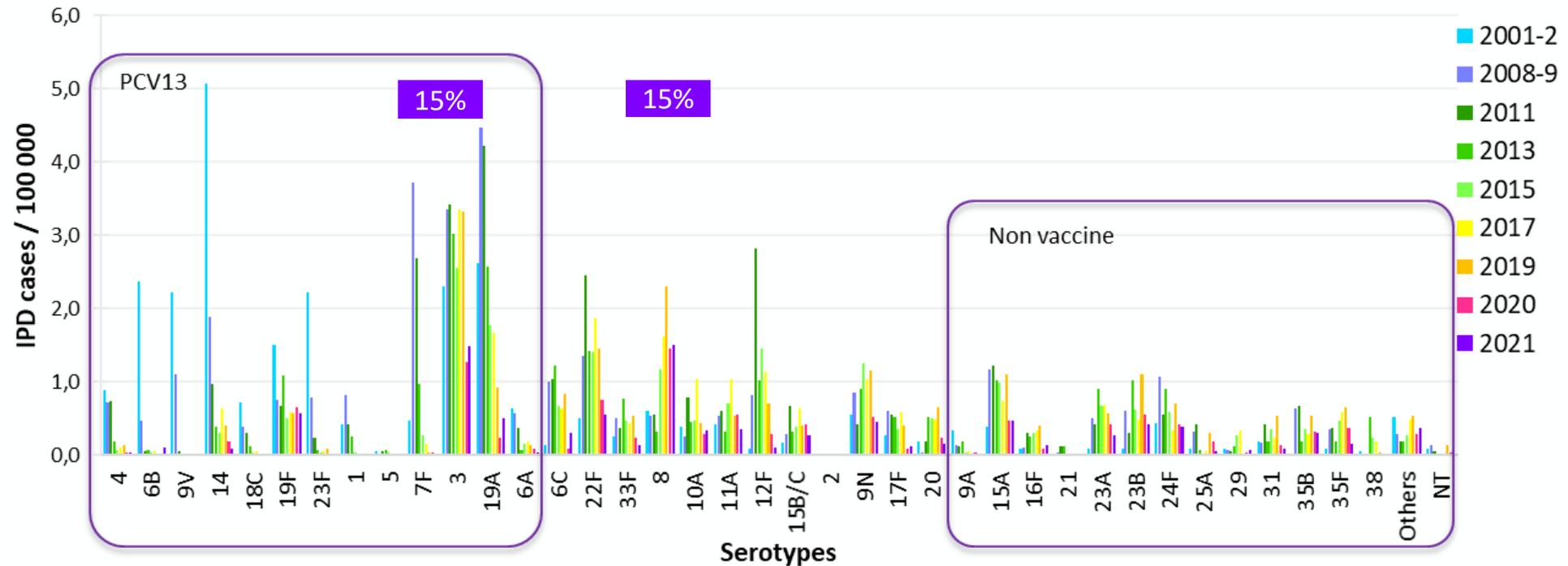


IPD 16-64 years	2001-02	2008-09	2011	2013	2015	2017	2019	2020	2021
Number of cases	932	974	549	342	331	336	353	194	476

Incidence rate: EPIBAC-SantéPublique France  
CNRP-ORP, 2021 unpublished data

# Serotype specific incidence rate of IPD, adults > 64 years

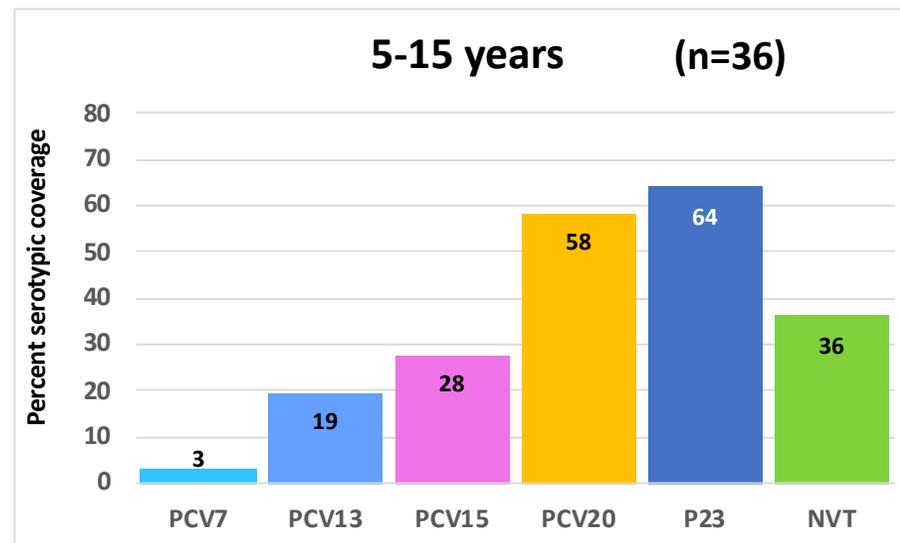
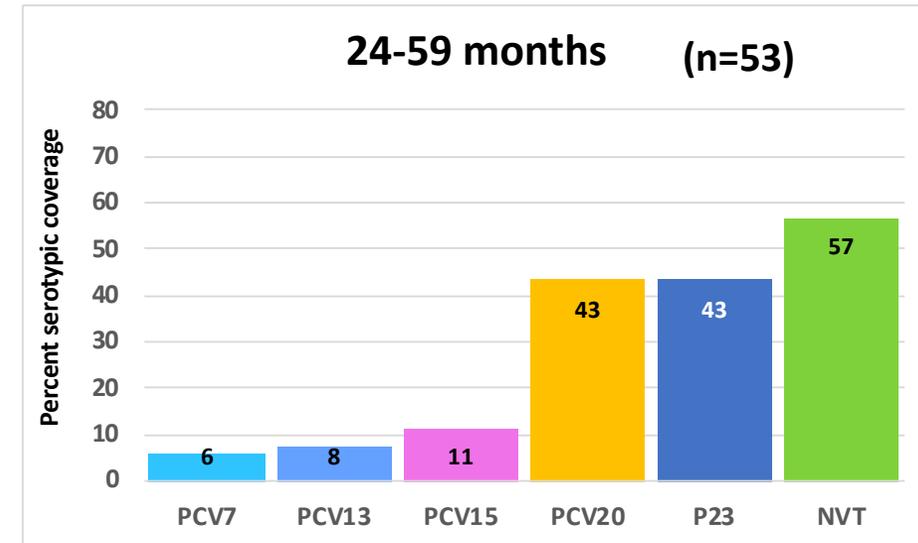
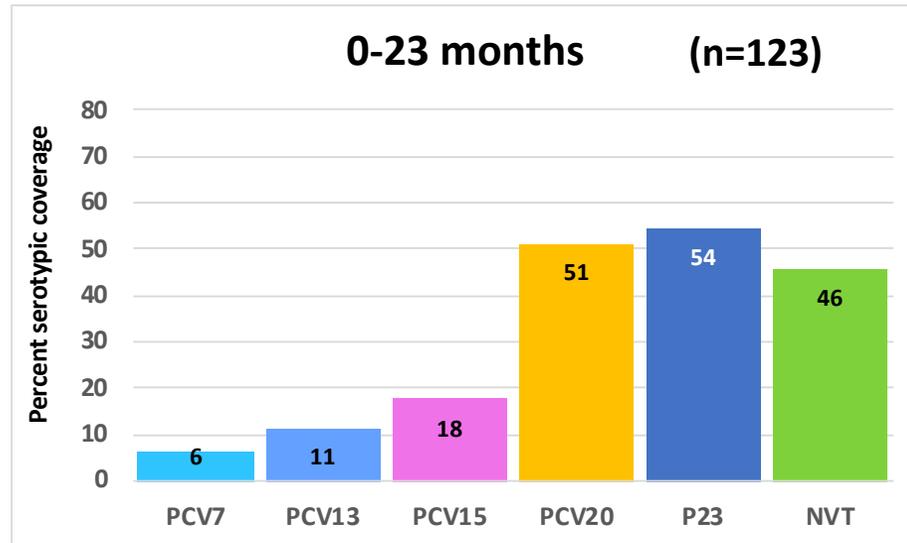
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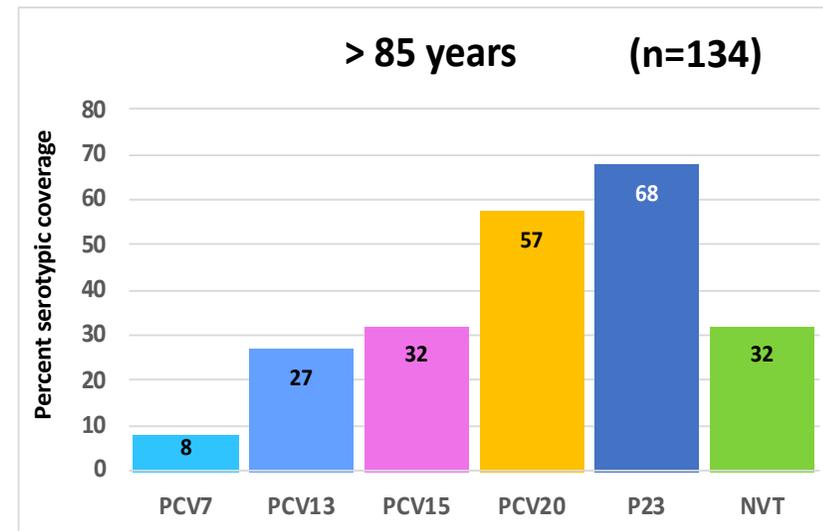
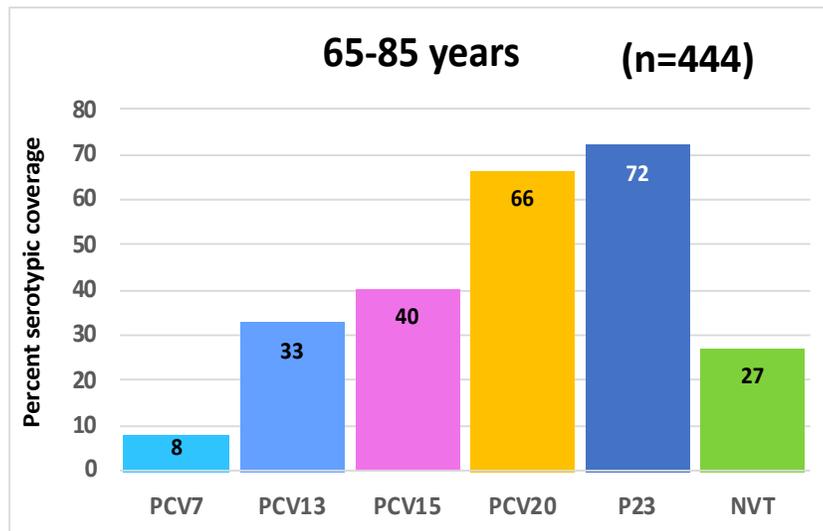
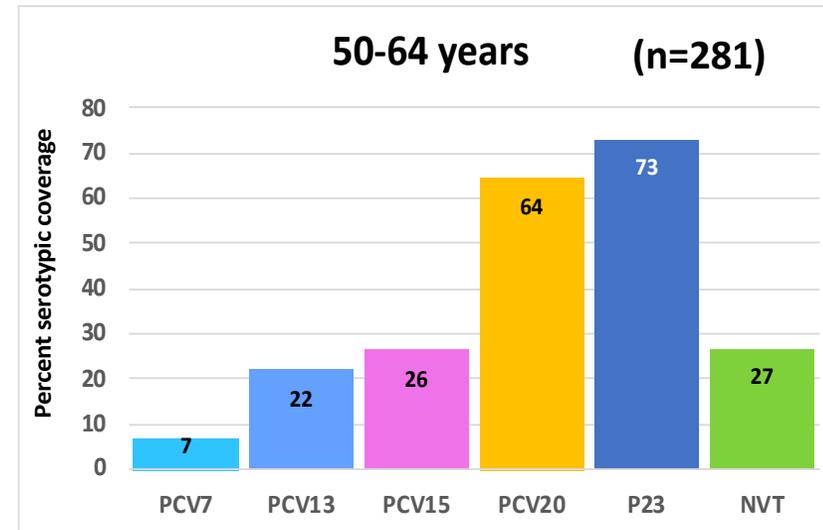
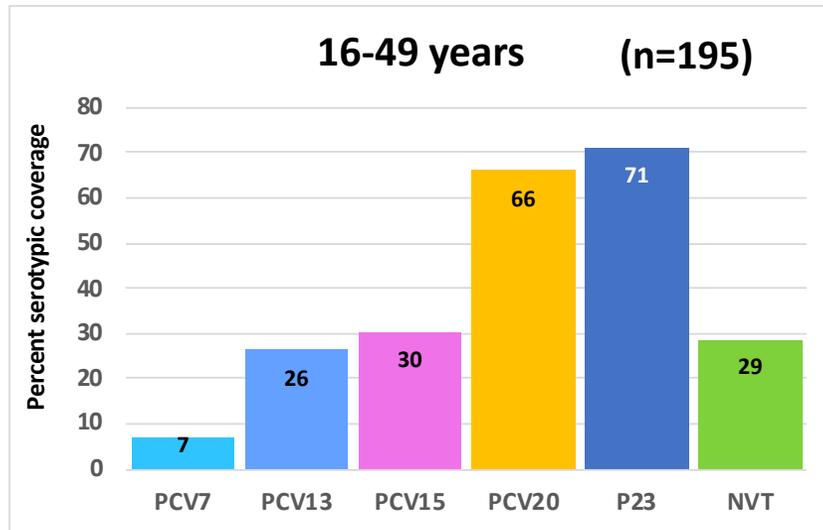
IPD > 64 years	2001-02	2008-09	2011	2013	2015	2017	2019	2020	2021
Number of cases	994	881	490	342	374	416	490	232	578

Incidence rate: EPIBAC-SantéPublique France  
 CNRP-ORP, 2021 unpublished data

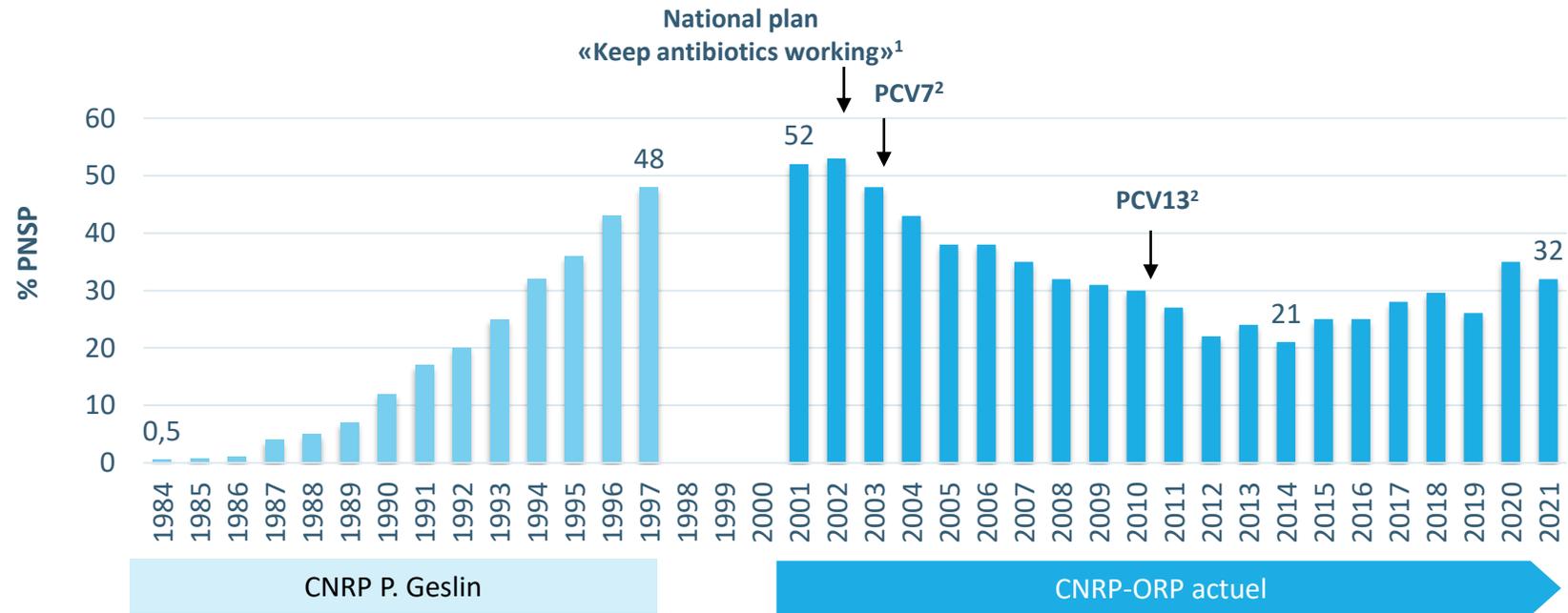
# IPD serotypes (%) covered by vaccines, France 2021



# IPD serotypes (%) covered by vaccines, France 2021



# Penicillin non susceptible *S. pneumoniae* (PNSP) in France



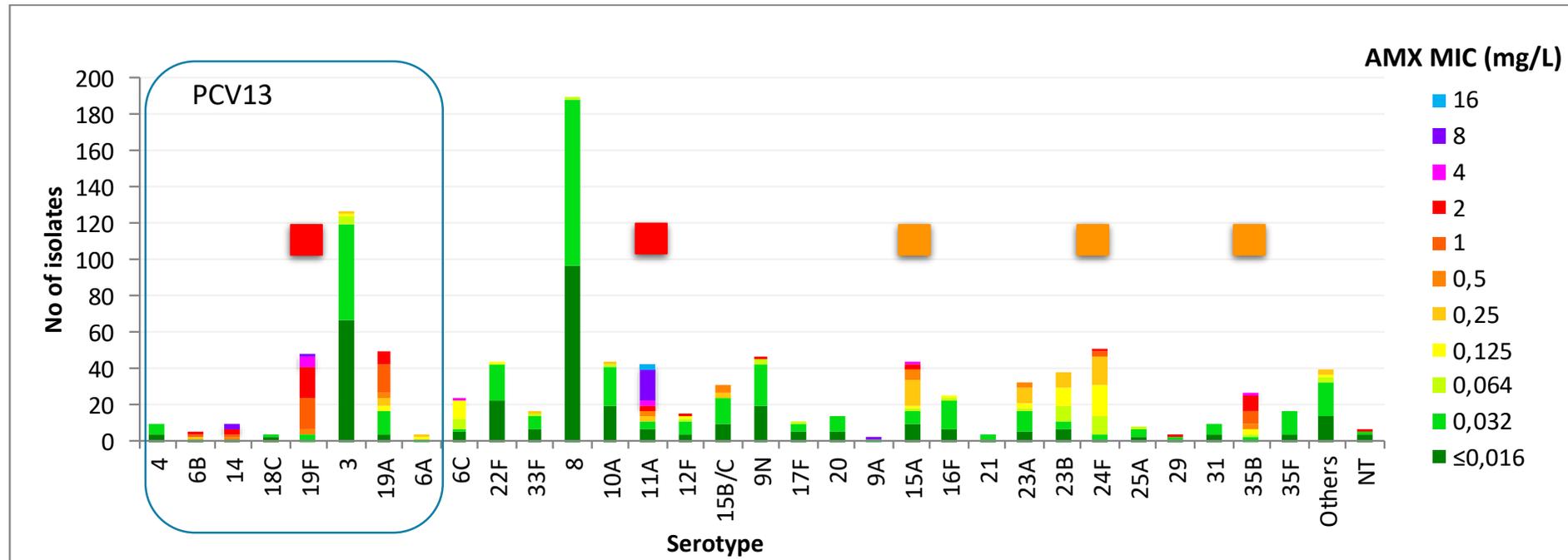
1984-2021: 67 985 isolates

<sup>1</sup>[http://www.sante.gouv.fr/htm/actu/34\\_01.htm](http://www.sante.gouv.fr/htm/actu/34_01.htm)

<sup>2</sup>Pneumococcal conjugate vaccine (PCV)

CNRP-ORP 2022, unpublished data

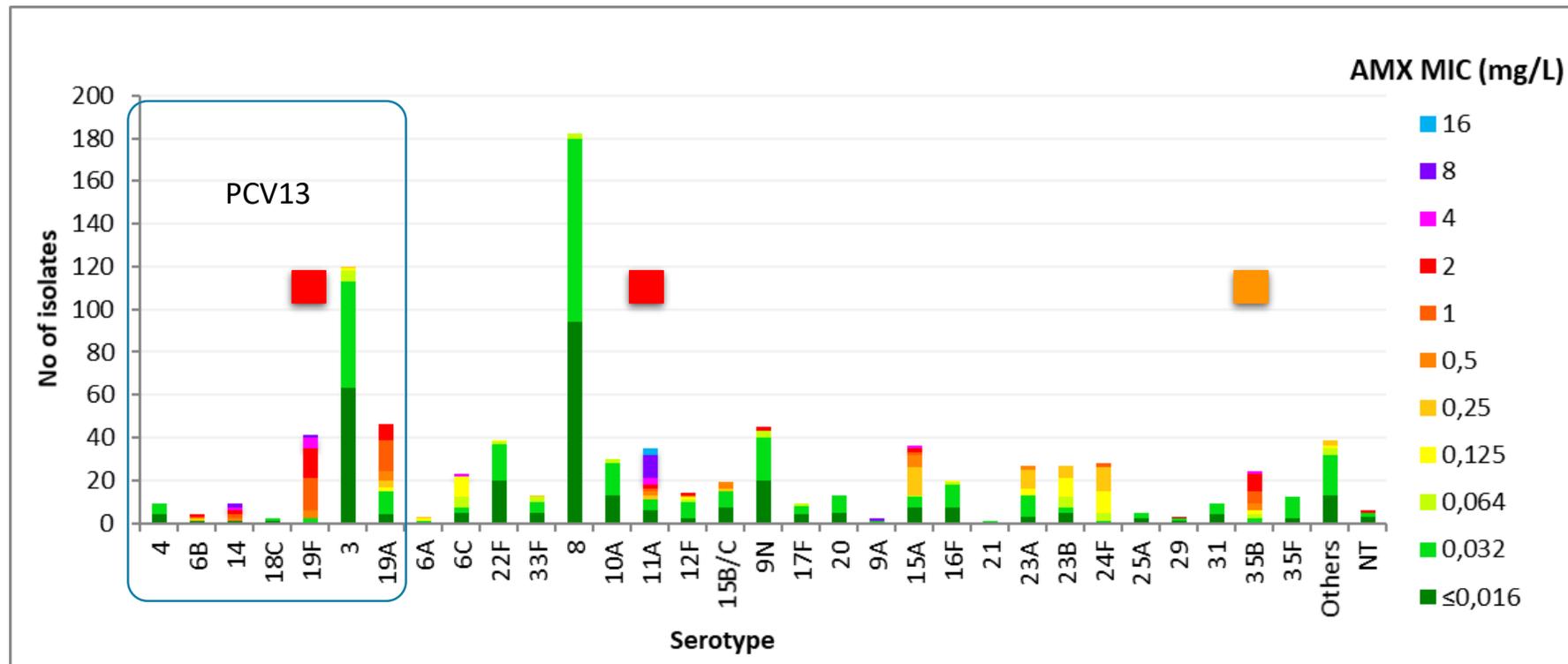
# Bacteremia (n=1029) : susceptibility to amoxicillin en 2021



94% of bacteremia isolates are susceptible to amoxicillin (MIC ≤ 2 mg/L) when considering pneumonia (CA-SFM EUCAST)

CNRP-ORP, unpublished data

# Bacteremia in adults > 15 years (n=895) : susceptibility to amoxicillin en 2021



97% of bacteremia isolates are susceptible to amoxicillin (MIC ≤ 2 mg/L) when considering pneumonia (CA-SFM EUCAST)

CNRP-ORP, unpublished data

# Etude SIIPA



- 7 ORP → un réseau de 27 hôpitaux
- Binôme infectiologue/microbiologiste
- Surveillance active : tous les cas d'IIP chez l'adulte (méningites exclues) en prospectif depuis juin 2014
- Objectifs
  - Présentation clinique des IIP de l'adulte
  - Terrain, comorbidités
  - Gravité, mortalité
  - Couverture vaccinale
- De juin 2014 à déc 2017 : 908 cas d'IIP
- De 2018 à 2021 : 779 cas d'IIP

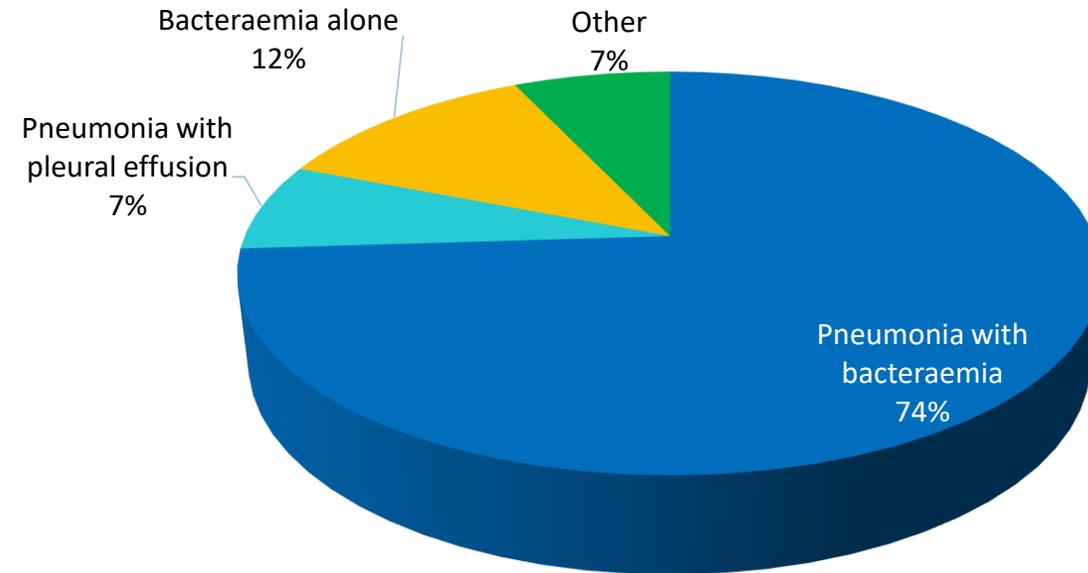
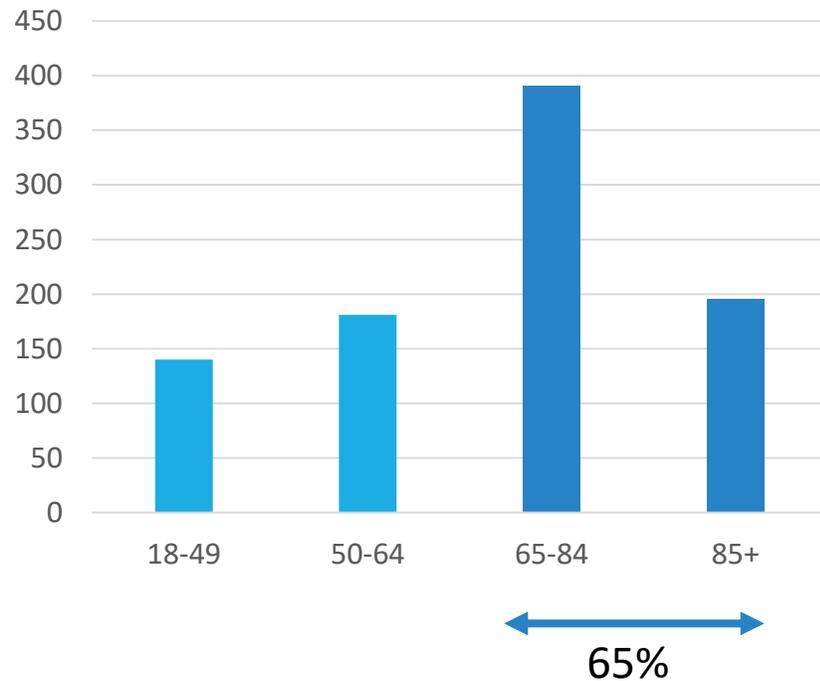
Figure 1. SIIPA network



Danis *et al.* OFID 2019

# SIIPA : répartition selon l'âge et la présentation clinique

Âge médian : 71 ans (18-101 ans)

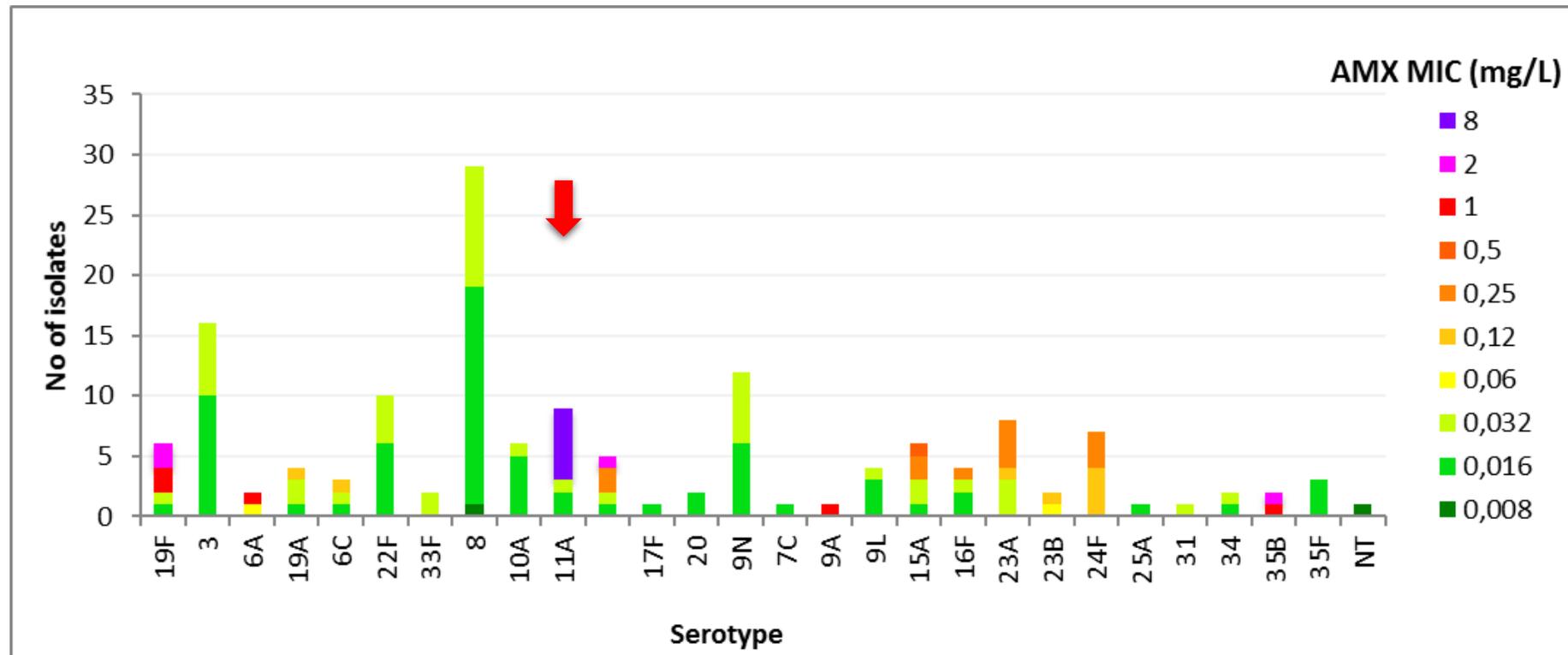


## Mortalité

- intra-hospitalière 22% (201/908)
- 30 j post admission 21% (dont 33% en 48h)

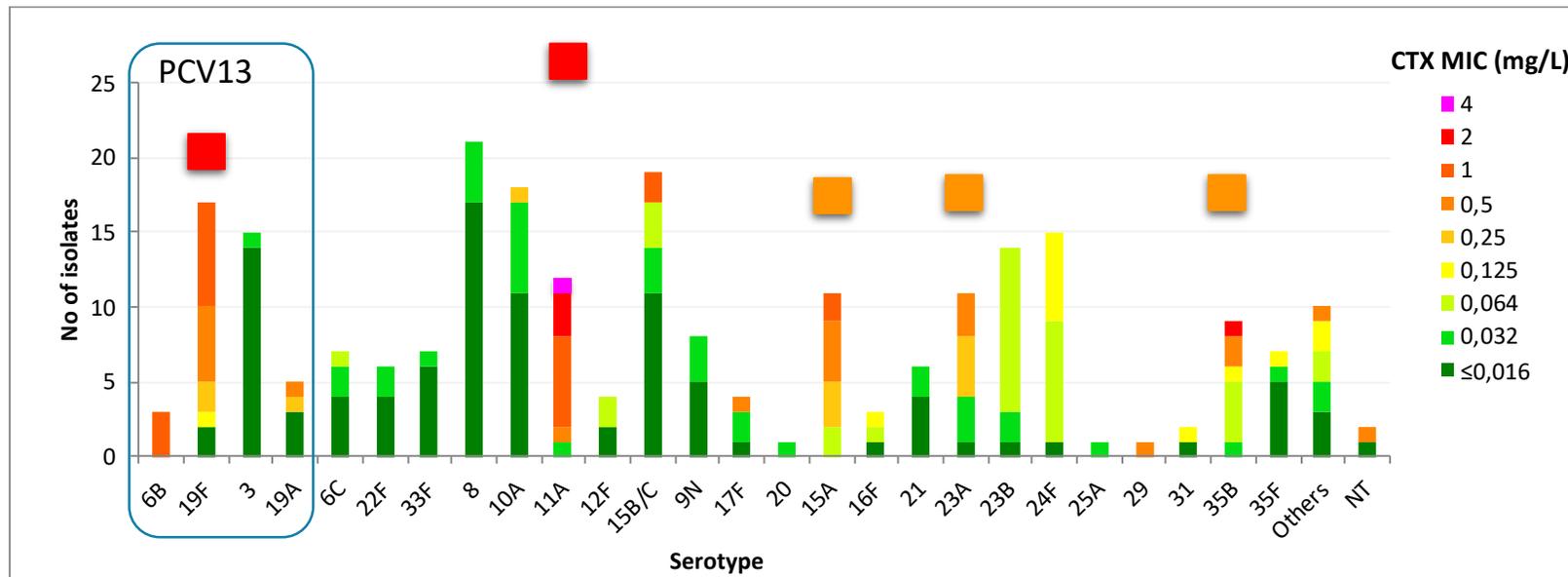
Danis *et al.* OFID 2019

# Etude SIIPA (n=150) : sensibilité à l'amoxicilline en 2021



CNRP-ORP 2022, unpublished data

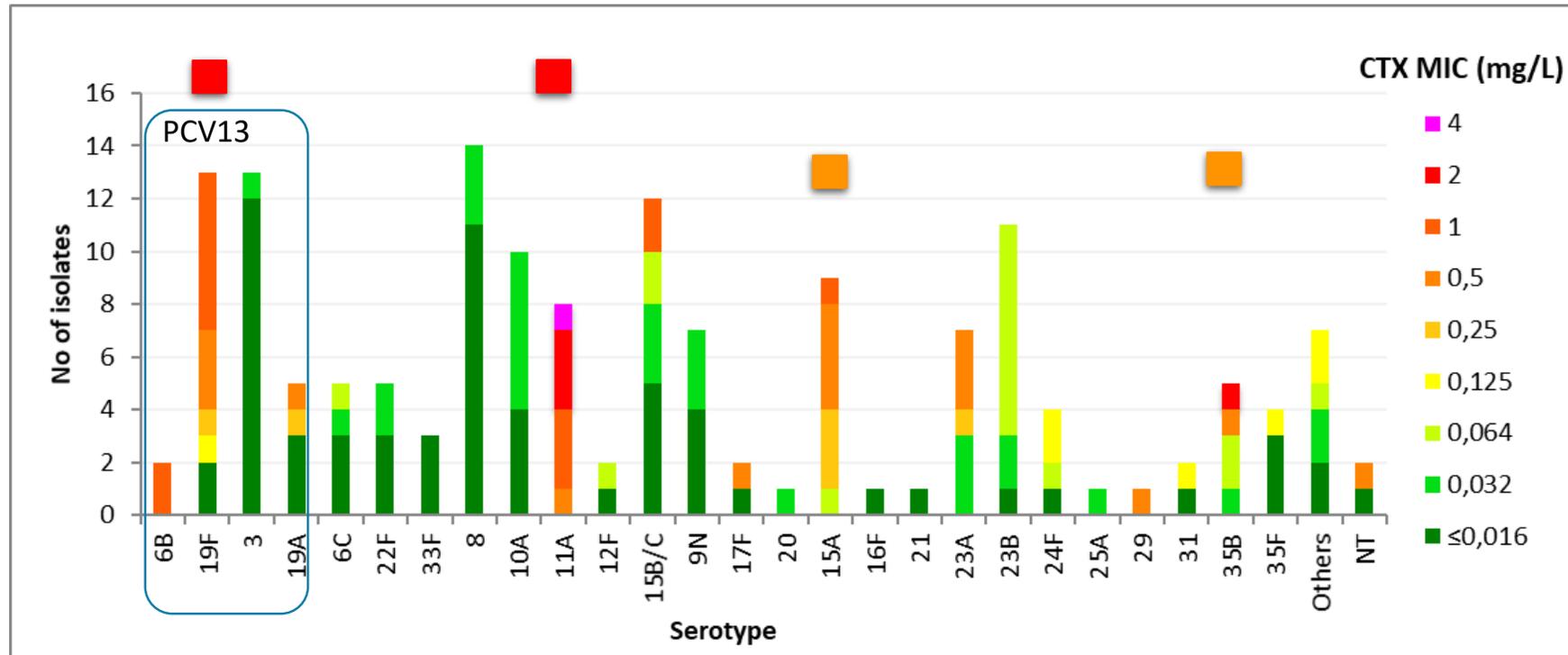
# Meningitis (n=239) : susceptibility to cefotaxime en 2021



10% of meningitis isolates are non-susceptible to cefotaxime (MIC > 0.5 mg/L) (CA-SFM EUCAST)

CNRP-ORP 2022, unpublished data

# Meningitis isolates in adults > 15 years (n=157) : susceptibility to cefotaxime en 2021



CNRP-ORP 2022, unpublished data

# 2021 : prescriptions d'antibiotiques en médecine de ville en hausse

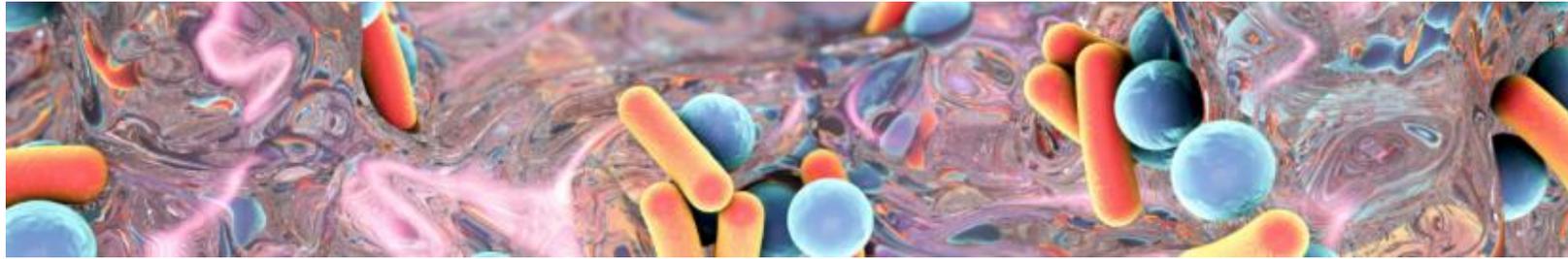
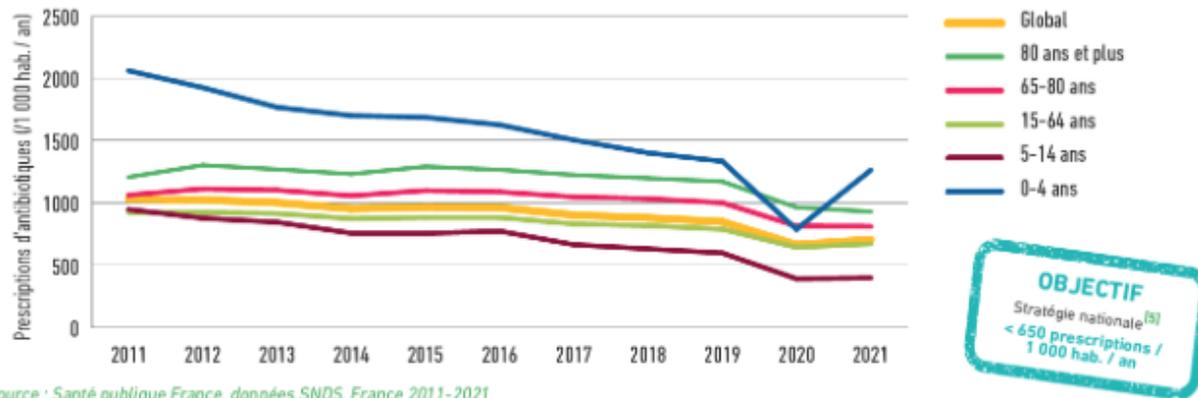


Fig - Prescriptions d'antibiotiques par classes d'âge et pour toute la population. France, santé humaine, 2011-2021



Source : Santé publique France, données SNDS, France 2011-2021

Par rapport à 2020 :

+ 5 % en Doses Définies Journalières ( DDJ )

+ 6 % en nombre de prescriptions

La France reste parmi les pays européens les plus consommateurs d'antibiotiques (4e rang depuis 2018) selon les données de la surveillance internationale ESAC-Net.

<https://www.santepubliquefrance.fr/les-actualites/2022/consommation-d-antibiotiques-et-prevention-de-l-antibiorésistance-en-france-en-2021-ou-en-sommes-nous>

# Conclusion

- Depuis PCVs, épidémiologie des pneumocoques a changé radicalement
  - ↳ ↳ ↳ Vaccinaux sauf 3, 19F et ↗ non vaccinaux → remplacement partiel
    - Péni-S : 8, 10A
    - Péni non S : 24F, 15A, 35B et 11A
  - ↳ ↳ Incidence des infections invasives puis ↗
    - Dans la population ciblée par le vaccin (effet direct)
    - Dans les autres groupes d'âge (effet indirect)
  - ↳ ↳ Pneumocoques de sensibilité diminuée aux bêta-lactamines puis ↗
- Avec la pandémie de COVID-19
  - ↳ ↳ Incidence des infections invasives entre 2019 et 2021, sans modification significative du portage, ni de la distribution des sérotypes, puis ↗ ↗ depuis fin 2022 ...
    - Dans un contexte de forte consommation ATB en médecine ambulatoire

Optimiser notre stratégie vaccinale en intégrant les nouveaux vaccins

# Remerciements

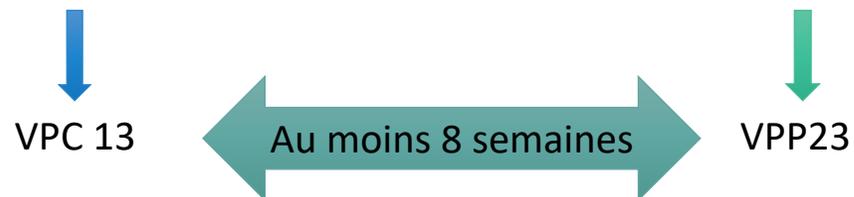
- **Les microbiologistes des ORP dont les coordinateurs :**
- Corentine ALAUZET, Gabriel AUGER, Julien BADOR, Nathalie BRIEU, Vincent CATTOIR, Julie CREMNITER, Paul-Louis WOERTHER, Alain GRAVET, Hélène GUET-REVILLET, Farida HAMDAD, Christophe ISNARD, Marie KEMPF, Philippe LANOTTE, Chrislène LAURENS, Nadine LEMAITRE, Isabelle PATRY, Isabelle PELLOUX, Olivia PEUCHANT, Céline PLAINVERT, Marie-Cécile PLOY, Frédéric ROBIN, Raymond RUIMY, Jennifer TETU, Véronique VERNET-GARNIER et Frédéric WALLET.
- **Coordination / Data Management des ORP :** Carole GRELAUD, Anaïs LABRUNIE, Sandrine LUCE, Eliza MUNTEANU.
- **Cécile JANSSEN, Jacques GAILLAT** et tous les infectiologues/cliniciens qui participent à SIIPA.
- **Santé publique France :** Céline FRANÇOIS, Isabelle PARENT du CHATELET et Delphine VIRIOT.
- **ACTIV :** Stéphane BECHET, Robert COHEN, Corinne LEVY, Naïm OULDALI, Alexis RYBAK, Isabelle RAMAY, Mathilde SERVERA et le réseau de pédiatres du GPIP-ACTIV.
- **CNRP :** Jameel BATAH, Cécile CULEUX, Assiya EL-MNIAI, Mélanie LORIN et Melissa AZOUAOU.

<http://cnr-pneumo.fr>

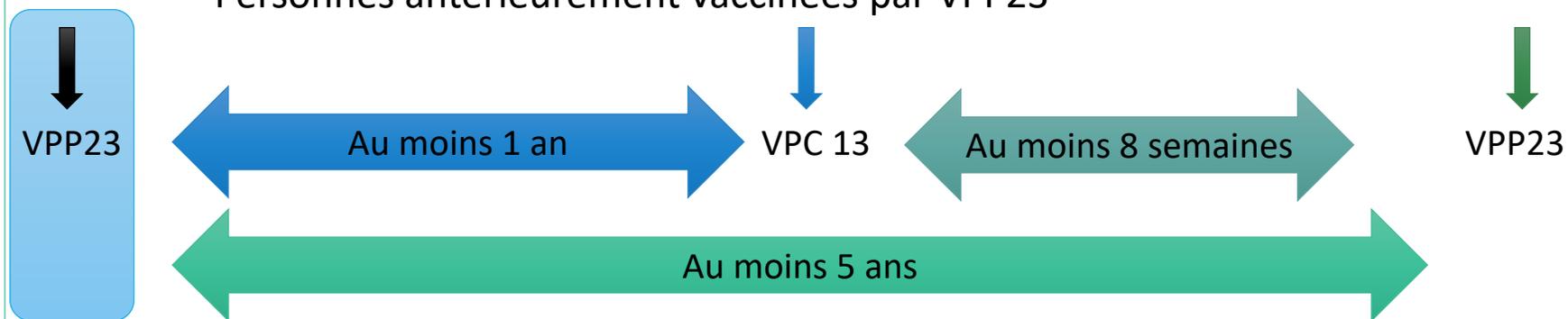


# Schémas vaccinaux

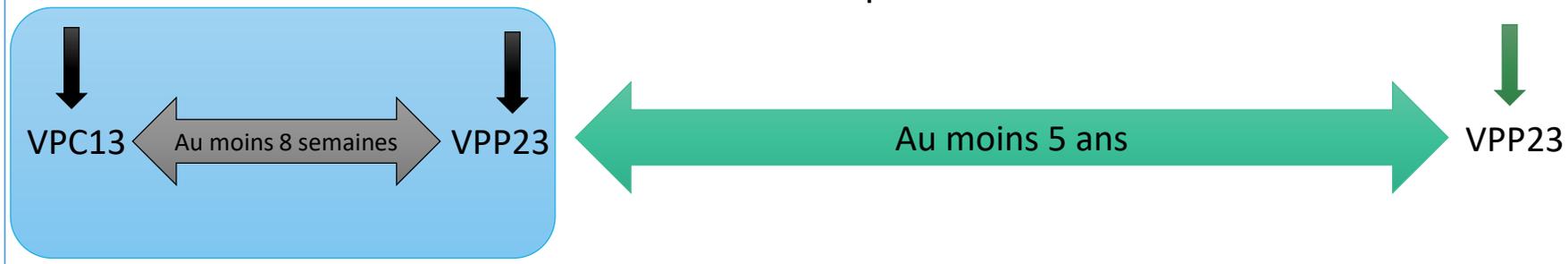
- Personnes non antérieurement vaccinées



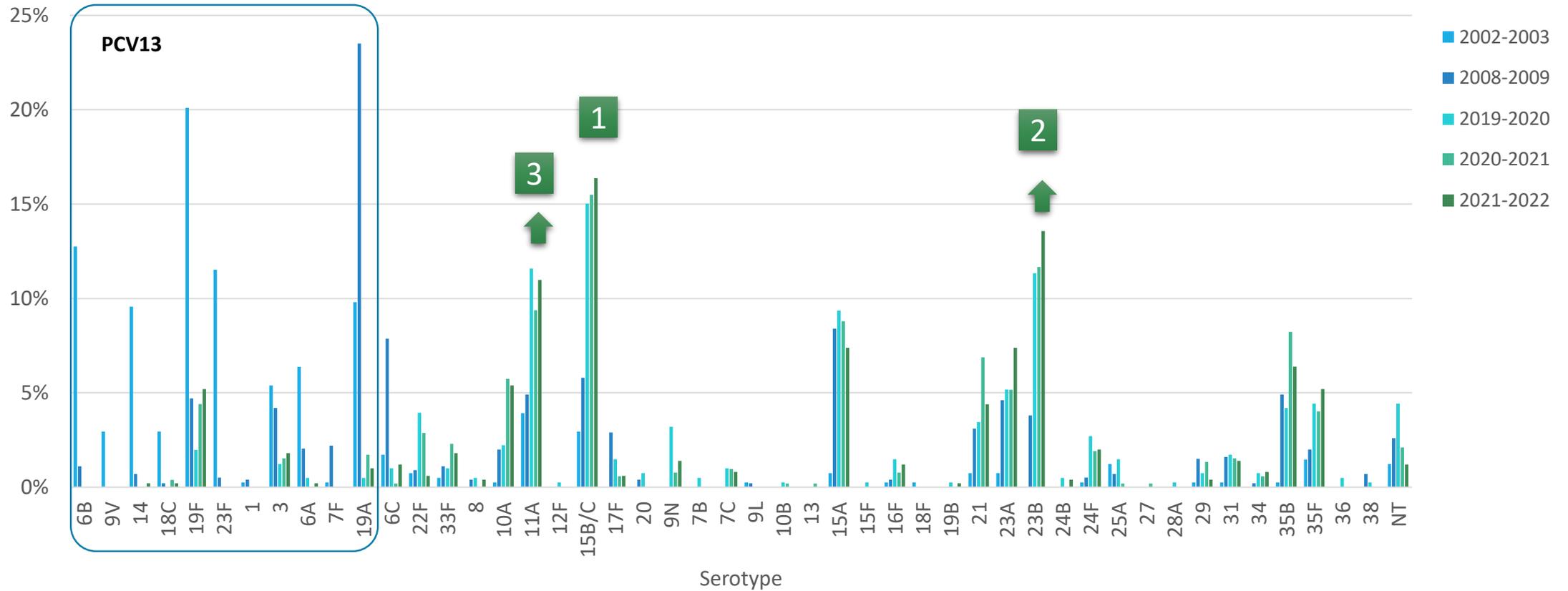
- Personnes antérieurement vaccinées par VPP23



- Personnes antérieurement vaccinées par PCV13+VPP23 : **revaccination VPP23**



# Distribution des sérotypes de *S. pneumoniae* isolés du rhinopharynx au cours d'OMA (Enfants de 6 à 24 mois)



	2002-2003	2008-2009	2019-2020	2020-2021	2021-2022
Nombre de cas	410	549	406	523	501

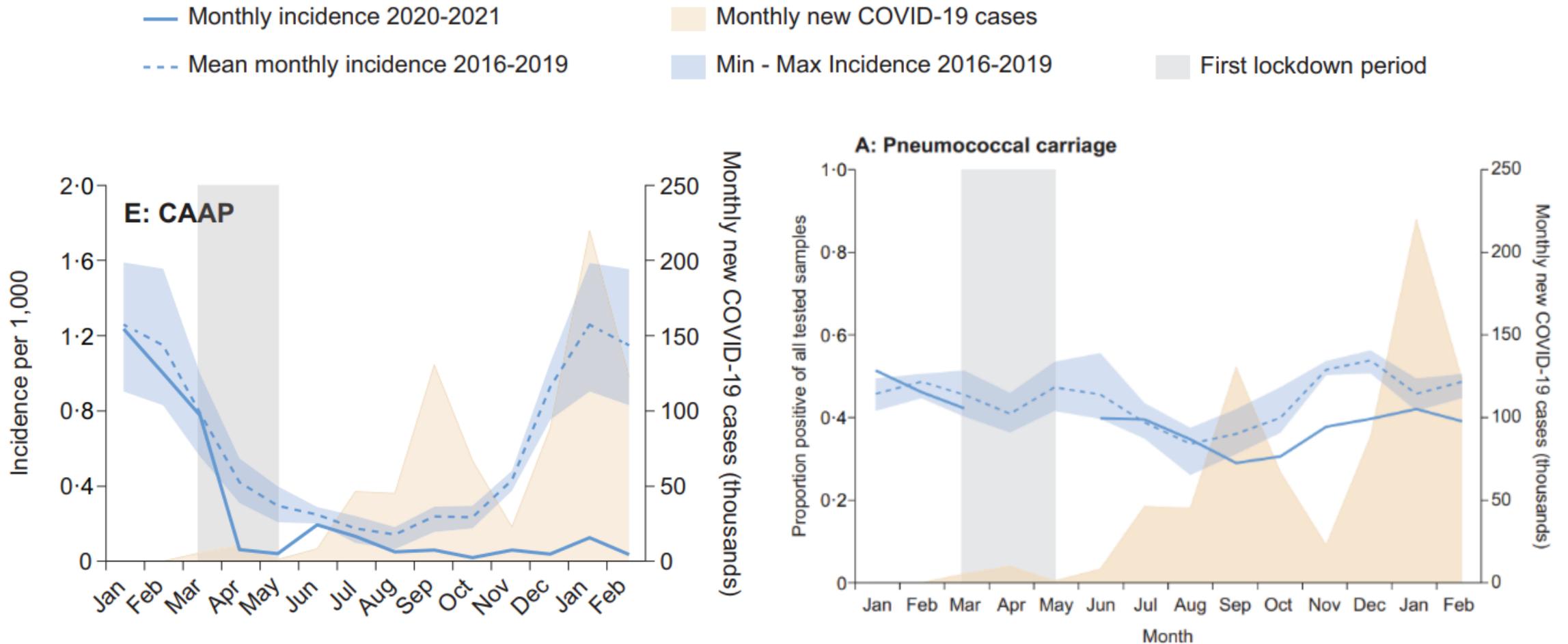
CNRP & ACTIV-GPIP, 2022

# NPI during the COVID-19 Pandemic, IPD, Pneumococcal Carriage, and Respiratory Viral Infections Among Children in France

Serotype	Estimated fraction of IPD					
	Influenza		RSV		Pneumococcal carriage	
	% (95% CI)	P value	% (95% CI)	P value	% (95% CI)	P value
Overall IPD	53 (28 to 78)	<.001	40 (15 to 65)	.002	4 (-7 to 15)	.49
IPD associated with non-PCV13 serotype						
High disease potential	53 (28 to 78)	<.001	41 (15 to 66)	.002	0.4 (-4 to 5)	.86
Low disease potential	56 (30 to 82)	<.001	38 (12 to 63)	.004	3 (-5 to 11)	.44
IPD associated with 24F serotype	54 (26 to 81)	<.001	37 (9 to 65)	.01	2 (-15 to 20)	.77

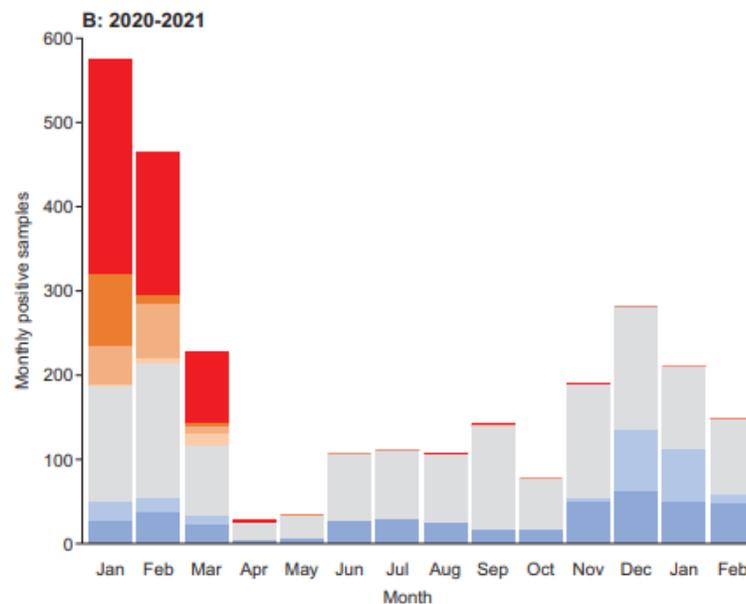
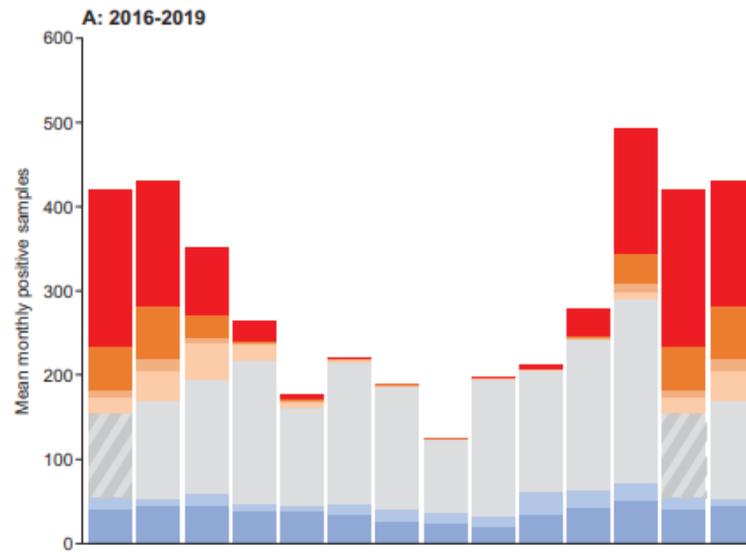
Rybak A. *et al.* JAMA Network Open. 2022;5(6):e2218959

# Decline in IPD in Young Children During the COVID-19 Pandemic in Israel



Danino D *et al.* Clin Infect Dis. 2022 Aug 24;75(1):e1154-e1164

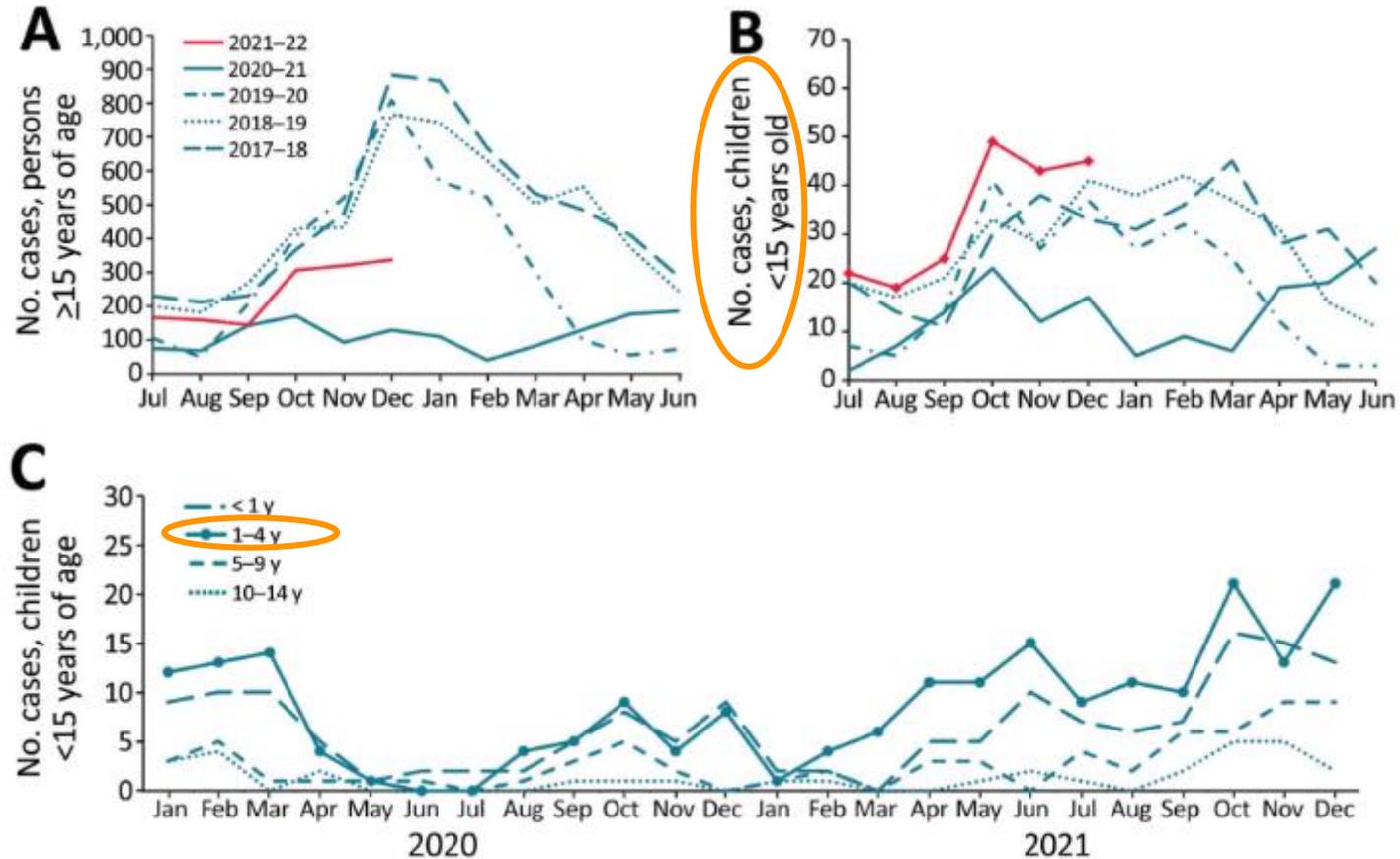
# Decline in IPD in Young Children During the COVID-19 Pandemic in Israel



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# Increased Incidence of Invasive Pneumococcal Disease among Children after COVID-19 Pandemic, England

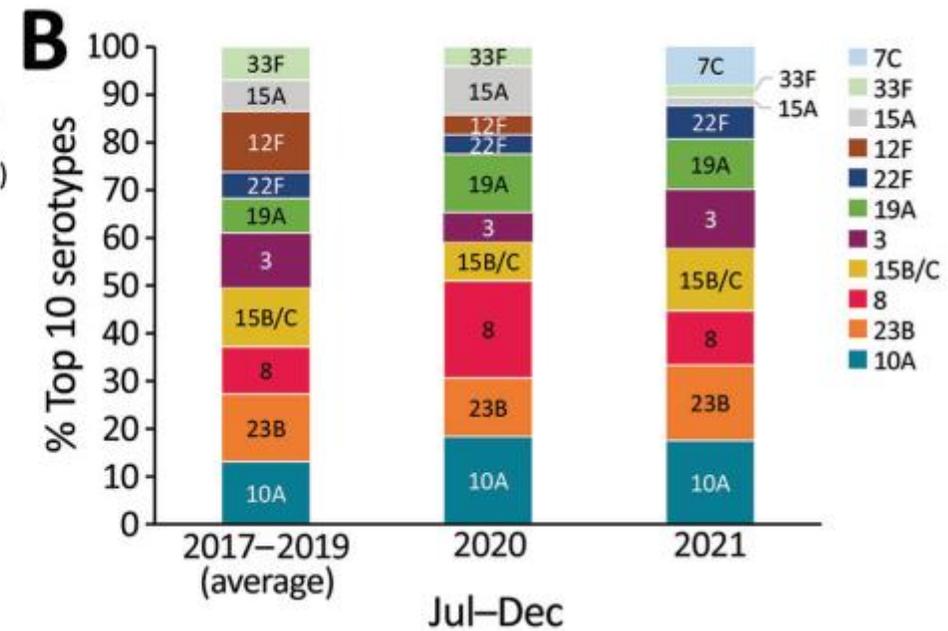
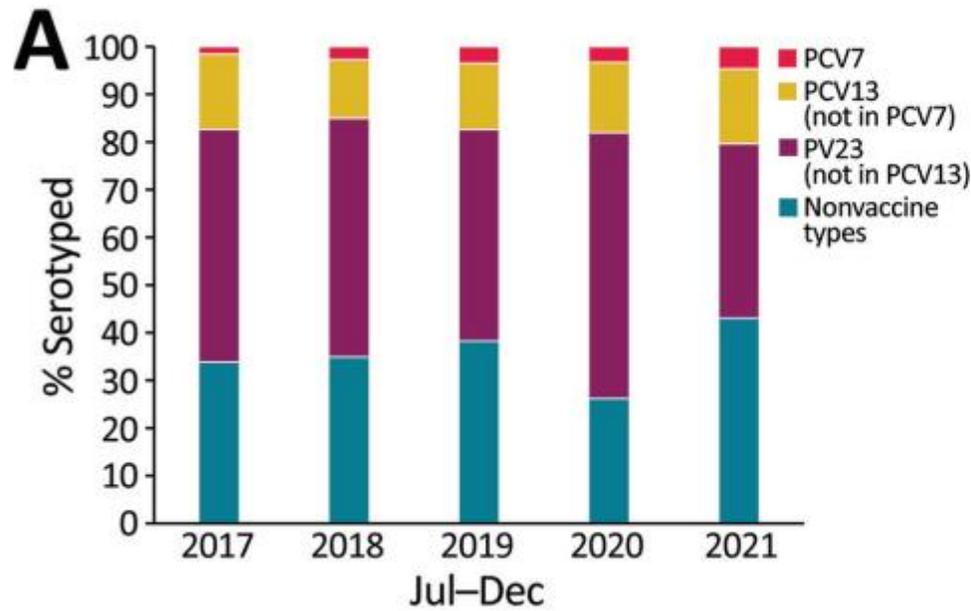
Marta Bertran, Zahin Amin-Chowdhury, Carmen L. Sheppard, Seyi Eletu, Dania V. Zamarreño, Mary E. Ramsay, David Litt, Norman K. Fry, Shamez N. Ladhani



Emerg Infect Dis. 2022;28(8):1669-1672.

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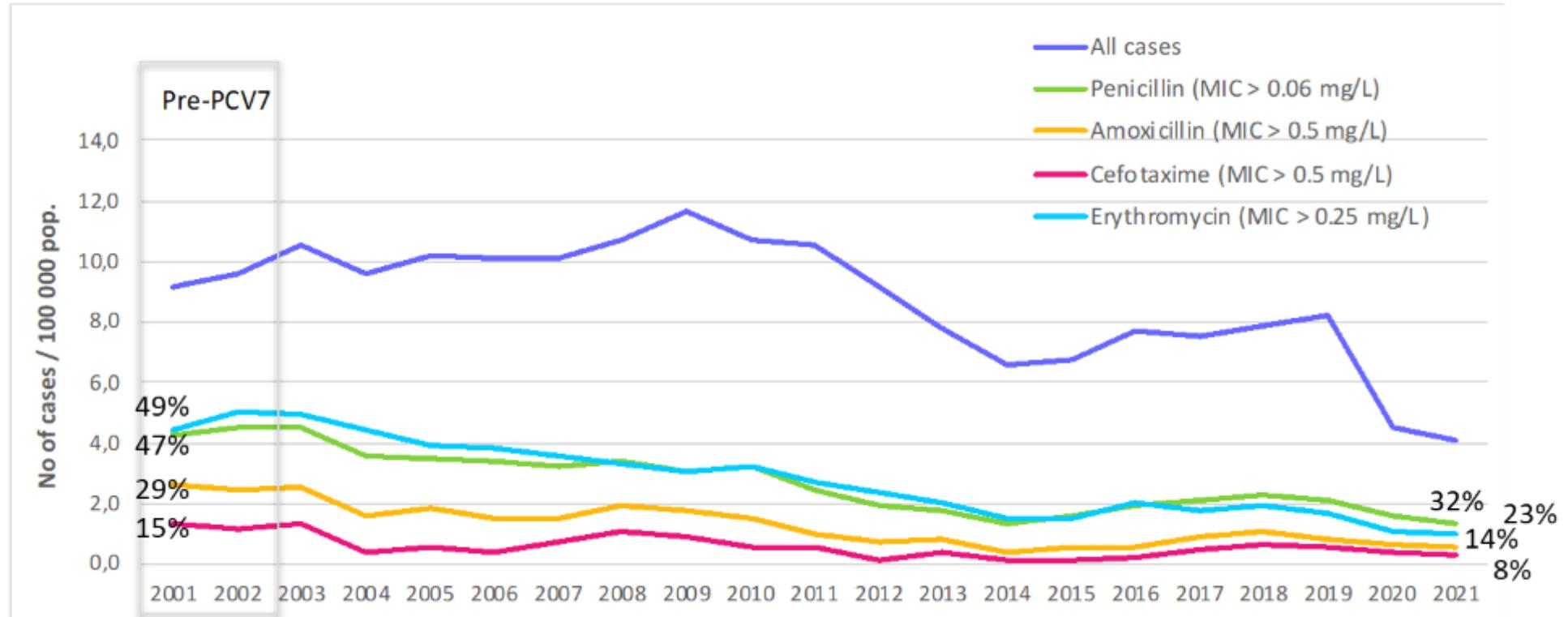
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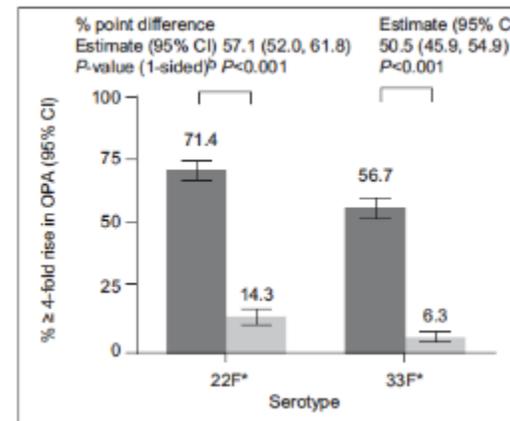
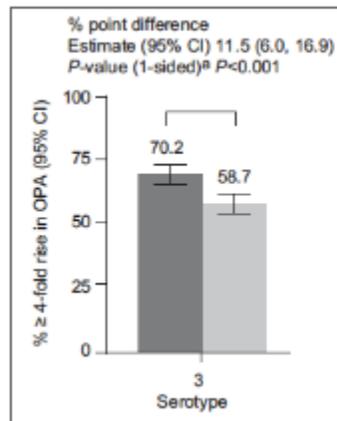
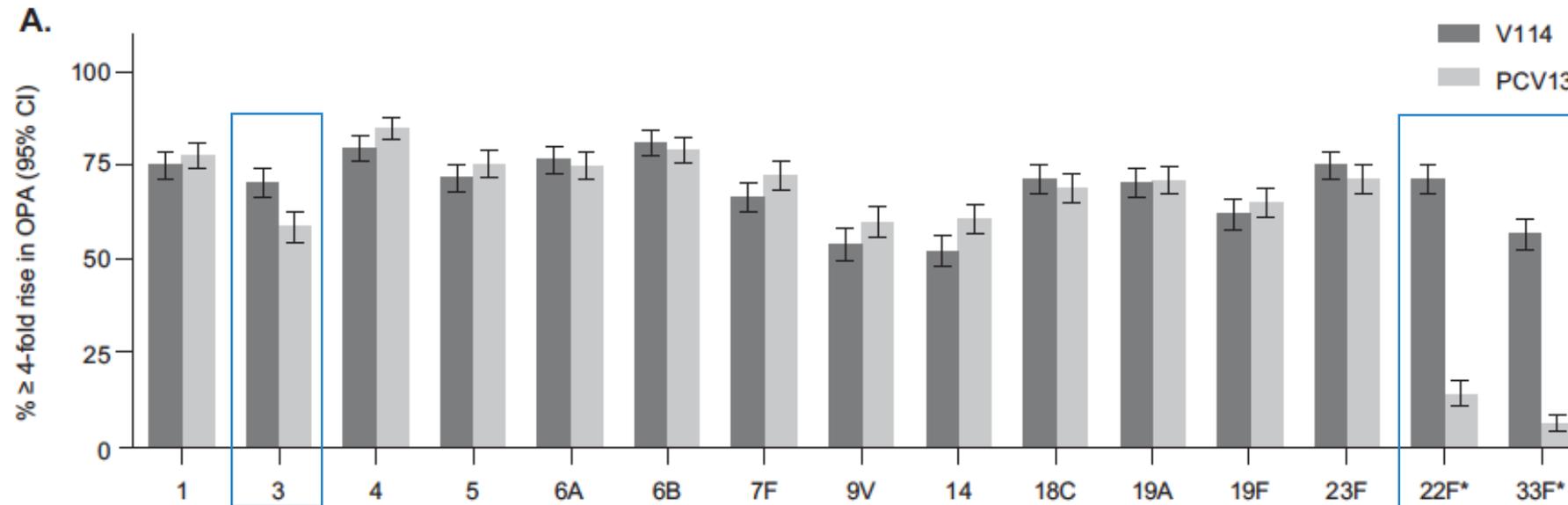
# Antibiotic susceptibility among IPD isolates, France, 2001-2021

↓ IPD isolates  
↑ % PNSP



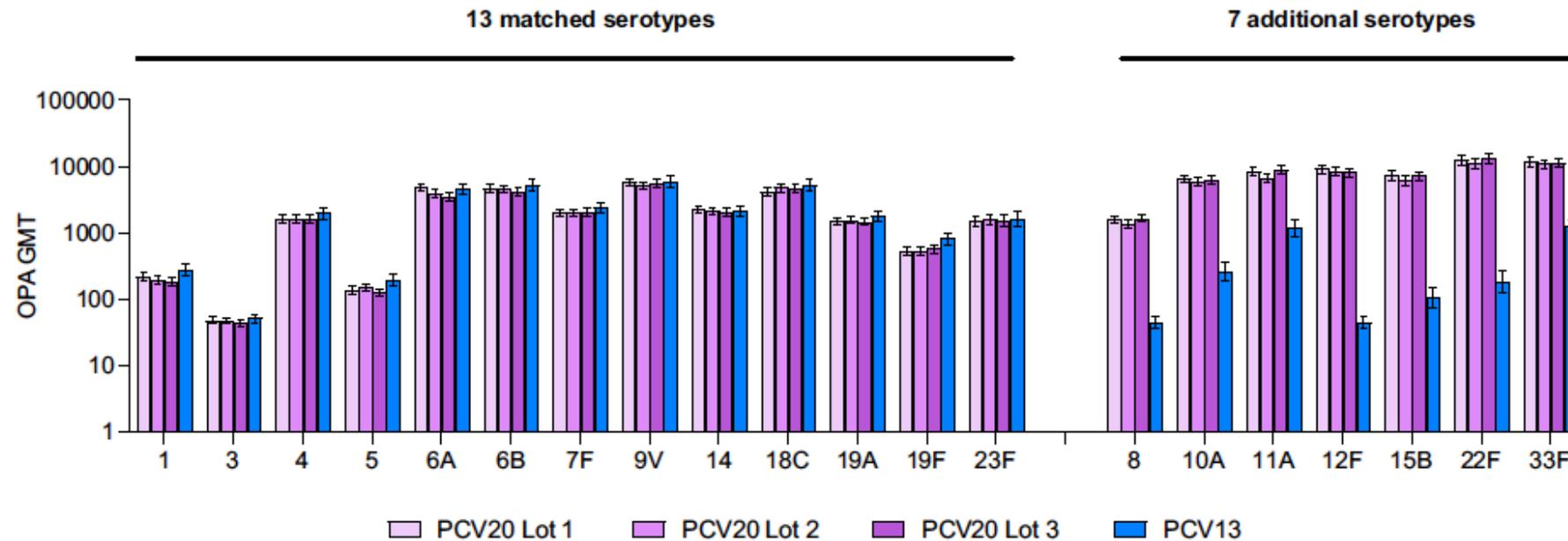
Incidence rate: EPIBAC-Santé Publique France  
 CNRP-ORP, 2021 unpublished data

# V114 (PCV15) - Essai de phase 3 PNEU-AGE (adultes 50-75 ans)



Platt *et al.* Vaccine 2022

# PCV20 – Essai de phase 3 (adultes 18-49 ans)



Klein *et al.*, Vaccine 2021