



كلية الطب
و الصيدلة - مراكش
FACULTÉ DE MÉDECINE
ET DE PHARMACIE - MARRAKECH



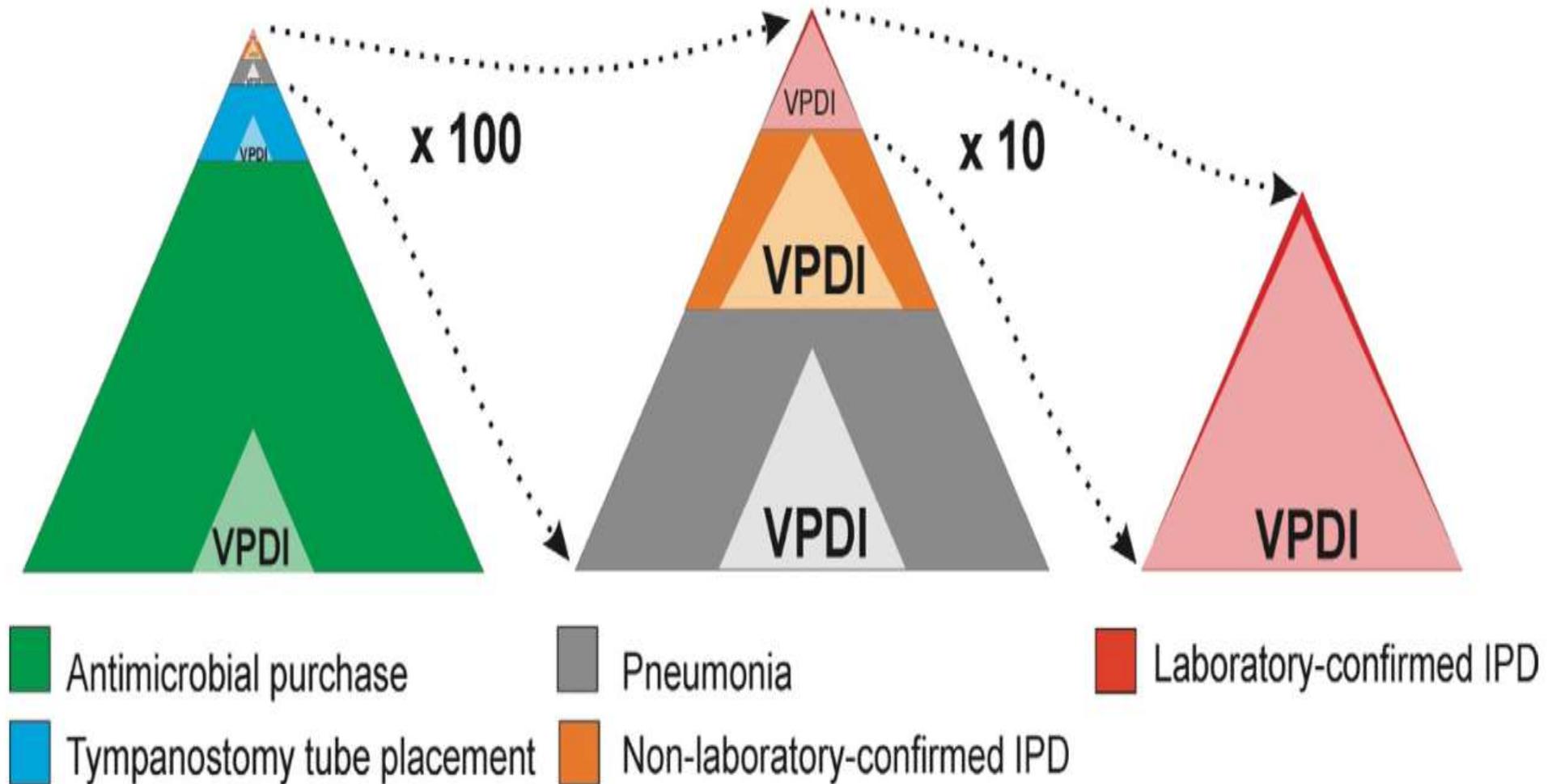
المركز الاستشفائي الجامعي
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مراكش
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La vaccination contre le pneumocoque

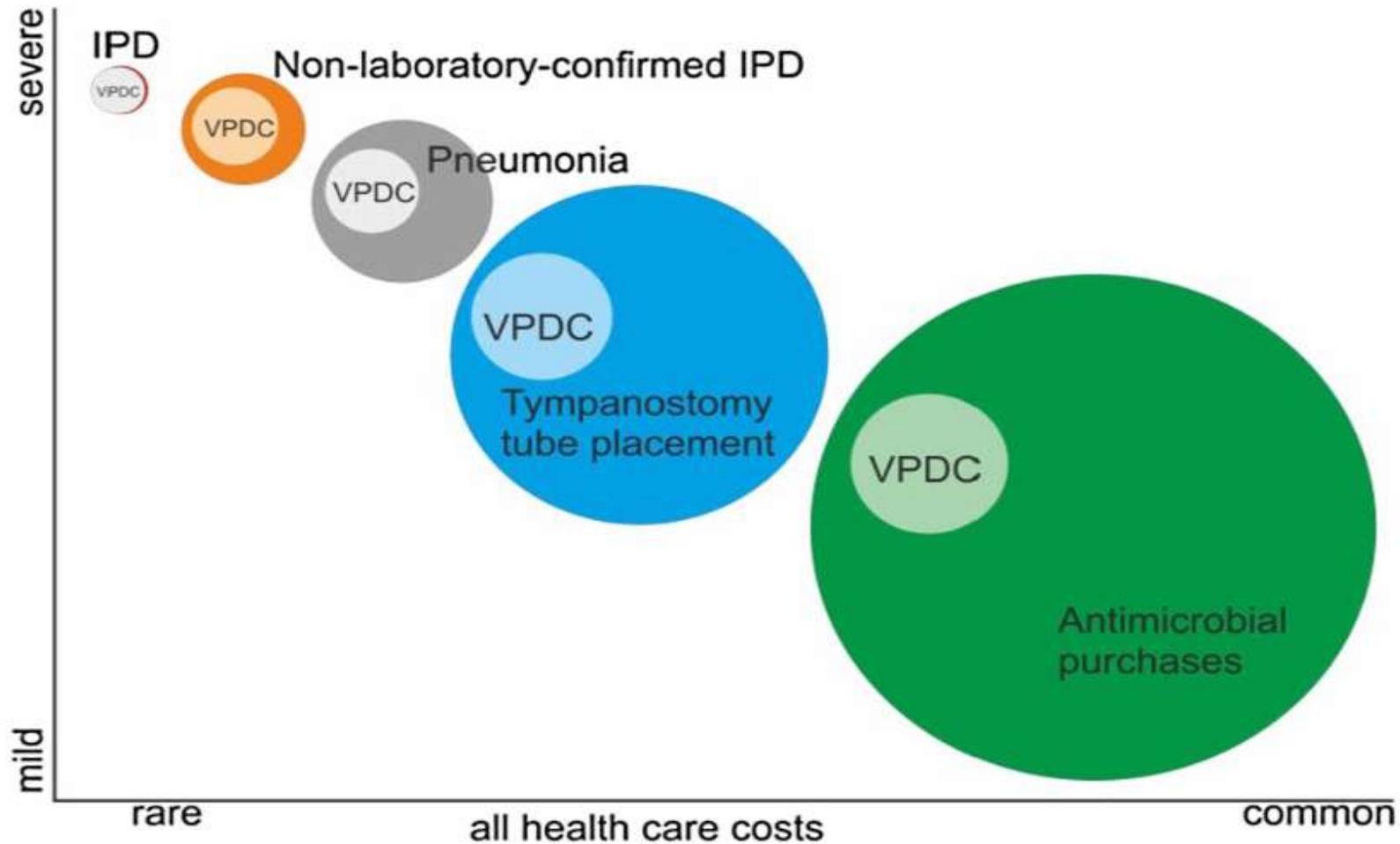
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Incidence de la maladie évitable par la vaccination (VPDI) chez les enfants vaccinés avec PHiD-CV10



Les coûts des soins évitables par la vaccination (VPDC) chez les enfants vaccinés avec PHiD-CV10

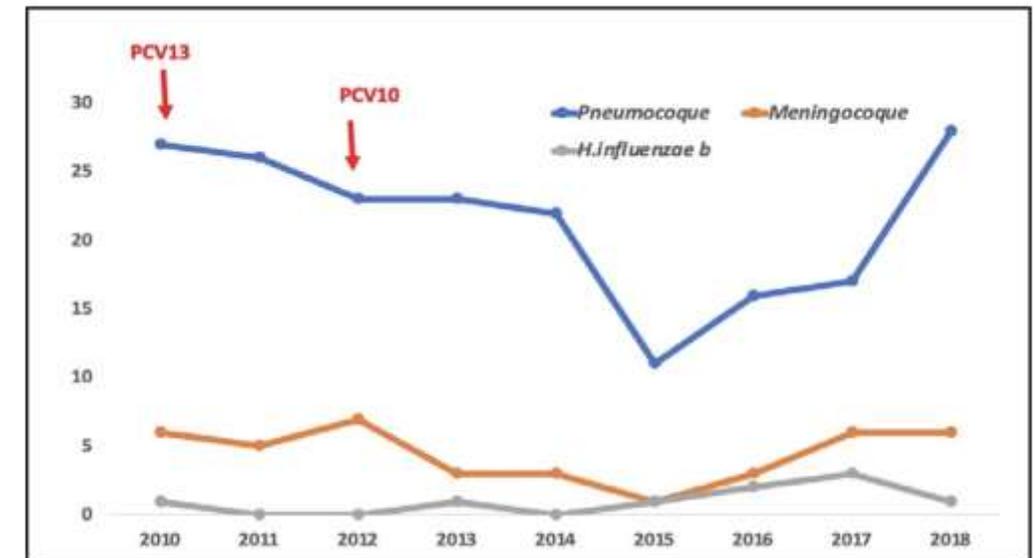
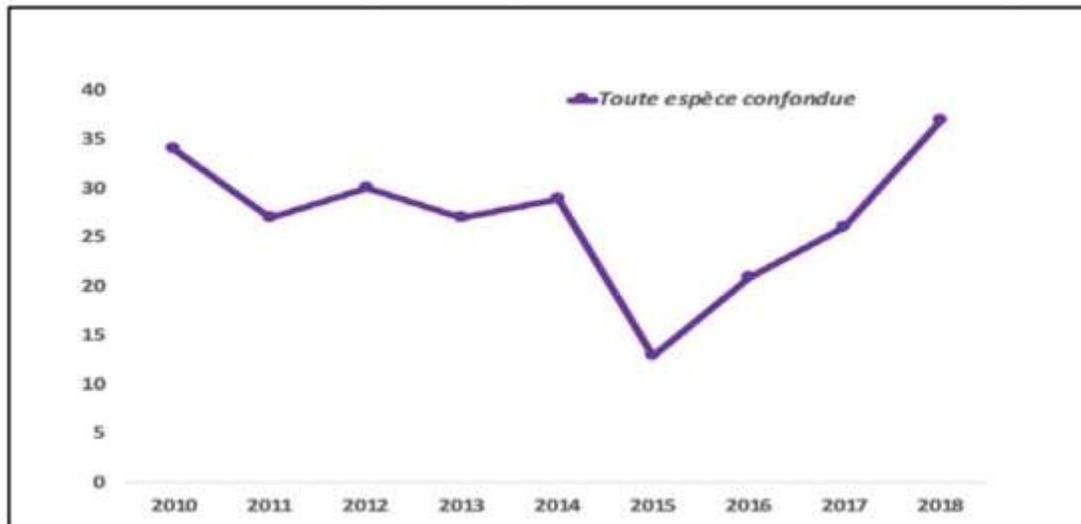
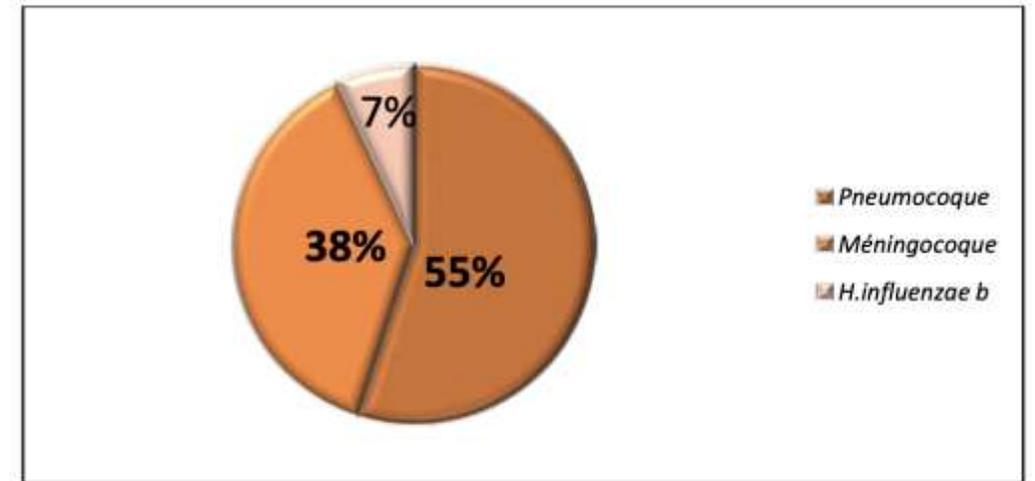
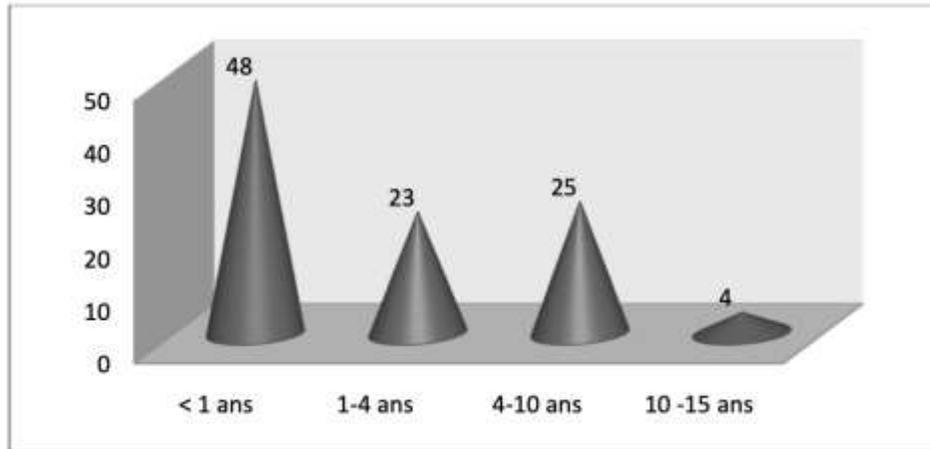


Vaccination contre le pneumocoque

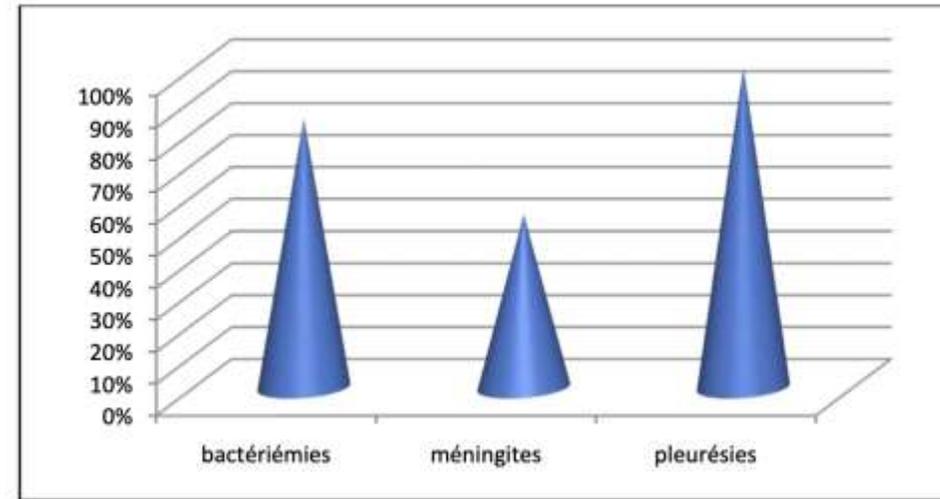
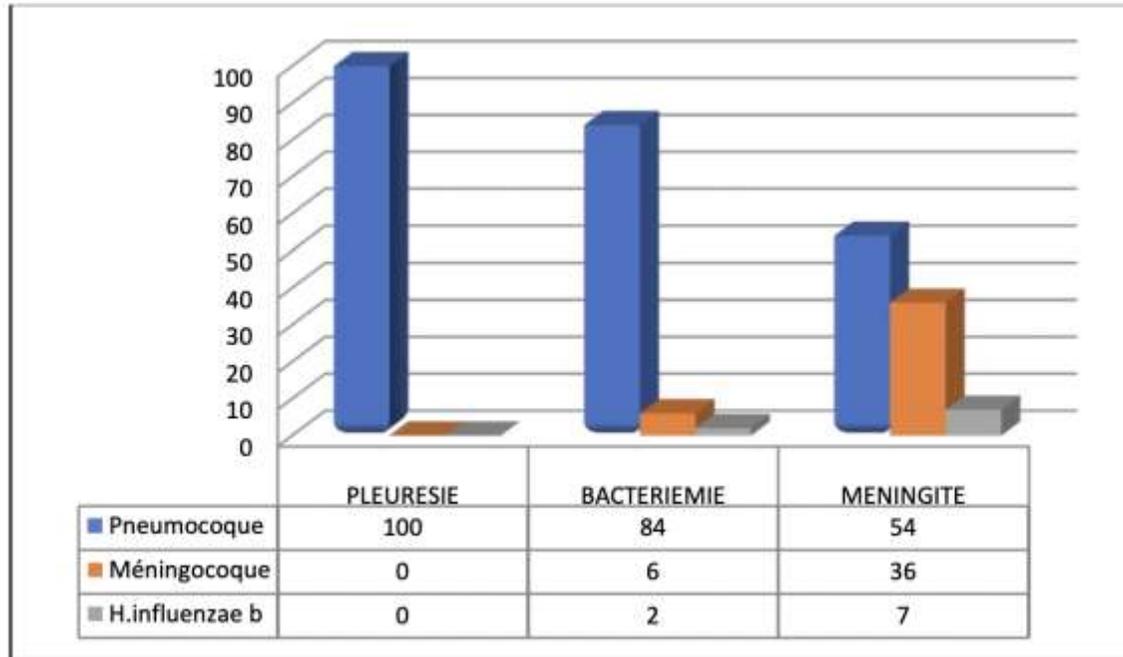
Quelle surveillance épidémiologique ?

- Portage
- Echech otite
- Méningites
- Bactériémie
- Pneumonie et pleuro-pneumopathie

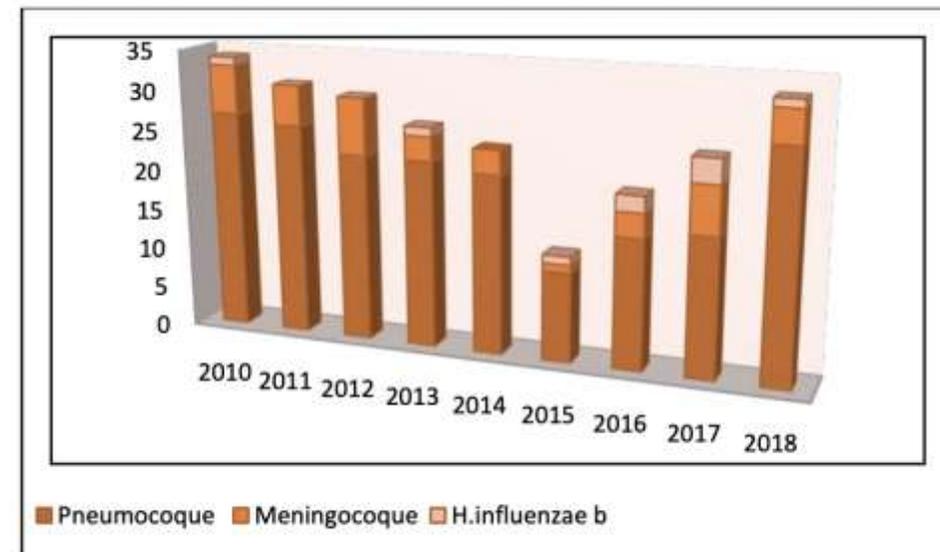
Les infections invasives bactériennes chez L'Enfant au CHU de marrakech



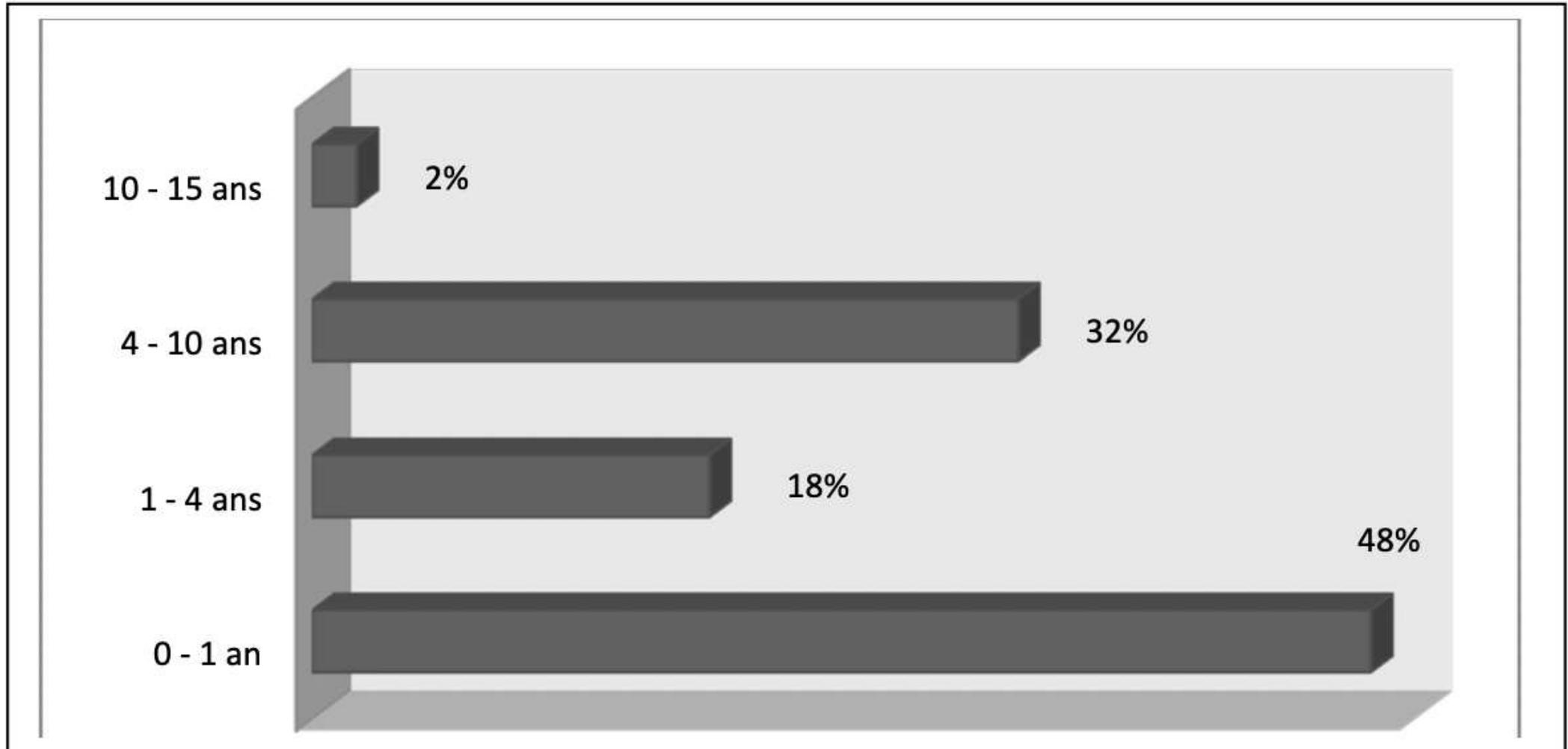
Les infections invasives bactériennes chez L'Enfant au CHU de marrakech



Année 2020 Thèse N° 103

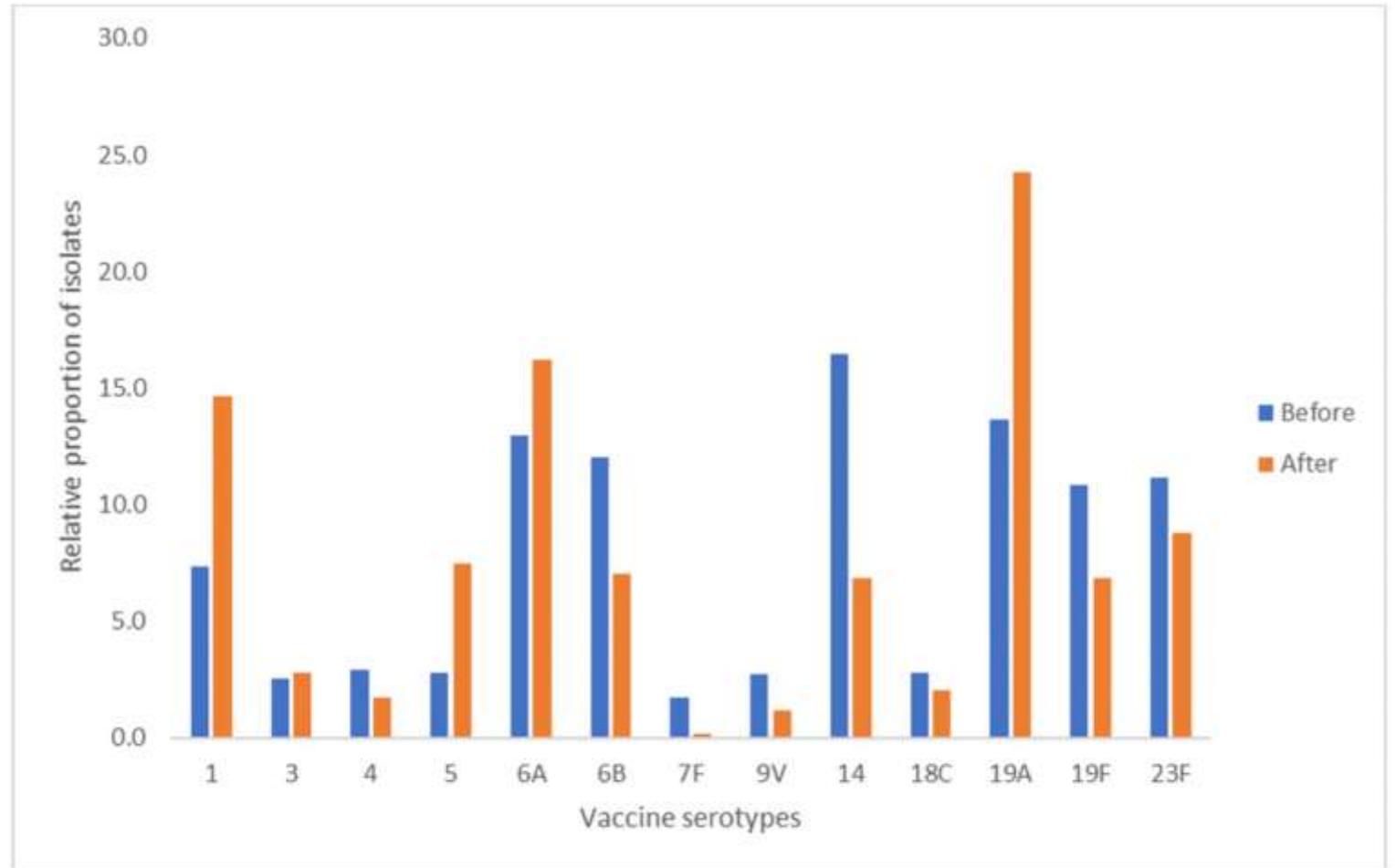


Distribution des infections invasives à pneumocoque selon les tranches d'âge



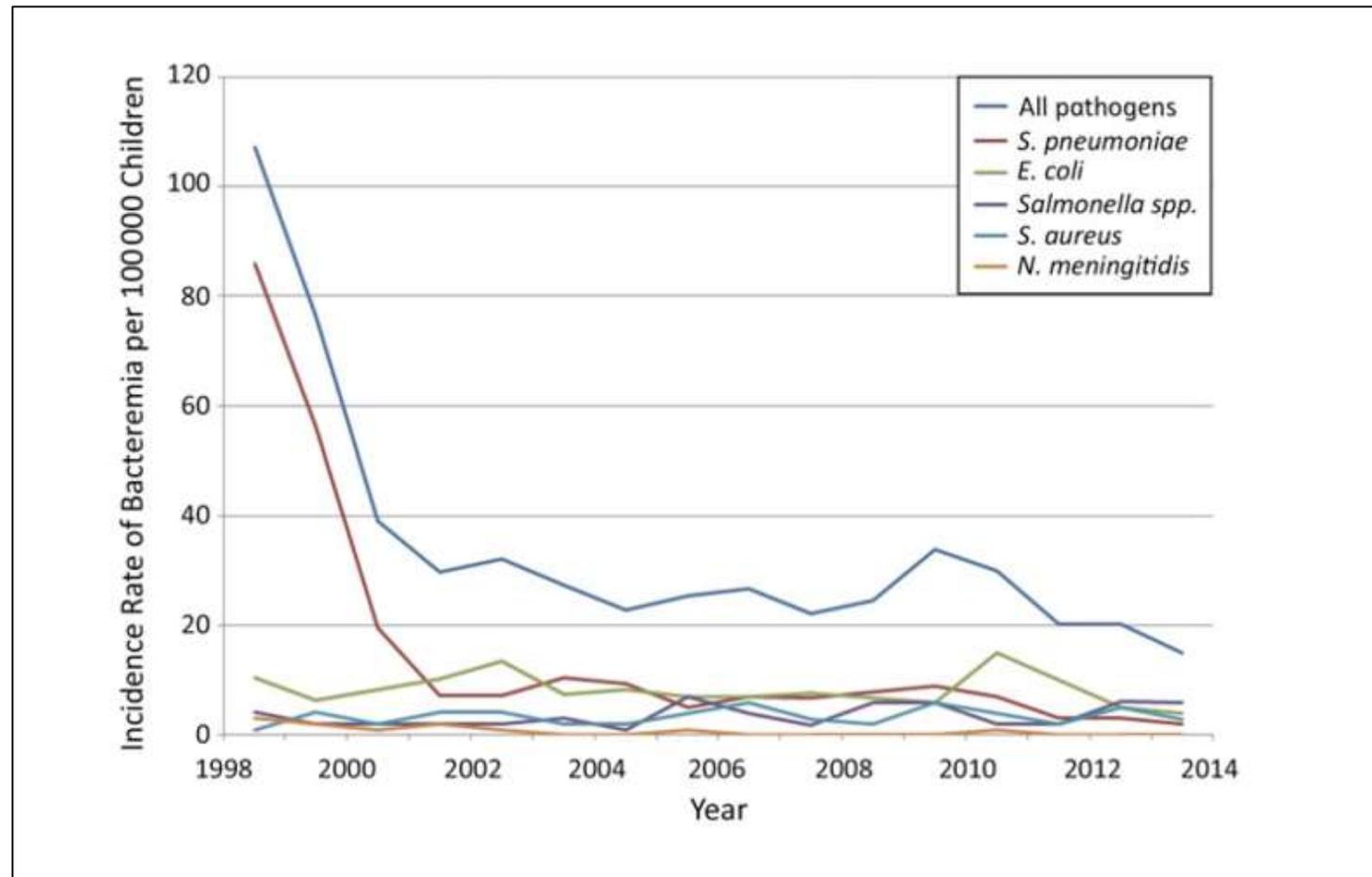
Efficacité des vaccins anti-pneumococciques conjugués contre les infections invasives à pneumocoque chez les enfants de moins de cinq ans en Afrique

PLoS ONE 14(2): e0212295.



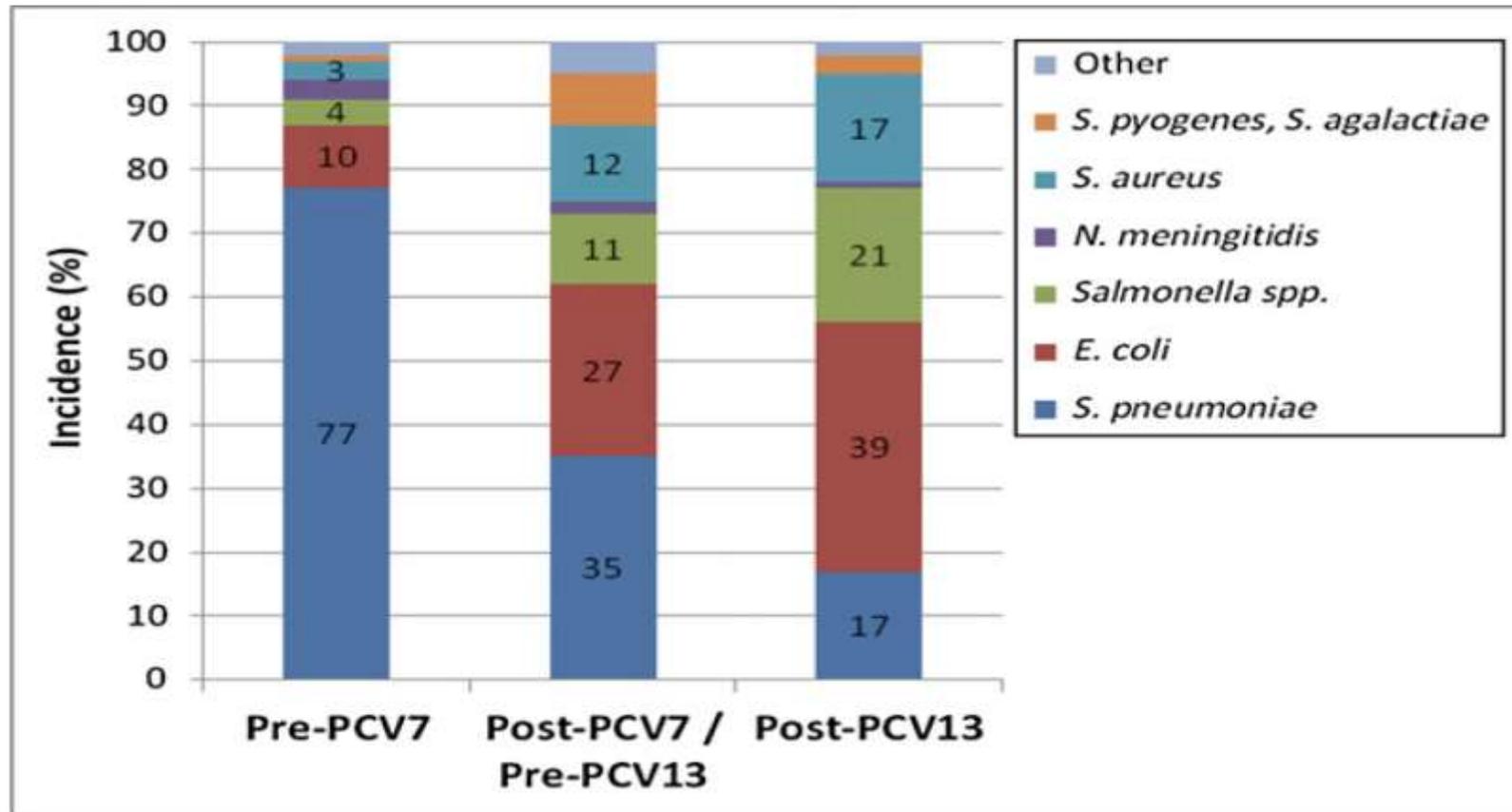
Bacteremia in Children 3 to 36 Months Old After Introduction of Conjugated Pneumococcal Vaccines

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



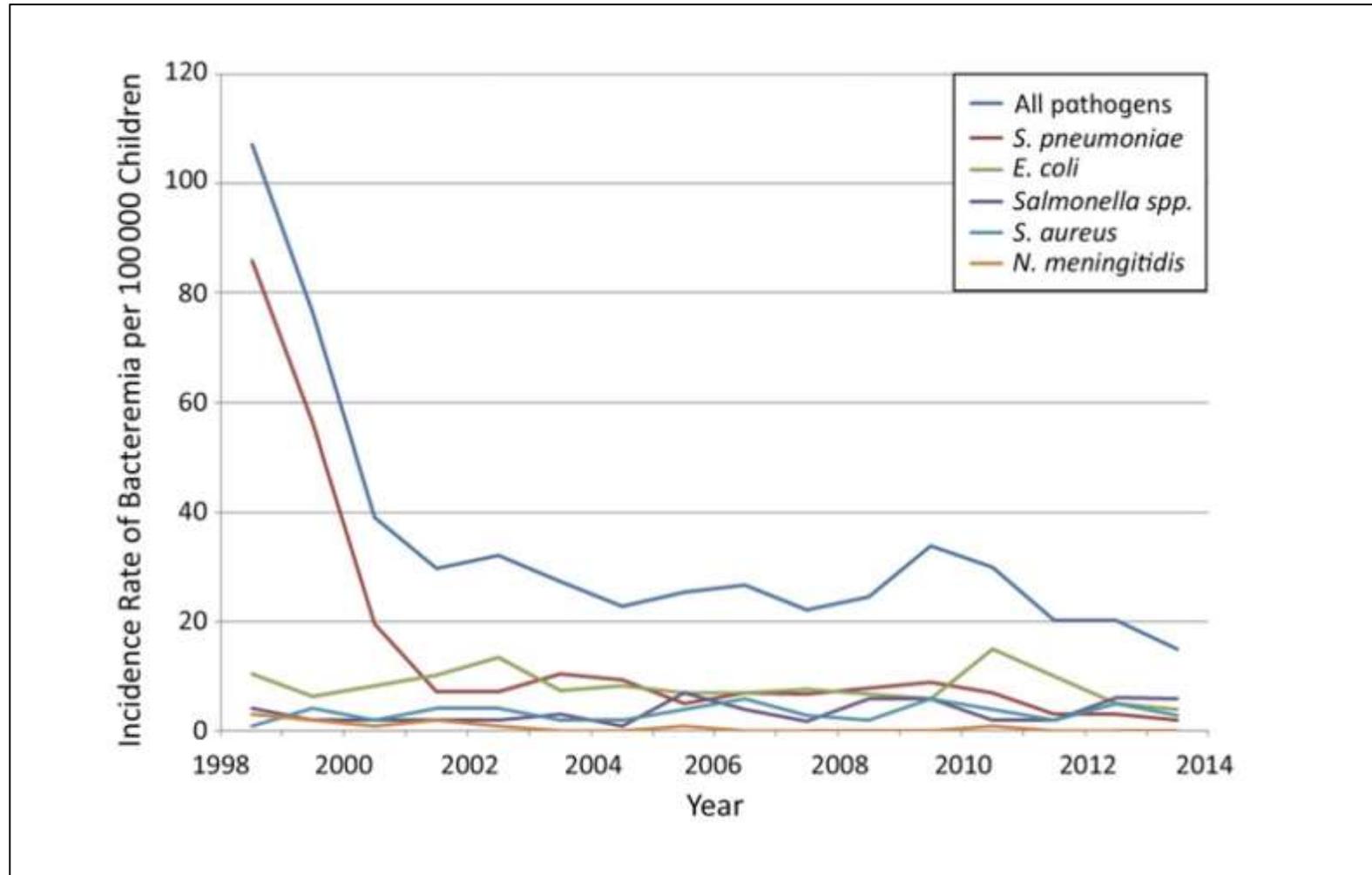
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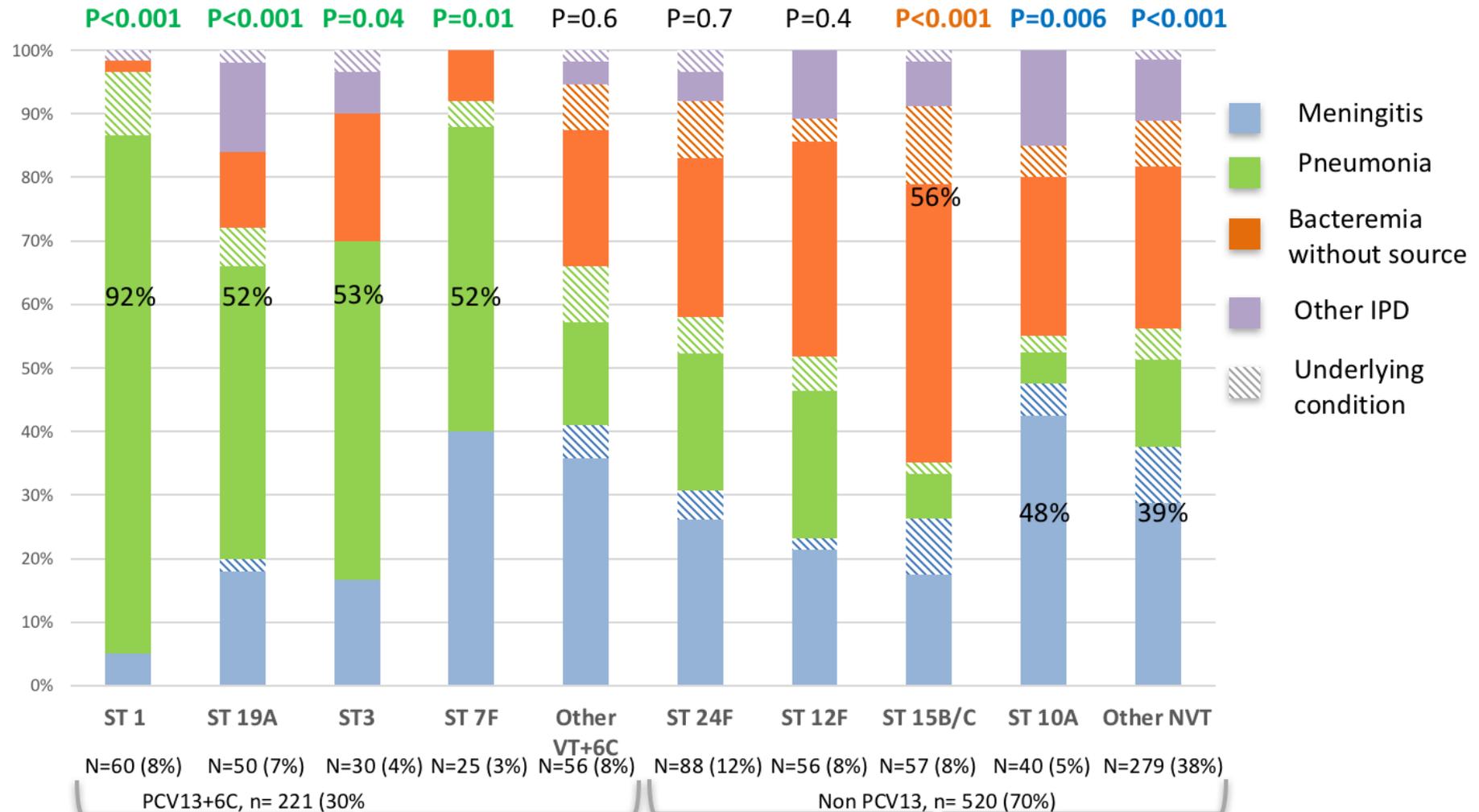
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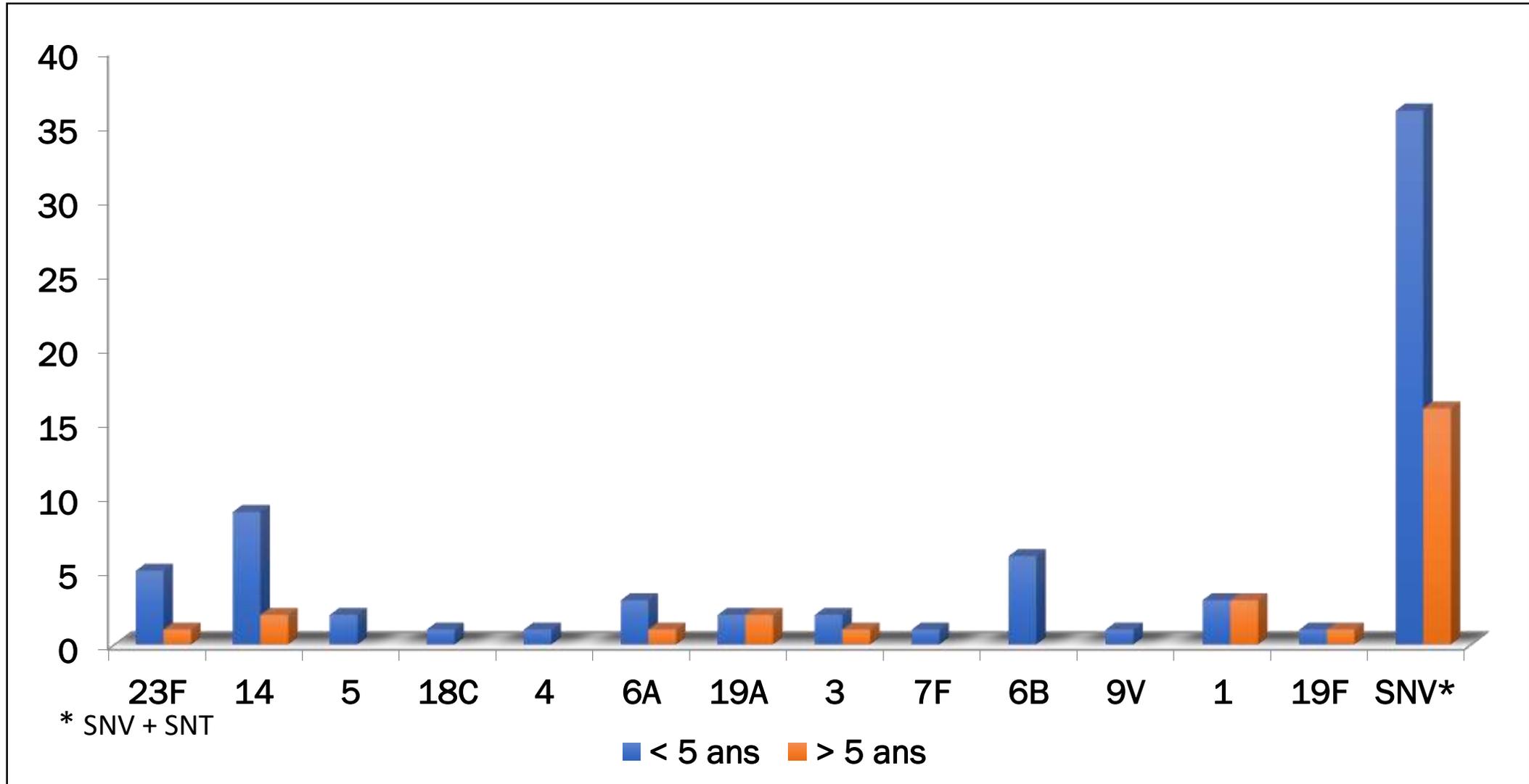


Variation of IPD profiles according to serotypes

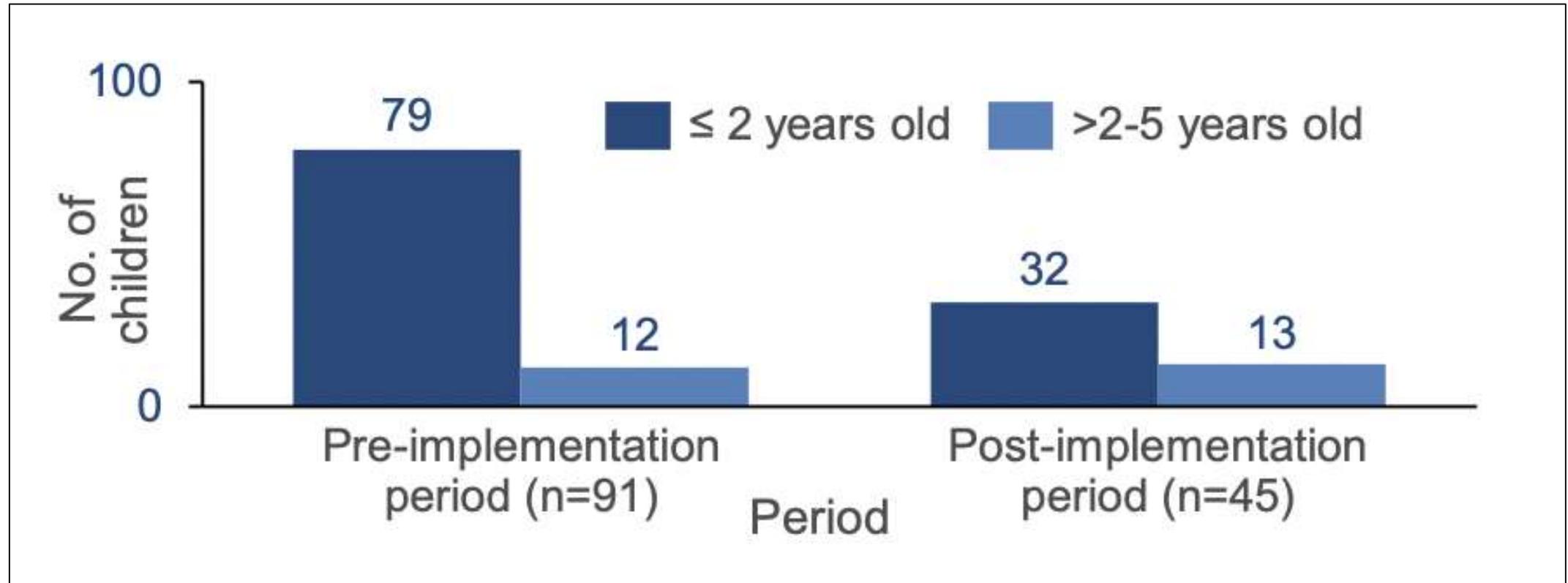
594 children with IPD recorded after PCV13 implementation, from 2011 to 2015



Sérotypes des infections invasives de l'enfant à Casablanca et Marrakech

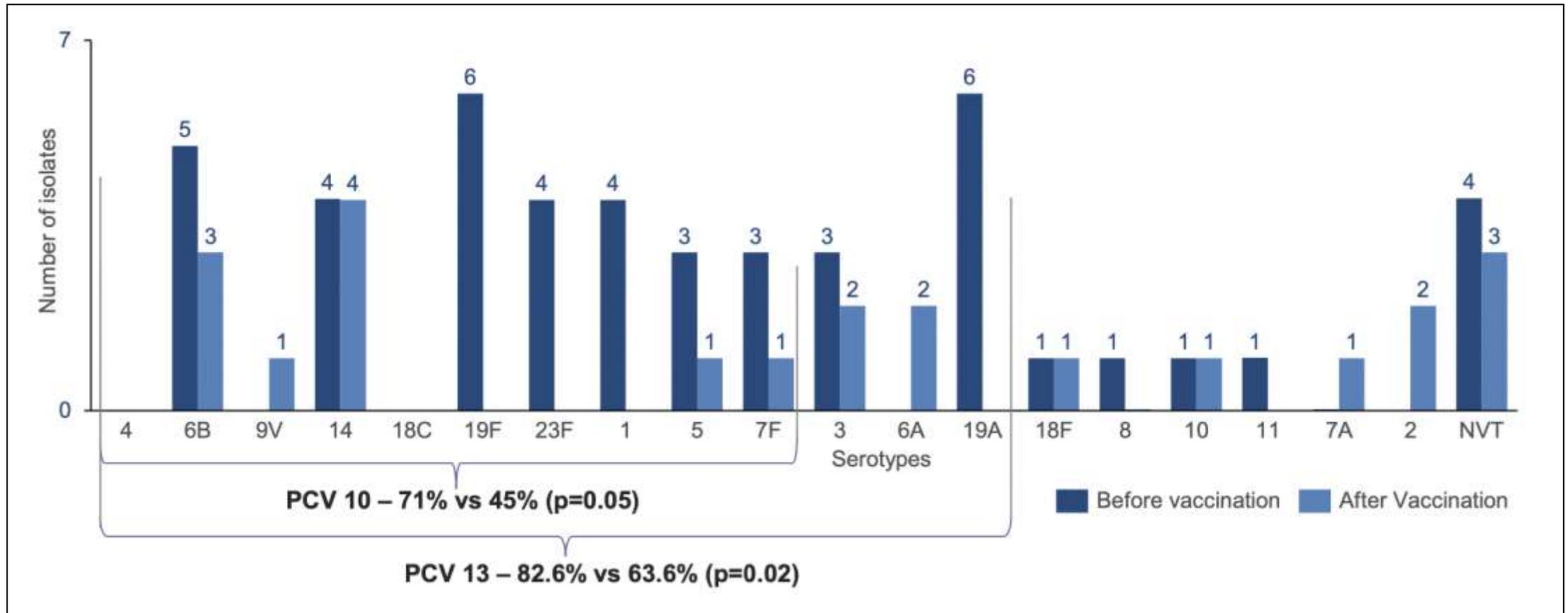


Maladie invasive à pneumocoque chez les enfants de moins de 5 ans avant et après l'introduction du vaccin anti-pneumococcique conjugué à Casablanca, Maroc

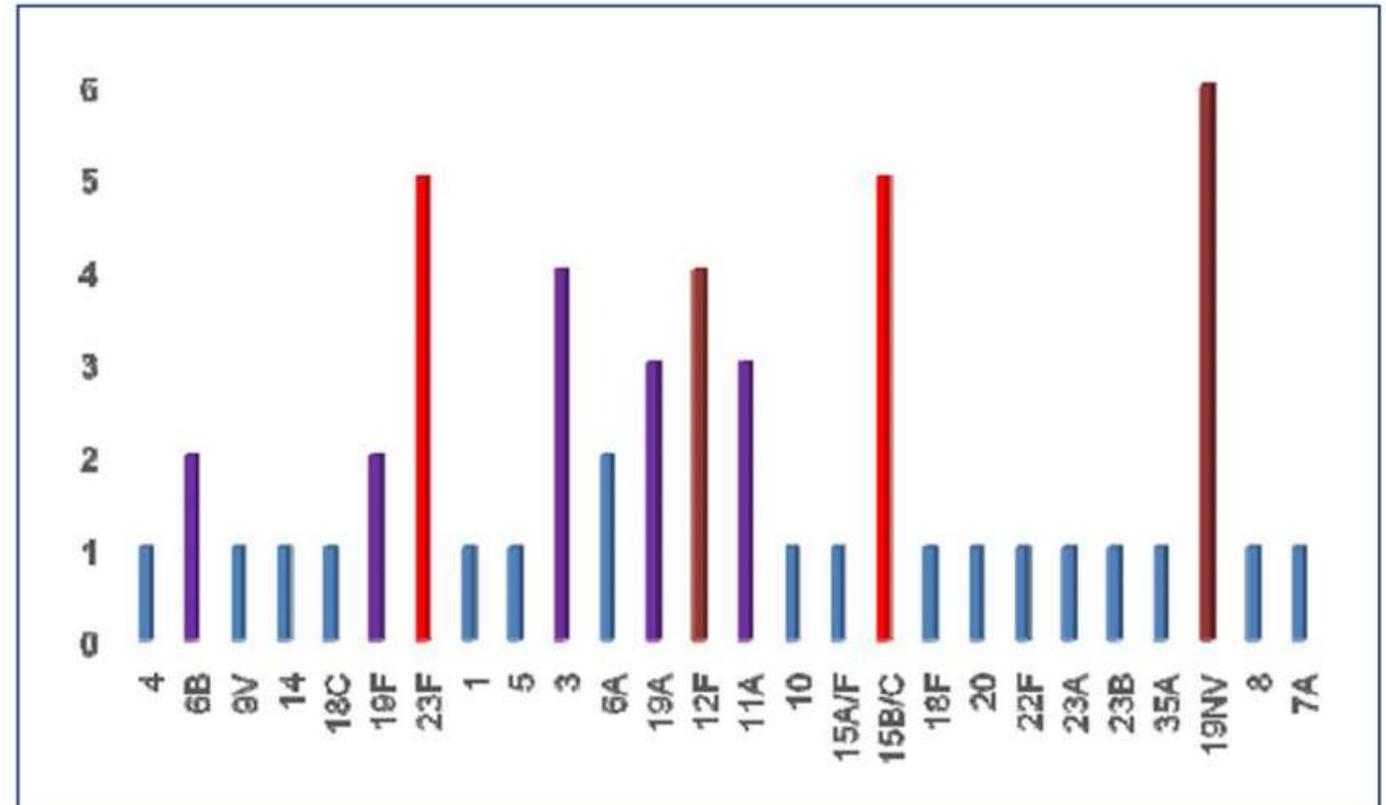
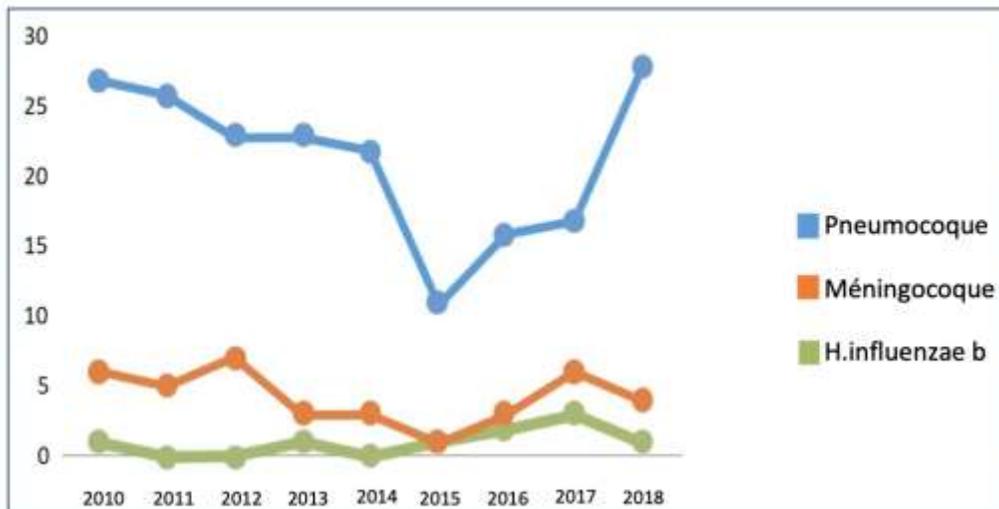


Répartition de *S. pneumoniae* dans enfants de ≤ 2 ans et $>2-5$ ans pendant la période de pré et post mise en œuvre

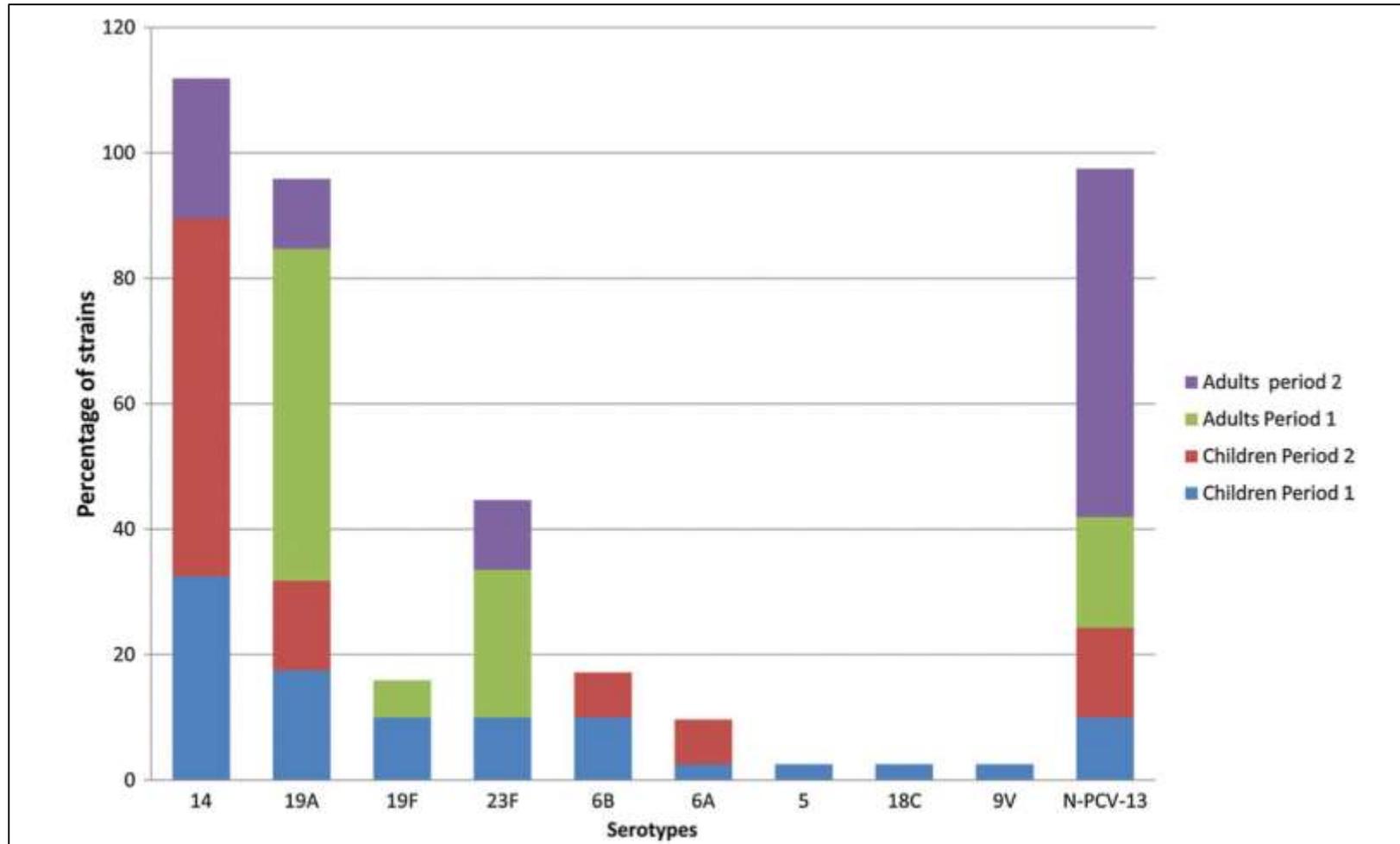
Répartition des sérotypes des souches invasives de pneumocoque chez les enfants de moins de 5 ans avant et après l'introduction du vaccin PCV



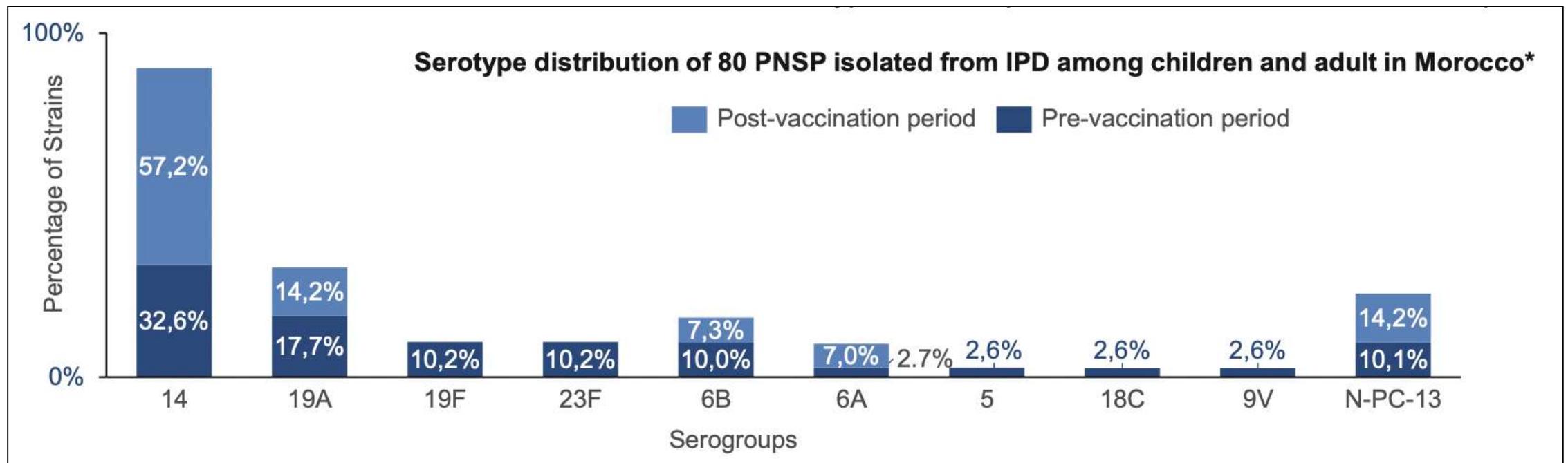
Epidémiologie des infections invasives communautaires chez l'enfant au CHU de Marrakech (2010-2018)



Caractérisation moléculaire de *Streptococcus pneumoniae* non sensible à la pénicilline isolé avant et après la mise en œuvre du vaccin conjugué contre le pneumocoque à Casablanca, Maroc

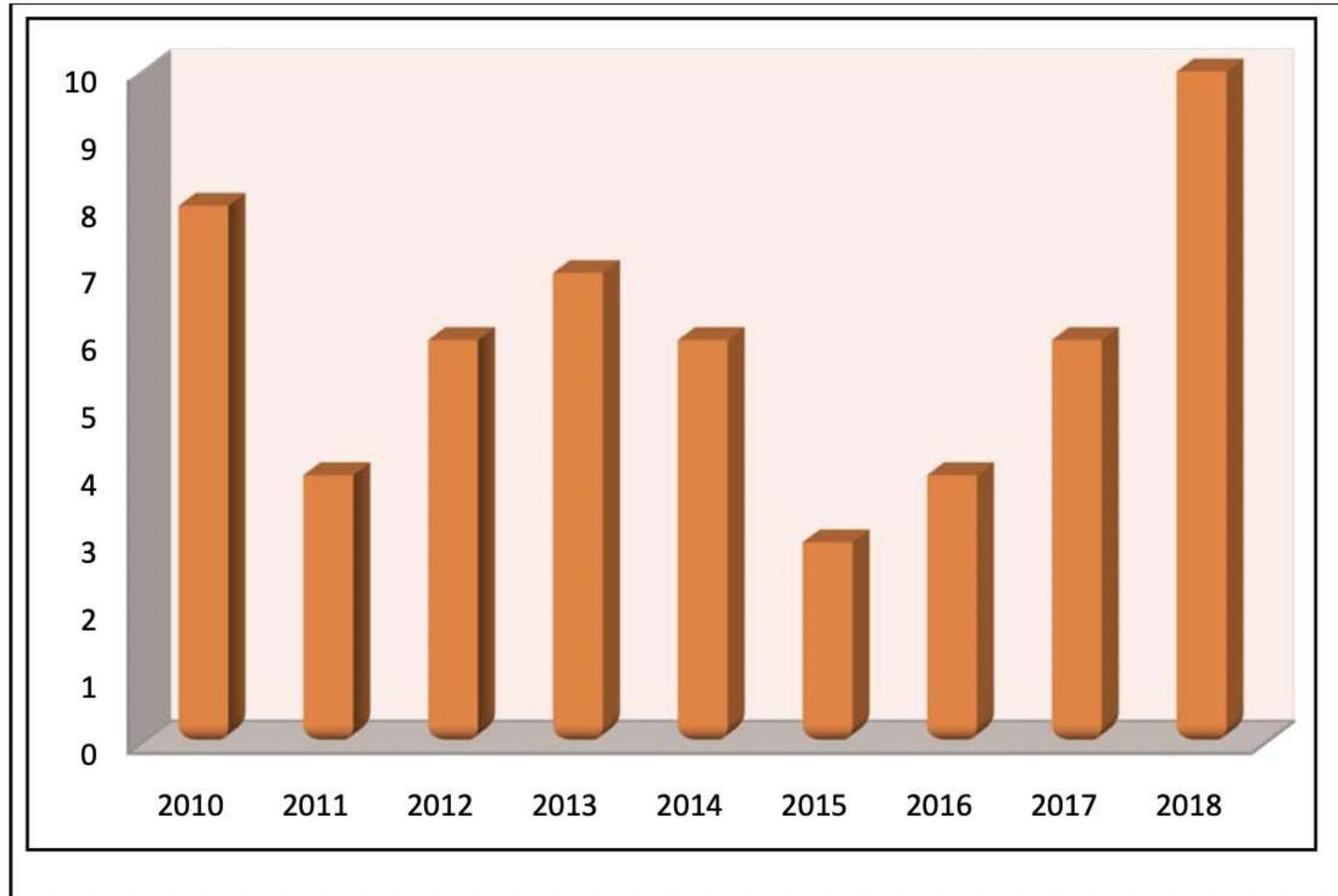


Caractérisation moléculaire de *S. pneumoniae* non sensible à la pénicilline isolé avant et après la mise en place du vaccin conjugué contre le pneumocoque à Casablanca, Maroc



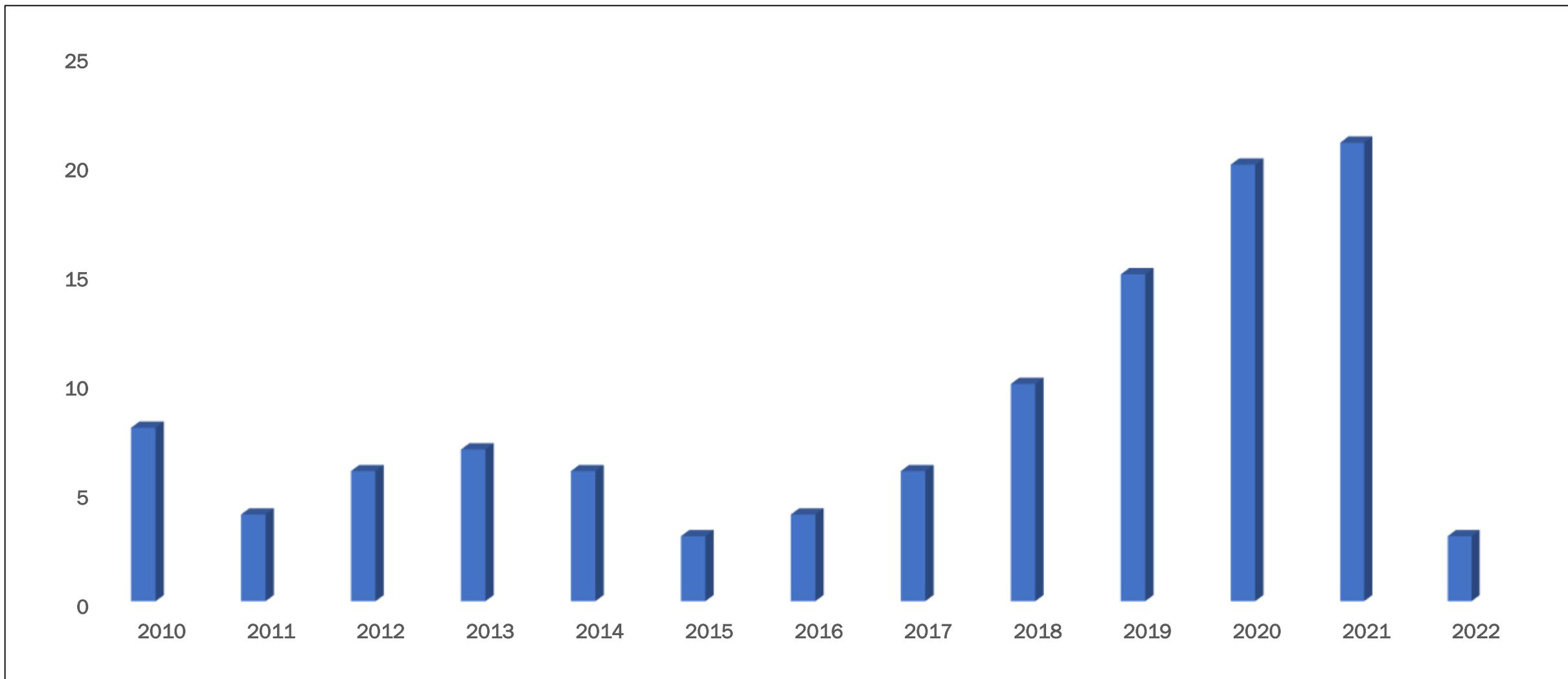
Diawara I. et al., 2017

Répartition des Méningites à Pneumocoque entre 2010 et 2018 (n = 52) à Marrakech

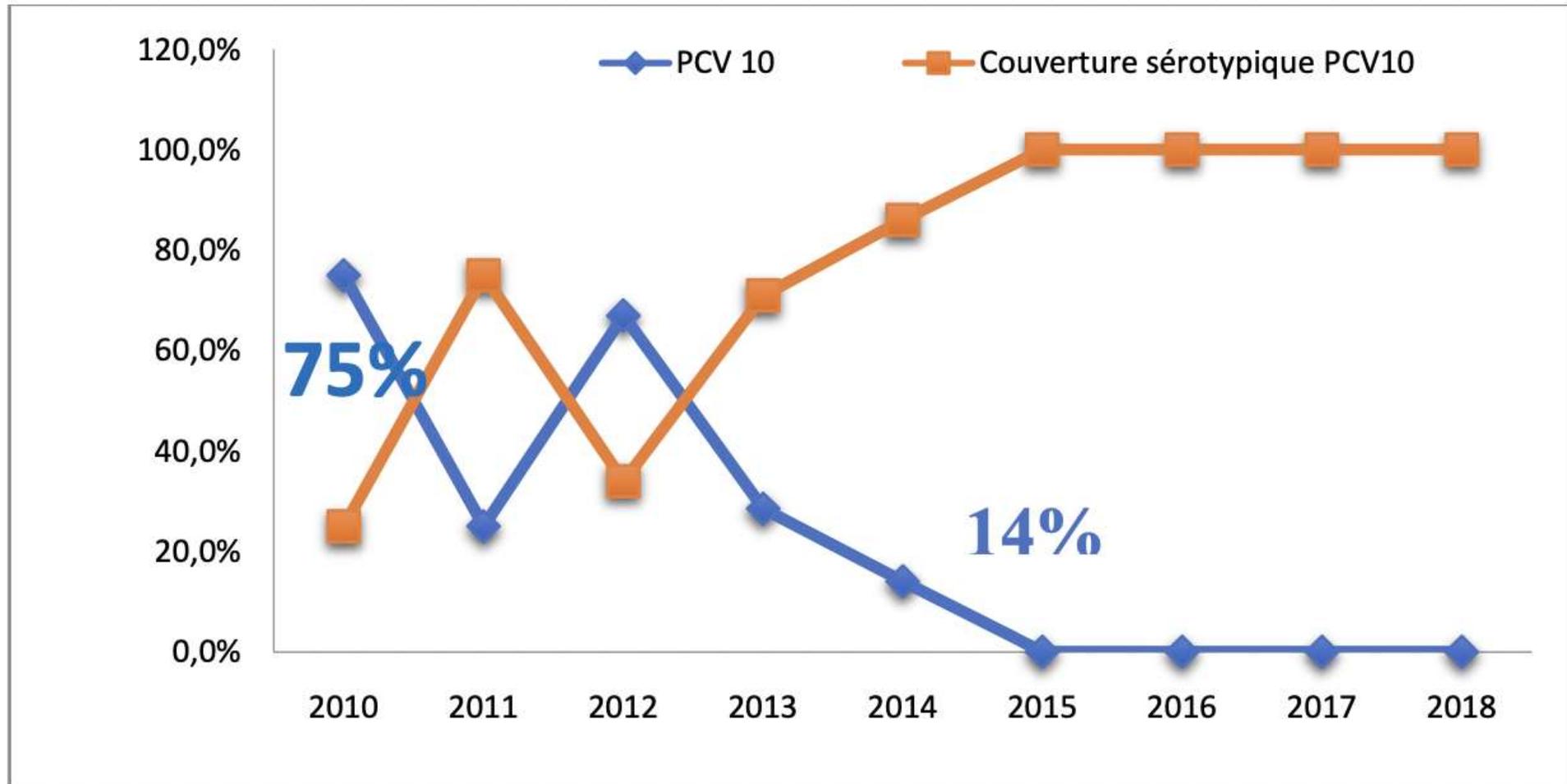


Méningites à Pneumocoque

CHU de Marrakech 2010 - JUILLET 2022 (n = 119)



Impact de la vaccination et l'évolution de la couverture sérotypique du PCV 10 dans les méningites à Pneumocoque

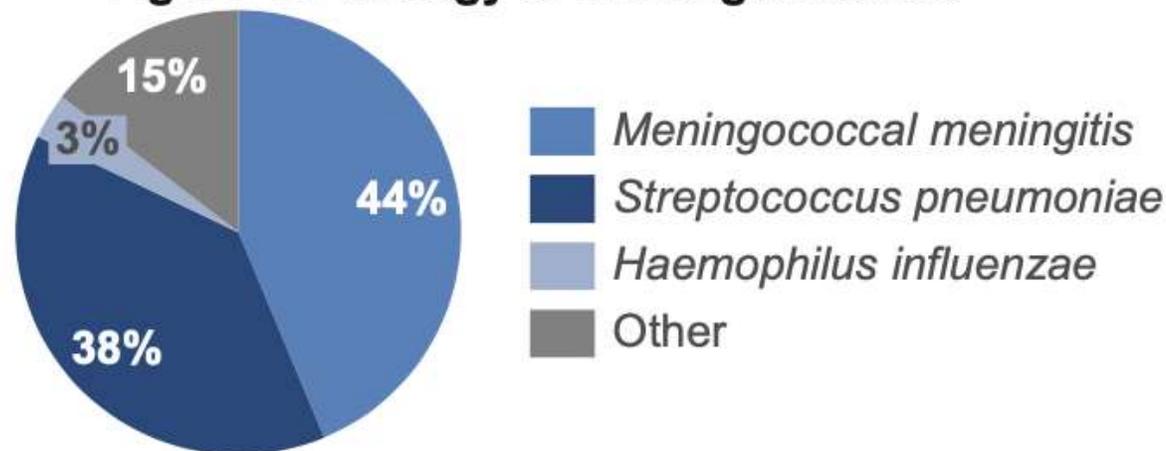


Les résultats de l'observatoire communautaire ont confirmé la méningite bactérienne aiguë chez l'enfant portant six centres hospitalo-universitaires marocains (2012-2017)

Etiology:

- Most meningitis cases were caused by *meningococcal meningitis* (43.7%) and *streptococcus pneumoniae* (38.42%)

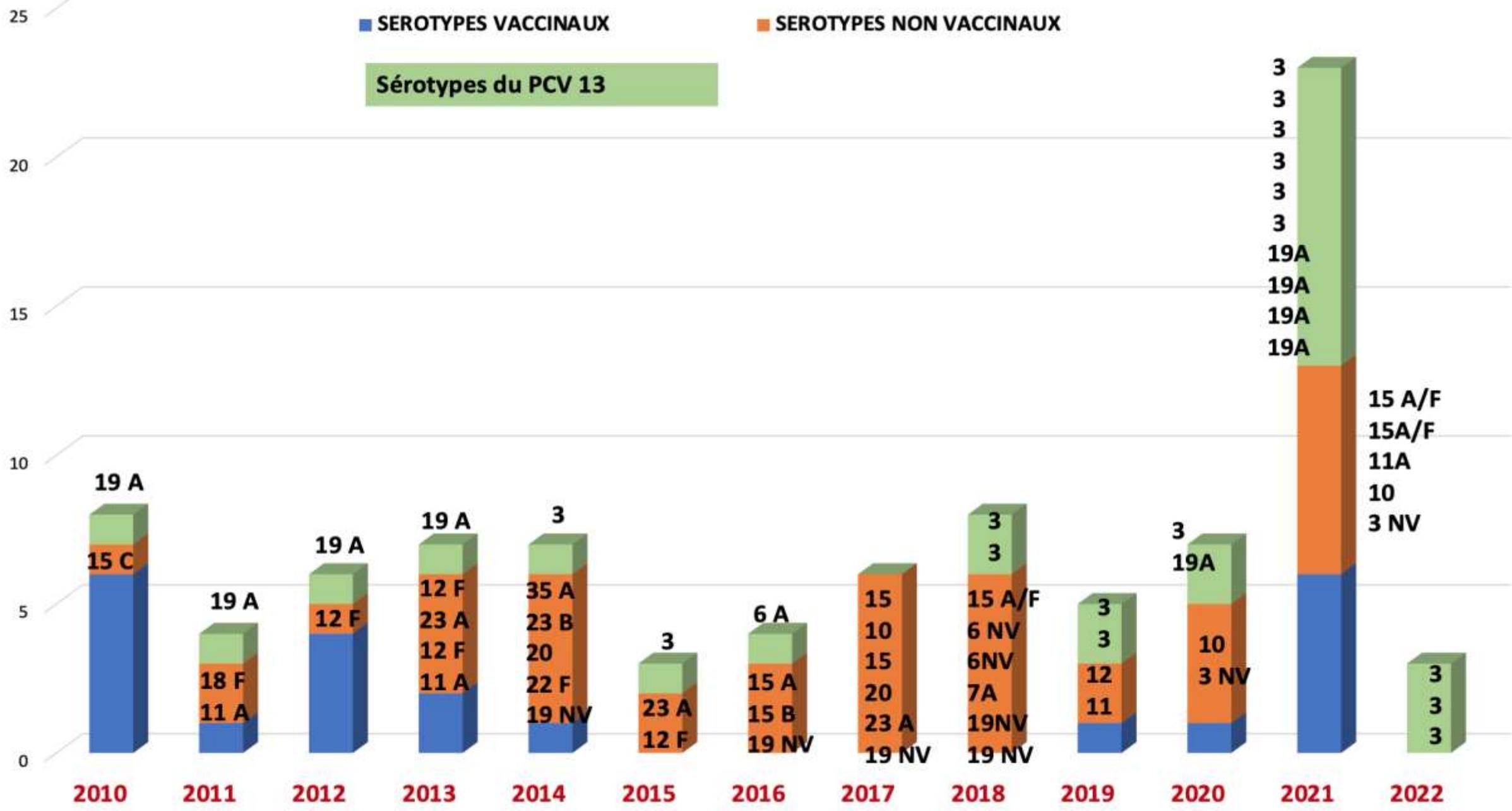
Figure 1: Etiology of Meningitis cases



■ SEROTYPES VACCINAUX

■ SEROTYPES NON VACCINAUX

Sérotypes du PCV 13



Distribution des méningites à Pneumocoque selon les sérotypes et leur sensibilité aux Pénicillines

Année	Souche de SDP	Souche sensibles aux pénicillines	Sérotypes des souches de SDP
2010	2	8	19A – 15C
2011	1	4	11A
2012	3	3	14 - 5 - 19A *
2013	1	6	12F
2014	3	4	3* – 20 – 23F
2015	-	3	-
2016	-	4	-
2017	2	4	15 - 10
2018	0	8	-
2019	1	14	11
2020	1	19	10
2021	1	20	15A/F
2022	0	3	-

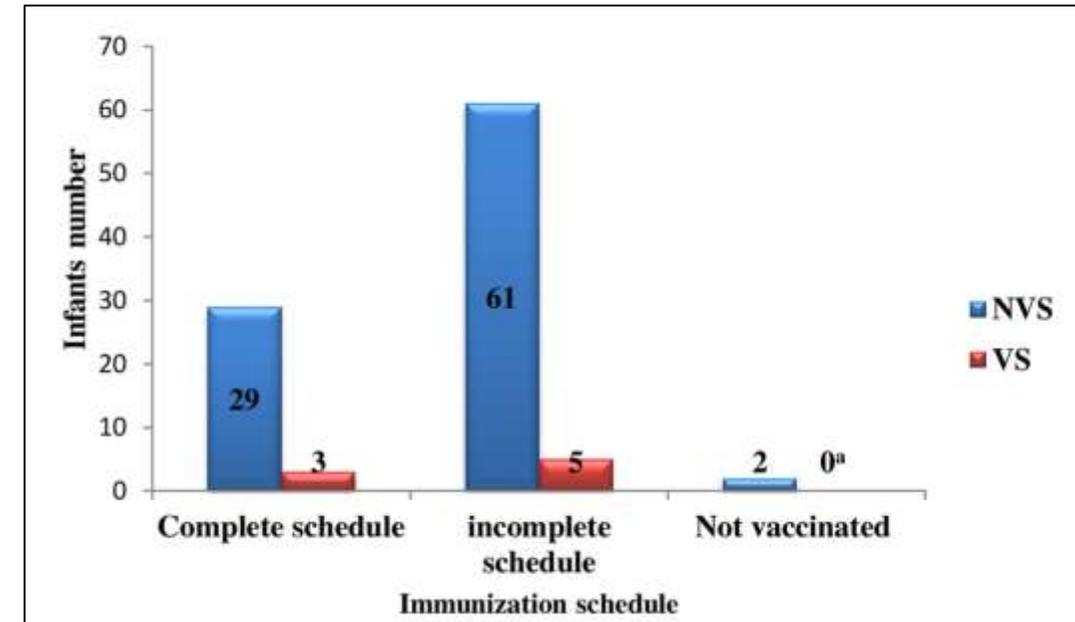
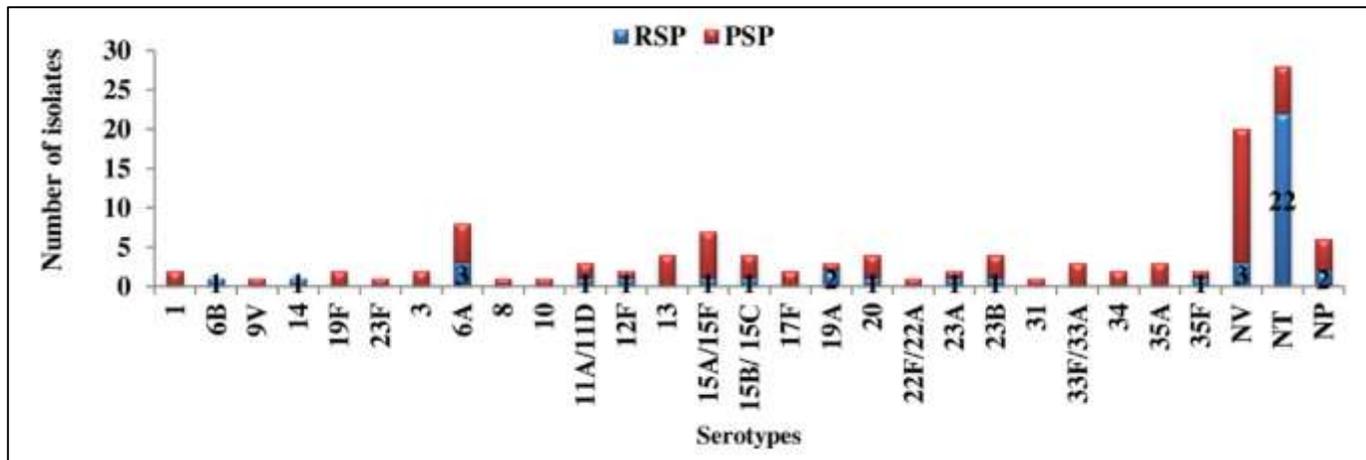
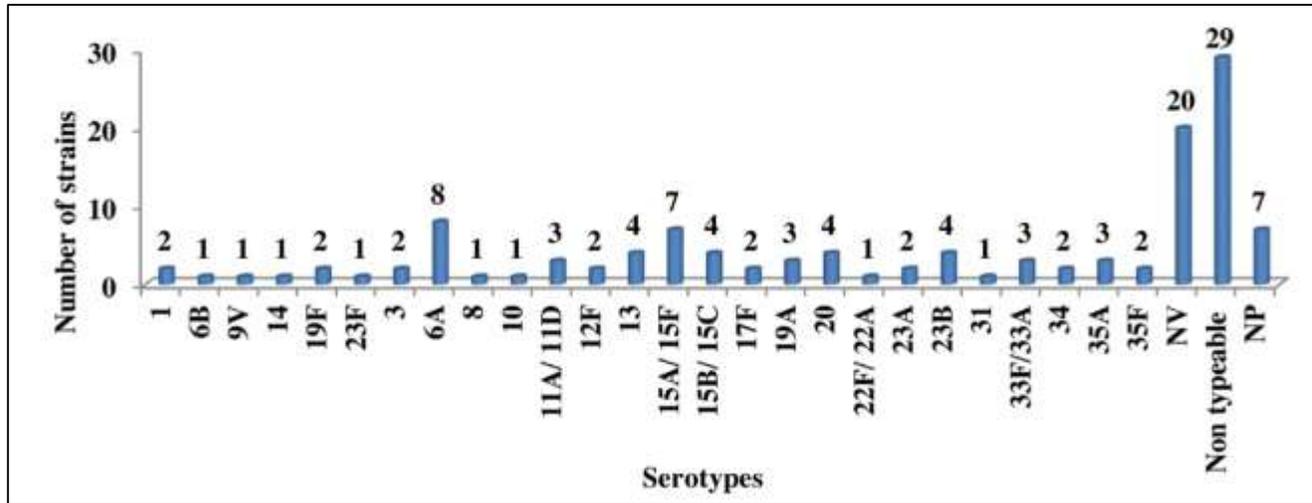
PSDP : 13 %

* PCV 13

Etat de sensibilité et sérotypage des souches invasives de Pneumocoque isolées en 2022 chez l'enfant

PC	SEXE	AGE	SITE	PSDP (OXA)	PENIG	AMX	CTX	CLINDA	LEVO	ERY	SXT	SEROTYPE
1	M	9 ans	LCR	S	<0.016	<0.016	<0.016	S	S	S	S	3
2	F	1 AN	LCR	S	0.016	0.032	0.016	S	S	S	S	3
3	M	1 AN	LCR	S	0.016	0.032	0.016	S	S	S	R	3
4	M	2 MOIS	HEMOCULTURE	R	0.064	0.064	0.125	R	S	I	S	3
5	M	9 ANS	ASCITE	S	0.016	0.016	0.016	S	S	R	S	6B
6	F	1 AN	ASCITE	R	2	2	0.5	S	S	I	R	11
7	F	-	ASCITE	R	1	0.125	0,5	R	S	I	S	3
8	M	5 ANS	PDP	S	0.5	0.125	0.25	S	S	S	S	19 A
9	M	4 ANS	PDP	R	2	2	1	R	S	I	S	19F
10	M	14 ANS	PDP	R	0.5	0.5	0.125	R	S	R	S	23B
11	F	1 AN	PDP	S	0.032	0.032	0.032	S	S	S	S	3

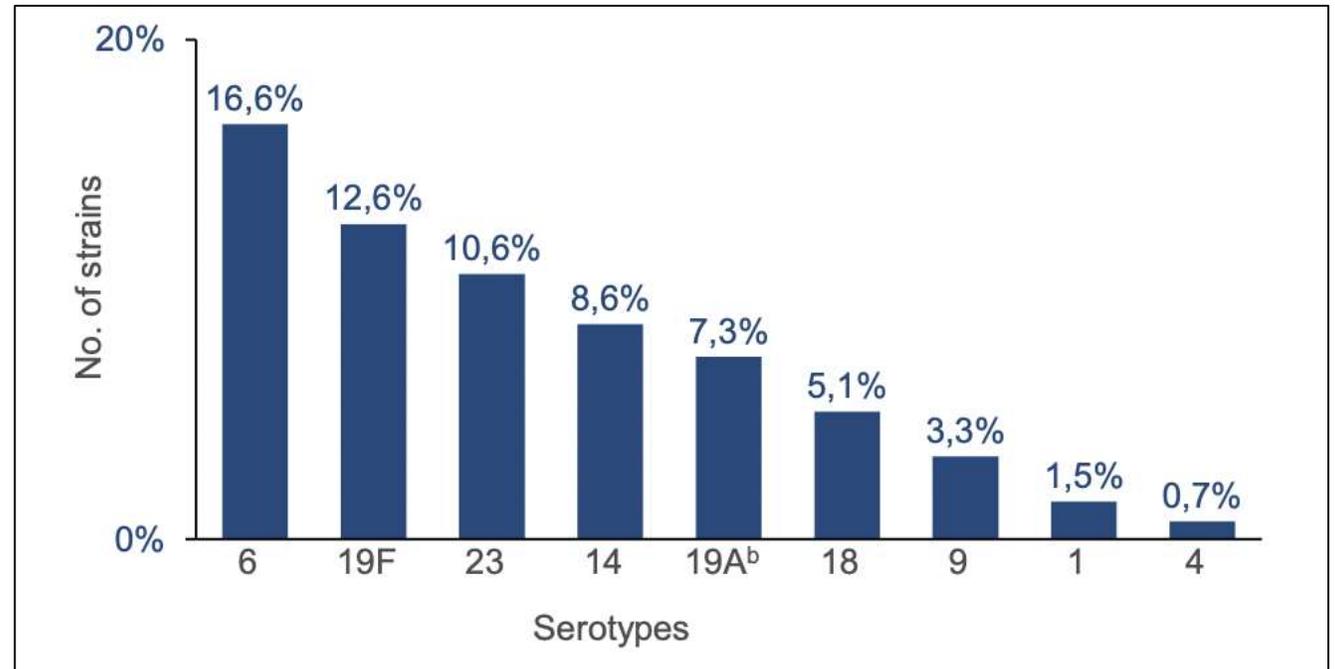
Portage de *Streptococcus pneumoniae* chez les enfants fébriles au moment de la vaccination par le PCV-10 aux urgences pédiatriques au CHU Mohammed VI de Marrakech (Maroc)



I. Dilagui et al. / Archives de Pédiatrie (2019)

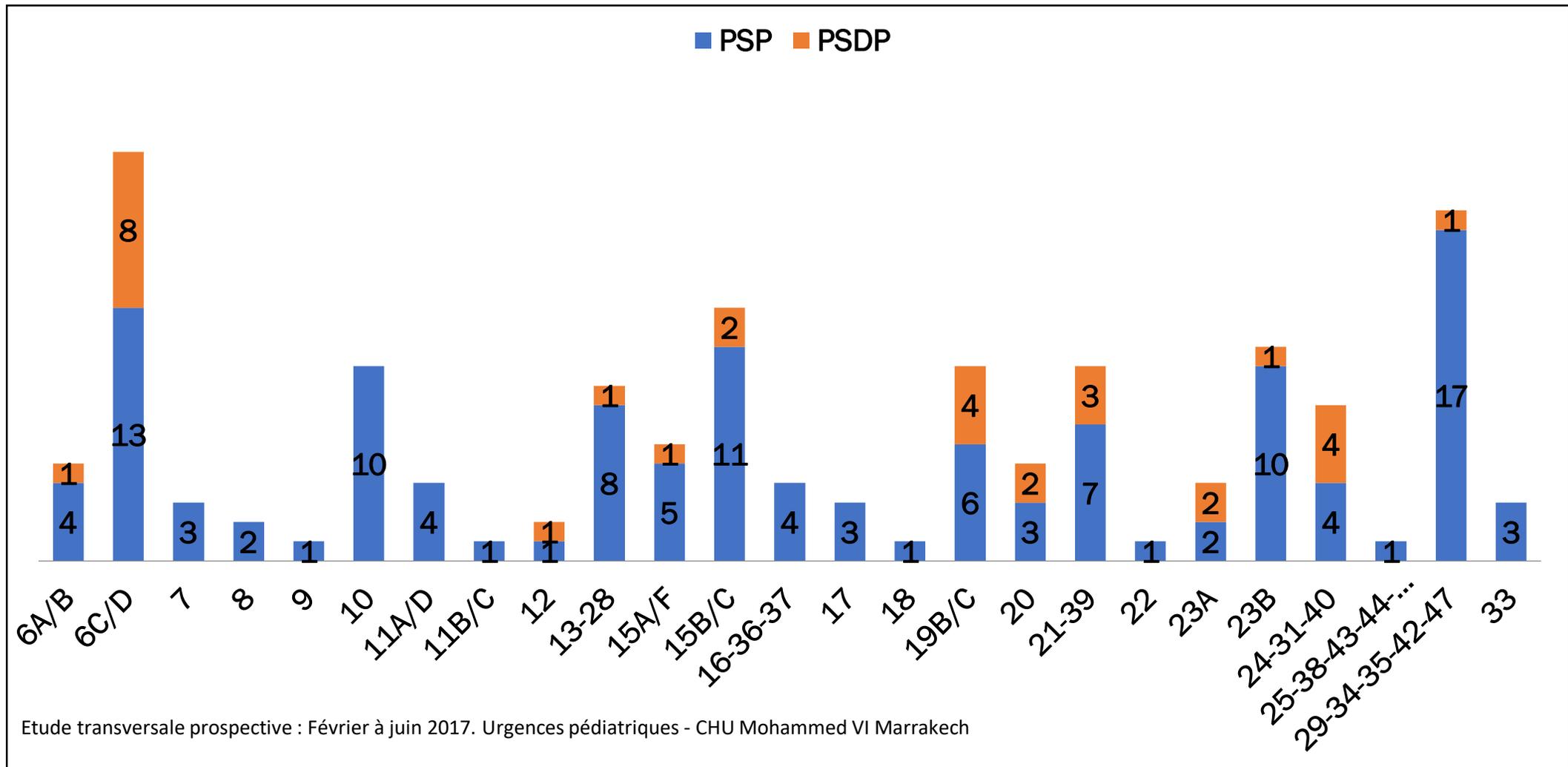
Etude du portage nasopharyngé de *Streptococcus pneumoniae* et de sa résistance aux antibiotiques chez des enfants sains de moins de 2 ans dans la région de Marrakech (Maroc)

Serotypes / Serogroups ^a	N (%)
6	25 (16.6%)
19F	19 (12.6%)
23	16 (10.6%)
14	13 (8.6%)
19A ^b	11 (7.3%)
18	7 (5.1%)
9	5 (3.3%)
1	2 (1.5%)
4	1 (0.7%)



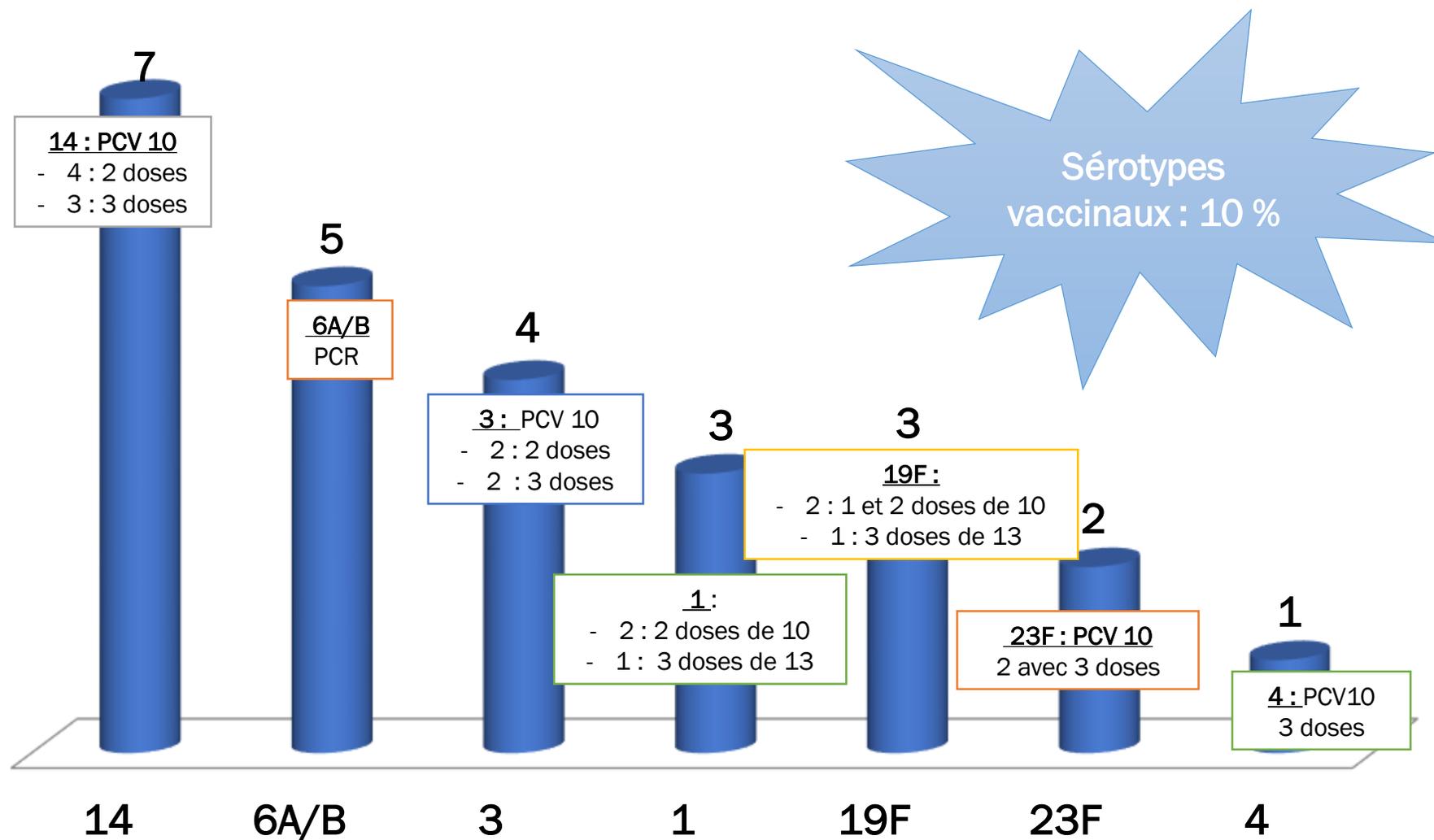
Portage rhino-pharyngé du pneumocoque à Marrakech

Distribution des sérotypes non vaccinaux en fonction de la sensibilité aux pénicillines



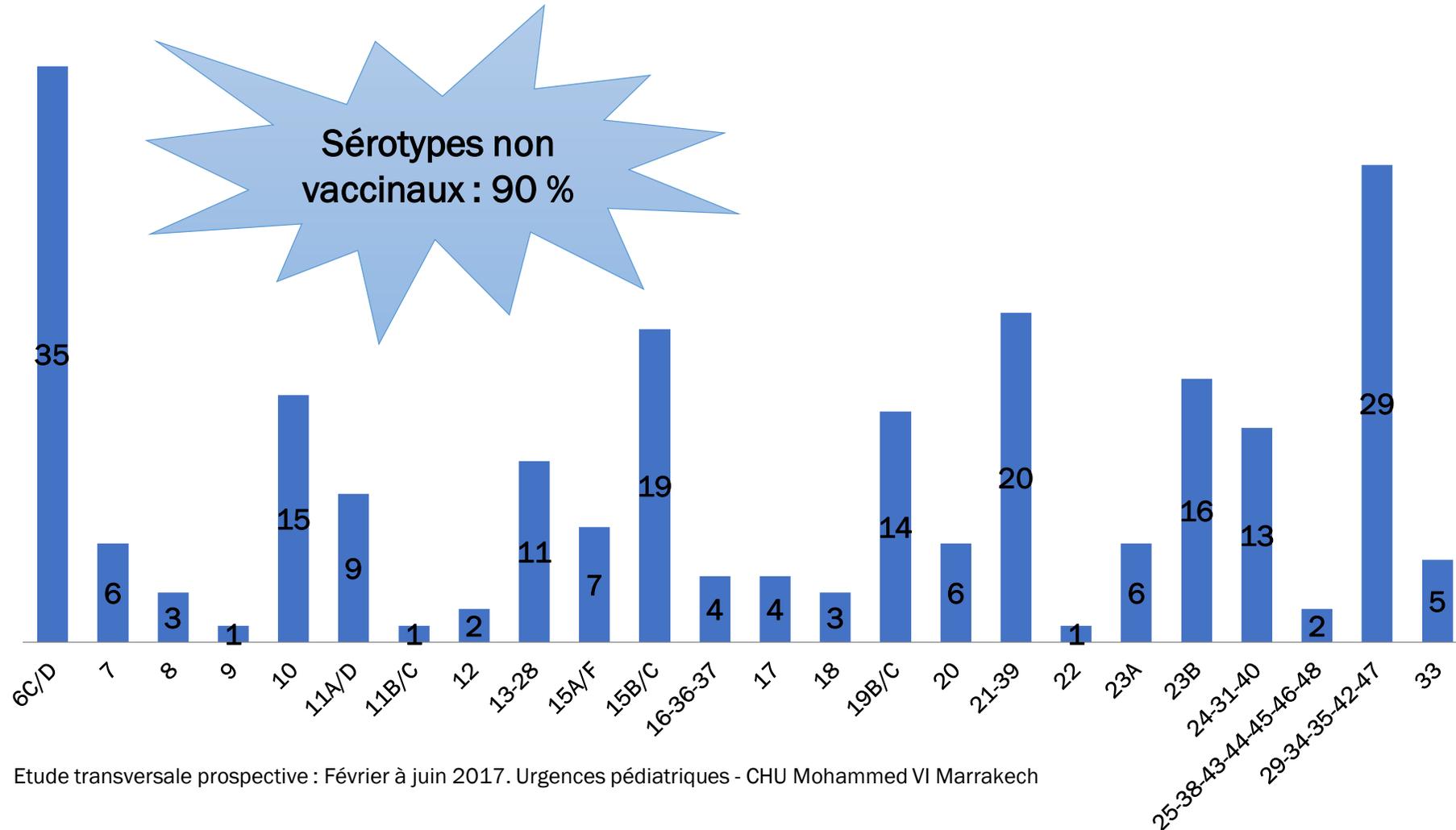
Portage rhino-pharyngé du pneumocoque à Marrakech

Distribution des sérotypes vaccinaux (N=25)



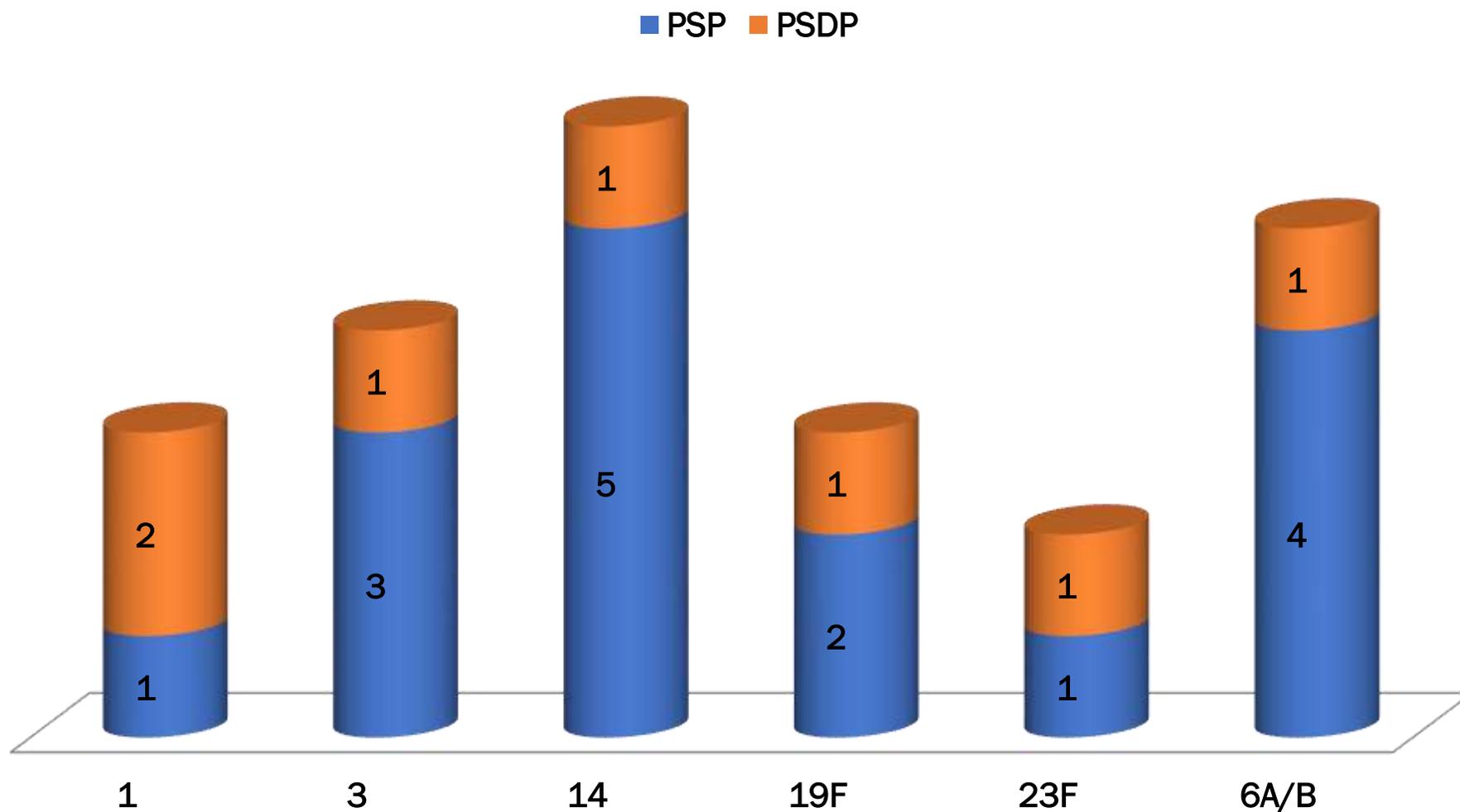
Portage rhino-pharyngé du pneumocoque à Marrakech

Distribution des sérotypes non vaccinaux (N : 232)



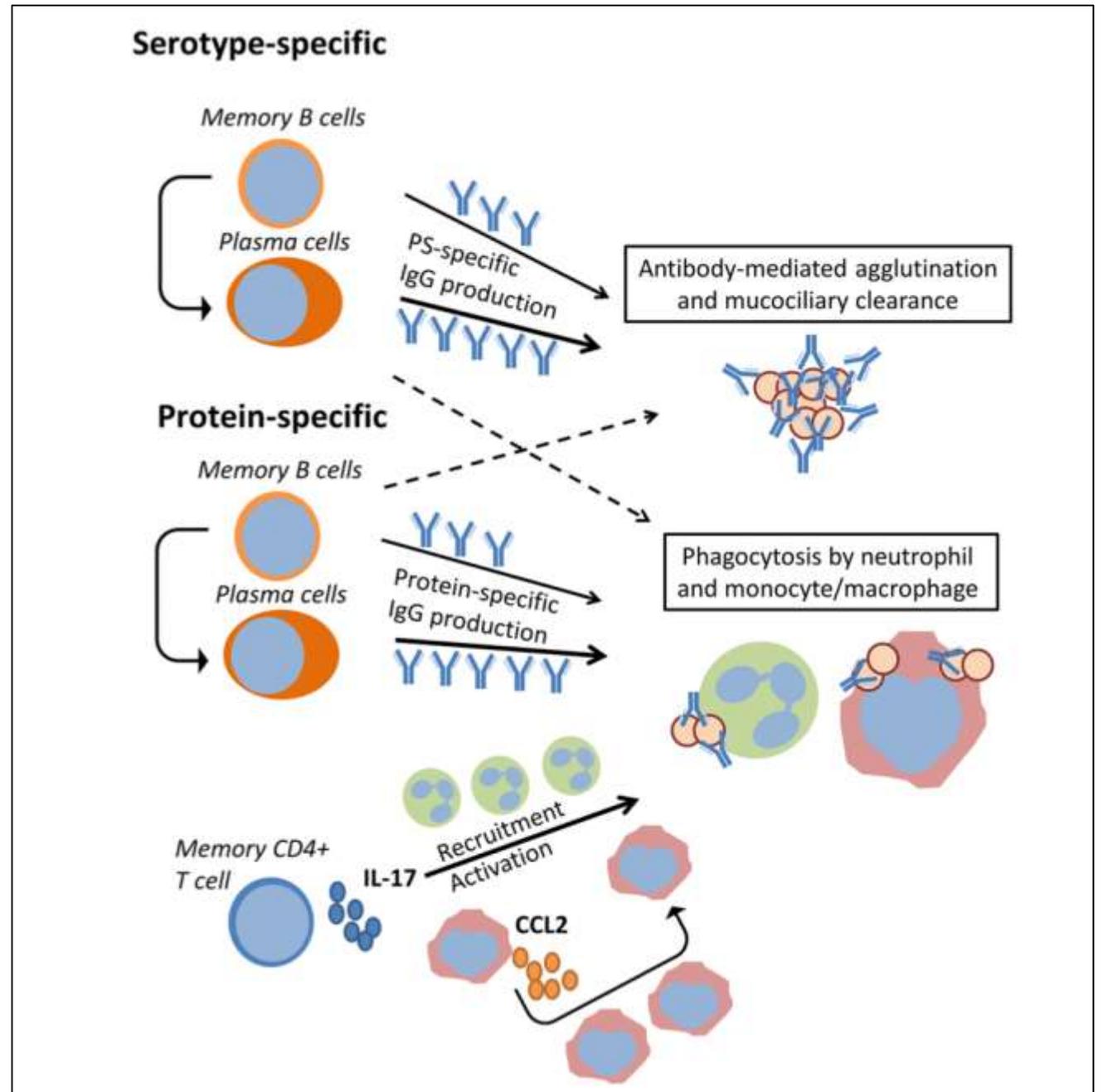
Portage rhino-pharyngé du pneumocoque à Marrakech

Distribution des sérotypes vaccinaux selon la sensibilité aux pénicillines

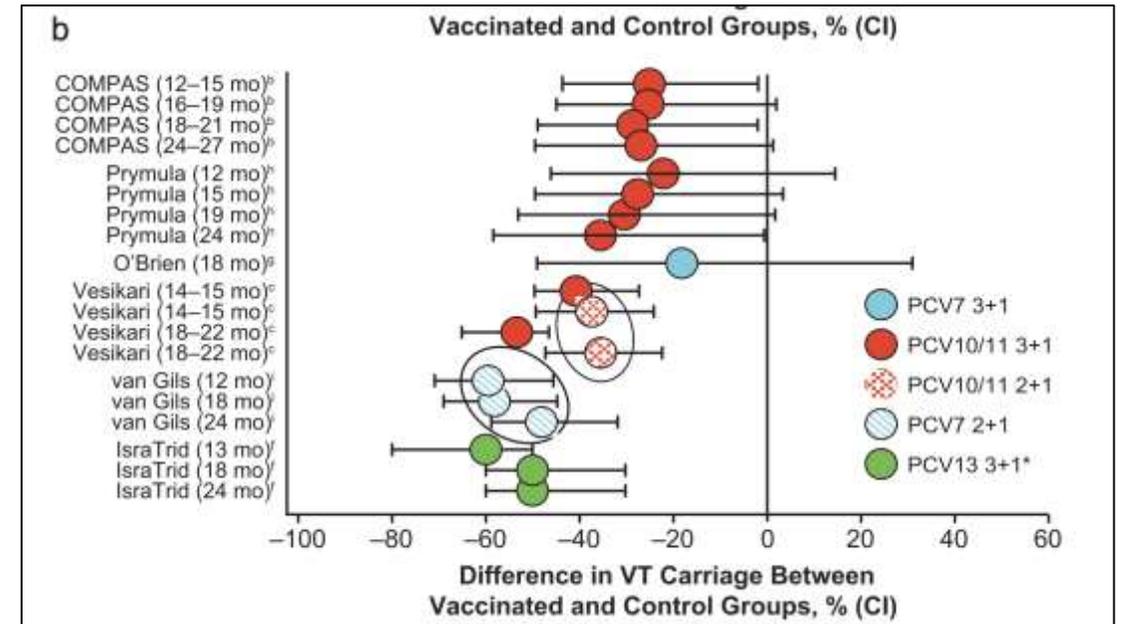
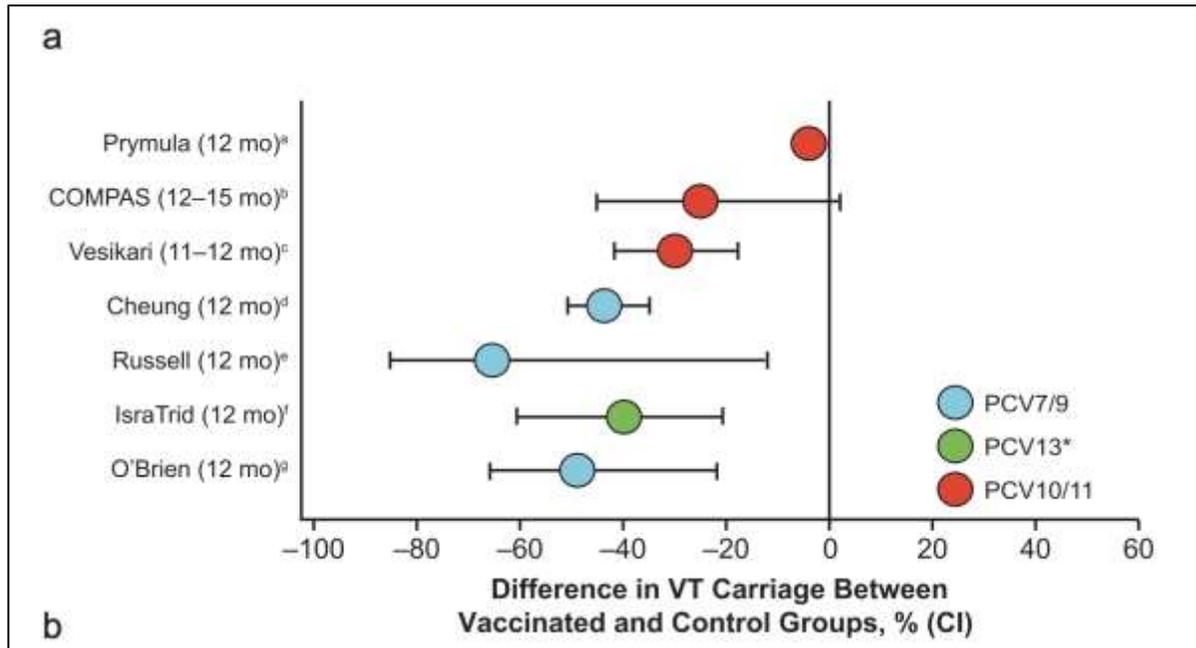


Les mécanismes immunologiques qui contrôlent le portage pneumococcique

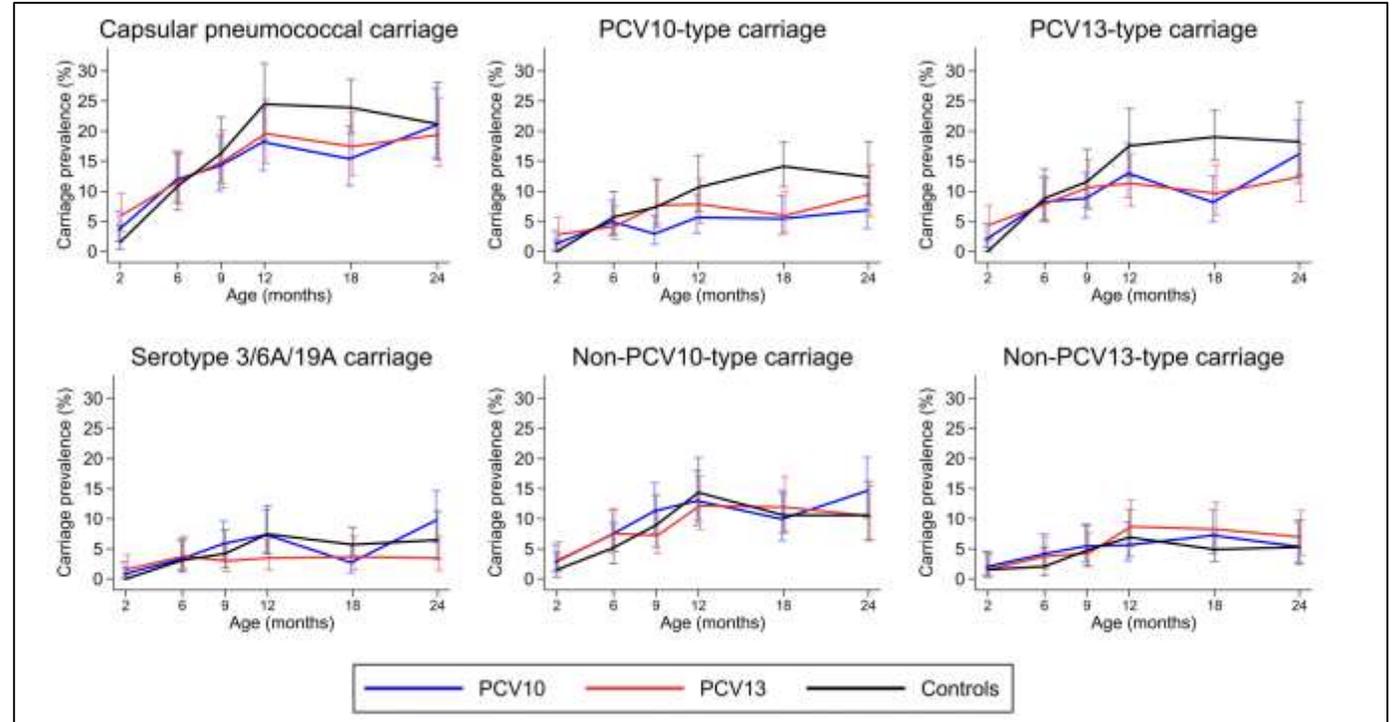
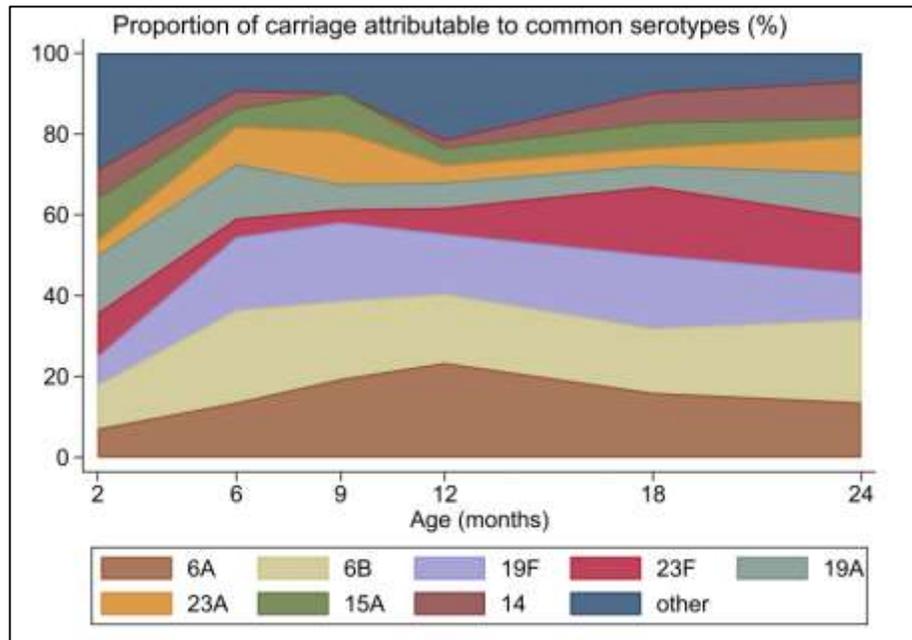
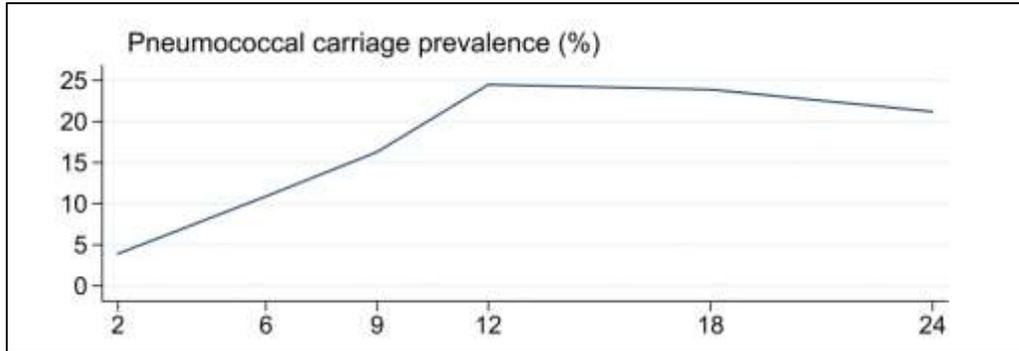
PLOS Pathogens | <https://doi.org/10.1371/journal.ppat.1006665>
December 21, 2017



Études de portage examinant l'efficacité des vaccins conjugués au CRM197 (PCV7/PCV13) et des vaccins conjugués à la protéine D



Effet d'un schéma 2+1 de vaccin conjugué antipneumococcique 10-valent versus 13-valent sur le portage pneumococcique



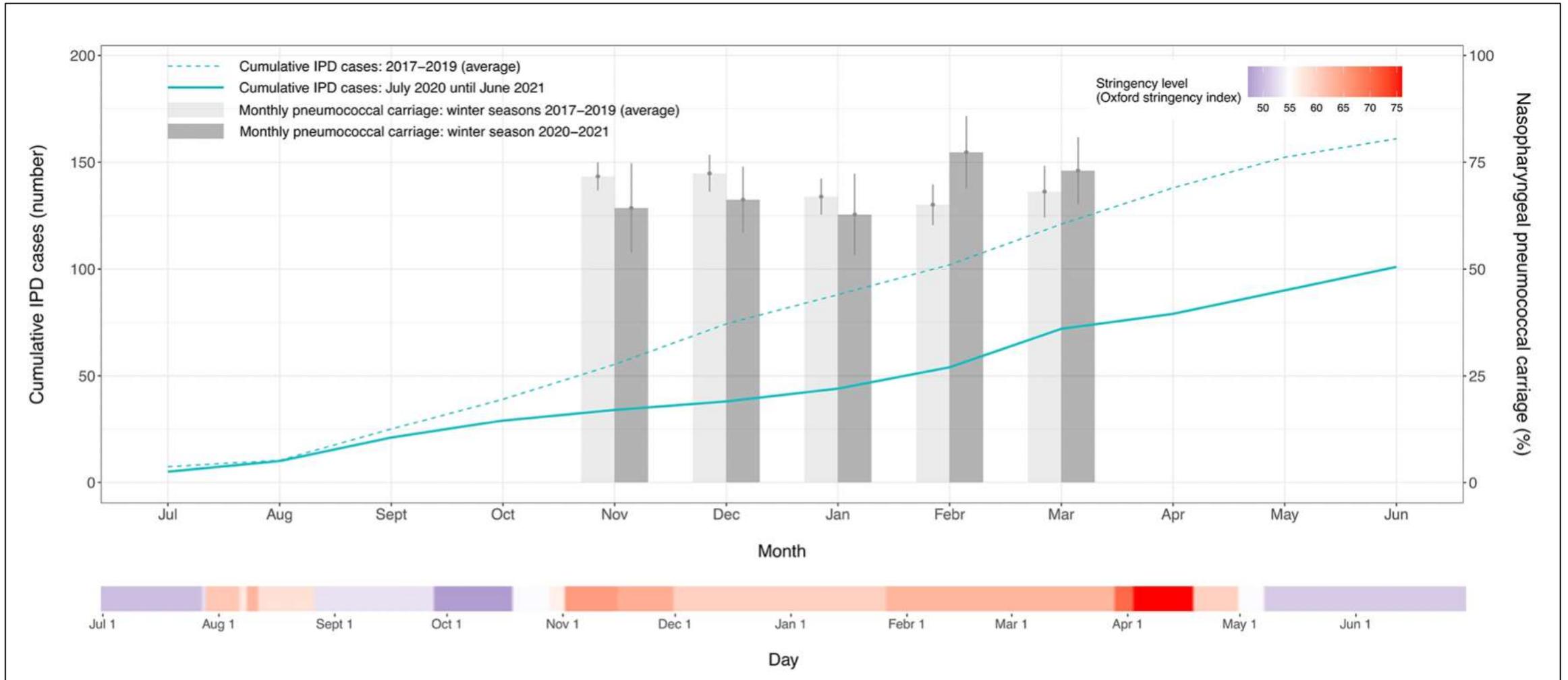
B. Temple, M. L. Nation, V. T. T. Dai et al, Vaccine 39 (2021) 2303–2310

Facteurs influençant le remplacement des sérotypes dans la flore nasopharyngée

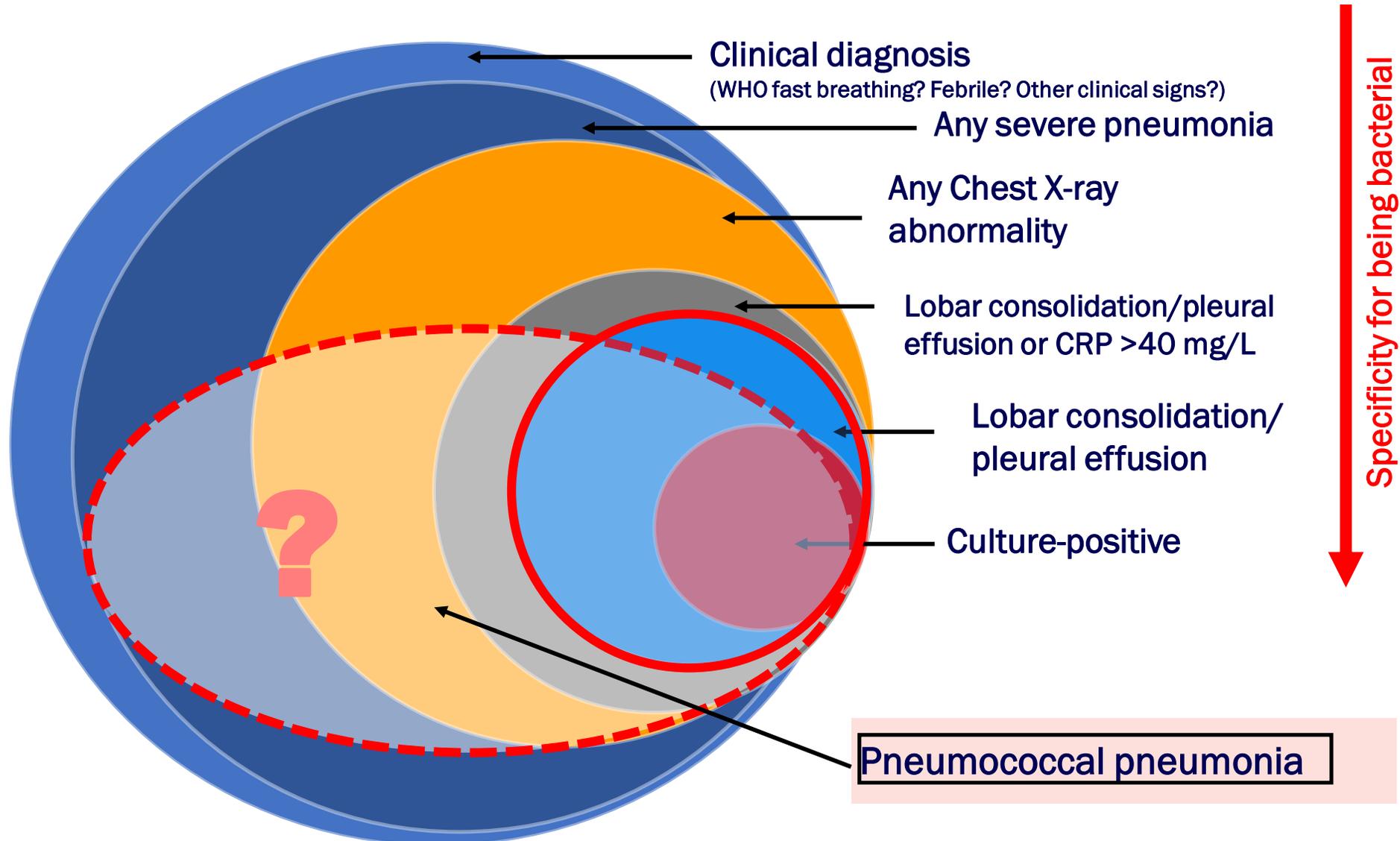
- Le facteur le plus évident est la composition de la population pneumococcique : avant la vaccination le NVT le plus courant avant la mise en place du PCV nettement augmenté et a été plus fréquemment porté après
- L'utilisation d'antibiotiques est le deuxième facteur impliqué dans le portage (co-sélection)
- Vaccination
- Couverture
- Rapidité de mise en œuvre
- Programme de rattrapage

Loo PIDJ 2014

Le portage des nourrissons à pneumocoque en Belgique n'est pas concerné par les mesures de confinement liées au COVID-19

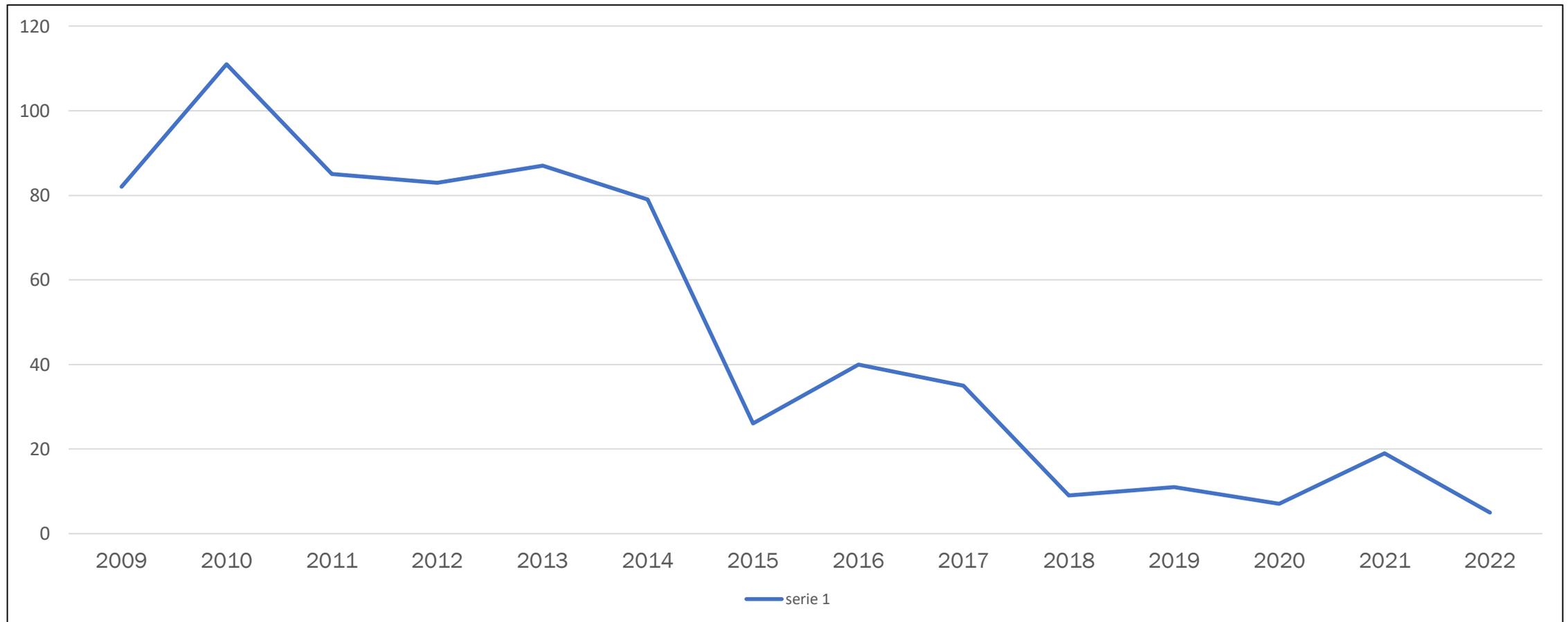


Définition de la pneumonie pneumococcique



Evolution du profil épidémiologique des pneumonies de l'enfant après la vaccination anti-pneumocoque

Hôpital Mère-Enfant – CHU Marrakech

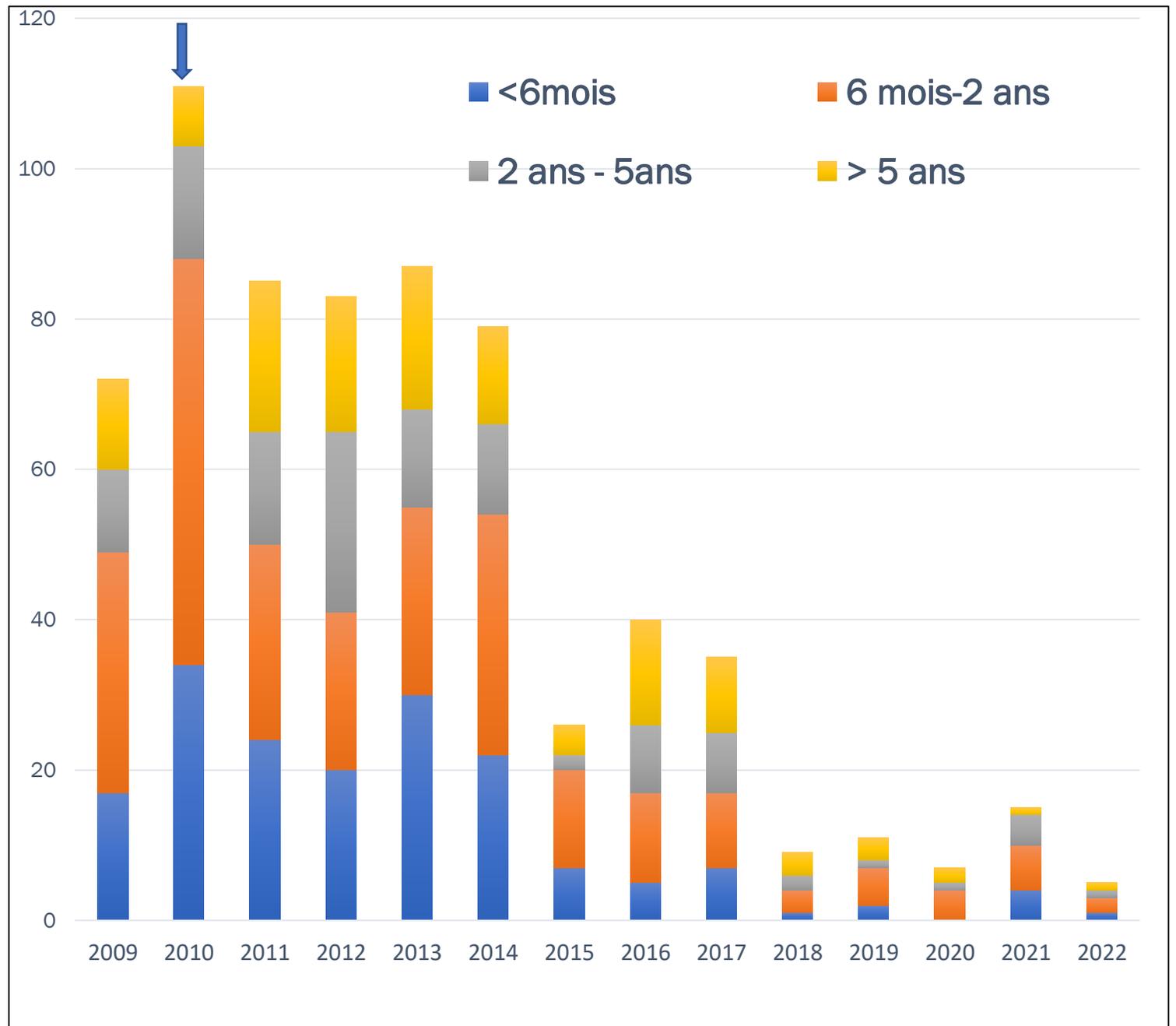


Données personnelles

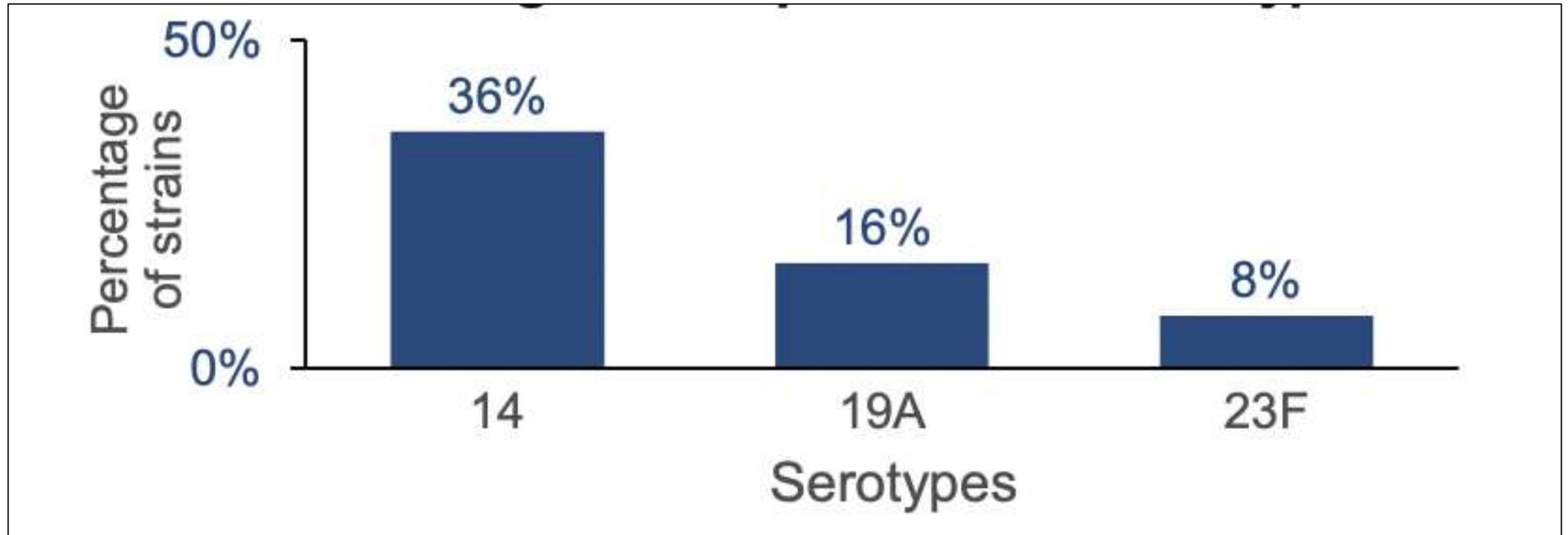
Répartition des pneumonies selon les tranches d'âges

Hôpital Mère-Enfant – CHU Marrakech

Données personnelles



Pneumopathie pneumococcique chez l'enfant de moins de 14 ans à l'hôpital Ibn Rochd Casablanca : résultats de 8 ans de surveillance (2007-2014)

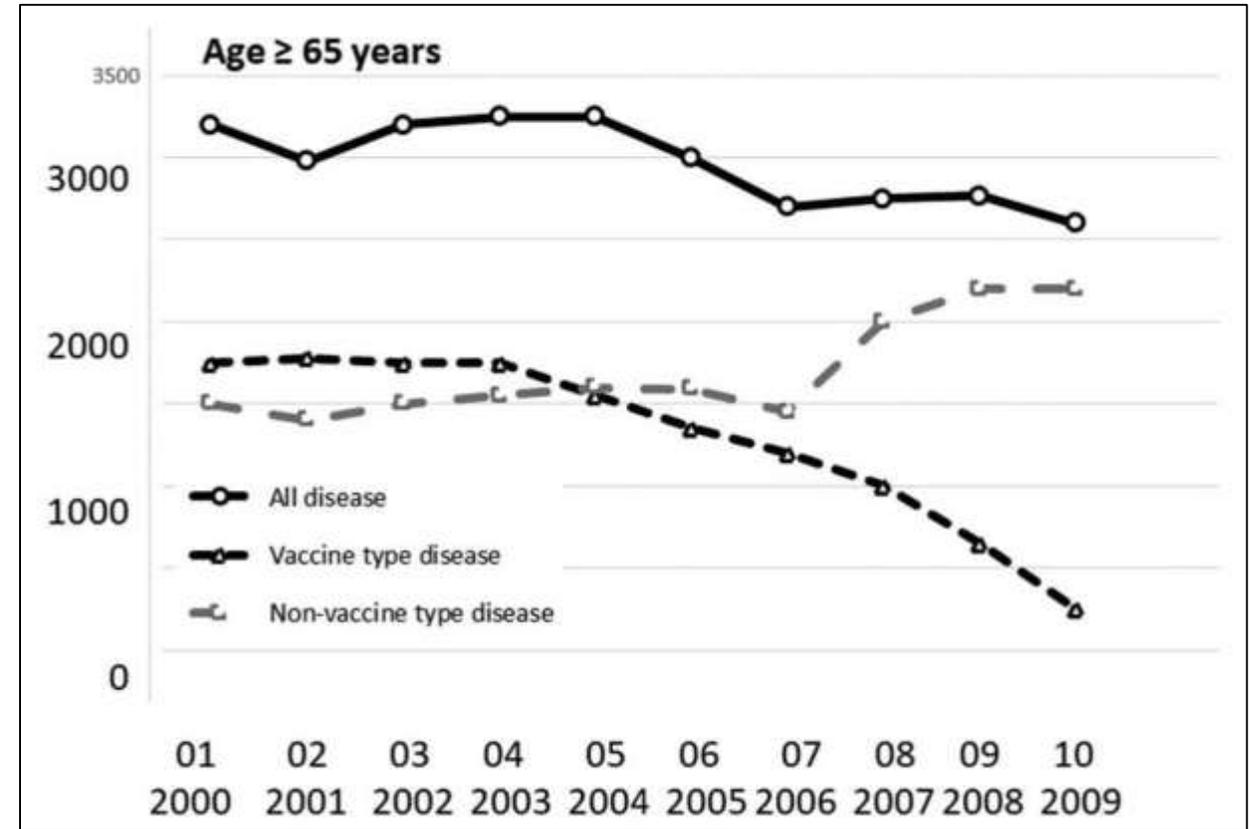
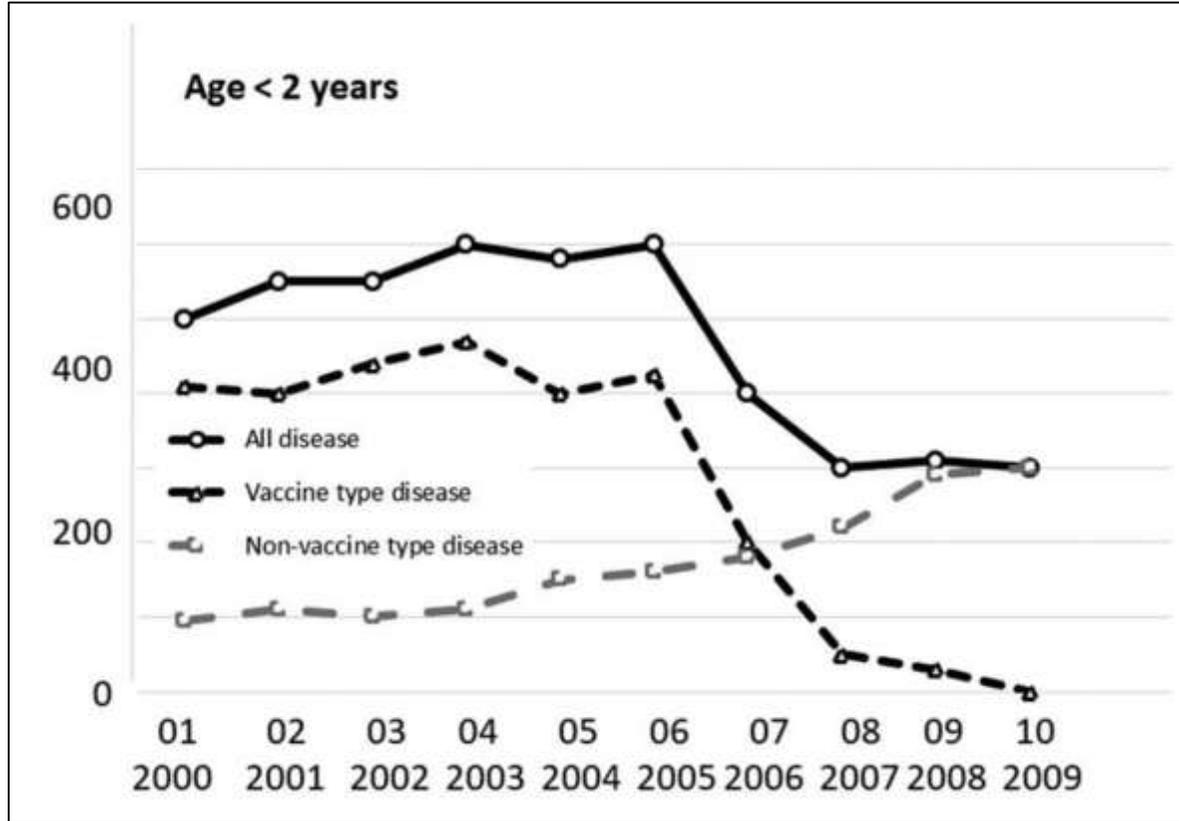


Baisse de la mortalité infantile d'origine respiratoire après l'introduction du vaccin anti-pneumococcique conjugué au Maroc

Total number of deaths in children under 5 years in Morocco in 2007–13, and estimated mortality rate per 100,000 children before and after the introduction of the pneumococcal conjugate vaccine (PCV) in 2010.

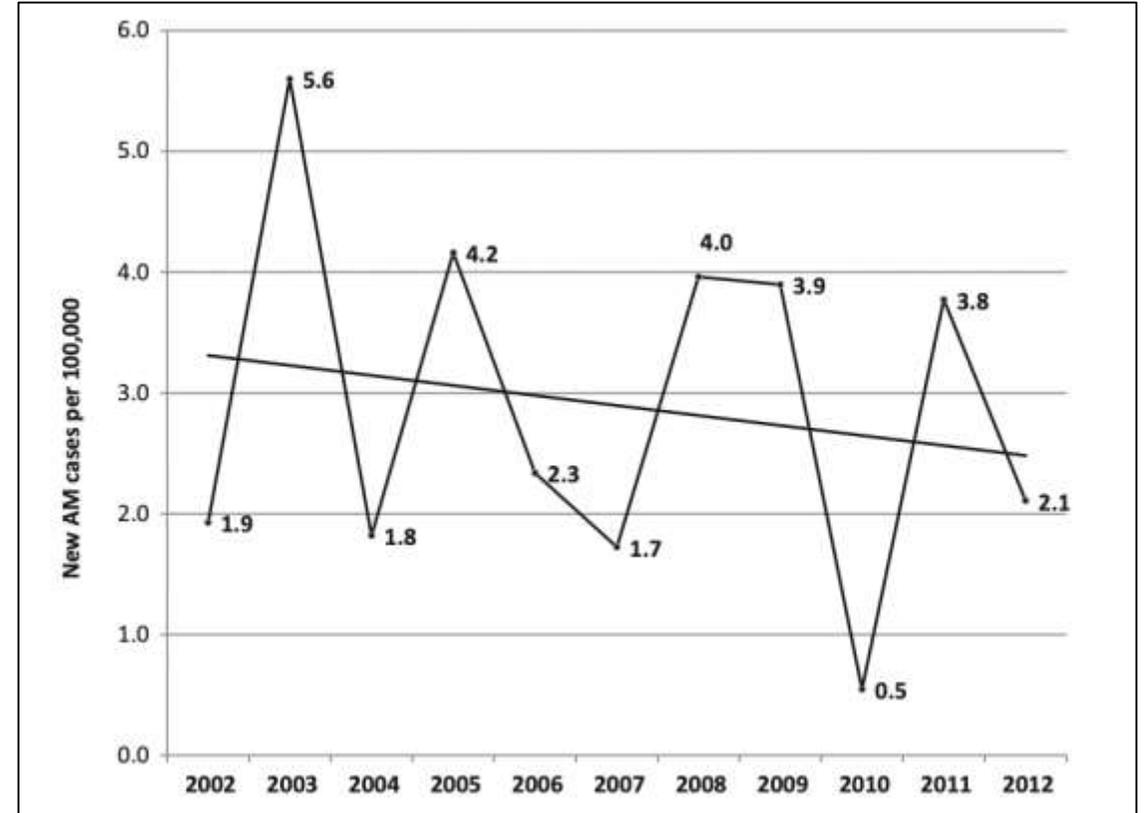
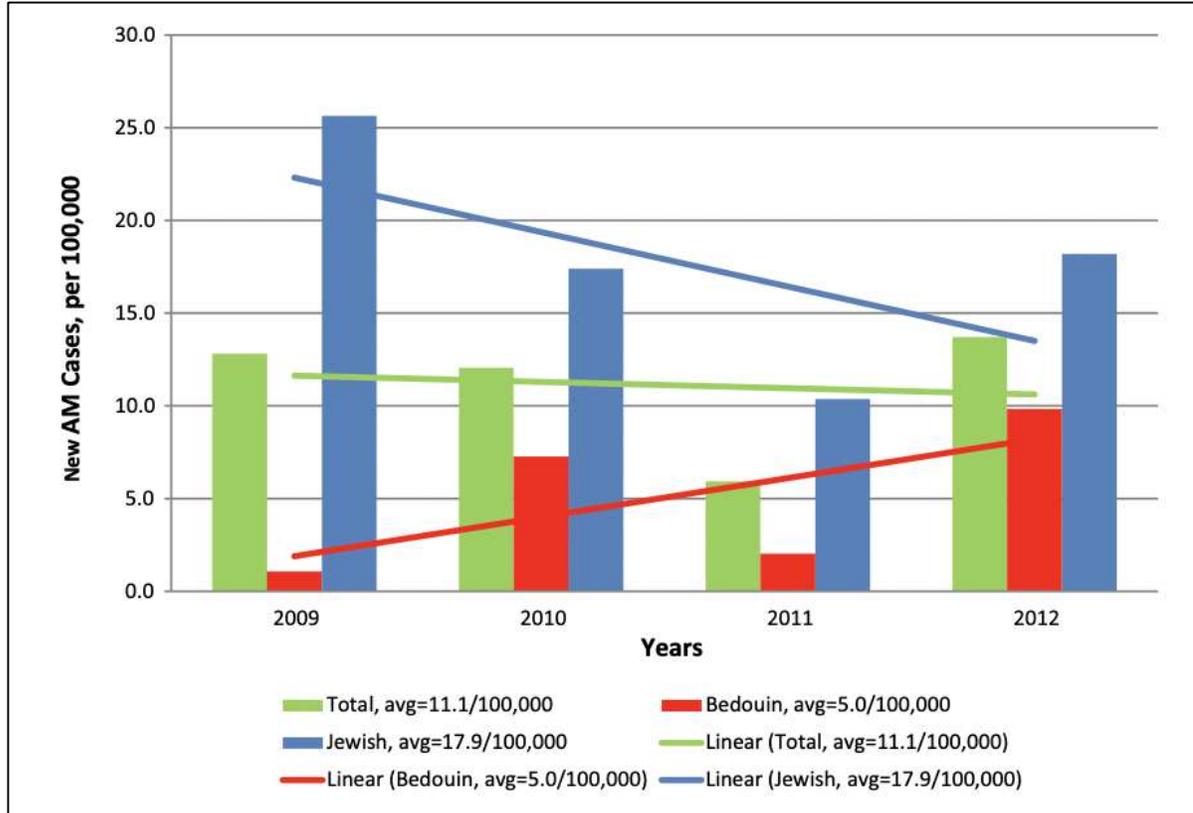
Cause of death	Total number of death No. (%)	Estimated mortality per 100,000	
		Before the introduction of PCV	After the introduction of PCV
Respiratory			
<1 year	1077 (80.7)	8.30	5.21
Total (<5 years)	1334 (100.0)	1.14	0.81
Congenital and chromosomal			
<1 year	1797 (90.2)	10.37	12.79
Total (<5 years)	1992 (100.0)	1.67	2.07

Pourquoi le taux de pneumonie à pneumocoque est-il en baisse ?



Mastoidite aiguë chez les enfants de moins de 15 ans dans le sud d'Israël suite à l'introduction des vaccins anti-pneumococciques conjugués

Une étude rétrospective de 4 ans (2009-2012)



Efficacité des vaccins conjugués anti-pneumococciques 10-valents versus 13-valents

	Study type	Age	Vaccine efficacy or effectiveness (95% CI)
Invasive pneumococcal disease ³	Meta-analysis	≤5 years	63.5% (37.3–89.7)
Clinical community-acquired pneumonia ^{4*}	Randomised controlled trial	≥65 years	61.5% (17.6–83.4)
Chest radiology-confirmed community-acquired pneumonia ^{4†}	Randomised controlled trial	≥65 years	60.0% (5.2–84.8)

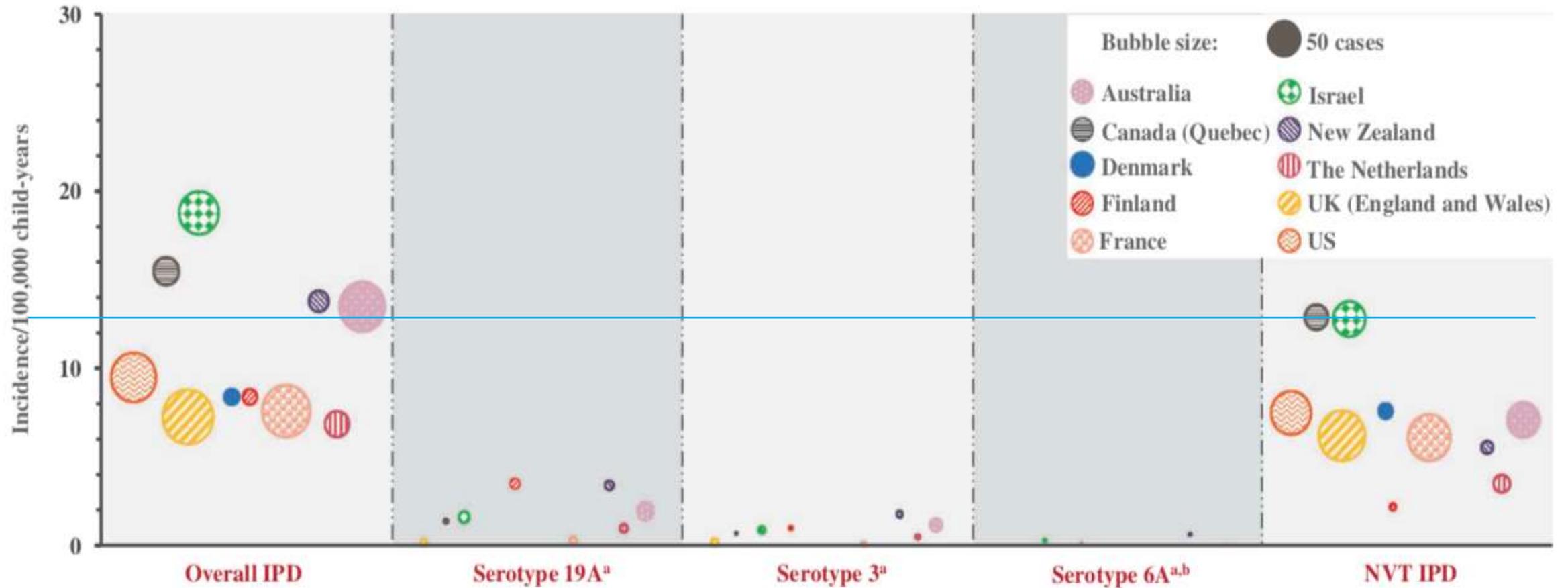
Introduction du PCV Maroc

VP13
Octobre 2010



VP10
Juillet 2012

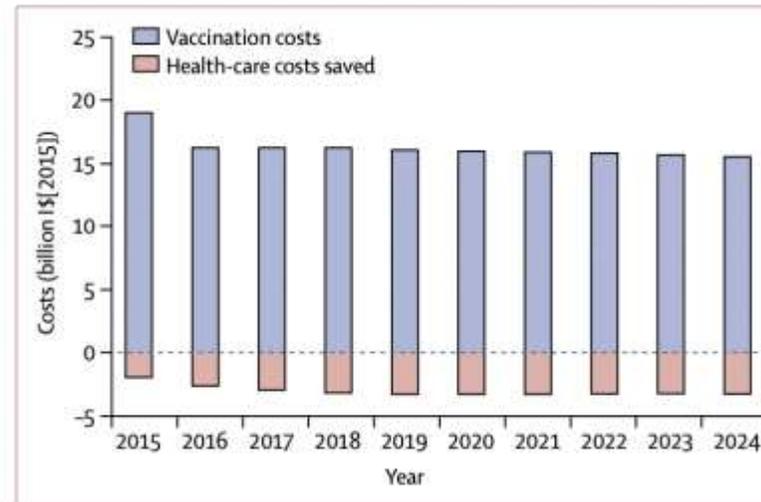
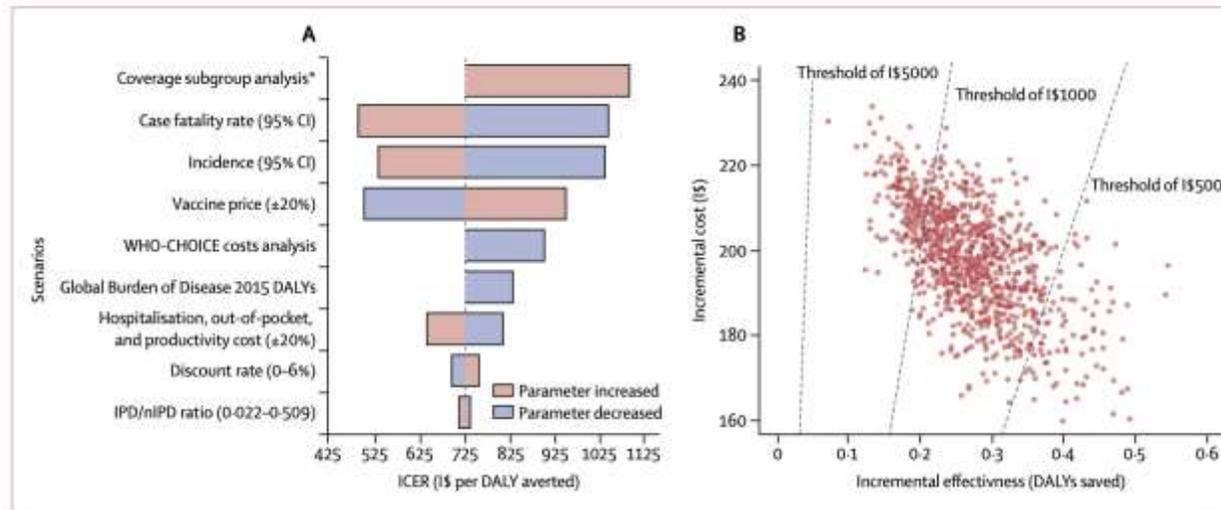
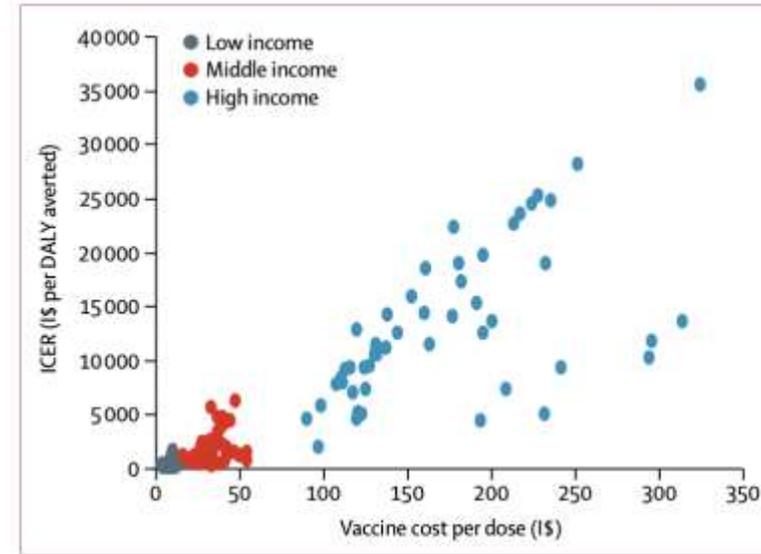
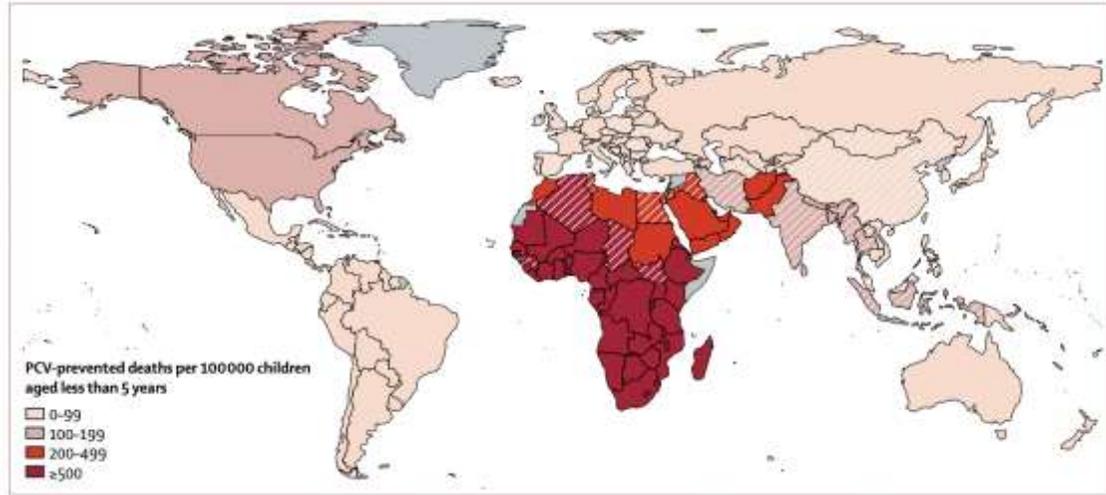
Public health impact of pneumococcal conjugate vaccine infant immunization programs: assessment of invasive pneumococcal disease burden and serotype distribution



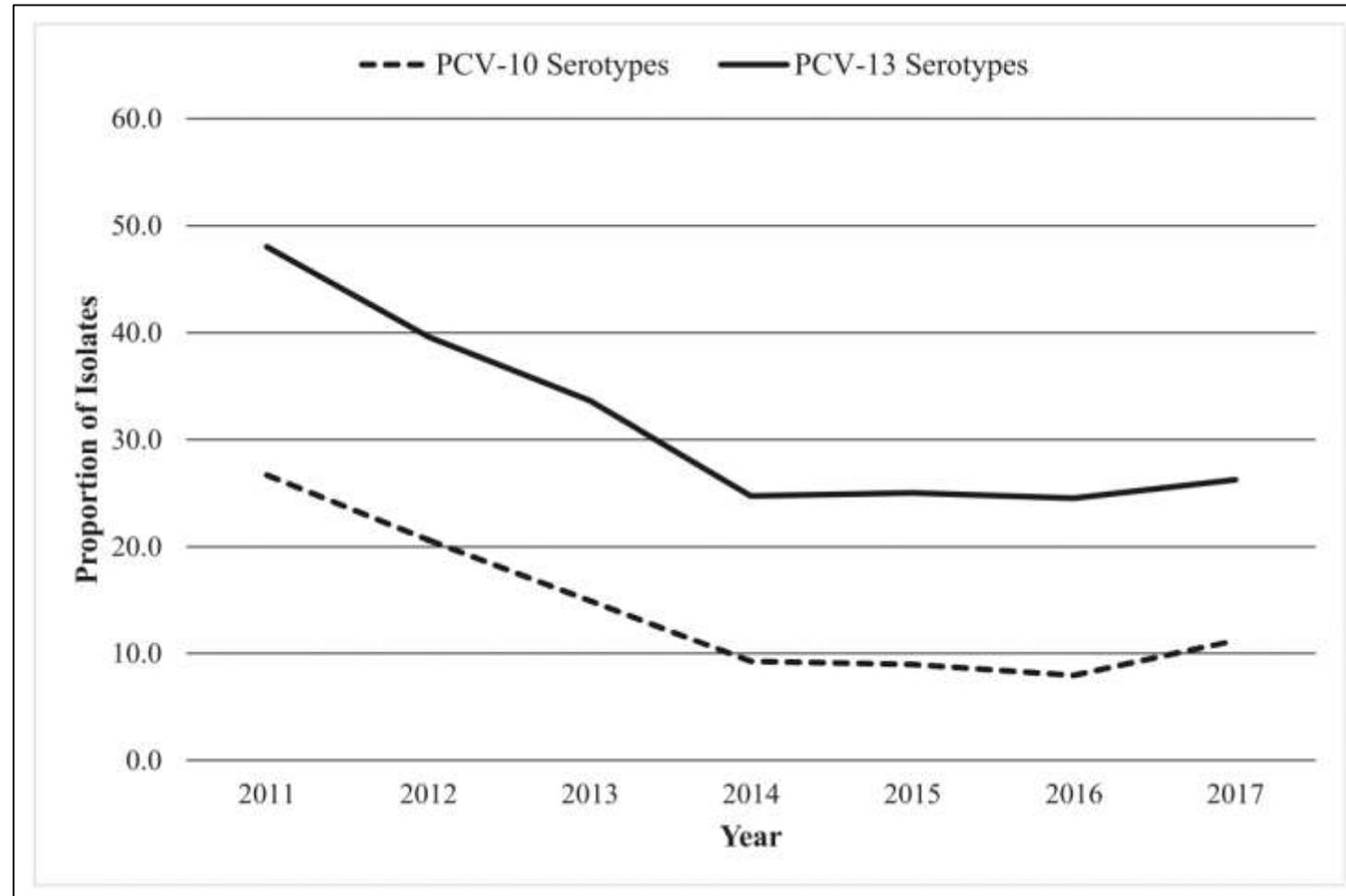
PCV10 ou PCV13 ?

- Etude coût-efficacité PCV 10/13
- Recommande de passer à une valence plus élevée, en raison des augmentations non PCV7
- On ne sait pas quel vaccin serait le plus rentable
- Dépend de l'effet PCV10 sur l'OMA et 19A, et le remplacement du sérotype
- Le PCV 13 serait plus rentable si le PCV10 et le PCV13 avaient des prix similaires
- Le sérotype 19A en hausse Avis GTCV en 2010
- Manque de données (efficacité sur les sérotypes 3 et 19A, remplacement des sérotypes, effet de troupeau) PCV13 préféré en raison d'une plus grande protection contre les sérotypes, sur la base des données actuelles A réviser lorsque de nouvelles données

Effet et coût-efficacité de la vaccination conjuguée contre le pneumocoque : une analyse de modélisation globale



Comparaison de la couverture vaccinale contre le PCV-10 et le PCV-13 pour les isolats de pneumocoques invasifs obtenus dans toutes les régions géographiques canadiennes, SAVE 2011 à 2017

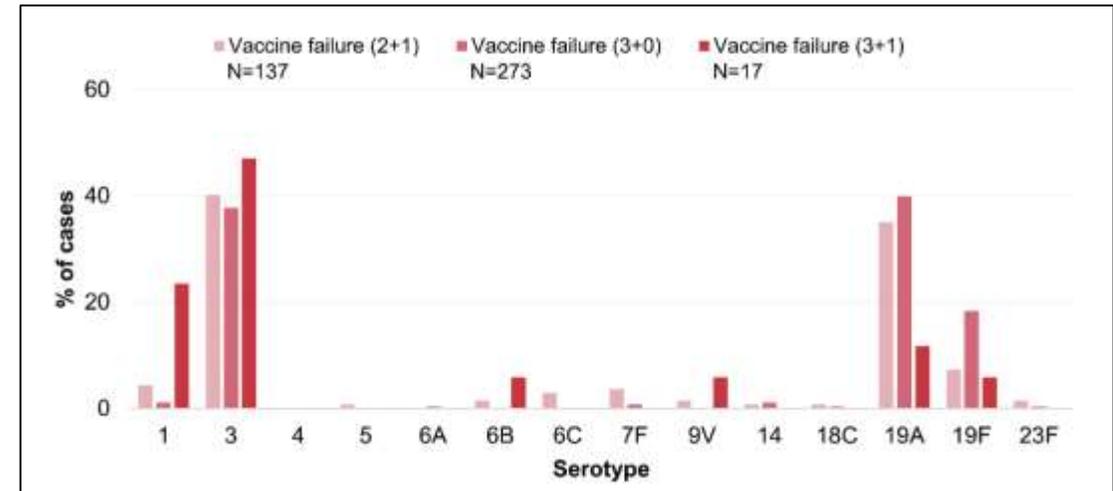
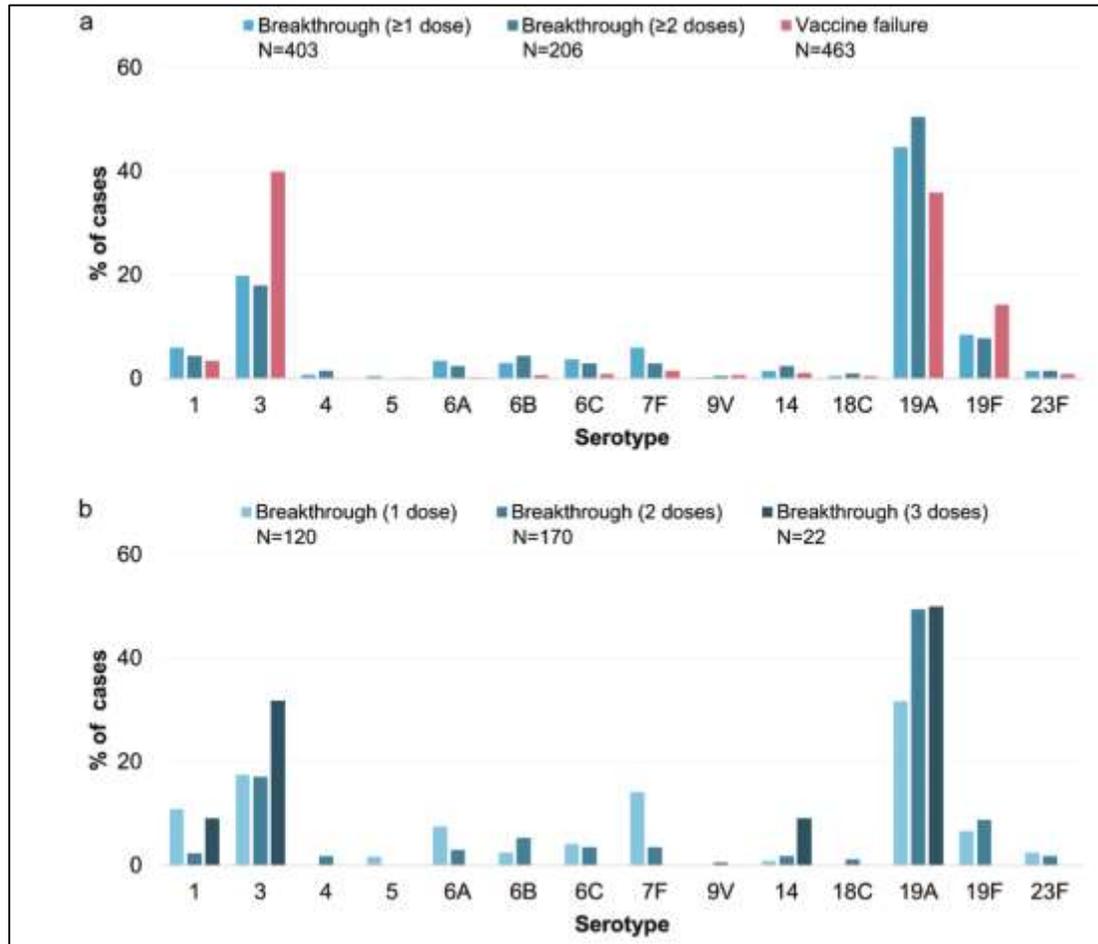


Une revue systématique des échecs des vaccins contre les maladies invasives à pneumocoque et des percées avec des vaccins conjugués contre le pneumocoque à valence plus élevée chez les enfants

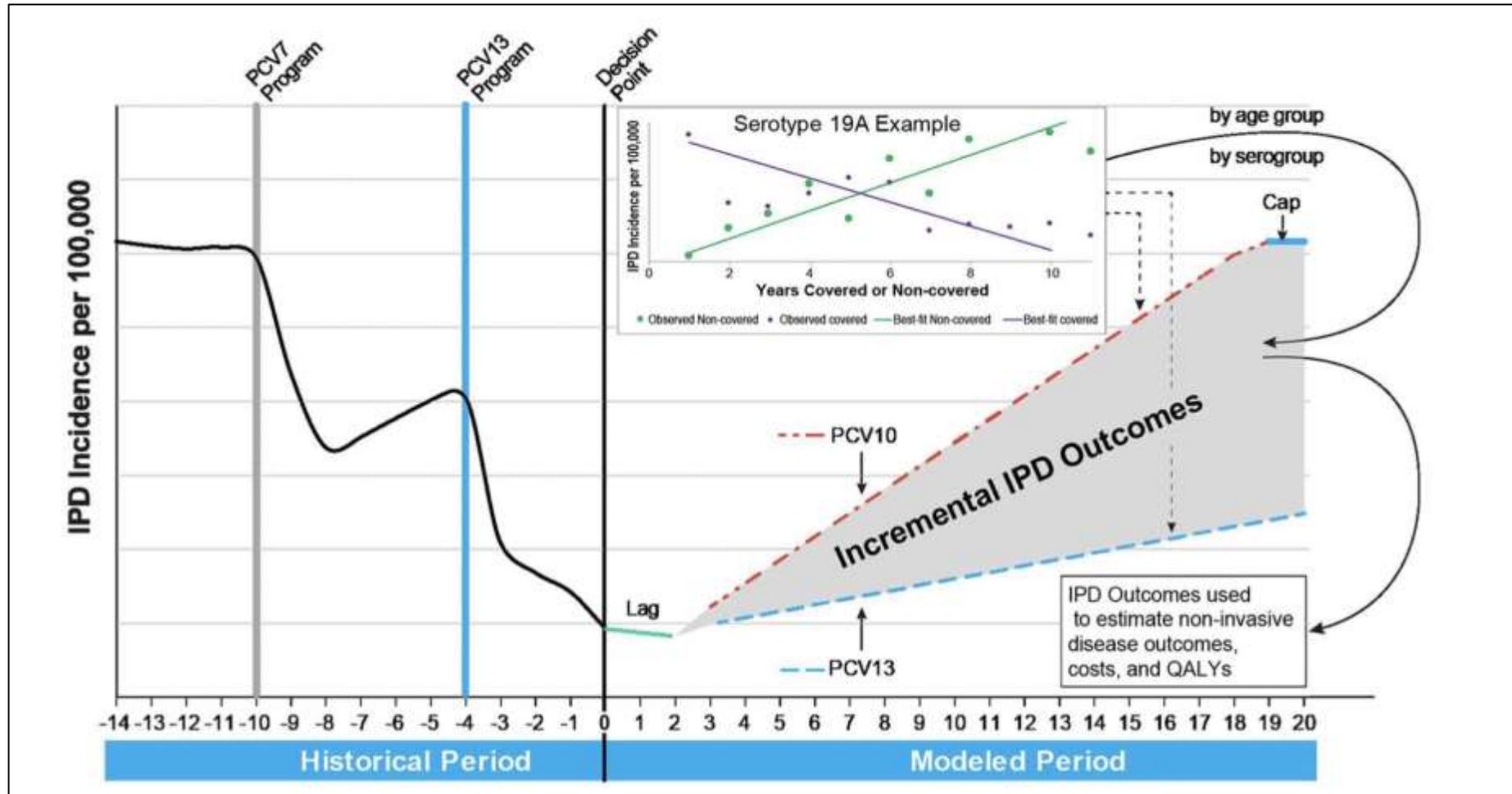
Author [ref]	Study period (PCV10/PCV13 assessment)	Country (Region)	PCV	Schedule	Study design	Age of cases
Agler [23]	2010–2014	France	PCV13	2+1	National pharmacovigilance survey	<6 years*
Almeida [24]	2012–2014	Portugal	PCV13	3+1	Retrospective, observational; hospital records (1 hospital)	<5 years
Andrews [25] ^a	2010–2018	United Kingdom (England)	PCV13	2+1	Case-control (indirect cohort); enhanced, national, laboratory-based, surveillance	<9 years*
Antachopoulos [26]	2012	Greece	PCV7/ PCV13	3+1	Descriptive analysis, national, laboratory-based, passive surveillance	<6 years*
Asner [27]	2011–2015	Switzerland	PCV7/ PCV13	2+1	Prospective, national, observational cohort; hospital records (10 hospitals)	<17 years*
Blyth [28]	2012–2017	Australia	PCV13	3+0	Descriptive analysis of vaccine failures; national, laboratory-based, passive surveillance	<5 years
Cohen [29] ^b	2012–2014	South Africa	PCV13	2+1	Case-control; national, laboratory-based, active surveillance (sentinel hospitals)	<5 years
Corcoran [47]	2012–2018	Ireland	PCV7/ PCV13	2+1	Descriptive analysis; national, laboratory-based, enhanced surveillance	<6 years*
De Wals [30]	2011–2016	Canada (Quebec)	PCV13	2+1	Descriptive analysis; provincial and sentinel, laboratory-based surveillance	<5 years
Deceuninck [6] ^b	2009–2013	Canada (Quebec)	PCV7/ PCV10/ PCV13	2+1	Case-control; provincial, laboratory-based, surveillance	<5 years
Diawara [31]	2011–2014	Morocco (Casablanca)	PCV10/ PCV13	2+1	Descriptive analysis; laboratory-based, passive surveillance (1 hospital)	<5 years
Dominguez [32] ^c	2012–2016	Spain (Barcelona)	PCV13	3+1	Case-control; hospital records (3 hospitals)	<5 years
Godot [33]	2011–2013	France	PCV13	2+1	Descriptive analysis; national hospital-based active surveillance	<5 years
Guevara [34] ^b	2010–2014	Spain (Navarra)	PCV10/ PCV13	3+1	Population-based cohort with nested case-control; active, laboratory-based surveillance	<5 years
Harboe [35]	2011–2013	Denmark	PCV13	2+1	Population-based cohort; national, laboratory-based surveillance	<2 years
Jayasinghe [36] ^a	2011–2014	Australia	PCV13	3+0	Case-control; national, passive, laboratory-based surveillance	<4 years
Lataza [37] ^b	2010–2015	Spain (Madrid)	PCV13	3+1	Case-control; regional, laboratory-based surveillance	<5 years
Mackenzie [38]	2013–2014	Gambia (Upper River Region)	PCV13	3+0	Prospective observational; population-based surveillance	≤2 years
Madhi [39]	2013	France	PCV13	2+1	Case report	3 years
Moore [41] ^b	2010–2014	United States	PCV13	3+1	Case-control; active, sentinel laboratory-based surveillance (13 sites)	<5 years
Novak [42]	2012	Sweden	PCV13	2+1	Case report	1 year
Okorji [43]	2012–2014	Czechia	PCV10/ PCV13	3+1/ (2+1)	Descriptive analysis; national, laboratory-based surveillance	<5 years
Ong [44]	2009–2014	Singapore	PCV13	2+1	Retrospective; hospital records (1 hospital)	<5 years
Sütçü [45]	NA	Turkey	PCV13	3+1	Case report	2 years
van der Linden [46] ^b	2010–2015	Germany	PCV10/ PCV13	3+1	Case-control (indirect cohort); national, laboratory-based surveillance	<2 years
Verani [9] ^c	2010–2012	Brazil	PCV10	3+1	Case-control (indirect cohort); laboratory-based surveillance (10 states)	<5 years

Author [ref]	PCV (schedule)	N IPO (PCV-vaccinated)	Breakthrough cases	Serotypes in breakthrough cases (n)	Vaccine failures	Serotypes in vaccine failures (n)
Agler [23]	PCV13 (2+1)	54	NA	NA	16	19A (5), 19F (5) ^d
Almeida [24]	PCV13 (3+1)	9	3	2 doses: 19A (1) 3 doses: 3 (2)	4	3 (4)
Andrews [25] ^a	PCV13 (2+1)	2,642	158	1 dose: 1 (11), 3 (19), 5 (1), 6A (3), 6B (1), 4C (5), 7F (13), 14 (1), 19A (19), 19F (3), 23F (1) 2 doses: 1 (2), 3 (24), 6A (2), 6B (1), 6C (0), 7F (5), 14 (1), 18C (2), 19A (29), 19F (8), 23F (1)	90	1 (6), 3 (36), 6B (1), 6C (4), 7F (4), 9V (2), 18C (1), 19A (26), 19F (8), 23F (2)
Antachopoulos [26]	PCV7/PCV13 (3+1)	NA	0	0	5	Catch-up: 3 (5)
Asner [27]	PCV7/PCV13 (2+1)	25	NA	NA	11	3 (11) ^d
Blyth [28]	PCV13 (3+0)	1,147	NA	NA	241	1 (1), 3 (96), 6A (1), 7F (1), 14 (1), 18C (1), 19A (93), 19F (46), 23F (1), 3 (1), 5 (1), 19A (3), 19F (2)
Cohen [29] ^b	PCV13 (2+1)	230	38	1 dose: 1 (1), 5 (1), 6A (6), 6B (1), 19A (1), 19F (3), 23F (2) 2 doses: 1 (1), 3 (1), 4 (3), 6A (2), 6B (6), 19A (3), 19F (4), 23F (1)	7	3 (1), 5 (1), 19A (3), 19F (2)
Corcoran [47]	PCV7/PCV13 (2+1)	NA	5	2 doses PCV7 + 1 dose PCV13: 19A (2) 1 dose PCV7 + 2 doses PCV13: 19A (1)	8	3 (1), 6B (1), 7F (1), 19A (5)
De Wals [30]	PCV13 (2+1)	NA	21	2 doses PCV13: 19A (2) 1 dose: 3 (1), 19A (1)	9	3 (3), 19A (6)
Deceuninck [6] ^b	PCV7/ PCV10/ PCV13 (2+1)	128	PCV10 or PCV7 + PCV10: 22 PCV13: 10	1 dose: 7F (1), 19A (9) 2 doses: 6A (1), 19A (11) PCV13: 10	PCV10: 4 PCV10 + PCV13: 2	PCV10: 19A (4) PCV10 + PCV13: 19A (2)
Diawara [31]	PCV10/ PCV13 (2+1)	18	PCV10: 5 PCV13: 5	1 dose: 3 (1) 2 doses: 19A (9) PCV10: 1 dose: 1 (1), 6B (1) 2 doses: 1 (1), 6B (1), 14 (1) PCV13: 1 dose: 7F (1)	0	0
Dominguez [32] ^c	PCV13 (3+1)	75	17	2 doses: 3 (1), 6B (1), 9V (1), 14 (1) 1, 2 or 3 doses: 1 (2), 3 (10), 19A (5)	15	1 (3), 3 (12), 14 (1), 19A (1)
Godot [33]	PCV13 (2+1)	NA	12	1 dose: 7F (2), 19A (2), 19F (1) 2 doses: 19A (5), 19F (2)	1	19A (1)
Guevara [34] ^b	PCV10/ PCV13 (3+1)	18	0	0	3	PCV10 + PCV13: 19A (1) PCV13: 3 (2)
Harboe [35]	PCV13 (2+1)	NA	1	2 doses: 3 (1)	0	0
Jayasinghe [36] ^a	PCV13 (3+0)	256	60	1 or 2 doses: 3 (32), 6C (4), 7F (1), 19A (33), 19F (10)	26	3 (7), 7F (1), 19A (14), 19F (4)
Lataza [37] ^b	PCV13 (3+1)	173	14	2 or 3 doses: 1 (3), 3 (1), 19A (9), 19F (1)	6	Catch-up: 1 (2), 3 (2), 19A (1), 23F (1)
Mackenzie [38]	PCV13 (3+0)	NA	1	2 doses: 23F (1)	5	1 (2), 14 (2), 19A (1)
Madhi [39]	PCV13 (2+1)	NA	NA	NA	1	3 (1)
Moore [41] ^b	PCV13 (3+1)	487	NA	86 (failure or breakthrough) ≥7 doses: 3 (25), 6C (4), 7F (2), 9V (1), 14 (1), 19A (50), 19F (3)	1	3 (1)
Novak [42]	PCV13 (2+1)	NA	NA	NA	1	3 (1)
Okorji [43]	PCV10/ PCV13 (3+1/2+1)	NA	PCV10: 1 PCV13: 1	PCV10 3 primary doses: 14 (1) PCV13 3 primary doses: 3 (1)	PCV10: 4 PCV13: 2	PCV10: 1 (3), 14 (1) PCV13: 1 (1), 3 (1)
Ong [44]	PCV13 (2+1)	NA	NA	NA	3	3 (1), 19A (2)
Sütçü [45]	PCV13 (3+1)	NA	NA	NA	1	9V (1)
van der Linden [46] ^b	PCV10/ PCV13 (3+1)	339	PCV10: 5 PCV13: 24	PCV10: 2 doses: 19A (2) 3 doses: 14 (1), 19A (2) PCV13: 1 dose: 19A (4), 19F (1) 2 doses: 3 (1), 7F (1), 19A (1), 19F (1) 3 doses: 1 (2), 3 (4), 19A (9)	PCV10: 2 PCV13: 2	PCV10: 6B (1), 19F (1) PCV13: 3 (1), 19A (1)
Verani [9] ^c	PCV10 (3+1)	187	NA	92 (failure or breakthrough) ≥7 doses: 6A (16), 6B (16), 14 (28), 18C (6), 19A (15), 19F (4), 23F (2)	NA	NA

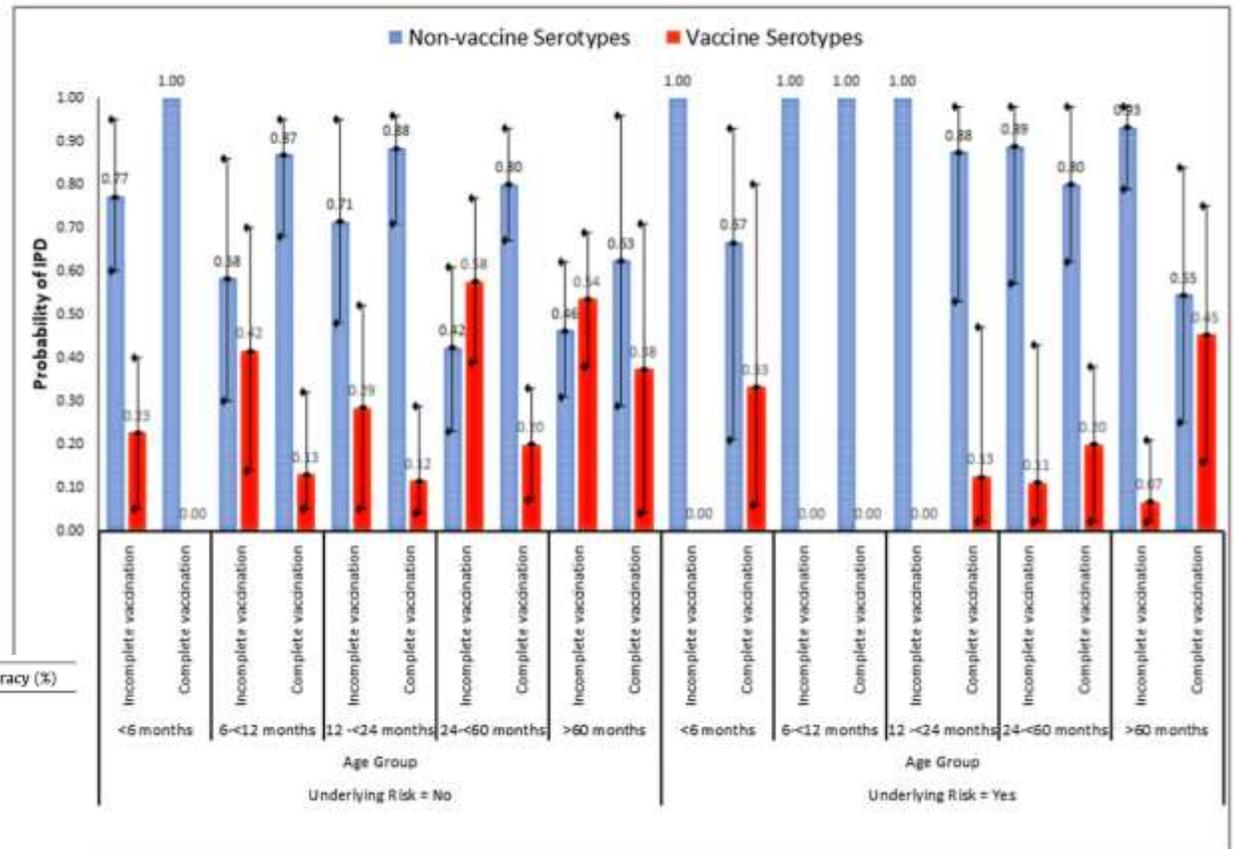
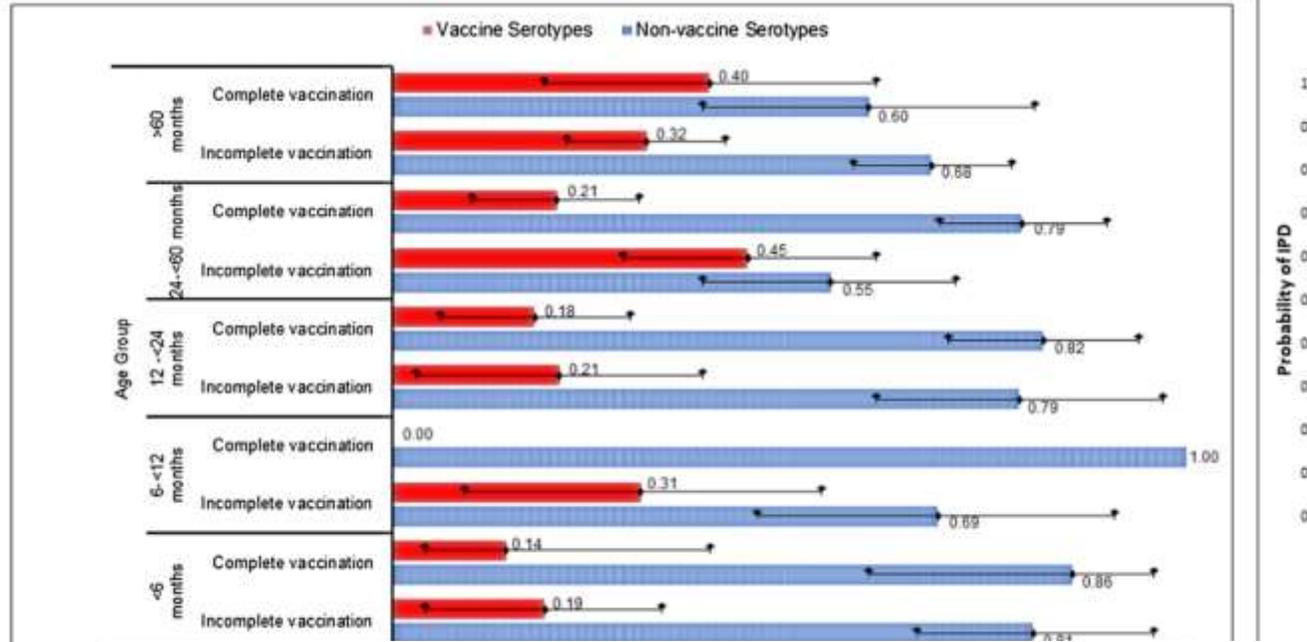
Une revue systématique des échecs des vaccins contre les maladies invasives à pneumocoque et des percées avec des vaccins conjugués contre le pneumocoque à valence plus élevée chez les enfants



Impact clinique et économique d'un passage potentiel de la vaccination conjuguée contre le pneumocoque à 13 valents à 10 valents au Canada



Qui est à risque d'échec du vaccin anti-pneumococcique conjugué 13-valent ?

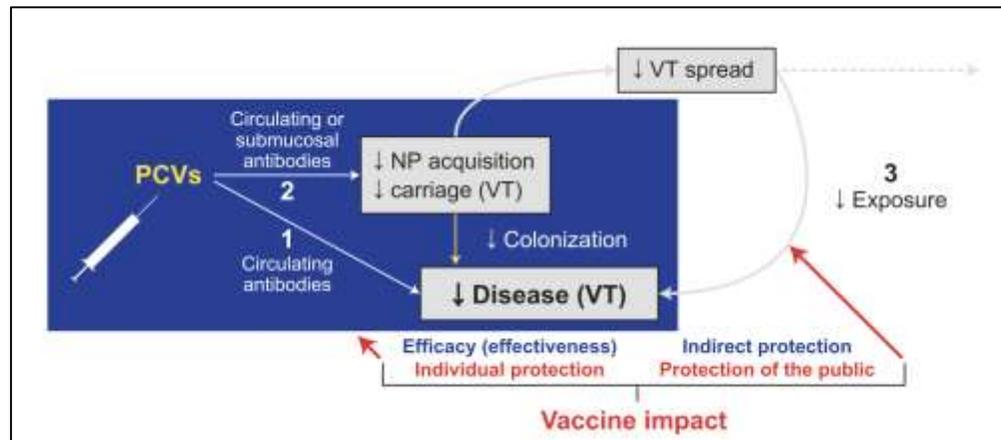
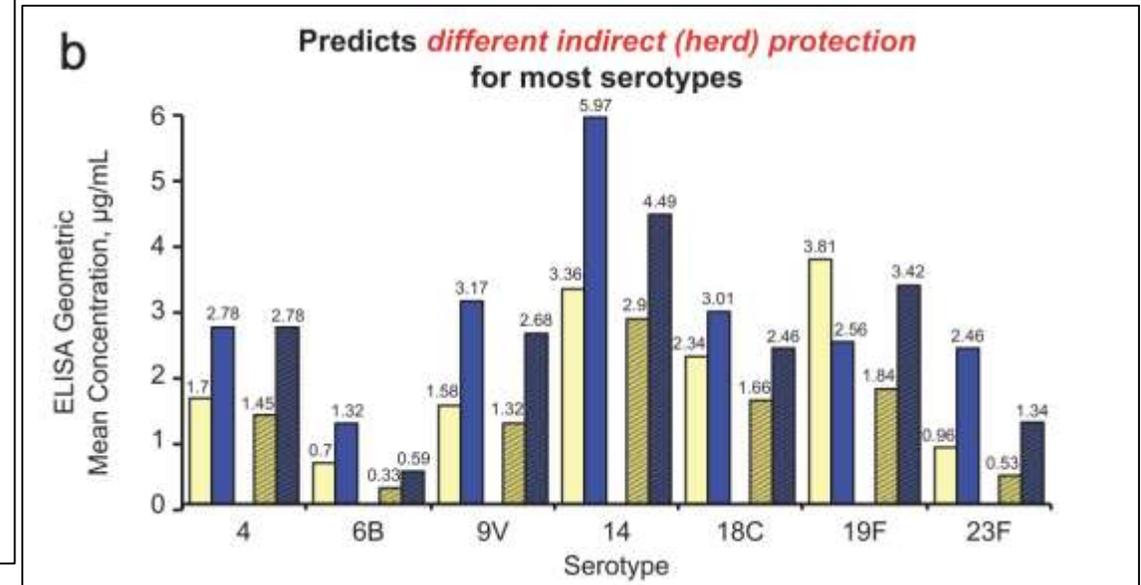
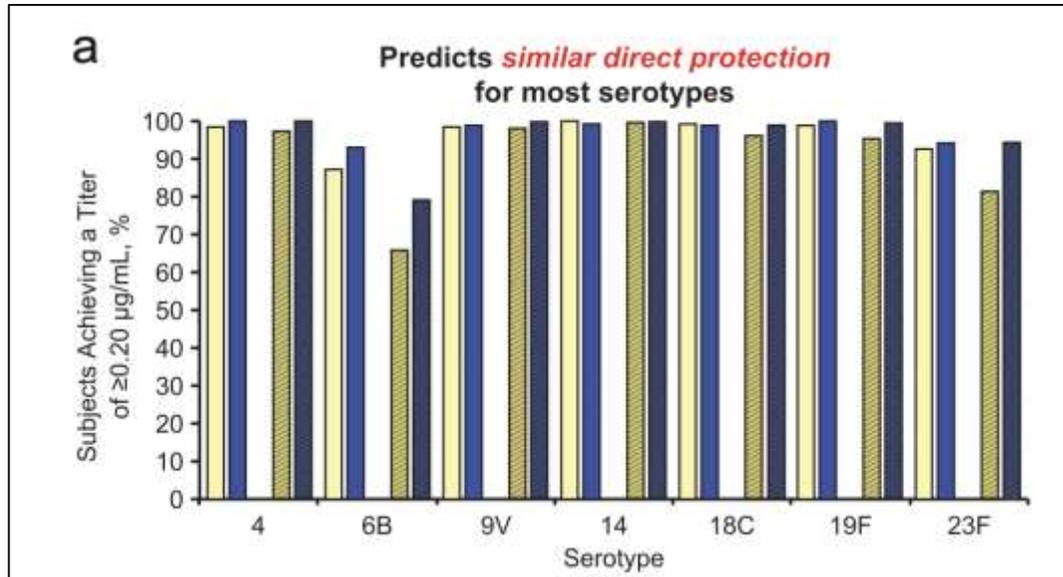


Characteristics	PCV13 schedule	Probability of Vaccine Serotype Disease (95% CI)*	Prediction Accuracy (%)
Whole cohort	2p+0 (N=34)	0.26 (0.14, 0.40)	91.2
	3p+0 (N=16)	0.25 (0.14, 0.39)	81.3
	3p+1 (N=7)	0.14 (0.09, 0.16)	100
Children with comorbidity	2p+0 (N=11)	0.18 (0.13, 0.23)	100
	3p+0 (N=4)	0 (0, 0.03)	100
	3p+1 (N=5)	0 (0, 0.06)	80
Children without any comorbidity	2p+0 (N=23)	0.30 (0.17, 0.43)	87
	3p+0 (N=12)	0.33 (0.23, 0.52)	75
	3p+1 (N=2)	0.50 (0, 1)	50
Clinical Presentation Pneumonia	2p+0 (N=12)	0.33 (0.13, 0.54)	100
	3p+0 (N=5)	0.60 (0.32, 0.82)	60
	3p+1 (N=2)	0.50 (0, 1)	50
Bacteremia	2p+0 (N=18)	0.22 (0.05, 0.33)	88.9
	3p+0 (N=10)	0.10 (0.01, 0.21)	90
	3p+1 (N=4)	0 (0, 0.05)	75

CI - Confidence interval (Bootstrap).

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Relation entre la réponse immunitaire aux vaccins anti-pneumococciques conjugués chez les nourrissons et la protection indirecte après la mise en œuvre du vaccin



PCV10 (n = 173)
 PCV7 (n = 170)
 PCV10 (n = 1107)
 PCV7 (n = 375)

Ron Dagan (2019) Relationship between immune response to pneumococcal conjugate vaccines in infants and indirect protection after vaccine implementation, *Expert Review of Vaccines*, 18:6, 641-661

Vaccins anti-pneumococciques

Combien de sérotypes suffisent ?

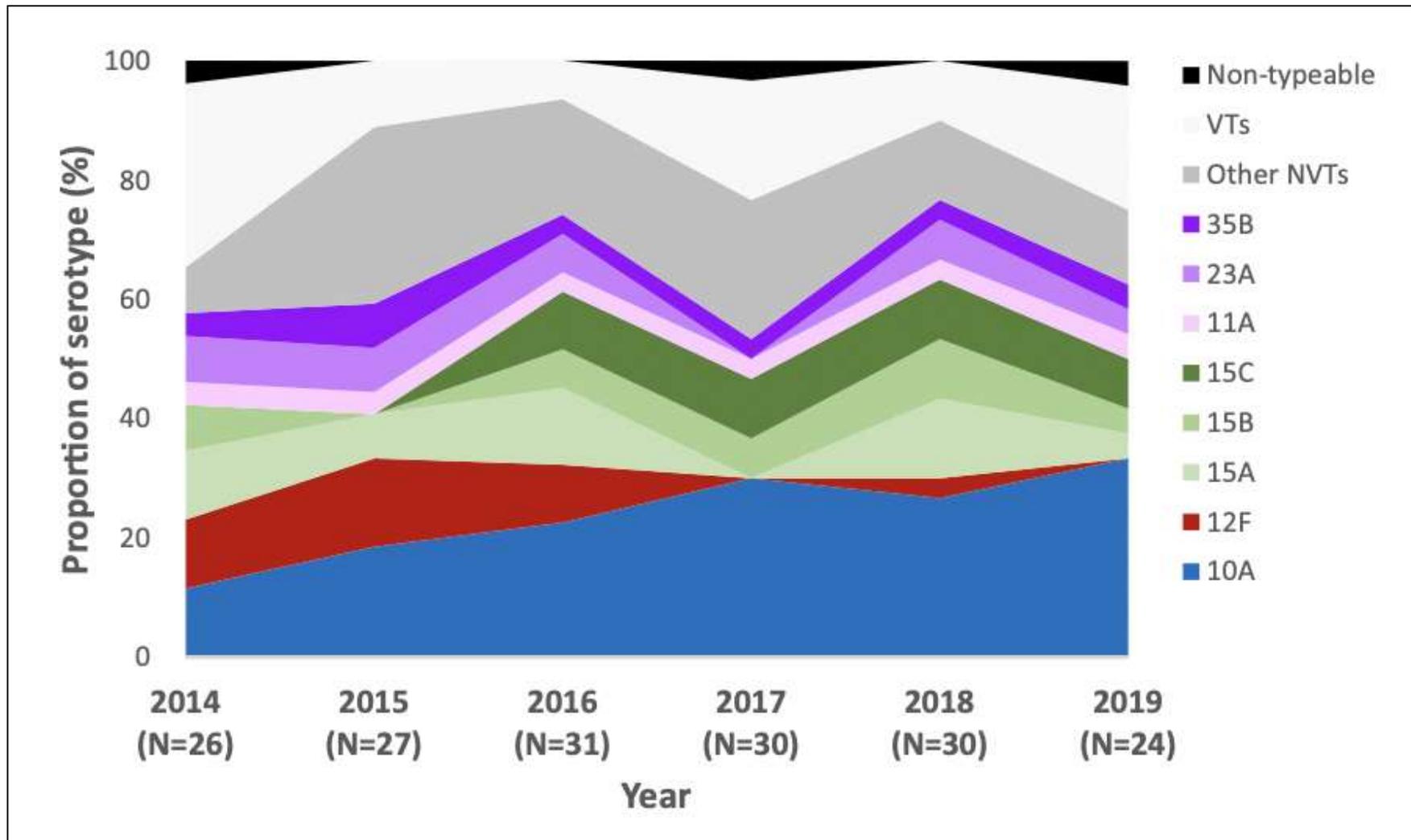
Studies	Regions	Serotypes	Serotype coverage by PCVs
Balaji et al. [9]	South India	14(19.5%), 19F (12.2%), 5(8.7%), 6A (8.7%), 6B (8, 7%)	PCV10–64% PCV13–74.6%
Shariff et al. [10]	Delhi	19 (26%), 6 (11%), 7 (10%), 1 (9%), 14 (7%), 9 (5%), 33 (4%), 17 (4%), 11 (2%), 3 (2%), 18 (1%), 23 (1%), 12 (1%), 32A (1%), 15B (1%), 22F (1%), 5 (1%), 29 (1%), non-vaccine type E (1%), F (1%), H (7%), 19 A (6%)	PCV10–54% PCV13–73%
ANSORP study [11]	11 Asian countries	19F (23.5%), 23F (10%), 19A (8.2%), 14(7.3%), 6B (7.3%), 3(6.2%), 6A (4.2%)	PCV7–52.5%
IBIS group, INCLIN [12]	India	6,1,19,14,4,5,45,12,7. Serotypes 1 and 5 account for 29% isolates	

Vaccine	Serotypes covered	Routine vaccination	Catch up vaccination
PCV 10 (synflorix)	4,6B,9V,14,18C,19F 23F (covered by PCV7) plus additional 3–1,5,7F	Primary vaccination –6,10,14 wk of age Booster at 12–15 mo of age	6–12 mo age 12 mo – 5 y
PCV 13 (Prevanar13)	Serotypes covered by PCV10 plus additional 3–3, 6A, 19A	Primary vaccination – 6,10,14 wk of age Booster at 12–15 mo of age	6–12 month 12–23 mo 24 mo – 5 y

Disease	Pooled vaccine efficacy
Invasive pneumococcal disease (IPD) [26]	For vaccine serotypes – 80% (95% CI 58% to 90%, $P < 0.0001$) For all serotypes – 58% (95% CI 29% to 75%, $P = 0.001$)
Radiologically defined pneumonia [27, 28]	27% (95% CI 15% to 36%, $P < 0.0001$)
Clinically defined pneumonia [29]	6% (2% to 9%, $P 0.0006$)
Otitis media [30–32]	Recurrent otitis media – 10–50% Severe otitis media – 39–66%
Nasopharyngeal carriage [33, 34]	16.6% – 18.3%

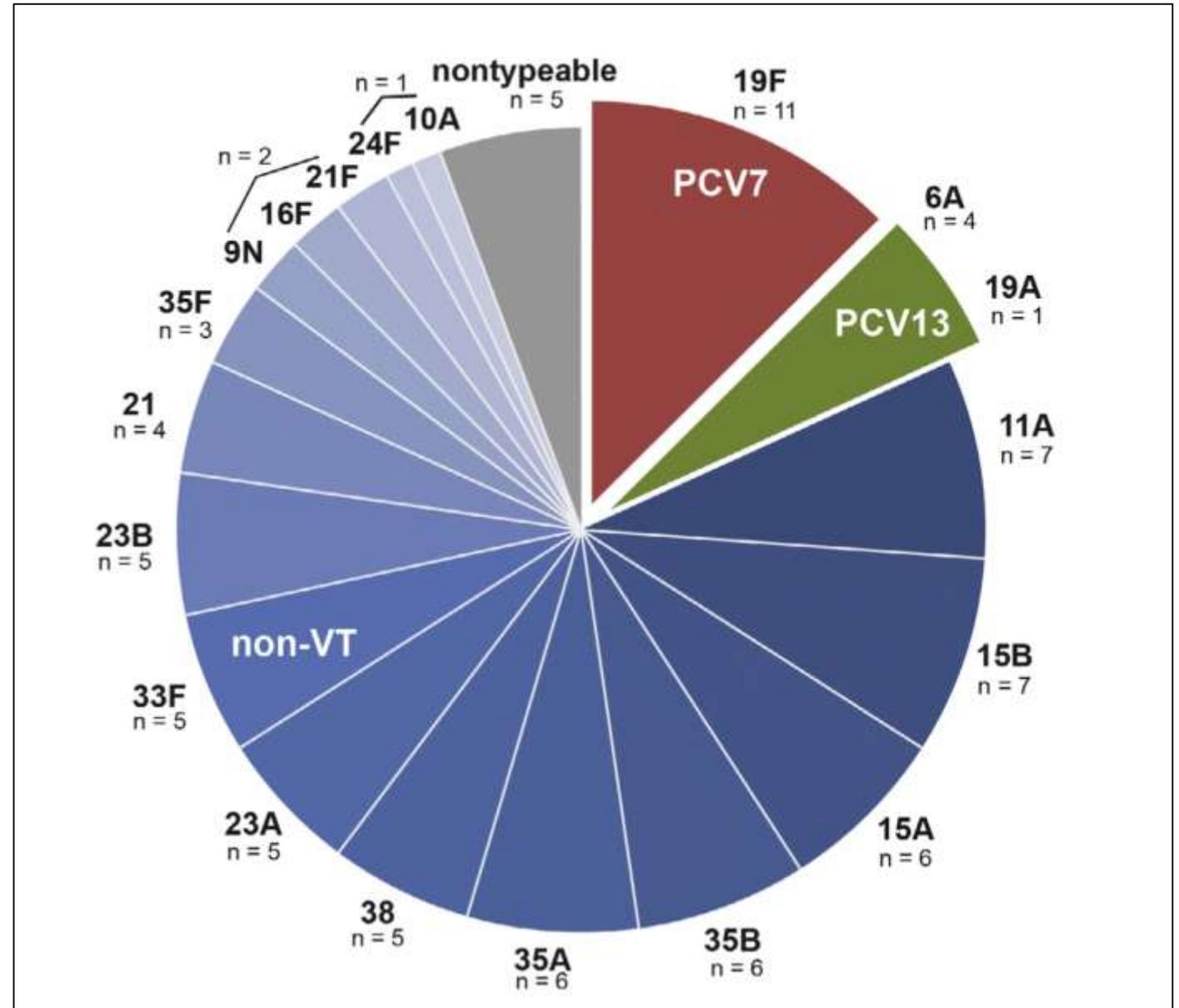
Dosing schedule		Primary doses	3p + 0 schedule		2p + 1 schedule	
			3 doses at 6,10,14 wk or 2, 4, 6 mo alongwith pentavac and rotavirus vaccines	No booster	< 6 mo	2 doses. As early as 6 wk and 8 wk gap between 2 doses
		Booster			>6 mo	4 wk gap between two doses
					1 booster at 15 mo of age with measles and vit A	
	1–2 y		2 doses 8 wk apart		2 doses 8 wk apart	
	>2 y with high risk		2 doses 8 wk apart		2 doses 8 wk apart	
Immunogenicity after primary doses			More		Less	
Immunogenicity after full doses			Less		More	

Émergence du sérotype 10A-ST11189 parmi les maladies pédiatriques invasives à pneumocoque, Corée du Sud, 2014-2019

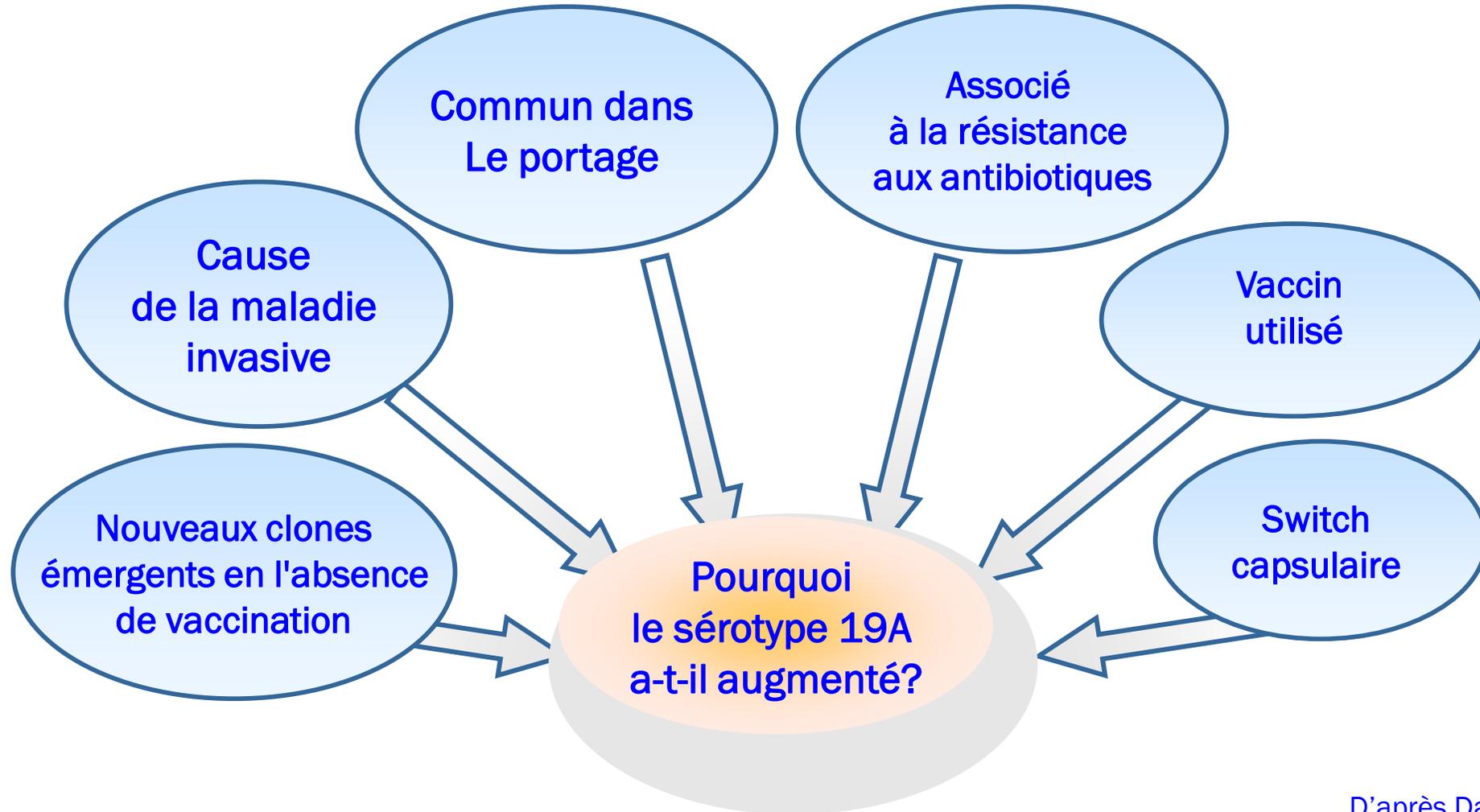


Colonisation par le 19F et d'autres sérotypes de vaccins anti-pneumococciques conjugués chez des enfants à St. Louis, Missouri, États-Unis

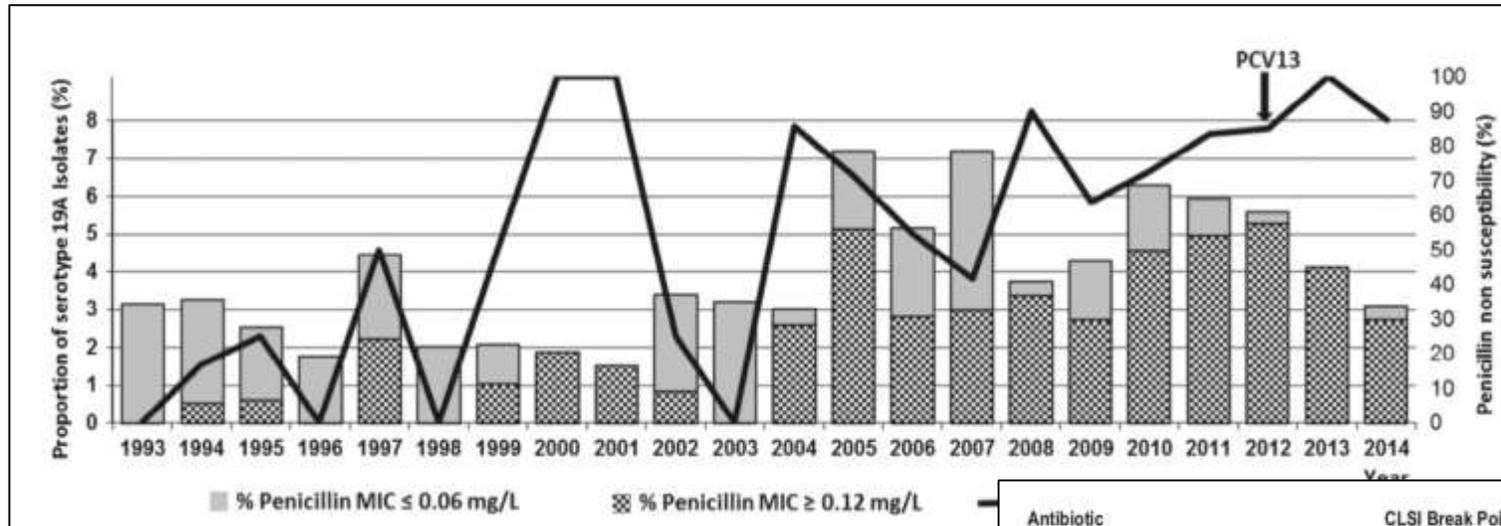
Vaccine 35 (2017) 4389-4395



Facteurs contribuant à l'émergence du 19A



Caractérisation des isolats invasifs de *Streptococcus pneumoniae* sérotype 19A d'Argentine (1993-2014)



P. Gagetti et al. / Vaccine xxx (2017) xxx–xxx

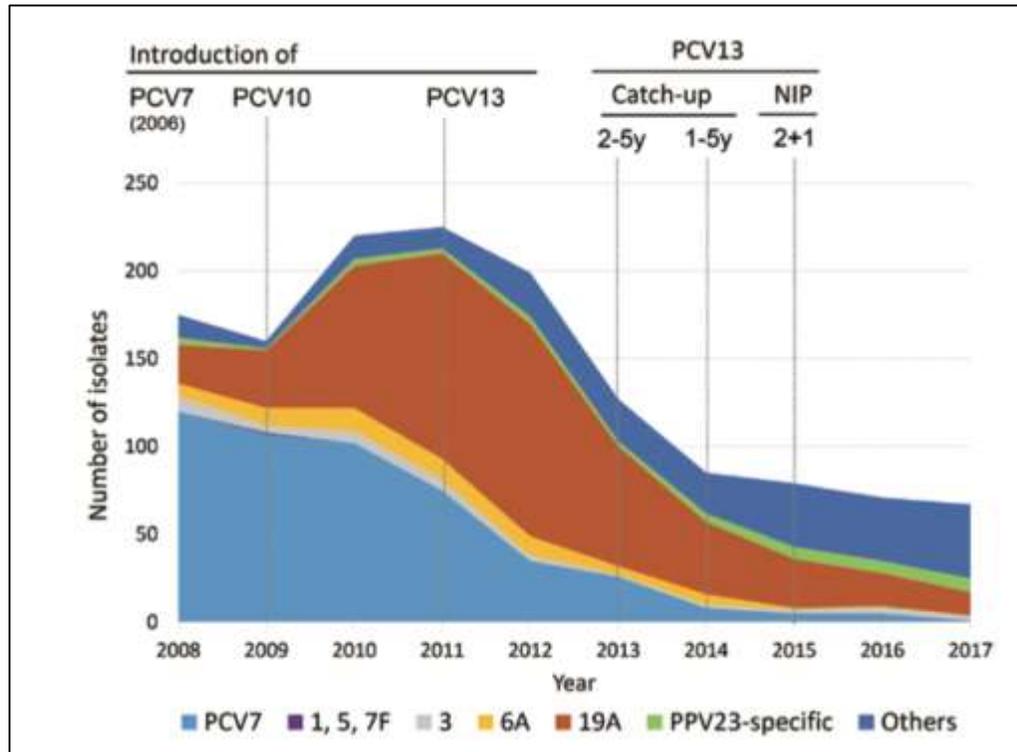
Antibiotic	CLSI Break Point (mg/L)	Resistance Profile			MIC (mg/L)												
		% S	% I	% R	0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16
Penicillin	S≤0.06 R≥0.12	34.1	-	65.9*	[MIC distribution bars]												
Amoxicillin	S≤2 I4 R≥8	97.5	2.5	0	[MIC distribution bars]												
Cefotaxime	S≤0.5 I1 R≥2	93.2	4.5	2.3	[MIC distribution bars]												
Meropenem	S≤0.25 I0.5 R≥1	94.8	2.3	2.9	[MIC distribution bars]												
Erythromycin	S≤0.25 I0.5 R≥1	84.1	0	15.9	[MIC distribution bars]												
Tetracycline	S≤1 I2 R≥4	89.2	0	10.8	[MIC distribution bars]												
Chloramphenicol	S≤4 R≥8	100	0	0	[MIC distribution bars]												
Trimethoprim-sulfamethoxazole	S≤0.5/9.5 I1/19-2/38 R≥4/76	73.9	9.6	16.5	[MIC distribution bars]												
Levofloxacin	S≤2 I4 R≥8	100	0	0	[MIC distribution bars]												
Rifampin	S≤1 I2 R≥4	100	0	0	[MIC distribution bars]												
Vancomycin	S≤1	100	0	0	[MIC distribution bars]												

MIC₅₀
 MIC₉₀
 Range
 CLSI break point

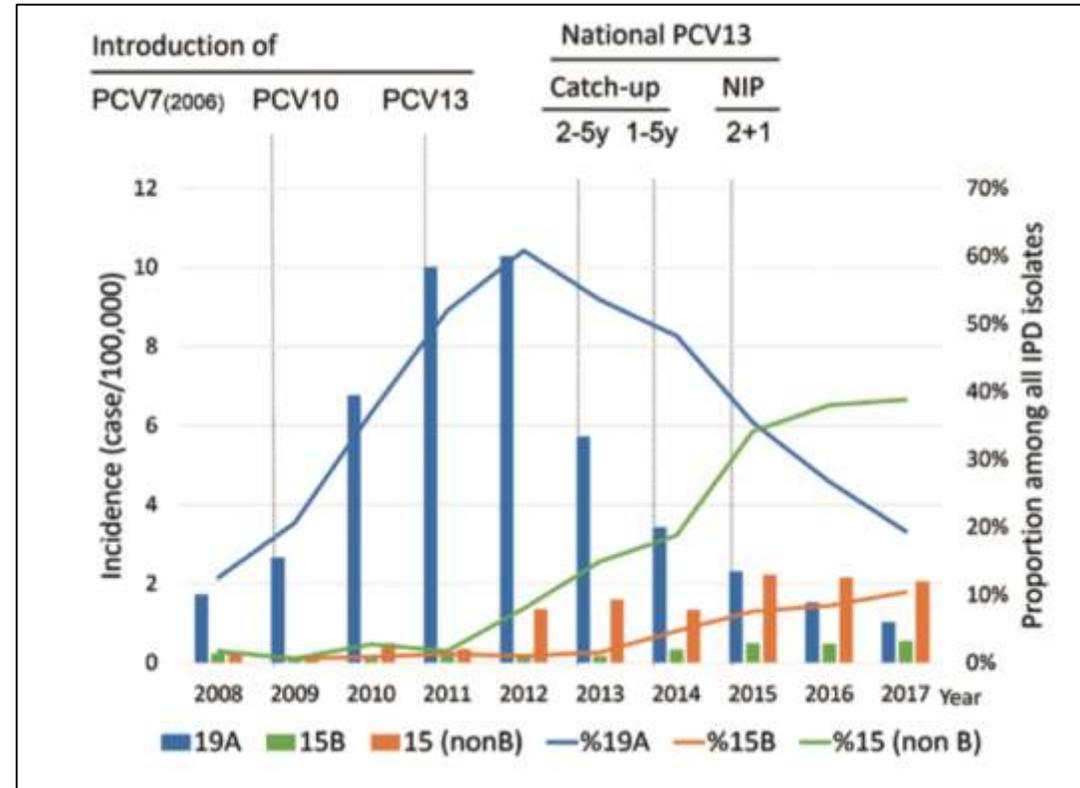
Contrôle réussi de *Streptococcus pneumoniae* 19A

Remplacement par une vaccination primaire de rattrapage

Programme à Taiwan



Nombre d'isolats de pneumococcie invasive, basé sur les sérotypes contenus dans différents PCV pour différentes années à Taiwan. L'historique de l'introduction et de la mise en œuvre du programme de vaccination contre le PCV est indiqué.
 Abréviations: NIP, programme national de vaccination; PCV, vaccin antipneumococcique conjugué.



Incidences (barres) et proportions (lignes) des cas de PI provoqués par le sérotype 19A et le sérotype 15 (15B et non-B) entre 2008 et 2017 à Taiwan. L'historique de l'introduction et de la mise en œuvre du programme de vaccination contre le PCV est indiqué.

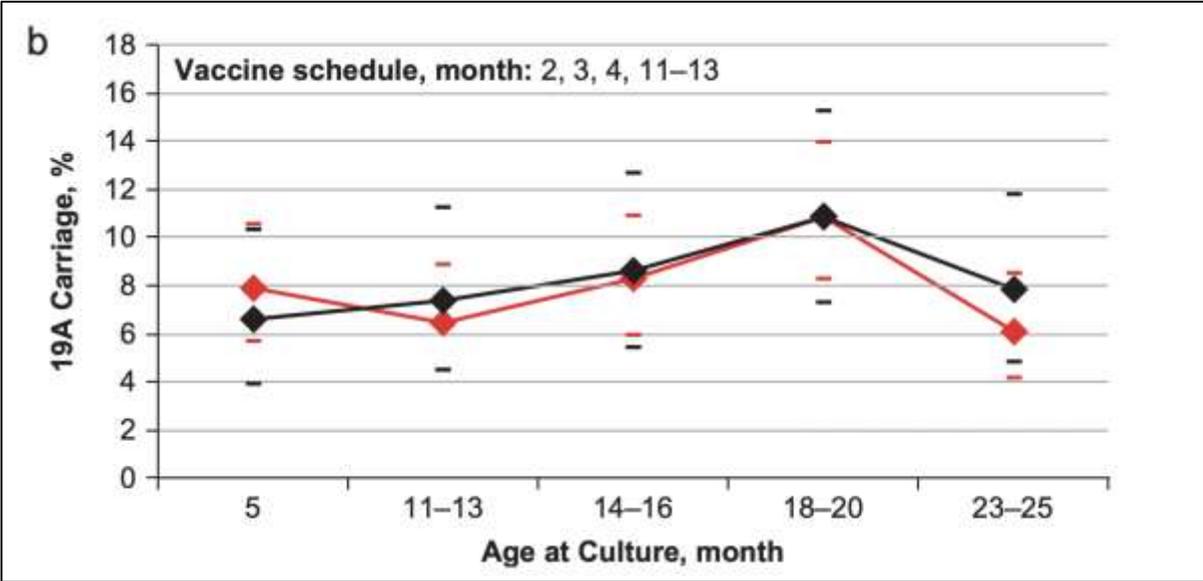
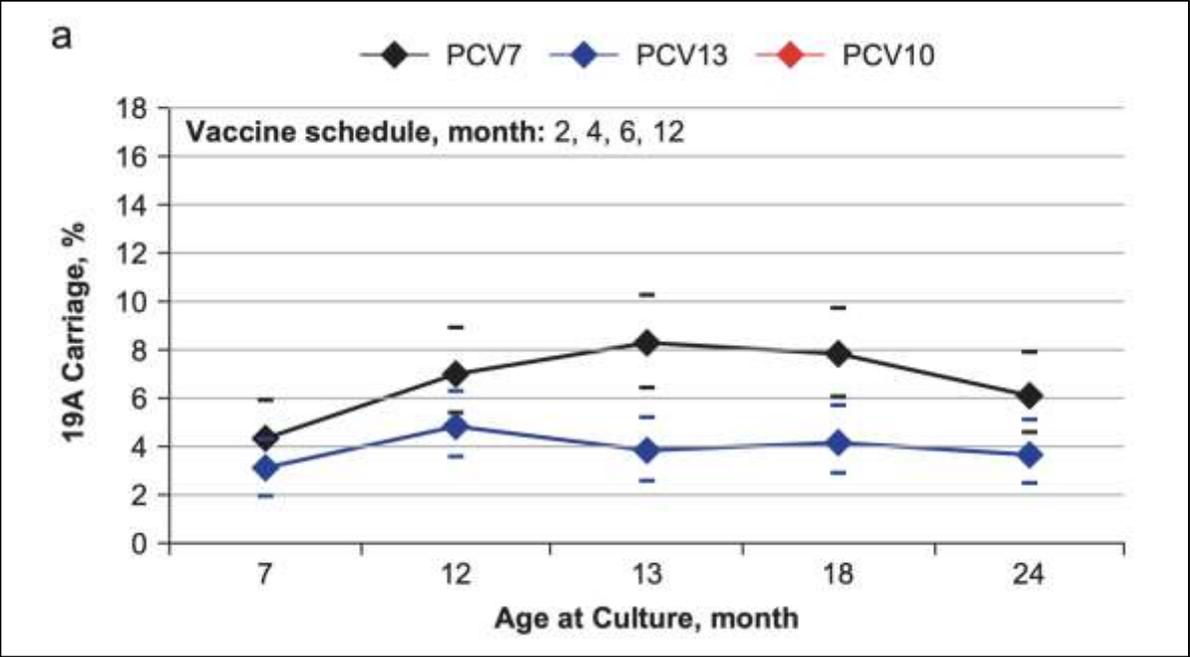
Abréviations: IPD, pneumococcie invasive; NIP, programme national de vaccination; PCV, vaccin antipneumococcique conjugué.

Réponse immunitaire au sérotype 19A après immunisation avec le vaccin anti-pneumococcique conjugué contenant du 19F chez les enfants coréens âgés de 12 à 23 mois

Table 1. Immune Response to Pneumococcal Serotypes 19F and 19A according to Vaccination Status with 7-valent Pneumococcal Conjugate Vaccine

		Booster (N=18)		Primary (N=21)		Control (N=6)	
		19F	19A	19F	19A	19F	19A
ELISA	GMC (µg/mL)	10.68* [†]	5.75 [†]	1.50	1.60	0.98	0.58
	95% CI	6.70-17.10	3.70-9.00	1.10-2.10	1.20-2.10	0.41-2.36	0.24-1.43
	%≥0.35 µg/mL	100	100	100	100	83.0	66.7
OPKA	GMI	3,124* [†]	172 [†]	54 [†]	15	10	10
	95% CI	1,539-6,342	51-580	29-103	10-23	NA	NA
	% ≥ 20	100* [†]	61.1 [†]	66.7*	19.0	0	0

La protection croisée induite par des antigènes de sérotype à réaction croisée ne fournit pas un niveau de protection similaire à celui induit par l'antigène de sérotype spécifique contre le portage du sérotype 19A

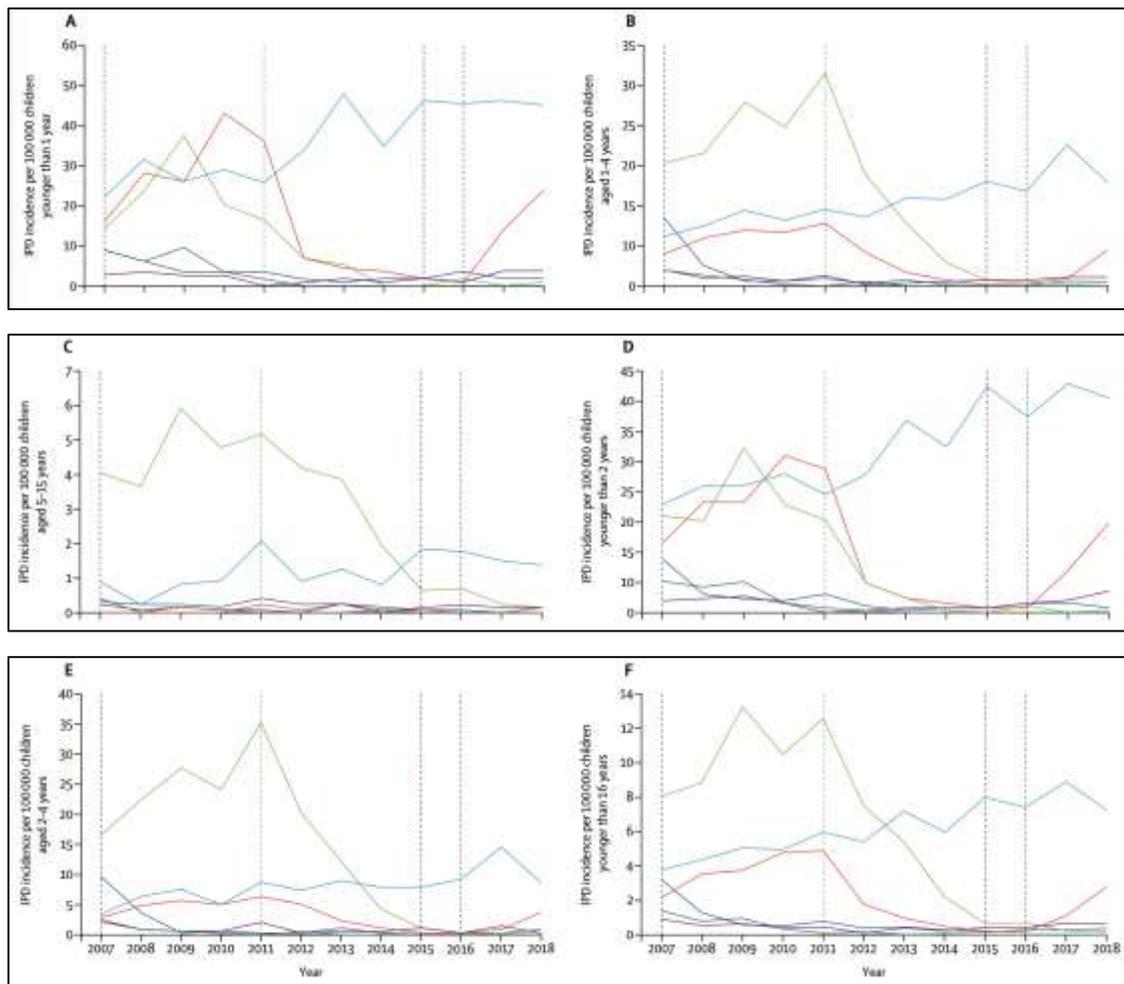


Analyse pangénomique de *Streptococcus pneumoniae* sérotype 19 dans la décennie qui a suivi l'introduction du pneumocoque vaccins conjugués en Australie

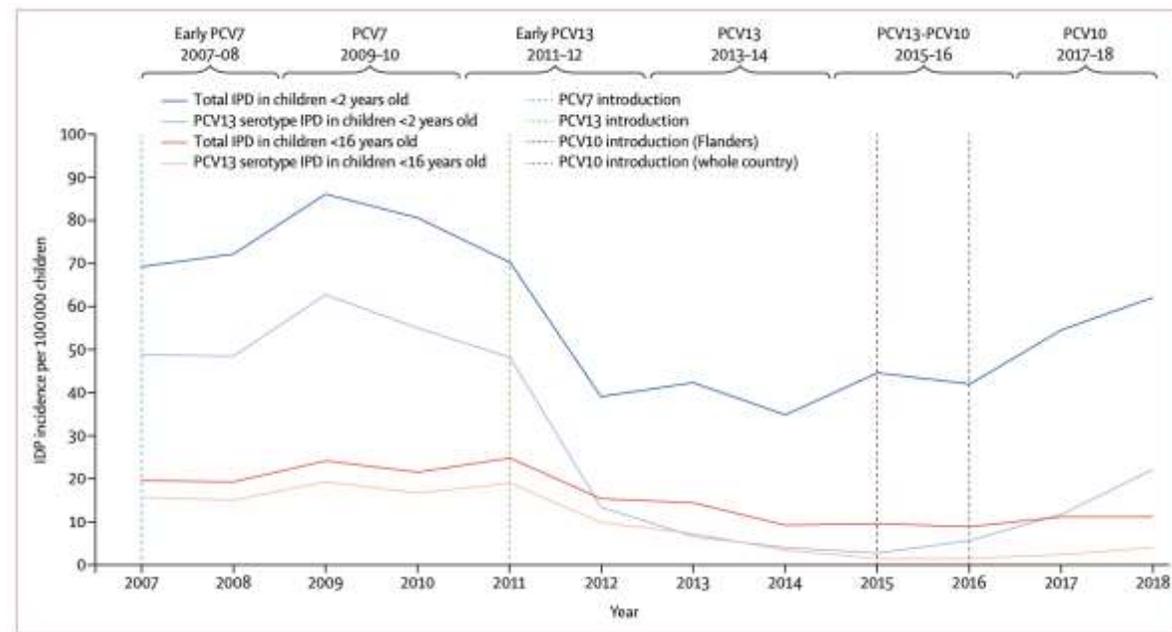
Serogroup 19/total (%)													
Year	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Total IPD isolates from children <5 yrs (all serotypes)	245 ^a	141	71	81	99 ^{a,b}	73	95	73	66	60	80 ^b	58	63
Total serogroup 19	41 ^a (17)	33 (23)	21 (30)	35 (43)	60 ^{a,b} (61)	42 (58)	40 (42)	40 (55)	22 (33)	13 (22)	23 ^{a,b} (29)	19 (33)	10 (16)
Serotype 19F	32 ^c (13)	19 (14)	8 (11)	4 (5)	4 ^{3,4} (4)	5 (6)	1 (1)	3 (4)	2 (3)	—	7 ^e (9)	10 (17)	6 (10)
Serotype 19A	9 ³ (4)	14 (10)	13 (18)	31 (38)	56 ^c (57)	37 (51)	39 (41)	37 (55)	20 (30)	13 (22)	16 ^d (20)	9 (16)	4 (6)
Vaccine Failure ^e - Serotype 19F	—	N/A	N/A	N/A	3 (3)	3 (4)	1 (1)	—	2 (3)	—	3 ^{f,g} (4)	7 (12)	4 (6)
Vaccine Failure ^e - Serotype 19A	—	N/A	N/A	N/A	—	—	—	—	—	5 (8)	9 ^{h,i} (11)	6 (10)	4 (6)

Year	Serogroup 19 (%) [19A]		
	2004	2008	2014
Total serogroup 19 isolates	41 [9]	60 [56]	23 [16]
MDR isolates	3 (7) [0]	5 (8) ^a [3]	4 (17.4) ^a [3]
Penicillin resistant (MIC <2 µg/mL)	5 (12) [0]	—	1 (4.3) [1]
Penicillin intermediate (MIC 0.12–1 µg/mL)	8 (20) [5] ^b	36 (60) [35] ^{b,c}	1 (4.3) ^c [1]
Penicillin susceptible (MIC <0.06 µg/mL)	25 (61) [3]	19 (32) [17]	17 (74) [11]

Changements dynamiques de la pneumococcie invasive pédiatrique après des changements séquentiels de vaccin conjugué en Belgique

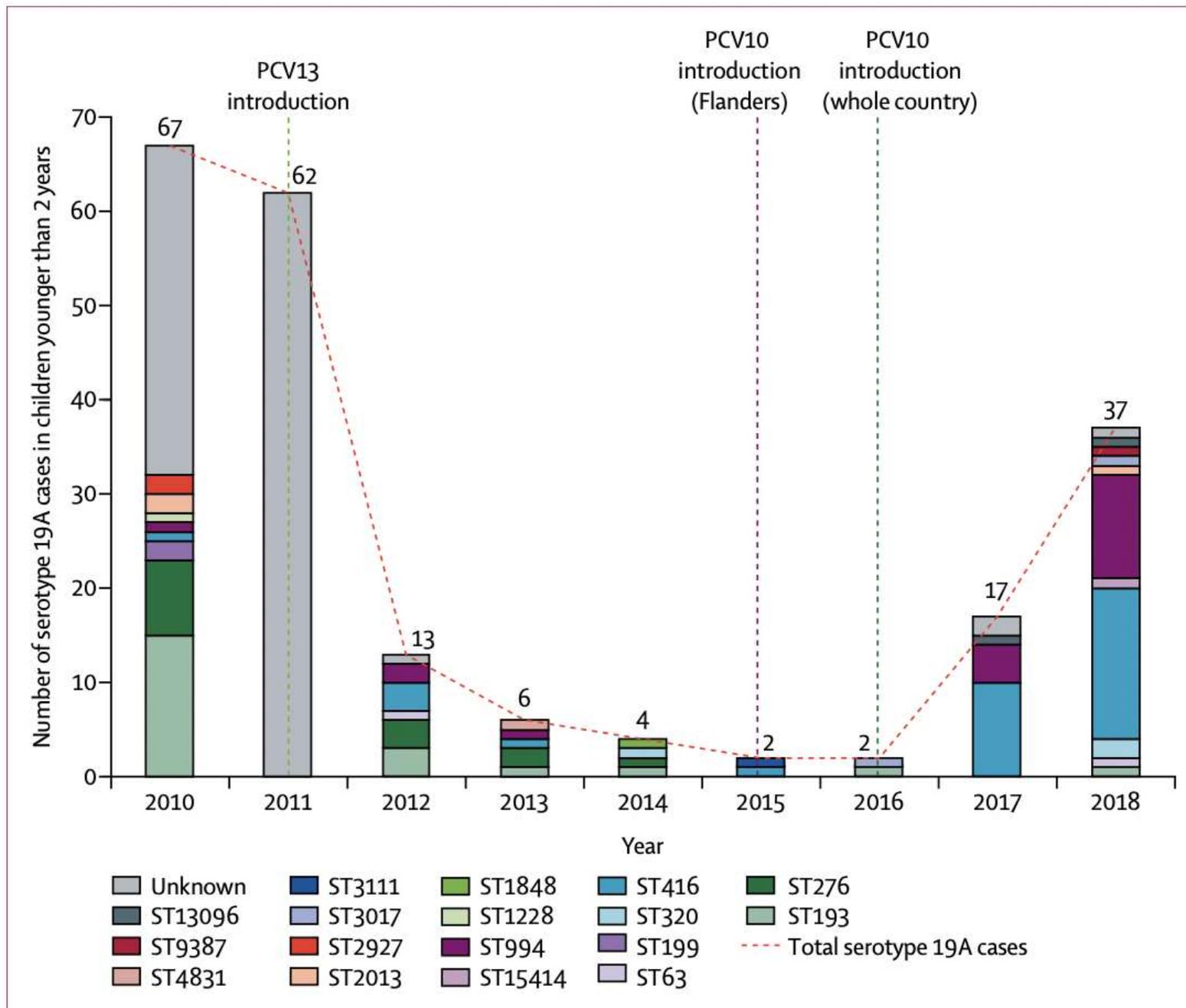


— PCV7 serotype — Serotype 3 — Serotype 19A - - - - PCV7 introduction - - - - PCV10 introduction (Flanders)
 — PCV10 non-PCV7 serotype — Serotype 6A — Non-PCV13 serotype - - - - PCV13 introduction - - - - PCV10 introduction (whole country)



Lancet Infect Dis 2020

Évolution des IPD de sérotype 19A et des types de séquences apparentés



Expérience avec PCV10

- Pserenade, 31 pays dans le monde
- Dans les sites PCV10, le sérotype 19A a également augmenté, parfois avec retard, et était le principal sérotype Mais l'IPD a généralement diminué Sauf dans les pays avec un ancien PCV7 de ≥ 4 ans à ≥ 70 % d'absorption
- Qu'est-ce qui est différent en Belgique ?
 - Taux d'incidence plus élevé
 - Transmission plus élevée en raison d'une densité plus élevée et de la fréquentation des garderies
 - Taux d'hémoculture plus élevés
 - La dynamique des sérotypes serait-elle plus marquée ?

Émergence de sérotype 19A dans la population pédiatrique à Bogotá comme principale cause de pneumococcie invasive après l'introduction du PCV10

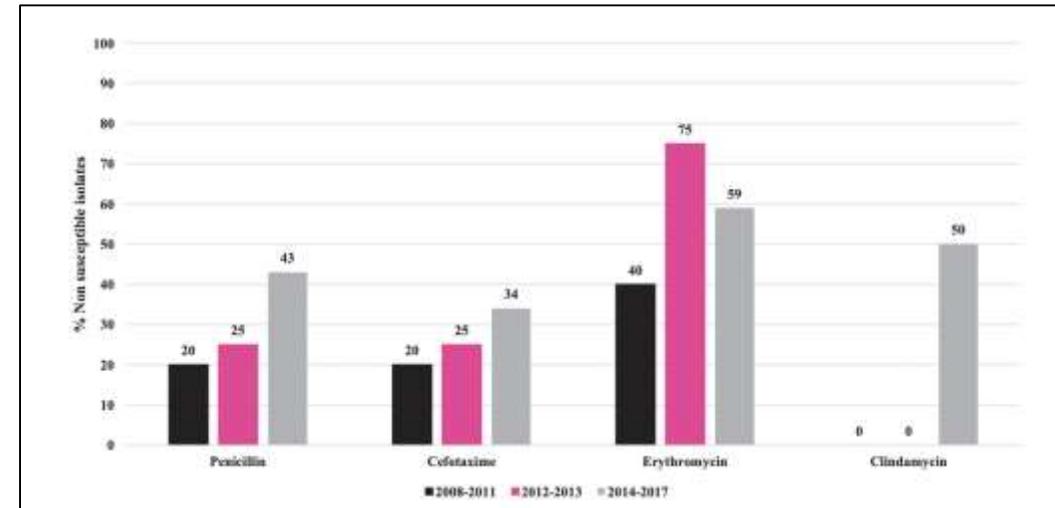
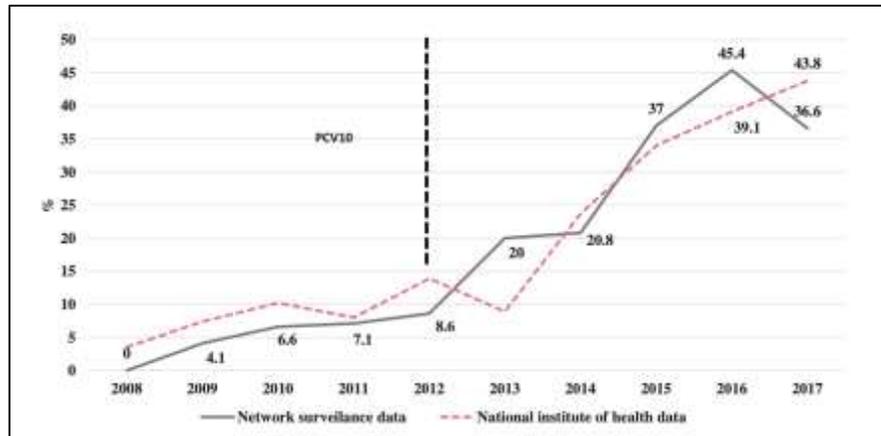
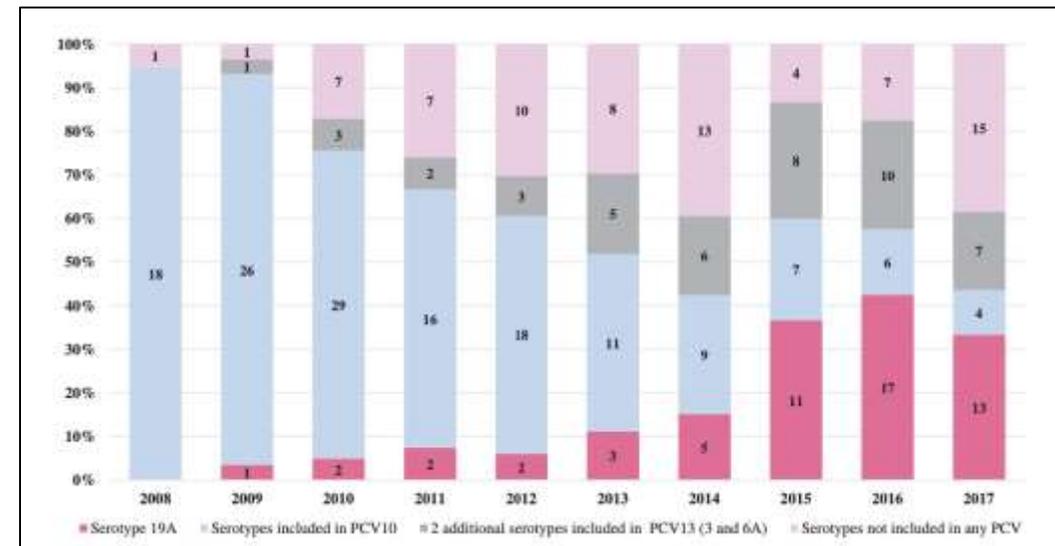
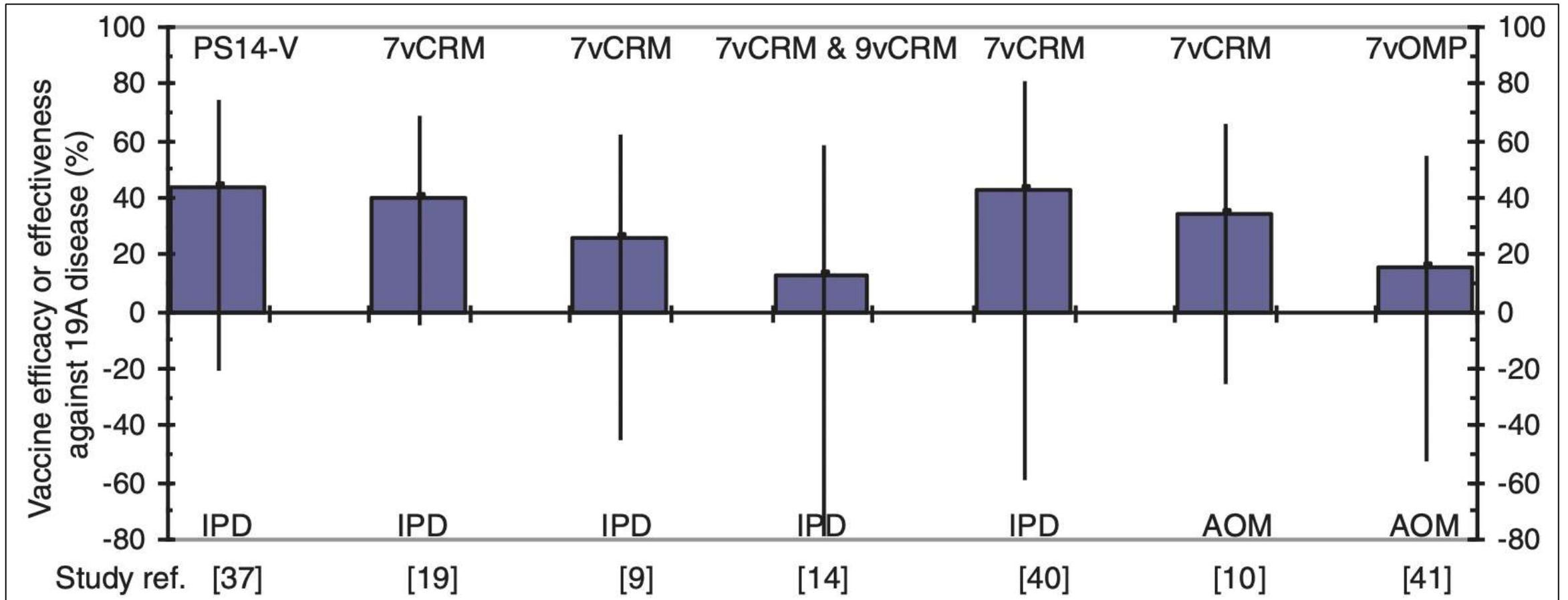


Table 1. Diagnostics by age group in cases of IPD by Spn19A.

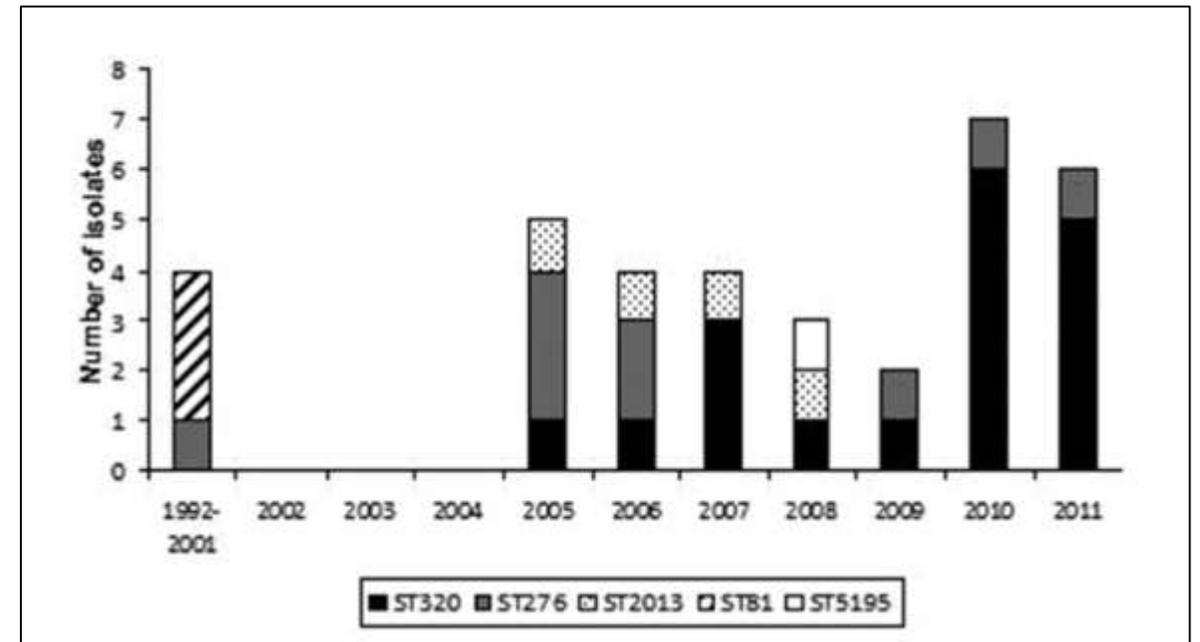
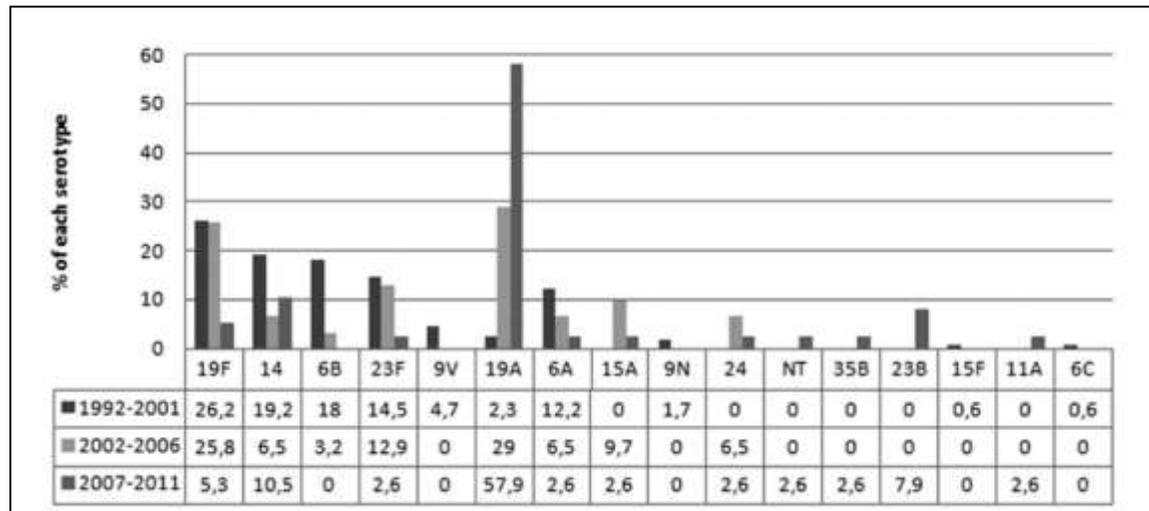
Age group	0 – 2 years	2 – 5 years	> 5 years	Total
Pneumonia	9	30	6	45
Bacteremia	1	5	0	6
Meningitis	1	2	0	3
Other	1	1	0	2
Total	12	38	6	56



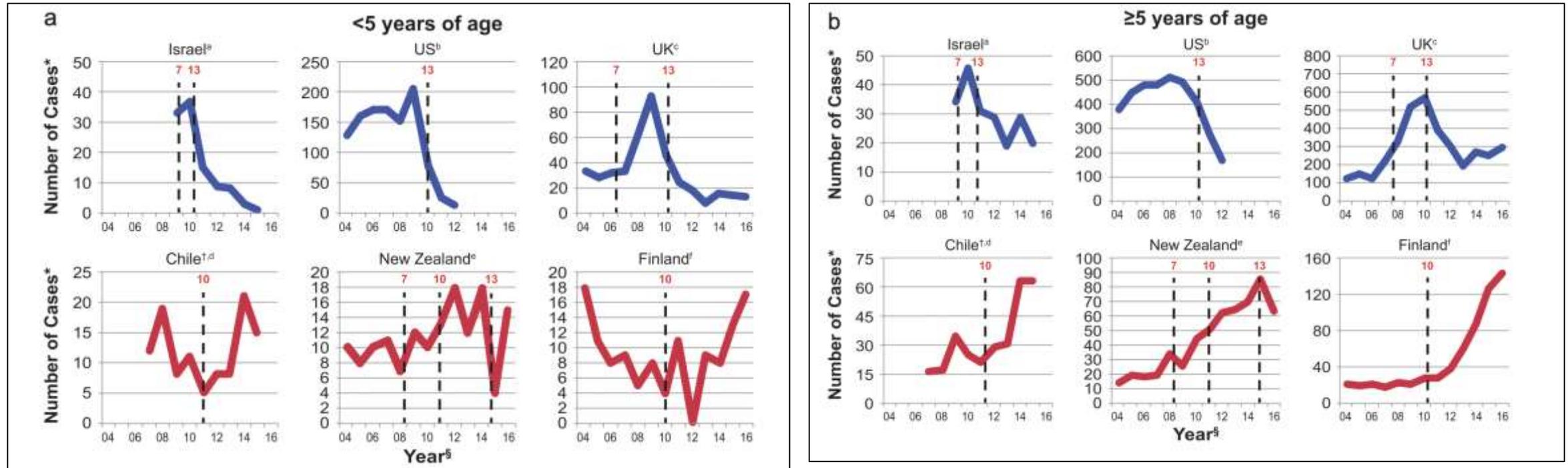
Les vaccins anti-pneumococquiques conjugués offrent-ils une protection croisée contre le sérotype 19A ?



Sérotypes pneumococciques provoquant une otite moyenne aiguë chez les enfants de Barcelone (1992-2011) : émergence de la Clone multirésistant ST320 du sérotype 19A



Impact différentiel sur la mise en œuvre des IPD de sérotype 19A post-PCV10 vs post-PCV13 dans six pays : trois pays après l'introduction du PCV13 (Israël, États-Unis États-Unis, Royaume-Uni) et trois pays après l'introduction du PCV10 (Chili, Nouvelle-Zélande, Finlande).



Émergence de Streptococcus pneumoniae sérotype 19A dans la population pédiatrique à Bogotá, Colombie comme principale cause de pneumococcie invasive après l'introduction du PCV10

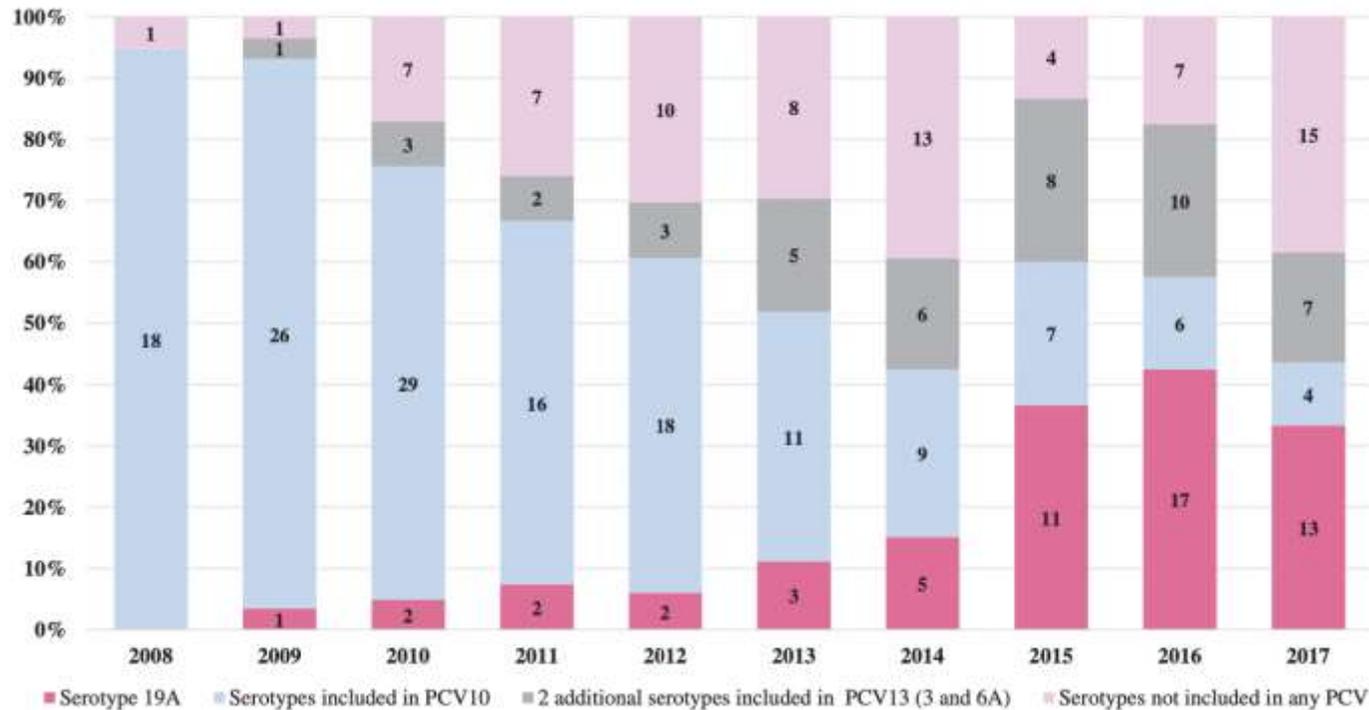
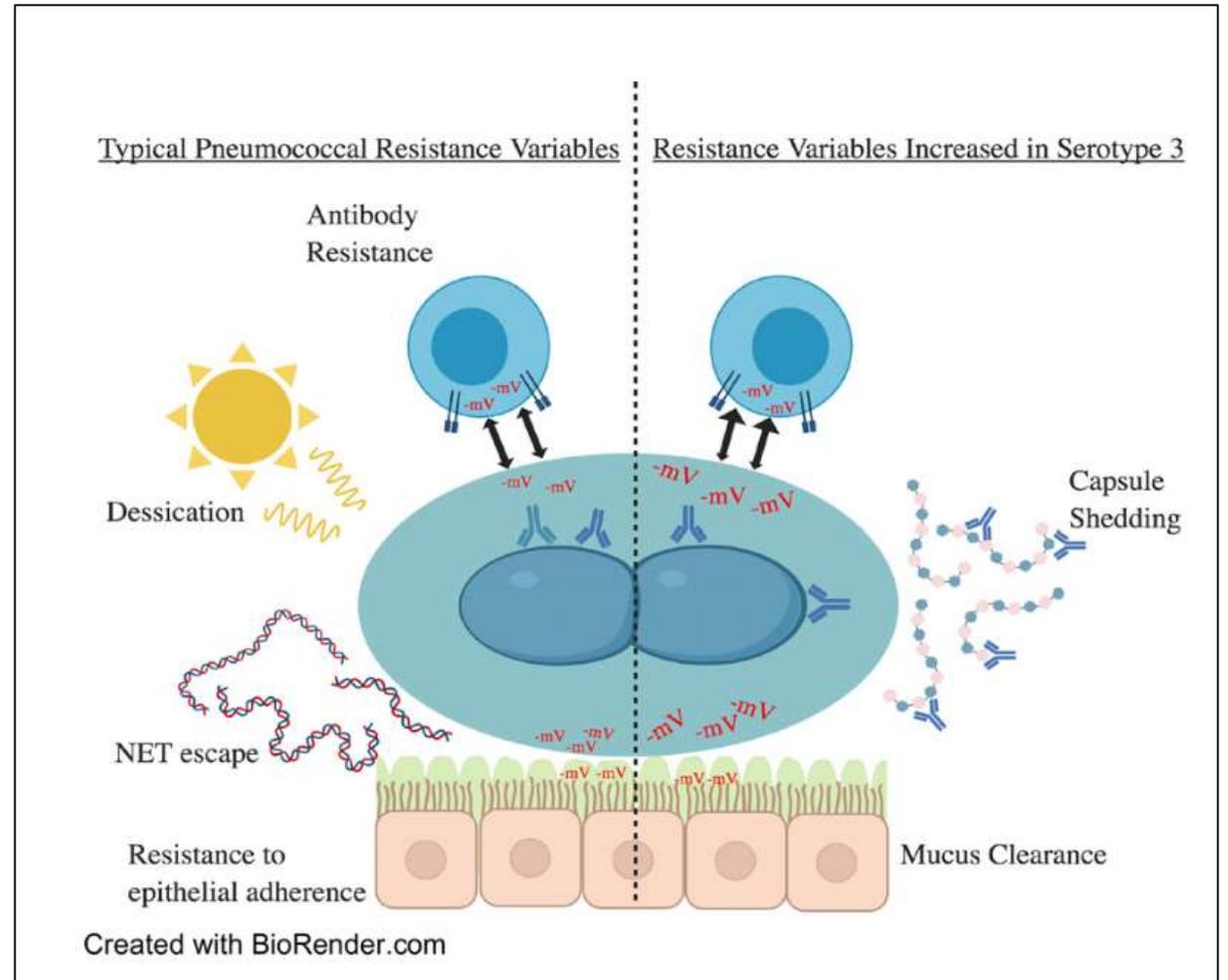


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Age group	0 – 2 years	2 – 5 years	> 5 years	Total
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Bacteremia	1	5	0	6
Meningitis	1	2	0	3
Other	1	1	0	2
Total	12	38	6	56

Tueur enrobé de sucre : maladie pneumococcique de sérotype 3



Capsule et réponse immunitaire

- La capsule offre un avantage pour la colonisation muqueuse en limitant la clairance muqueuse
- La capsule module l'activation de la voie alternative du complément et l'opsono-phagocytose
- La capsule influence la quantité d'anticorps nécessaire à l'activation de la voie classique du complément.

Tous les sérotypes ne sont pas identiques

- Différents sérotypes entraînent des présentations cliniques et une gravité de la maladie différentes
- Les différents sérotypes ont une capacité invasive et des caractéristiques épidémiologiques variables
- Efficacité vaccinale variable et impact sur différents sérotypes

Pneumoniae due au Serotype 3

- Provoque une maladie grave avec un taux de mortalité élevé
- Taux élevés de foyers extra-pulmonaires
- Le risque de maladie augmente avec l'âge
- Taux de colonisation relativement faible dans la population et capacité invasive élevée

Pneumoniae due au Serotype 3

- Le sérotype 3 a une capsule épaisse entourée d'une couche de « vase » et un aspect mucoïde caractéristique sur les plaques de gélose au sang.

Summary of key points

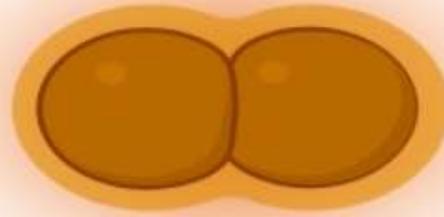
- Le type de capsule est un facteur de virulence majeur
- Le sérotype 3 a une capsule épaisse et mucoïde
- Le PCV13 a un impact limité sur les maladies invasives de sérotype 3 et la colonisation

Comment le sérotype 3 échappe-t-il au vaccin ?

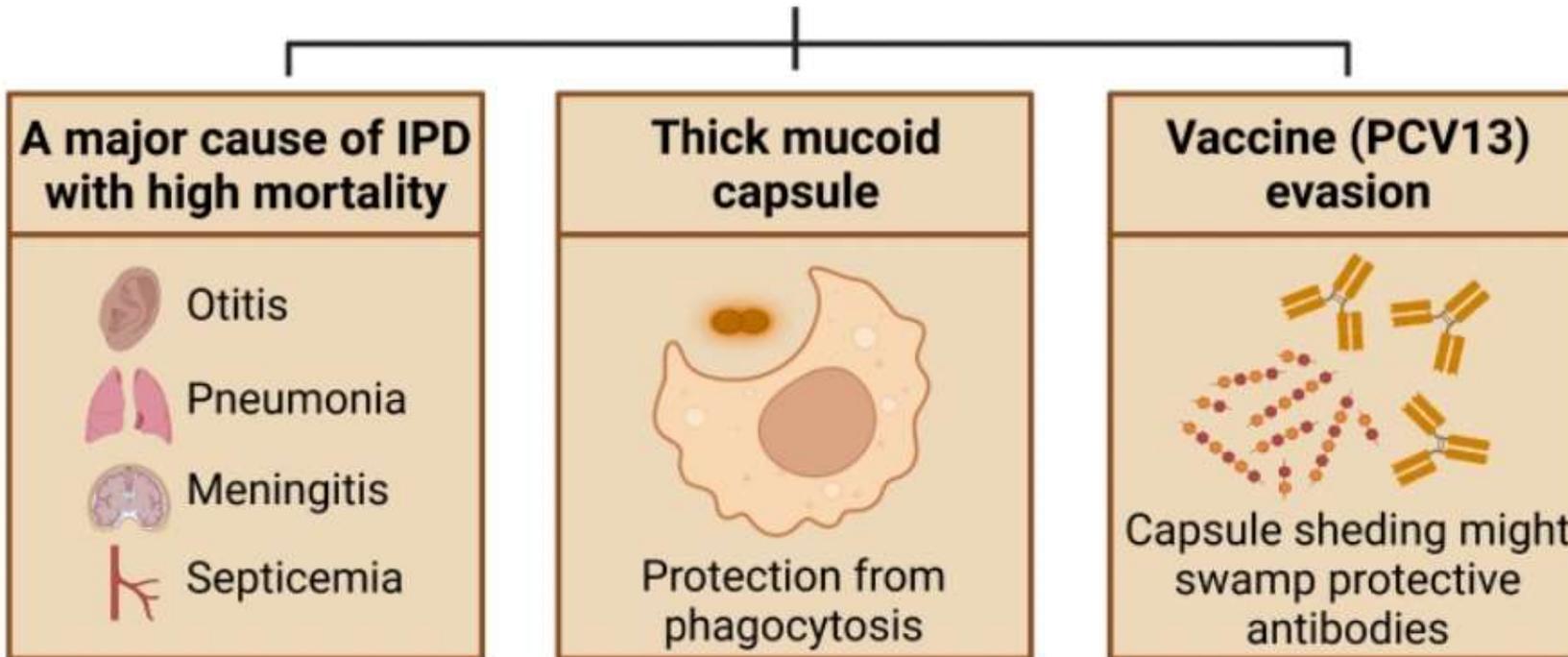
- Immunogénicité insuffisante de l'antigène de sérotype 3?
- Induit une réponse relativement faible des niveaux d'anticorps par rapport aux autres sérotypes
- Excrétion de la capsule
- Baisse de l'immunité avec le temps ?
- La pression vaccinale provoquant l'expansion du clade II ?

Activation du complément des souches de sérotype 3

- Par cytométrie en flux, nous avons mesuré la liaison du complément humain à 80 isolats cliniques de sérotype 3 : Liaison de C3-commune à toutes les voies Liaison de C4-exclusif à la voie classique



Streptococcus pneumoniae
serotype 3
(SPN3)



Impact du vaccin conjugué antipneumococcique 13-valent sur les maladies invasives graves causées par *Streptococcus Pneumoniae* de sérotype 3 chez Enfants italiens

Study Groups	Ser3 IPD	Ser3 Pneumonias	Ser3 Sepsis/Meningitis
Children born before 2011 Crude incidence rates	0.99 (0.96–1.02)	0.76 (0.60–0.92)	0.24 (–0.04–0.52)
Children born after 2011 Age-standardized incidence rates	0.87 (0.73–1.01)	0.85 (0.70–1.01)	0.02 (–0.25–0.29)
Vaccinated children Age-standardized incidence rates	0.62 (0.38–0.86)	0.62 (0.38–0.86)	0.00 (NaN)

Children Born before PCV13 Introduction	Type of Infection	Children Born after PCV13 Introduction	Children Vaccinated with PCV13
29	Complicated Pneumonias	21	16
11	- with effusion	11	8
17	- with empyema	9	8
1	- necrotizing/massive	1	0
4	Sepsis	0	0
5	Meningitis	1	0
38	Total	22	16

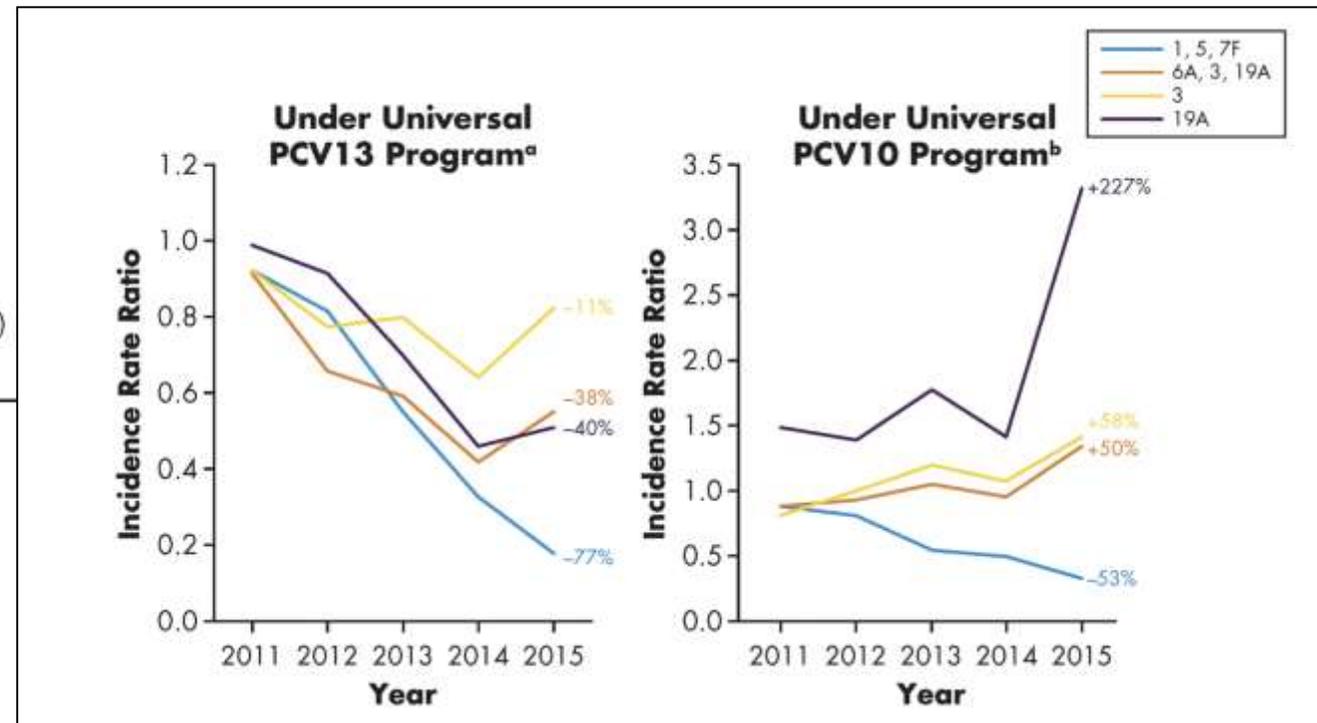
Impact du vaccin antipneumococcique conjugué sur le sérotype 3 : examen des données de surveillance

End point	Study type	Age, years	% Vaccine efficacy or effectiveness (95% CI)
IPD [2]	Meta-analysis	≤ 5	50.5 (8.2, 73.3) ^a
IPD [5] ^b	Randomized-controlled trial	≥ 65	80 (−79, 100)
Clinical CAP [4] ^{b,c}	Randomized-controlled trial	≥ 65	61.5 (17.6, 83.4)
Chest radiology confirmed CAP [3, 4] ^{b,d}	Randomized-controlled trial	≥ 65	60.0 (5.2, 84.8)
Chest radiology confirmed CAP [6]	Hierarchical statistical model	≥ 65	50 (6.4, 83.4)
Chest radiology confirmed CAP [5]	Test negative design	≥ 65	52.8 (−100, 88.9)
Chest radiology confirmed CAP [5]	Pooled analysis	≥ 65	52.5 (6.2, 75.9)

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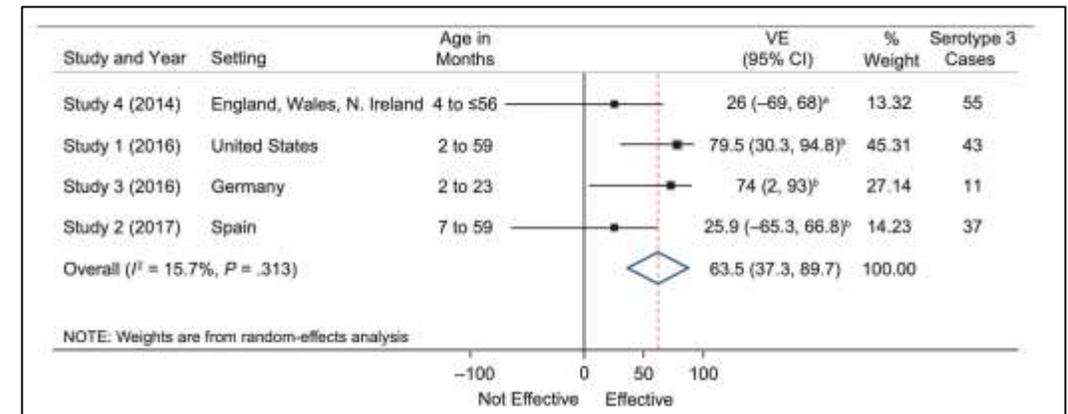
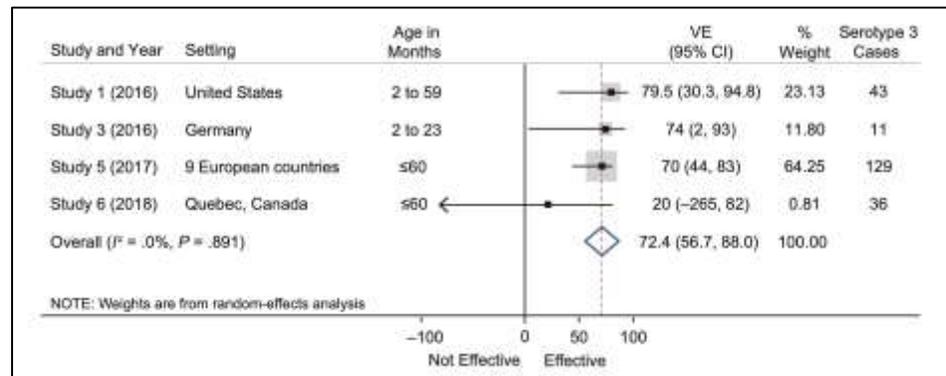
^aFrance, Denmark, Norway, England & Wales, Scotland, Ireland.

^bNetherlands, Finland, Czech Republic (PCV10/PCV13), Sweden (PCV10/PCV13).

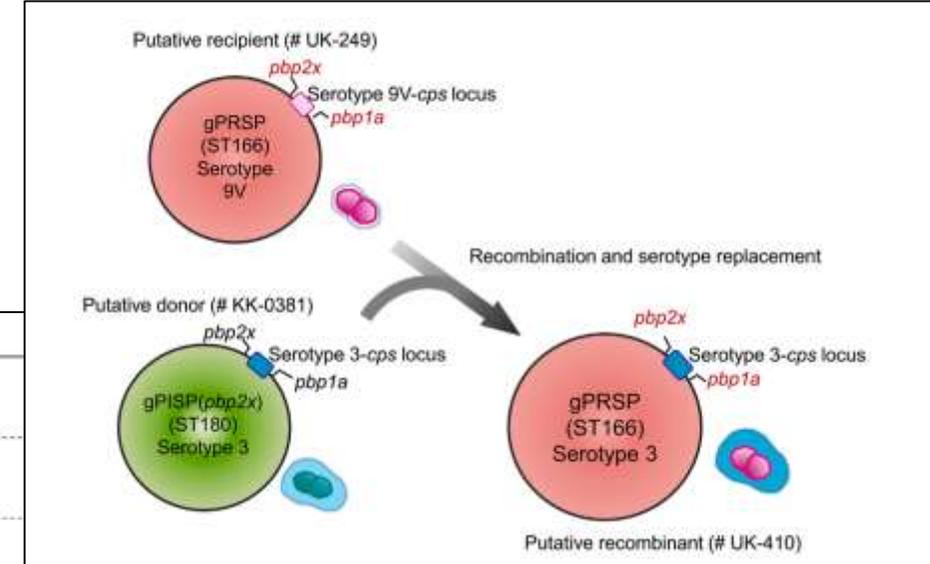
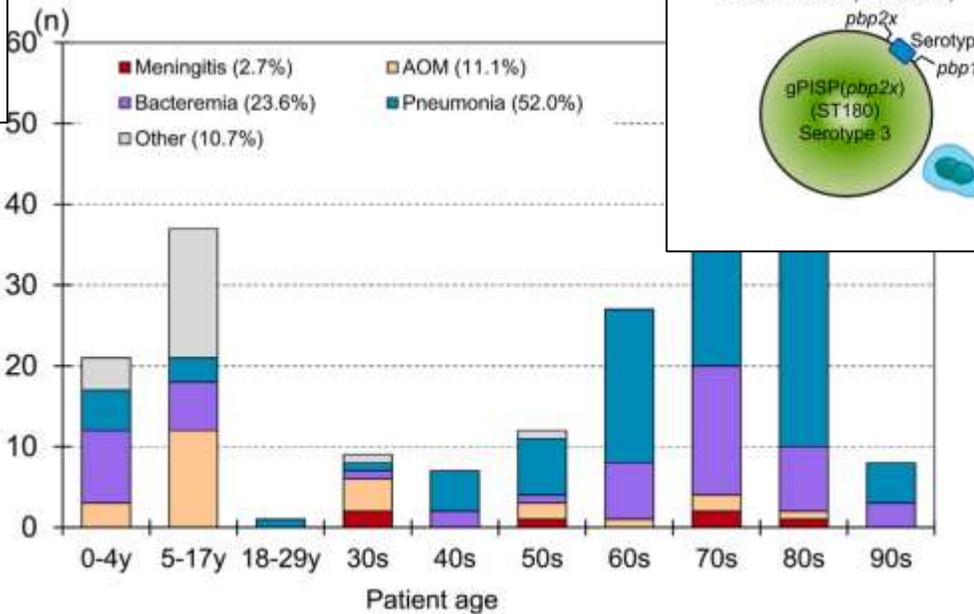
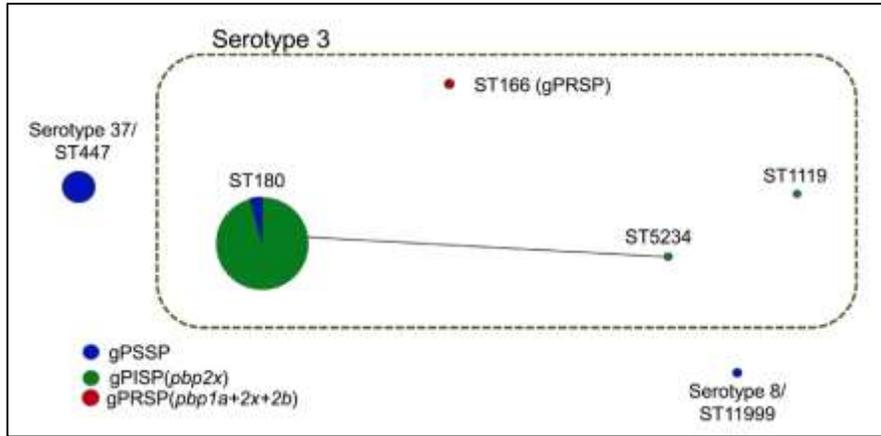
Efficacité du conjugué pneumococcique 13-valent Vaccin contre les maladies invasives causées par le sérotype 3 chez les enfants

Study Location	Design	Setting/Data Source	Study Period	PCV Use in Infant/NP	Definition/Identification of Cases	Definition/Identification of Controls	Adjustment or Matching of Cases and Controls	Ascertainment of Vaccination Status	Children Immunized With Lower Valent Vaccines Included in VE Analyses for Serotype 3
Published studies									
Study 1, United States [6]	Matched case-control	Population-based IPD surveillance system: ABCs	Jan 2010 to Dec 2014	PCV7: 2000, 3+1 PCV13: 2010, 3+1	Children with IPD and resident of ABC site	4 controls per case identified via state birth certificate registry	Controls matched for age and location	Medical record	No
Study 2, Spain [13]	Matched case-control	3 pediatric hospitals in Barcelona	Jan 2012 to June 2016	See footnote*	Children hospitalized with IPD	4 controls per case; patients admitted to same hospital as cases for cause other than IPD	Controls matched for age, sex, date of hospitalization, and underlying medical condition	Medical record	No
Study 3, Germany [14]	Indirect cohort	Voluntary national IPD surveillance system: German National Reference Center for Streptococci	July 2006 to June 2015	PCV7: 2006, 3+1 PCV13: 2009, 3+1*	Children with IPD reported to National Reference center. Cases = vaccine type IPD	Children with IPD reported to National Reference center. Controls = nonvaccine-type IPD	VE adjusted for age and time period	Questionnaire (diagnostic laboratory)	No
Study 4, United Kingdom [15]	Indirect cohort	National IPD surveillance system: PHE	Apr 2010 to Oct 2013	PCV7: 2006, 2+1 PCV13: 2010, 2+1	Children with IPD identified by national IPD surveillance system. Cases = vaccine type IPD	Children with IPD identified by national IPD surveillance system. Controls = nonvaccine-type IPD	VE adjusted for age and time period	Questionnaire (general practitioner)	Yes; PCV7
Conference posters									
Study 5, European Union [24]	Indirect cohort	Streptococcus pneumoniae invasive disease network	Jan 2012 to Dec 2014	PCV7: 2009-2011, 2+1 or 3+1; PCV13: 2009-2010, 2+1 or 3+1	Children with IPD identified by active surveillance system. Cases = vaccine type IPD	Children with IPD identified by active surveillance system. Controls = nonvaccine-type IPD	VE adjusted for site, age, sex, underlying conditions, and year of notification	Not reported	Not reported
Study 6, Canada [25]	Unmatched case-control	Children residing in province of Quebec	2006-2016	PCV7: 2002, 2+1 or 3+1; PCV10: 2008, 2+1; PCV13: 2011, 2+1	Children with IPD notified to regional public health authority	Children randomly selected in the Quebec Health Insurance Registry	VE adjusted for age, season, calendar year, and presence of high-risk medical conditions	Medical record	PCV7 or PCV10 immunized children considered "not vaccinated"

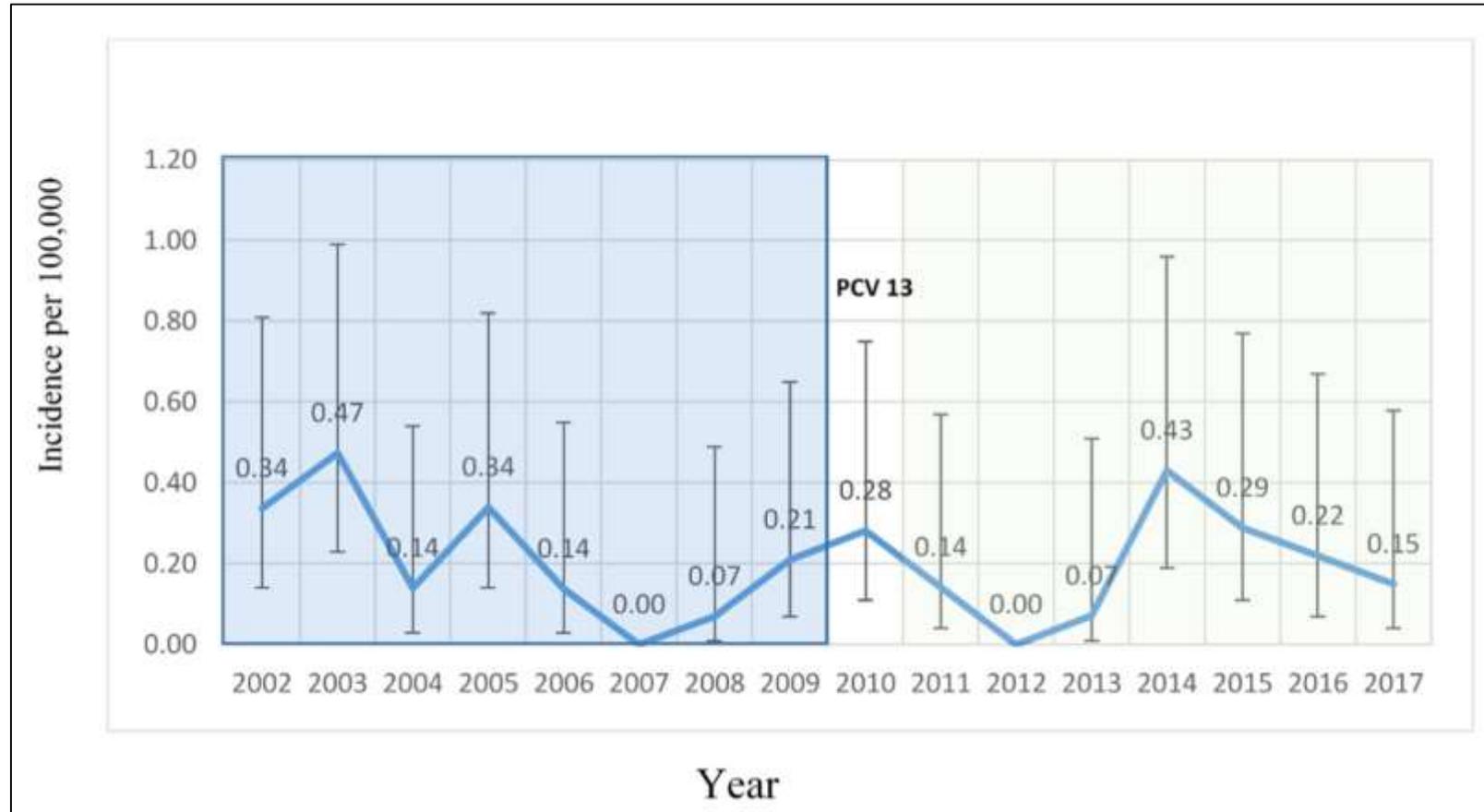
Study, Location	Age	Cases Vaccinated: Unvaccinated*	Controls Vaccinated: Unvaccinated*	No. of Doses	Serotype 3 VE, % (95% CI) ^b	Reported Range of VE, % (Lowest and Highest) for Other PCV13 Serotypes ^c
Published studies						
Study 1, United States [6]	2-59 m (median, 21-27 m)	16 discordant pairs ^d		At least 1 dose	79.5 (30.3-94.8) ^e	19A: 85.6 (70.6-93.5) 7F: 96.5 (92.7-100)
Study 2, Spain [13]	7-59 m	22/15	91/48	At least 1 dose	25.9 (-65.3 to 66.8)	19A: 96.0 (51.2-99.7) 5A: 96.3 (70.4-99.7)
		9/15	22/49	At least 2 doses before 12 m or 2 doses on or after 12 m or 1 dose on or after 24 m	63.3 (-56.2 to 91.4)	The only other serotype with data reported for this schedule was 19A: 85.6 (6.7-99.8)
Study 3, Germany [14]	74-729 d	6/5	194/43	At least 1 dose	74 (2-93)	19A: 84.1 (-92.1 to 98.7) 14: 94.2 (41.8-99.4)
		1/2	34/20	Postprimary	80 (-68 to 98)	1: 49 (-614 to 99) 7F: 95.1-100 to 100)
		3/3	33/16	Postcohort	63 (-30 to 97)	7F: 32 (-8066 to 98) 19A: 88 (25-98)
Study 4, United Kingdom [15]	4 to ≤56 m	28/21 ^f	280/76	At least 2 doses before 12 m or 1 dose on or after 12 m	26 (-69 to 88)	19A: 67 (23-84) 8A: 95 (64-99.8)
		4 to <13 m	3/2	118/20	2 doses before 12 m	66 (-322 to 92)
Conference posters						
Study 5, European Union [24]	<5 y	79/50	908/833	At least 1 dose	70 (44-83) ^g	1: 66 (66-93) ^h 14: 96 (90-100) ^h
Study 6, Quebec [25]	<6 y	57/34	423/390	Fully vaccinated	57 (5-81) ⁱ	1: 84 (57-94) ^j 14: 96 (89-100) ^j
Study 6, Quebec [25]	<6 y	8/27	858/1712	At least 1 dose	20 (-265 to 82)	Not reported



Caractérisation épidémiologique moléculaire dans des isolats de *Streptococcus pneumoniae* de type mucoïde obtenus à partir de patients atteints de pneumococcie invasive au Japon



Caractéristiques de la maladie pneumococcique invasive de sérotype 3 avant et après l'immunisation universelle de l'enfance avec le PCV13 au Massachusetts

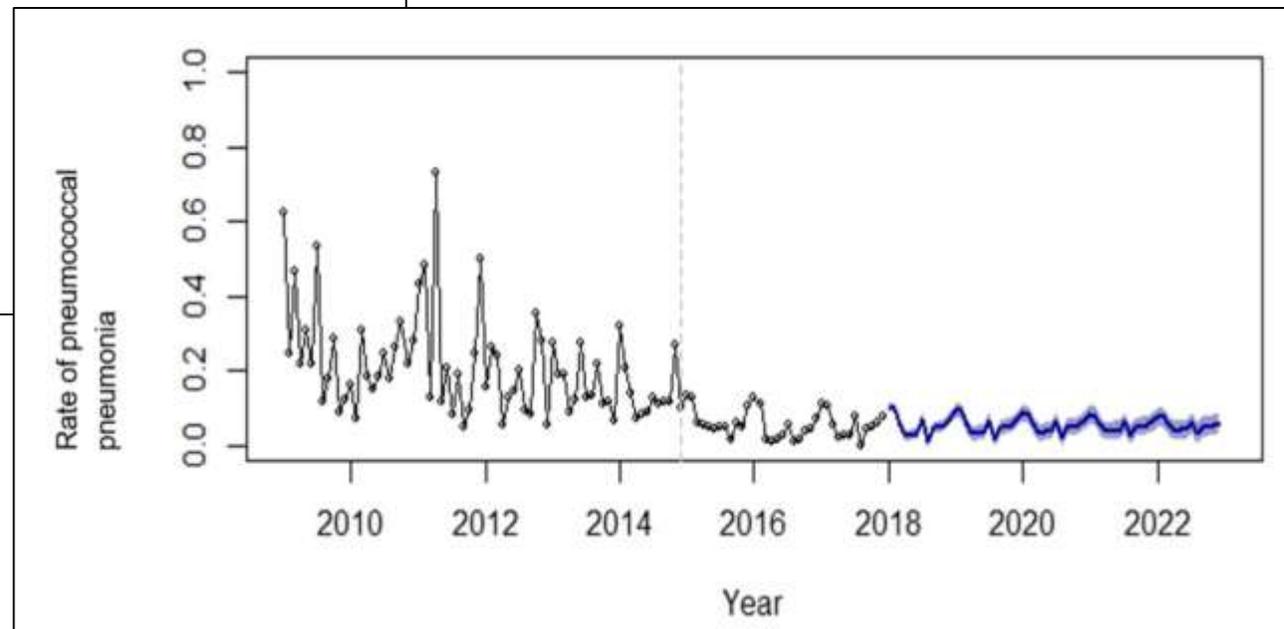
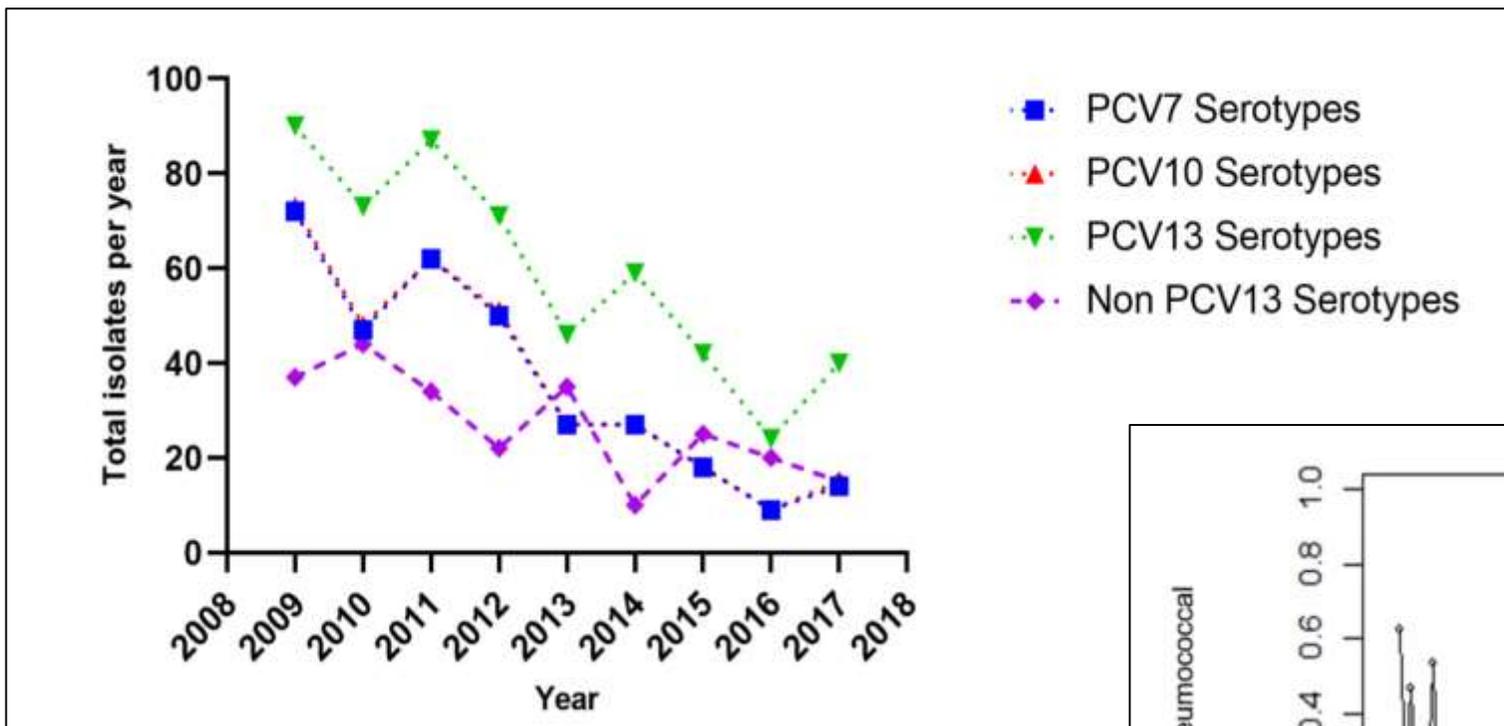


Incidence annuelle des cas de pneumococcie invasive de sérotype 3 (PI) dans le Massachusetts » les enfants.

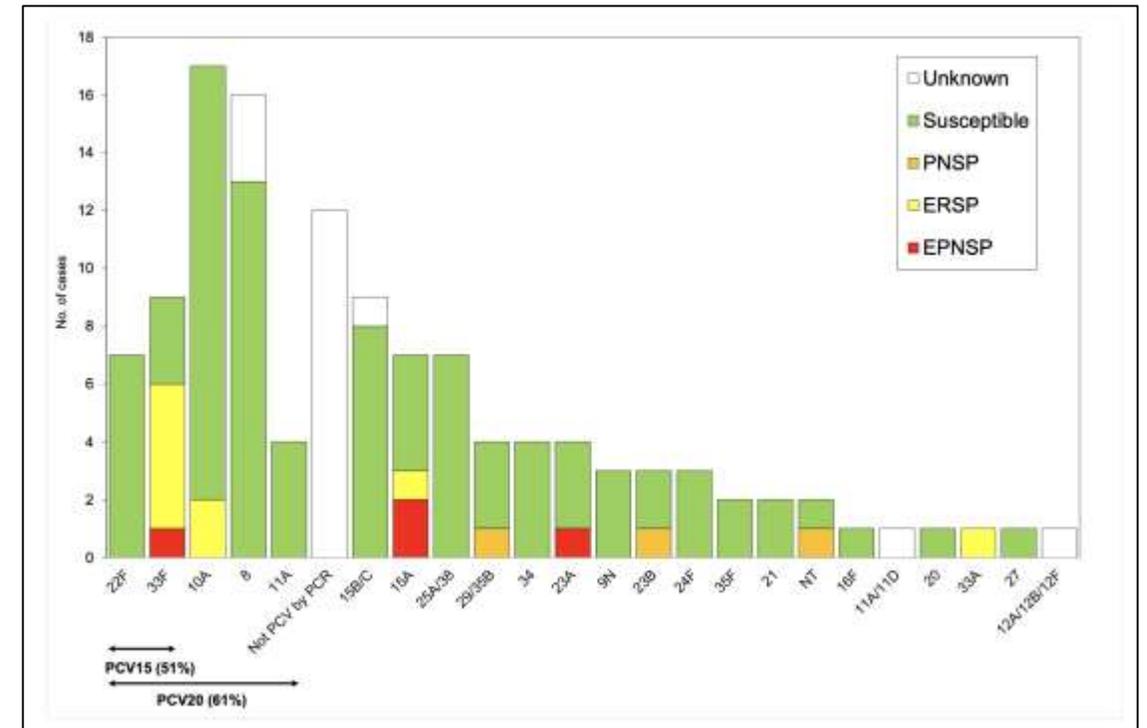
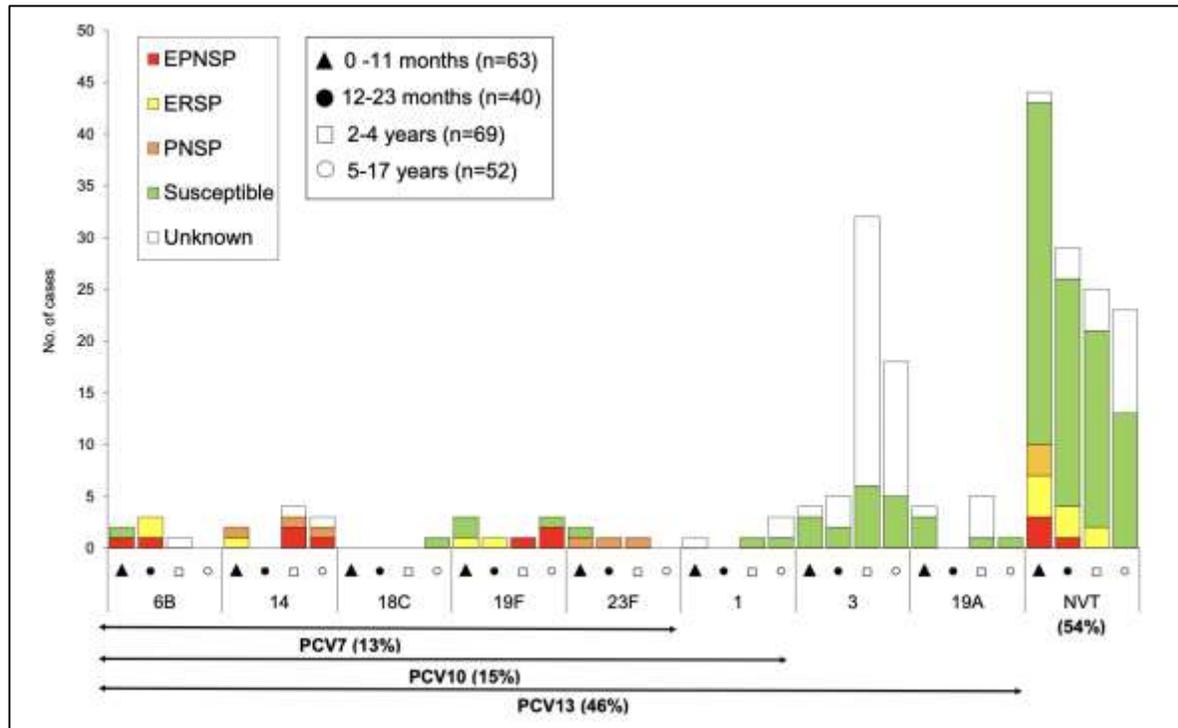
Vaccin anti-pneumococcique conjugué contre la pneumonie à pneumocoque de sérotype 3 chez l'adulte

Study Population/Method	Serotype 3 Cases (PCV13/No PCV13)	Test-negative Controls (PCV13/No PCV13)	VE	95%CI
CAPiTA [23] as TND Modified intent-to-treat "TND-like" all episodes of CAP analysis	9/20	806/826	53.9	-1.9 to 79.1
Louisville TND [30] All episodes of CAP	2/25	285/1681	52.8	-100 to 88.9
Argentina TND [33] (unpublished) All episodes of CAP	0/11	17/283	100 (29.6)*	-1145 to 96.0
Pooled TND Analysis All episodes of CAP	11/56	1108/2790	52.5 [†]	6.2 to 75.9 [†]

Persistence du sérotype pneumococcique 3 dans la maladie pneumococcique adulte à Hong Kong

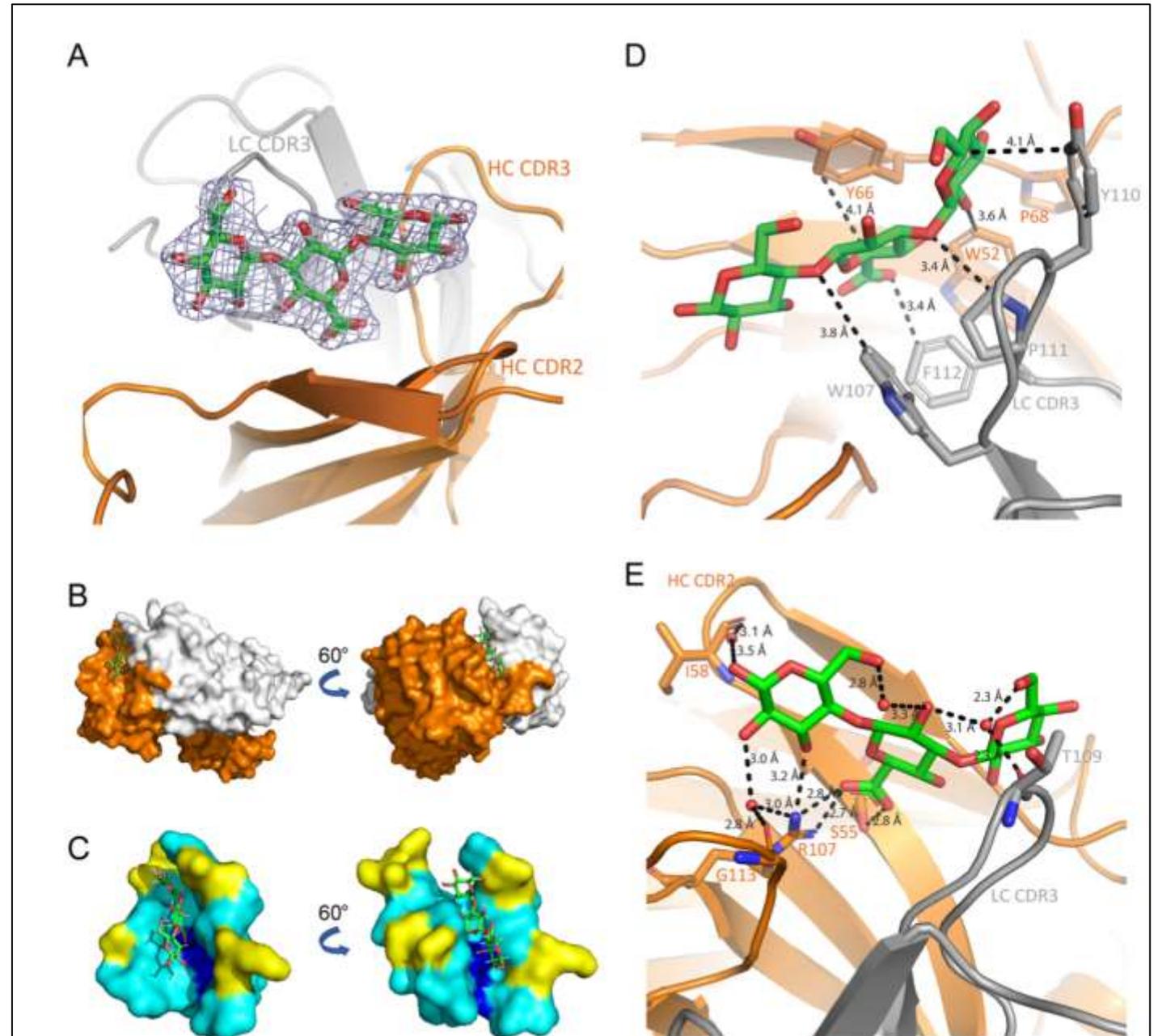


Maladie pneumococcique invasive pédiatrique trois ans après l'introduction du PCV13 dans le plan national de vaccination - L'importance continue du sérotype 3

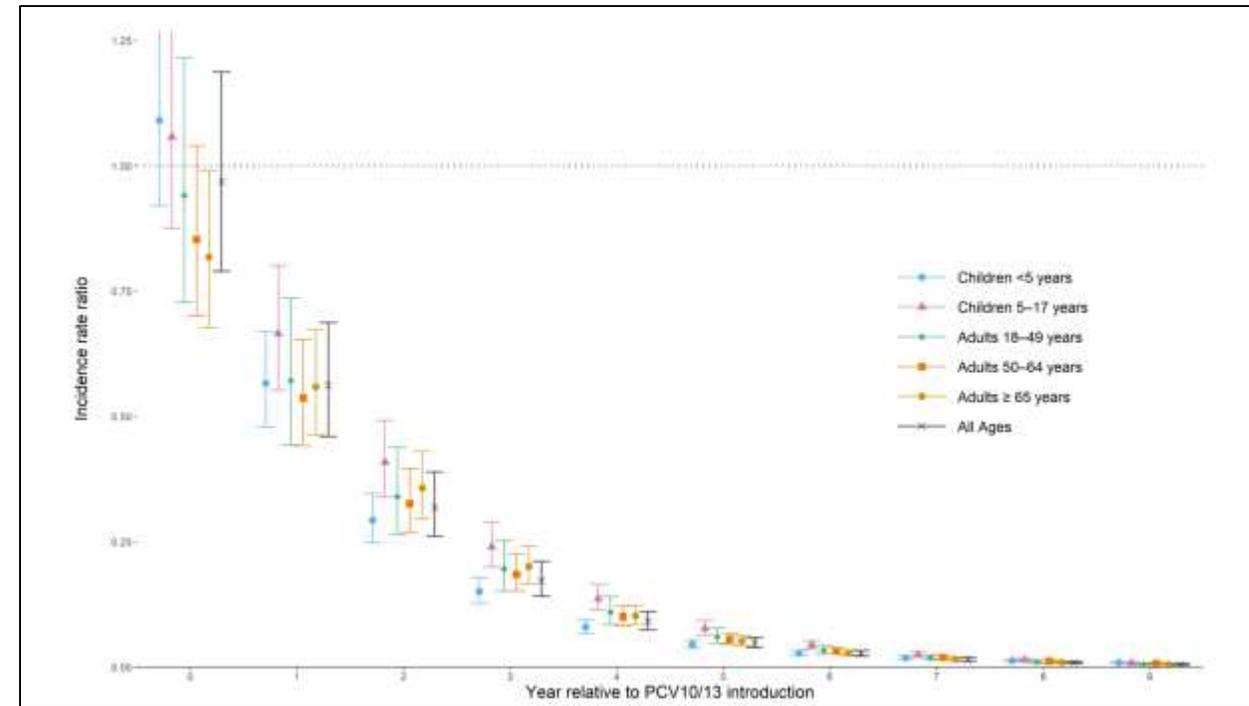
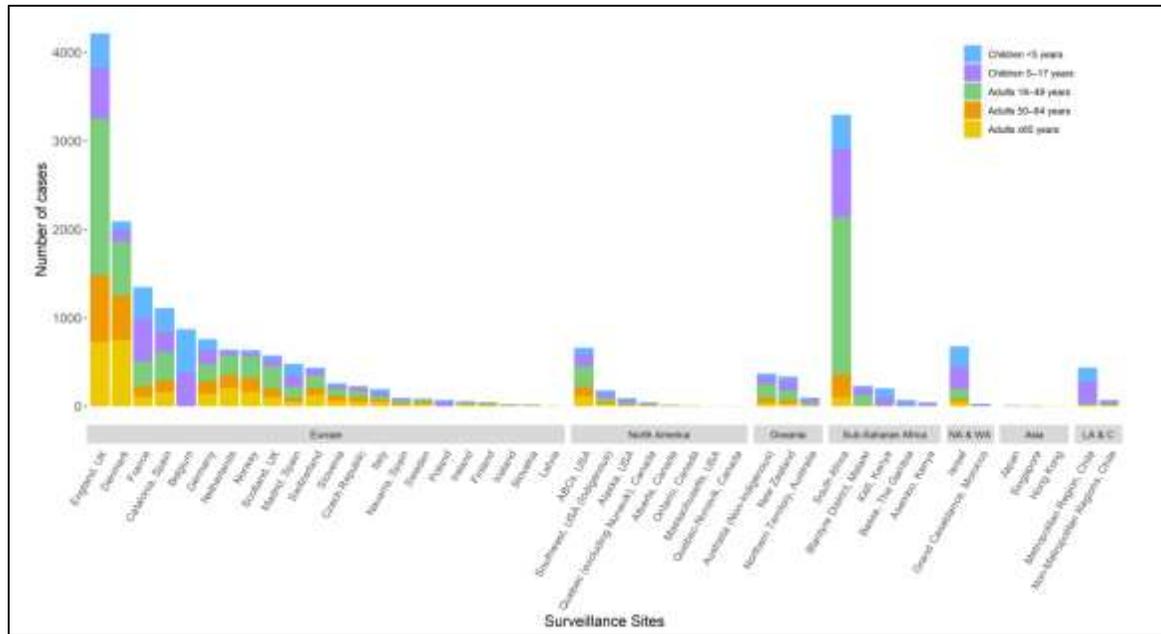


Un modèle structurel pour la liaison au ligand des anticorps protecteurs spécifiques au polysaccharide capsulaire du sérotype 3 du pneumocoque

May/June 2021 Volume 12 Issue 3 e00800-21



Changements dans la maladie pneumococcique invasive causée par *Streptococcus pneumoniae* sérotype 1 suite à l'introduction du PCV10 et du PCV13 : résultats du projet PSERENADE



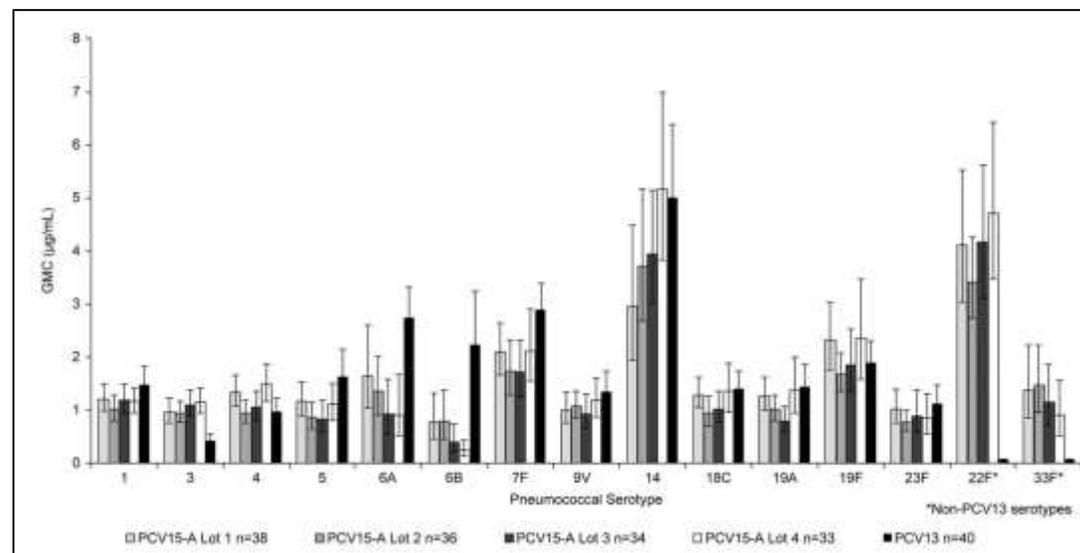
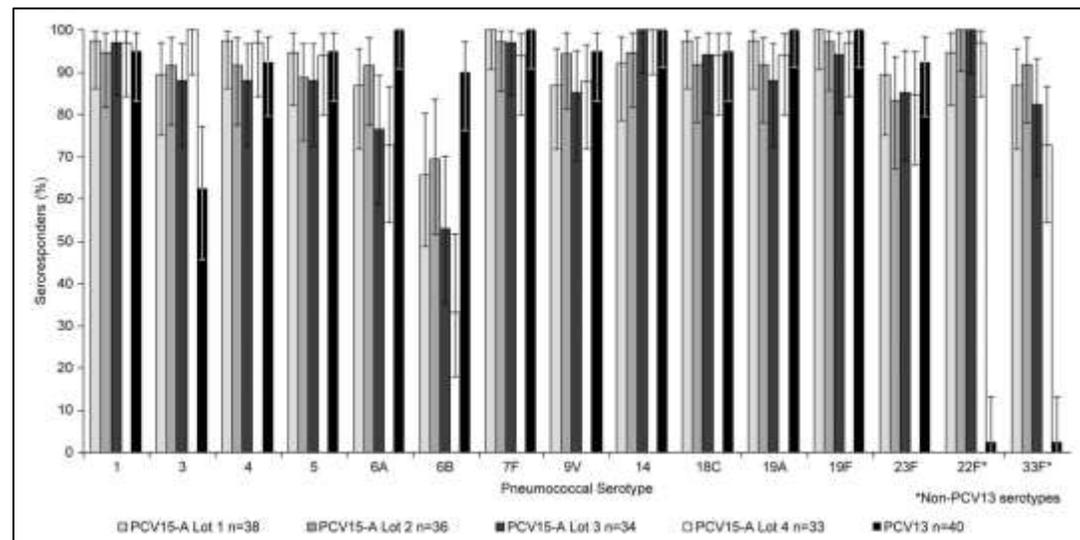
Une étude de dosage de 2 formulations différentes de vaccin conjugué anti-pneumococcique 15-valent chez des nourrissons en bonne santé

Table 1. Vaccine Lots Evaluated in Study #1 (PCV15-Formulation A) and Study #2 (PCV15-Formulation B) (Infant Per-Protocol Population).

Vaccine	Lot	Pneumococcal Polysaccharide Composition	Aluminum Phosphate Adjuvant	Planned Infant Enrollment
Study #1 (PCV15-Formulation A) (NCT02037984 [V114-004])				
PCV15-A	1	All serotypes at 2 µg/dose, except 6B at 4 µg/dose	125 µg/dose	50
	2	All serotypes at 1 µg/dose, except 6B at 2 µg/dose	250 µg/dose	50
	3	All serotypes at 2 µg/dose, except 6B at 4 µg/dose	250 µg/dose	50
	4	All serotypes at 4 µg/dose, except 6B at 8 µg/dose	250 µg/dose	50
PCV13	Comparator	All serotypes at 2.2 µg/dose, except 6B at 4.4 µg/dose	125 µg/dose	50
Study #2 (PCV15-Formulation B) (NCT02531373 [V114-005])				
PCV15-B	5	All serotypes at 2 µg/dose, except 6B at 4 µg/dose	125 µg/dose	50
	6	All serotypes at 4 µg/dose, except 6B at 8 µg/dose	250 µg/dose	50
PCV13	Comparator	All serotypes at 2.2 µg/dose, except 6B at 4.4 µg/dose	125 µg/dose	50

Table 2. Subjects Reporting Local and Systemic Adverse Events Within 14 Days Postvaccination – Study #1 (PCV15-Formulation A) (Infant Per-Protocol Population).

	PCV15-A					PCV13
	Lot 1	Lot 2	Lot 3	Lot 4		
	n	(%)	n	(%)	n	(%)
Subjects With Safety Follow-up	50		48		50	
Injection-site AEs (Day 1 to Day 14 Following Any Vaccination)						
Injection-site pain	47 (94.0)	43 (89.6)	46 (92.0)	43 (86.0)	44 (86.3)	
Injection-site erythema	22 (44.0)	29 (60.4)	28 (56.0)	26 (52.0)	27 (52.9)	
Injection-site induration	21 (42.0)	26 (54.2)	18 (36.0)	19 (38.0)	14 (27.5)	
Injection-site swelling	19 (38.0)	25 (52.1)	22 (44.0)	21 (42.0)	20 (39.2)	
Systemic AEs (Day 1 to Day 14 Following Any Vaccination)						
Irritability	47 (94.0)	40 (83.3)	42 (84.0)	47 (94.0)	47 (92.2)	
Somnolence	42 (84.0)	36 (75.0)	37 (74.0)	42 (84.0)	37 (72.5)	
Decreased appetite	23 (46.0)	27 (56.3)	26 (52.0)	32 (64.0)	27 (52.9)	
Urticaria	2 (4.0)	2 (4.2)	2 (4.0)	3 (6.0)	2 (3.9)	
Serious AEs (Duration of the Study)						
with serious adverse events	1 (2.0)	3 (6.3)	0 (0.0)	3 (6.0)	5 (9.8)	
with vaccine-related serious adverse events	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
who died	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
who discontinued due to adverse event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Elevated Body Temperature (Day 1 to Day 7 Following Any Vaccination)						
<100.4°F (38.0°C)	41 (82.0)	34 (72.3)	37 (78.7)	37 (75.5)	42 (82.4)	
≥100.4°F (38.0°C) and <102.2°F (39.0°C)	8 (16.0)	13 (27.7)	10 (21.3)	11 (22.4)	9 (17.6)	
≥102.2°F (39.0°C) and <103.1°F (39.5°C)	1 (0.0)	1 (0.0)	0 (0.0)	1 (0.0)	0 (0.0)	
≥103.1°F (39.5°C)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	



Fardeau sanitaire et économique associé aux sérotypes du vaccin anti-pneumococcique conjugué 15-valent chez les enfants aux États-Unis

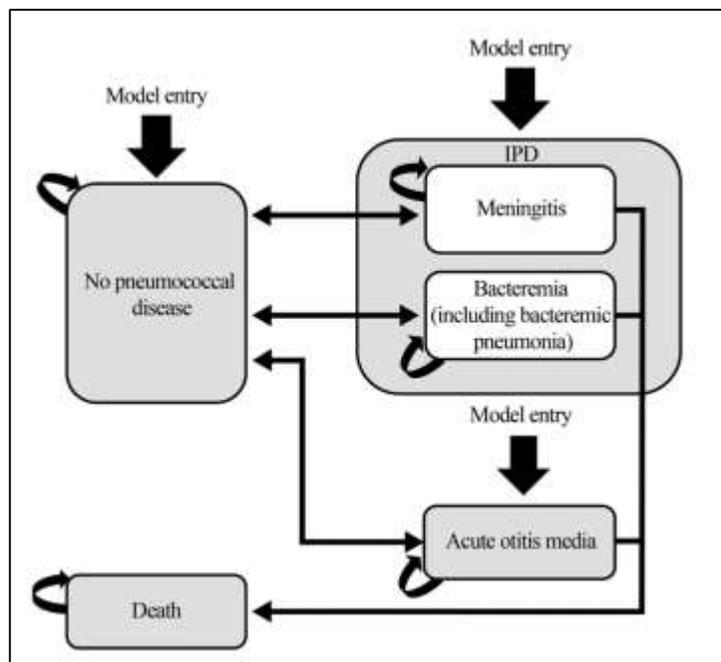


Table 1. Epidemiological inputs[†].

	Age group [†] (years)	Pre-PCV7 period			Pre-PCV13 period			Post-PCV13 period		
		PCV7 serotypes	PCV13 not PCV7 serotypes	V114 not PCV13 serotypes	PCV7 serotypes	PCV13 not PCV7 serotypes	V114 not PCV13 serotypes	PCV7 serotypes	PCV13 not PCV7 serotypes	V114 not PCV13 serotypes
IPD incidence rate (100,000 person-years) ³⁹	<1	138.9	6.9	2.4	0.4	25.7	4.5	0.5	2.0	1.4
	1	175.4	8.7	3.1	0.3	22.2	3.9	0.3	1.4	1.0
	2–4	25.8	2.6	0.5	0.3	9.6	1.2	0.5	1.1	0.7
	5–20	2.5	0.9	0.1	0.1	2.3	0.2	0.2	0.3	0.1
Pneumococcal AOM incidence rate (100,000 person-years) ^{12,16,31,38†}	<2	24,381.7	5,257.3	304.8	562.1	12,647.7		81.3	975.2	325.1
	2–4	7,822.2	1,686.7	97.8	198.3	4,462.7		32.1	385.6	128.5
	5–20	2,538.5	547.4	31.7	74.3	1,670.9		11.6	138.6	46.2

Table 3. IPD cases attributable to V114 serotypes in the pre-PCV7, pre-PCV13, and post-PCV13 periods.

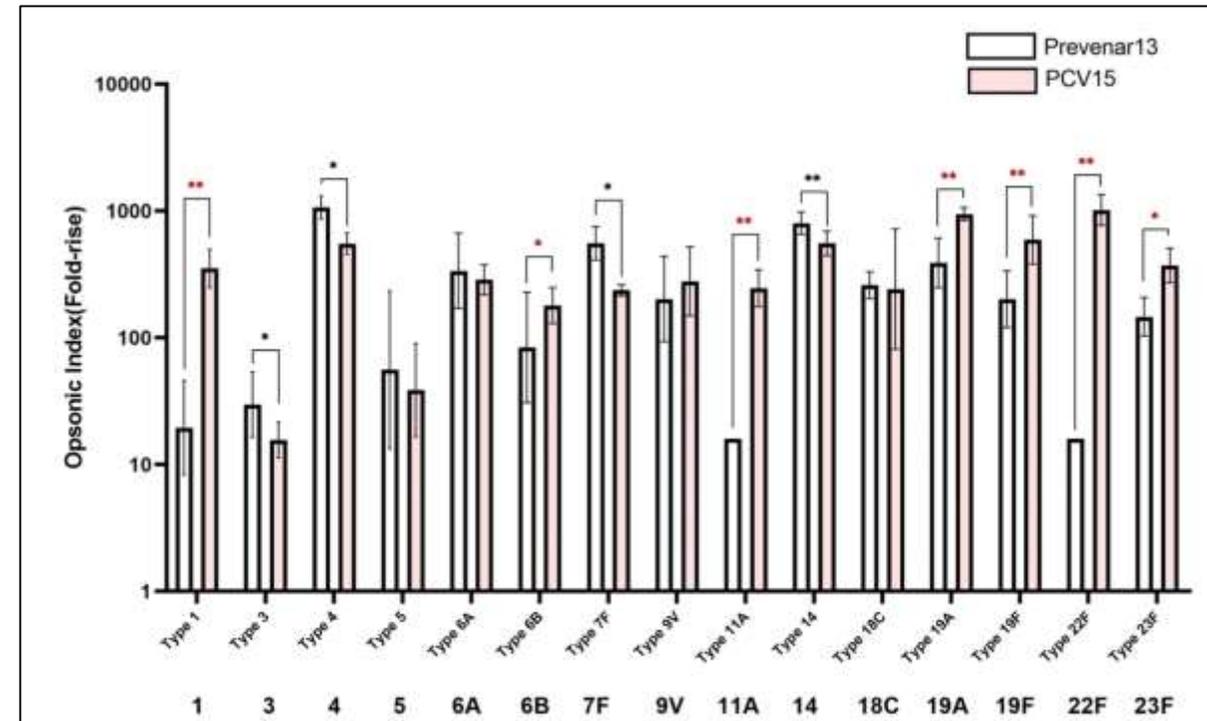
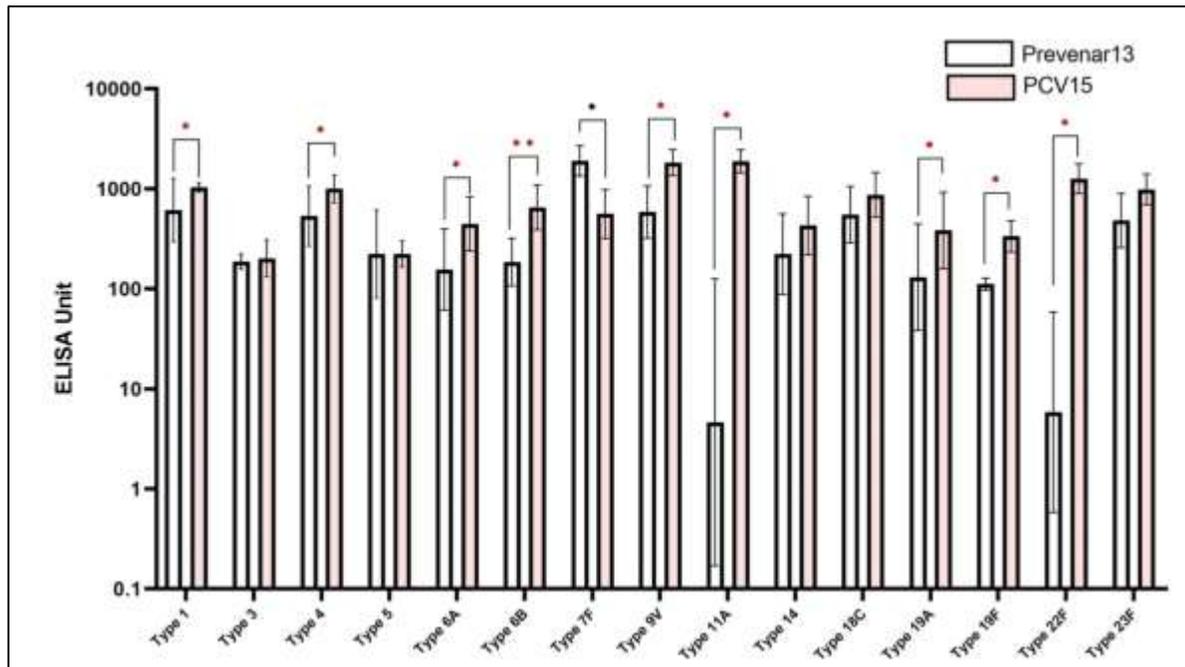
Cases, n (%)	Pre-PCV7 period	Pre-PCV13 period	Post-PCV13 period
PCV7 serotypes	16,321 (86)	147 (3)	224 (24)
ST18C	1,863 (10)	41 (1)	11 (1)
ST4	1,421 (7)	9 (0)	
ST6B	1,960 (10)		
ST9V	1,343 (7)	19 (0)	
ST14	6,326 (33)	27 (1)	
ST19F	2,156 (11)	42 (1)	214 (23)
ST23F	1,252 (7)	9 (0)	
PCV13, but not PCV7 serotypes	2,338 (12)	4,009 (85)	427 (45)
ST3	147 (1)	226 (5)	202 (21)
ST19A	514 (3)	2,081 (44)	214 (23)
ST6A	1,056 (6)	27 (1)	
ST1	358 (2)	243 (5)	
ST5	17 (0)	32 (1)	
ST7F	246 (1)	1,400 (30)	11 (1)
V114, but not PCV13 serotypes	324 (2)	545 (12)	298 (31)
ST22F	185 (1)	229 (5)	181 (19)
ST33F	139 (1)	315 (7)	116 (12)
Total V114 serotypes	18,983 (100)	4,697 (100)	948 (100)

Abbreviations. IPD, invasive pneumococcal disease; PCV, pneumococcal conjugate vaccine; ST, serotype.

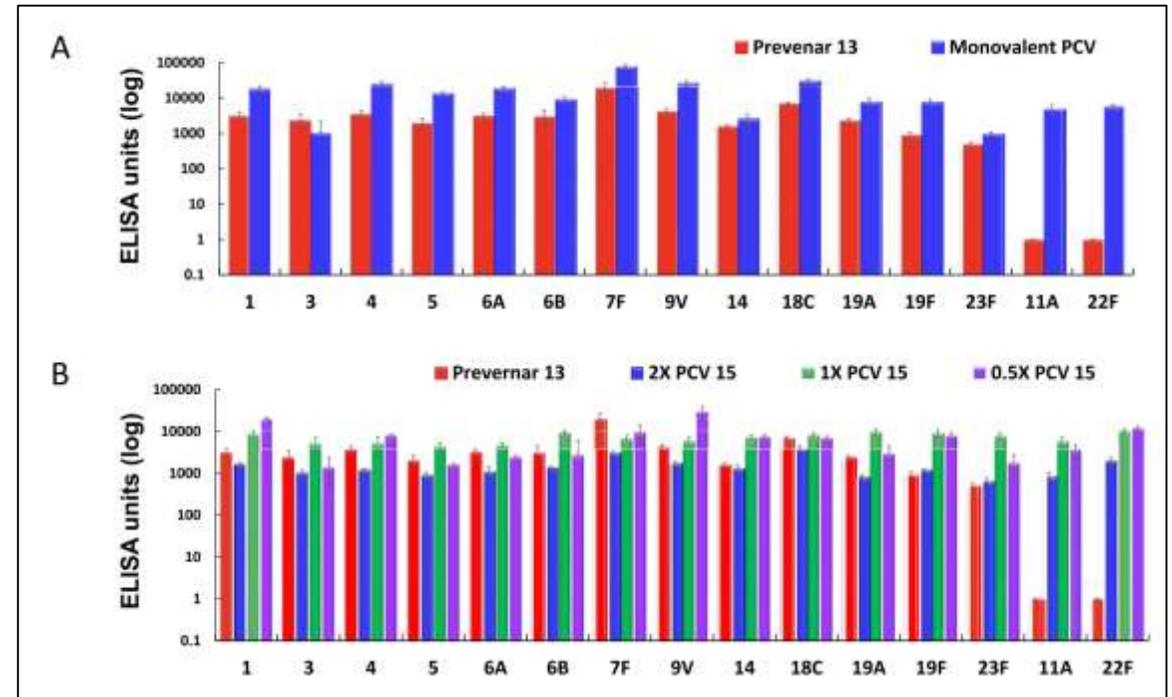
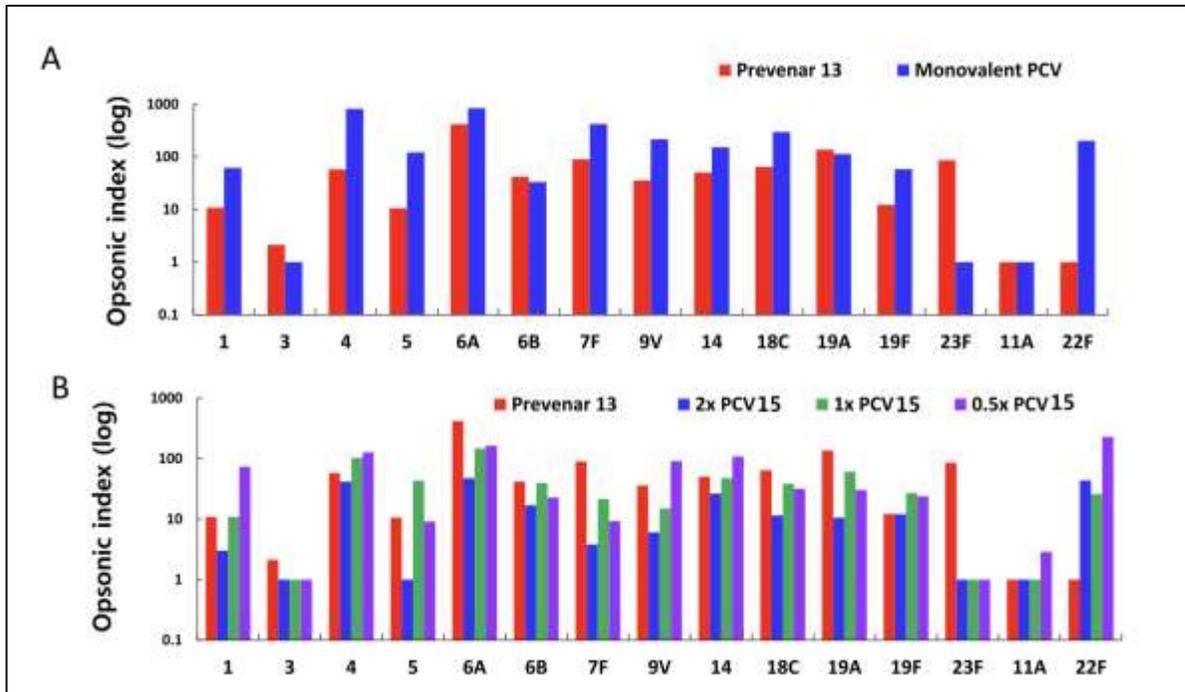
Table 4. IPD deaths attributable to V114 serotypes in the pre-PCV7, pre-PCV13, and post-PCV13 periods.

Deaths, n (%)	Pre-PCV7 period			Pre-PCV13 period			Post-PCV13 period		
	Bacteremia	Meningitis	Total	Bacteremia	Meningitis	Total	Bacteremia	Meningitis	Total
PCV7 serotypes	418 (87)	240 (83)	657 (85)	4 (3)	1 (3)	5 (3)	6 (24)	3 (24)	9 (24)
PCV13, but not PCV7 serotypes	60 (12)	34 (12)	94 (12)	109 (85)	38 (85)	147 (85)	5 (45)	3 (45)	17 (45)
ST5	0 (0)	0 (0)	1 (0)	1 (1)	0 (1)	1 (1)	0 (0)	0 (3)	0 (0)
ST3	4 (1)	2 (1)	6 (1)	6 (5)	2 (5)	8 (5)	6 (21)	3 (21)	8 (21)
ST7F	6 (1)	4 (1)	10 (1)	38 (30)	13 (30)	51 (30)	0 (0)	0 (1)	0 (0)
ST1	9 (2)	5 (2)	14 (2)	7 (5)	2 (5)	9 (5)	0 (0)	0 (0)	0 (0)
ST19A	13 (3)	8 (3)	21 (3)	57 (44)	20 (44)	76 (44)	8 (23)	3 (23)	6 (23)
ST6A	27 (6)	16 (5)	43 (6)	1 (1)	0 (1)	1 (1)	0 (0)	0 (0)	0 (0)
V114, but not PCV13 serotypes (ST22F and ST33F)	5 (1)	13 (5)	18 (2)	15 (12)	5 (12)	20 (12)	8 (31)	4 (31)	12 (31)
Total V114 serotypes	482 (100)	287 (100)	769 (100)	128 (100)	44 (100)	172 (100)	25 (100)	12 (100)	37 (100)

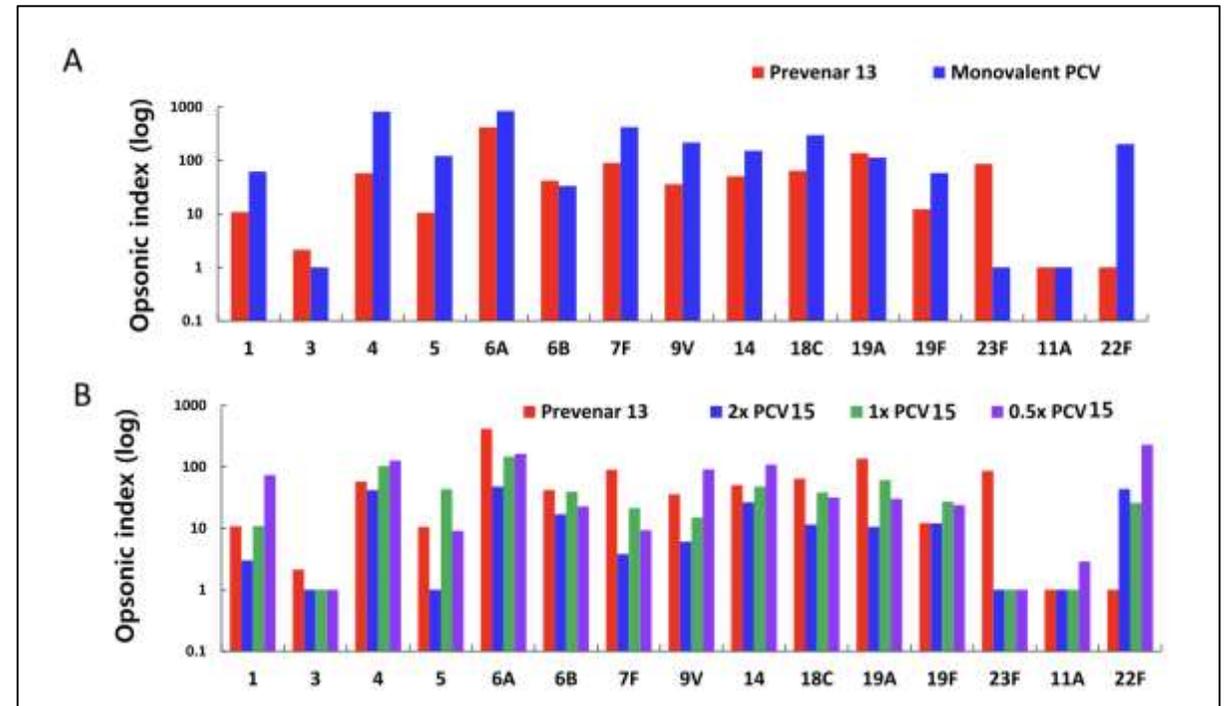
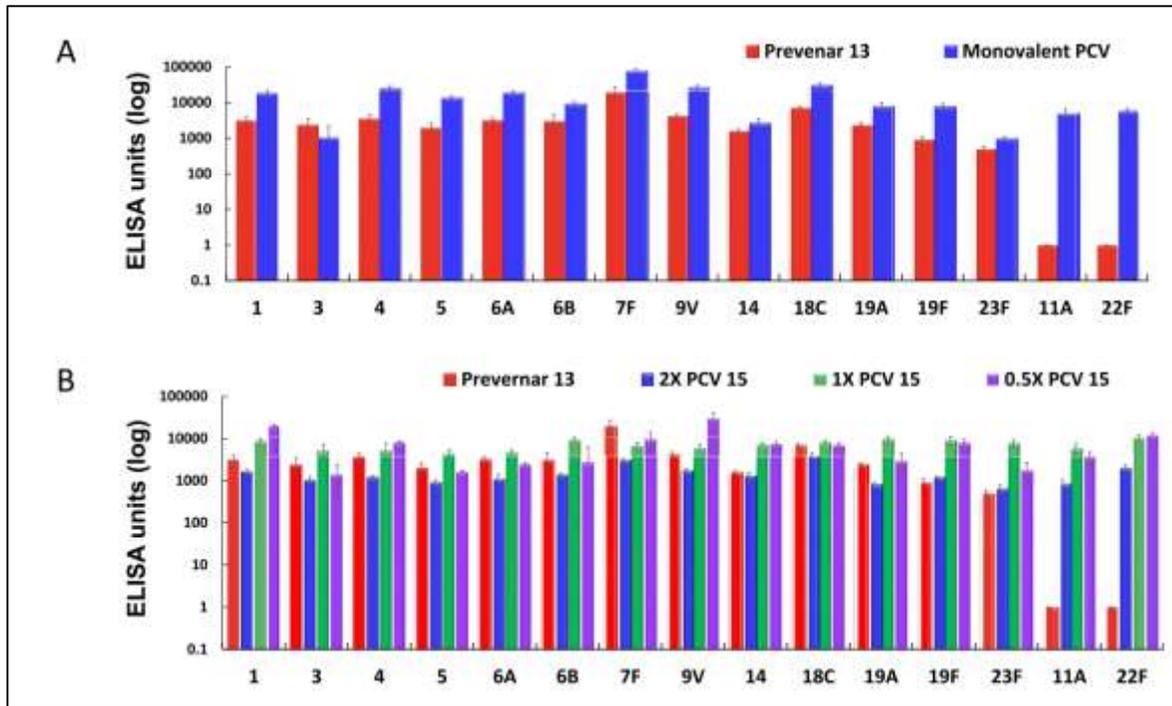
Réduction de la contamination par les polysaccharides libres dans la production d'un vaccin conjugué antipneumococcique 15-valent



Développement d'un nouveau vaccin conjugué anti-pneumococcique 15-valent (PCV15) T et évaluation de son immunogénicité

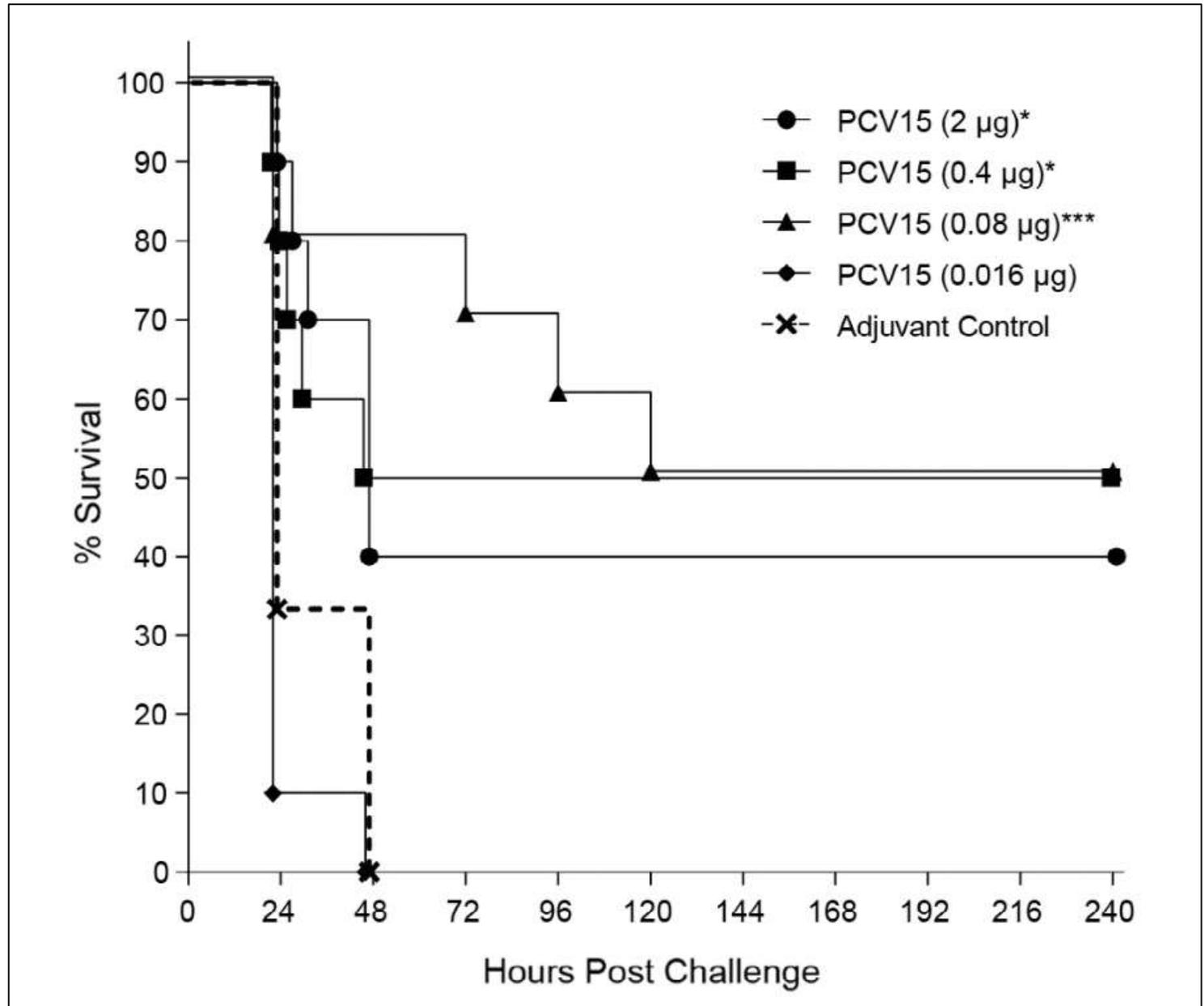


Développement d'un nouveau vaccin conjugué antipneumococcique 15-valent (PCV15) T et évaluation de son immunogénicité



Différences d'immunogénicité
d'un vaccin conjugué
polyosidique anti-
pneumococcique 15-valent en
fonction de la dose de vaccin, de
la voie d'immunisation et de la
souche de souris

I. Caro-Aguilar et al. / Vaccine 35 (2017) 865–872



Fardeau sanitaire et économique associé aux sérotypes du vaccin anti-pneumococcique conjugué 15-valent en Corée et à Hong Kong

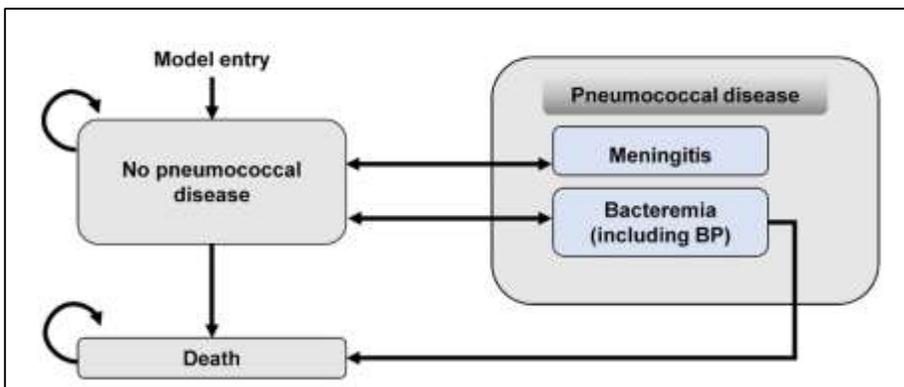


Table 3. IPD cases attributable to V114 serotypes in the pre-PCV7, pre-PCV13, and post-PCV13 periods in Korea and Hong Kong^a

	Korea			Hong Kong	
	Pre-PCV7	Pre-PCV13	Post-PCV13	Pre-PCV7	Post-PCV13
PCV7-specific serotypes	46 (75)	5 (19)	1 (17)	59 (96)	3 (6)
PCV13-specific serotypes	15 (25)	21 (78)	5 (67)	3 (4)	43 (94)
1	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
3	0 (0)	0 (0)	0 (0)	1 (2)	38 (83)
5	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
6A	8 (12)	3 (11)	1 (11)	1 (2)	0 (0)
7F	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)
19A	8 (12)	18 (67)	4 (44)	0 (0)	5 (10)
V114-specific serotypes	0 (0)	1 (3)	1 (17)	0 (0)	0 (0)
All V114 serotypes	62	26	8	62	46

Table 2. Cost inputs for Korea and Hong Kong.

	Korea	Hong Kong
Direct medical cost per episode ^a		
Meningitis	\$13,033	\$18,425
Bacteremia	\$6,078	\$12,230
Indirect medical cost per episode ^b		
Meningitis	\$1,024	\$473
Bacteremia	\$651	\$528

Table 4. Discounted direct and indirect costs associated with IPD in Korea^a

\$ in millions (%)	Pre-PCV7			Pre-PCV13			Post-PCV13		
	Direct costs	Indirect costs	Total costs	Direct costs	Indirect costs	Total costs	Direct costs	Indirect costs	Total costs
Korea									
PCV7-specific serotypes	0.296 (75)	0.973 (75)	1.269 (75)	0.033 (19)	0.111 (19)	0.144 (19)	0.008 (17)	0.028 (17)	0.035 (17)
PCV13-specific serotypes	0.098 (25)	0.323 (25)	0.442 (25)	0.134 (78)	0.444 (78)	0.578 (78)	0.031 (67)	0.111 (67)	0.141 (67)
1	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
3	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
5	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
6A	0.049 (12)	0.162 (12)	0.211 (12)	0.019 (11)	0.063 (11)	0.082 (11)	0.005 (11)	0.018 (11)	0.024 (11)
7F	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.005 (11)	0.018 (11)	0.024 (11)
19A	0.049 (12)	0.162 (12)	0.211 (12)	0.115 (67)	0.381 (67)	0.496 (67)	0.020 (44)	0.074 (44)	0.094 (44)
V114-specific serotypes	0 (0)	0 (0)	0 (0)	0.005 (3)	0.015 (3)	0.020 (3)	0.008 (17)	0.028 (17)	0.035 (17)
All V114 serotypes	0.394	1.297	1.691	0.172	0.570	0.743	0.046	0.166	0.212
Hong Kong									
PCV7-specific serotypes	0.719 (96)	1.508 (96)	2.227 (96)	-	-	-	0.033 (6)	0.078 (6)	0.110 (6)
PCV13-specific serotypes	0.030 (4)	0.065 (4)	0.096 (4)	-	-	-	0.479 (94)	1.137 (94)	1.616 (94)
1	0 (0)	0 (0)	0 (0)	-	-	-	0 (0)	0 (0)	0 (0)
3	0.014 (2)	0.031 (2)	0.044 (2)	-	-	-	0.419 (82)	1.000 (82)	1.419 (82)
5	0 (0)	0 (0)	0 (0)	-	-	-	0.003 (1)	0.007 (1)	0.010 (1)
6A	0.017 (2)	0.035 (2)	0.051 (2)	-	-	-	0 (0)	0 (0)	0 (0)
7F	0 (0)	0 (0)	0 (0)	-	-	-	0 (0)	0 (0)	0 (0)
19A	0 (0)	0 (0)	0 (0)	-	-	-	0.056 (11)	0.130 (11)	0.187 (11)
V114-specific serotypes	0 (0)	0 (0)	0 (0)	-	-	-	0 (0)	0 (0)	0 (0)
All V114 serotypes	0.749	1.573	2.322	-	-	-	0.512	1.215	1.726

Fardeau sanitaire et économique des infections invasives à pneumocoque associées aux sérotypes conjugués du 15-valent chez les enfants dans huit pays européens

Table 2. Epidemiological inputs.^a

Country	Age group (years)	IPD serotype-specific incidence rates by age group (per 100,000 person-years)									Case fatality rate meningitis/ bacteremia (%)
		Pre-PCV7			Pre-PCV13			Post-PCV13			
		PCV7 Serotypes	PCV13 not PCV7 serotypes	V114 not PCV13 serotypes	PCV7 Serotypes	PCV13 not PCV7 serotypes	V114 not PCV13 serotypes	PCV7 Serotypes	PCV13 not PCV7 serotypes	V114 not PCV13 serotypes	
UK ^{61,62}	<2	37.0	8.1	1.0	1.5	13.6	2.3	0.2	1.9	1.8	9.6/4.1
	2-4	11.6	2.5	0.3	0.7	4.9	0.7	0.1	0.6	0.5	
France ^{63,64,65,66,67}	5-20	2.1	1.4	0.2	0.8	1.1	0.2	0.0	0.1	0.1	11.0/4.1
	<2	20.5	7.6	0.8	1.1	18.4	0.7	0.8	1.8	1.0	
Germany ^{64,67,68}	2-4	5.3	2.0	0.2	0.5	7.8	0.3	0.0	0.5	0.3	7.5/2.0
	5-20	1.1	0.4	0.0	0.1	2.5	0.1	0.4	0.4	0.3	
Italy ^{69,70,71,72}	<2	13.5	4.0	0.2	2.6	6.1	0.5	0.4	1.9	1.2	4.8-12.9 ^b
	2-4	3.6	0.9	0.1	1.8	2.9	0.2	0.1	0.2	0.1	
Spain ^{73,74,75}	5-20	0.4	0.5	0.0	0.4	1.1	0.1	0.0	0.3	0.1	0.0-2.90 ^b
	<2	12.1	5.3	0.5	2.3	6.3	0.4	0.6	0.3	0.2	
Denmark ^{76,77,78,79,80}	1-4	9.4	4.1	0.4	1.0	2.8	0.2	0.2	0.1	0.1	8.0/1.0
	5-9	2.3	1.0	0.1	0.3	0.7	0.0	0.0	0.0	0.0	
Norway ^{81,82,83}	10-20	2.3	1.0	0.1	0.1	0.3	0.0	0.0	0.0	0.0	5.6/2.0
	<2	45.3	12.7	1.2	13.2	30.0	0.0	6.5	10.4	0.7	
Switzerland ^{84,85,86,87}	2-4	20.2	5.7	0.5	4.2	17.4	0.0	2.1	7.0	0.2	9.0/1.0
	5-20	6.8	1.7	0.2	1.7	5.6	0.1	0.9	0.2	0.2	
Denmark ^{76,77,78,79,80}	<2	34.2	14.6	0.6	2.4	18.8	1.2	0.0	1.2	1.2	8.0/1.0
	2-4	5.2	2.2	0.1	1.0	7.6	0.5	0.0	0.6	0.3	
Norway ^{81,82,83}	5-20	0.8	1.0	0.1	0.2	1.4	0.1	0.0	1.4	0.3	8.0/1.0
	<2	48.4	11.2	0.6	3.6	11.7	2.2	0.0	1.7	1.7	
Switzerland ^{84,85,86,87}	2-4	12.6	2.9	0.2	0.8	2.3	0.9	0.5	0.9	1.4	9.0/1.0
	5-20	1.9	0.8	0.2	0.1	0.4	0.2	0.3	1.4	2.1	
Switzerland ^{84,85,86,87}	<2	25.8	2.3	0.0	1.9	12.3	0.0	1.0	0.0	2.0	9.0/1.0
	2-4	4.7	5.2	0.0	2.6	5.9	0.5	2.5	0.0	0.0	
Switzerland ^{84,85,86,87}	5-20	1.8	1.2	0.0	0.9	1.7	0.2	0.2	0.2	0.0	

Table 5. IPD deaths attributable to V114 serotypes in the pre-PCV7, pre-PCV13, and post-PCV13 periods.

Deaths, n (%)	Pre-PCV7 period			Pre-PCV13 period			Post-PCV13 period		
	Bacteremia	Meningitis	Total	Bacteremia	Meningitis	Total	Bacteremia	Meningitis	Total
PCV7 serotypes	80 (73)	49 (72)	129 (72)	11 (15)	7 (17)	19 (15)	5 (24)	3 (24)	8 (24)
PCV13, but not PCV7 serotypes	27 (25)	17 (26)	45 (25)	63 (80)	34 (79)	97 (80)	11 (55)	7 (49)	18 (53)
ST3	3 (3)	2 (3)	5 (3)	5 (7)	3 (8)	9 (7)	4 (21)	3 (24)	8 (23)
ST19A	6 (6)	4 (6)	10 (6)	16 (21)	9 (20)	25 (20)	2 (10)	1 (10)	3 (10)
ST6A	4 (4)	2 (4)	7 (4)	2 (2)	1 (2)	3 (2)	1 (4)	0 (2)	1 (3)
ST1	8 (8)	5 (7)	13 (7)	21 (27)	10 (24)	32 (26)	3 (13)	1 (7)	4 (10)
ST5	1 (1)	1 (1)	2 (1)	2 (2)	1 (2)	3 (2)	0 (1)	0 (1)	0 (1)
ST7F	4 (4)	3 (5)	8 (4)	17 (21)	9 (22)	26 (21)	1 (7)	1 (5)	2 (6)
ST22F and 33F (V114, but not PCV13 serotypes)	3 (2)	1 (2)	4 (2)	4 (5)	2 (4)	6 (5)	4 (20)	4 (27)	8 (23)
Total V114 serotypes	110 (100)	67 (100)	178 (100)	78 (100)	43 (100)	121 (100)	20 (100)	14 (100)	34 (100)

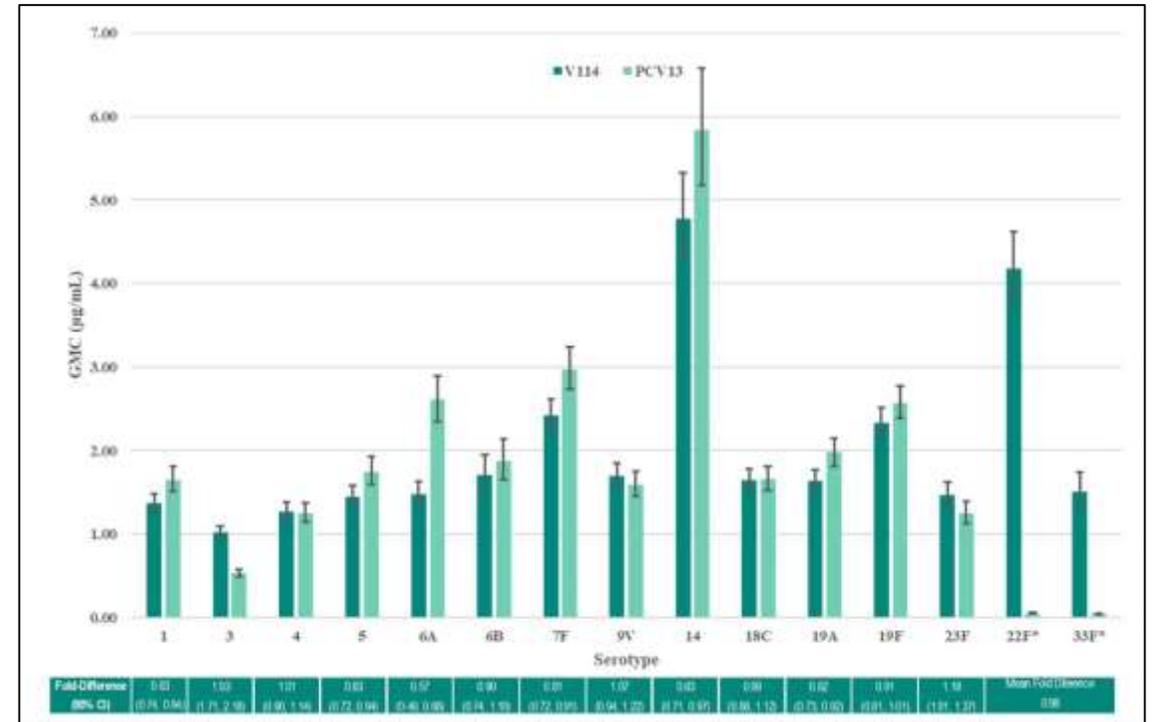
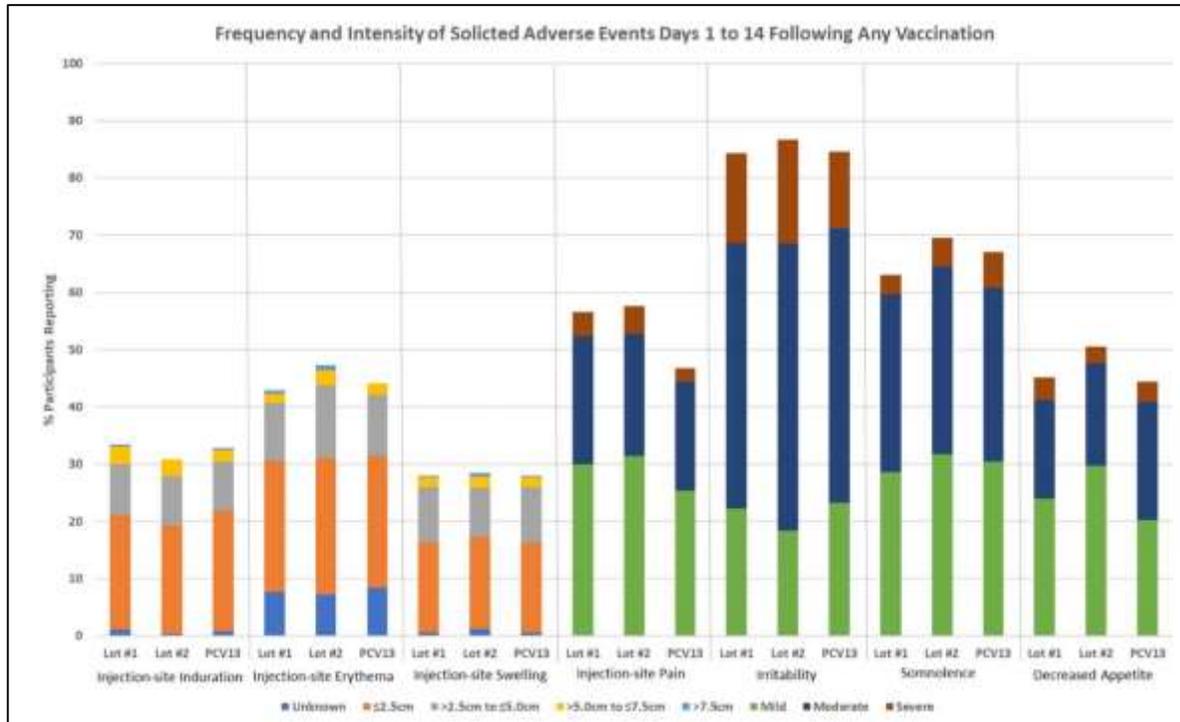
Table 3. Cost inputs (2018 Euros).^a

Country	Manifestation	Direct medical cost (per episode)	Indirect cost (per episode) ^b
UK ⁶⁶	Meningitis	€9,780	€1,262
	Bacteremia	€8,194	€742
France ^{66-68,69,70}	Meningitis	€6,089	€954
	Bacteremia	€2,422	€561
Germany ⁶²	Meningitis	€7,162	€459
	Bacteremia	€6,897	€459
Italy ^{5,66,71,72}	Meningitis	€8,228	€971
	Bacteremia	€3,239	€571
Spain ^{66,73-75c}	Meningitis	€10,874-€11,789	€687
	Bacteremia	€3,786-€4,039	€404
Denmark ^{59,63,76,77}	Meningitis	€12,245	€606
	Bacteremia	€8,258	€493
Norway ^{59,78,77}	Meningitis	€19,862	€834
	Bacteremia	€18,054	€679
Switzerland ^{59,61,79,80}	Meningitis	€10,675	€1,014
	Bacteremia	€4,887	€592

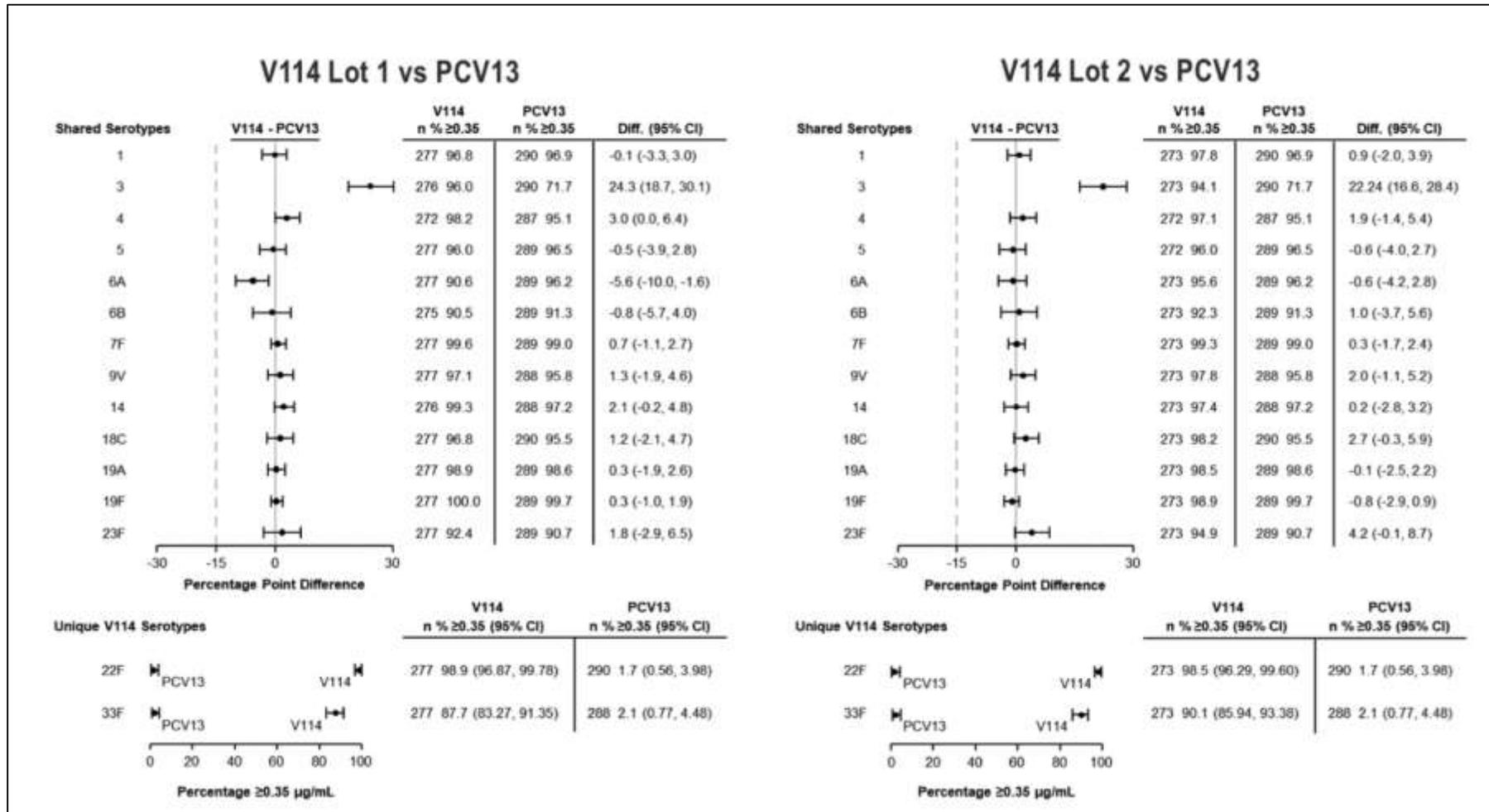
Table 7. One-way sensitivity analyses results (2018 Euros).

€millions (% change from base cost)	PCV7 serotypes		PCV13 but not PCV7 serotypes		V114 but not PCV13 serotypes	
	Discounted indirect costs due to premature death	Discounted total costs	Discounted indirect costs due to premature death	Discounted total costs	Discounted indirect costs due to premature death	Discounted total costs
Base case	59.1	79.4	20.6	27.3	1.8	2.4
Incidence -20%	47.3 (-20)	63.5 (-20)	16.5 (-20)	21.8 (-20)	1.5 (-20)	2.0 (-20)
Incidence +20%	71.0 (20)	95.3 (20)	24.7 (20)	32.7 (20)	2.2 (20)	2.9 (20)
CFR -20%	47.3 (-20)	67.6 (-15)	16.5 (-20)	23.1 (-15)	1.5 (-20)	2.1 (-15)
CFR +20%	71.0 (20)	91.3 (15)	24.7 (20)	31.4 (15)	2.2 (20)	2.8 (15)
Cost -20%	59.1 (0)	75.4 (-5)	20.6 (0)	25.9 (-5)	1.8 (0)	2.3 (-5)
Cost +20%	59.1 (0)	83.1 (5)	20.6 (0)	28.5 (4)	1.8 (0)	2.6 (4)
Discount factor 0%	239.9 (306)	262.8 (231)	83.4 (305)	91.2 (235)	7.6 (311)	8.3 (238)
Discount factor 5%	26.9 (-54)	46.0 (-42)	9.4 (-54)	15.5 (-43)	0.8 (-55)	1.4 (-43)

Un essai de phase II sur l'innocuité, la tolérabilité et l'immunogénicité du V114, un vaccin conjugué contre le pneumocoque à 15 valences, par rapport au vaccin conjugué contre le pneumocoque à 13 valences chez des nourrissons en bonne santé



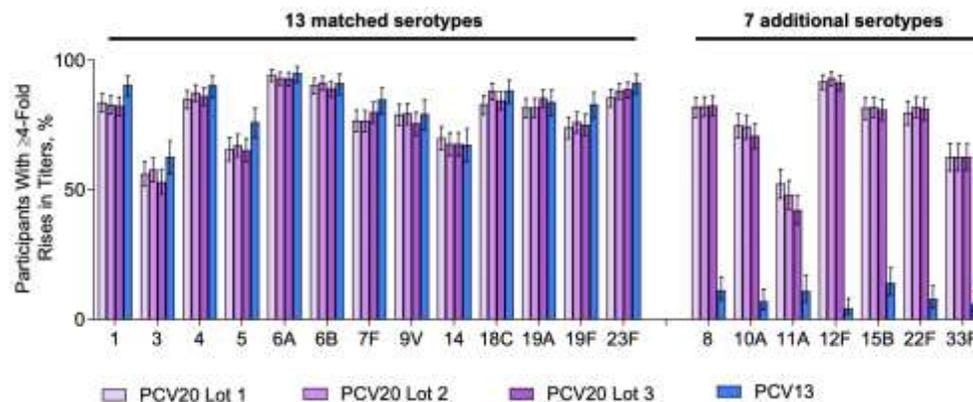
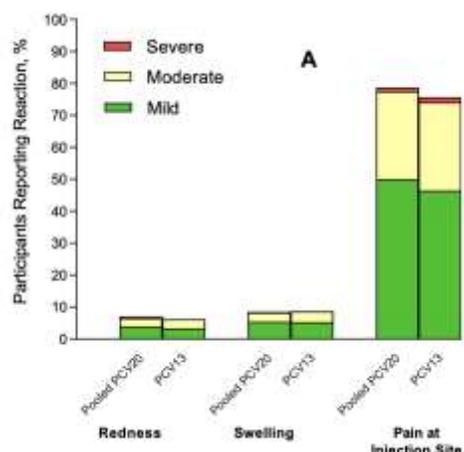
Un essai de phase II sur l'innocuité, la tolérabilité et l'immunogénicité du V114, un vaccin conjugué contre le pneumocoque à 15 valences, par rapport au vaccin conjugué contre le pneumocoque à 13 valences chez des nourrissons en bonne santé



Un essai de phase II sur l'innocuité, la tolérabilité et l'immunogénicité du V114, un vaccin conjugué contre le pneumocoque à 15 valences, par rapport au vaccin conjugué contre le pneumocoque à 13 valences chez des nourrissons en bonne santé

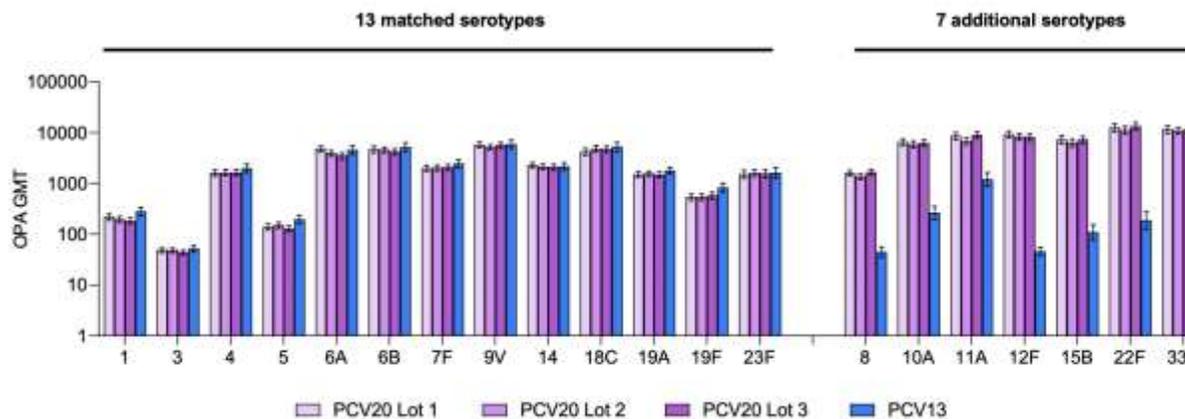
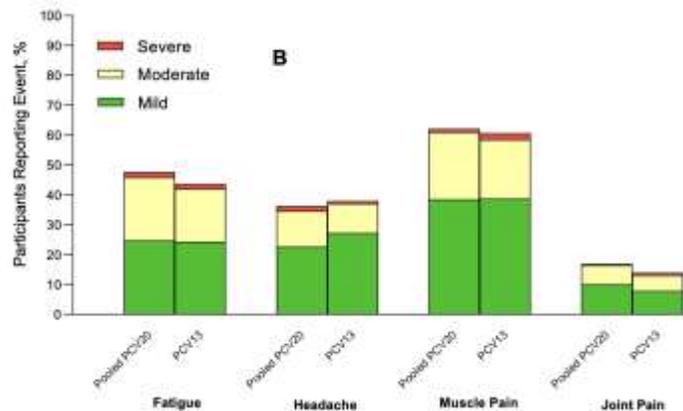
Serotype	Endpoint	V114 Lot 1 (N = 128)			V114 Lot 2 (N = 136)			PCV13 (N = 128)		
		N	Observed Response	95% CI	N	Observed Response	95% CI	N	Observed Response	95% CI
Shared serotypes										
1	% ≥ 1:9	104	81%	(72–88)	112	80%	(71–87)	104	76%	(67–84)
	OPA GMT	104	31	(24–40)	112	28	(22–36)	104	28	(22–37)
3	% ≥ 1:19	105	100%	(97–100)	111	99%	(95–100)	103	95%	(89–98)
	OPA GMT	105	160	(142–179)	111	144	(127–165)	103	129	(108–155)
4	% ≥ 1:34	102	100%	(96–100)	110	98%	(94–100)	95	98%	(93–100)
	OPA GMT	102	970	(812–1158)	110	904	(758–1077)	95	1043	(835–1303)
5	% ≥ 1:27	105	97%	(92–99)	114	96%	(90–99)	106	97%	(92–99)
	OPA GMT	105	419	(341–514)	114	392	(319–483)	106	402	(323–502)
6A	% ≥ 1:232	95	98%	(93–100)	101	99%	(95–100)	88	100%	(96–100)
	OPA GMT	95	2144	(1799–2556)	101	1948	(1659–2288)	88	2593	(2115–3179)
6B	% ≥ 1:40	101	100%	(96–100)	108	97%	(92–99)	98	100%	(96–100)
	OPA GMT	101	1261	(1049–1516)	108	1223	(998–1498)	98	1135	(942–1367)
7F	% ≥ 1:61	99	100%	(96–100)	108	100%	(97–100)	94	100%	(96–100)
	OPA GMT	99	2309	(1679–2693)	108	3691	(3230–4217)	94	3128	(2604–3757)
9V	% ≥ 1:151	105	91%	(84–96)	109	95%	(90–98)	103	96%	(91–99)
	OPA GMT	105	981	(788–1220)	109	1386	(1109–1731)	103	1203	(966–1497)
14	% ≥ 1:62	107	100%	(97–100)	111	97%	(92–99)	105	99%	(95–100)
	OPA GMT	107	1248	(1039–1500)	111	1492	(1203–1850)	105	1160	(937–1437)
18C	% ≥ 1:115	108	99%	(95–100)	114	100%	(97–100)	106	98%	(94–100)
	OPA GMT	108	733	(617–872)	114	1091	(947–1257)	106	916	(763–1100)
19A	% ≥ 1:31	96	99%	(94–100)	102	100%	(96–100)	93	100%	(96–100)
	OPA GMT	96	936	(766–1144)	102	993	(832–1186)	93	1409	(1178–1686)
19F	% ≥ 1:113	106	97%	(92–99)	112	98%	(94–100)	105	98%	(93–100)
	OPA GMT	106	394	(780–1133)	112	1122	(949–1326)	105	917	(754–1115)
23F	% ≥ 1:55	100	100%	(96–100)	107	98%	(93–100)	86	100%	(96–100)
	OPA GMT	100	2089	(1775–2459)	107	2087	(1714–2541)	86	2414	(1981–2942)
Unique V114 serotypes										
22F	% ≥ 1:15	79	100%	(95–100)	84	100%	(96–100)	61	20%	(11–32)
	OPA GMT	79	1814	(1501–2192)	84	1817	(1549–2131)	61	12	(9–18)
33F	% ≥ 1:20	88	93%	(86–97)	86	95%	(89–99)	87	47%	(36–58)
	OPA GMT	88	3779	(2496–5722)	86	3677	(2512–5381)	87	61	(38–97)

Une étude de phase 3, randomisée, en double aveugle pour évaluer l'immunogénicité et l'innocuité de 3 lots de vaccin conjugué anti-pneumococcique 20-valent chez des adultes naïfs de vaccin antipneumococcique âgés de 18 à 49 ans

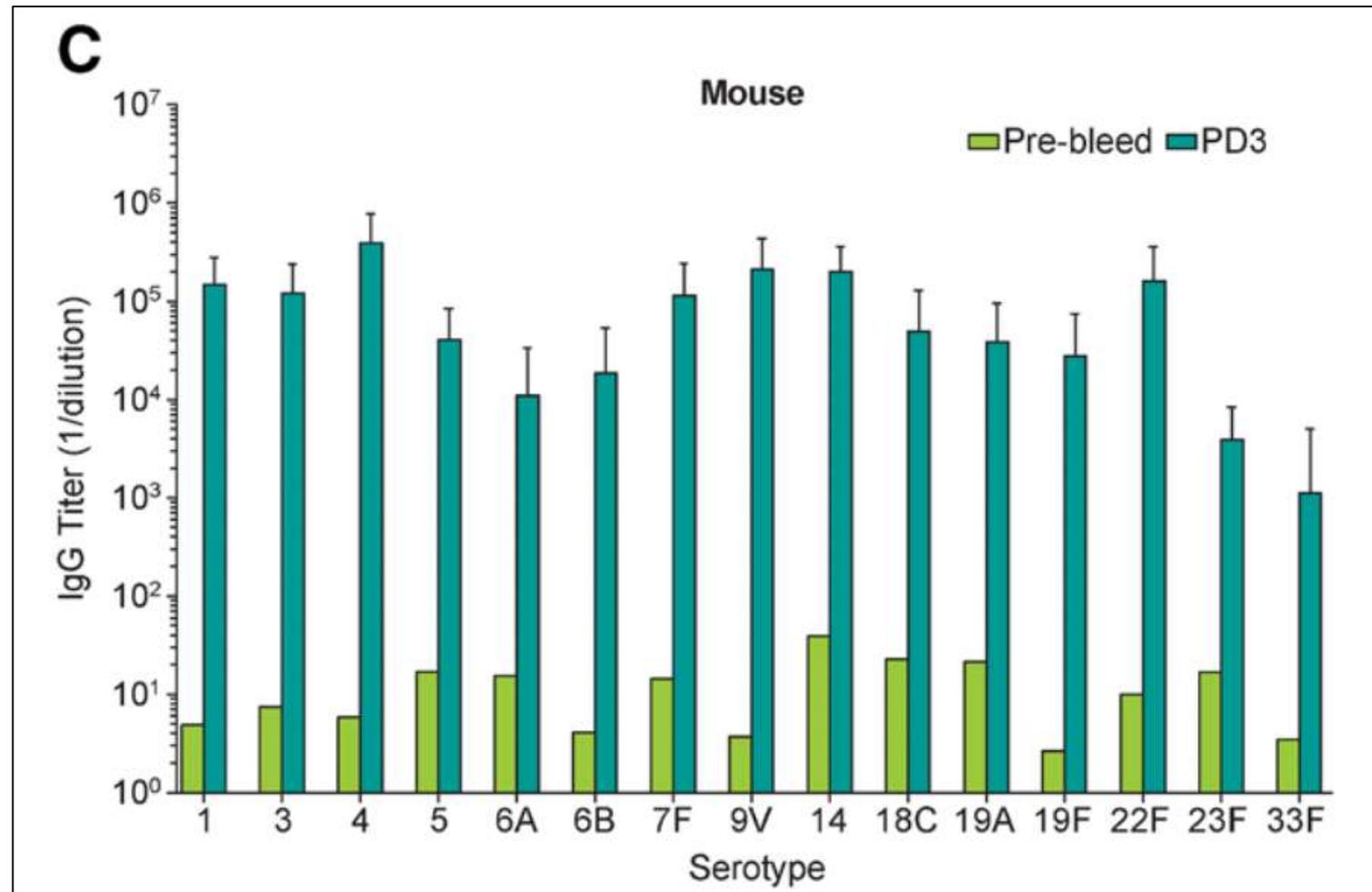


Summary of adverse events.

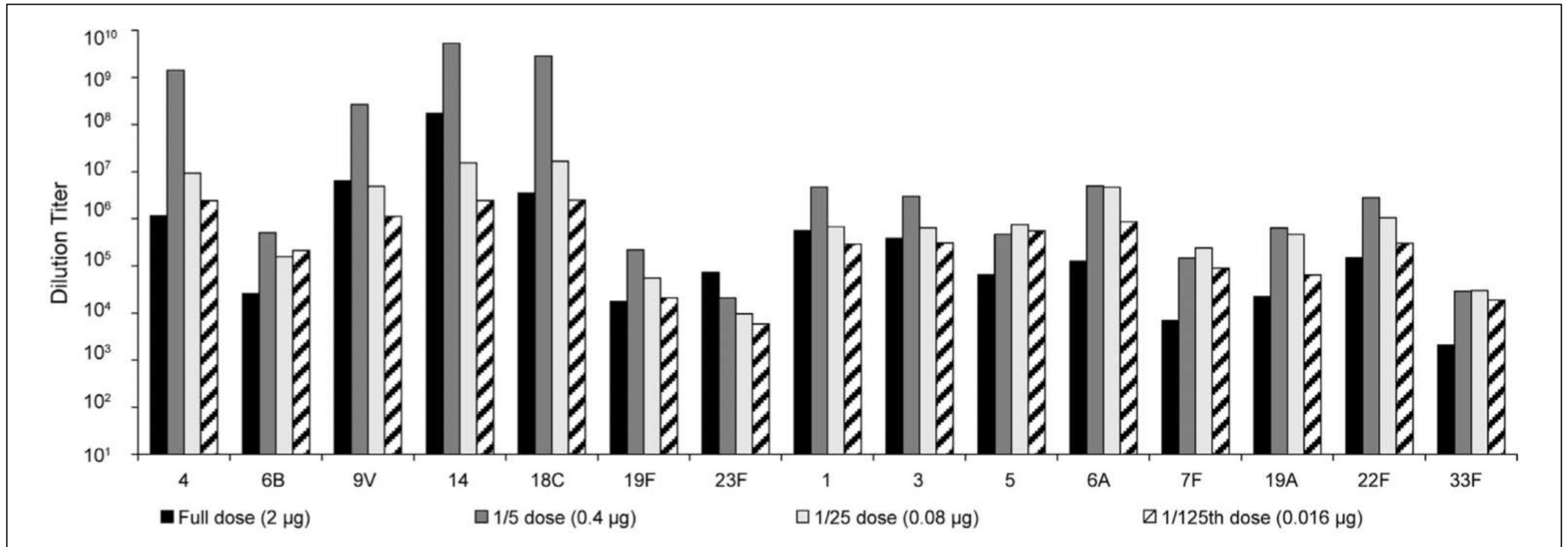
Time point AE type	Pooled PCV20 (N = 1463 ^a) n ^b (%)	PCV13 (N = 245 ^a) n ^b (%)
Through 1 month after vaccination		
Any AE	100 (6.8)	13 (5.3)
Related	5 (0.3)	2 (0.8)
Severe	7 (0.5)	2 (0.8)
Through 6 months after vaccination		
SAE	10 (0.7)	0
NDCMC	15 (1.0)	5 (2.0)



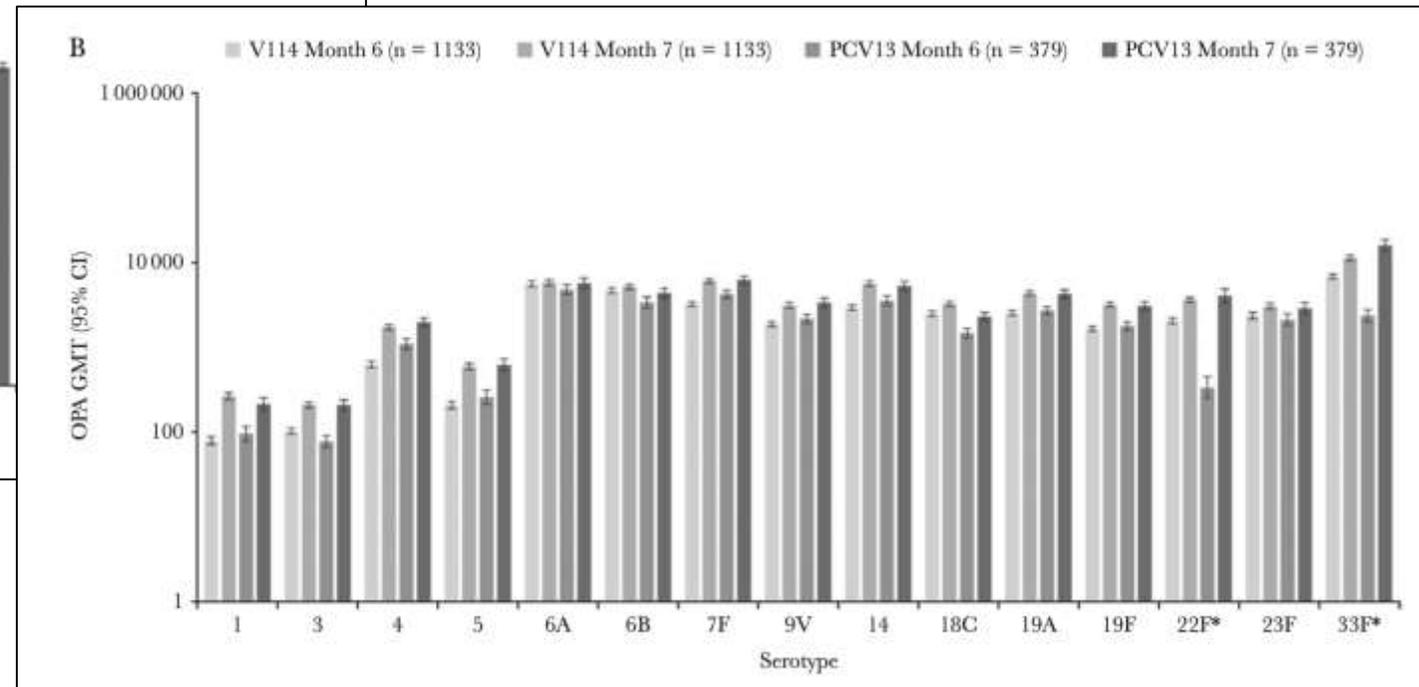
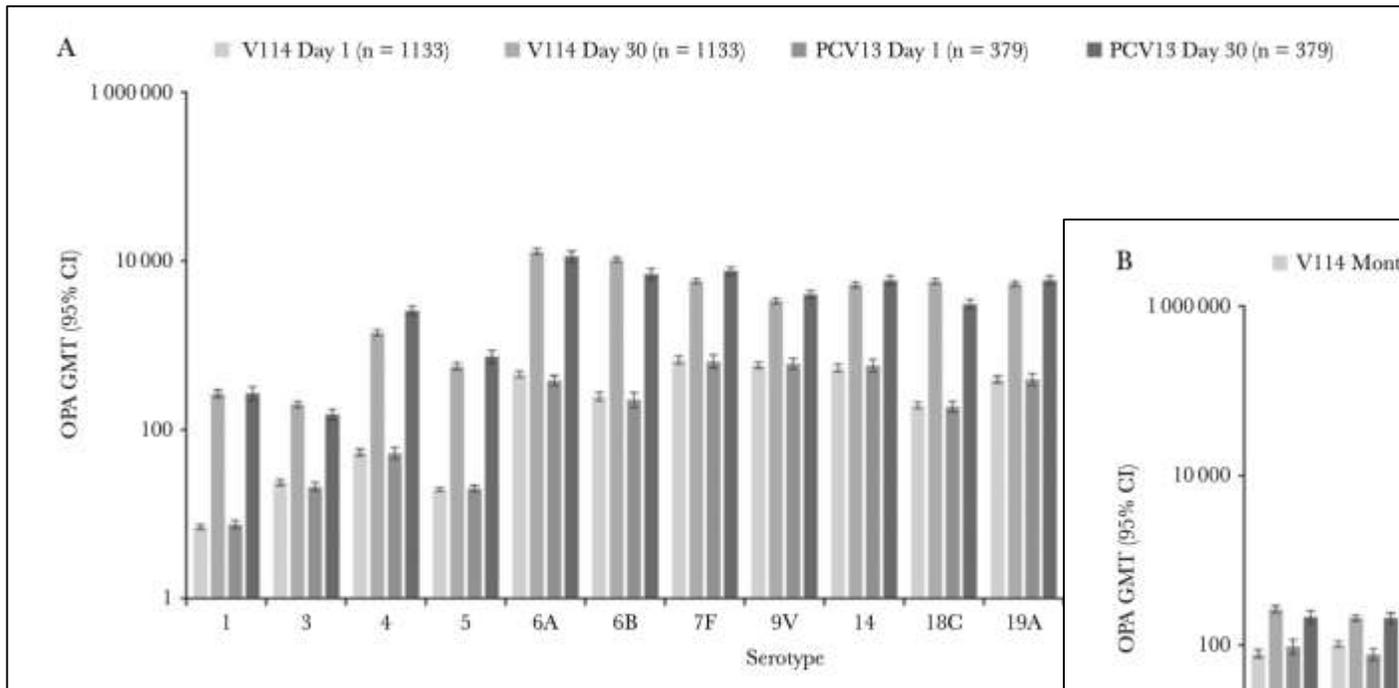
Comparaison de l'immunogénicité d'un vaccin conjugué contre le pneumocoque de nouvelle génération chez des modèles animaux et des nourrissons humains



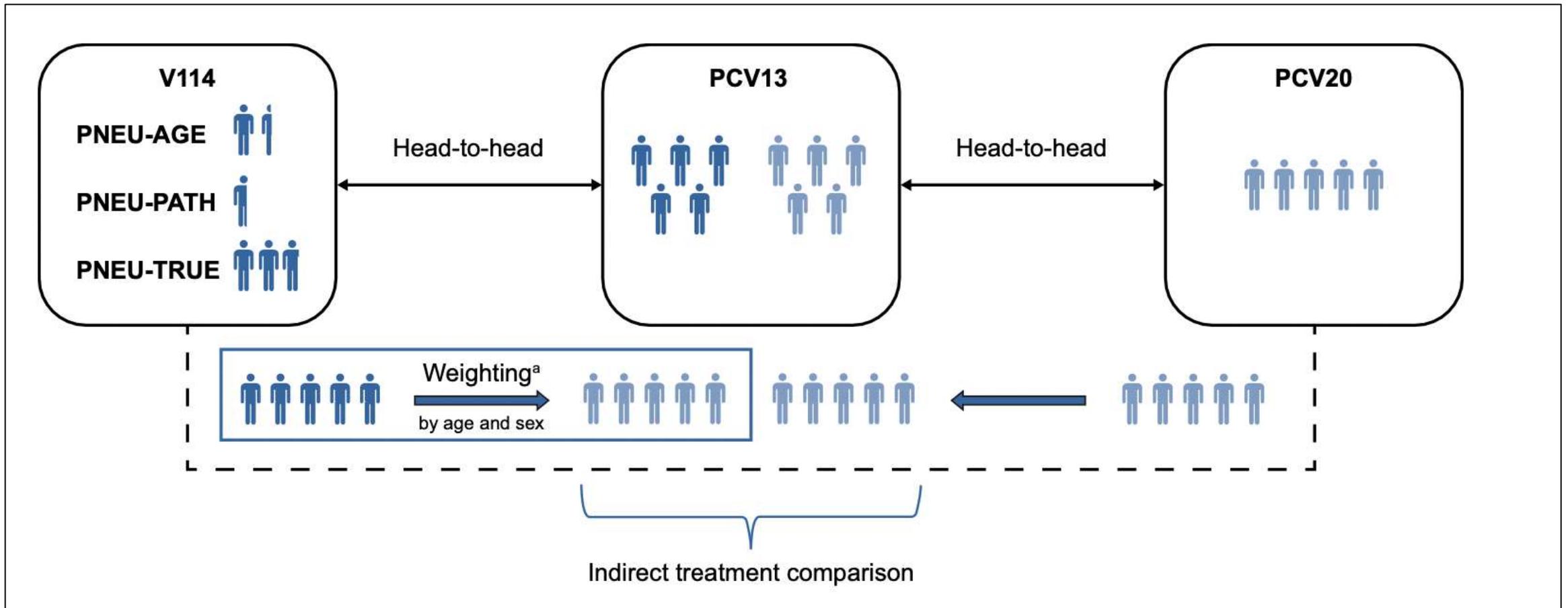
Différences d'immunogénicité d'un vaccin conjugué polysidique antipneumococcique 15-valent (PCV15) en fonction de la dose de vaccin, de la voie d'immunisation et de la souche de souris



Immunogénicité, innocuité et tolérabilité du V114, un vaccin conjugué antipneumococcique 15-valent, chez des adultes immunocompétents âgés de 18 à 49 ans avec ou sans facteurs de risque de maladie pneumococcique : un essai randomisé de phase 3 (PNEU-DAY)



Comparaison indirecte ajustée par appariement des vaccins antipneumococciques V114 et PCV20



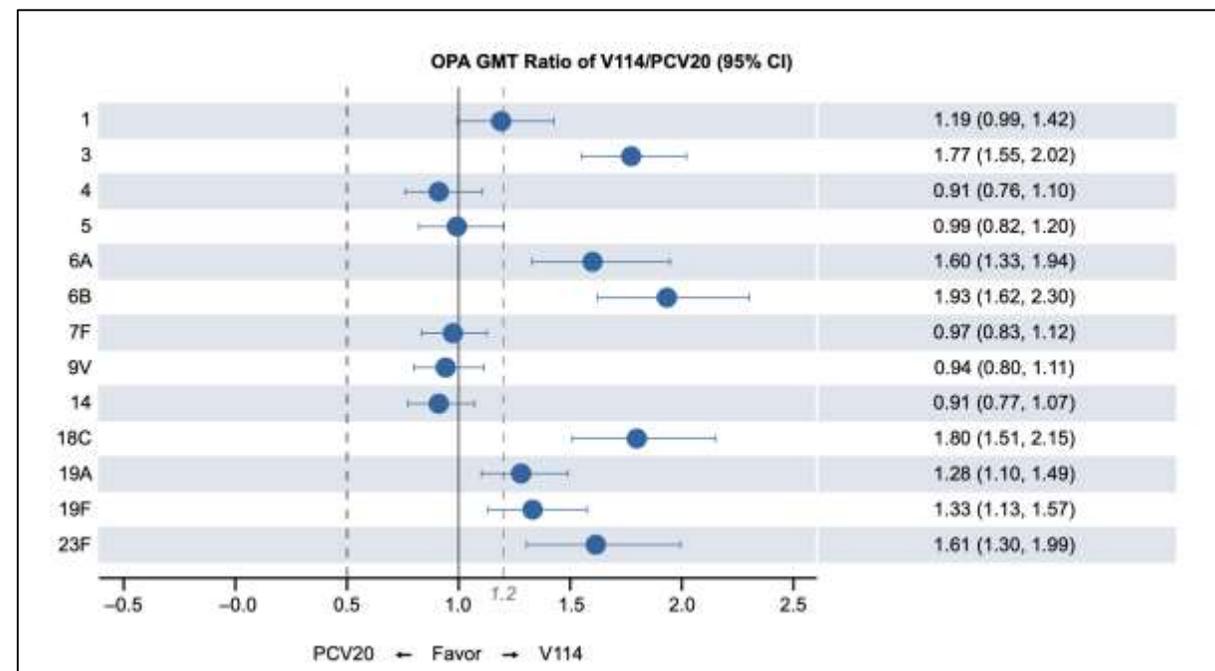
Comparaison indirecte ajustée par appariement des vaccins antipneumococciques V114 et PCV20

Table 3. Unadjusted and matching-adjusted indirect comparison (MAIC) analyses of OPA GMT ratio for V114 versus PCV20.

Serotype	V114:PCV13		PCV20:PCV13	V114:PCV20			
	Before matching (N1/N2 = 2,196/843)	After matching (N1/N2 = 1,580/562)	(N1/N2 = 1,507/1,490)	Before matching		After matching	
	GMT ratio (95% CI)	GMT ratio (95% CI)	GMT ratio (95% CI)	GMT ratio (95% CI)	p-value ^a	GMT ratio (95% CI)	p-value ^a
1	0.93 (0.81, 1.07)	0.95 (0.83, 1.09)	0.80 (0.71, 0.90)	1.17 (0.97, 1.40)	<0.001	1.19 (0.99, 1.42)	<0.001
3	1.65 (1.49, 1.82)	1.51 (1.36, 1.67)	0.85 (0.78, 0.93)	1.94 (1.69, 2.21)	<0.001	1.77 (1.55, 2.02)	<0.001
4	0.72 (0.64, 0.82)	0.74 (0.65, 0.84)	0.81 (0.71, 0.93)	0.89 (0.74, 1.07)	<0.001	0.91 (0.76, 1.10)	<0.001
5	0.78 (0.67, 0.90)	0.82 (0.71, 0.95)	0.83 (0.74, 0.94)	0.94 (0.78, 1.13)	<0.001	0.99 (0.82, 1.20)	<0.001
6A	1.09 (0.96, 1.23)	1.22 (1.08, 1.38)	0.76 (0.66, 0.88)	1.43 (1.18, 1.73)	<0.001	1.60 (1.33, 1.94)	<0.001
6B	1.48 (1.30, 1.67)	1.60 (1.42, 1.80)	0.83 (0.73, 0.95)	1.78 (1.48, 2.14)	<0.001	1.93 (1.62, 2.30)	<0.001
7F	0.80 (0.72, 0.88)	0.83 (0.75, 0.92)	0.86 (0.77, 0.96)	0.93 (0.80, 1.07)	<0.001	0.97 (0.83, 1.12)	<0.001
9V	0.87 (0.78, 0.96)	0.88 (0.79, 0.98)	0.93 (0.82, 1.05)	0.93 (0.79, 1.10)	<0.001	0.94 (0.80, 1.11)	<0.001
14	0.95 (0.85, 1.07)	0.91 (0.81, 1.02)	1.00 (0.89, 1.13)	0.95 (0.81, 1.13)	<0.001	0.91 (0.77, 1.07)	<0.001
18C	1.35 (1.21, 1.51)	1.53 (1.37, 1.71)	0.85 (0.74, 0.97)	1.59 (1.33, 1.89)	<0.001	1.80 (1.51, 2.15)	<0.001
19A	0.91 (0.83, 1.01)	1.03 (0.93, 1.13)	0.80 (0.71, 0.90)	1.14 (0.98, 1.33)	<0.001	1.28 (1.10, 1.49)	<0.001
19F	1.00 (0.91, 1.11)	1.07 (0.96, 1.18)	0.80 (0.70, 0.91)	1.25 (1.06, 1.48)	<0.001	1.33 (1.13, 1.57)	<0.001
23F	1.31 (1.15, 1.51)	1.34 (1.17, 1.53)	0.83 (0.70, 0.97)	1.58 (1.28, 1.96)	<0.001	1.61 (1.30, 1.99)	<0.001

Abbreviations: CI, confidence interval; GMT, geometric mean titer; ITC, indirect treatment comparison; MAIC, matching-adjusted indirect comparison; N1/N2, number of participants randomized/number of participants vaccinated (sum of weights by arm after matching); OPA, opsonophagocytic activity; PCV13, 13-valent pneumococcal conjugate vaccine; PCV20, 20-valent pneumococcal conjugate vaccine; V114, 15-valent pneumococcal conjugate vaccine.

^aOne-sided p-value calculated from the test statistic associated with the ITC estimate and its standard error with a non-inferiority margin equal to 0.5.



Serotypes Contained in Current and New Pneumococcal Vaccines

	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F	22F	33F	8	10A	11A	12F	15B	2	9N	17F	20	
PCV13	Yellow	White	White	White	White																				
PCV15	Yellow	Green	Green	White	White	White	White																		
PCV20	Yellow	Green	Green	Blue	Blue	Blue	Blue	Blue	Blue	White	White	White	White												
PPSV23	Yellow	Yellow	Yellow	Yellow	White	Yellow	Green	Green	Blue	Blue	Blue	Blue	Blue	Blue	Orange	Orange	Orange	Orange							

PCV13: 13-valent pneumococcal conjugate vaccine

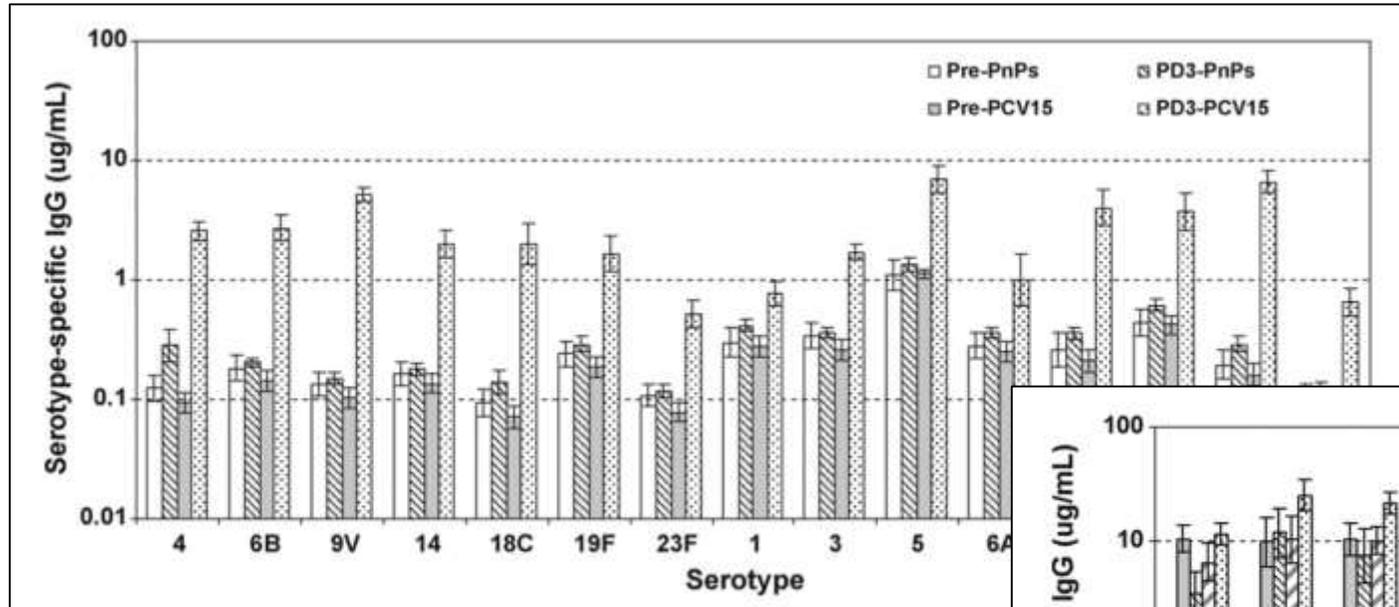
PPSV23: 23-valent pneumococcal polysaccharide vaccine

Serotypes Contained in Current and New Pneumococcal Vaccines

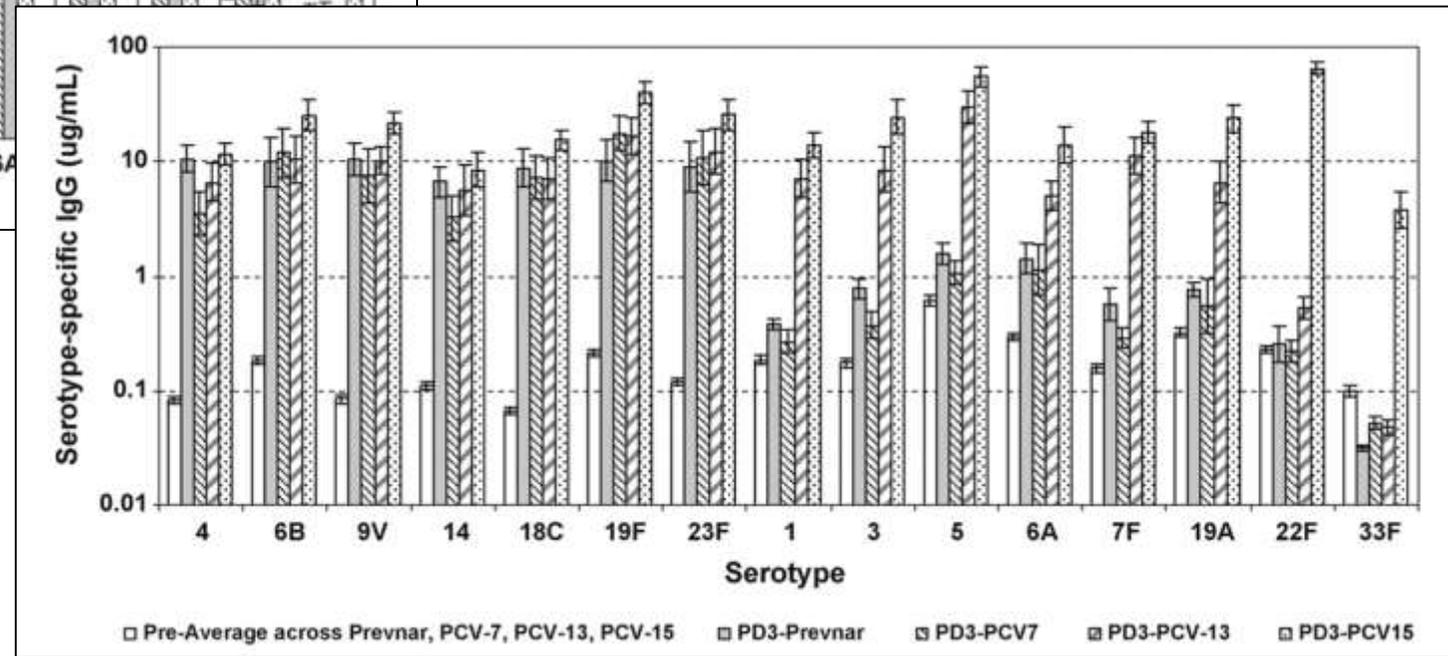
	1	3	4	5	6A	6B	7 F	9V	14	18 C	19 A	19 F	23 F	22 F	33 F	8	10 A	11 A	12 F	15 B	2	9N	17 F	20		
PCV13	Yellow																									
PCV15	Yellow	Green	Green																							
PCV20	Yellow	Green	Green	Blue	Blue	Blue	Blue	Blue	Blue																	
PPSV23	Yellow	Yellow	Yellow	Yellow	White	Yellow	Green	Green	Blue	Blue	Blue	Blue	Blue	Blue	Orange	Orange	Orange	Orange								

- **PCV15 non-PCV13:** includes serotypes **22F** and **33F**
- **PCV20 non-PCV13:** includes serotypes **22F, 33F, 8, 10A, 11A, 12F, and 15B**
- **PPSV23 non-PCV20:** includes serotypes **2, 9N, 17F, and 20**

Évaluation pré-clinique d'un vaccin conjugué antipneumococcique 15-valent (PCV15-CRM197) dans un modèle d'immunogénicité nourrisson-singe rhésus



Vaccine 29 (2011) 8870–8876



Prédire l'efficacité du vaccin V114 contre la maladie pneumococcique invasive chez les enfants

Serotype	Vaccine effectiveness		Geometric mean serotype-specific antibody concentration (µg/mL)			
	PCV7 (95% CI) ^A	PCV13 (95% CI) ^B	Placebo (95% CI) ^C	PCV7 (95% CI) ^D	PCV13 (95% CI) ^E	V114 (95% CI) ^E
PCV7						
4	93% (65–99)	–	0.03 (0.03–0.04)	1.36 (1.20–1.56)	0.87 (0.83–0.91)	0.89 (0.86–0.93)
6B	94% (77–98)	–	0.08 (0.07–0.08)	3.34 (2.75–4.05)	1.60 (1.50–1.70)	1.50 (1.40–1.60)
9 V	100% (88–100)	–	0.06 (0.05–0.06)	1.60 (1.41–1.83)	0.86 (0.83–0.90)	0.88 (0.84–0.91)
14	94% (81–98)	–	0.22 (0.20–0.24)	4.68 (4.07–5.40)	4.50 (4.20–4.90)	3.60 (3.40–3.90)
18C	97% (85–99)	–	0.06 (0.06–0.07)	1.96 (1.71–2.25)	1.00 (0.96–1.10)	0.87 (0.83–0.90)
19 F	87% (65–95)	–	0.14 (0.13–0.15)	1.44 (1.26–1.65)	2.30 (2.20–2.40)	2.00 (1.90–2.00)
23 F	98% (80–100)	–	0.08 (0.08–0.09)	1.44 (1.22–1.70)	1.10 (1.10–1.20)	1.10 (1.00–1.20)
PCV13						
1	–	87% (77–93)	0.05 (0.04–0.05)	–	1.20 (1.20–1.30)	0.91 (0.87–0.95)
3	–	80% (30–95)	0.06 (0.06–0.06)	–	0.47 (0.45–0.49)	0.79 (0.76–0.82)
5	–	87% (77–93)	0.12 (0.11–0.13)	–	0.98 (0.92–1.00)	0.79 (0.75–0.83)
6A	–	86% (76–92)	0.08 (0.08–0.08)	–	1.90 (1.80–2.00)	1.20 (1.10–1.20)
7 F	–	97% (83–100)	0.09 (0.08–0.09)	–	2.20 (2.10–2.30)	1.70 (1.70–1.80)
19A	–	86% (71–94)	0.25 (0.23–0.26)	–	1.50 (1.40–1.60)	1.20 (1.20–1.30)

Serotype	PCV13 observed effectiveness, median % (95% CI) ^A	Protective antibody concentration (median (95% CI) µg/mL)	Predicted effectiveness, median % (95% CI)
3	26% (–69–68)	0.66 (0.34–∞)	62% (0–93)
1	84% (54–95)	0.64 (0.42–1.10)	72% (37–89)
6A	98% (64–100)	0.41 (0.05–1.53)	93% (37–100)

CI, confidence interval; PCV, pneumococcal conjugate vaccine; V114, 15-valent PCV; VE, vaccine effectiveness

^ASource: Andrews *et al.* (2014) [15].

Prédire l'efficacité du vaccin V114 contre la maladie pneumococcique invasive chez les enfants

Serotype	PCV7/13 Observed effectiveness, median % (95% CI) ^A	V114 Predicted effectiveness, median % (95% CI)
PCV7		
4	93% (65–99)	95% (41–100)
6B	94% (77–98)	86% (58–93)
9 V	100% (88–100)	99% (85–100)
14	94% (81–98)	91% (79–97)
18C	97% (85–99)	94% (62–99)
19 F	87% (65–95)	99% (90–100)
23 F	98% (80–100)	99% (81–100)
PCV13		
1	87% (77–93)	76% (58–86)
3	80% (30–95)	97% (67–100)
5	87% (77–93)	84% (69–91)
6A	86% (76–92)	59% (47–71)
7 F	97% (83–100)	93% (73–100)
19A	86% (71–94)	78% (55–88)

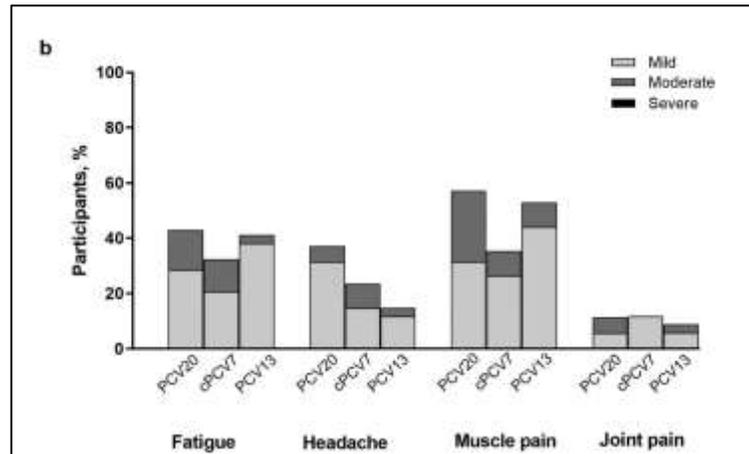
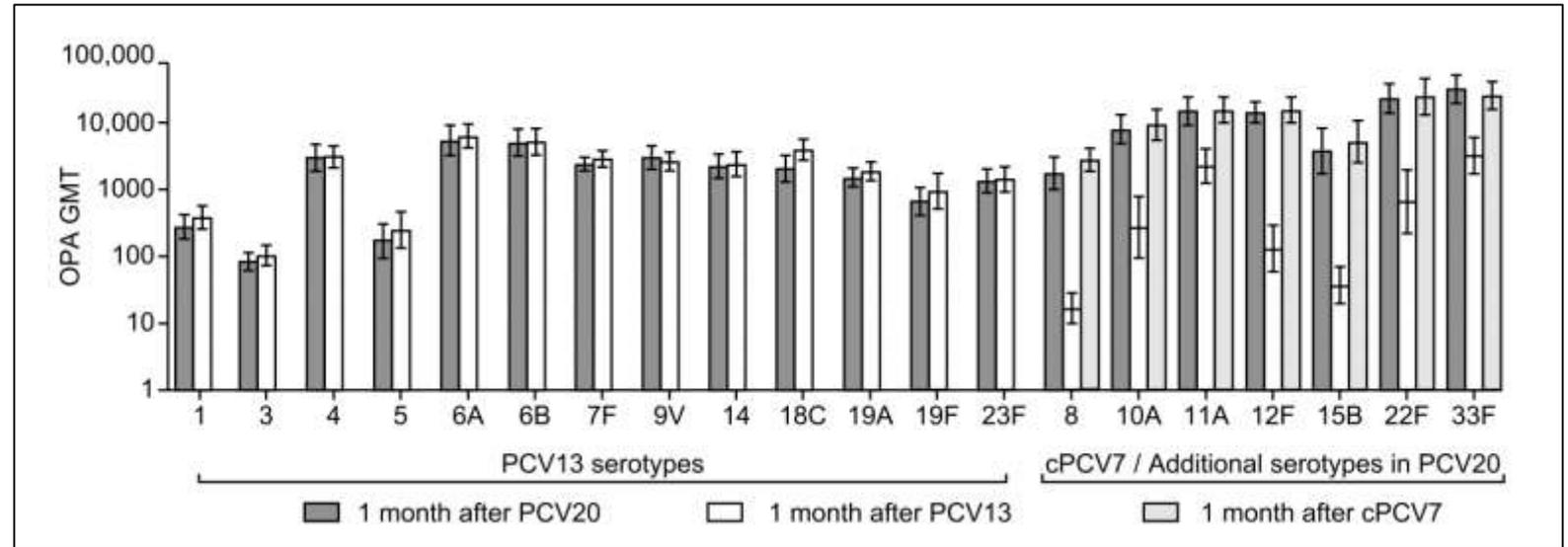
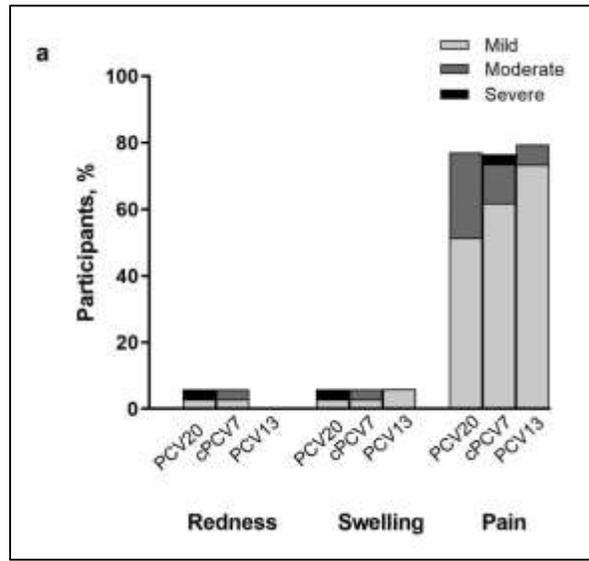
CI, confidence interval; PCV, pneumococcal conjugate vaccine; IPD, invasive pneumococcal disease; V114, 15-valent PCV

^ASources: for PCV7, De Serres *et al.* (2012) [21] and, for PCV13, Moore *et al.* (2016) [22].

Serotype	Protective antibody concentration (median (95% CI) µg/mL)
PCV7	
4	0.31 (0.13–0.98)
6B	0.40 (0.11–1.37)
9 V	0.13 (0.05–0.51)
14	0.95 (0.45–2.02)
18C	0.32 (0.13–0.74)
19 F	0.41 (0.17–1.04)
23 F	0.11 (0.03–0.55)
PCV13	
1	0.59 (0.47–0.79)
3	0.27 (0.17–0.61)
5	0.39 (0.29–0.53)
6A	1.04 (0.85–1.29)
7 F	0.62 (0.06–1.22)
19A	0.83 (0.68–1.16)

CI, confidence interval; PCV, pneumococcal conjugate vaccine; V114, 15-valent PCV

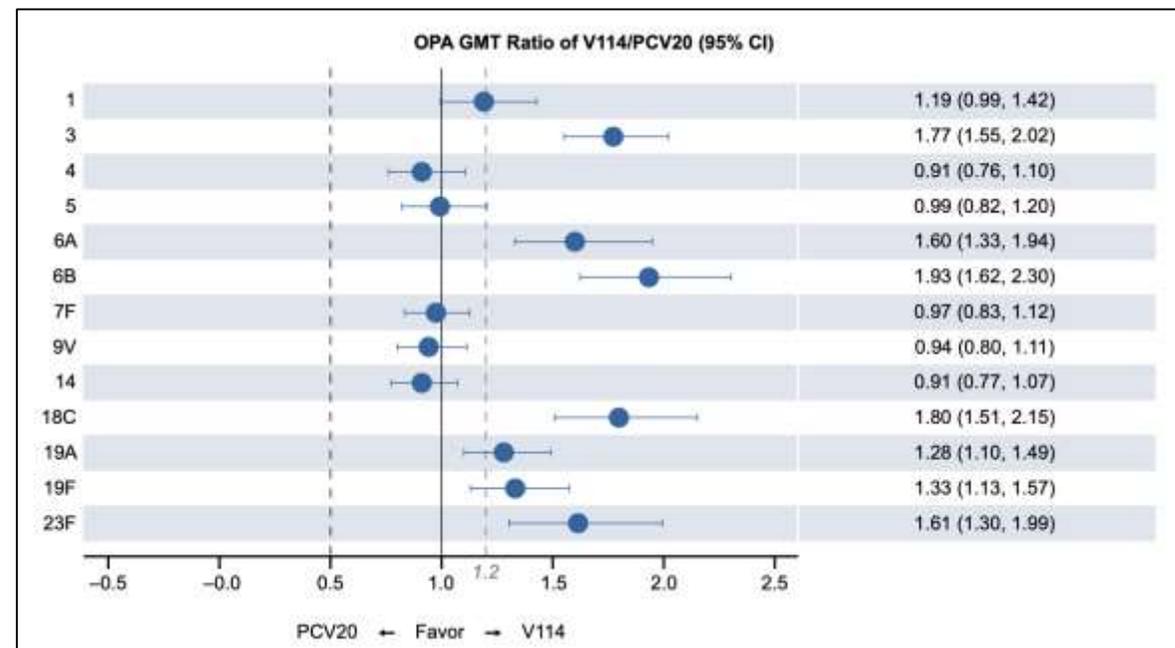
Une étude randomisée de phase 1 sur l'innocuité et l'immunogénicité de 2 nouveaux vaccins anti-pneumococciques conjugués chez des adultes japonais en bonne santé aux États-Unis



HUMAN VACCINES & IMMUNOTHERAPEUTICS 2021, VOL. 17, NO. 7, 2249–2256

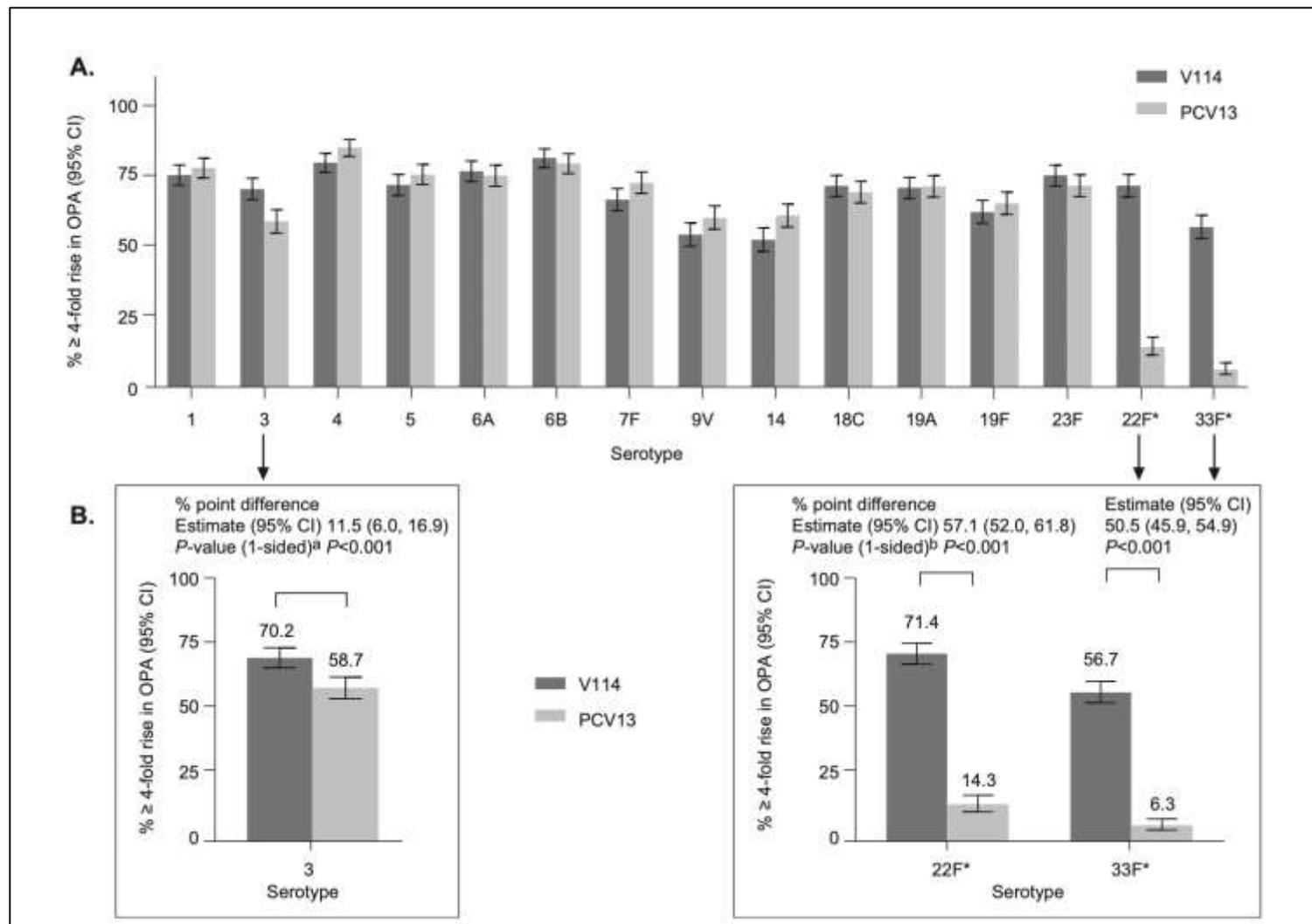
Comparaison indirecte ajustée par appariement des vaccins anti-pneumococciques V114 et PCV20

Serotype	V114:PCV13		PCV20:PCV13	V114:PCV20			
	Before matching (N1/N2 = 2,196/843)		After matching (N1/N2 = 1,580/562)	Before matching		After matching	
	GMT ratio (95% CI)	GMT ratio (95% CI)	GMT ratio (95% CI)	GMT ratio (95% CI)	p-value ^a	GMT ratio (95% CI)	p-value ^a
1	0.93 (0.81, 1.07)	0.95 (0.83, 1.09)	0.80 (0.71, 0.90)	1.17 (0.97, 1.40)	<0.001	1.19 (0.99, 1.42)	<0.001
3	1.65 (1.49, 1.82)	1.51 (1.36, 1.67)	0.85 (0.78, 0.93)	1.94 (1.69, 2.21)	<0.001	1.77 (1.55, 2.02)	<0.001
4	0.72 (0.64, 0.82)	0.74 (0.65, 0.84)	0.81 (0.71, 0.93)	0.89 (0.74, 1.07)	<0.001	0.91 (0.76, 1.10)	<0.001
5	0.78 (0.67, 0.90)	0.82 (0.71, 0.95)	0.83 (0.74, 0.94)	0.94 (0.78, 1.13)	<0.001	0.99 (0.82, 1.20)	<0.001
6A	1.09 (0.96, 1.23)	1.22 (1.08, 1.38)	0.76 (0.66, 0.88)	1.43 (1.18, 1.73)	<0.001	1.60 (1.33, 1.94)	<0.001
6B	1.48 (1.30, 1.67)	1.60 (1.42, 1.80)	0.83 (0.73, 0.95)	1.78 (1.48, 2.14)	<0.001	1.93 (1.62, 2.30)	<0.001
7F	0.80 (0.72, 0.88)	0.83 (0.75, 0.92)	0.86 (0.77, 0.96)	0.93 (0.80, 1.07)	<0.001	0.97 (0.83, 1.12)	<0.001
9V	0.87 (0.78, 0.96)	0.88 (0.79, 0.98)	0.93 (0.82, 1.05)	0.93 (0.79, 1.10)	<0.001	0.94 (0.80, 1.11)	<0.001
14	0.95 (0.85, 1.07)	0.91 (0.81, 1.02)	1.00 (0.89, 1.13)	0.95 (0.81, 1.13)	<0.001	0.91 (0.77, 1.07)	<0.001
18C	1.35 (1.21, 1.51)	1.53 (1.37, 1.71)	0.85 (0.74, 0.97)	1.59 (1.33, 1.89)	<0.001	1.80 (1.51, 2.15)	<0.001
19A	0.91 (0.83, 1.01)	1.03 (0.93, 1.13)	0.80 (0.71, 0.90)	1.14 (0.98, 1.33)	<0.001	1.28 (1.10, 1.49)	<0.001
19F	1.00 (0.91, 1.11)	1.07 (0.96, 1.18)	0.80 (0.70, 0.91)	1.25 (1.06, 1.48)	<0.001	1.33 (1.13, 1.57)	<0.001
23F	1.31 (1.15, 1.51)	1.34 (1.17, 1.53)	0.83 (0.70, 0.97)	1.58 (1.28, 1.96)	<0.001	1.61 (1.30, 1.99)	<0.001

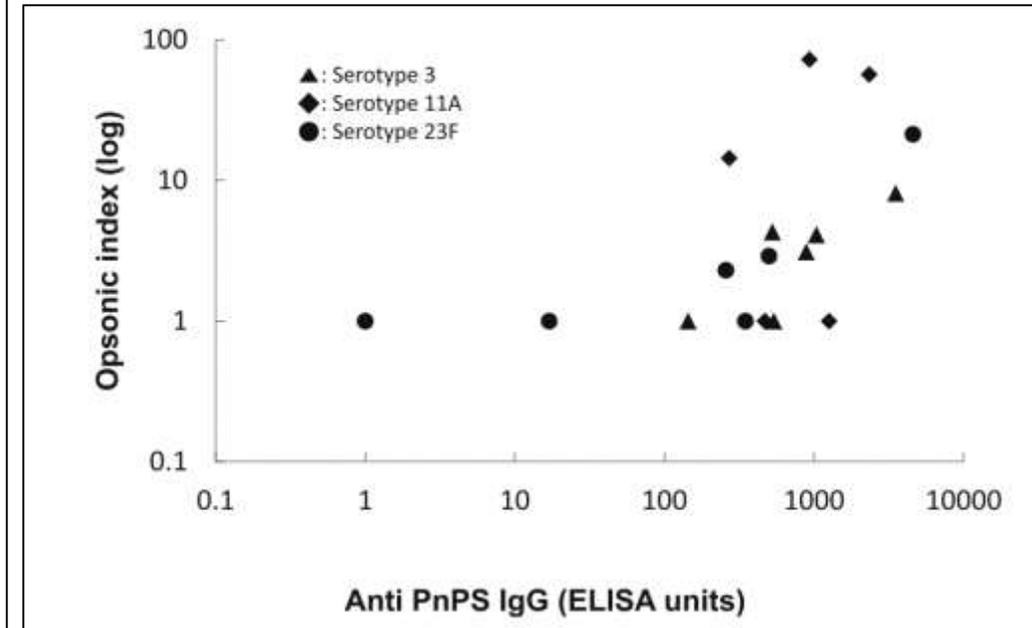
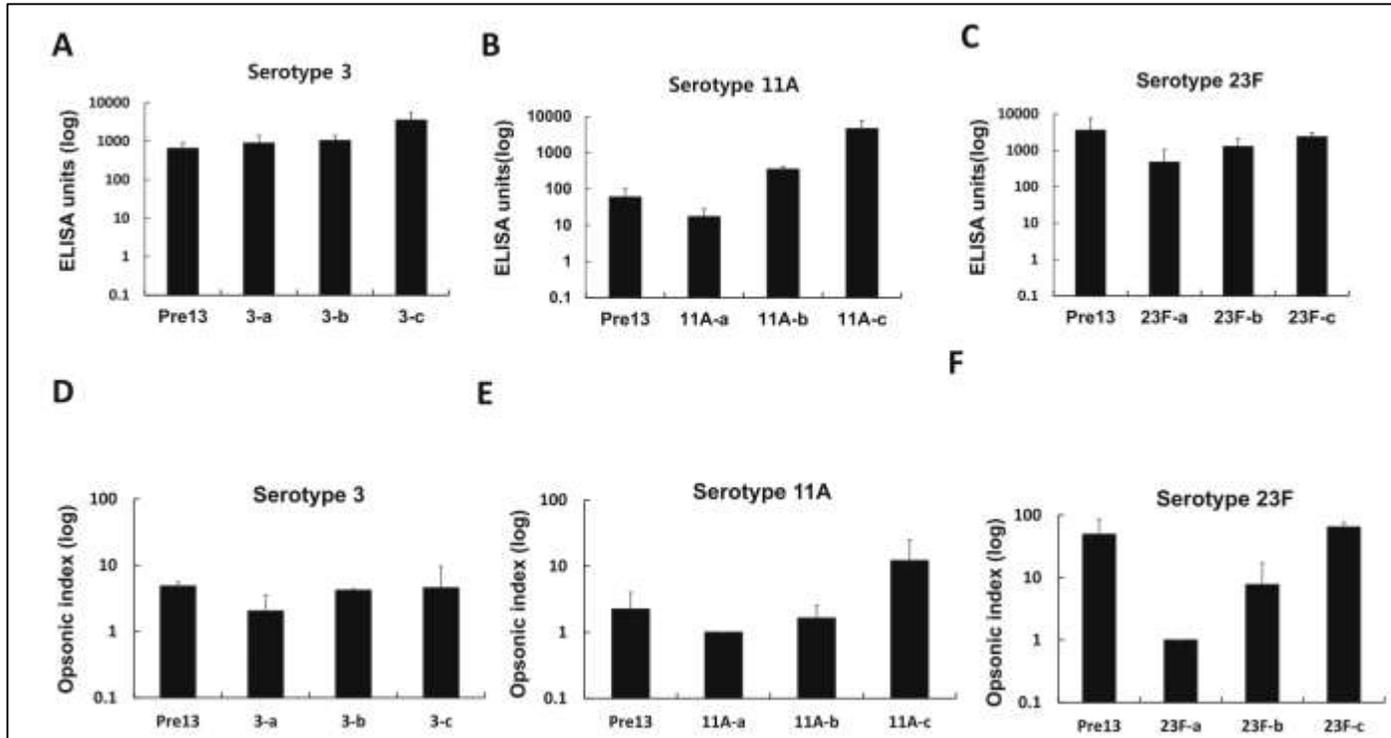


Un essai de phase 3 sur l'innocuité, la tolérabilité et l'immunogénicité du V114, vaccin conjugué contre le pneumocoque 15-valent, par rapport au vaccin conjugué contre le pneumocoque 13-valent chez les adultes de 50 ans et plus (PNEU-AGE)

Vaccine 40 (2022) 162–172



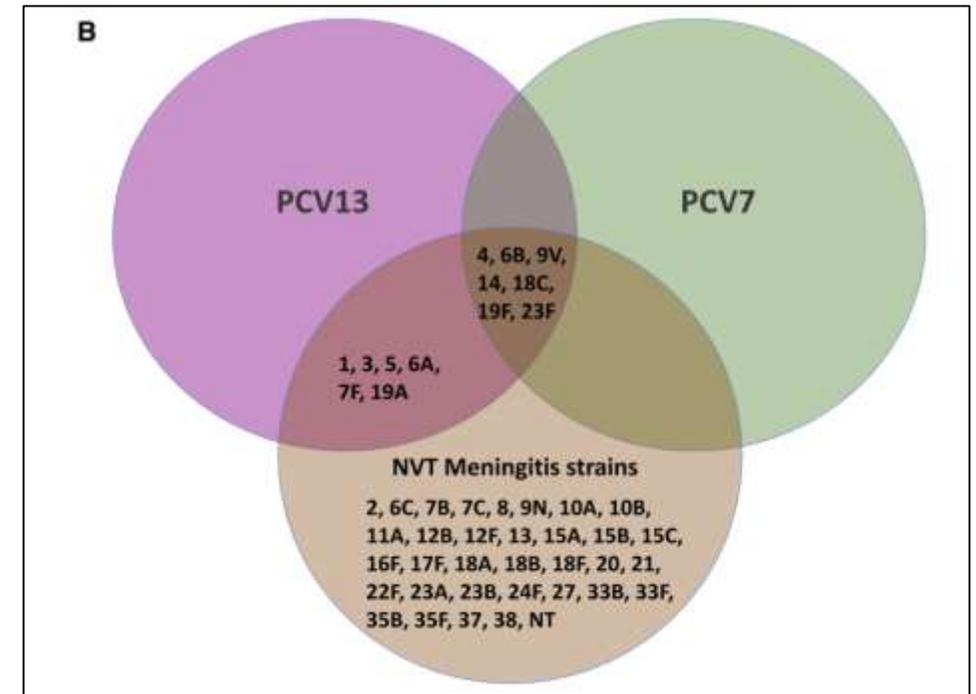
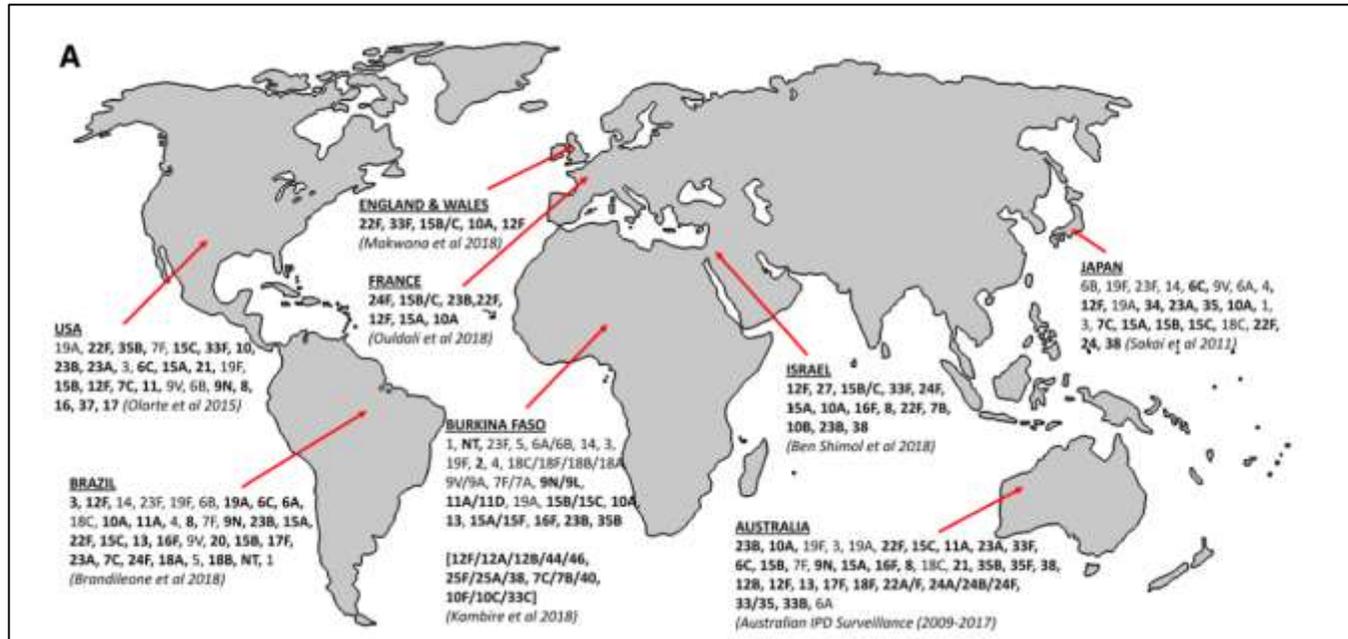
Développement d'un nouveau vaccin conjugué anti-pneumococcique 15-valent (PCV15) T et évaluation de son immunogénicité



Comparaison de l'immunogénicité d'un vaccin conjugué contre le pneumocoque de nouvelle génération chez des modèles animaux et des nourrissons humains

Pediatr Infect Dis J 2020;39:70-77

Une nouvelle stratégie est nécessaire pour prévenir la méningite à pneumocoques



Conclusions

- Vacciné n'est pas totalement protégé
- Sérotypes non vaccinaux
- Les vaccins ne sont pas efficaces à 100%
- Sérotipe 3 Reste une cause majeure d'IPD (pneumonies compliquées)
- Les méthodes moléculaires sont essentielles pour la détection
- Aucun autre avantage du PCV13 ne peut être attendu
- Principale cause de percées (efficacité du vaccin ?)
- Sérotipe 19A en baisse mais plus lent

Conclusions

- "Autres" sérotypes PCV13 toujours avec nous
- Le sérotype 19F est souvent le plus important
 - Résistant aux antimicrobiens
 - Diminution de l'importance mais maladie résiduelle résiliente



EQUALITY

EQUITY