Vaccins anti-méningocoque

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Paris : 28/02/2023

FOR RESEARCH, FOR HEALTH,
FOR OUR FUTURE

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Liens d'intérêt

- Travaux scientifiques à l'Institut Pasteur en collaboration et financement par GSK, Pfizer et Sanofi Pasteur.
- Conférences et advisory Boards pour GSK, Pfizer et Sanofi Pasteur.
- Financement des travaux de recherche par la Fondation TOTAL
- Brevet Bexsero *Neisseria meningitidis* X (Novartis/GSK).
- Brevets des tests rapides de diagnostic de *Neisseria meningitidis.*
- Crédit institutionnel pour réaliser des formations internationales sur la méningite (Pfizer).
- Président de l'European Meningococcal and Haemophilus Disease Society (EMGM).
- Membre du Global Meningococcal Initiative (GMI)
- Membre du Task Force de l'OMS pour « Defeating meningitis by 2030)

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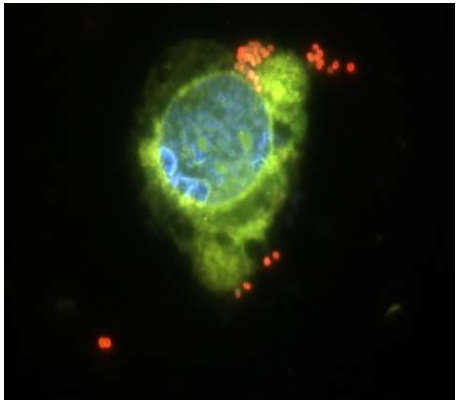
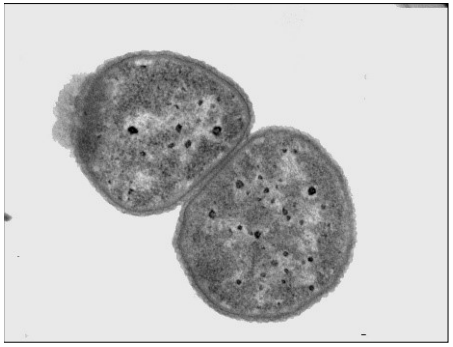
Neisseria meningitidis





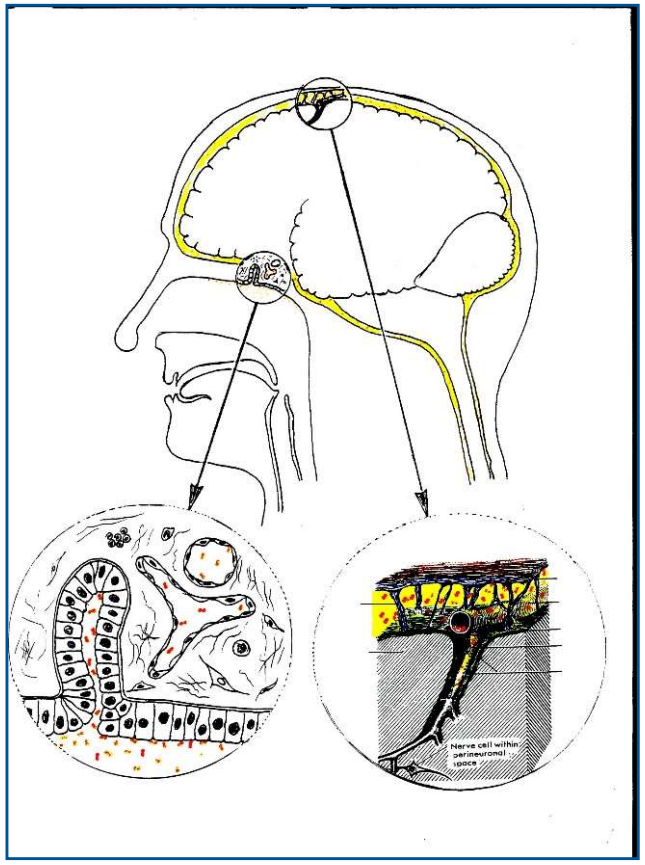
- **Encapsulated bacterium**
- **Only encountered in humans**
- **Inter-human transmission (respiratory but also sexual transmission)**
- **Highly variable (Transformation & recombination)**

Frequent asymptomatic carriage (10%)

Invasive infections:
Even treated, IMD still has a case fatality rate of about 10%

Invasive infections:
Sporadic forms : Europe. America
Incidence 0.11-2 per 100 000 (Europe)

Epidemic forms : Africa (meningitis belt).
Incidence up to 1000 per 100 000



Source data WHO and ECDC; Photo MK Taha

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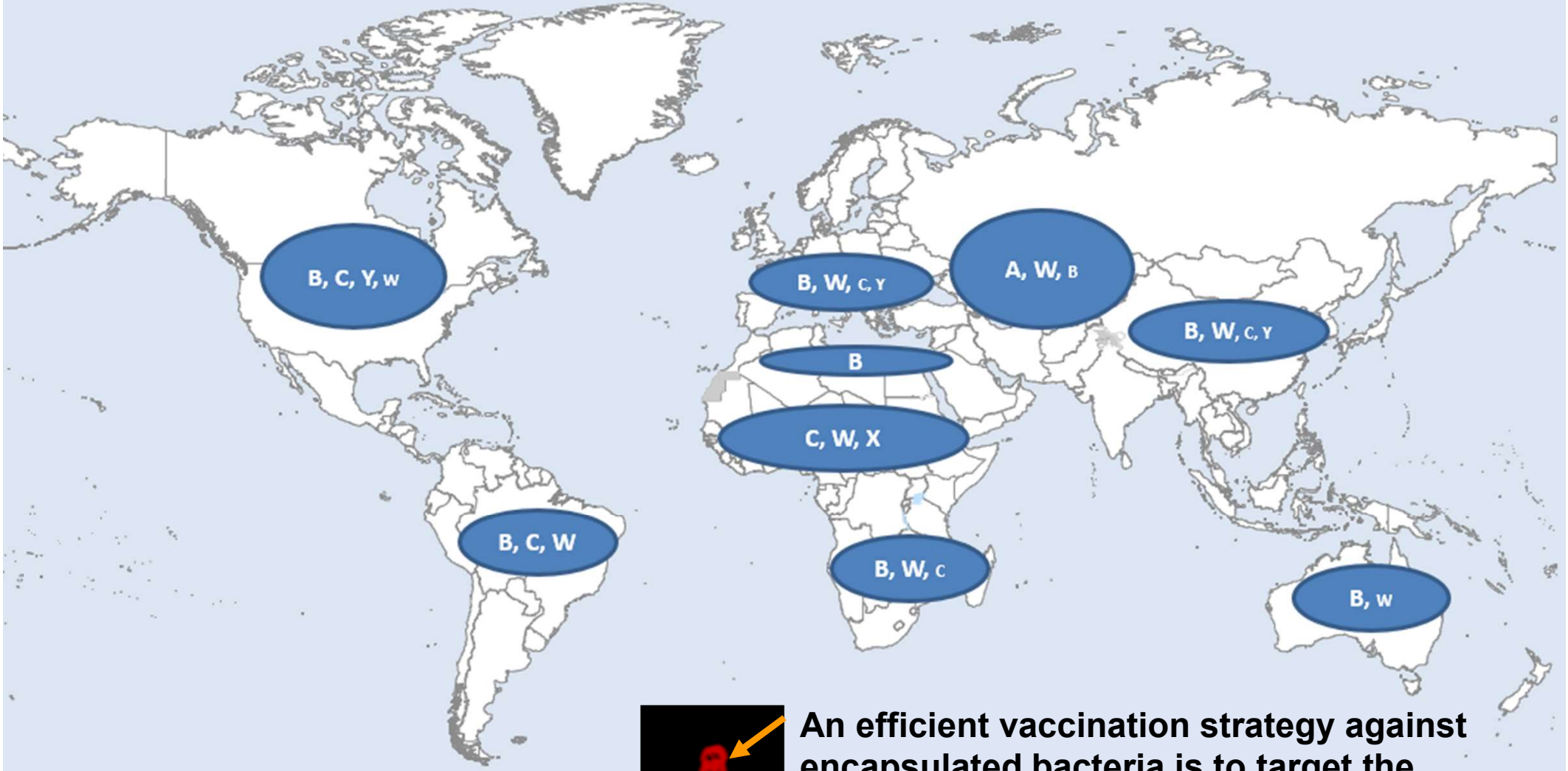
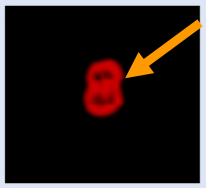
Invasive Meningococcal Disease – Serogroup distribution, 2019

World Health Organization

Map date: January 2020





An efficient vaccination strategy against encapsulated bacteria is to target the capsule (abundant surface exposed antigen)

SEROGROUP Most frequent

SEROGROUP Less frequent

Data Source: World Health Organization
Map Production: WHO Health Emergencies Programme

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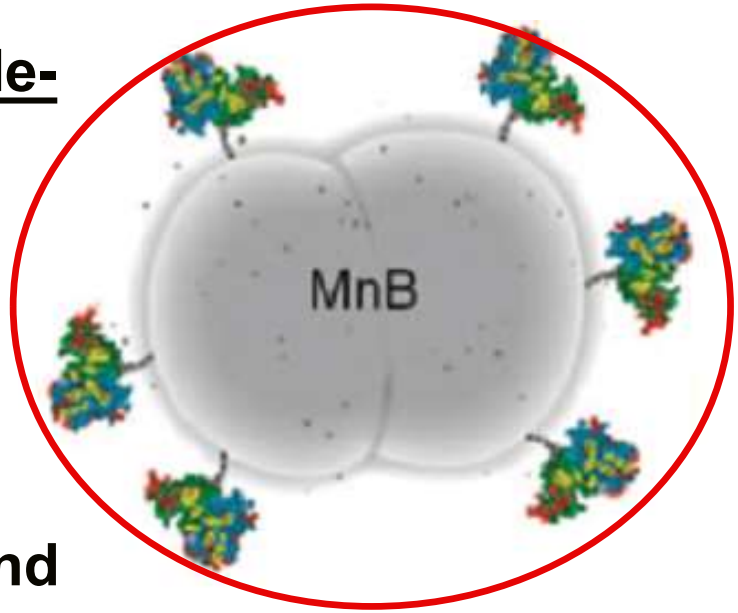
Vaccines against meningococci

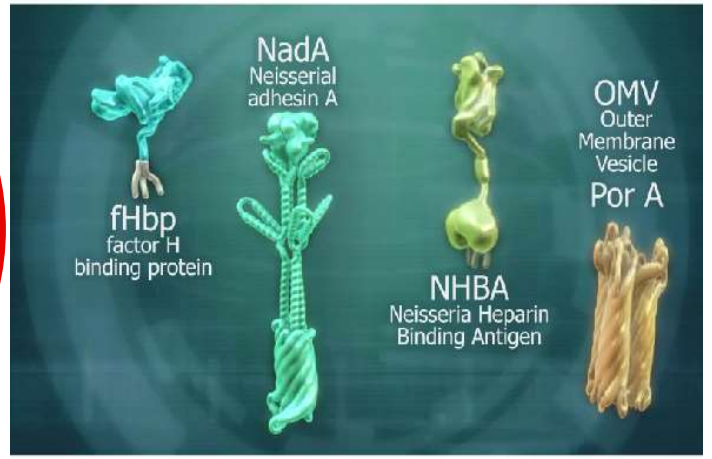
Capsular polysaccharide-based vaccines:

Monovalent: A, C

Tetravalent ACWY

Pentavalents ACWYX and ABCWY
(underdevelopment)





Conjugate capsular polysaccharide-based vaccines

- Impact on carriage
- Persistence of the immune response

4CMenB (2 months)

50 µg each
25 µg of OMV NZ98/254,
1.5 of mg aluminum hydroxide

Bivalent MenB-FHbp (10 years old)

60 µg of each fHBP variant
0.25 mg aluminum phosphate

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Les vaccins disponibles

Serogroup	**Type of the vaccine**	Brand	PS	carrier	**Use**
A	Conjugate monovalent	MenAfriVac® Serum Institute of India		TT	• 1-29 y (catch-up ≥ 9 months
C	Conjugate monovalent	Neisvac ® (PFIZER) Menjugate ® (GSK)	10 10	TT CRM-197	• ≥ 2 months
A **C** **Y** **W**	Conjugate tetravalent	Menveo® (GSK)	10, 5, 5,5	CRM-197	• ≥ 2 y
		Nimenrix® (PFIZER)	5, 5, 5,5	TT	•≥ 6 weeks
		Mencatra® Menquad® SANOFI PASTEUR	4, 4, 4, 4 10, 10, 10, 10	Diphtheria toxoid TT	US 9 months-55 y ≥ 2 y
B	Protein-based vaccines	Bexsero ® (GSK)			•≥ 2 months
		Trumenba ® PFIZER			• ≥ 10 y

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Conjugated Vaccines vs plain polysaccharide vaccines

- Higher quantity of IgG (conjugated vaccines)
- IgG:IgM ration increases (booster) for conjugated vaccines
- Hypo-responsiveness after repeated doses with plain polysaccharide vaccines
- Avidity maturation of antibodies upon booster (conjugated vaccines)
- Memory cell response (conjugated vaccines)
- Impact on carriage acquisition (conjugated vaccines)

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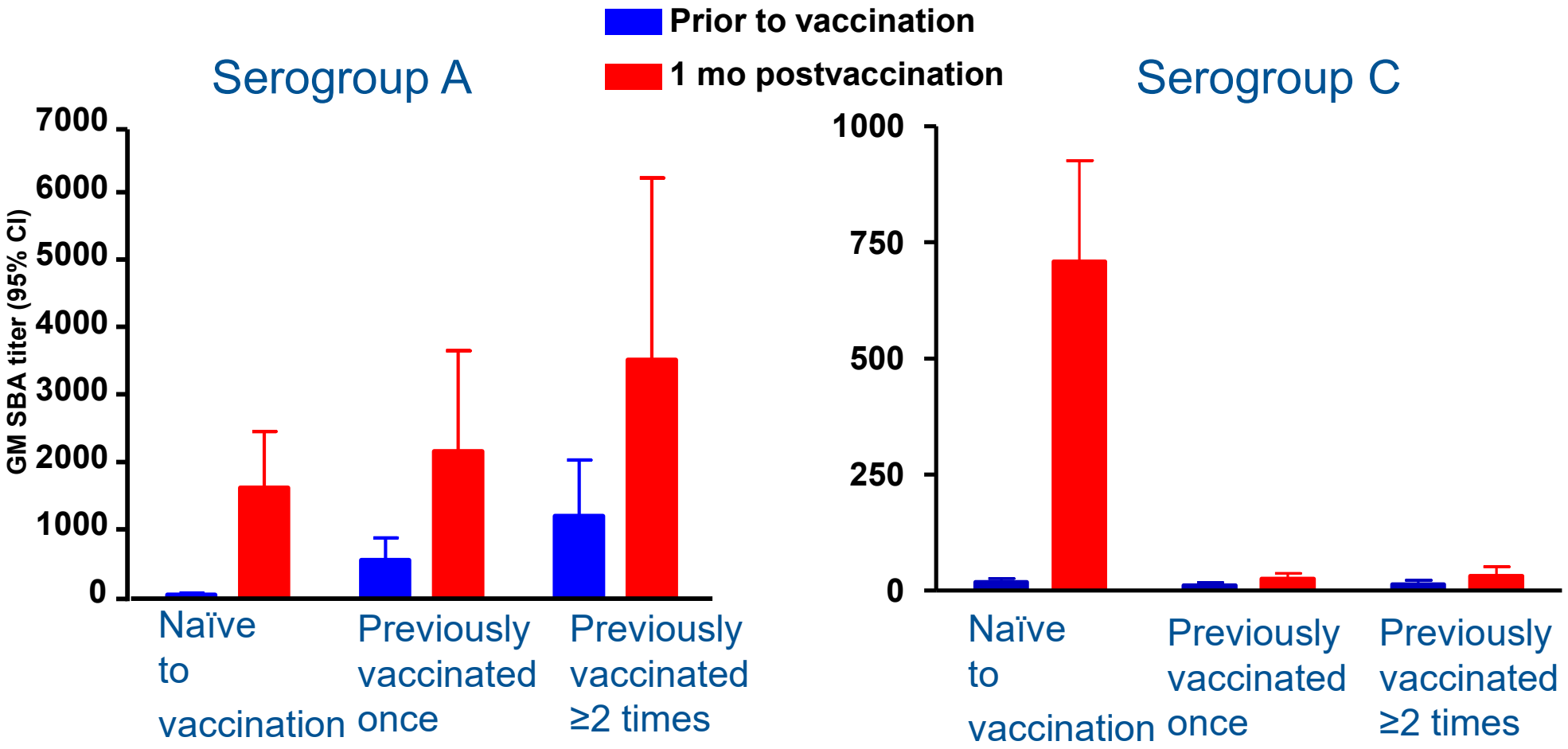
Hyporesponsiveness

Saudi Arabia: **Subjects aged 10 to 29 : 38 subjects naïve, 79 subjects with one prior vaccination with the MACP vaccine, and113 subjects with two or more prior vaccinations with the MACP vaccine.**



Jokhdar et al., 2004

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Correlate of protection

	Bactericidal titer ≥4		
	Group Cases	Group Control	*P*
Bacterial strain tested	**3/54 (5,6%)**	**444/540 (82%)**	**<0.001**

Three values are considered for vaccine licensure:

% of subjects with a titer ≥4

% of subjects with four fold increase of bactericidal titer

Geometric mean of titers of all subjects

Goldschneider et al., 1969 J Exp Med

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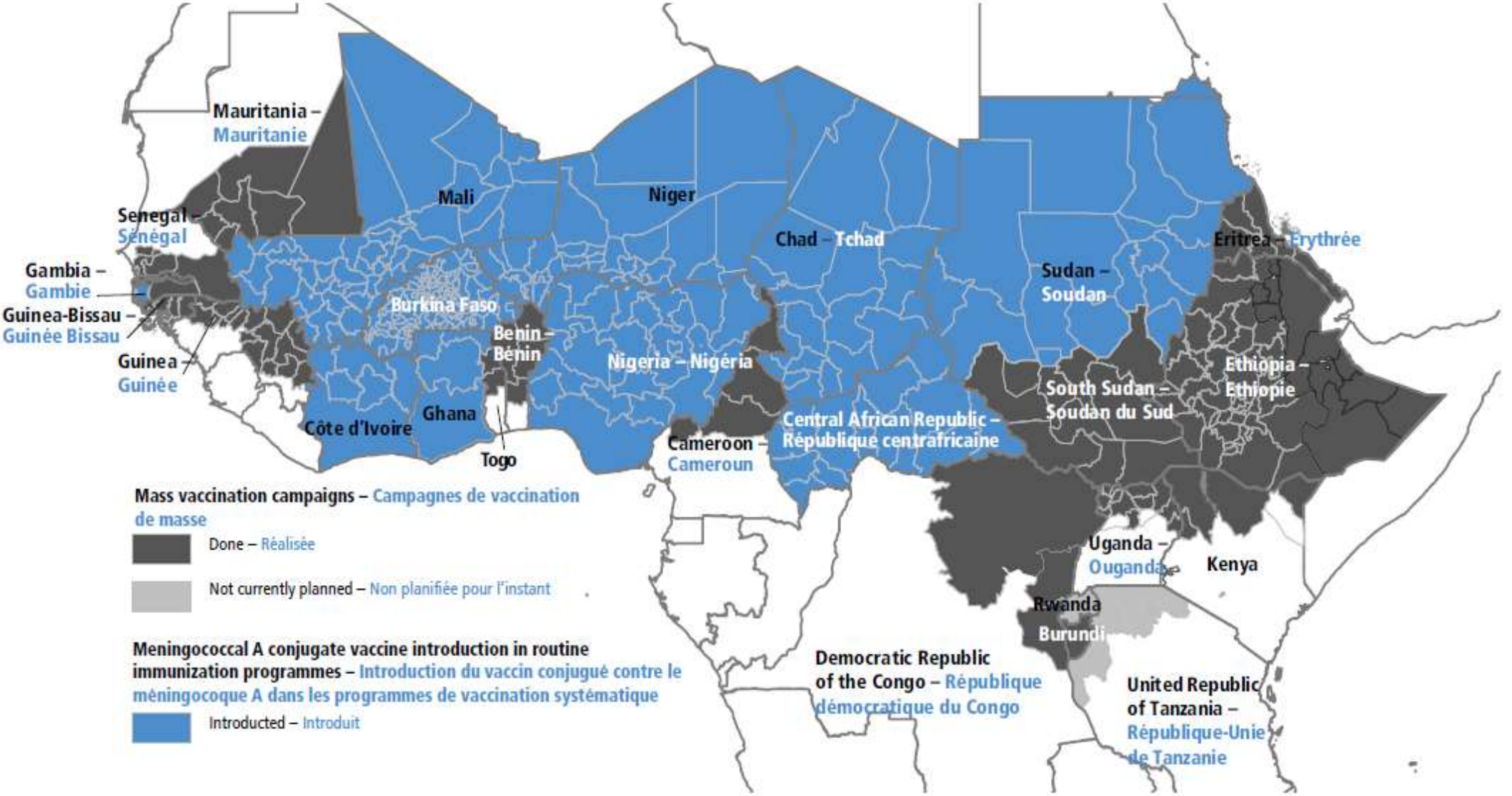
Map 1 **Meningococcal A conjugate vaccine introduction in countries of the African meningitis belt. 2010–2019[a]**

Carte 1 **Introduction du vaccin conjugué contre le méningocoque A dans les pays de la ceinture africaine de la méningite, 2010-2019[a]**



[a] Countries depicted as having introduced in routine immunization, also conducted mass vaccination campaigns (not shown), either nation-wide or only on high-risk areas. – Les pays représentés comme ayant été introduits dans les programmes de vaccination systématique, ont également mené des campagnes de masse préventive (non illustré), soit à l'échelle du pays ou dans les zones où le risque est élevé.

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. – Les appellations employées dans la présente publication et la présentation des données qui y figurent n'impliquent de la part de l'Organisation mondiale de la Santé aucune prise de position quant au statut juridique des pays, territoires, villes ou zones, ou de leurs autorités, ni quant au tracé de leurs frontières ou limites. Les lignes en pointillé sur les cartes représentent des frontières approximatives dont le tracé peut ne pas avoir fait l'objet d'un accord définitif.

Table 2 **Number of cerebrospinal fluid (CSF) samples collected and pathogens identified from suspected meningitis cases, in countries under enhanced surveillance in Africa, 2019[a]**

Tableau 2 **Nombre d'échantillons de liquide céphalorachidien (LCR) prélevés et agents pathogènes identifiés chez les cas suspects de méningite dans les pays placés en surveillance renforcée en Afrique, saison 2019[a]**

Country – Pays	No. CSF samples – Nombre d'échantillons de LCR		No. CSF positive samples – Nombre d'échantillons de LCR positifs		*N.m.* A		*N.m.* C		*N.m.* X		*N.m.* W		Other *N.m.* – Autres *N. m.*		*Spn*		*Hib*		Other pathogens – Autres pathogènes	
	Season – Saison	Annual – Annuel	Season – Saison	Annual – Annuel	Season – Saison	Annual – Annuel	Season – Saison	Annual – Annuel	Season – Saison	Annual – Annuel	Season – Saison	Annual – Annuel	Season – Saison	Annual – Annuel	Season – Saison	Annual – Annuel	Season – Saison	Annual – Annuel	Season – Saison	Annual – Annuel
Benin – Bénin	236	400	3	11	0	0	0	5	0	0	1	1	0	0	2	3	0	2	0	0
Burkina Faso	1596	1754	142	215	0	0	59	75	12	20	0	0	0	0	57	95	12	17	2	8
Cameroon – Cameroun	46	60	3	3	0	0	0	0	0	0	1	1	0	0	1	1	1	1	0	0
Central African Republic – République centrafricaine	260	661	2	32	0	0	0	0	0	0	0	2	0	0	0	21	0	0	2	9
Chad – Tchad	629	739	200	229	0	0	0	0	22	25	81	91	NI	7	65	84	14	20	1	2
Ghana	632	952	50	88	0	0	1	1	0	0	10	11	0	0	11	41	0	0	28	35
Mali	310	648	57	86	0	0	3	3	1	1	0	0	0	0	34	49	14	17	5	16
Niger	865	1092	290	310	0	0	124	129	56	56	3	3	NI	0	92	105	14	17	0	0
Nigeria – Nigéria	337	441	101	122	0	0	31	47	16	19	2	7	NI	0	39	42	6	7	0	0
Senegal – Sénégal	126	126	1	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0
South Sudan – Soudan du Sud	9	9	2	2			0	0	0	0	0	0	0	0	2	2	0	0	0	0
Togo	1102	1924	136	141	0	0	104	104	6	6	1	1	0	0	20	22	3	3	2	5
Total	**6148**	**8806**	**962**	**1240**	**0**	**0**	**322**	**364**	**113**	**127**	**100**	**118**	**NI**	**7**	**323**	**465**	**64**	**84**	**40**	**75**

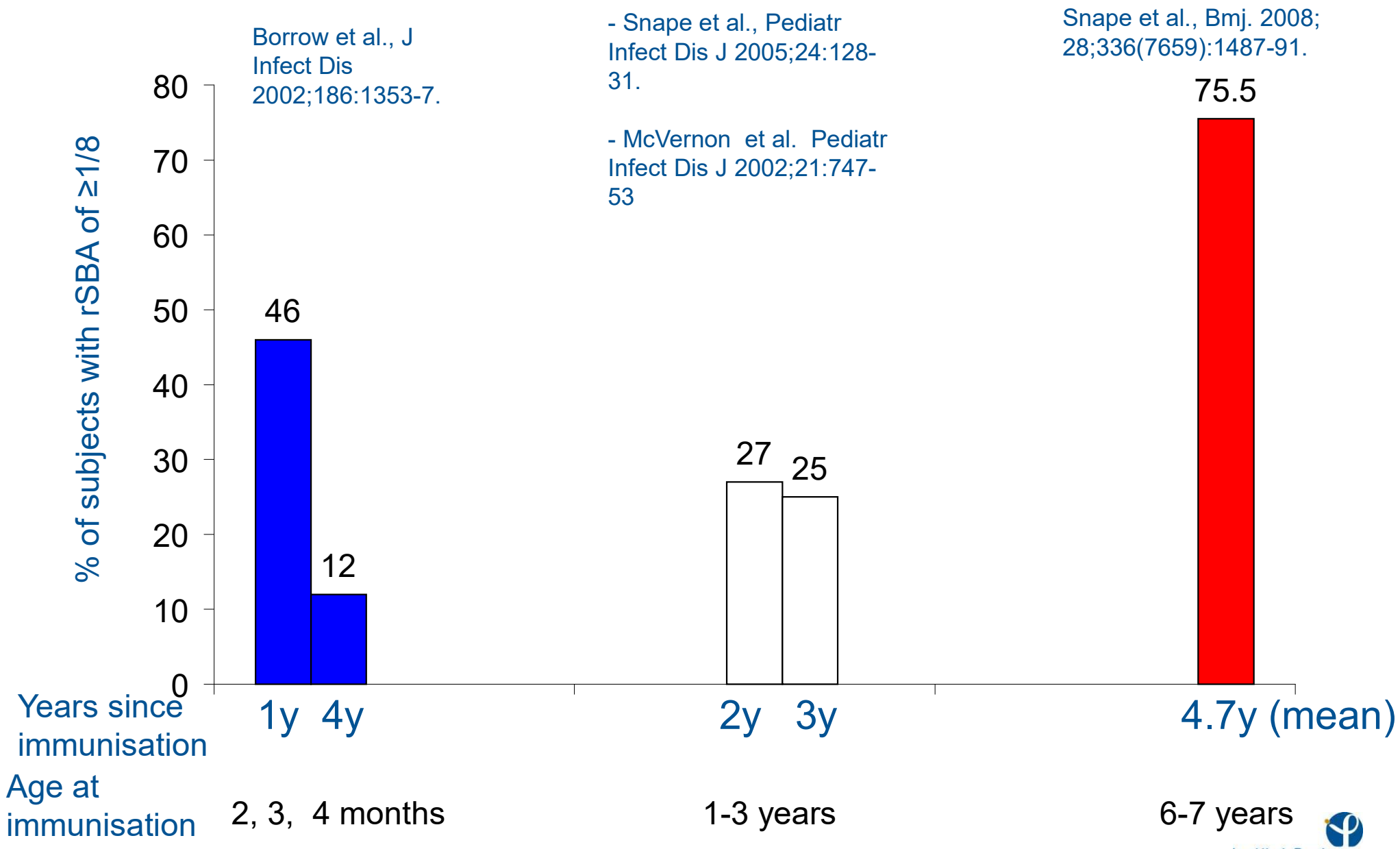
[a] Data for epidemic seasons (weeks 1–26) and for the whole year (weeks 1–52). – Données pour la saison épidémique (semaines 1-26) et pour toute l'année (semaines 1-52).

N.m. – Neisseria meningitidis; *Spn* – *Streptococcus pneumoniae*; *Hib* – *Haemophilus influenzae* type b.

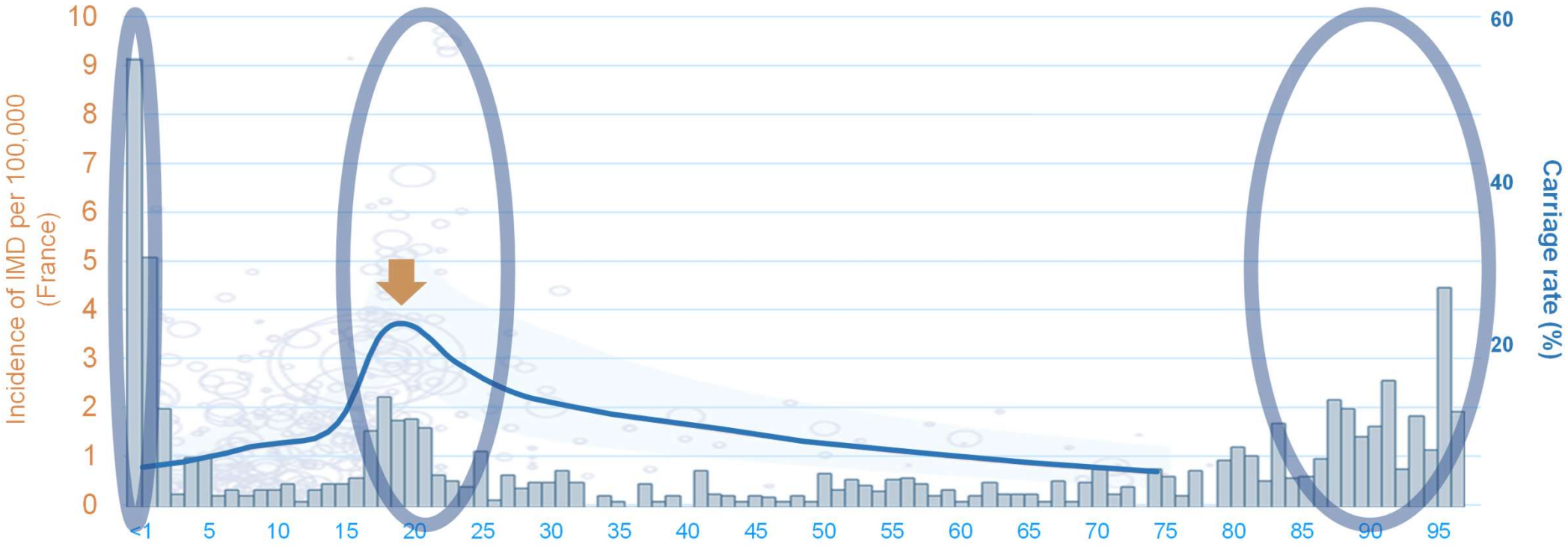
NI: noninterpretable. – NI: non interprétable.

Source: WHO/AFRO Inter country Support Team for West Africa. Meningitis Weekly Bulletin. – Source: OMS/AFRO Equipe d'appui inter-pays pour Afrique de l'Ouest. Bulletin hebdomadaire sur la méningite cérébrospinale.

Persistence of bactericidal titers



Invasive meningococcal disease and meningococcal carriage



https://www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-a-prevention-vaccinale/infections-invasives-a-meningocoque/documents/bulletin-national2/les-infections-invasives-a-meningocoque-en-france-en-2019 [Accessed.
Christensen H, et al., Lancet Infect Dis. 2010;10(12):853-861.

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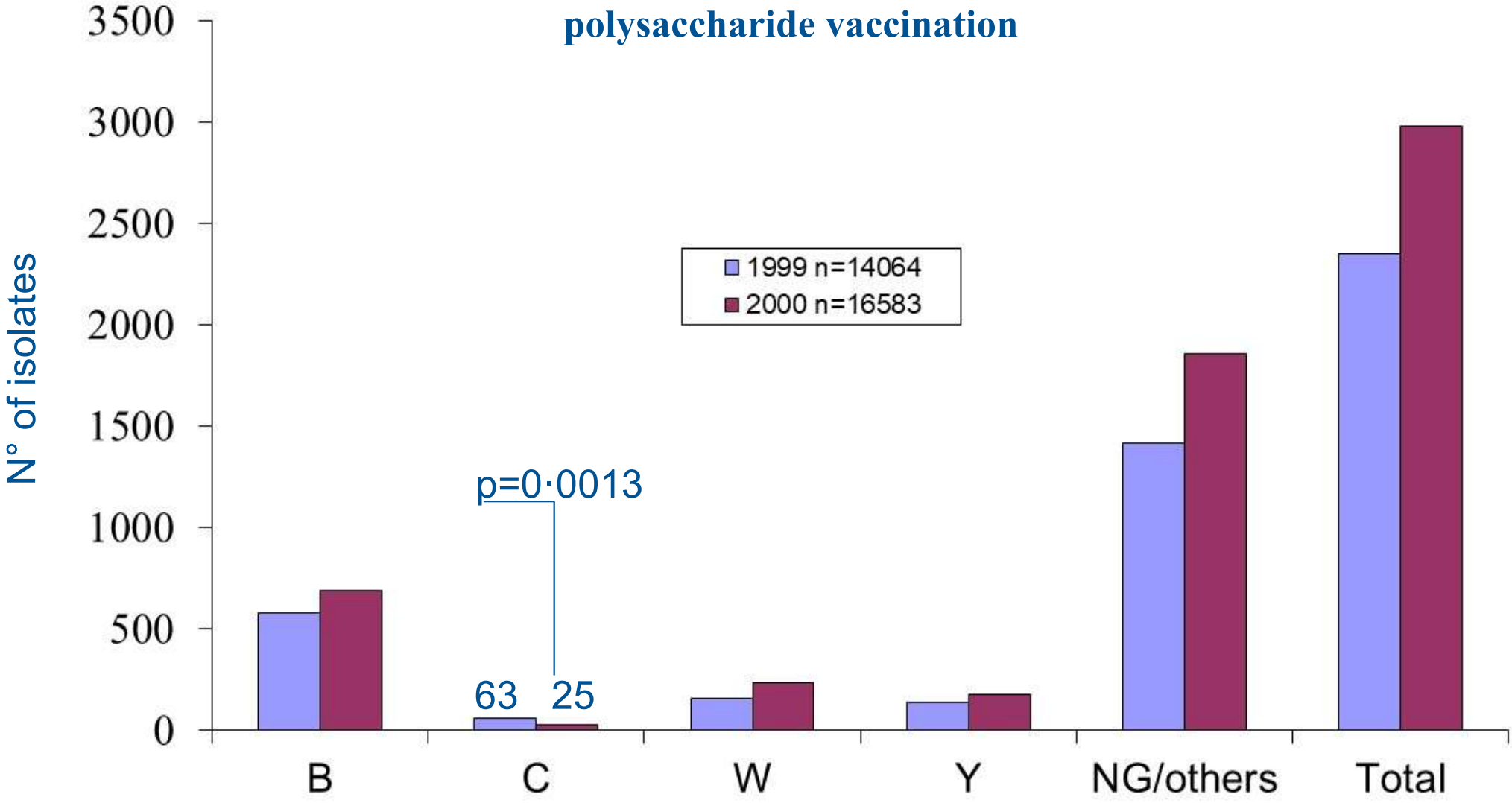
Impact of MenCC on carriage

Carriage of serogroup C meningococci 1 year after meningococcal C conjugate polysaccharide vaccination



Maiden and Stuart, Lancet. 2000

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Evolution des recommandations de la vaccination contre MenC : Royaume-Uni

Introduction de la vaccination	Classes d'âge ciblées par la vaccination
Novembre 1999	Nourrissons <1an: 3 doses; Nourrissons de 12-15mois: 1 dose; Ado 15-17 ans: 1 dose;
De janvier à octobre 2000	Rattrapage avec une dose unique des enfants de <24 mois + aux ado jusqu'à 19 ans
Janvier 2002	Extension du rattrapage avec une dose unique chez les 20-24 ans
Septembre 2006	Changement de schéma pour les <12 mois: 2 doses + une dose à 12 mois
Juin 2013	Changement de schéma pour les <12 mois: une dose + une dose à 12 mois+ un rappel à14 ans MCC

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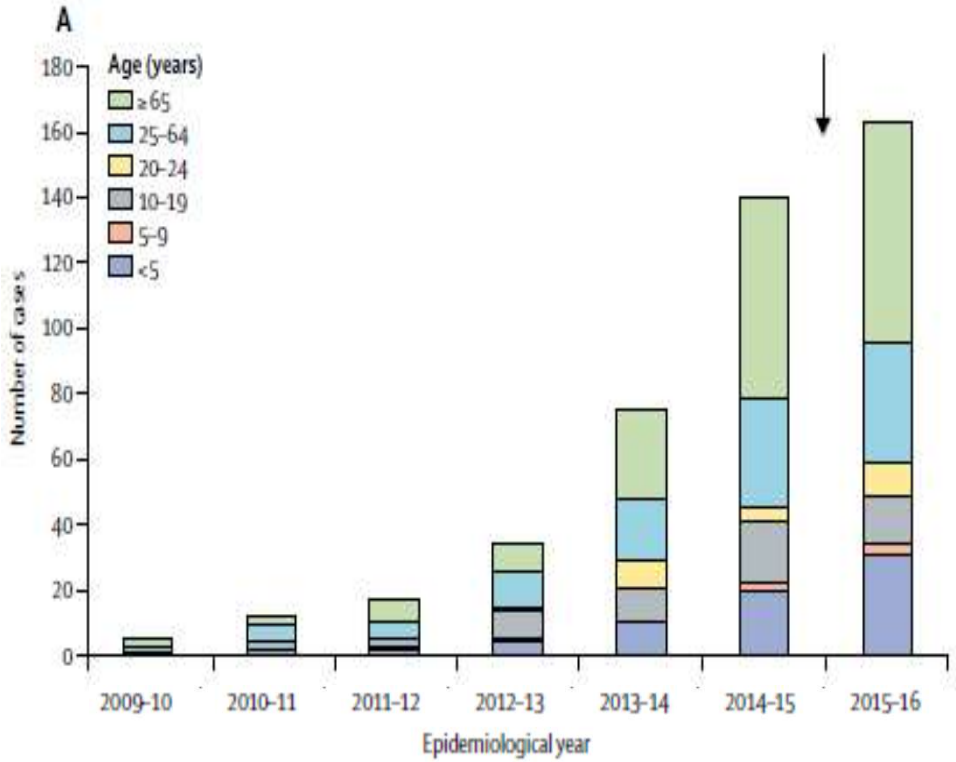
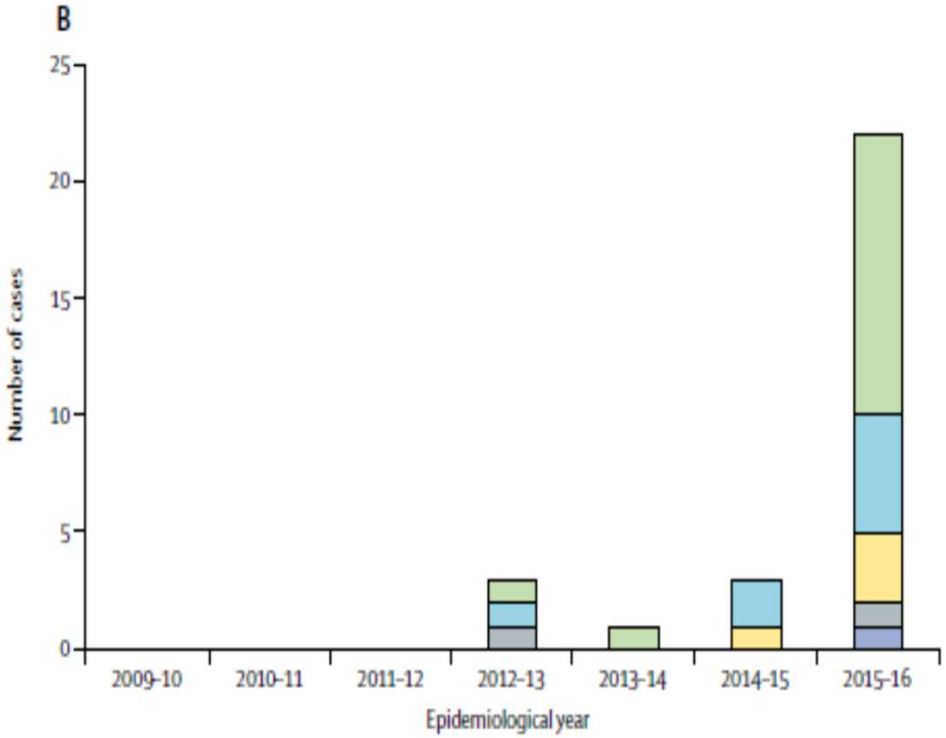
N° IMDW disease caused by the South American MenW:cc11 strain sublineages

England



The Netherlands



Knol et al., 2017 Lancet Public Health

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Juin 2013	Changement de schéma pour les <12 mois: une dose + une dose à 12 mois+ un rappel à14 ans MCC
Septembre 2015	Changement de schéma pour les <12 mois: une dose à 12 mois+ un ACWY à14 ans + Rattrapage (ACWY) 13-18 ans 4CMenB (2+1: 2, 4, and 12 mois).
Août 2022 JCVI interim statement 05/08/22 la protection directe pendant la petite enfance n'est plus nécessaire	Abandonner la dose contenant du MenC pour les nourrissons un ACWY à14 ans 4CMenB (2+1: 2, 4, and 12 mois).

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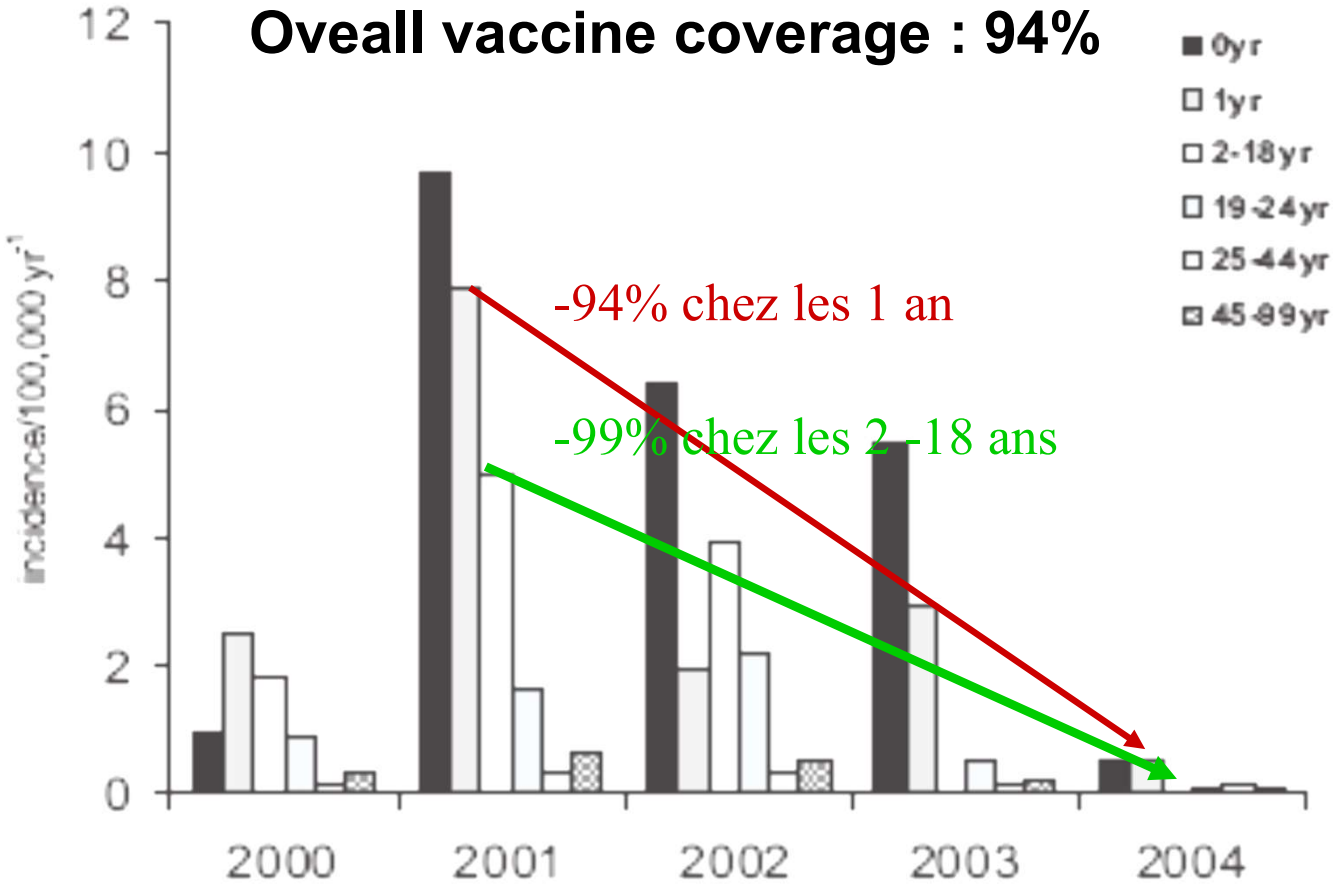
Direct and indirect impacts of MCC Vaccination: The Netherlands

Recommendation June 2002 = 1 dose at 14 months + catch-up 2-18 years-old



- May 2018, MenACWY vaccination replaces MenC vaccination at age 14 months
- and from October 2018, 13–14 year-olds are offered MenACWY vaccination.
- If risk group, a bosster every 5 years if risk persists

Knol et al., EUROSURVEILLANCE, 2018 (April) : 23 (16): 2-6

de Greeff SC et al., Pediatr Infect Dis J 2006; 25:79-80.

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Stratégie vaccinale : France

AVIS DU CONSEIL SUPERIEUR D'HYGIENE PUBLIQUE DE FRANCE
SECTION MALADIES TRANSMISSIBLES

Relatif à la vaccination par le vaccin conjugué contre le méningocoque C

(Séance du 15 novembre 2002)

- Il n'y a pas lieu de recommander la vaccination généralisée aux nourrissons, enfants, adolescents ou adultes jeunes à l'échelon national.

- La vaccination reste recommandée pour les groupes à risque suivants :

sujets contacts

dans les zones délimitées où l'incidence du méningocoque de sérogroupe C est particulièrement élevée.

enfants souffrant de déficit en fractions terminales du complément, en properdine ou ayant une asplénie anatomique ou fonctionnelle.

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Pourquoi ne pas recommander la vaccination généralisée?

- Variation cyclique des IIMC
- Différence de l'épidémiologie entre les pays en Europe
- Capsule switching

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Men-C vaccination campaigns at a district level, France

	Clermont-Ferrand (1 district)	South-West (3 districts)	Haute-Vienne (1 district)
Year	2001	2002	2007
Total population	600,000	220,000 600,000 300,000	350,000
Number of cases within 52 weeks (Inc rates)	11 (1.7)	7 (3.1) 12 (2.0) 6 (1.8)	7 (2.0)
% of serogroup C	71 %	93 %	100 %
CFR	27 %	20 %	43 %
Strains group/CC	C/CC11	C/CC11	C/CC11

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Rationnel d'une recommandation généralisée

- **La France montrait l'un des taux d'incidence d'infections invasives (IIMC) à méningocoque C les plus élevés d'Europe**
- **Augmentation des alertes.**
- **Association spatio-temporelle entre grippe et IIM**
- **Émergence d'un nouveau clone virulent (++Mortalité et %PF)**
- **Analyse médico-économique**
- **Efficacité clinique démontrée à travers les programmes de vaccination généralisée en Europe**
- **Pas d'expansion de switch capsulaire**

Avis du HCSP du 24 avril et 26 juin 2009 relatif à la vaccination par le vaccin méningococcique conjugué de sérogroupe C

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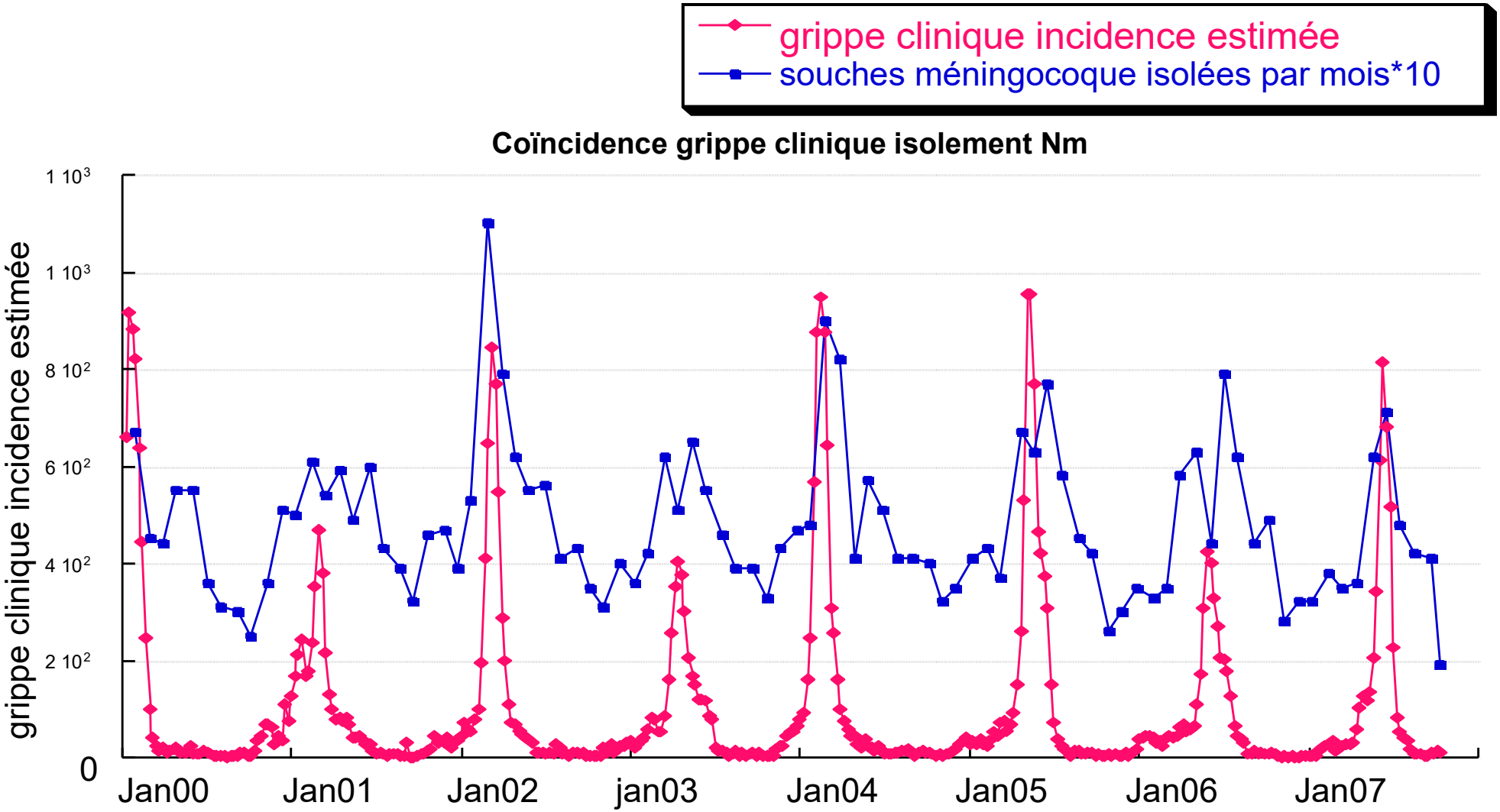
Grippe et méningocoque



Données du CNR du Méningocoque et des réseaux sentinelles de surveillance de la grippe

Rameix-Welti MA et al. Infect Immun 2009.

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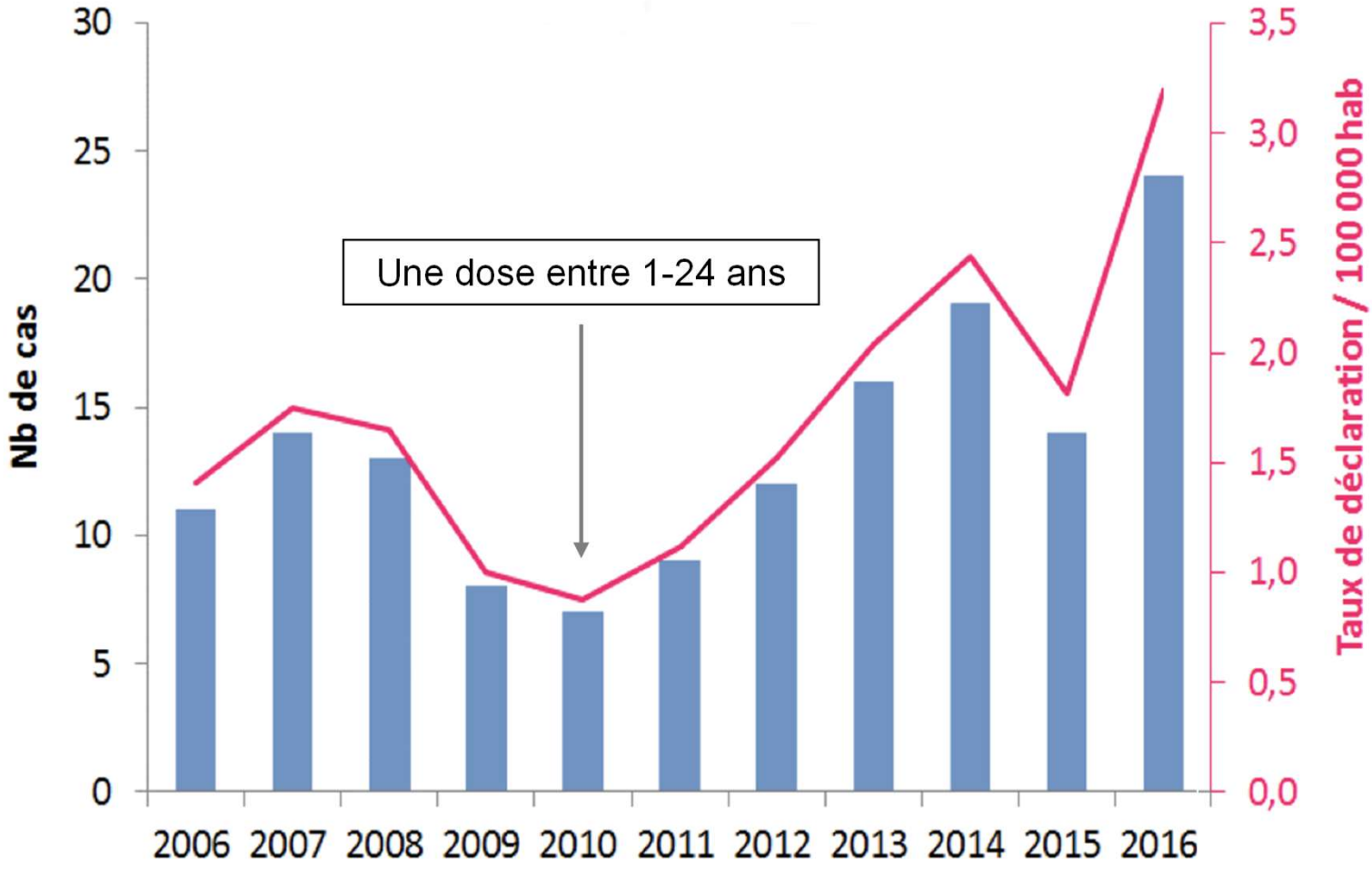
Evolution des recommandations vaccinales contre les IIMC, France, 2006-2016



https://www.santepubliquefrance.fr/content/download/288813/2762761

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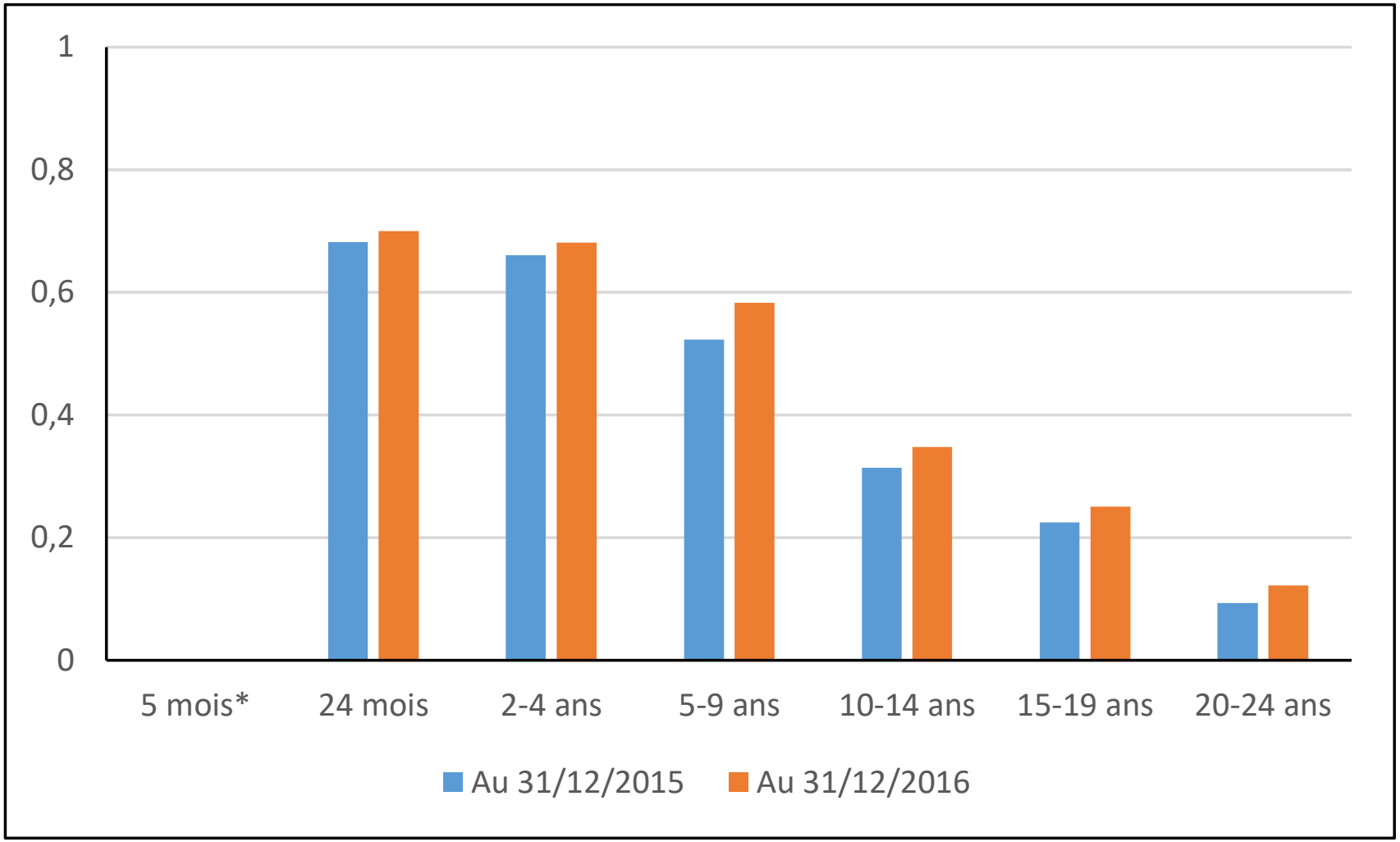
Couverture vaccinale en France MCC: France



source : SNDS-DCIR, données au 31/12/20)

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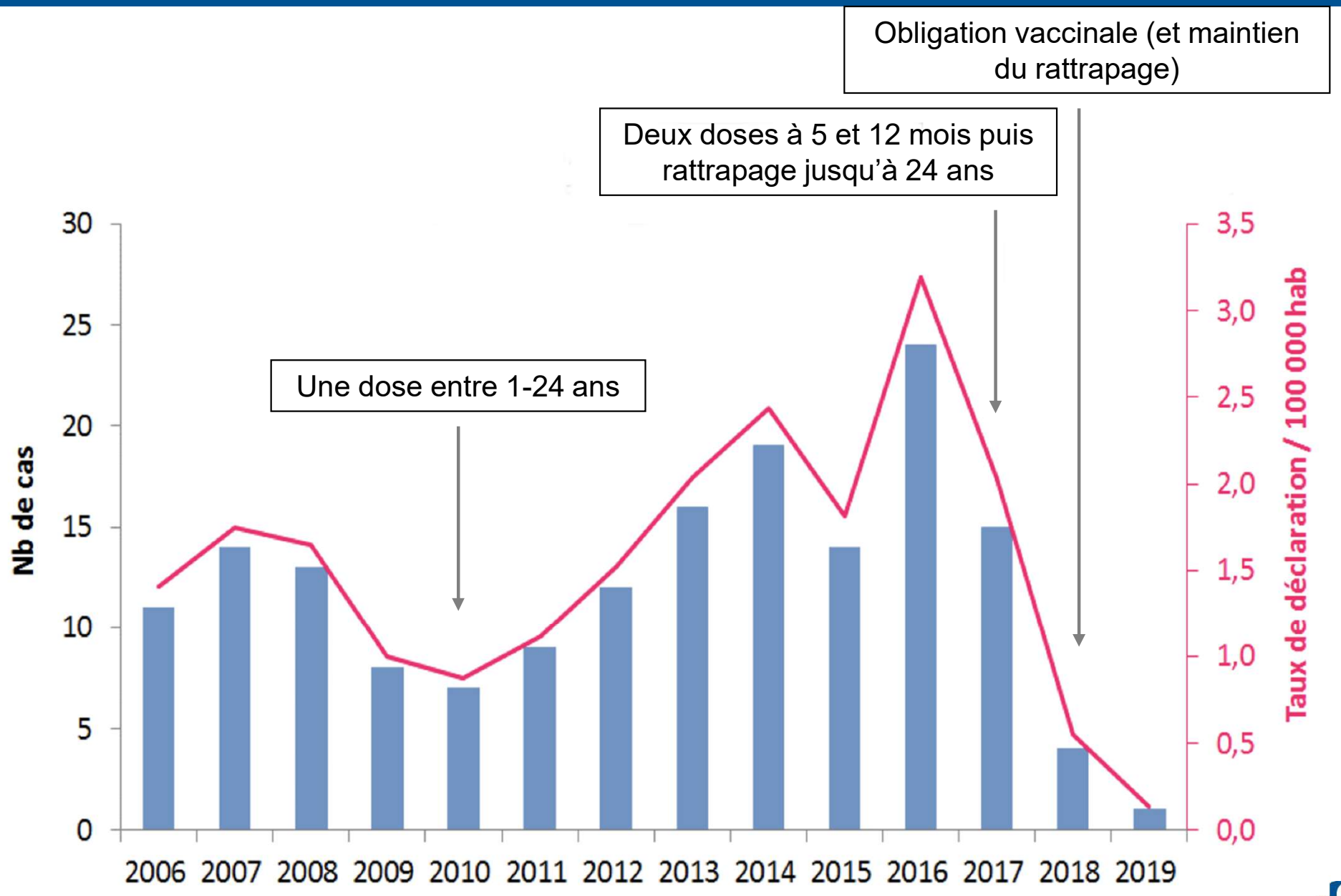
Evolution des recommandations vaccinales contre les IIMC, France, 2006-2019



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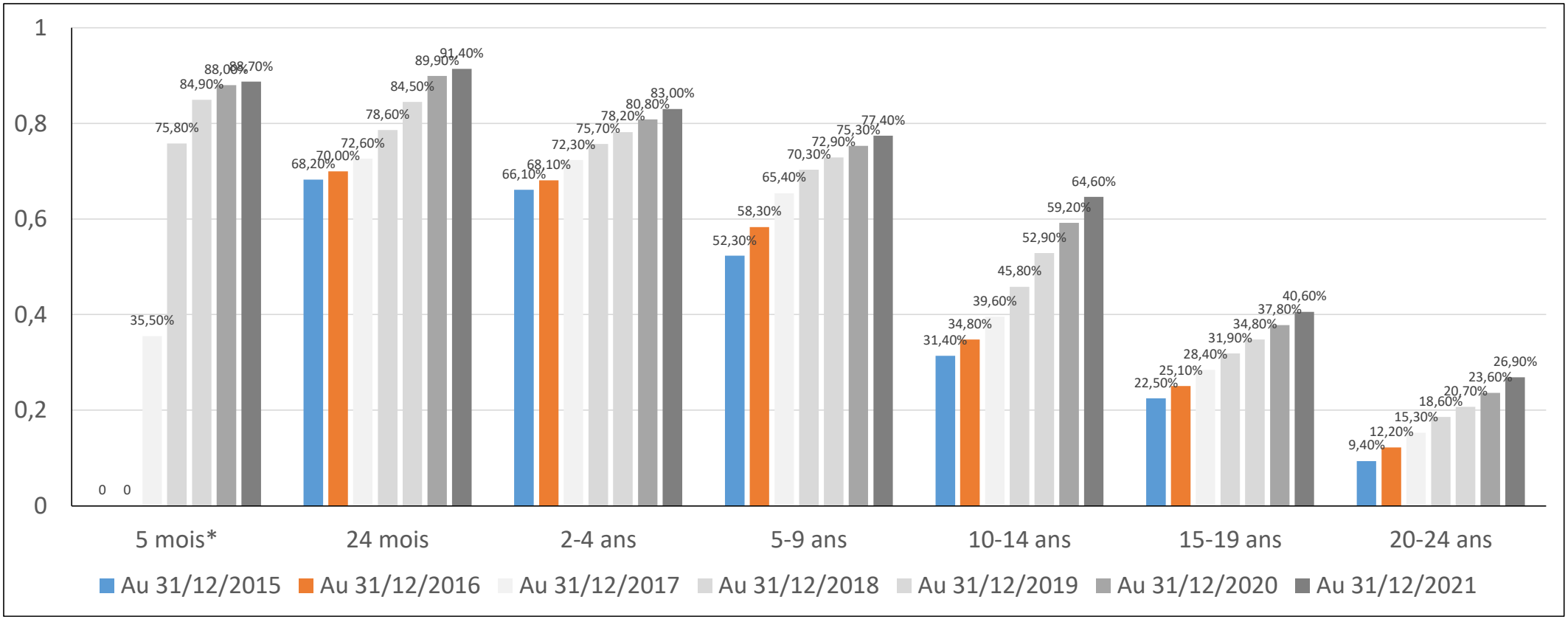
Couverture vaccinale en France MCC: France



source : SNDS-DCIR, données au 31/12/20)

https://www.santepubliquefrance.fr/content/download/288813/2762761

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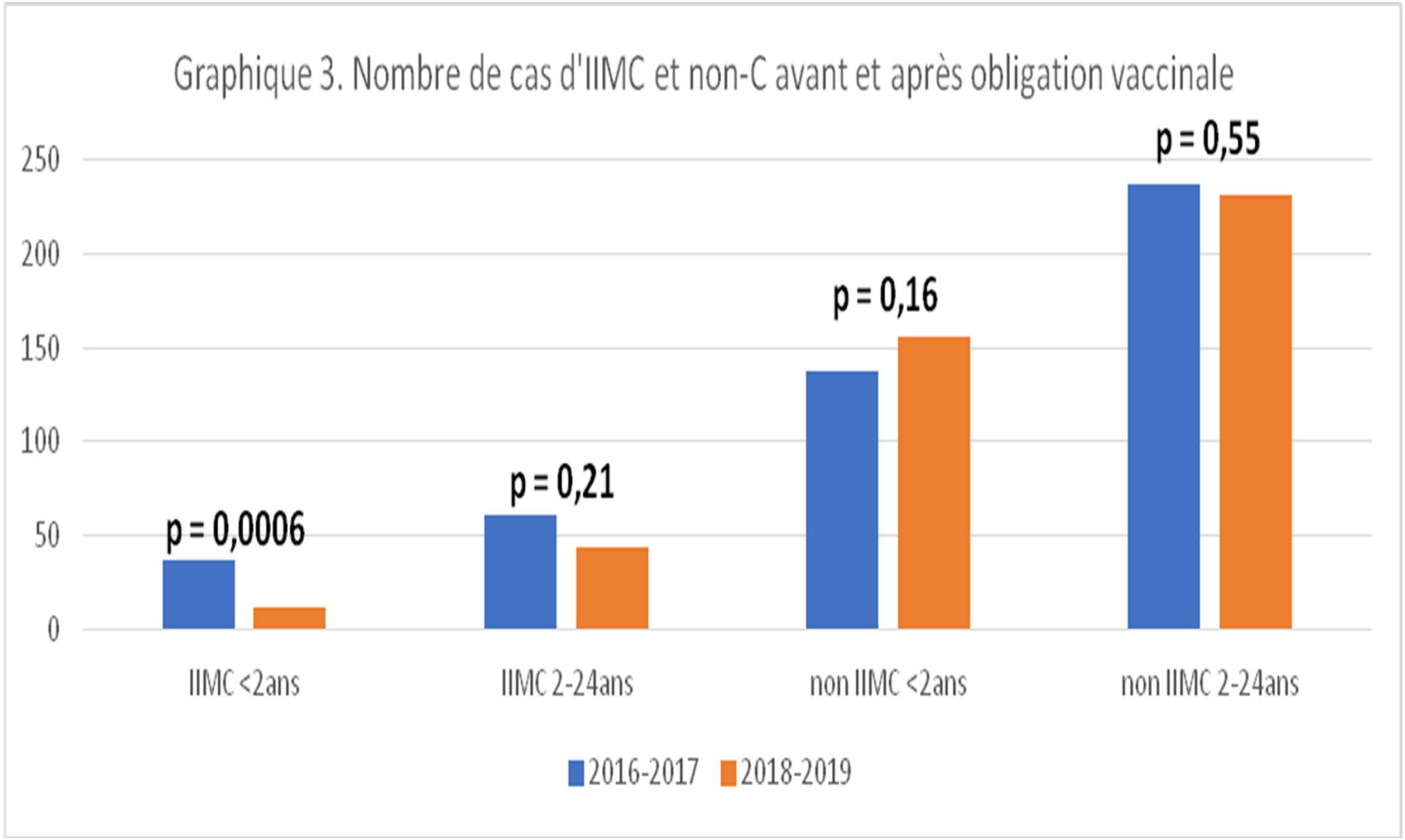
Evolution des cas d'IIM liées aux principaux sérogroupes, France entière, 2016-2019



Samy Taha 2021 Thèse de médecine générale Universite Paris Saclay faculté de médecine Paris-Sud

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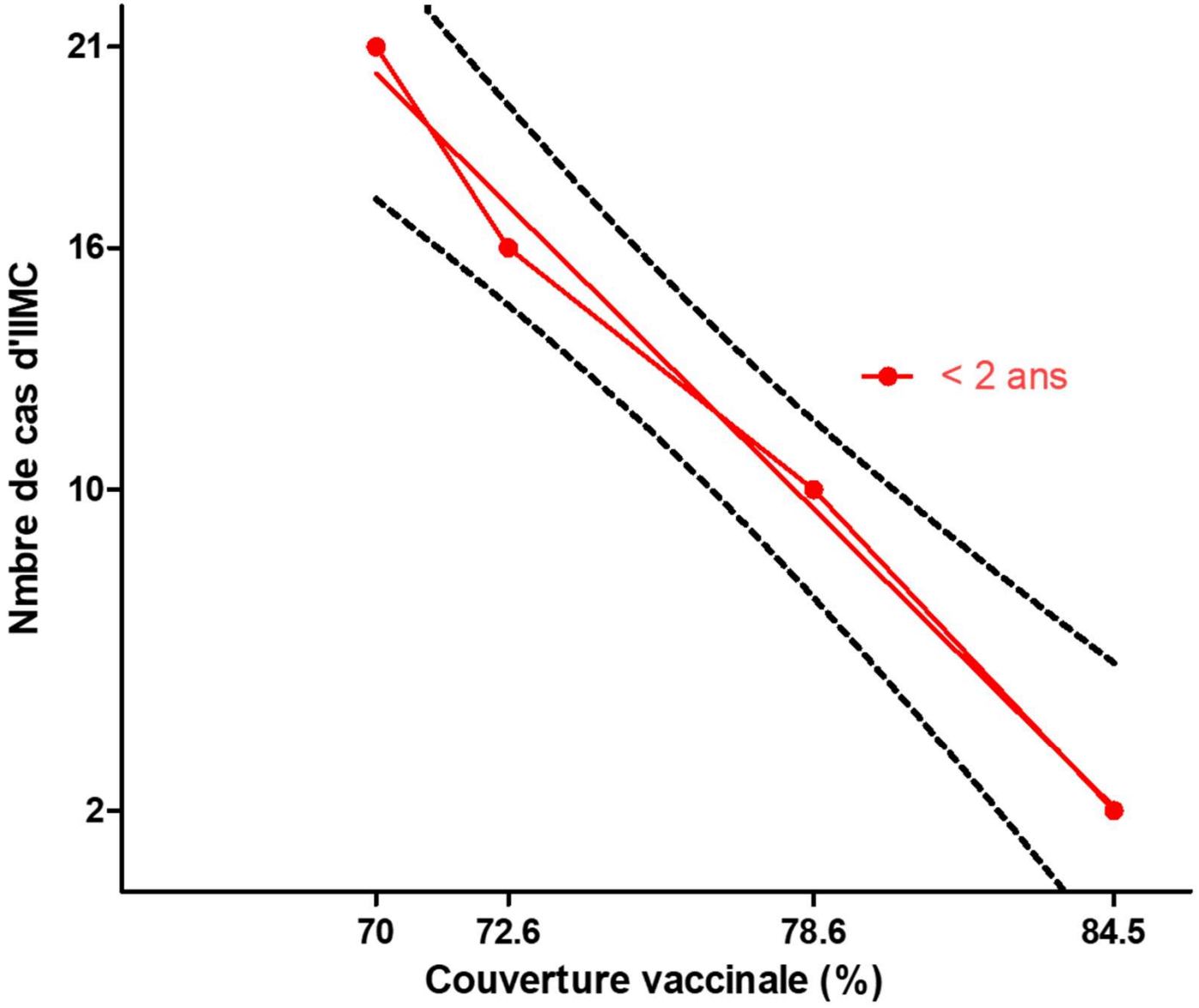
Nombre de cas d'IIMC en fonction de la couverture vaccinale chez les < 2 ans



Taha S. et al, 2022 npj Vaccines (2022) 7:73 ; https://doi.org/10.1038/s41541-022-00488-8

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MenB vaccines

	Two MenB vaccines	
Vaccines	4CMenB Bexsero	Bivalent rLP2086 Trumemba
composition	*4 components*  fHbp variant 1 (subfamily B) (50 µg) NadA (50 µg) NHBA (50 µg) PorA P1.4 (25 µg)	*2 variants of fHbp*  fHbp variant 1 (subfamily B) (60 µg) fHbp variant 3 (subfamily A) (60 µg)
Licensure	**EMA (2013) : ≥ *2 mo* FDA (2015) : ≥ 10 y**	**FDA (2015) /EMA (2017) : ≥10 y**
Schemes	**> 2 Mo: 2+1** **> 2 y: 2 doses (0-2mo)** **> 10 y: 2 doses (0-1mo)**	**> 10 y : 2 doses (0-6mo) or 3 doses (0-1/2-6mo)**
Persistence	**24-36 mo after booster,** **3y "real life data"** **Adolescent: 7.5 y** **Booster: non determined**	**4 – 5 y** **Booster: non determined**
Real life data (impact)	**In routine: UK, Italy, Portugal** **Epidemic situations: France, Canada, several US universities USA**	**Epidemic situations : 2 universities USA**
acquisition of carriage	**No**	**No**
Cross-protection	**In vitro : Against non-B (immunogenicity)** **Real life data: impact MenW** **Protection against *Neisseria gonorrhoeae***	**In vitro : against non-B (immunogenicity)**

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Immunogenicity of 4CMenB vaccine: <1y

	Concomitant	Intercalated	Accelerated	Control
Strain 44/76-SL fHBP	9.0 (6.7 to 11.7)	7.2 (5.1 to 10.0)	5.9 (3.4 to 9.4)	6.5 (3.7 to 10.3)
	99.2 (98.1 to 99.8)	99.4 (98.4 to 99.9)	99.3 (97.4 to 99.9)	4.4 (2.2 to 7.8)
Strain 5/99 NadA	5.4 (3.6 to 7.7)	6.6 (4.6 to 9.1)	4.5 (2.3 to 7.7)	6.6 (3.7 to 10.7)
	99.4 (98.3 to 99.9)	99.2 (98.0 to 99.8)	100 (98.6 to 100)	5.3 (2.8 to 9.1)
Strain NZ98/254 PorA	3.4 (2.0 to 5.3)	1.0 (0.3 to 2.2)	2.2 (0.8 to 4.8)	0.8 (0.1 to 2.9)
	79.0 (75.2 to 82.4)	86.1 (82.9 to 89.0)	81.7 (76.6 to 86.2)	4.4 (2.2 to 7.7)

Gossger et al., 2012 JAMA

% of hSBA≥ 1:5

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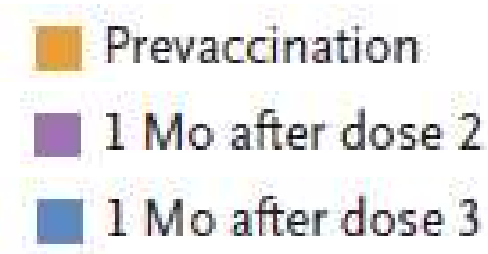
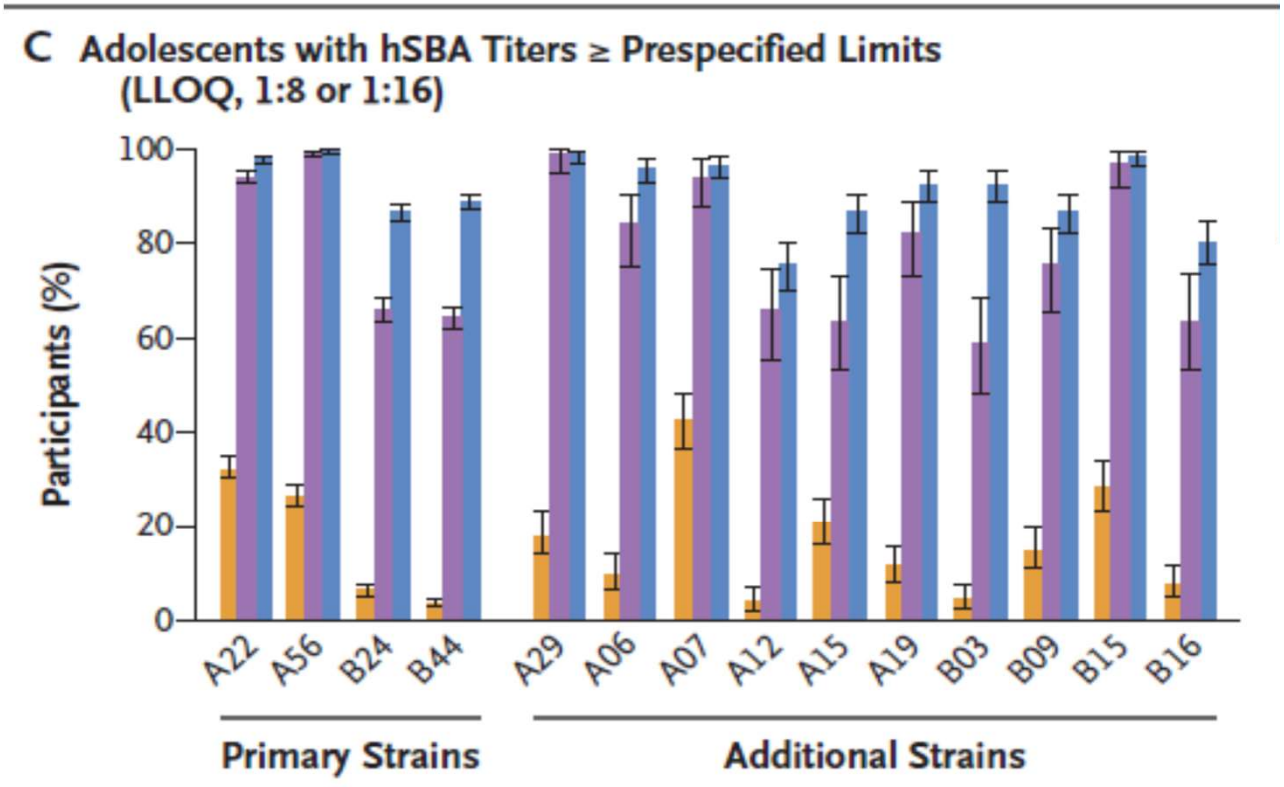
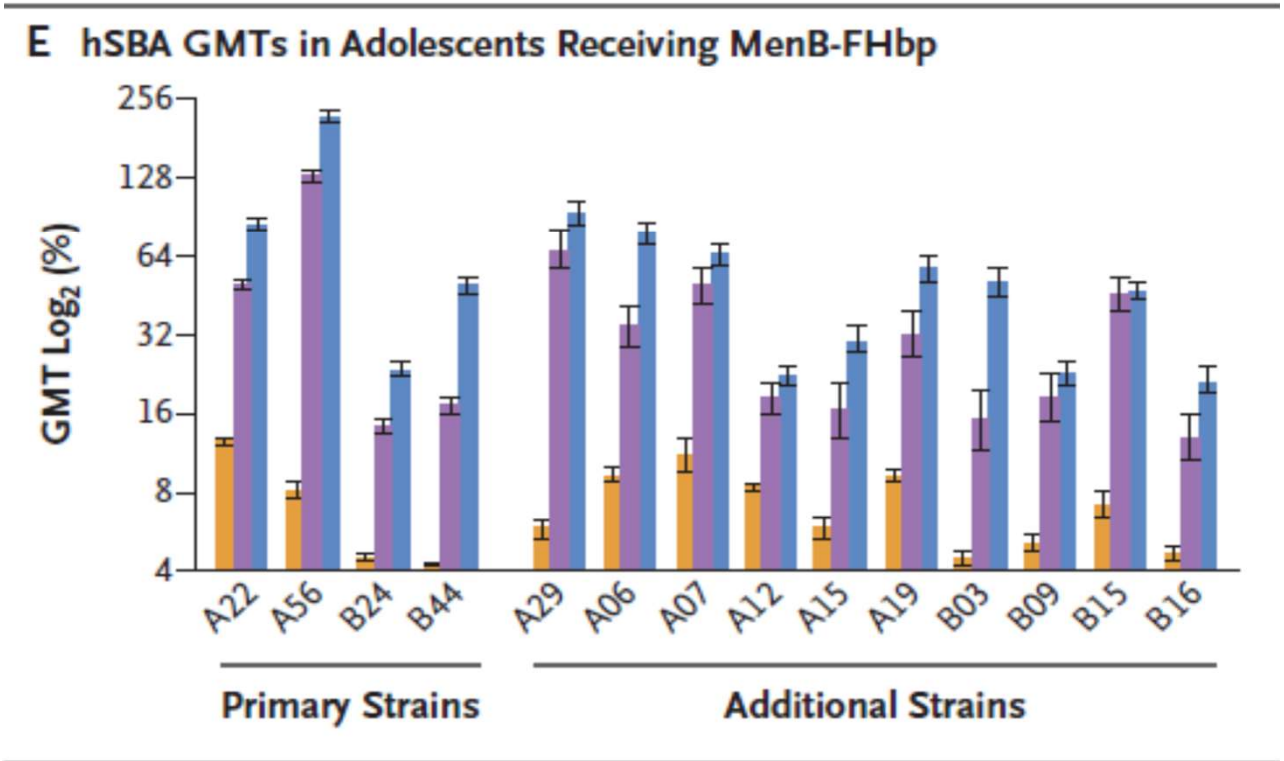
Immunogenicity of MenB-FHbp vaccine

Three doses at 0, 2 and 6 months

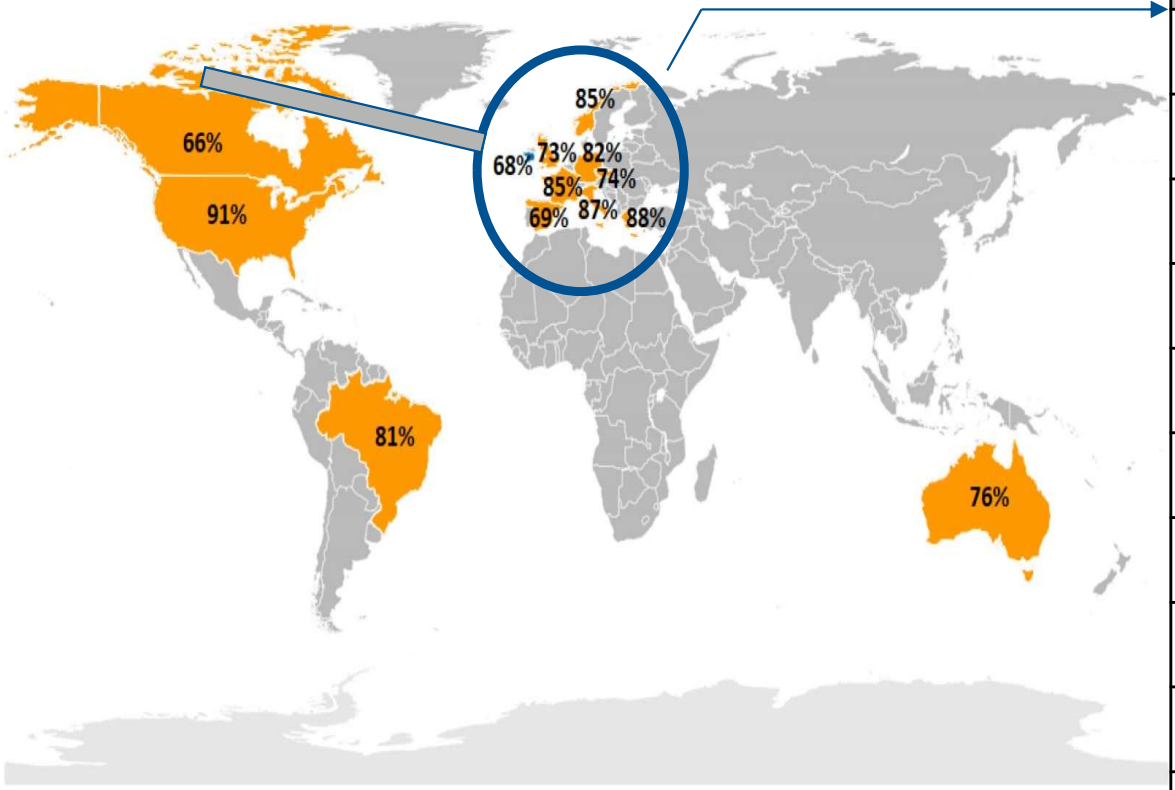






Ostergaard et al., 2017 NEJM

Predicated Coverage of 4CMenB Vaccine



	Predicted coverage (95% CI)
England & Wales	73% (57–87)
France	85% (69–93)
Germany	82% (69–92)
Italy	87% (70–93)
Norway	85% (76–98)
Czech Republic	74% (58–87)
Spain	69% (48–85)
Greece	89% (64-99)
Poland	84% (79-91)
Combined*	78% (63–90)

MATS assay
Meningococcal Antigen Typing System

*Excludes Czech Republic, Greece and Poland and Spain

Vogel *et al.*, 2013 Lancet Infect Dis
Bettinger et al., 2013 Vaccine Tzanakaki et al.,2014 BMC Microbiol; Wasko et al., 2016 Vaccine

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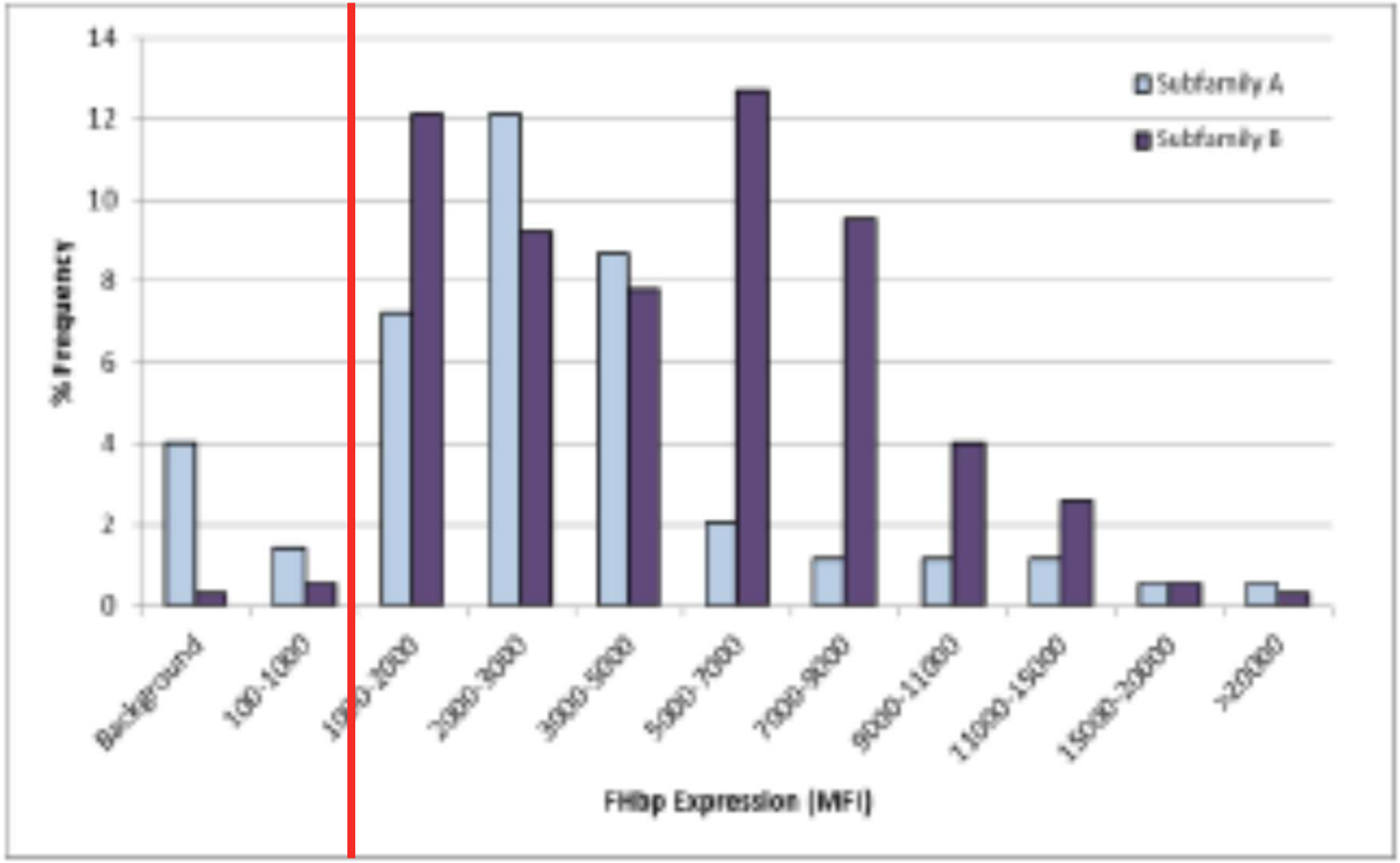
Predicted Coverage by MenB-FHbp Vaccine

MEASURE (Meningococcal Antigen Surface Expression) assay
1923 isolates (US, UK, France Norway, Czech Republic, Spain and Germany)



91% predicted coverage

McNeil et al., 2018 MBio

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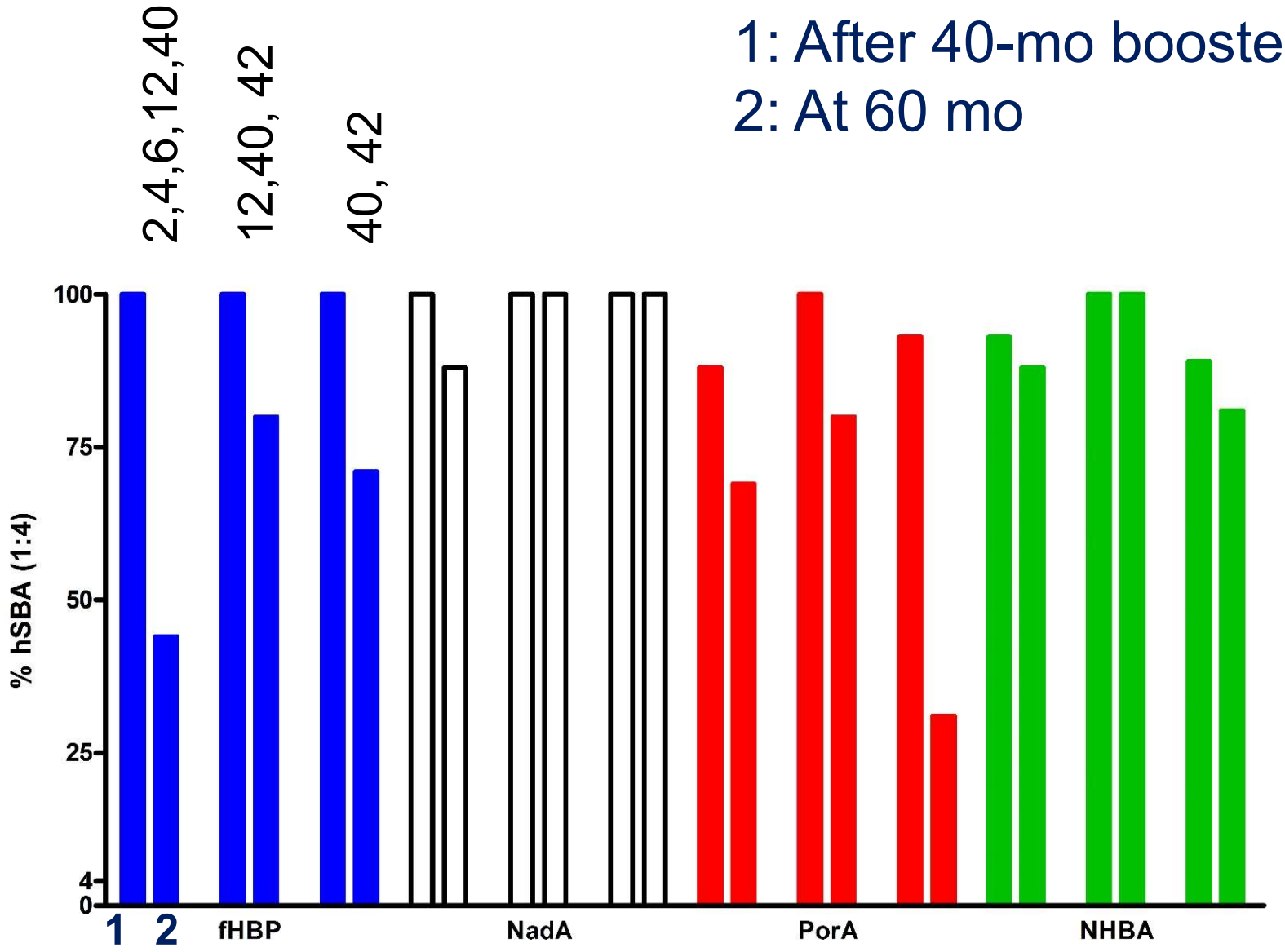
Five-years Persistence of hSBA (hSBA ≥ 1:4) 4CMenB



McQuaid et al., CMAJ 2015

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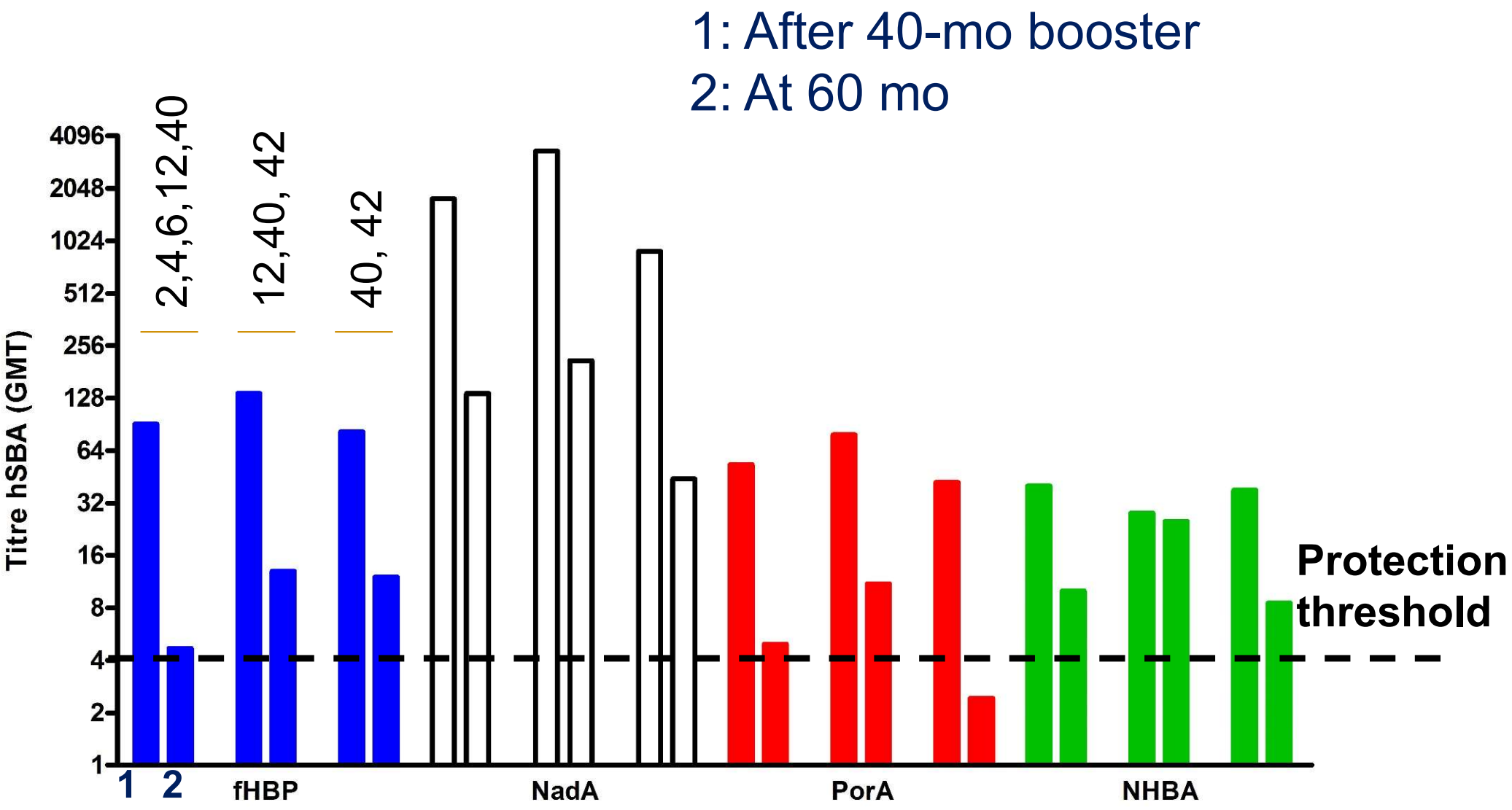
Five-years Persistence of hSBA (GMT) 4CMenB



McQuaid et al., CMAJ 2015

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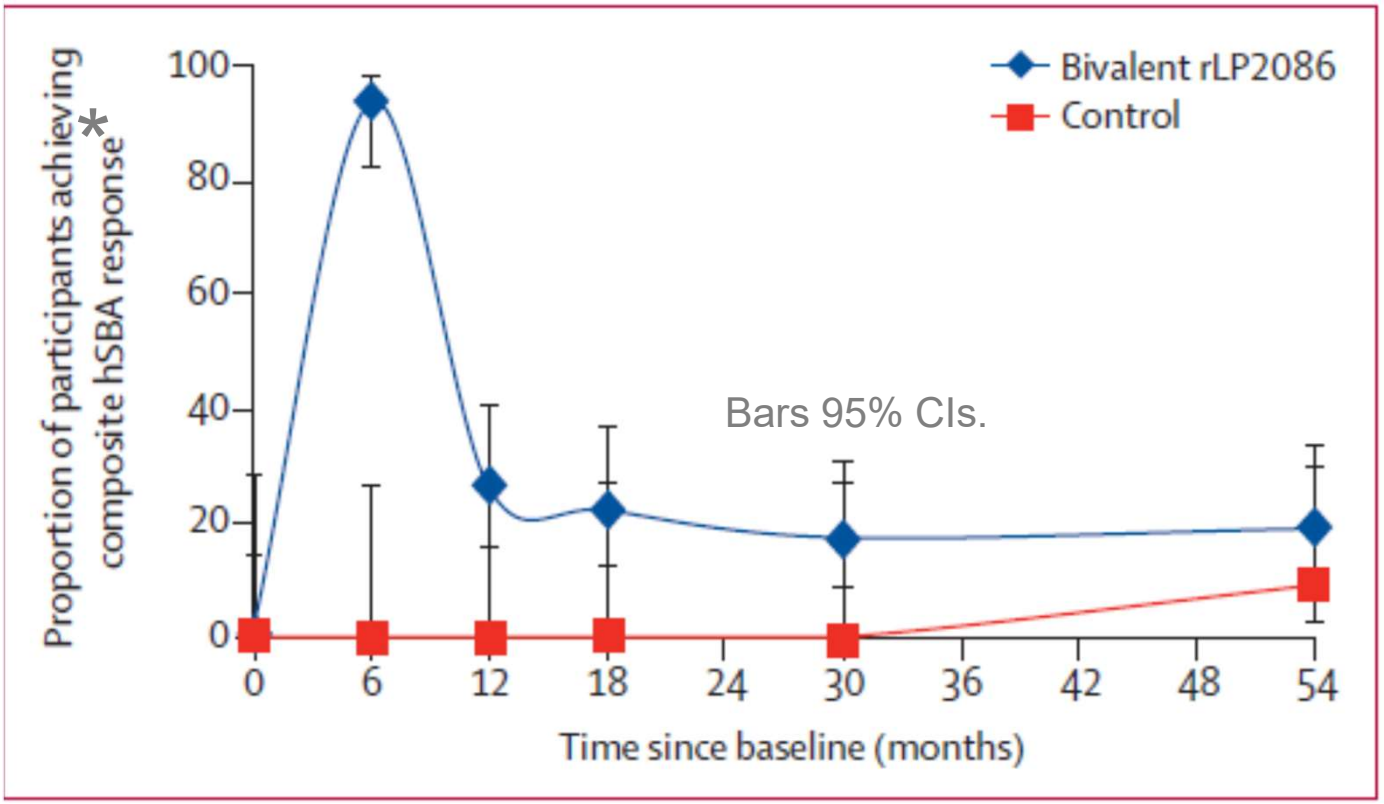
Bivalent rLP2086: 4 year follow-up

- **A phase 2 trial25 sites in Australia, Poland, and Spain.**
- **Three dosese (60 µg, 120 µg, and 200 µg) or placebo at months 0, 2, and 6mo.**
- **hSBA at months 6, 12, 24, and 48 post-vaccination against 4 strains (2 subfamily A and 2 subfamily B).**



hSBA titres greater than or equal to the lower limit of quantification for all four test strains combined.

Marshall *et al.*, *Lancet Infect Dis* 2017.

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Effect of 4CMenB vaccine on meningococcal carriage

Outcome	Vaccination Group (N=12,746)	Control Group (N=11,523)	Odds Ratio (95% CI)†
	no. (%)		
Carriage of disease-causing genogroup	326 (2.55)	291 (2.52)	1.02 (0.80–1.31)‡
Carriage of any *N. meningitidis*	547 (4.29)	561 (4.87)	0.85 (0.70–1.04)
Carriage of genogroup B	164 (1.29)	135 (1.18)	1.10 (0.81–1.47)
Carriage of genogroup Y	117 (0.92)	131 (1.13)	0.81 (0.56–1.18)
Carriage of genogroup W§	17 (0.16)	18 (0.18)	0.89 (0.43–1.85)
Carriage of genogroup C§	12 (0.11)	7 (0.07)	1.87 (0.63–5.55)
Carriage of genogroup X§	8 (0.07)	1 (0.01)	7.59 (0.98–58.83)¶
Acquisition of any *N. meningitidis*	430 (3.38)	427 (3.70)	0.91 (0.73–1.13)
Acquisition of disease-causing genogroup	272 (2.13)	238 (2.07)	1.03 (0.79–1.34)

April2016-June 2017,
24,269 surdents (15 to 18 years)
South Australia

Marshall et al., 2020 NEJM

	Odds ratio (95% CI)	Carriage reduction, (95% CI)
All NmB	**0·8 (0·6–1·1)**	**15.6% (-11·0 to 35·9)**
Disease associated MenB	**0·9 (0·7–1·2)**	**12·6% (-15 to 34·1)**
BCWY	**0·7 (0·6–0·9)**	**26·6% (10·5 to 39·9)**
CWY	**0·7 (0·5–0·9)**	**29·6% (8·1 to 46·0)**

Autumn 2010; 2954 participants aged 18–24 years. UK
987 control group; carriage rate 31%.
979 4CMenB group; carriage rate 33%.

Read et al., 2014, The Lancet

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Meningococcal carriage after MenB-FHbp vaccine Rhode Island, 2015

20%–24% of participants carried any meningococcal bacteria and 4% carried group B

- 71% remained noncarriers,
- 8% cleared carriage,
- 5% remained carriers,
- 7% acquired carriage.

Ten students acquired serogroup B carriage: 3 after 1 MenB-FHbp dose, 4 after 2 doses, and 3 after 3 doses.

➔ MenB-FHbp vaccine did not reduce meningococcal carriage or prevent serogroup B carriage acquisition

Soeters et al., 2017 CID

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4CMenB: UK

Meningitis B vaccine to be introduced in UK after U turn on its cost effectiveness

BMJ 2014;348:g2327 doi: 10.1136/bmj.g2327 (Published 24 March 2014)

Jacqui Wise

An abbreviated schedule was likely to be sufficiently immunogenic →cost-effectiveness could be improved by using a three-dose (2+1) schedule (2, 4, and 12 months).

- Provision of prophylactic paracetamol at the time of or shortly after vaccination, with a further 2 doses every 4-6 hours thereafter
- Reduce likelihood or intensity of fever without diminishing immune response

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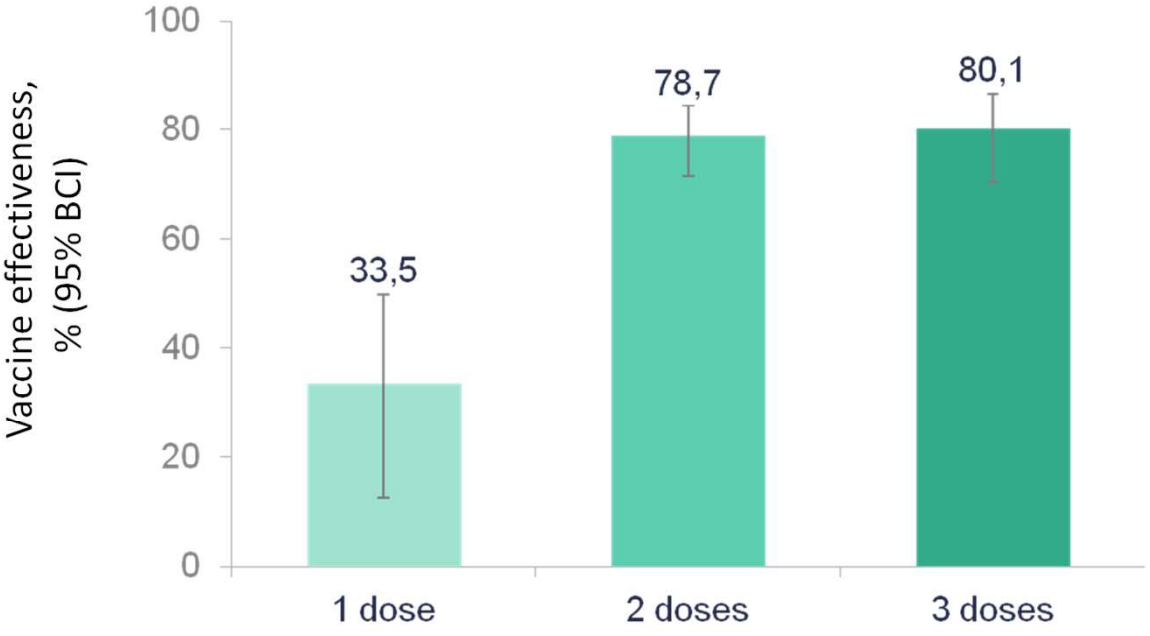
The UK MenB national immunisation programme

United Kingdom

2 4 12

Months

Introduced in **September 2015**



After the first three years, vaccine uptake was high:

- 2 doses: **92.5%**
- 3 doses: **87.9%**

Reduction of MenB disease across all fully eligible age cohorts:
75.2% (95% BCI, 65.5%–81.9%)

BCI, Bayesian credible interval

The programme prevented an estimated 312 cases between 2015 and 2018

Argante L *et al. BMC Infect Dis* 2021;21:1244

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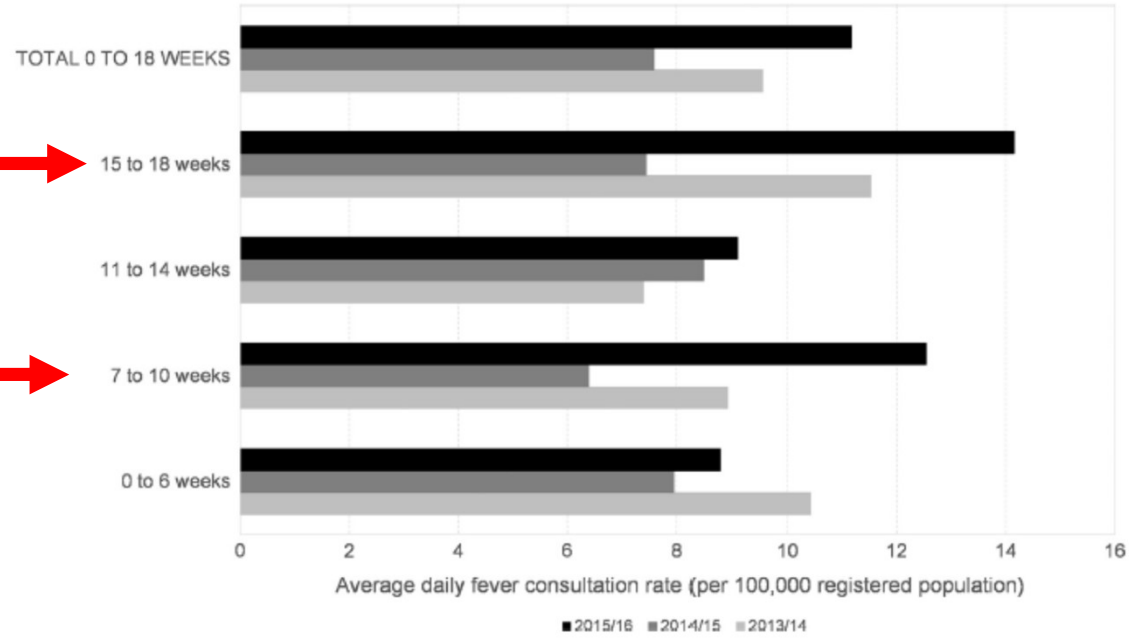
Safety of 4CMenB in routine infant immunisation in the UK

Fever consultations were identified using Read (CTV3) codes, a concept-based clinical coding system used by UK GPs

Twelve month periods (September to August) 2013-2015

Second dose
1.5-fold increase
(IRR 1.47,
95% CI 1.17 to 1.86,
p < .05)

First dose
1.6-fold increase
(IRR 1.58,
95% CI 1.22 to 2.05,
p < .05)



A small but significant difference in all-cause fever consultation rates in vaccine eligible infants who would have received 4CMenB with other vaccines.

Harcourt et al., Vaccine 2018

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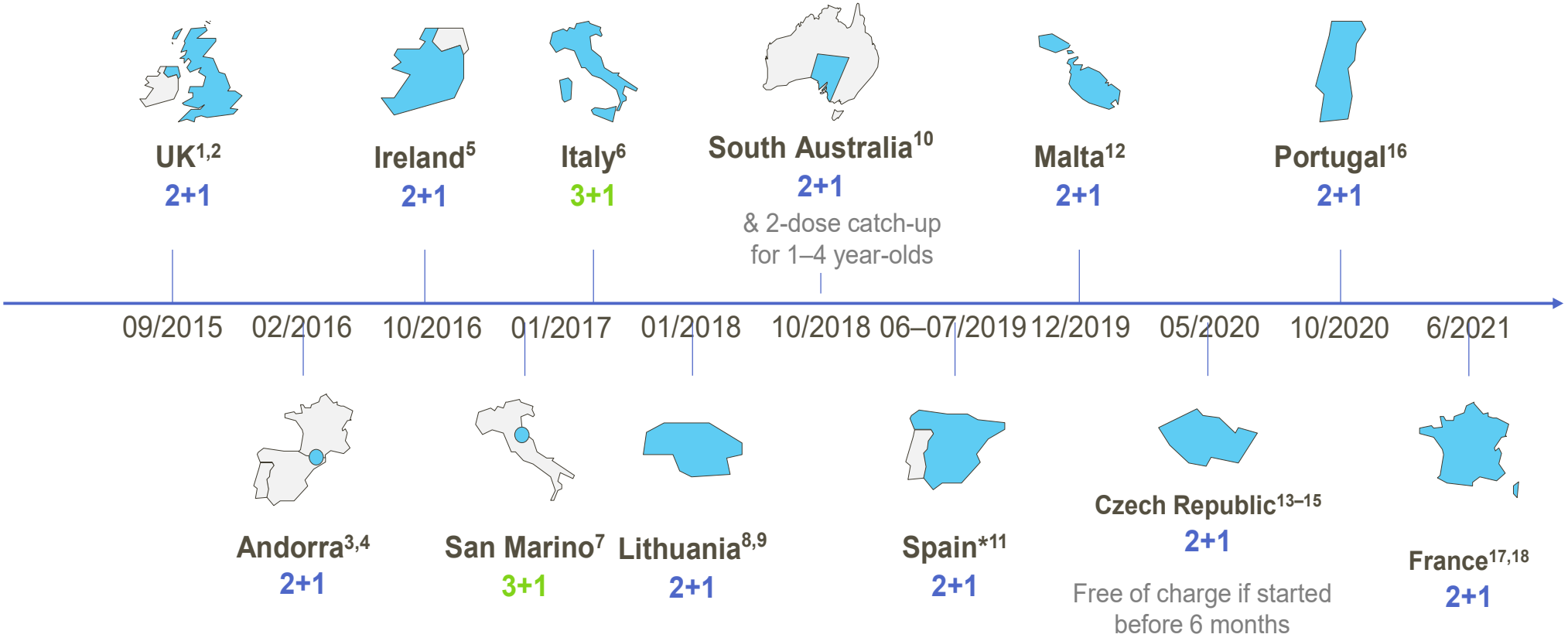
Growing and consistent evidence of real-world effectiveness of 4CMenB in infants

England[1]	**Italy**[2]	**Portugal**[3]
Infant NIP	Infant NIP	Endemic setting
80% vaccine effectiveness	**>90% vaccine effectiveness**	**79% vaccine effectiveness**
1 case averted every 4 days		
Three doses VE: 80.1% (95% BCI: 70.3, 86.7%)	Tuscany VE: 93.6% (95% CI: 55.4, 99.1%) Veneto VE 91% (95% CI: 59.9, 97.9%)	Appropriate for age VE: 79% (95% CI: 45, 92%) from case–control study in individuals aged 2 months to 18 years

Argante L *et al. BMC Infect Dis* 2021;21:1244; 2. Azzari C *et al. Vaccines* 2020;8:E469; 3. Rodrigues FMP *et al. JAMA* 2020;324:2187–2194

National and regional infant MenB immunisation programmes



Dates represent when program was announced and/or implemented. MenB, meningococcal serogroup B
*For Canarias and Castilla y León

1. National Health Service (NHS), 2022; 2. Ladhani SM *et al. N Engl J Med* 2020;382:309–317; 3. Government of Andorra: Calendari de vacunacions; 4. Andorra Department of Health, 2016; 5. HSE, 2020; 6. Ministry of Health for Italy, 2017; 7. World Health Organization, 2019; 8. Ministry of Health of the Republic of Lithuania, 2018; 9. Ministry of Health of the Republic of Lithuania, 2018 (annex); 10. Government of South Australia, 2021. Meningococcal B Immunisation Program; 11. Asociación Española de Pediatría de Atención Primaria (AEPap), 2021; 12. Malta National Immunisation Schedule 2020; 13. Česká vakcinologická společnost ČLS JEP, 2020; 14. Czech General Medical Council; 15. Czech Vaccination Society, 2018; 16. SIP/SPP, 2020; 17. France: Haute Autorite De Sante recommendation 2021. 18. France: Calendrier des vaccinations et recommandations vaccinales 2022. URLs in slide notes

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4CenB in France: targeted recommendation in 2013

High Council for Public Health considered:

- **Low/lack of impact on the acquisition of meningococcal carriage**
- **The decline in antibody titers after vaccination**
- **The reactogenicity (especially fever) of the vaccine when co-administered with other early childhood vaccines**
- **Unfavorable cost-effectiveness**

Use of 4CMenB was recommended only for targeted use:

- **At risk subjects**
- **Outbreak control**
- **Epidemics**

Cas groupés :
Survenue d'au moins 2 cas d'IIM B :

- **dans une même collectivité ou un même groupe social ;**
- **dans un délai ≤ à 4 semaines;**
- **survenus et rattachables à des souches identiques couvertes par le vaccin 4CMenB ou ne pouvant être différenciées.**

Epidémie :
Survenue d'au moins 3 cas sans contact direct entre eux dans un délai de ≤ trois mois, rattachables à des souches identiques ou ne pouvant être différenciées

Haut Conseil de la Santé Publique, 2013. Vaccination contre les infections invasives à méningocoque B. Place du vaccin Bexsero
http://www.hcsp.fr/Explore.cgi/avisrapportsdomaine?clefr=386 (accessed March 2022)

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Targeted use of 4CMenB in Beaujolais Region, France, 2016

Background

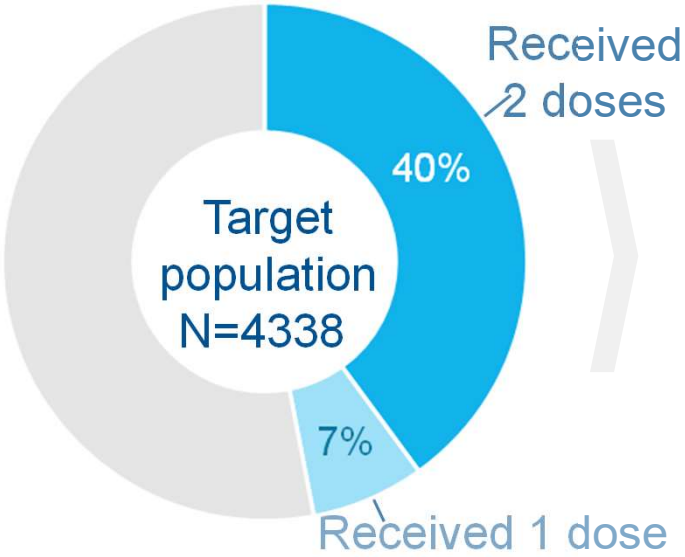
4 cases of IMD reported in February/March

Genotype: B:P1.19,15:F4–28:cc32

Covered by 4CMenB

Vaccination campaign

Ages: 2 mo–24 y, from 12 municipalities in affected region



Reinforced pharmacovigilance follow-up was set up

Outcomes

No new cases reported

Rate of adverse effects: 3.5%

Alert lifted July 2016

Thabuis A *et al. Euro Surveill* 2018;23:1700590

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4CMenB in France: new recommendations were made on 22 June 2021

The French National Authority for Health (HAS) considered:[1]

- Data that emerged since 2013 on **real-world effectiveness** in England, Portugal and Italy
- The impact of social inequalities on risk of IMD and access to the 4CMenB vaccine: **Equity**
- Seriousness of IMD in terms of **morbidity and mortality**

French scientific societies strongly supported generalised infant vaccination against MenB[2]

- **Equity** was a key consideration

Use of 4CMenB was recommended:[1]

- For all infants aged <1 y
- According to a 2 primary dose + booster schedule

1. Haute Autorité de Santé, France. Stratégie de vaccination pour la prévention des infections invasives à méningocoques : Le sérogroupe B et la place de BEXSERO. 2021. https://www.has-sante.fr/jcms/p_3066921/fr/strategie-de-vaccination-pour-la-prevention-des-infections-invasives-a-meningocoques-le-serogroupe-b-et-la-place-de-bexsero (accessed March 2022); 2. Gras-Le Guen C *et al. Infect Dis Now* 2021;51:407–409

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Parcours de soins des patients d'IIM en France : une analyse de la base de données du système national d'information inter-régime de l'Assurance Maladie (SNIIRAM)

Care pathways in invasive meningococcal disease: a retrospective analysis of the French national public health insurance database

Catherine Weil-Olivier, Muhamed-Kheir Taha, Stéphane Bouée, Corinne Emery, Véronique Loncle-Provot, Gaëlle Nachbaur, Ekkehard Beck & Céline Pribil

HUMAN VACCINES & IMMUNOTHERAPEUTICS 2022, VOL. 18, NO. 1, e2021764 (11 pages)
https://doi.org/10.1080/21645515.2021.2021764

Une cohorte historique a été constituée à partir de la base de données du SNIIRAM sur une période de 6 ans

Au total, 3 532 cas hospitalisés pour IIM ont été inclus : d'âge médian de 21 ans, ils sont majoritairement de sexe masculin et hospitalisés via les urgences.

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Risk factors for invasive meningococcal disease: a retrospective analysis of the French national public health insurance database

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2021, VOL. 17, NO. 6, 1858–1866
https://doi.org/10.1080/21645515.2020.1849518

Muhamed-Kheir Taha, Catherine Weil-Olivier, Stéphane Bouée, Corinne Emery, Gaëlle Nachbaur, Céline Pribil & Véronique Loncle-Provot

Universal health coverage for low-income individuals

Social deprivation index calculated based on quintiles of municipality-level deprivation

Odds ratios of socioeconomic risk factors (CI 95%)

CMU-C Status	1.7 (1.6–1.9)
SDI above median value	1.0 (1.0–1.1)

Socioeconomic risk factors

Odds ratios of most prominent statistically significant (CI 95%) medical risk factors per classification

Congenital immunodeficiency	39.1 (5.1–299.1)
Immunodeficiency (ALD)	10.3 (4.5–24.0)
Asplenia/hyposplenia	6.7 (3.0–14.7)
Autoimmune diseases	5.4 (2.5–11.8)
Haemophilia	4.7 (1.8–12.2)
Severe chronic respiratory disorders	4.3 (3.1–6.2)
Acute lower respiratory track infection	3.9 (2.6–5.8)
Acute upper respiratory track infection	3.3 (1.4–7.4)
Prematurity	2.7 (1.5–5.0)

European vaccination recommendations

History of severe chronic conditions based on ALD

Other risk factors

Odds ratio intervals are all ≥1

Taha MK *et al. Hum Vaccin Immunother* 2021;17:1858–1866

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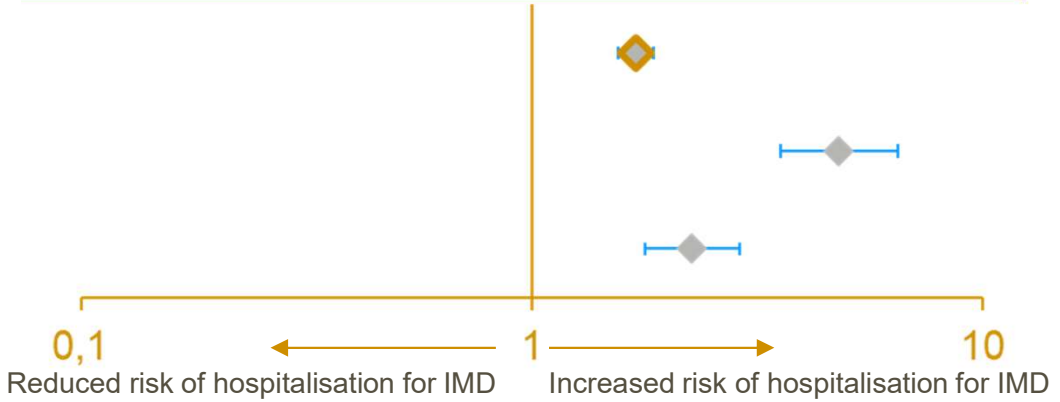
Hospitalisation pour IIM: Association CMU-c et âge

French national public health insurance database (SNDS) analysis assessed hospitalisation for IMD as a function of socioeconomic status

Risk of IMD-hospitalisation in CMU-C recipients versus controls[1]

Age group	Odds ratio (95% CI)
All ages	1.7 (1.56–1.86)
<1 year	4.81 (3.56–6.49)
1–4 years	2.27 (1.78–2.89)



- Les enfants de familles à faible revenu ont un risque plus élevé d' hospitalisation due à une IIM en particulier avant l'âge de 1 an
- Ce sont les enfants les moins susceptibles de bénéficier d'un vaccin disponible à l'achat, mais sans remboursement

22 Juin 2021
Le HAS recommande de vacciner tous les nourrissons en utilisant le Bexsero selon le schéma de 2 dose + un rappel

[1]Taha et al., Hum Vaccin Immunother. 2021:1-9. doi:10.1080/21645515.2020.1849518

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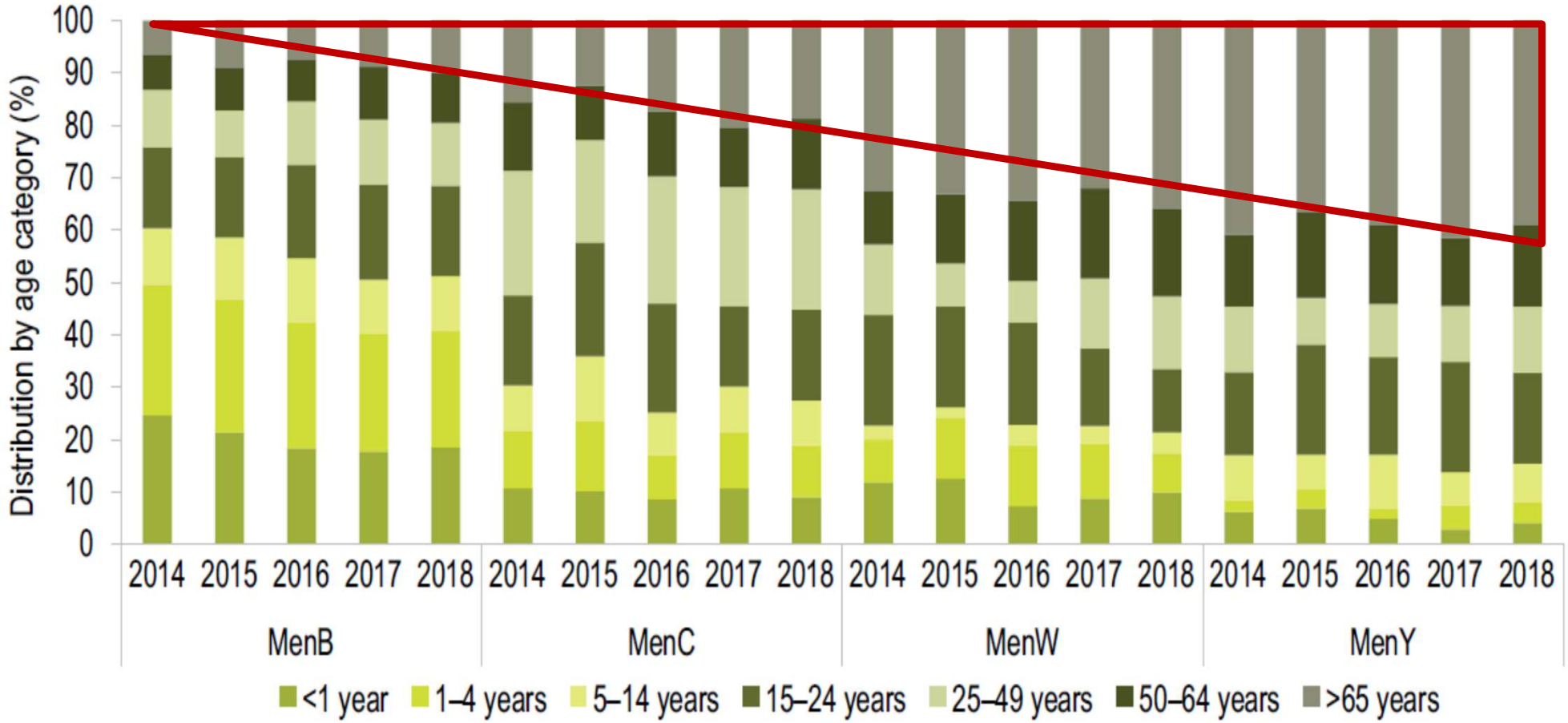
Evolving strategies for meningococcal vaccination in Europe: Overview and key determinants for current and future considerations

PATHOGENS AND GLOBAL HEALTH
https://doi.org/10.1080/20477724.2021.1972663

Federico Martinón-Torres[a], Muhamed-Kheir Taha[b], Markus Knuf[c], Victoria Abbing-Karahagopian[d], Michele Pellegrini[e], Rafik Bekkat-Berkani[f] and Véronique Abitbol[g]



Distribution of reported serogroup-specific IMD in European countries, 2014– 2018
ECDC data

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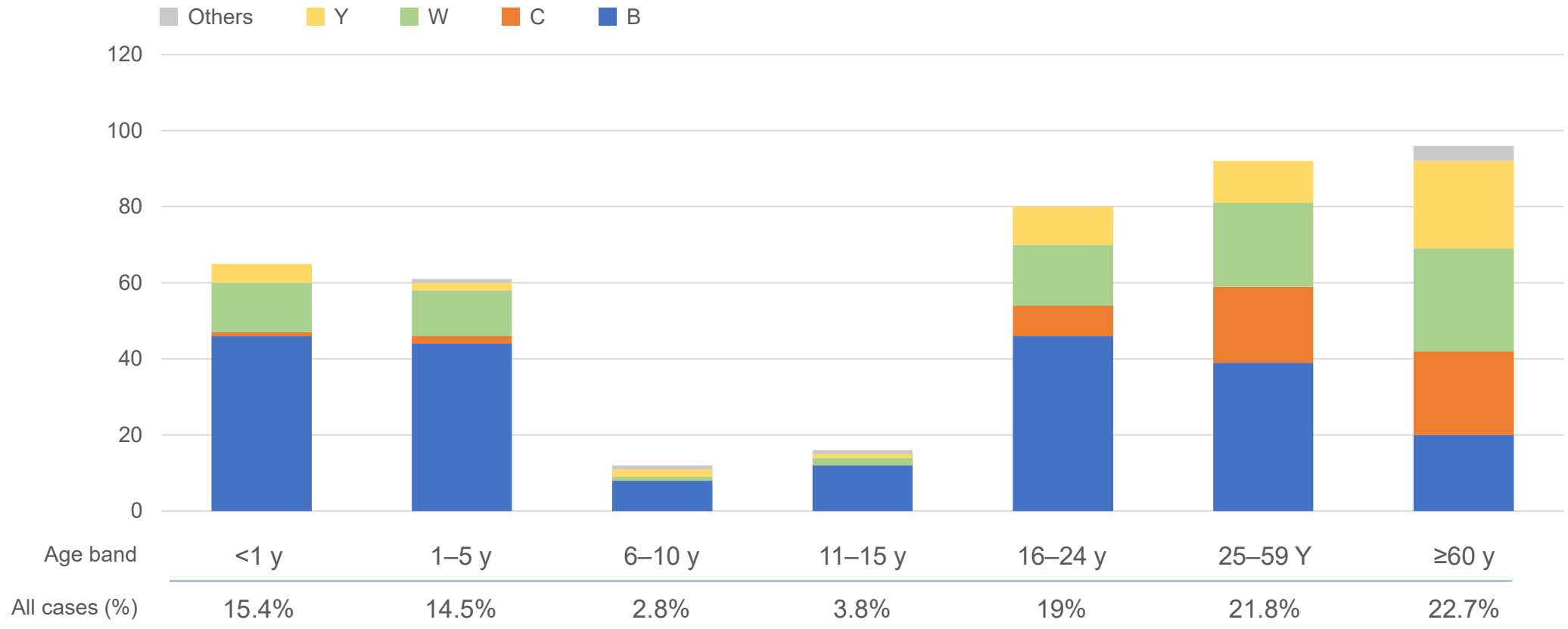
Age and serogroup distribution of IMD cases in France (2019)

No. of cases: The highest numbers are among seniors ≥60 years



Donnée CNR Taha MK,

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The case fatality rate is the highest among ≥60 years for all serogroups: France 2019

	IMD all groups		IMD B		IMD C		IMD W		IMD Y	
	No. cases	Deaths n (%)	No. cases	Deaths n (%)	No. cases	Deaths n (%)	No. cases	Deaths n (%)	No. cases	Deaths n (%)
<1 y	65	6 (9%)	45	1 (2%)	1	-	13	4 (31%)	4	1
1–4 y	62	4 (6%)	43	2 (5%)	2	-	12	2 (17%)	2	-
5–14 y	33	1 (3%)	24	-	0	-	3	1	1	-
15–24 y	93	4 (4%)	54	-	10	1 (10%)	16	3 (19%)	13	-
25–59 y	104	16 (15%)	48	5 (10%)	18	3 (17%)	22	8 (36%)	11	-
≥60 y	102	24 (23%)	26	8 (31%)	23	3 (13%)	27	7 (26%)	23	6 (26%)
Total	459	55 (12%)	240	16 (7%)	54	7 (13%)	93	25 (27%)	54	7 (13%)

https://www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-a-prevention-vaccinale/infections-invasives-a-meningocoque/documents/bulletin-national2/les-infections-invasives-a-meningocoque-en-france-en-2019

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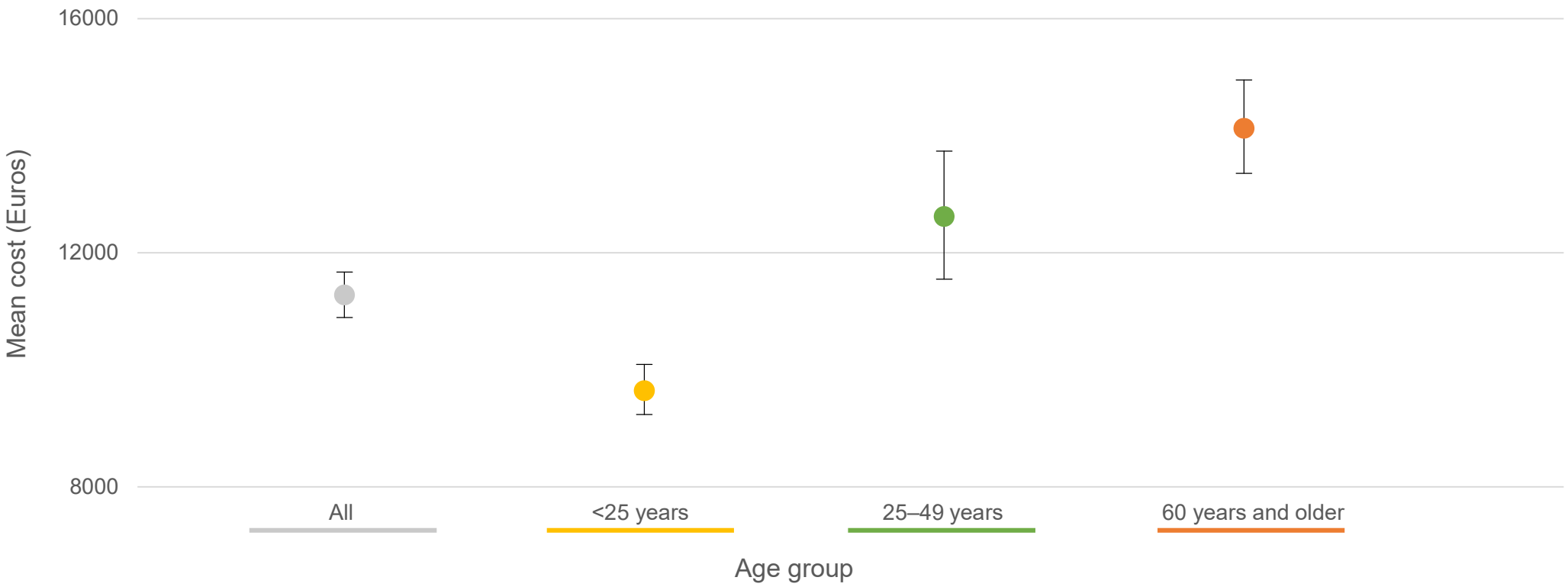
The mean cost per capita of the index hospitalisation increases with age (p<0.001): The highest among ≥60 years

- Unlike several other infectious diseases, IMD case management is systematically in hospital settings



Weil-Olivier C, et al. Infectious Diseases and Therapy. 2021;10:1607-1623.

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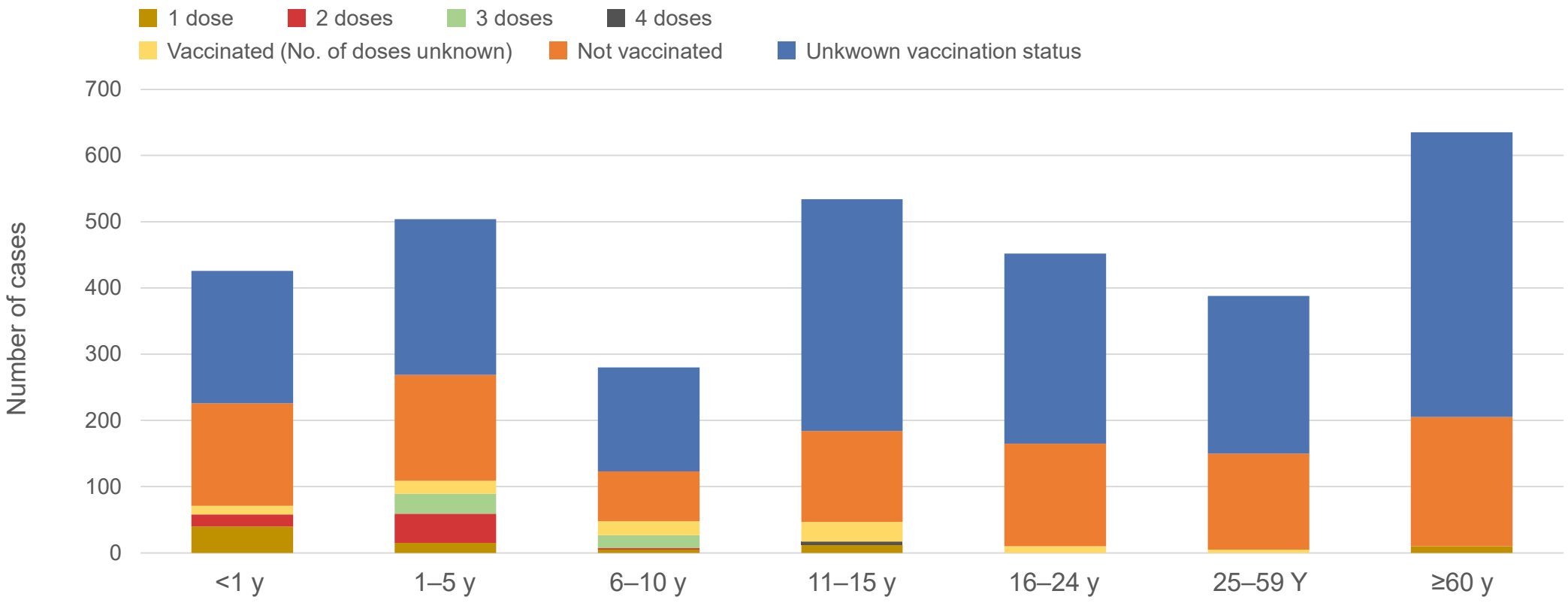
The vaccination status among cases by age-group, EU/EEA, 2014–2018: The lowest among ≥60 years



European Centre for Disease Prevention and Control (ECDC). Invasive meningococcal disease - Annual Epidemiological Report for 2018. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/AER-Invasive-meningococcal-disease-2018.pdf. [Accessed August 2022].

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Implementation of a prospective study for enhancing surveillance of invasive bacterial infections in North Africa

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	Algeria	Morocco	Tunisia	All
Number of samples (Number of patients)	83 (82)	451 (451)	218 (175)	752 (708)
Samples types % (N°)				
CSF	94% (78)	100% (451)	64% (141)	89.1% (670)
Blood	1.2% (1)		11% (24)	3.3 %(25)
CSF and blood	2.4% (2)		22% (48)	6.6% (50)
Skin biopsy	2.4% (2)			0.3% (2)
Pleural fluid			3% (5)	0.7% (5)
Number of positive samples % (N°)	31% (26)	14% (65)	20% (44)	18% (135)
N. meningitidis	17% (14)	7% (31)	9% (20)	9% (65)
S. pneumoniae	15% (12)	6% (28)	10% (22)	8% (62)
H. influenzae		1% (6)	1% (2)	1% (8)
Groups of *N. meningitidis* of all Nm				
B	50% (7)	90% (28)	65% (13)	74% (48)
C		3.2% (1)	10% (2)	4% (3)
Y	21% (3)	6.8% (2)	10% (2)	11%(7)
Non-determined	29% (4)		15% (3)	11% (7)

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Conclusions

- **Meningococcal epidemiology is unpredictable.**
- **Plain and conjugate capsular polysaccharide-based vaccines are available. Use preferentially conjugate vaccines.**
- **Protection for all age groups (including older adults)**
- **Vaccines targeting MenB were developed on the basis of sub-capsular proteins**

- Vaccination strategies should consider:
- Local epidemiology & coverage of isolates
- Cost-effectiveness (criteria?)
- Direct protection and herd immunity
- Persistence? Needs for boosters? When and frequencies?

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