



Nouveaux vaccins conjugués antipneumococciques

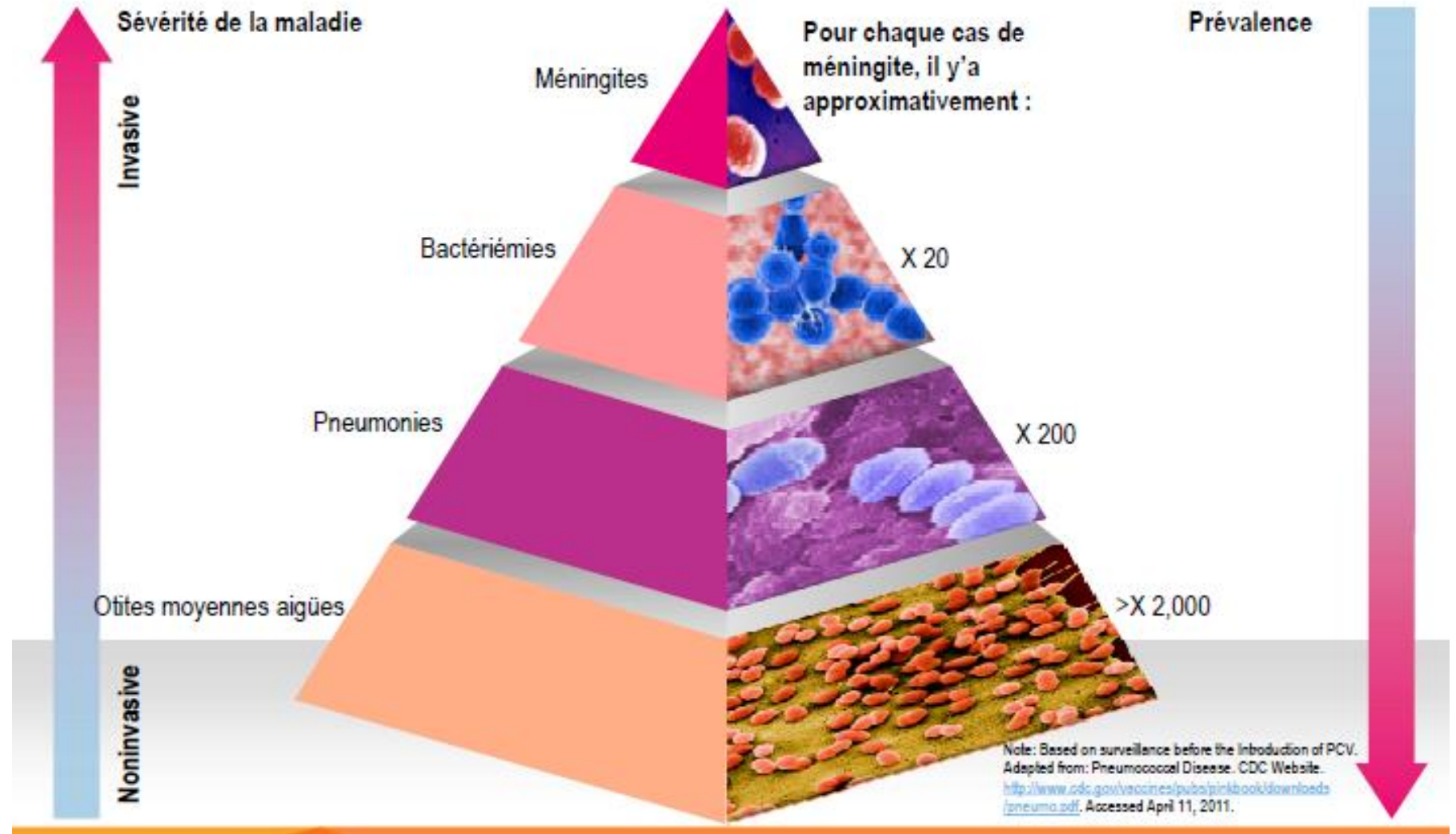
O. Epaulard

Infectiologie, CHU Grenoble Alpes

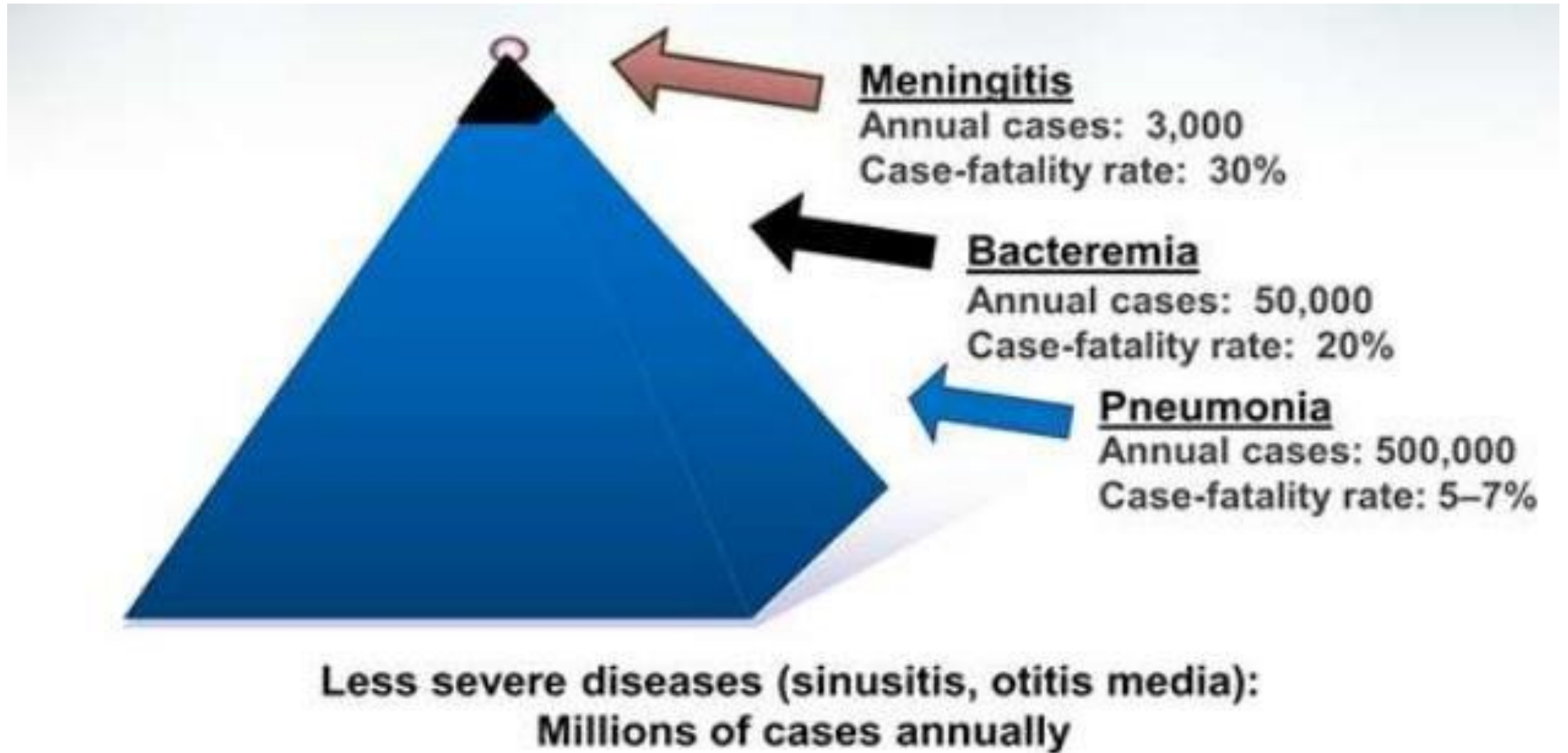
12 octobre 2023 – Journées en région du groupe Vaccination-Prévention

Pas de conflit d'intérêt à déclarer

Spectre des infections à pneumocoque de l'enfant

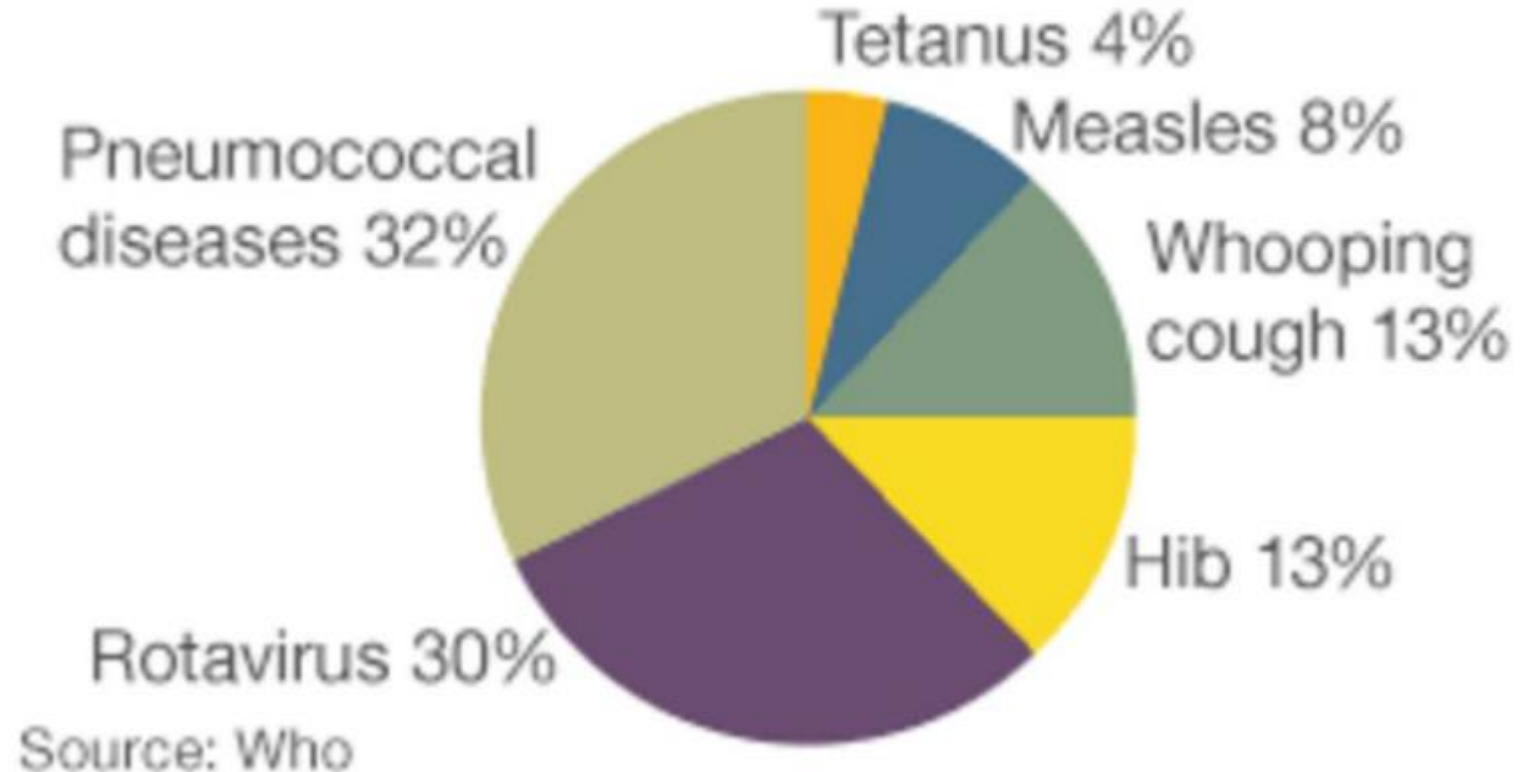


Chiffres aux USA



Chiffres OMS

The vaccine-preventable diseases responsible for 1.5 million infant deaths



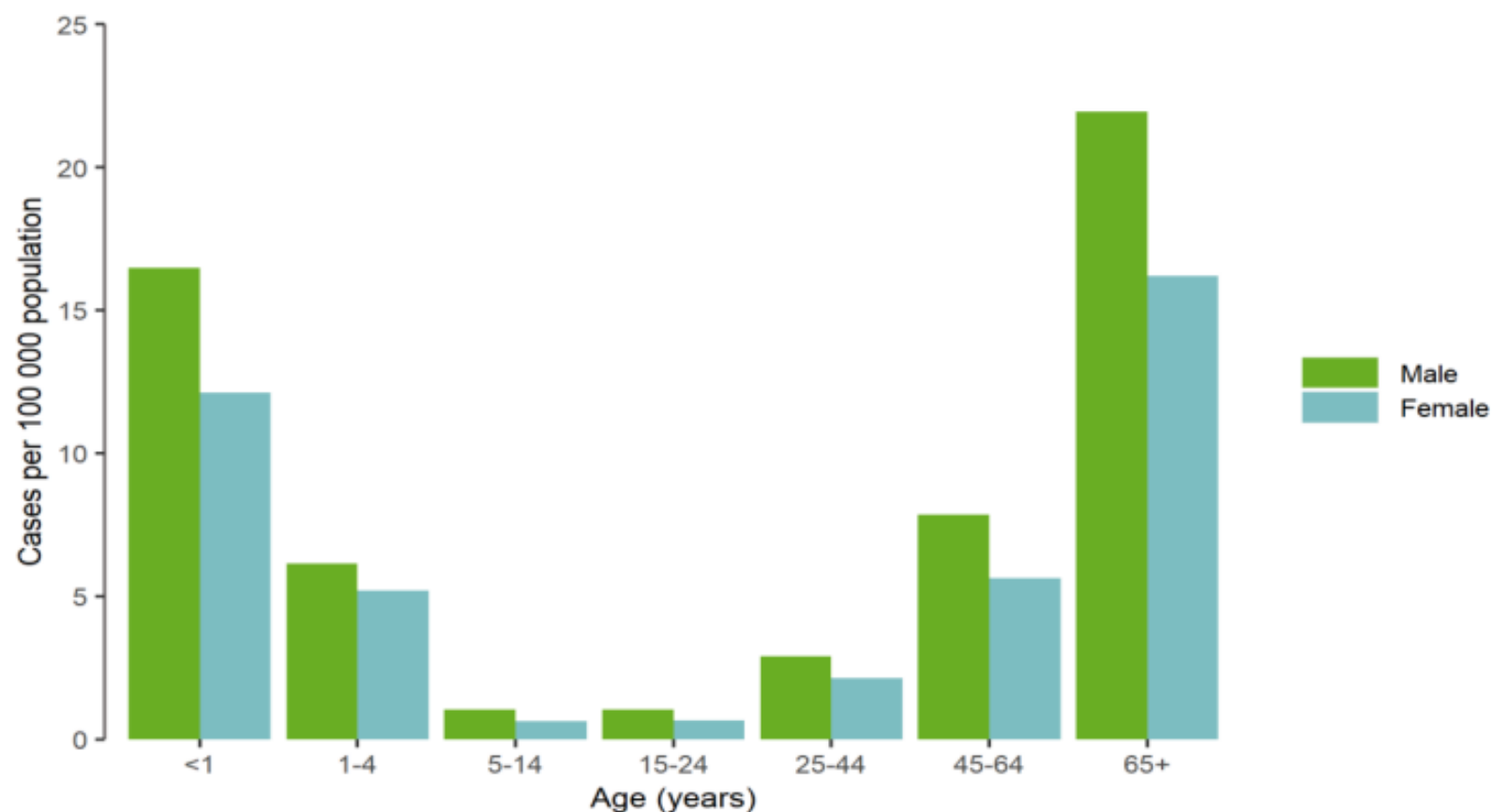


SURVEILLANCE REPORT

Invasive pneumococcal disease

Annual Epidemiological Report for 2018

Figure 2. Distribution of confirmed invasive pneumococcal disease cases per 100 000 population, by age and gender, EU/EEA, 2018



Source: Country reports from Austria, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

Invasive Pneumococcal Disease in Solid Organ Transplant Recipients—10-Year Prospective Population Surveillance

D. Kumar^{a,*}, A. Humar^a, A. Plevneshi^b,
K. Green^b, G.V. R. Prasad^c, D. Siegal^d,
the Toronto Invasive Bacterial Diseases
Network^e and A. McGeer^b

Received 26 September 2006, revised 21 November
2006 and accepted for publication 4 December 2006

Introduction

- Incidence of IPD in the transplant population:
146 per 100,000 persons / year
- General population incidence:
11.5 per 100,000 persons / year

Table 2: Clinical presentations of pneumococcal disease

Outcome	Cases (n = 21)
Clinical presentation	
Bacteremia	19 (90.5%)
Pneumonia	12 (57.1%)
Bacteremia without focus	7 (33.3%)
Peritonitis	1 (4.8%)
Parotitis	1 (4.8%)
Site of positive culture	
Blood	19 (90.5%)
Ascitic fluid	1 (4.8%)
Parotid gland	1 (4.8%)
Hospitalization	19 (90.5%)
Mean time in hospital (days)	16.2 ± 16.9
Range (days)	1–67
In-hospital mortality	6 (28.6%)

Capsule et sérotype

- Capsule : protection contre l'opsonisation
 - Par le complément
 - Par les anticorps
- 90 sérotypes capsulaires
- Hétérogénéité de leur invasivité
 - Ratio portage/invasion : variation de 2 log
- 20-30 sérotypes font 90% des cas d'IIP
- Cible d'anticorps efficaces

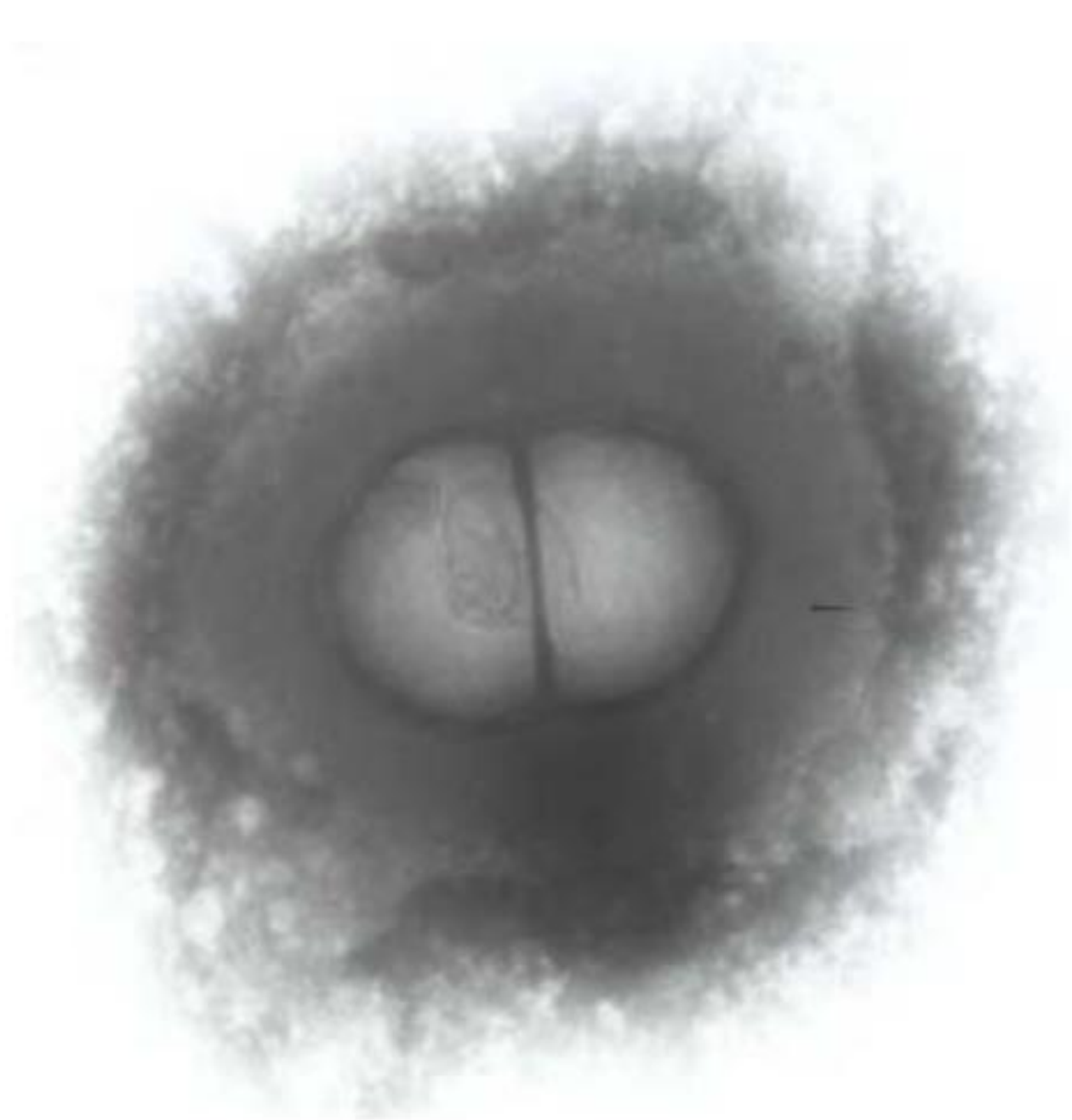
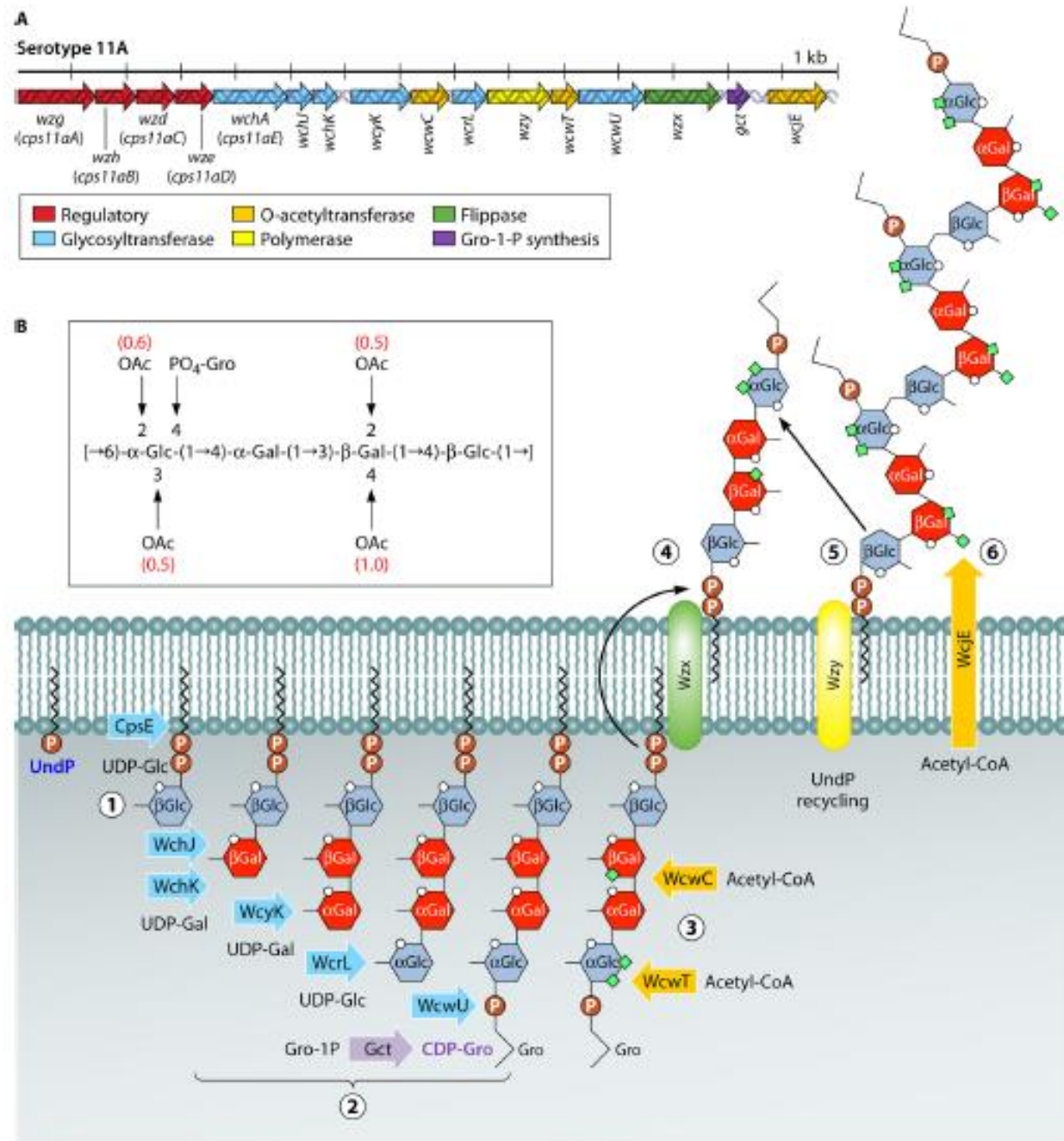


FIG 2 Serotype 3 has a divergent *cps* locus and utilizes synthase-dependent assembly. (A) The serotype 3 *cps* locus (based on GenBank accession no. CR931634.2). The *cps* locus occurs between *dexB* and *aliA* on the chromosome. Note that *ugd* (*cps3D*) and *wcbE* (*cps3S*) are necessary for capsular synthesis, and *wzd*, *galU*, and *pgm* (*) are dispensable (66, 73, 74, 275, 276). (B) The Cps3S synthase synthesizes serotype 3 PS (structure shown in the inset). Cps3S initiates synthesis by transfer of glucose (Glc) from UDP-glucose to a phosphatidyl glycerol (PG) acceptor (1), transfers glucuronic acid (GlcUA) from UDP-GlcUA to the PG-linked Glc (2), and extends the capsule to approximately an octosaccharide (3). Under favorable conditions (i.e., relatively high [GlcUA]), Cps3S translocates the PS chain to the external face of the membrane (4) and increases chain length by a processive capsular synthesis mechanism (5). PS is thought to be released when [GlcUA] becomes insufficient to fill the second-sugar binding site of Cps3S before the PS chain advances without a new sugar to bind in the first binding site.

11A

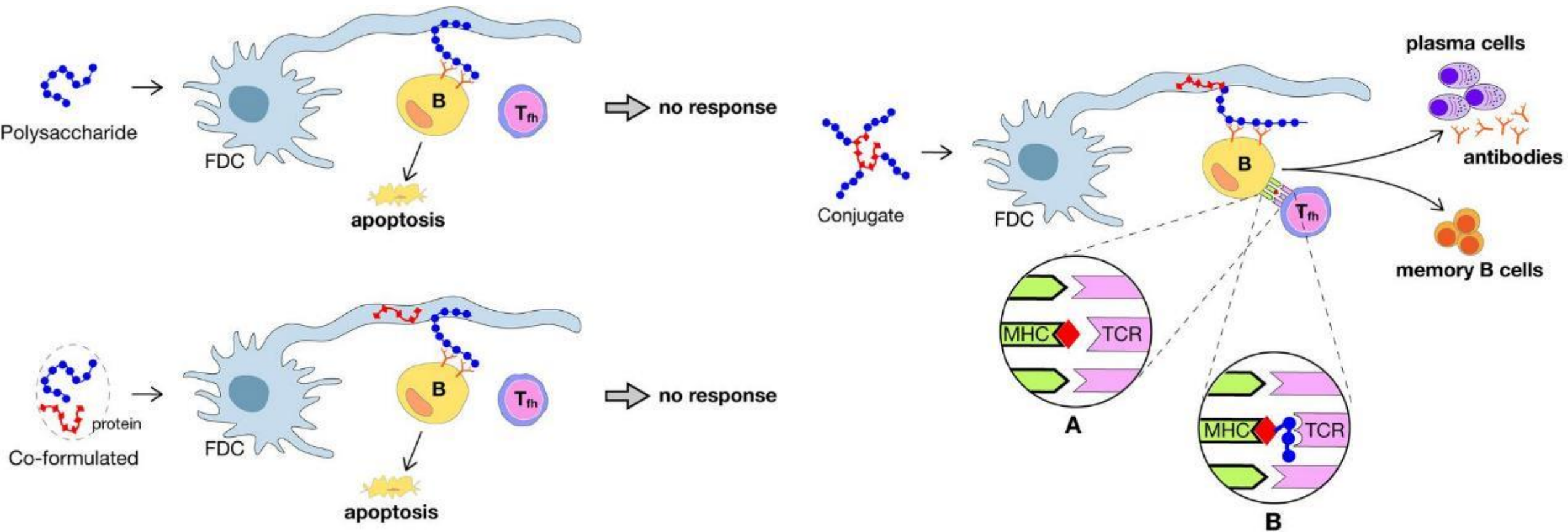


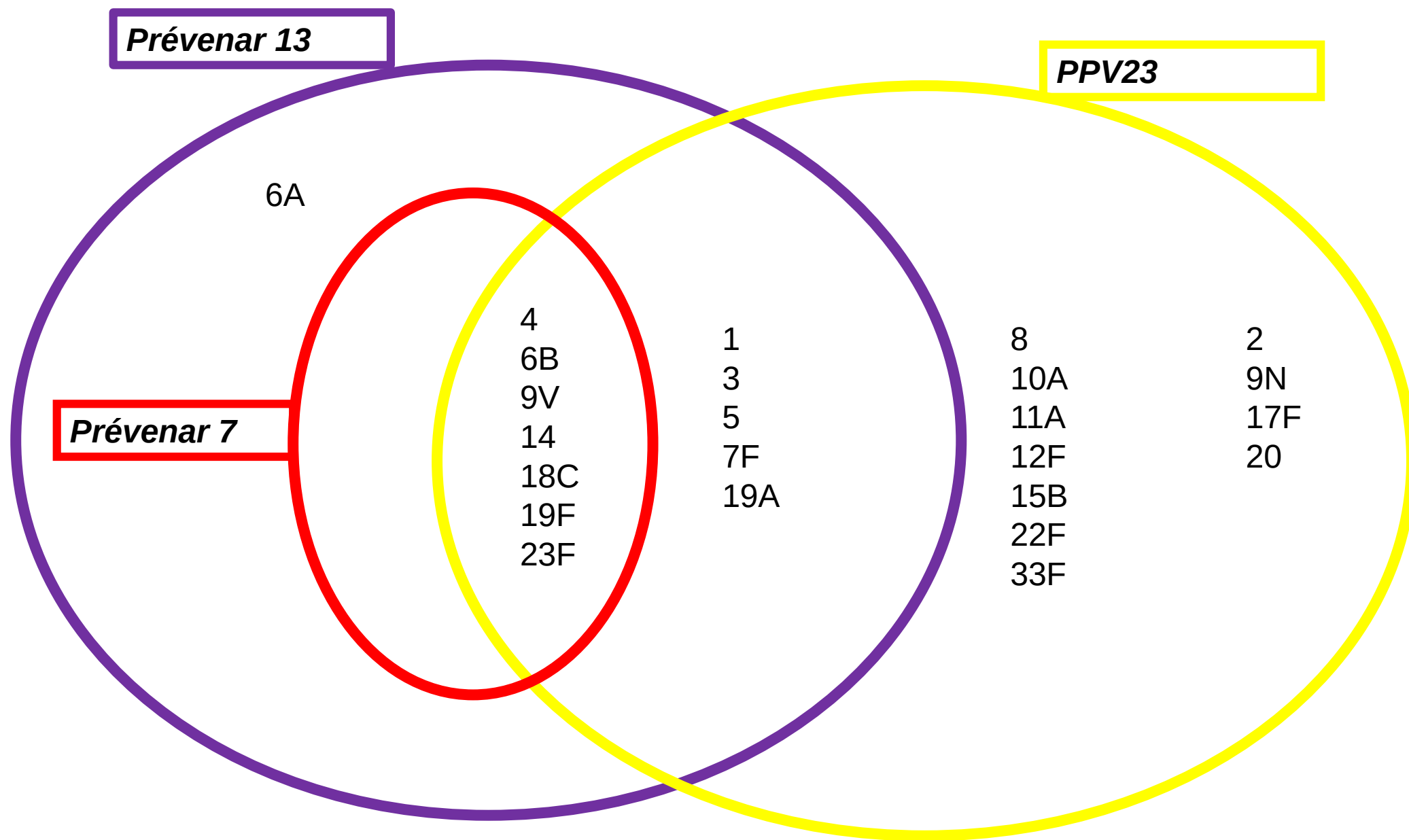
Vaccins anti-pneumococciques

- Vaccins polysaccharidiques
 - Pneumovax®, pneumo23®
 - 23 sérotypes
 - Mauvaise réponse chez le nourrisson
 - AMM après 5 ans
 - Peu ou pas d'induction de mémoire immunologique
 - Risque d'hyporéactivité si revaccination par vaccin conjugué ou pas
- Vaccins conjugués
 - Prévenar7® puis Prévenar13® puis ... Vaxneuvance (15v) et Apexxnar (20v)
 - Conjugaison à un dérivé de l'anatoxine diphtérique
 - Meilleure réponse chez le nourrisson, et chez l'immunodéprimé
 - AMM avant 5 ans et après 50 ans
 - Induction d'une mémoire immunologique
 - Efficacité sur le portage

On the mechanisms of conjugate vaccines

Rino Rappuoli^{a,b,1}, Ennio De Gregorio^a, and Paolo Costantino^c





ORIGINAL ARTICLE

Polysaccharide Conjugate Vaccine against Pneumococcal Pneumonia in Adults

M.J.M. Bonten, S.M. Huijts, M. Bolkenbaas, C. Webber, S. Patterson, S. Gault, C.H. van Werkhoven, A.M.M. van Deursen, E.A.M. Sanders, T.J.M. Verheij, M. Patton, A. McDonough, A. Moradoghli-Haftvani, H. Smith, T. Mellelieu, M.W. Pride, G. Crowther, B. Schmoele-Thoma, D.A. Scott, K.U. Jansen, R. Lobatto, B. Oosterman, N. Visser, E. Caspers, A. Smorenburg, E.A. Emini, W.C. Gruber, and D.E. Grobbee

84,496 adults 65 years of age or older

NB and NI : non bacteremic and non-invasive

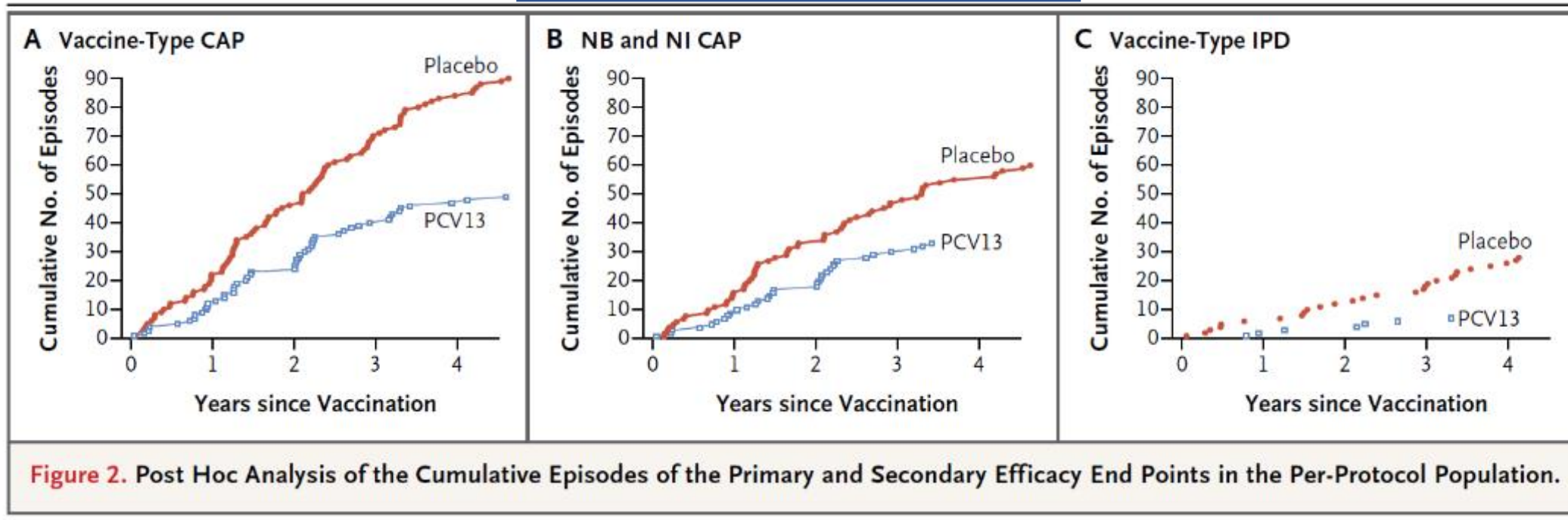
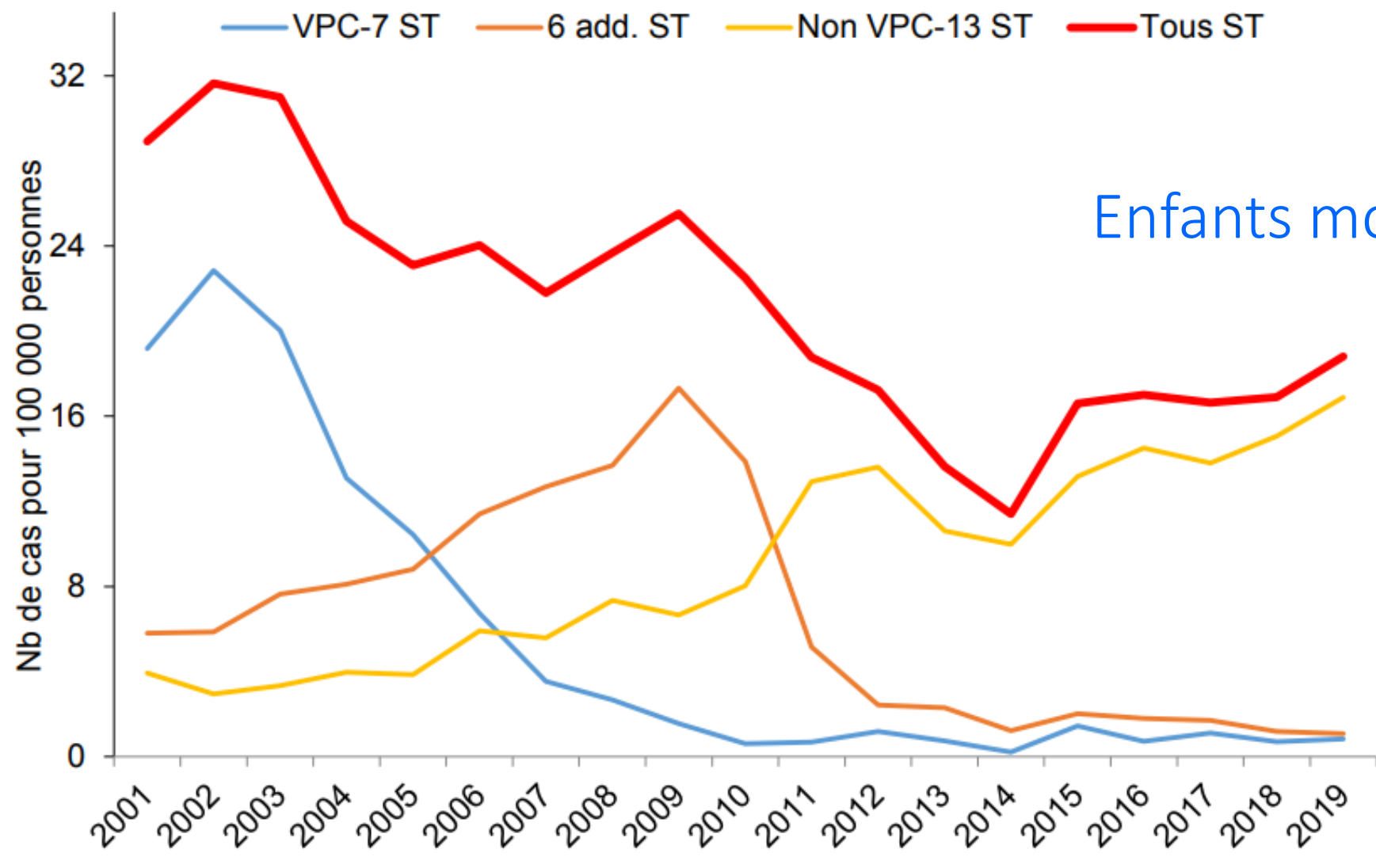
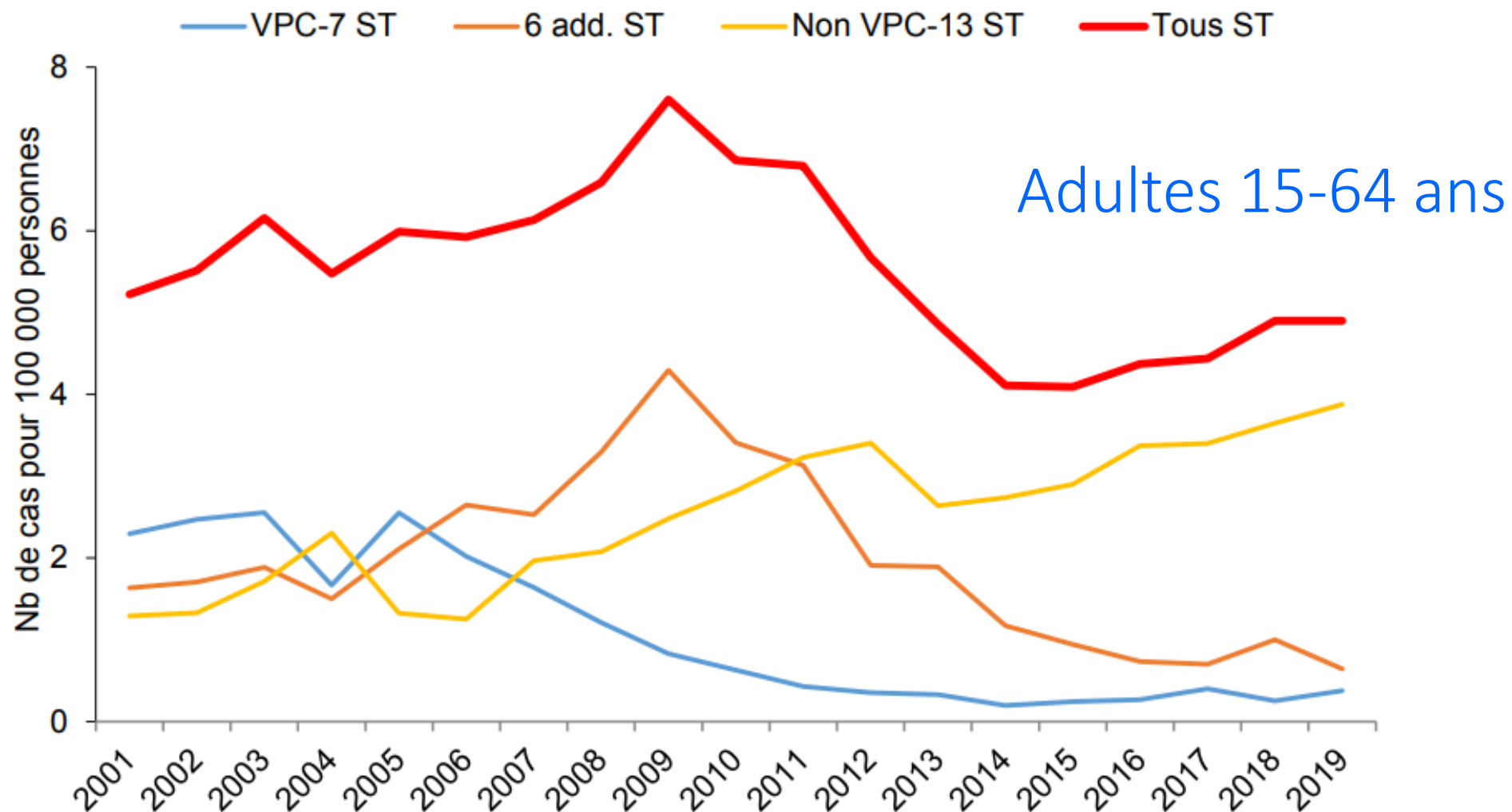


Figure 2 : Incidence des infections invasives à pneumocoques par groupe de sérotypes, chez les enfants âgés de moins de 2 ans, France métropolitaine, 2001-2019*



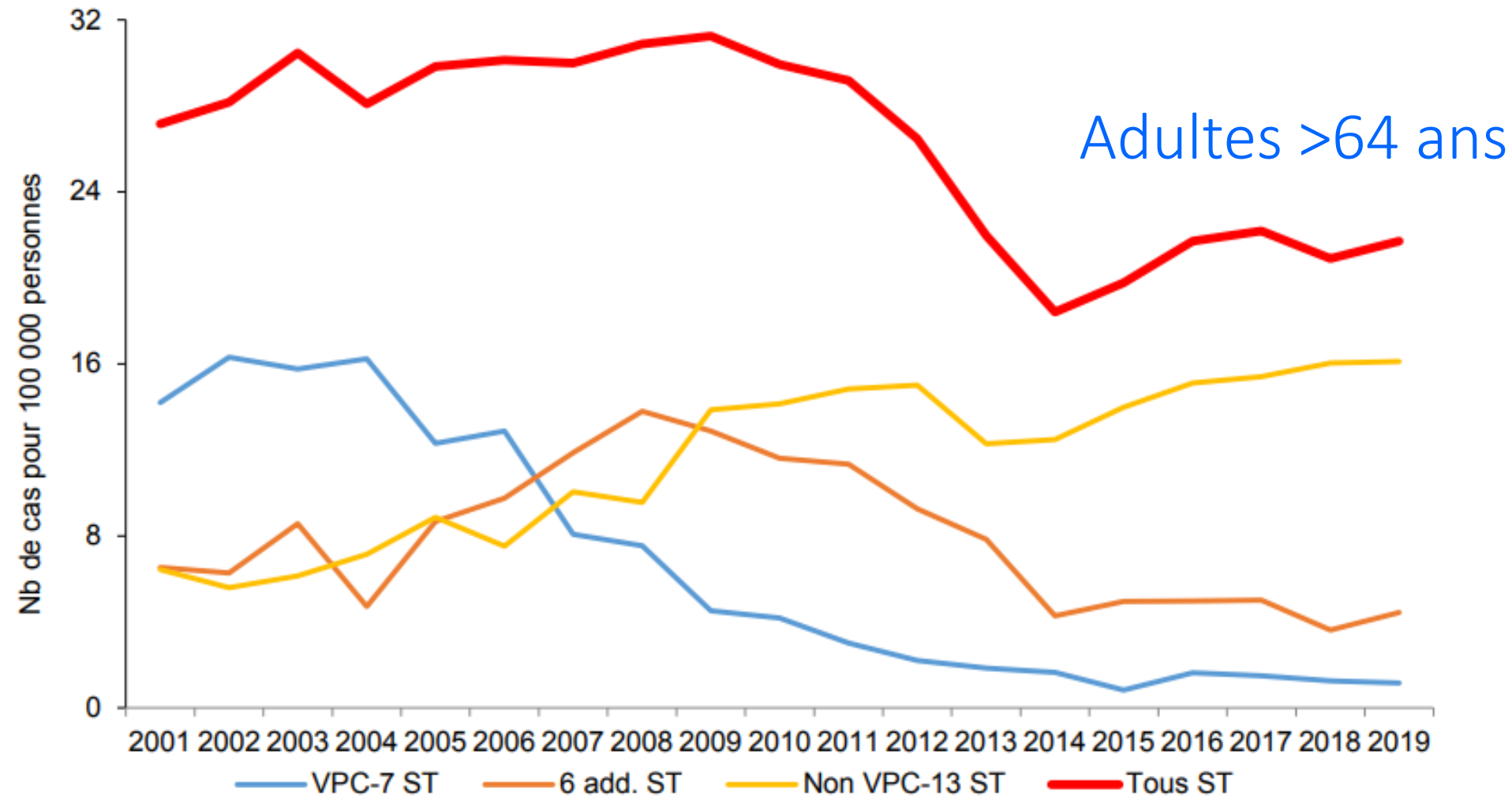
*VPC7 ST= sérotypes du VPC7, 6 add.ST= sérotypes additionnels du VPC13, Non VPC13 ST= sérotypes non contenus dans le VPC13, Tous ST= tous les sérotypes identifiés

Figure 5 : Incidence des infections invasives à pneumocoques par groupe de sérotypes, chez les enfants et adultes âgés de 15 à 64 ans, France métropolitaine 2001-2019*



*VPC7 ST= sérotypes du VPC7, 6 add.ST= sérotypes additionnels du VPC13 ; Non VPC13 ST= sérotypes non contenus dans le VPC13 ; Tous ST= tous les sérotypes identifiés

Figure 6 : Incidence des infections invasives à pneumocoques par groupe de sérotypes, chez les adultes âgés de 65 ans et plus, France métropolitaine 2001-2019*



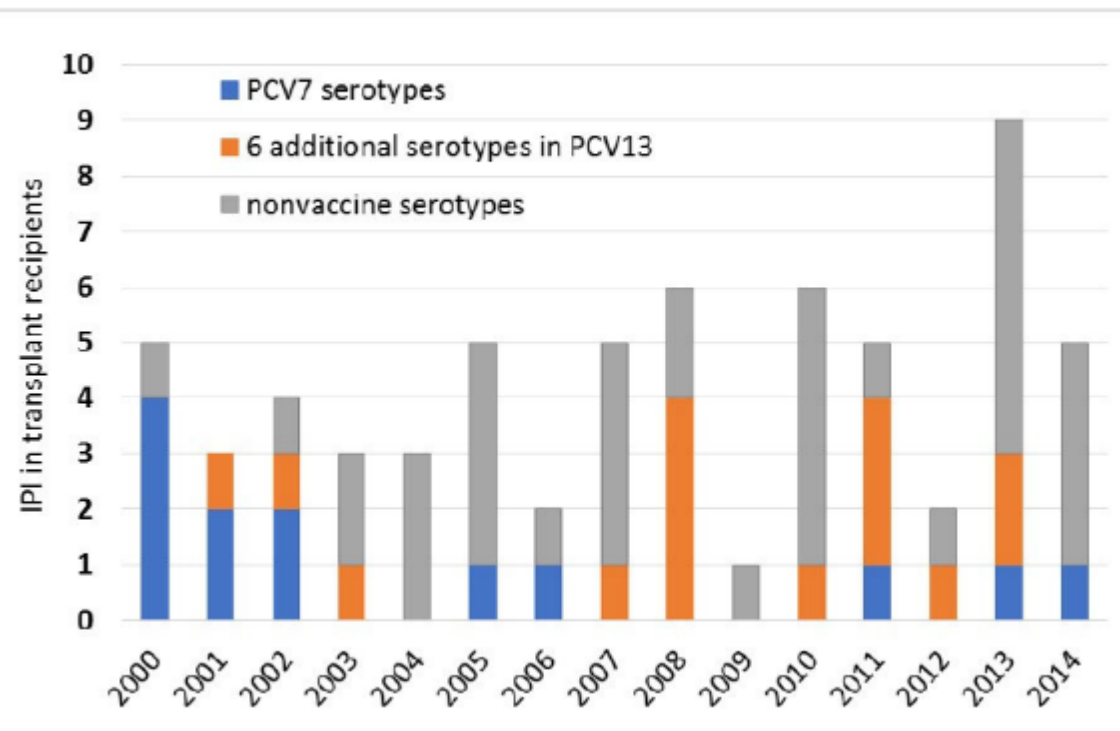
*VPC7 ST= sérotypes du VPC7, 6 add.ST= sérotypes additionnels du VPC13 ; Non VPC13 ST= sérotypes non contenus dans le VPC13 ; Tous ST= tous les sérotypes identifiés

ORIGINAL ARTICLE

WILEY

Invasive pneumococcal infections in children following transplantation in the pneumococcal conjugate vaccine era

Liset Olarte¹ | Philana Ling Lin² | William J. Barson³ | Jose R. Romero⁴ |
Tina Q. Tan⁵ | Laurence B. Givner⁶ | Jill A. Hoffman⁷ | John S. Bradley⁸ |
Kristina G. Hultén¹ | Edward O. Mason¹ | Sheldon L. Kaplan¹





In addition, many adults have to pay for pneumococcal vaccination, even if it is recommended. Only 15 countries in this report (36%) reimburse or cover the cost for all three groups through their national healthcare systems.

Indication vaccinale
chez les seniors (hors
comorbidités)

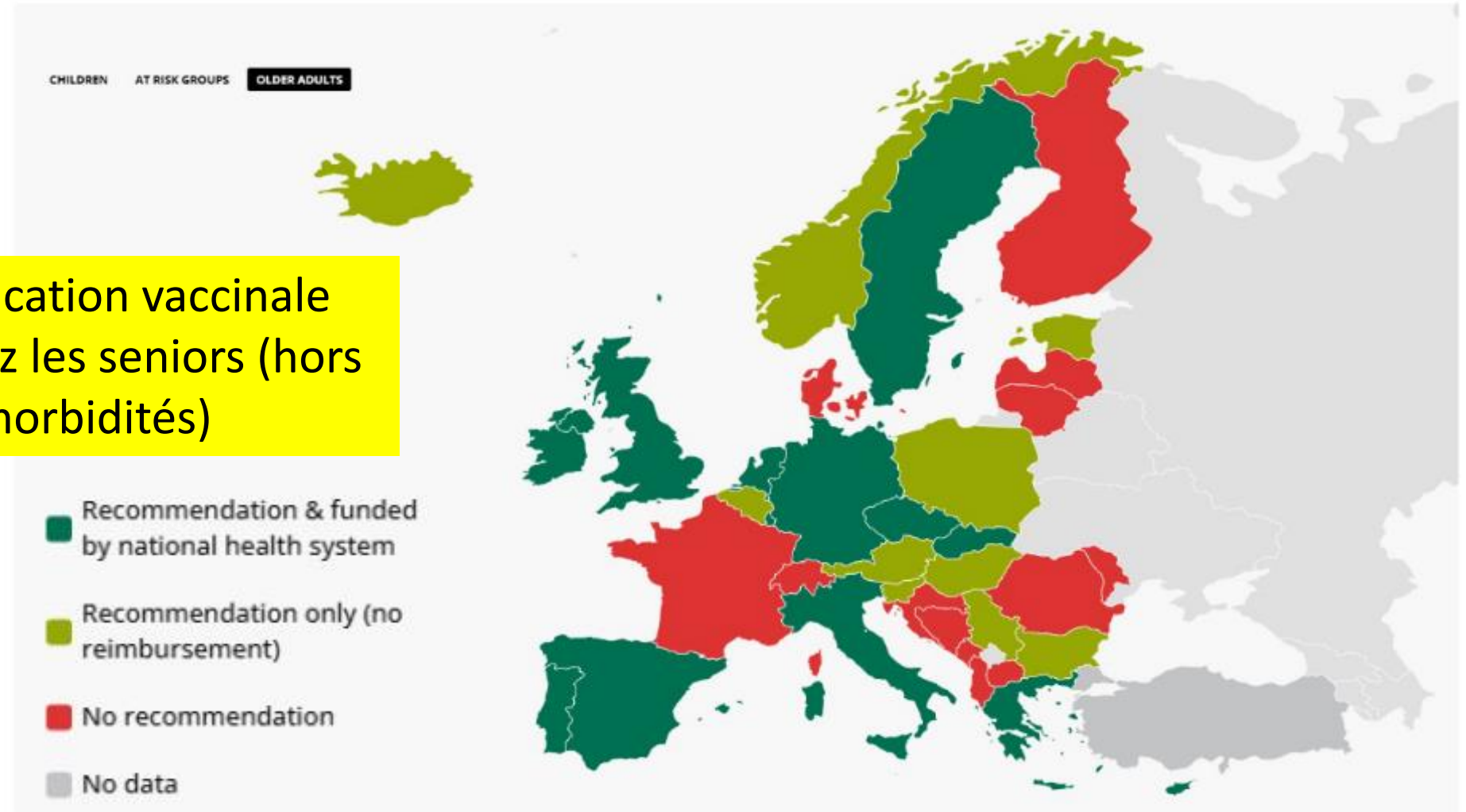


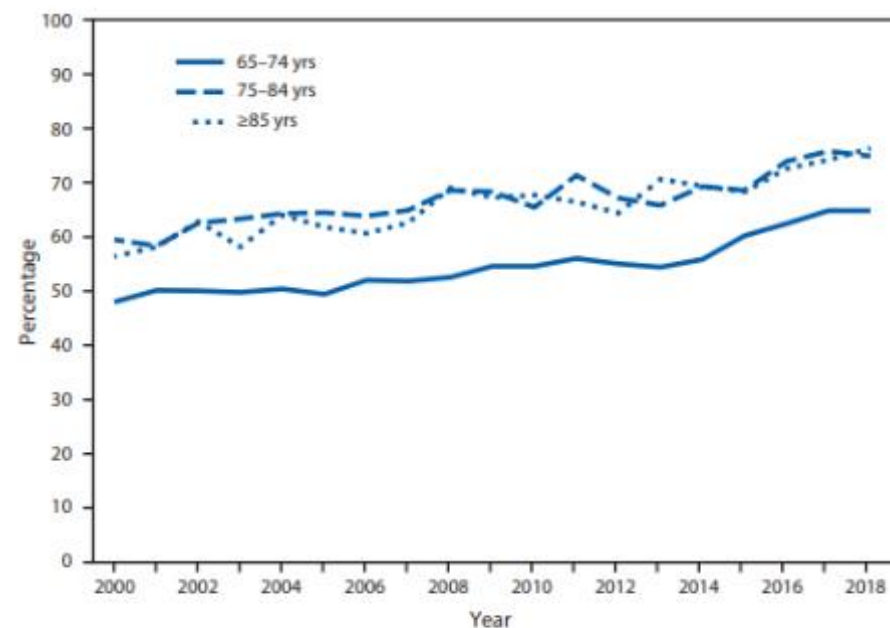
Figure 3: A patchwork of policies: In some countries, pneumococcal vaccination is recommended and funded for older adults; in others it is recommended but not reimbursed; and in several countries there is no recommendation for older people.

MMWR 2020

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage of Adults Aged ≥ 65 Years Who Had Ever Received Pneumococcal Vaccination,* by Age Group — National Health Interview Survey,[†] United States, 2000–2018



* Based on the survey question "Have you ever had a pneumonia shot? This shot is usually given only once or twice in a person's lifetime and is different from the flu shot. It is also called the pneumococcal vaccine." In 2000, the question wording included the following statement: "This shot is usually given only once in a person's lifetime and is different from the flu shot." Practice recommendations regarding who should receive pneumococcal vaccination and the types and number of vaccines have changed over time, and trends in vaccination receipt could reflect changes in recommendations.

[†] Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population and are derived from the National Health Interview Survey Sample Adult component. Unknowns for vaccination status were not included in the denominators when calculating percentages.

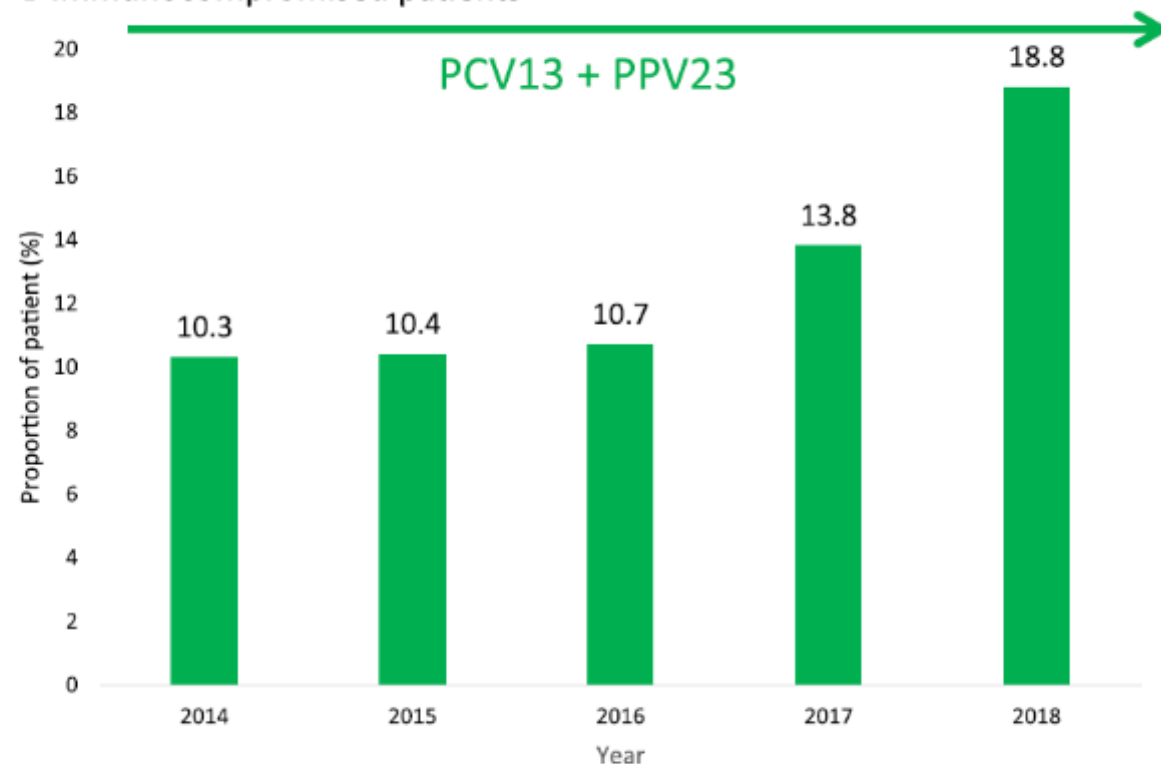


Pneumococcal and influenza vaccination coverage among at-risk adults: A 5-year French national observational study



Benjamin Wyplosz^{a,*}, Jérôme Fernandes^b, Ariane Sultan^c, Nicolas Roche^d, François Roubille
Bertrand Fougère^g, Bruno Moulin^h, Didier Duhotⁱ, Alexandre Vainchtock^j, Fanny Raguideau
Joannie Lortet-Tieulent^j, Emmanuelle Blanc^k, Jennifer Moïsi^k, Gwenaél Goussiaume^k

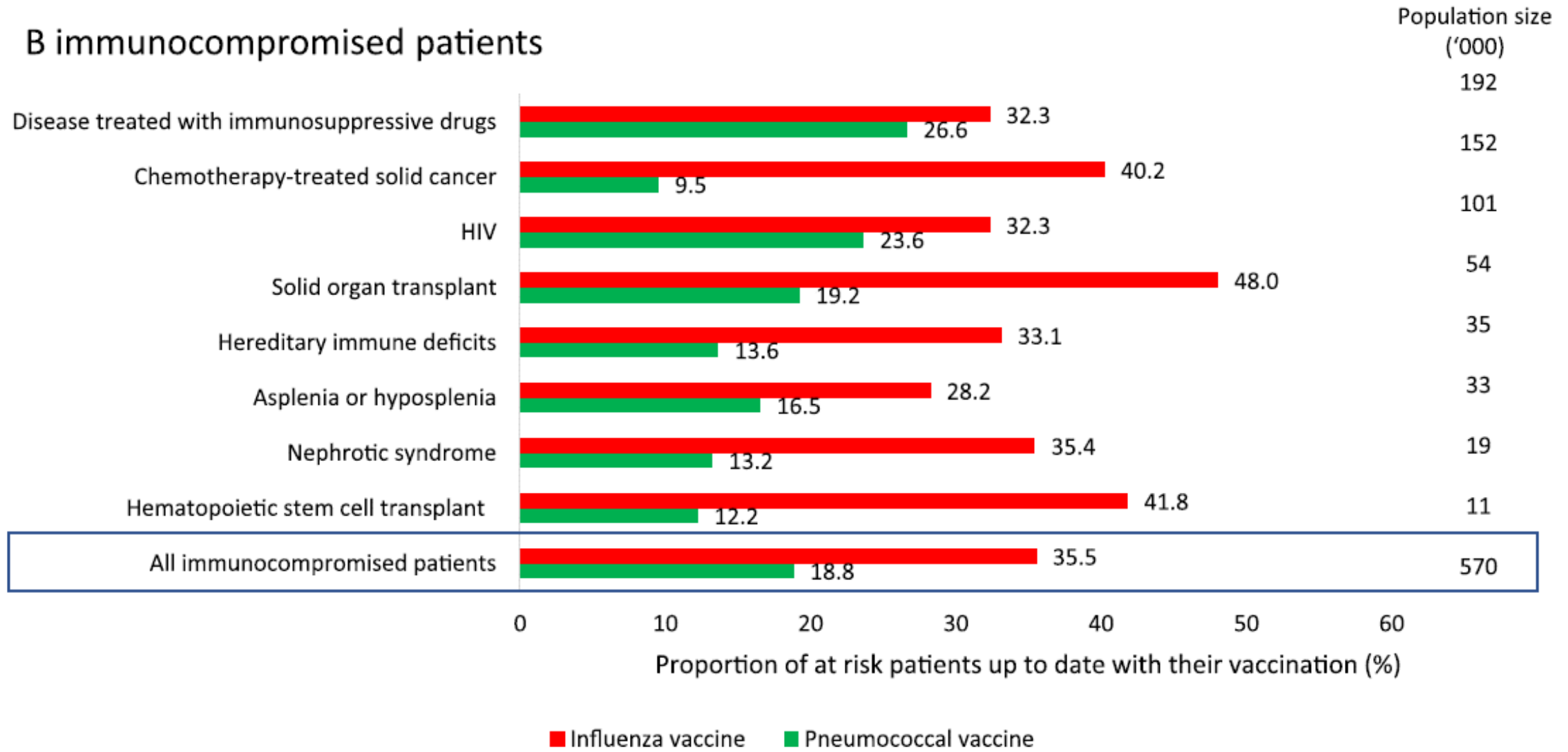
B Immunocompromised patients



■ 2013 Guidelines: PCV13 and PPV23, then PPV23 at least 5 years apart

No. of patients	490,556	513,137	536,645	562,134	570,035
-----------------	---------	---------	---------	---------	---------

B immunocompromised patients



ÉVALUER
LES TECHNOLOGIES DE SANTÉ

**RAPPORT
D'ÉVALUATION**

Stratégie de vaccination contre les infections à pneumocoque

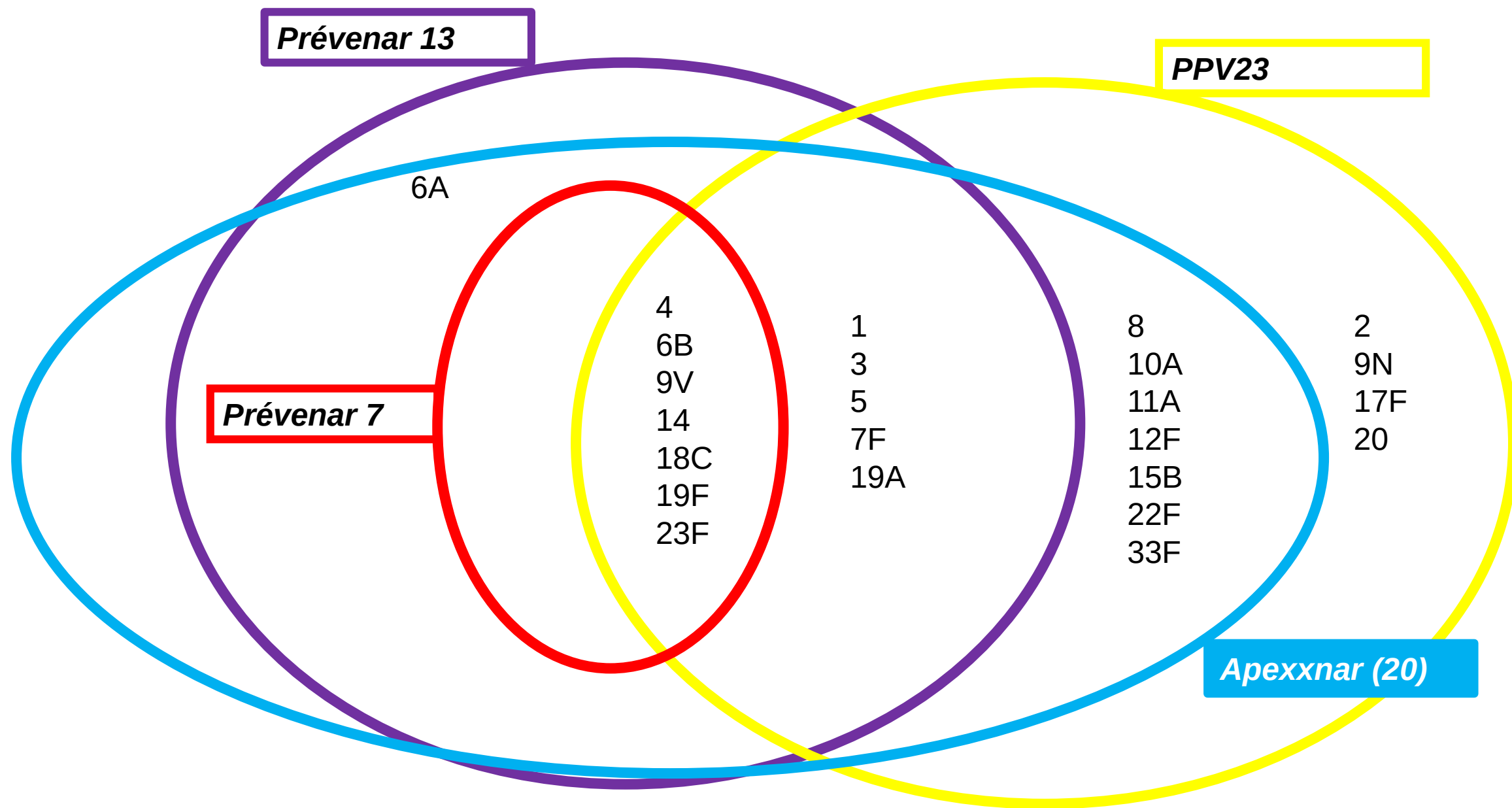
Place du vaccin pneumococcique
polyosidique conjugué (20-valent,
adsorbé) chez l'adulte

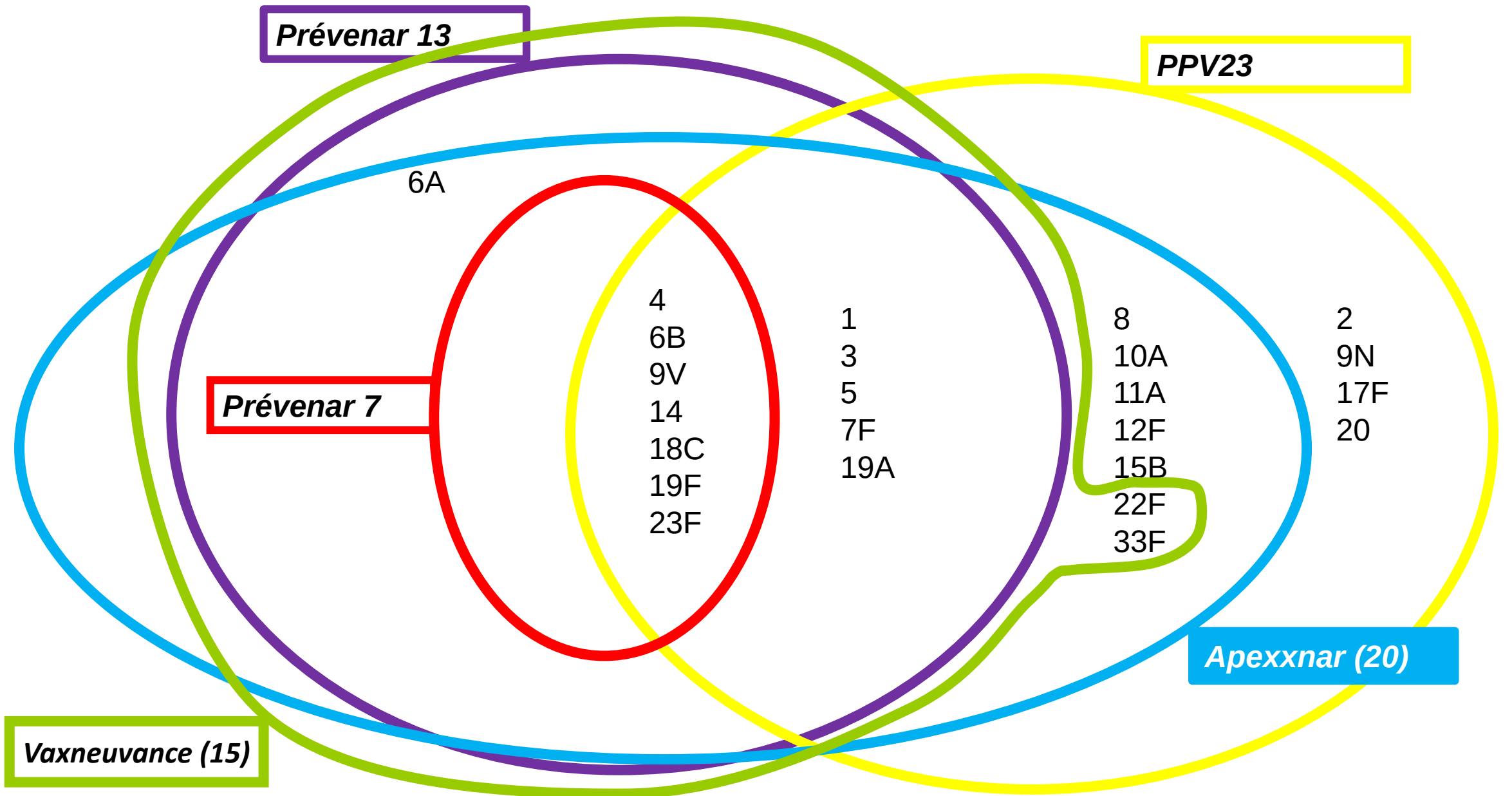
ÉVALUER
LES TECHNOLOGIES DE SANTÉ

**RAPPORT
D'ÉVALUATION**

Stratégie de vaccination contre les infections à pneumocoque

Place du vaccin VAXNEUVANCE
chez l'enfant de 6 semaines à 18
ans





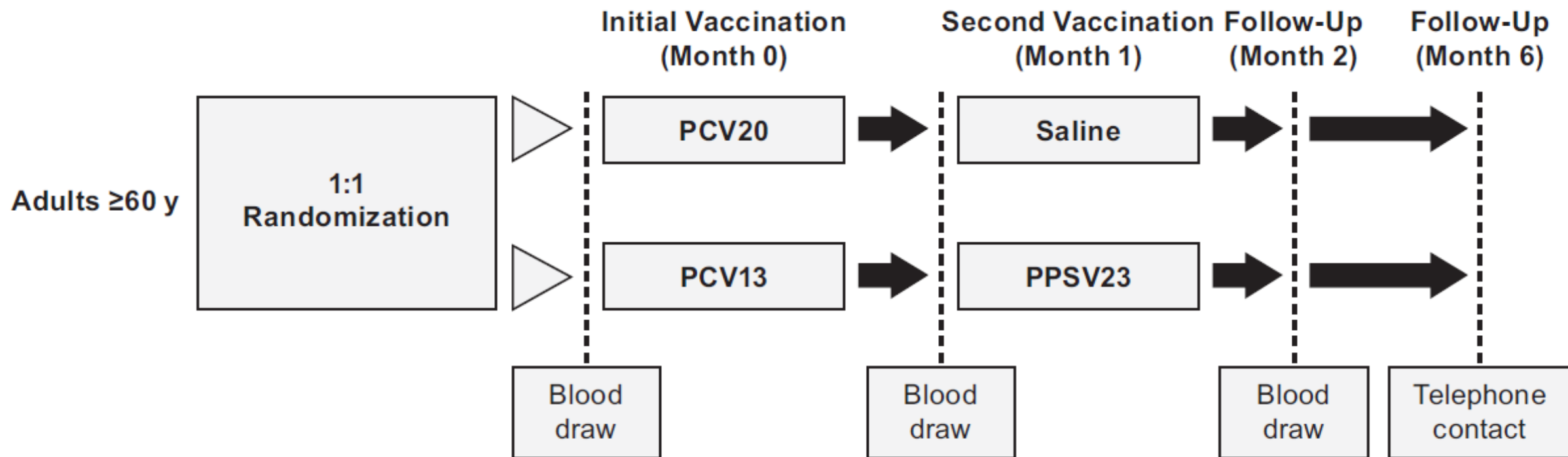
Pivotal Phase 3 Randomized Clinical Trial of the Safety, Tolerability, and Immunogenicity of 20-Valent Pneumococcal Conjugate Vaccine in Adults Aged ≥ 18 Years

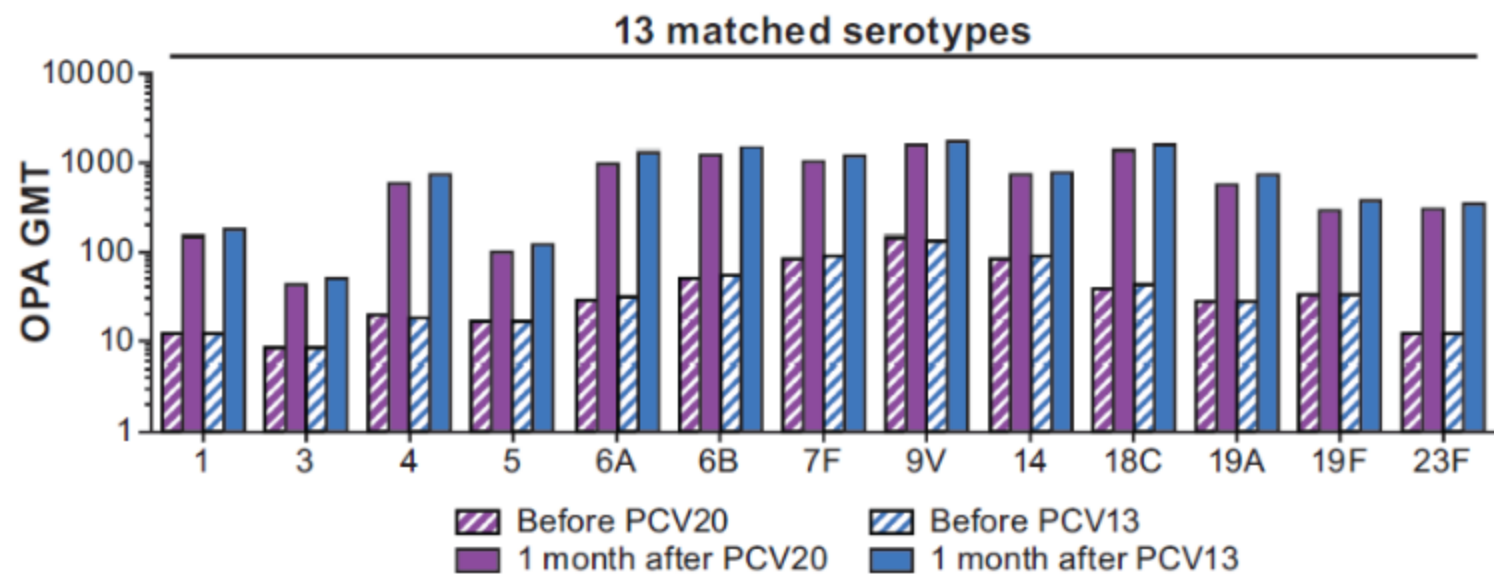
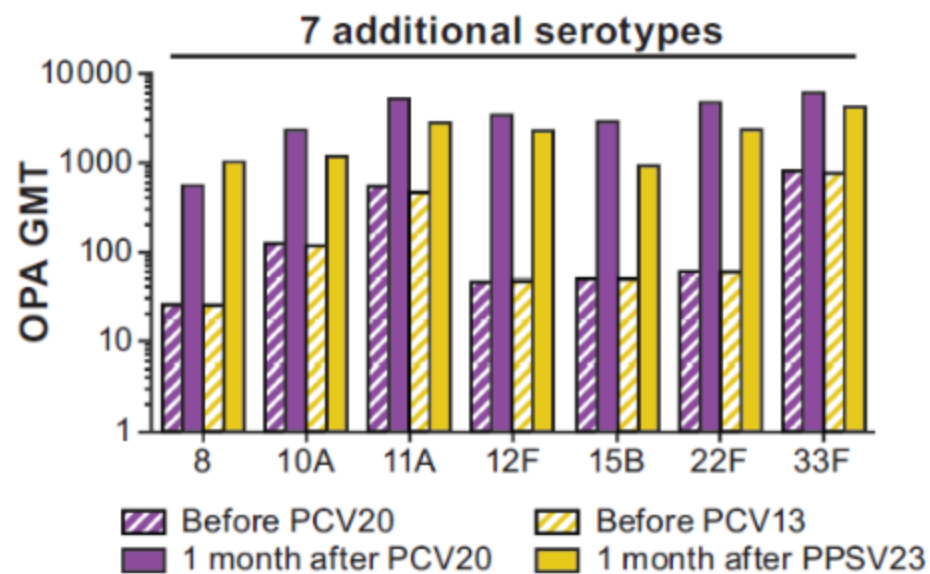
2023

Brandon Essink,¹ Charu Sabharwal,² Kevin Cannon,³ Robert Frenck,⁴ Himal Lal,⁵ Xia Xu,⁵ Vani Sundaraiyer,⁶ Yahong Peng,⁵ Lisa Moyer,⁵ Michael W. Pride,² Ingrid L. Scully,² Kathrin U. Jansen,² William C. Gruber,² Daniel A. Scott,⁵ and Wendy Watson⁵

¹Meridian Clinical Research, Omaha, Nebraska, USA; ²Vaccine Research and Development, Pfizer Inc, Pearl River, New York, USA; ³PMG Research of Wilmington, Wilmington, North Carolina, USA;

⁴Cincinnati Children's Hospital, Cincinnati, Ohio, USA; ⁵Vaccine Research and Development, Pfizer Inc, Collegeville, Pennsylvania, USA; and ⁶Syneos Health, Somerset, New Jersey, USA



A**B**

Immunogénicité par sérotype : étude B7471007

VPC20 ou VPC13 puis VPP23

13 sérotypes communs

Sujets >60 ans

Tableau 8 : Moyenne géométrique des titres OPA et ratio des moyennes géométriques un mois après la vaccination (par VPC 20 ou VPC 13 + VPP 23), pour les 13 sérotypes inclus dans VPC 13

	VPC 20			Groupe contrôle VPC 13/VPP 23			Comparaison	
Sérotype	N	MGT	IC95%	N	MGT	IC95%	Ratio MGT	IC95%
1	1430	123,4	112,3-135,5	1419	153,8	140,2-168,8	0,80	0,71-0,90
3	1415	40,7	38,0-43,6	1411	47,8	44,7-51,2	0,85	0,78-0,93
4	1415	508,7	456,5-566,9	1409	626,9	563,5-697,4	0,81	0,71-0,93
5	1418	91,6	83,4-100,5	1395	109,7	100,1-120,3	0,83	0,74-0,94
6A	1403	889,0	795,0-994,1	1390	1165,1	1043,3-1301,0	0,76	0,66-0,88
6B	1413	1115,2	1003,1-1239,8	1401	1341,3	1208,5-1488,8	0,83	0,73-0,95
7F	1409	968,8	887,0-1058,3	1391	1129,2	1034,7-1232,4	0,86	0,77-0,96
9V	1399	1455,5	1317,5-1608,0	1391	1567,8	1420,5-1730,5	0,93	0,82-1,05
14	1418	746,7	679,0-821,2	1408	746,7	679,8-820,1	1,00	0,89-1,13
18C	1420	1252,6	1123,1-1397,0	1403	1482,3	1330,5-1651,5	0,85	0,74-0,97
19A	1420	517,9	472,2-568,0	1398	645,3	588,9-707,1	0,80	0,71-0,90
19F	1421	265,8	240,2-294,1	1403	333,3	301,5-368,3	0,80	0,70-0,91
23F	1424	276,5	242,5-315,2	1409	335,1	294,4-381,4	0,83	0,70-0,97

Immunogénicité par sérotype : étude B7471007

VPC20 ou VPC13 puis VPP23

7 sérotypes additionnels

Tableau 11 : Moyenne géométrique des titres OPA et ratio des moyennes géométriques un mois après la vaccination (population d'immunogénicité évaluable pour les 7 sérotypes additionnels, Cohorte 1)

	VPC 20			Groupe contrôle VPC 13/VPP 23			Comparaison des groupes		
Sérotype	N	MGT	IC95%	N	MGT	IC95%	Ratio MGT	IC95%	p
8	1374	465,6	422,5-513,1	1319	848,1	769,1-935,2	0,55	0,49-0,62	>0,999
10A	1310	2007,6	1808,0-2229,1	1263	1079,9	972,1-1199,7	1,86	1,63-2,12	<0,001
11A	1198	4426,8	3965,5-4941,8	1209	2534,9	2276,8-2822,3	1,75	1,52-2,01	<0,001
12F	1294	2538,7	2255,3-2857,7	1222	1716,6	1521,8-1936,3	1,48	1,27-1,72	<0,001
15B	1283	2398,2	2090,6-2751,2	1249	768,5	669,7-881,9	3,12	2,62-3,71	<0,001
22F	1274	3666,2	3244,4-4143,0	1227	1846,2	1636,6-2082,6	1,99	1,70-2,32	<0,001
33F	1157	5125,9	4611,3-5698,0	1201	3720,6	3356,2-4124,6	1,38	1,21-1,57	<0,001

PREVNAR 20

[f Share](#) [X Post](#) [in LinkedIn](#) [✉ Email](#) [🖨 Print](#)

Vaccines

[Emergency Use Authorization
for Vaccines Explained](#)

[Approved Vaccine Products](#)

[Questions about Vaccines](#)

STN: 125731

Proper Name: Pneumococcal 20-valent Conjugate Vaccine

Tradename: PREVNAR 20

Manufacturer: Wyeth Pharmaceuticals LLC

Indication:

- Active immunization for the prevention of invasive disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, and 33F in individuals 6 weeks of age and older.
- Active immunization for the prevention of otitis media caused by *S. pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F in individuals 6 weeks through 5 years of age.
- Active immunization for the prevention of pneumonia caused by *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, and 33F in individuals 18 years of age and older.

Product Information

VAXNEUVANCE

[f Share](#) [X Post](#) [in LinkedIn](#) [✉ Email](#) [🖨 Print](#)

Vaccines

[Emergency Use Authorization
for Vaccines Explained](#)

[Approved Vaccine Products](#)

[Questions about Vaccines](#)

STN: 125741

Proper Name: Pneumococcal 15-valent Conjugate Vaccine

Tradename: VAXNEUVANCE

Manufacturer: Merck Sharp & Dohme LLC

Indication: Active immunization for the prevention of invasive disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F in individuals 6 weeks of age and older.

Product Information

- [Package Insert - VAXNEUVANCE](#)
- [Patient Information - VAXNEUVANCE](#)
- [Demographic Subgroup Information – Pneumococcal 15-valent Conjugate Vaccine \(VAXNEUVANCE\)](#)

Refer to Section 1.1 of the [Clinical Review Memo](#) for information about participation in the clinical trials and any analysis of demographic subgroup outcomes that is notable.

Que va-t-il se passer ?

- Le 20-valent conjugué et le vaxneuvance® n'ont pas encore leur ASMR
- Arrivée 2nd trimestre 2024 ?
- VPC20 : 1 injection pour l'adulte (hors GCSHP) ; rappels ?
- VPC15 : 1 injection suivie de VPP23 pour l'adulte ; rappels ?
- Le VPC20 va probablement « passer » aussi chez le nourrisson
- Quelle coexistence pour ces 2 vaccins ?
 - Ne prescrire que du VPC20 ...
 - Mais avoir le VPC15 disponible en cas de pénurie du 1^{er} ... (drôle de *business model* ...)