Actualités vaccinales

O. Epaulard

Infectiologie, CHU Grenoble Alpes

4 mai 2023- Semaine européenne de la vaccination

Deux « vagues » d’actualités vaccinales

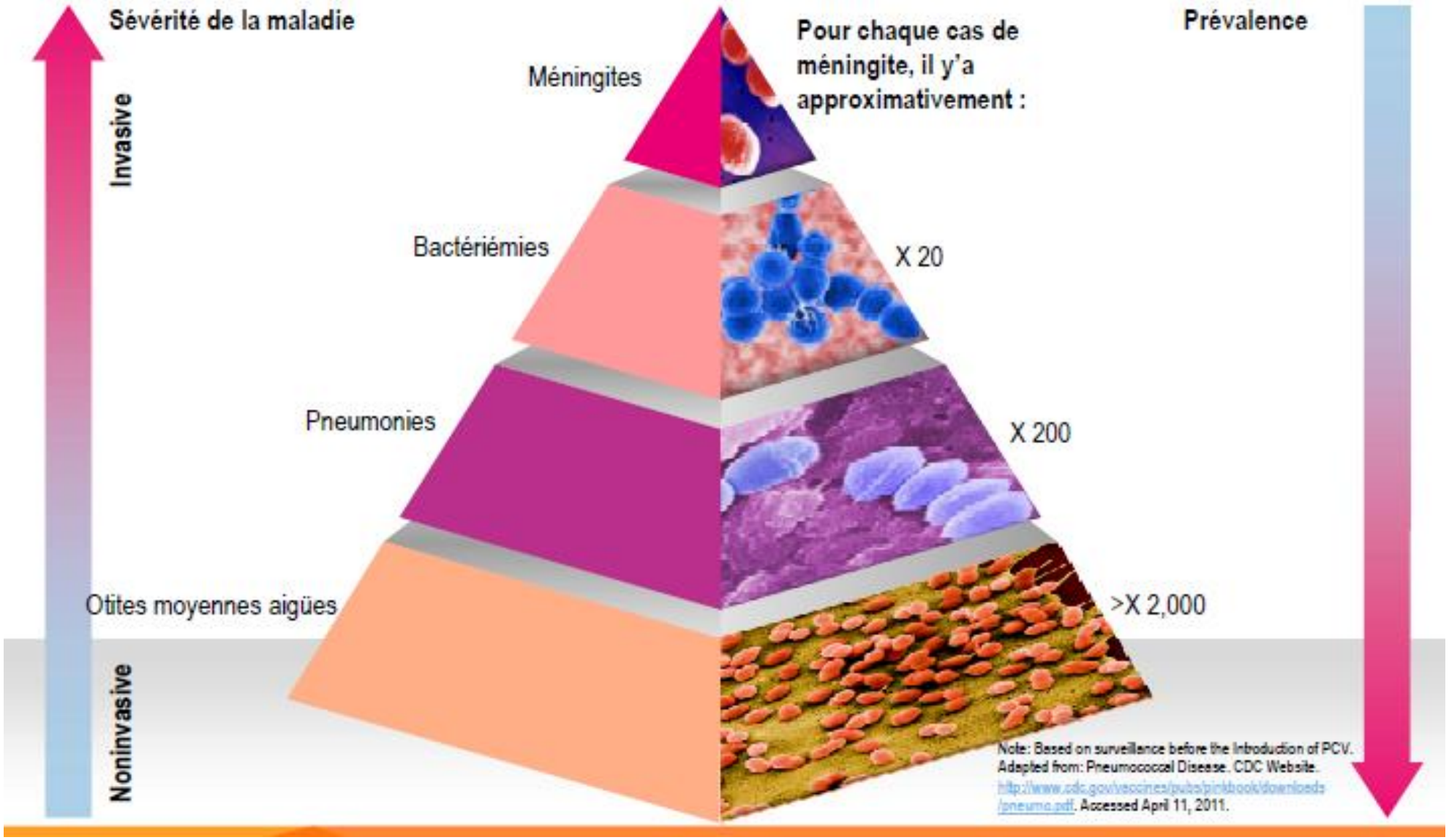
- À court terme :
  - Arrivée d’un nouveau vaccin zona
  - Arrivée d’un vaccin conjugué pneumocoque 20-valent

- À moyen terme (et assez vite) : nouveaux vaccins ARN
  - VRS
  - Grippe

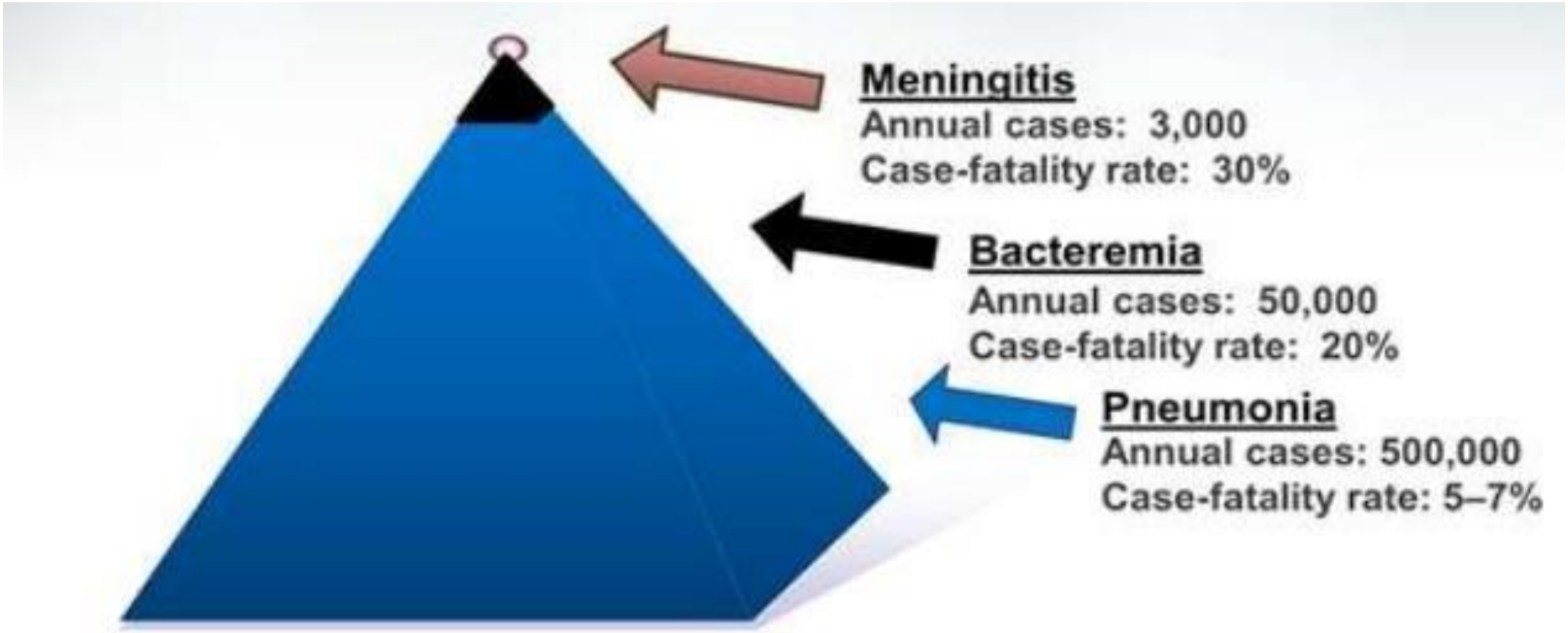
- Assez rapidement également : extensions de certains vaccins
  - HPV
  - Méningocoque tétravalent
  - Recommandation préférentielle du vaccin grippal haute dose

Pneumocoque

Spectre des infections à pneumocoque de l'enfant

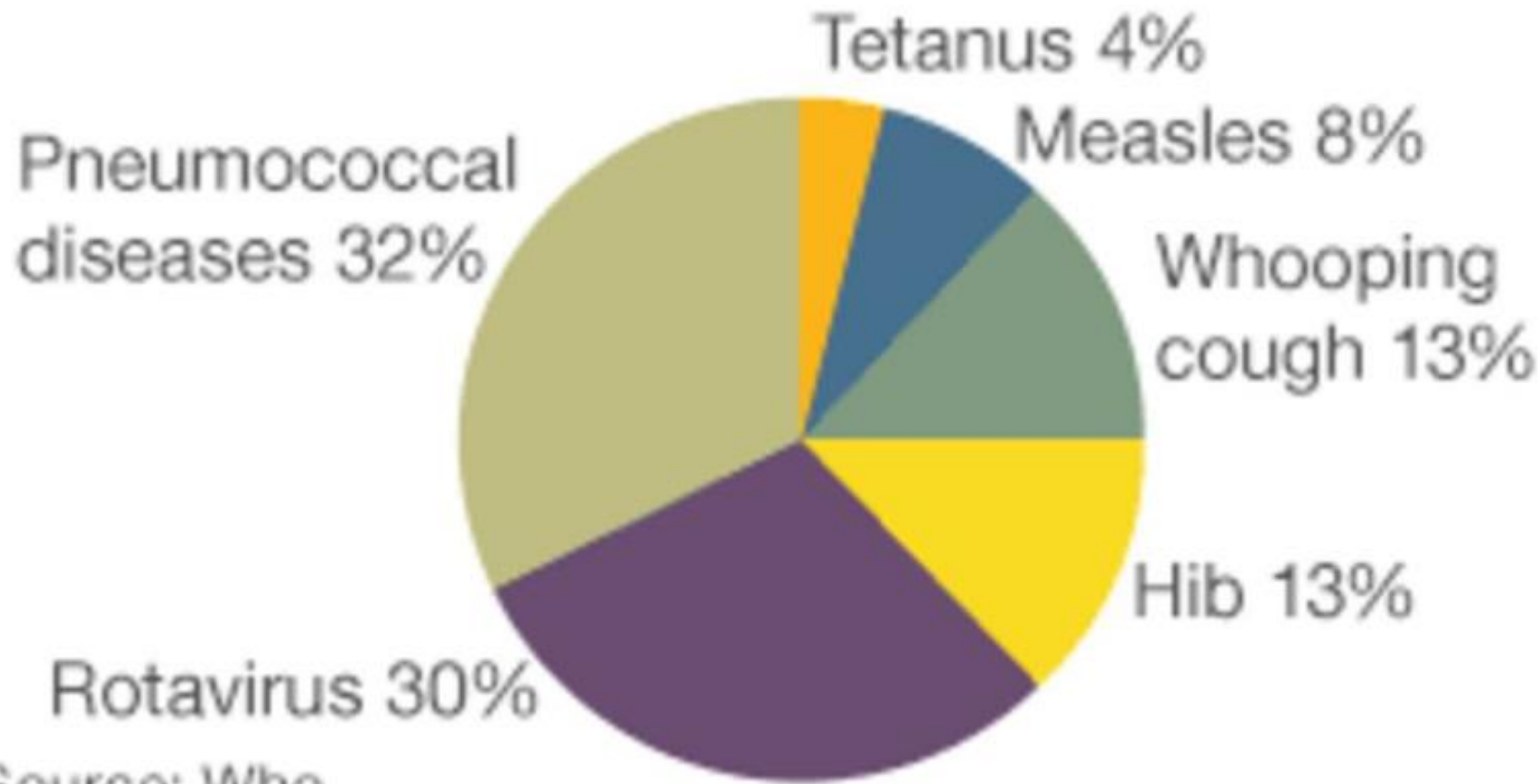


Chiffres aux USA



Less severe diseases (sinusitis, otitis media):
Millions of cases annually

The vaccine-preventable diseases responsible for 1.5 million infant deaths



Source: Who

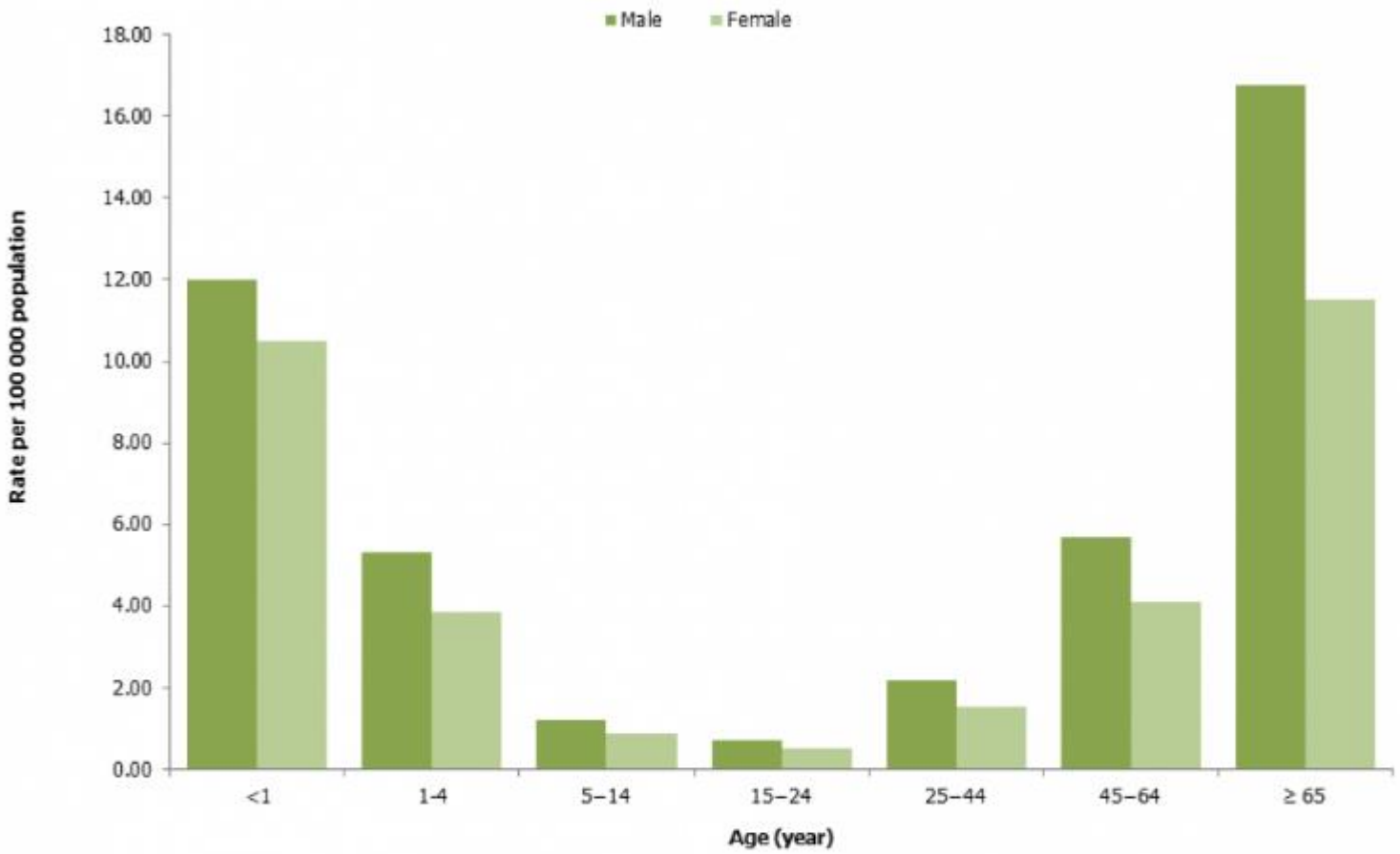
ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

SURVEILLANCE REPORT

Annual Epidemiological Report for 2016

Invasive pneumococcal disease

Figure 3. Cases of reported, confirmed invasive pneumococcal disease, by age and gender, EU/EEA, 2014



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

Suggested citation: European Centre for Disease Prevention and Control. Annual epidemiological report 2015. Invasive pneumococcal disease. Stockholm: ECDC; 2016.

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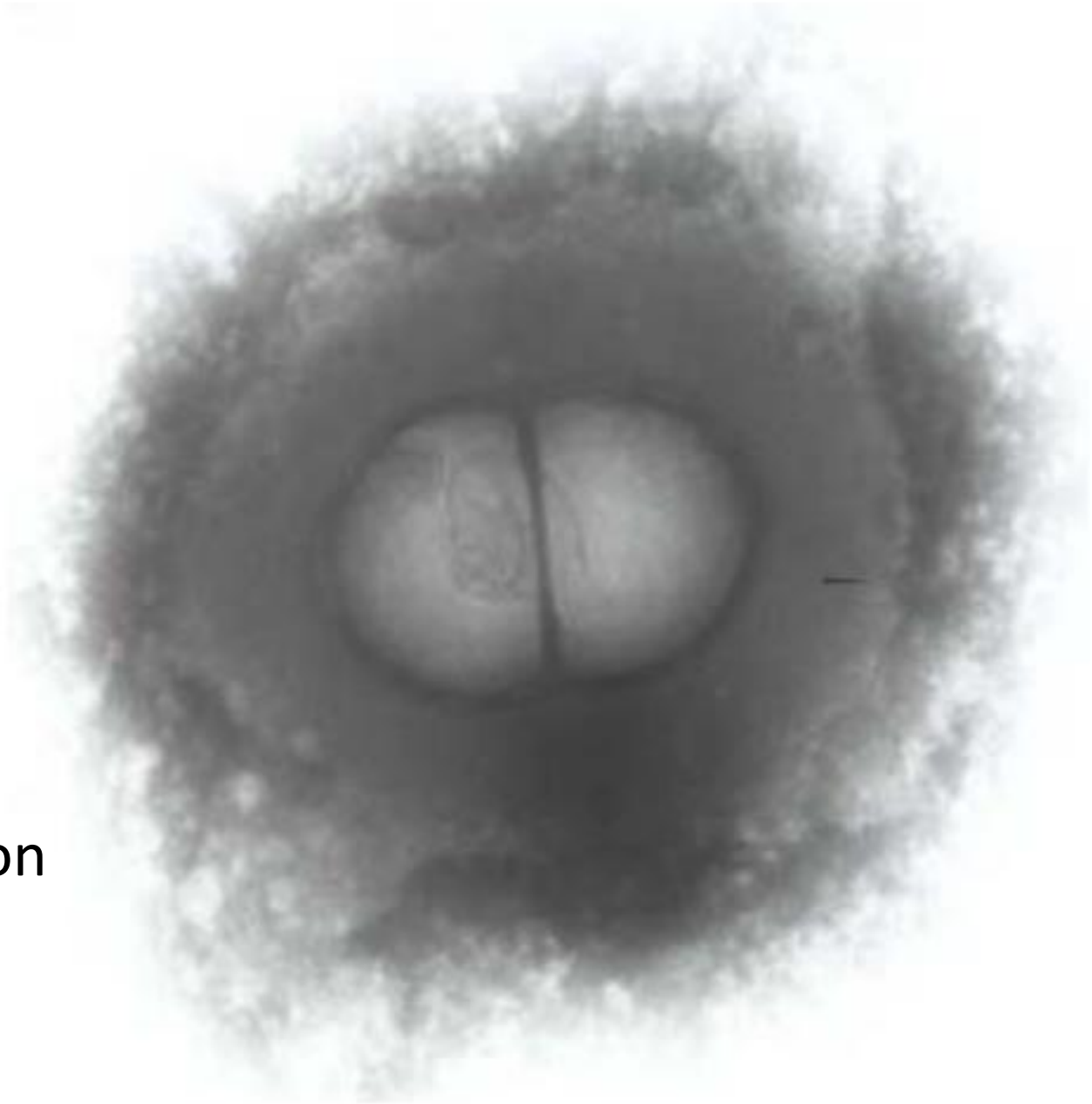
- 90 sérotypes capsulaires
- Hétérogénéité de leur invasivité
  - Ratio portage/invasion : variation de 2 log

- 20-30 sérotypes font 90% des cas d'IIP

- Capsule : protection contre l'opsonisation
  - Par le complément
  - Par les anticorps



3

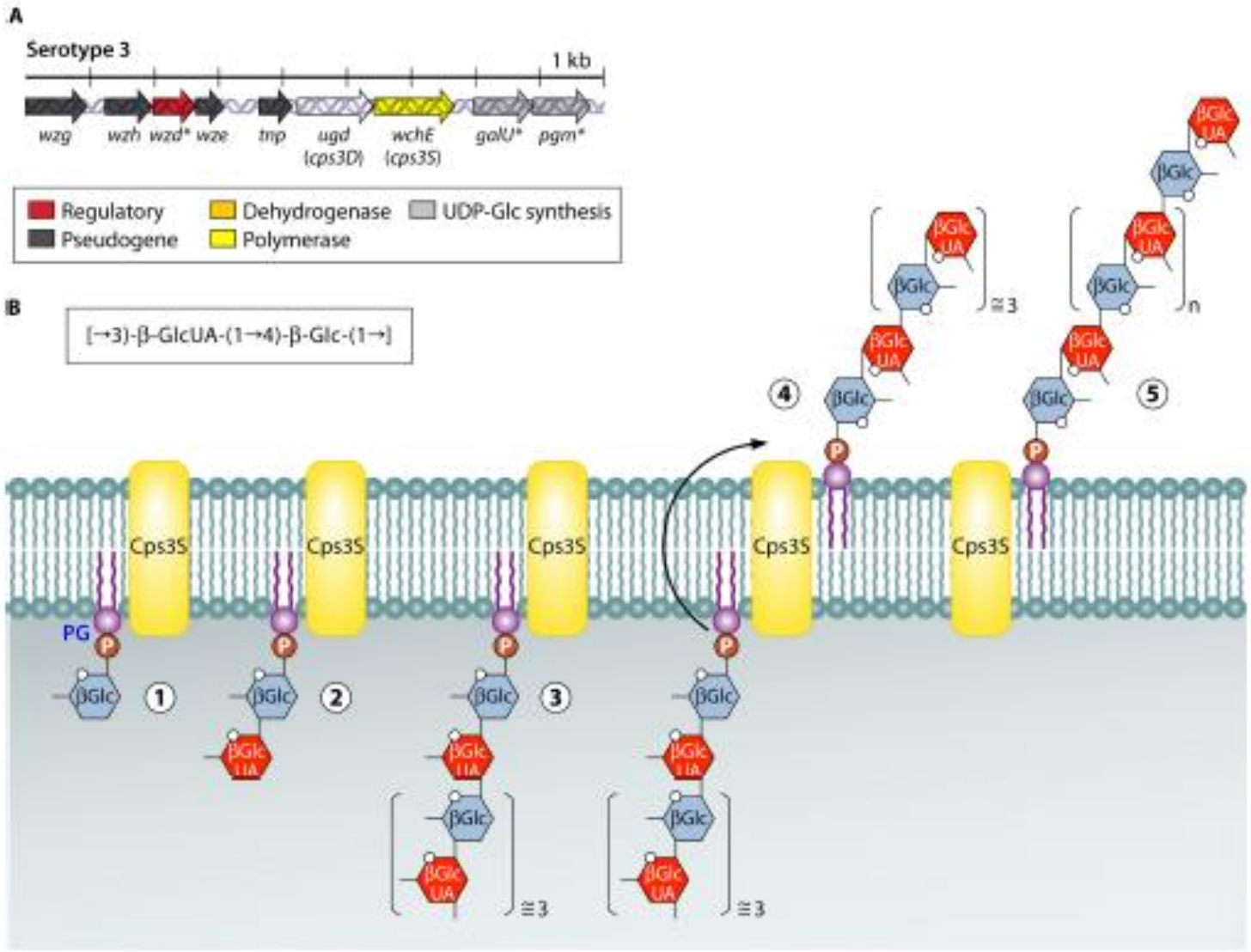
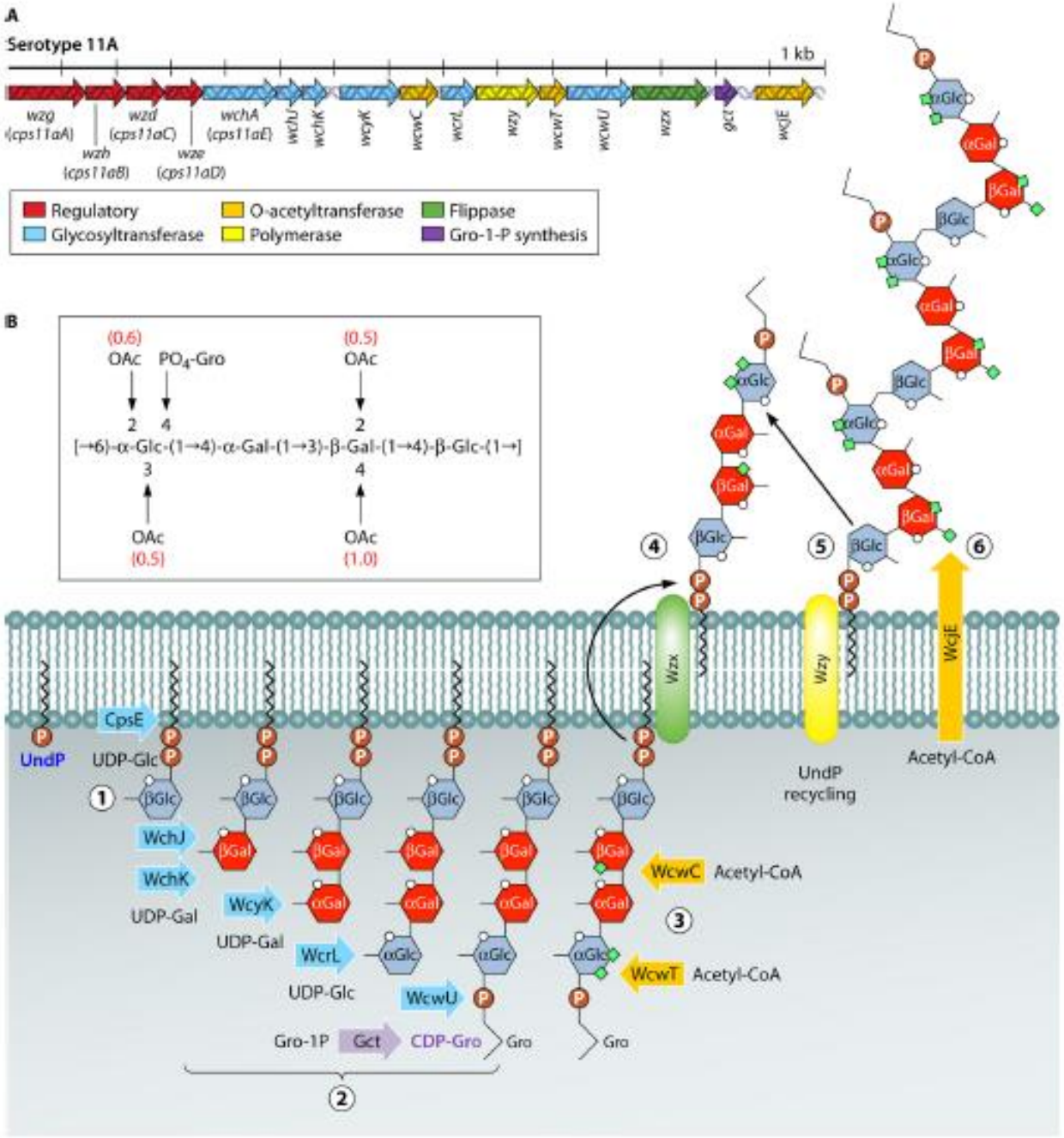


FIG 2 Serotype 3 has a divergent *cps* locus and utilizes synthase-dependent assembly. (A) The serotype 3 *cps* locus (based on GenBank accession no. CR931634.2). The *cps* locus occurs between *dexB* and *aliA* on the chromosome. Note that *ugd* (*cps3D*) and *wchE* (*cps3S*) are necessary for capsular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

11A


A
Serotype 11A
1 kb
wzg (cps11aA)
wzh (cps11aB)
wzd (cps11aC)
wze (cps11aD)
wchA (cps11aE)
wchJ
wchK
wcyK
wcwC
wcrL
wzy
wcwT
wcwU
wzx
gct
wcjE
Regulatory
Glycosyltransferase
O-acetyltransferase
Polymerase
Flippase
Gro-1-P synthesis
B
(0.6)
OAc
PO4-Gro
(0.5)
OAc
2
4
2
[→6)-α-Glc-(1→4)-α-Gal-(1→3)-β-Gal-(1→4)-β-Glc-(1→]
3
4
OAc
(0.5)
OAc
(1.0)
CpsE
UndP
UDP-Glc
WchJ
WchK
UDP-Gal
WcyK
UDP-Gal
WcrL
UDP-Glc
WcwU
Gro-1P
Gct
CDP-Gro
Gro
Gro
WcwC
Acetyl-CoA
WcwT
Acetyl-CoA
Wzx
Wzy
WcjE
UndP recycling
Acetyl-CoA
1
2
3
4
5
6

Vaccins anti-pneumococciques

- Vaccins polysaccharidiques
  - Pneumovax®, pneumo23®
  - 23 sérotypes
  - Mauvaise réponse chez le nourrisson
  - AMM après 5 ans
  - Peu ou pas d'induction de mémoire immunologique
  - Risque d'hyporéactivité si revaccination par vaccin conjugué ou pas

- Vaccins conjugués
  - Prévenar7® puis Prévenar 13®
  - Conjugaison à l'anatoxine tétanique
  - Meilleure réponse chez le nourrisson
  - AMM avant 5 ans et après 50 ans
  - Induction d'une mémoire immunologique
  - Efficacité sur le portage

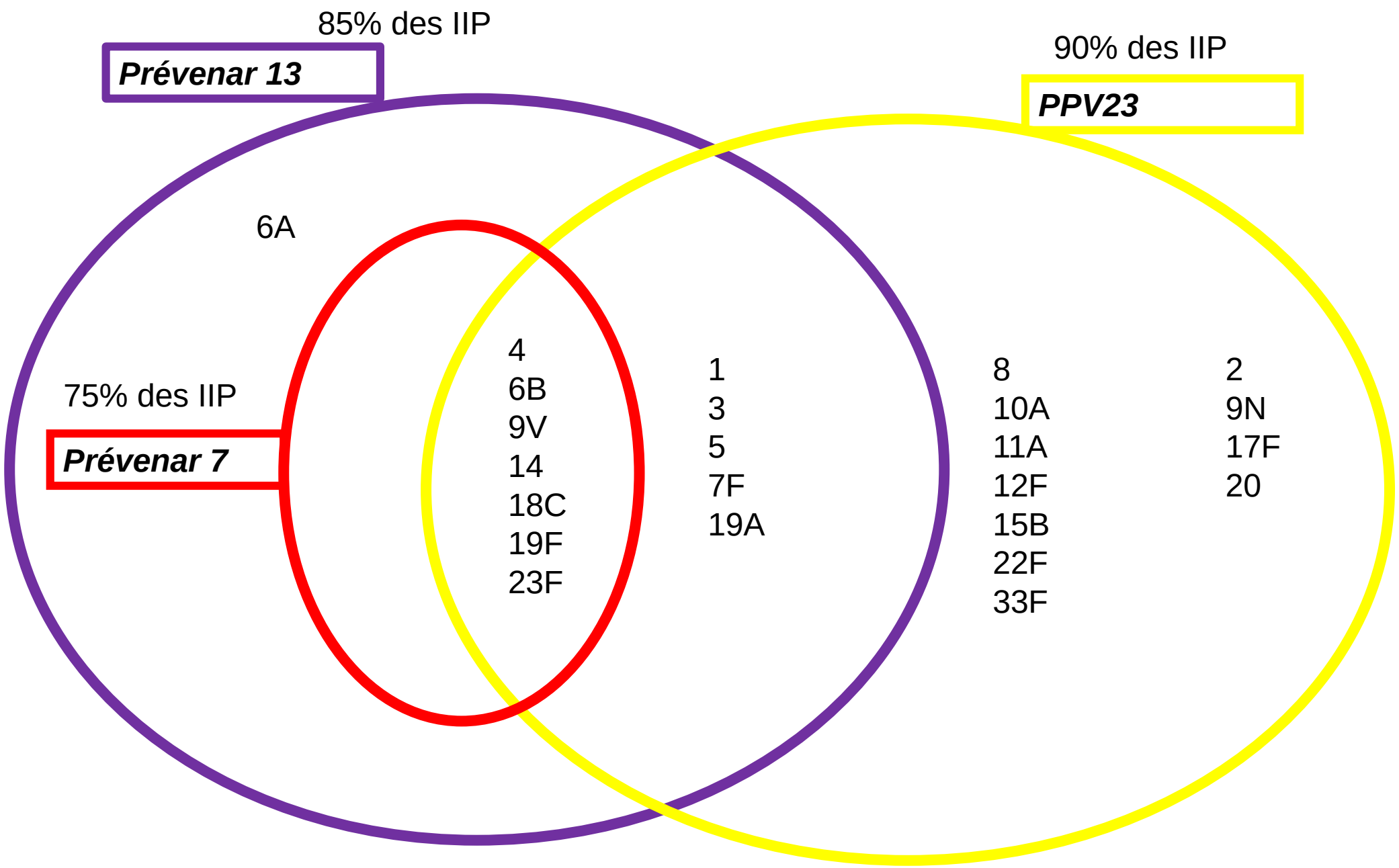
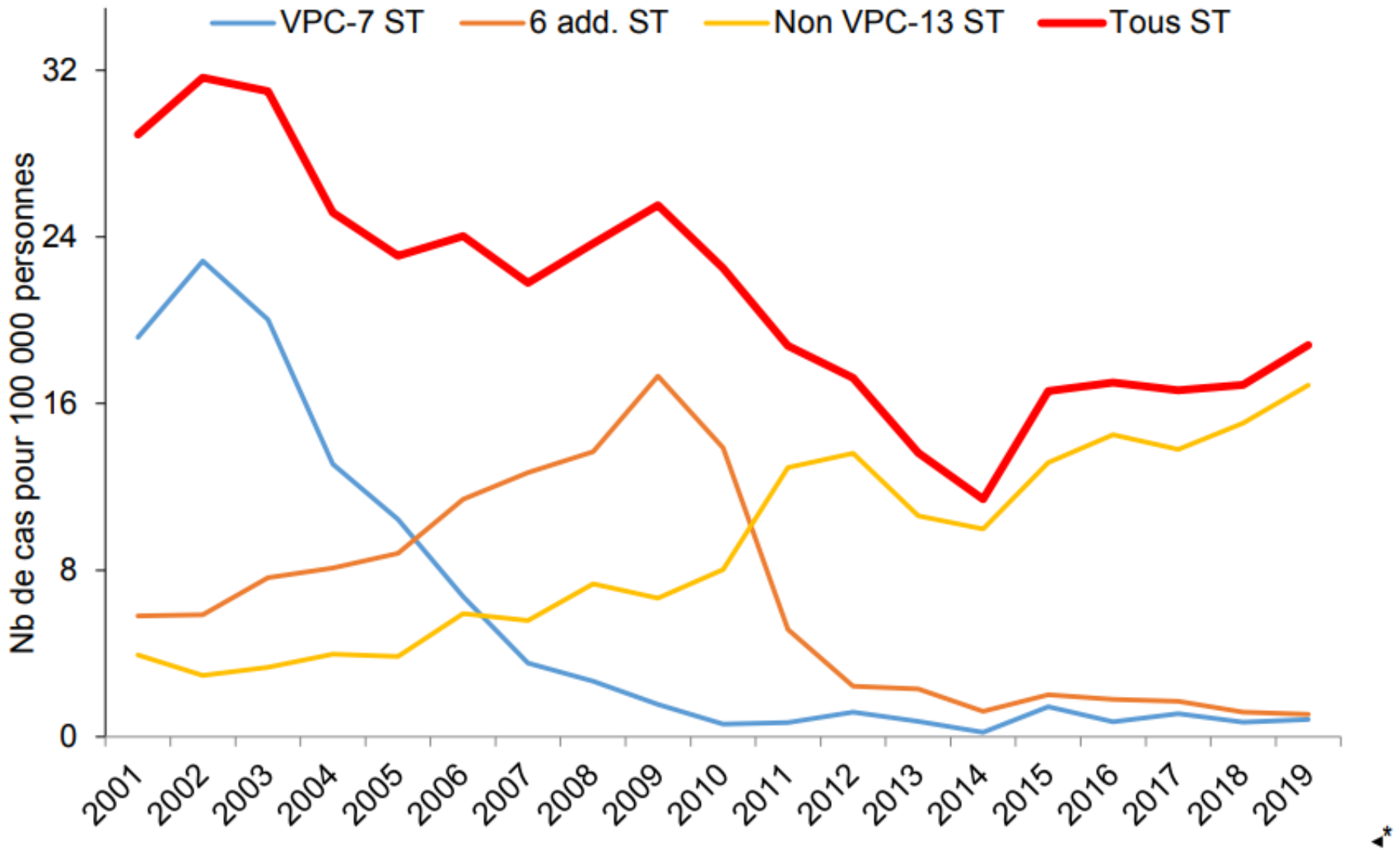

85% des IIP
Prévenar 13
90% des IIP
PPV23
6A
75% des IIP
Prévenar 7
4
6B
9V
14
18C
19F
23F
1
3
5
7F
19A
8
10A
11A
12F
15B
22F
33F
2
9N
17F
20

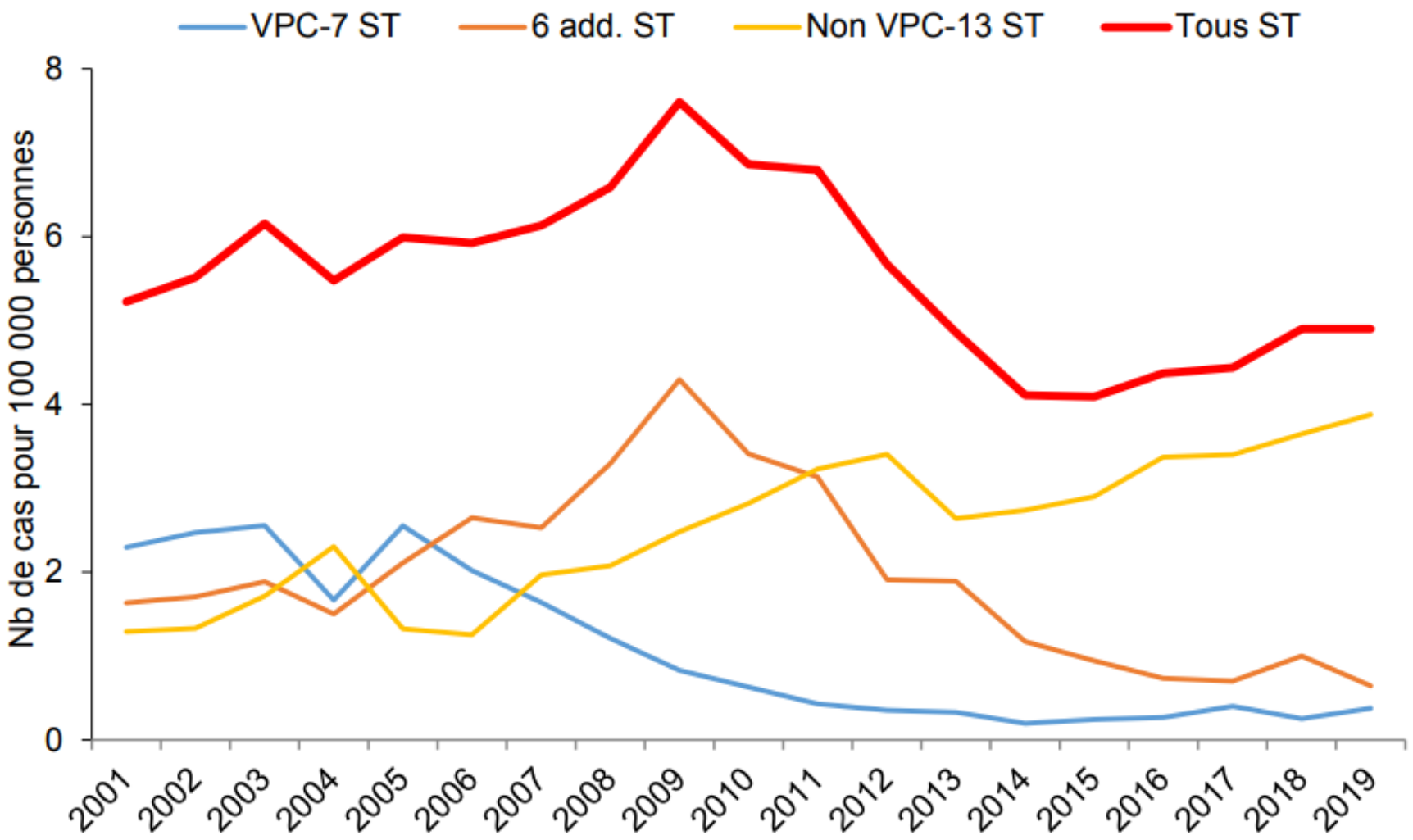
Figure 2 : Incidence des infections invasives à pneumocoques par groupe de sérotypes, chez les enfants âgés de moins de 2 ans, France métropolitaine, 2001-2019*



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

Santé Publique France

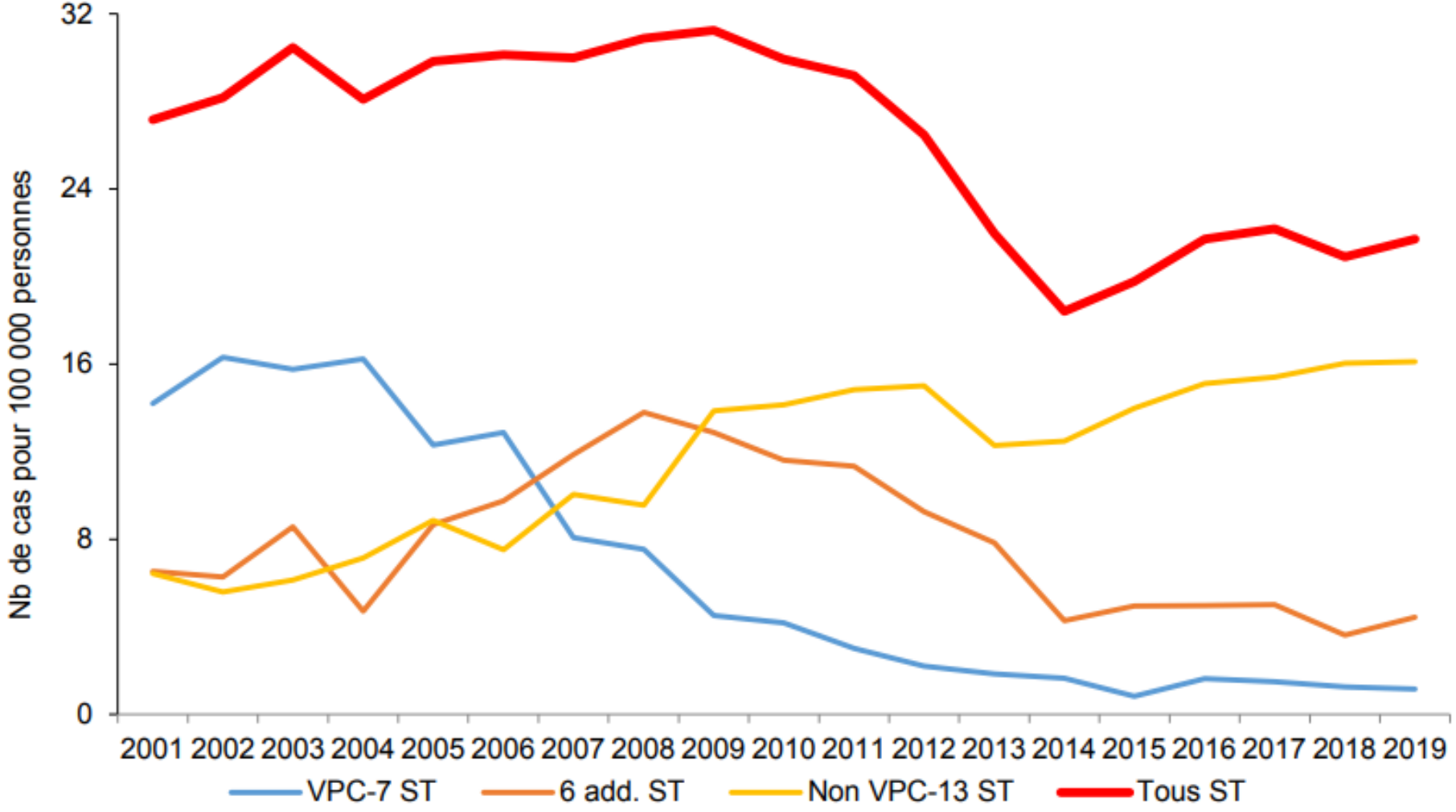
Figure 5 : Incidence des infections invasives à pneumocoques par groupe de sérotypes, chez les enfants et adultes âgés de 15 à 64 ans, France métropolitaine 2001-2019*



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

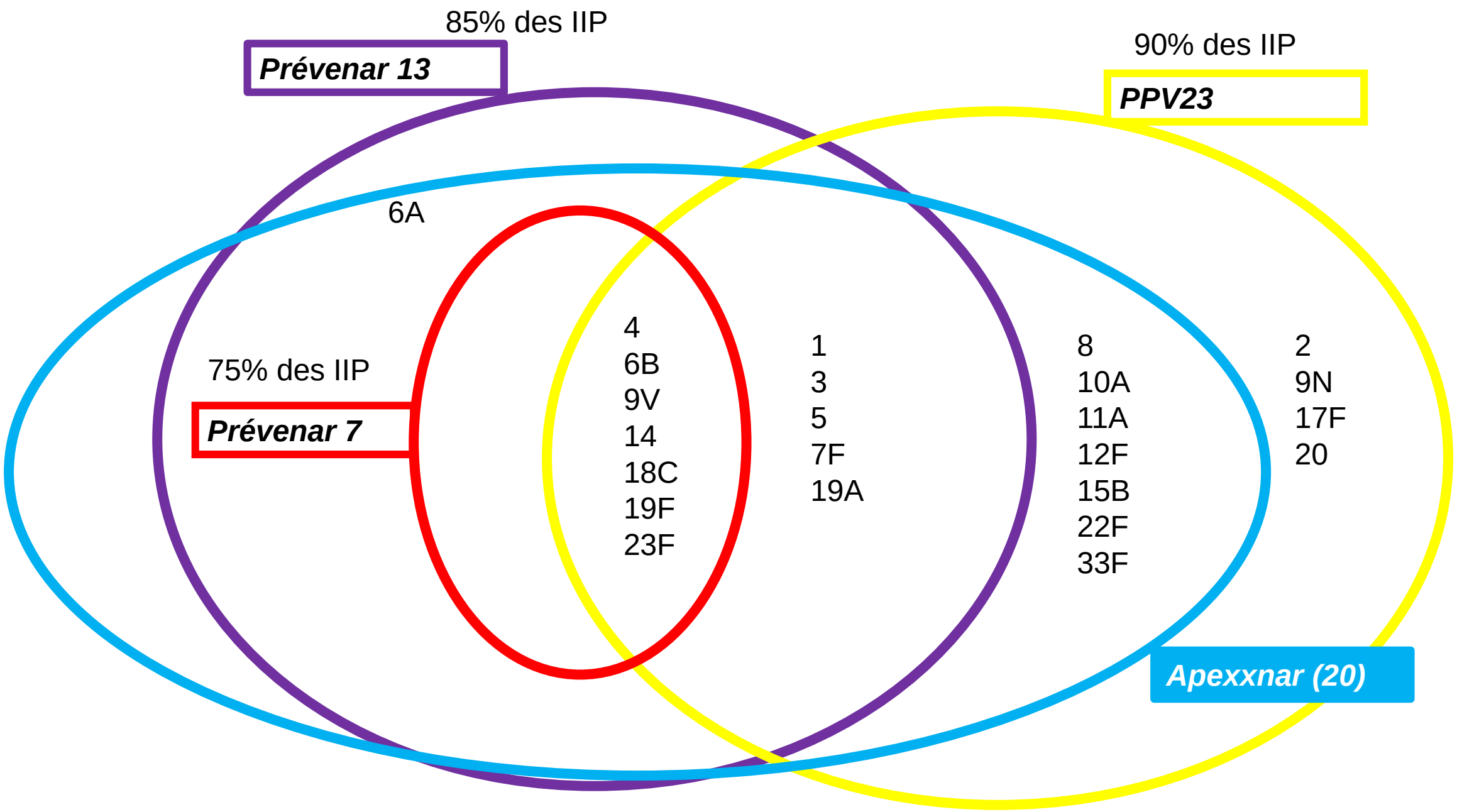
Santé Publique France

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



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

Santé Publique France


85% des IIP
Prévenar 13
90% des IIP
PPV23
6A
75% des IIP
Prévenar 7
4
6B
9V
14
18C
19F
23F
1
3
5
7F
19A
8
10A
11A
12F
15B
22F
33F
2
9N
17F
20
Apexxnar (20)

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

hivma hiv medicine association

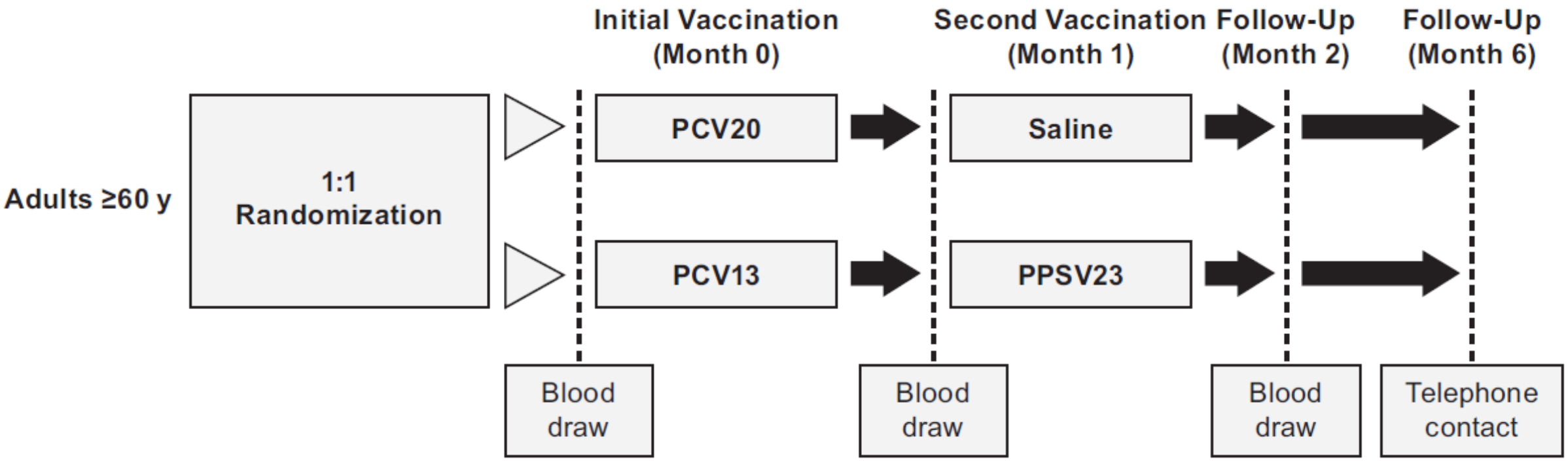
OXFORD

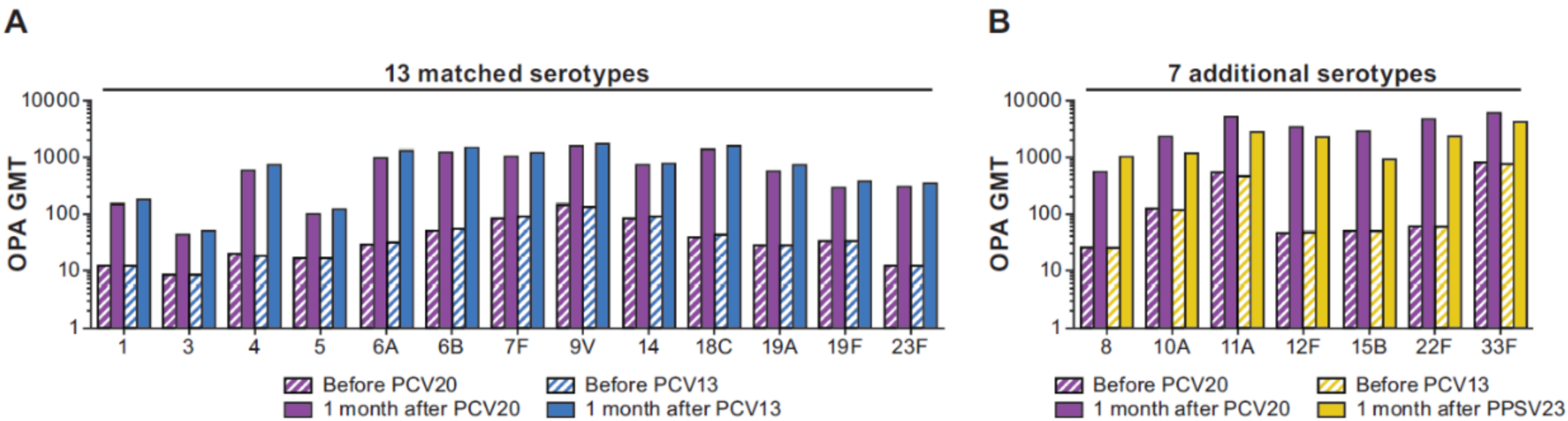
2023

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

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

[1]Meridian Clinical Research, Omaha, Nebraska, USA; [2]Vaccine Research and Development, Pfizer Inc, Pearl River, New York, USA; [3]PMG Research of Wilmington, Wilmington, North Carolina, USA; [4]Cincinnati Children's Hospital, Cincinnati, Ohio, USA; [5]Vaccine Research and Development, Pfizer Inc, Collegeville, Pennsylvania, USA; and [6]Syneos Health, Somerset, New Jersey, USA


Initial Vaccination
(Month 0)
Second Vaccination
(Month 1)
Follow-Up
(Month 2)
Follow-Up
(Month 6)
Adults ≥60 y
1:1
Randomization
PCV20
PCV13
Saline
PPSV23
Blood
draw
Blood
draw
Blood
draw
Telephone
contact

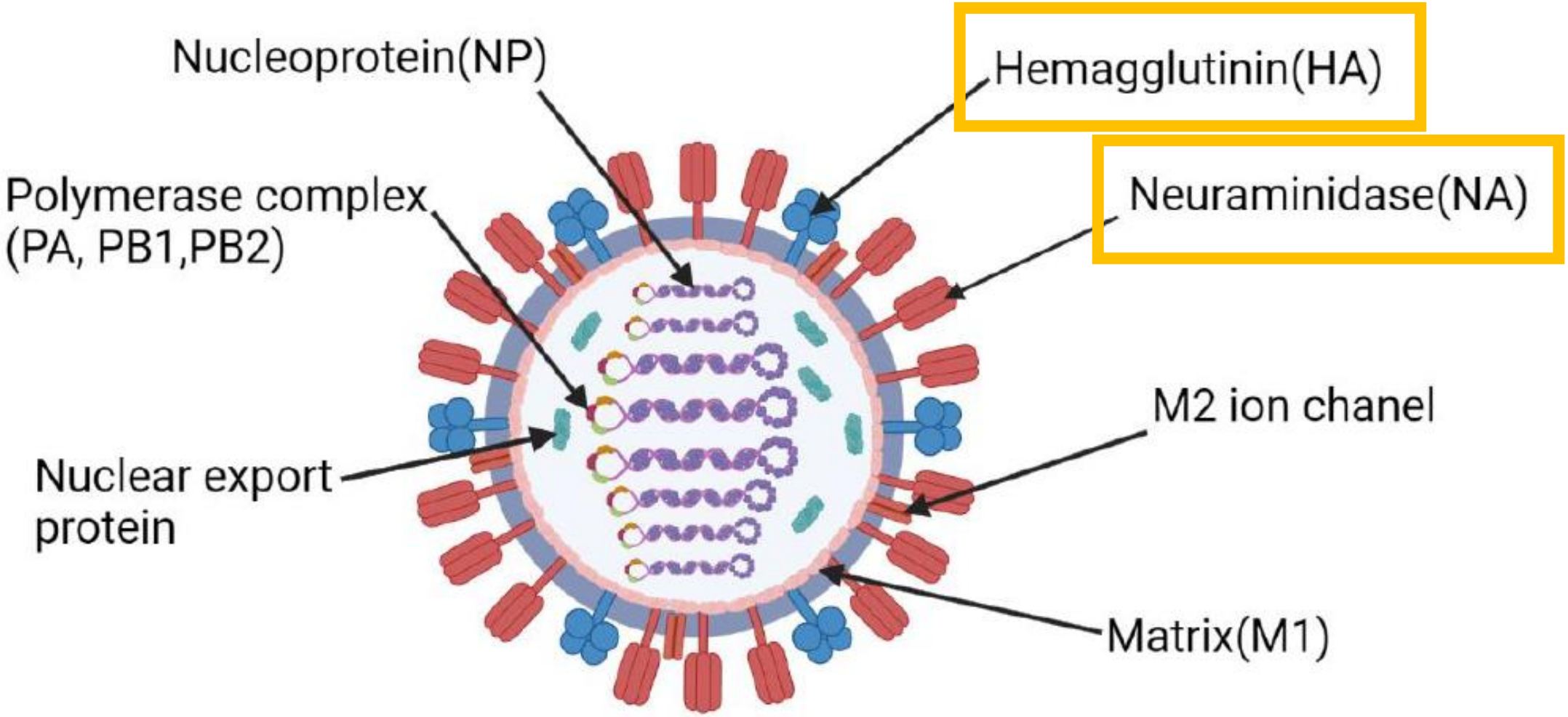

A
13 matched serotypes
OPA GMT
10000
1000
100
10
1
1
3
4
5
6A
6B
7F
9V
14
18C
19A
19F
23F
Before PCV20
Before PCV13
1 month after PCV20
1 month after PCV13
B
7 additional serotypes
OPA GMT
10000
1000
100
10
1
8
10A
11A
12F
15B
22F
33F
Before PCV20
Before PCV13
1 month after PCV20
1 month after PPSV23

Quelle évolution des schémas vaccinaux ?

- Actuellement :
  - Enfant : Prévenar 13 à 2-4-11 mois
  - Adultes avec comorbidités, immunodéprimé :
    - Prévenar 13 puis Pneumovax 2 mois après
    - Puis Pneumovac 5 ans après

- À venir dès 2023
  - Enfant : **Apexxnar à 2-4-11 mois**
  - Adultes avec comorbidités, immunodéprimé :
    - **Une dose d'Apexxnar ?**
    - **Un rappel à 5 an ?**
  - Un vaccin conjugué 15-valent sera probablement disponible aussi
    - En utilisation chez l'adulte : une injection suivi d'un Pneumovax
    - Avantage : disposer d'un autre fabricant si pénurie avec le premier …

Grippe



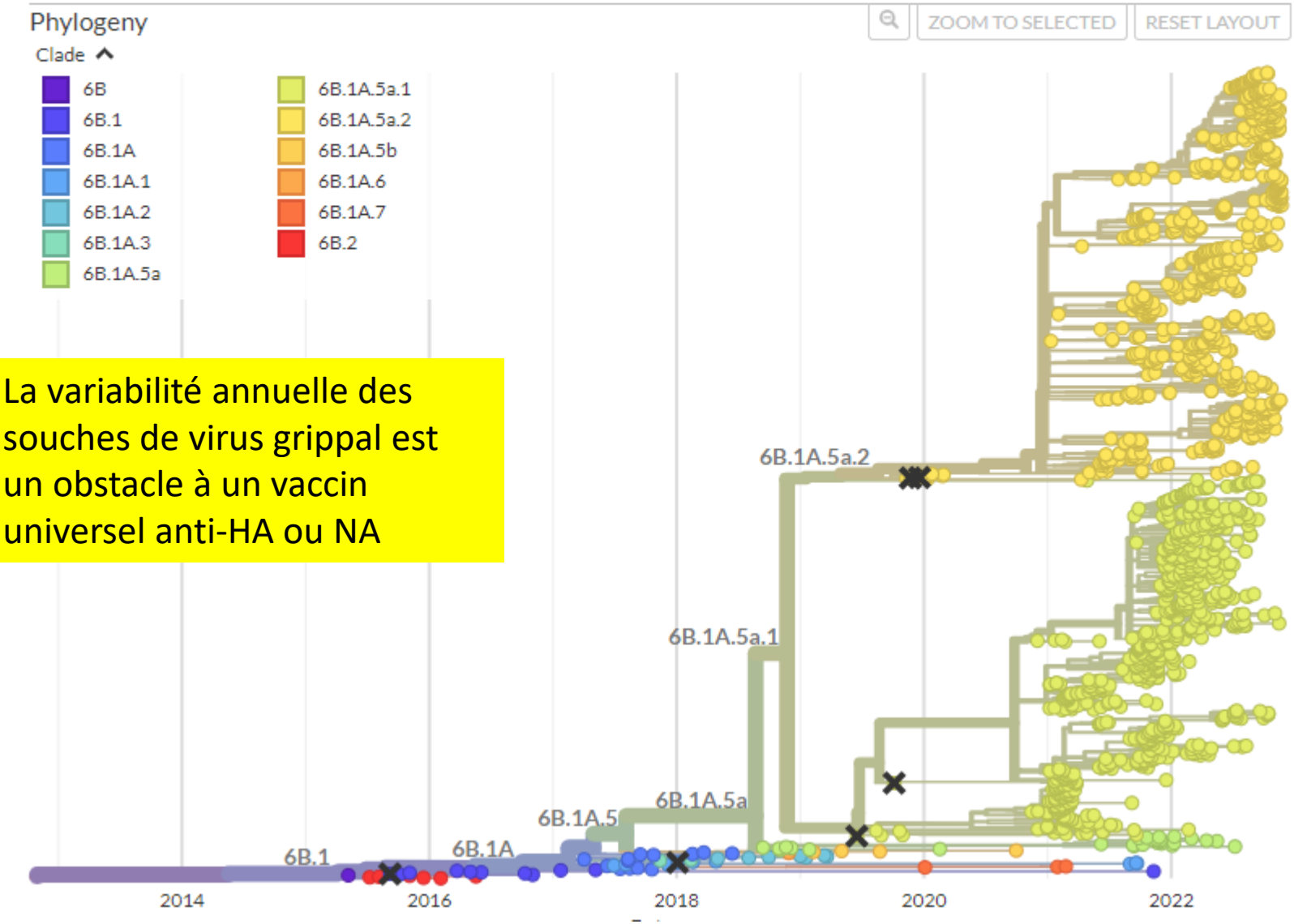
L'efficacité des vaccins annuels est diminuée par la variabilité des protéines ciblées, HA et NA
Des vaccins (en particulier déclenchant une réponse T cytotoxique) contre les protéines M et NP pourraient être « universels »

Nextstrain.org

Real-time tracking of influenza A/H1N1pdm evolution

Built with nextstrain/seasonal-flu. Maintained by Jover Lee, Richard Neher and Trevor Bedford. Enabled by data from GISAID.

Showing 1625 of 1625 genomes sampled between May 2015 and Nov 2022.



La variabilité annuelle des souches de virus grippal est un obstacle à un vaccin universel anti-HA ou NA

Dose d’antigène des vaccins anti-grippaux

- Vaccins inactivés
- Dose standard d’antigène : 15 µg pour chacune des 4 souches
- Haute dose (vaccin Efluelda®) : 60 µg pour chacune des 4 souches

2021

Contents lists available at ScienceDirect

Journal of Infection

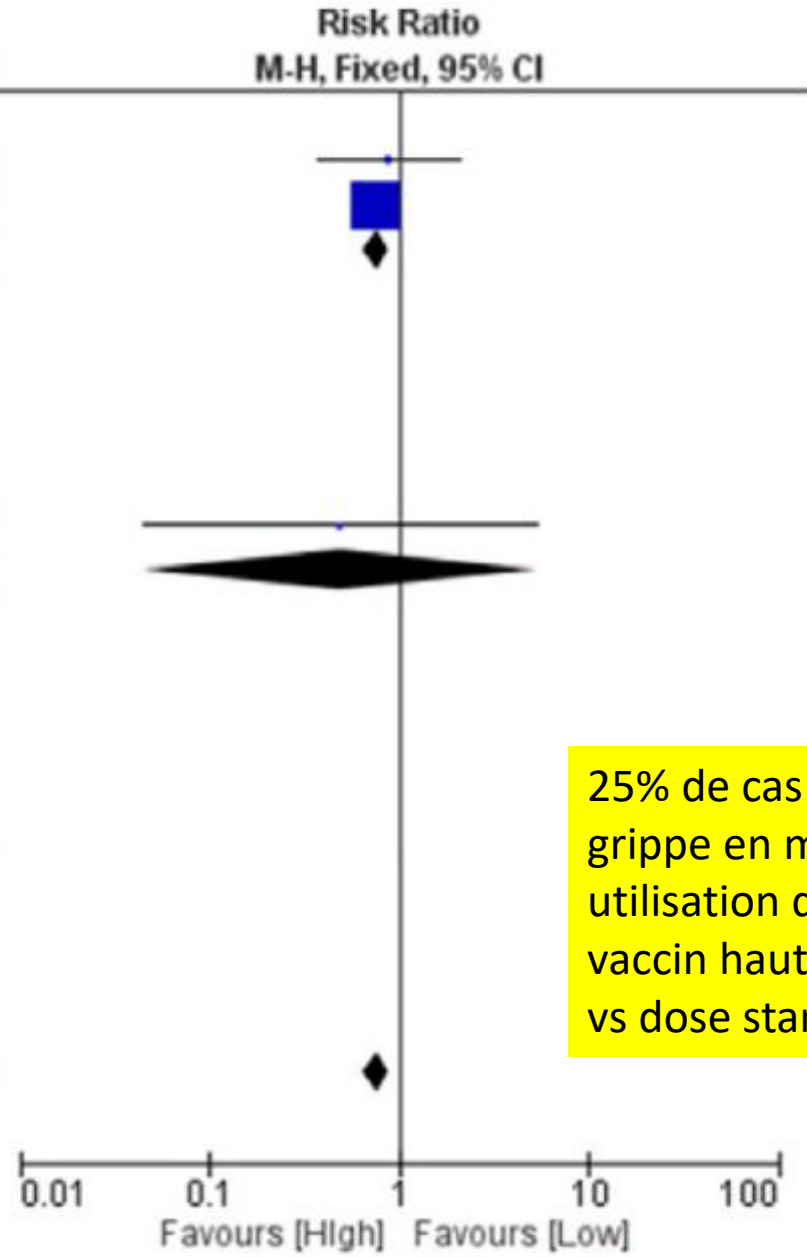
journal homepage: www.elsevier.com/locate/jinf

Clinical efficacy and safety of high dose trivalent influenza vaccine in adults and immunosuppressed populations – A systematic review and meta-analysis

Yaara Leibovici Weissman[a,b,*], Lisa Cooper[b,c], Neta Sternbach[b,d], Liat Ashkenazi-Hoffnung[b,e], Dafna Yahav[b,f]

[a] Internal medicine E, Rabin Medical Center, Beilinson Hospital, Petah Tikva, Israel
[b] Sackler School of Medicine, Tel Aviv University, Ramat Aviv, Israel
[c] Department of acuter geriatrics, Rabin Medical Center, Beilinson Hospital, Petah Tikva, Israel
[d] Internal medicine D, Rabin Medical Center, Beilinson Hospital, Petah Tikva, Israel
[e] Day Hospitalization Department and Infectious Diseases Unit, Schneider Childrens Medical Center of Israel, Petah Tikva, Israel
[f] Infectious Diseases Unit, Rabin Medical Center, Beilinson Hospital, Petah Tikva, Israel

Study or Subgroup	High Events	High Total	Low Events	Low Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.3.1 Elderly						
DiazGranados 2013	14	6107	8	3051	3.4%	0.87 [0.37, 2.08]
DiazGranados 2014 S1	228	15990	301	15993	96.0%	0.76 [0.64, 0.90]
Subtotal (95% CI)		**22097**		**19044**	**99.4%**	**0.76 [0.64, 0.90]**
Total events	242		309			
Heterogeneity: Chi² = 0.10, df = 1 (P = 0.75); I² = 0%						
Test for overall effect: Z = 3.19 (P = 0.001)						
1.3.2 Immunocompromised						
Natori 2017	1	87	2	85	0.6%	0.49 [0.05, 5.29]
Subtotal (95% CI)		**87**		**85**	**0.6%**	**0.49 [0.05, 5.29]**
Total events	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.59 (P = 0.56)						
1.3.3 Others						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**22184**		**19129**	**100.0%**	**0.76 [0.64, 0.90]**
Total events	243		311			
Heterogeneity: Chi² = 0.23, df = 2 (P = 0.89); I² = 0%						
Test for overall effect: Z = 3.22 (P = 0.001)						
Test for subgroup differences: Chi² = 0.13, df = 1 (P = 0.72), I² = 0%						



25% de cas de grippe en moins si utilisation du vaccin haute dose vs dose standard

Vaccine 39 (2021) A24–A35

Contents lists available at ScienceDirect

Vaccine

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

Review

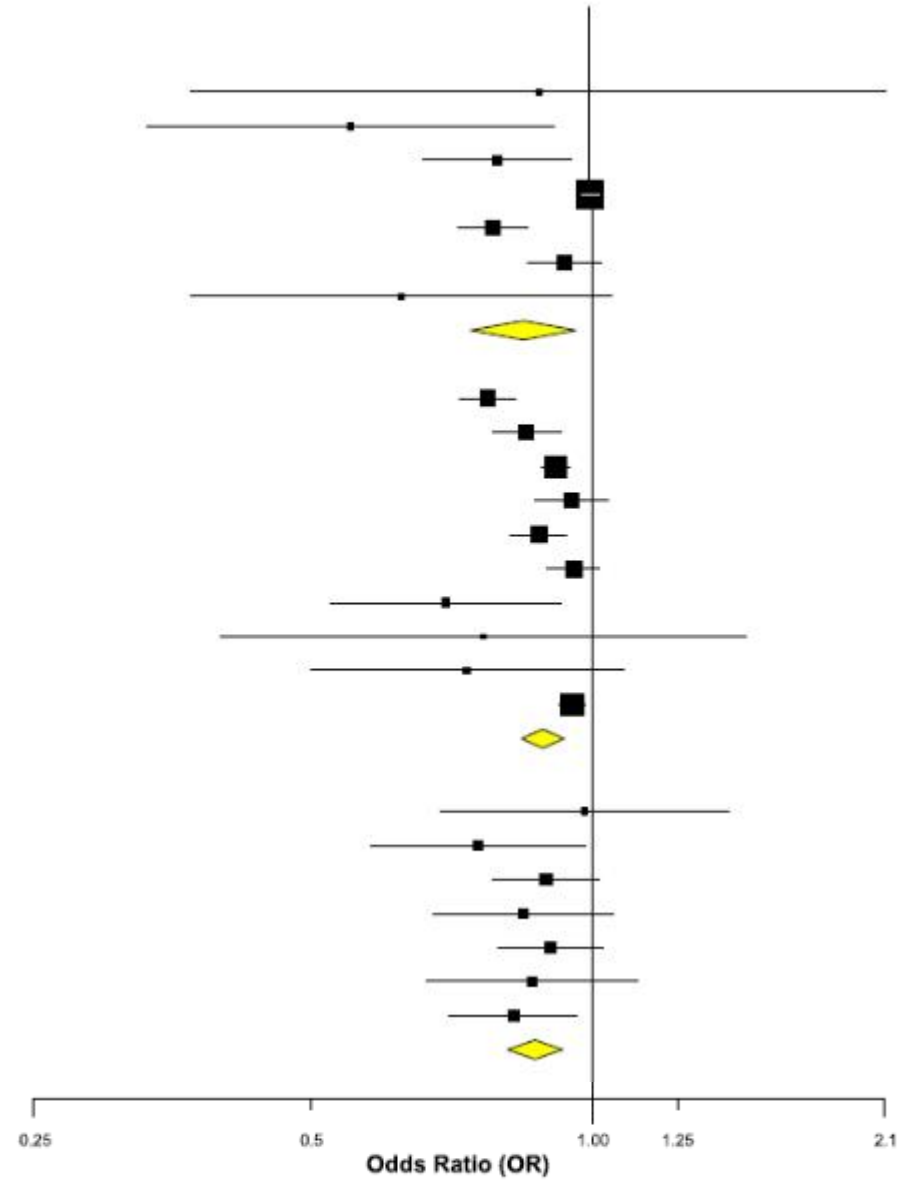
Efficacy and effectiveness of high-dose influenza vaccine in older adults by circulating strain and antigenic match: An updated systematic review and meta-analysis ☆

Jason K.H. Lee [a,b,*], Gary K.L. Lam [a,b], Thomas Shin [b,c], Sandrine I. Samson [d], David P. Greenberg [d], Ayman Chit [a,d]

[a] Leslie Dan School of Pharmacy, University of Toronto, Toronto, ON, Canada
[b] Sanofi Pasteur, Toronto, ON, Canada
[c] Department of Mathematics and Statistics, York University, Toronto, ON, Canada
[d] Sanofi Pasteur, Swiftwater, PA, USA

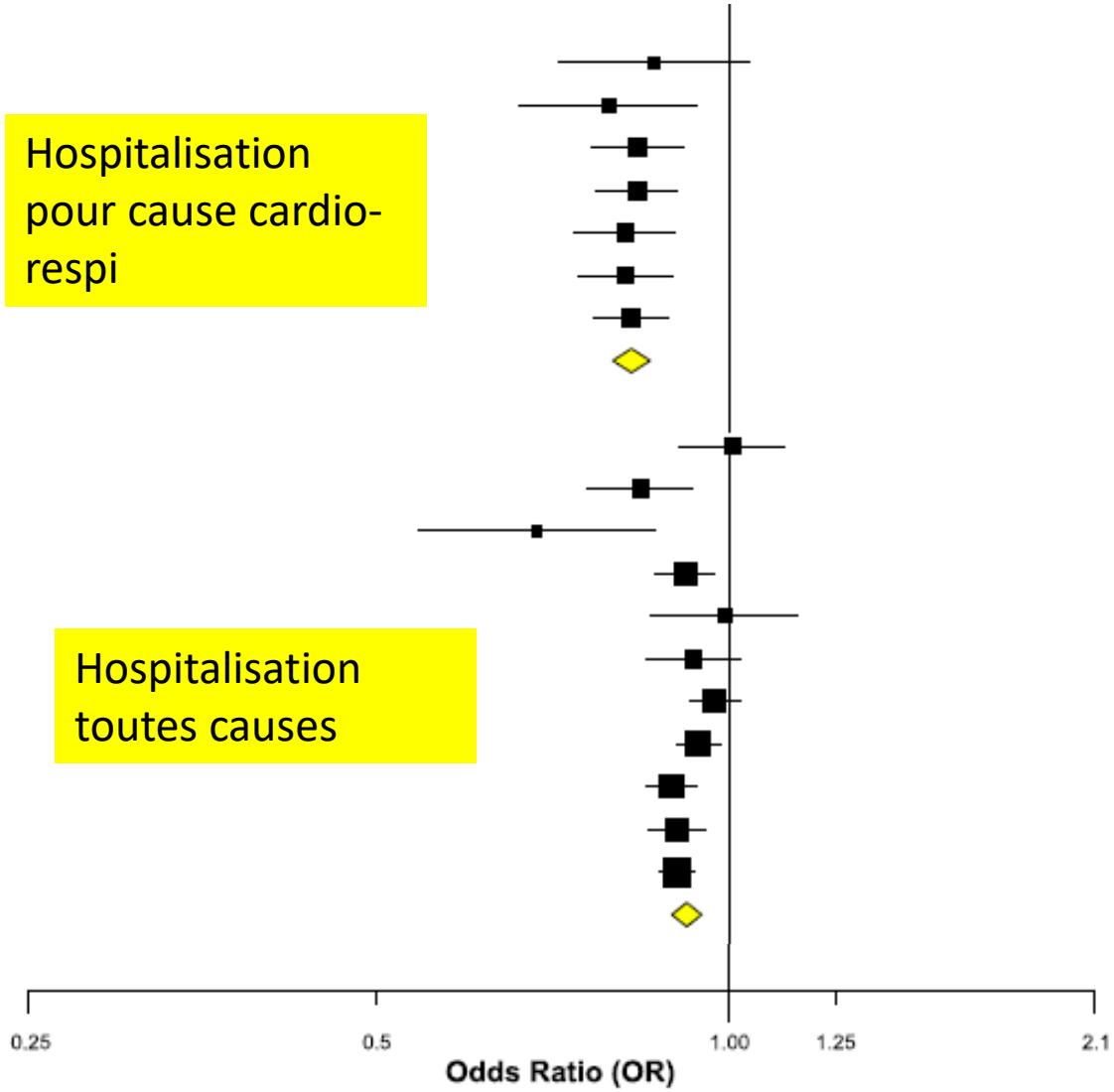
Évolution de l'efficacité selon les années

Studies (Influenza Season, Predominant Strain)	Odds Ratio (95% CI)
Syndrome grippal	
DiazGranados 2013 (2009–10)	0.87 (0.37, 2.09)
DiazGranados 2014 (2011–12)	0.55 (0.33, 0.91)
DiazGranados 2014 (2012–13)	0.79 (0.65, 0.95)
Izurieta 2018 (2017–18)	0.99 (0.97, 1.02)
Shay 2017 (2012–13)	0.78 (0.71, 0.85)
Shay 2017 (2013–14)	0.93 (0.85, 1.02)
Young–Xu 2018 (2015–16)	0.62 (0.37, 1.05)
Subgroup Influenza–like Illness (I^2=85.37% , het. P=0.00)	**0.84 (0.74, 0.96)**
Grippe hospitalisée	
Lu 2019 (2012–13)	0.77 (0.72, 0.82)
Lu 2019 (2013–14)	0.85 (0.78, 0.92)
Lu 2019 (2014–15)	0.91 (0.88, 0.94)
Lu 2019 (2015–16)	0.95 (0.86, 1.04)
Lu 2019 (2016–17)	0.87 (0.82, 0.94)
Lu 2019 (2017–18)	0.95 (0.89, 1.02)
Robison 2018 (2016–17)	0.69 (0.52, 0.92)
Doyle 2020 (2015–16)	0.76 (0.39, 1.47)
Doyle 2020 (2016–17)	0.73 (0.49, 1.08)
Izurieta 2020 (2018–19)	0.95 (0.92, 0.98)
Subgroup Influenza Hospitalization (I^2=77.97%, het. P=0.00)	**0.88 (0.84, 0.93)**
Grippe ou pneumonie hospitalisée	
Richardson 2015 (2010–11)	0.98 (0.68, 1.40)
Young–Xu 2018 (2015–16)	0.75 (0.57, 0.98)
Young–Xu 2019 (2010–11)	0.89 (0.78, 1.02)
Young–Xu 2019 (2011–12)	0.84 (0.67, 1.05)
Young–Xu 2019 (2012–13)	0.90 (0.79, 1.02)
Young–Xu 2019 (2013–14)	0.86 (0.66, 1.12)
Young–Xu 2019 (2014–15)	0.82 (0.70, 0.96)
Subgroup P&I Hospitalization (I^2=0%, het. P=0.86)	**0.87 (0.81, 0.93)**



Évolution de l'efficacité selon les années

DiazGranados 2015 (2011−12)	0.86 (0.71, 1.04)
DiazGranados 2015 (2012−13)	0.78 (0.66, 0.94)
Young−Xu 2019 (2010−11)	0.83 (0.76, 0.91)
Young−Xu 2019 (2011−12)	0.83 (0.77, 0.90)
Young−Xu 2019 (2012−13)	0.81 (0.73, 0.89)
Young−Xu 2019 (2013−14)	0.81 (0.74, 0.89)
Young−Xu 2019 (2014−15)	0.82 (0.76, 0.88)
Subgroup Cardiorespiratory Hospitalization (I^2=5.89%, het. P=0.38)	**0.82 (0.79, 0.86)**
DiazGranados 2015 (2011−12)	1.00 (0.90, 1.12)
DiazGranados 2015 (2012−13)	0.84 (0.75, 0.93)
Gravenstein 2017 (2012−13)	0.68 (0.54, 0.86)
Gravenstein 2017 (2013−14)	0.92 (0.86, 0.97)
Richardson 2015 (2010−11)	0.99 (0.86, 1.15)
Young−Xu 2018 (2015−16)	0.93 (0.85, 1.02)
Young−Xu 2019 (2010−11)	0.97 (0.92, 1.02)
Young−Xu 2019 (2011−12)	0.94 (0.90, 0.98)
Young−Xu 2019 (2012−13)	0.89 (0.85, 0.94)
Young−Xu 2019 (2013−14)	0.90 (0.85, 0.95)
Young−Xu 2019 (2014−15)	0.90 (0.87, 0.93)
Subgroup All−Cause Hospitalization (I^2=54.78%, het. P=0.01)	**0.92 (0.89, 0.95)**



Évolution de l'efficacité selon les années

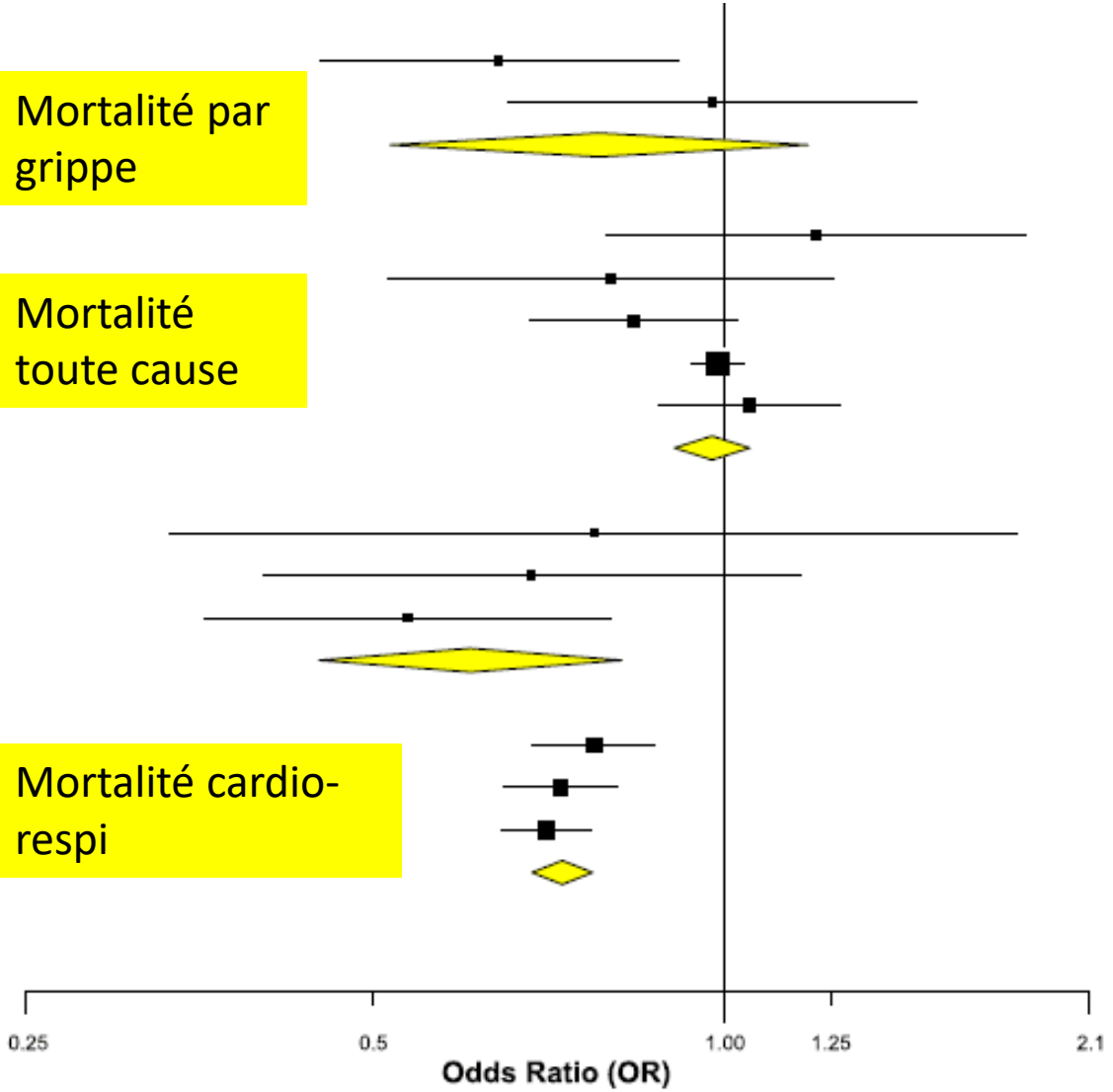
Shay 2017 (2012−13)	0.64 (0.44, 0.91)
Shay 2017 (2013−14)	0.97 (0.65, 1.47)
Subgroup Post−Influenza Mortality (I^2=57.81%, het. P=0.12)	**0.78 (0.51, 1.18)**
DiazGranados 2015 (2011−12)	1.20 (0.79, 1.83)
DiazGranados 2015 (2012−13)	0.80 (0.51, 1.24)
Gravenstein 2017 (2012−13)	0.83 (0.68, 1.03)
Gravenstein 2017 (2013−14)	0.99 (0.93, 1.04)
Richardson 2015 (2010−11)	1.05 (0.88, 1.26)
Subgroup All−Cause Mortality (I^2=13.85%, het. P=0.33)	**0.98 (0.90, 1.05)**
Young−Xu 2020 (2012−13)	0.77 (0.33, 1.80)
Young−Xu 2020 (2013−14)	0.68 (0.40, 1.17)
Young−Xu 2020 (2014−15)	0.53 (0.35, 0.79)
Subgroup P&I Mortality (I^2=0%, het. P=0.64)	**0.60 (0.44, 0.81)**
Young−Xu 2020 (2012−13)	0.77 (0.68, 0.87)
Young−Xu 2020 (2013−14)	0.72 (0.64, 0.81)
Young−Xu 2020 (2014−15)	0.70 (0.64, 0.77)
Subgroup Cardiorespiratory Mortality (I^2=0%, het. P=0.47)	**0.72 (0.68, 0.77)**

Mortalité par grippe

Mortalité toute cause

Mortalité grippe / pneumonie

Mortalité cardio-respi



En conclusion

- Nombreux arguments pour favoriser le vaccin hautement dosé (Efluelda) chez les sujets âgés et immunodéprimés

Zona

Épidémiologie

- **Incidence du zona en augmentation**
  - Car plus de personnes âgées
  - Et plus de personnes très âgées

- **Plus de 2/3 des cas surviennent après 45 ans**
- **50% des plus de 80 ans feront un zona**

- **Âge = hospitalisation plus fréquente**
- **Âge = douleurs post-zostériennes plus fréquentes et plus durables**

Terrains du zona

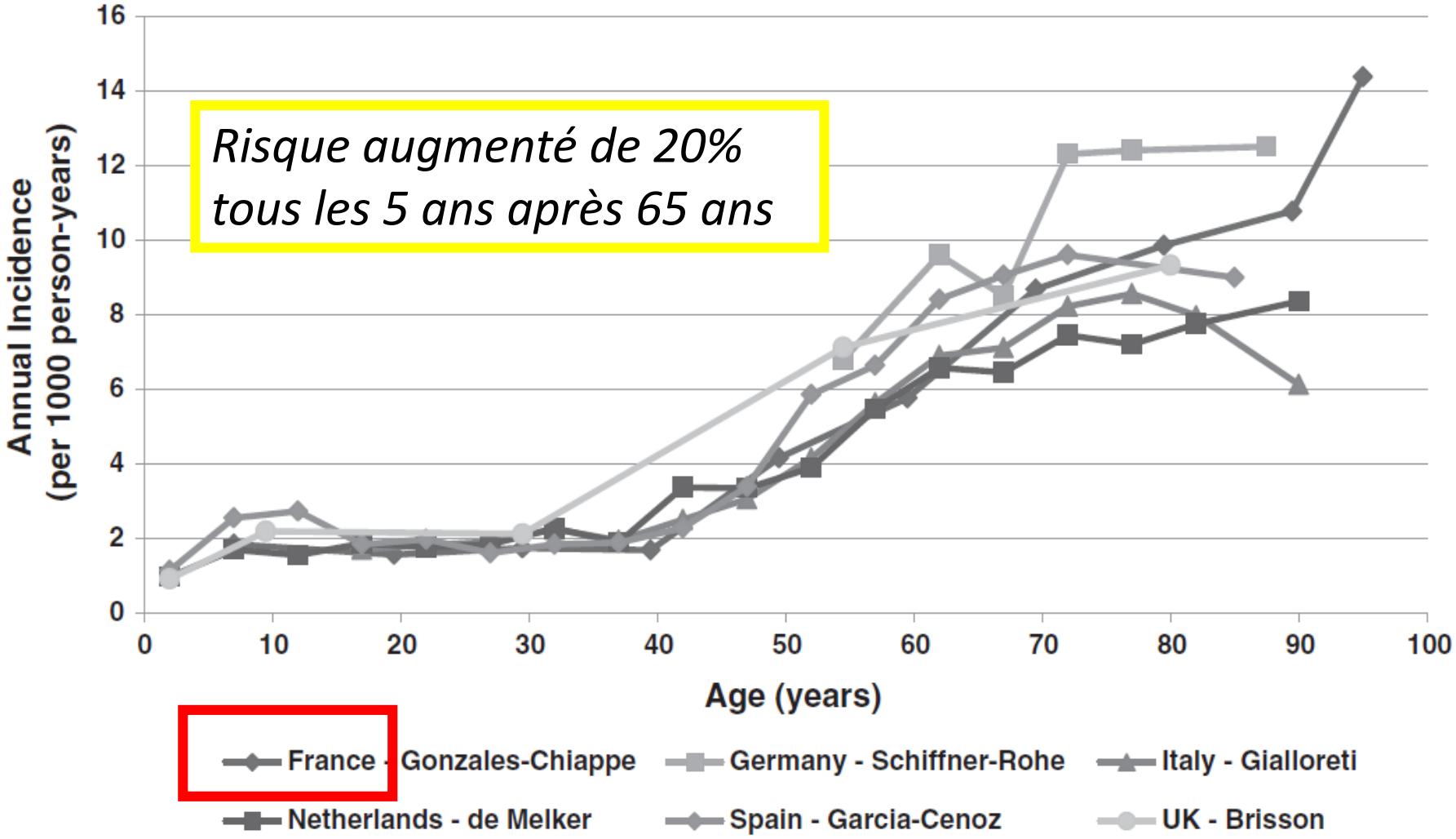
- **Essentiellement l'âge**

Immunodépression	Effectifs	%
Oui	36	5,2
Non	652	94,8
Total	688	100,0

Type d'immunodépression	Effectifs	%
Acquise non médicamenteuse	6	19,4
Médicamenteuse	25	80,6
Total	31	100,0

Données sentinelles 2008

Incidence selon l'âge



Risque augmenté de 20% tous les 5 ans après 65 ans

Pinchinat 2013

Zona : taux d'hospitalisation selon l'âge

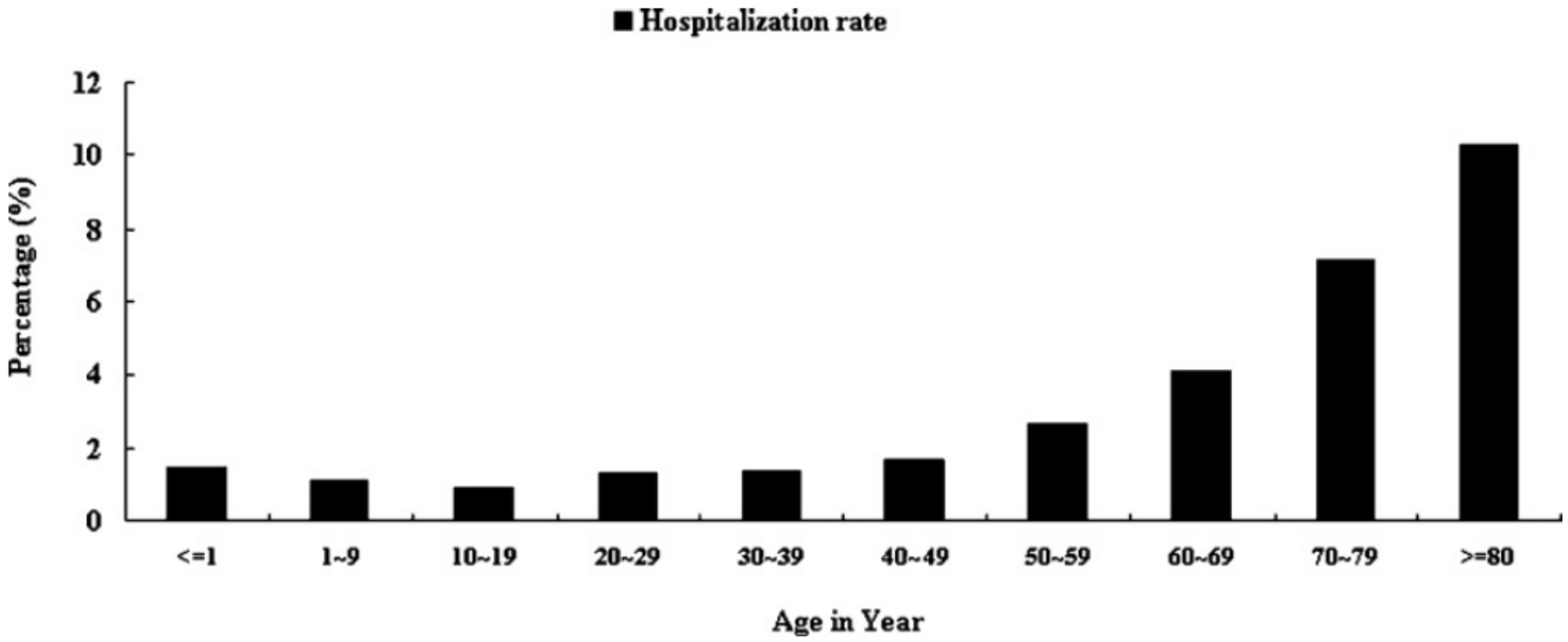
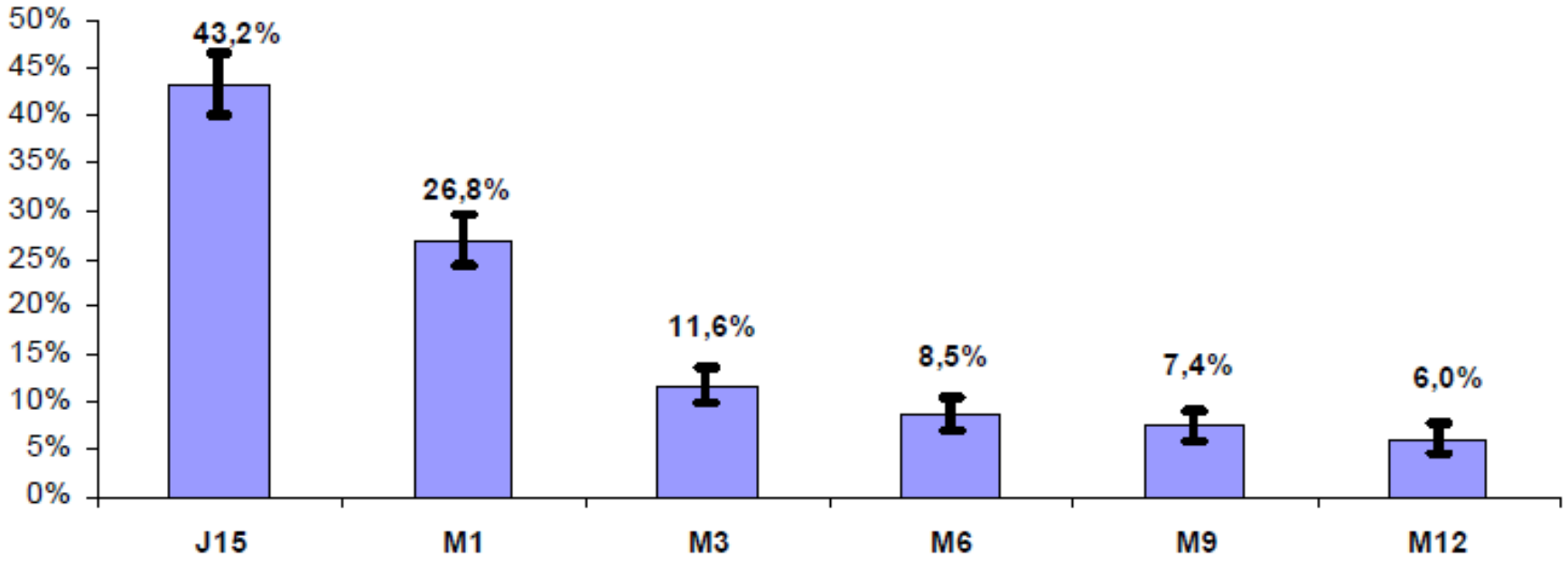


Fig. 3. Age-specific zoster-related hospitalization rate.

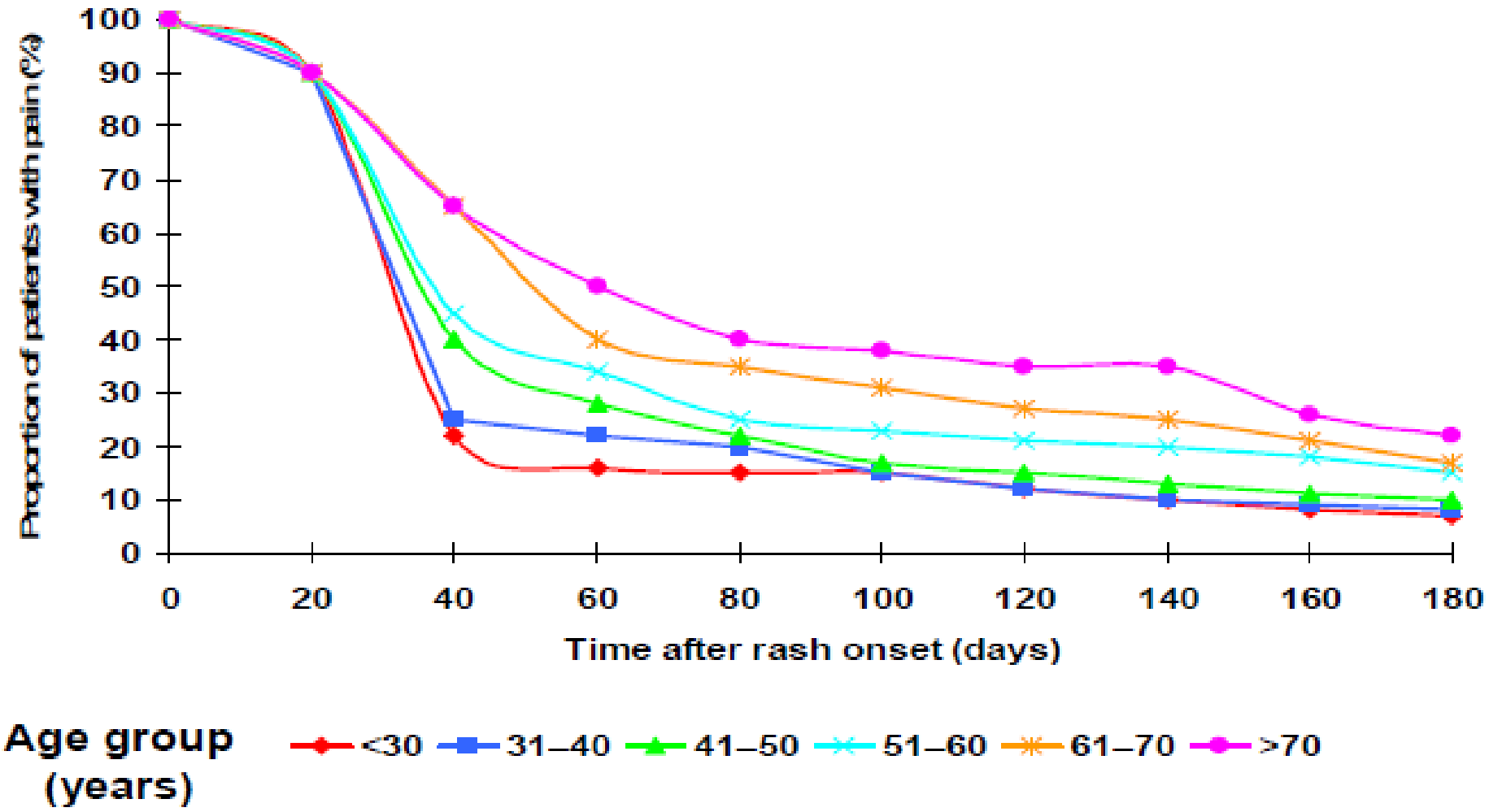
Lin 2010

Proportion d'algies post-zostériennes : étude française AriZona



Temps écoulé depuis l'éruption

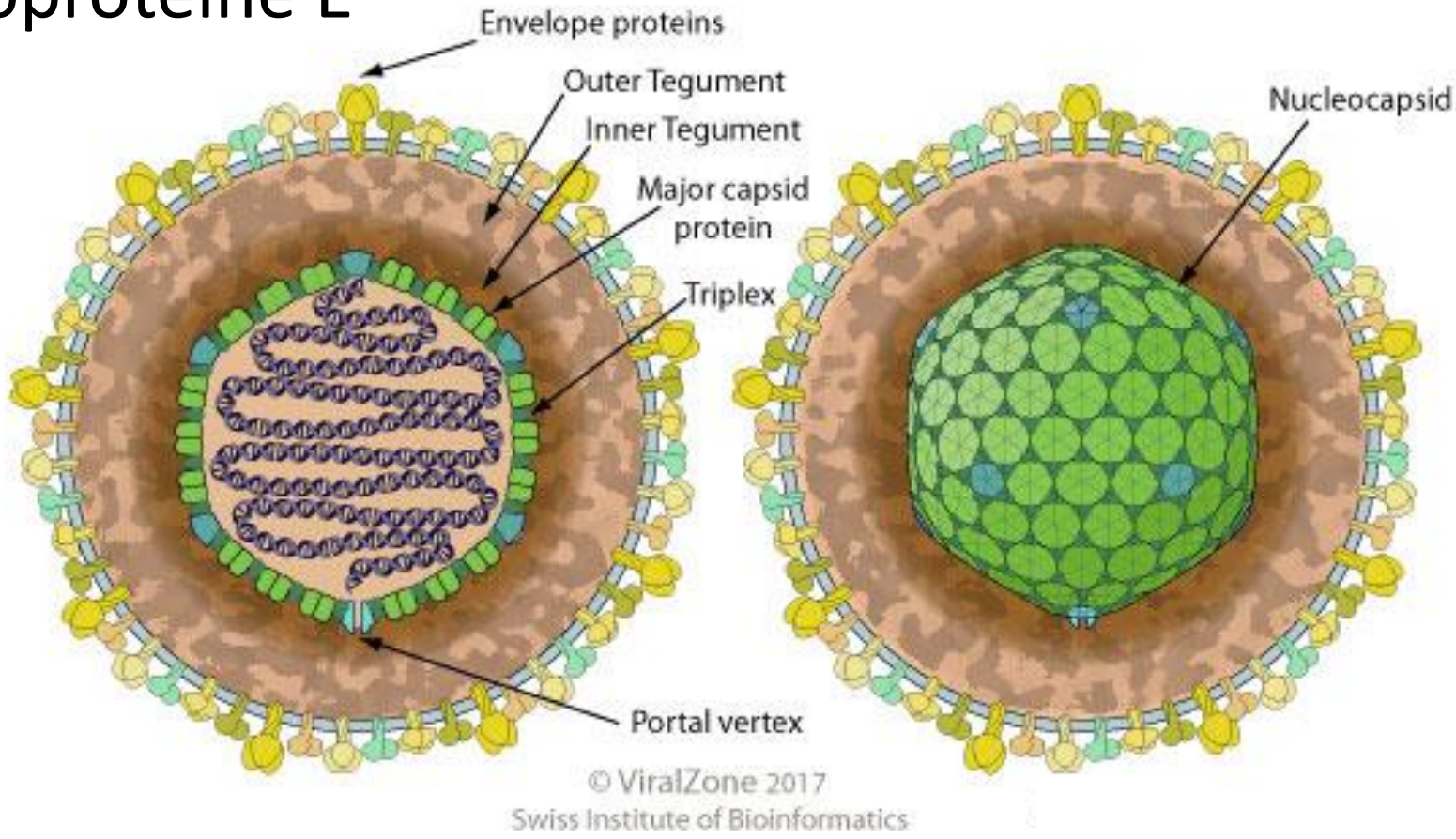
Âge et durée des algies post-zostériennes



Meister 1998

- Vaccin actuel : vivant : Zostavax®

- Arrivée prochaine du vaccin Shingrix®
- Vaccin subunitaire : glycoprotéine E
- Adjuvanté



programme de développement du vaccin Shingrix

- Deux études de phase III, contrôlées versus placebo, avec observateur en aveugle, évaluant **l'efficacité de Shingrix**, **menées chez des adultes âgés de 50 ans** et plus avec deux doses administrées à deux mois d'intervalle (38, 39) ;
- **Deux études phase III visant à évaluer l'efficacité et l'immunogénicité** à long terme du vaccin Shingrix chez les adultes de 50 ans et plus (40, 41) ;
- Des études de phase II et III, contrôlées versus placebo, **avec observateur en aveugle, évaluant l'efficacité de Shingrix, menées chez les adultes immunodéprimés** âgés de 18 ans et plus avec deux doses administrées à 1-2 mois d'intervalle (42-45). Des études incluant des patients transplantés rénaux (43), traités pour cancer (44, 46), infectés par le VIH (47), patients après transplantation de cellules souches hématopoïétiques (48), ou des analyses en sous-groupe des essais de phase III *post hoc* chez des sujets fragiles (49) ou chez des sujets présentant des maladies **immuno-médiées** (50) ;
- Des études **d'immunogénicité/sécurité** chez les sujets ayant des antécédents de zona (51), ou encore des études selon différents schémas d'administration (52) ou en administration sous-cutanée (53) ou avec un plus grand recul de six (54) ou neuf ans (55) ;

The NEW ENGLAND JOURNAL of MEDICINE

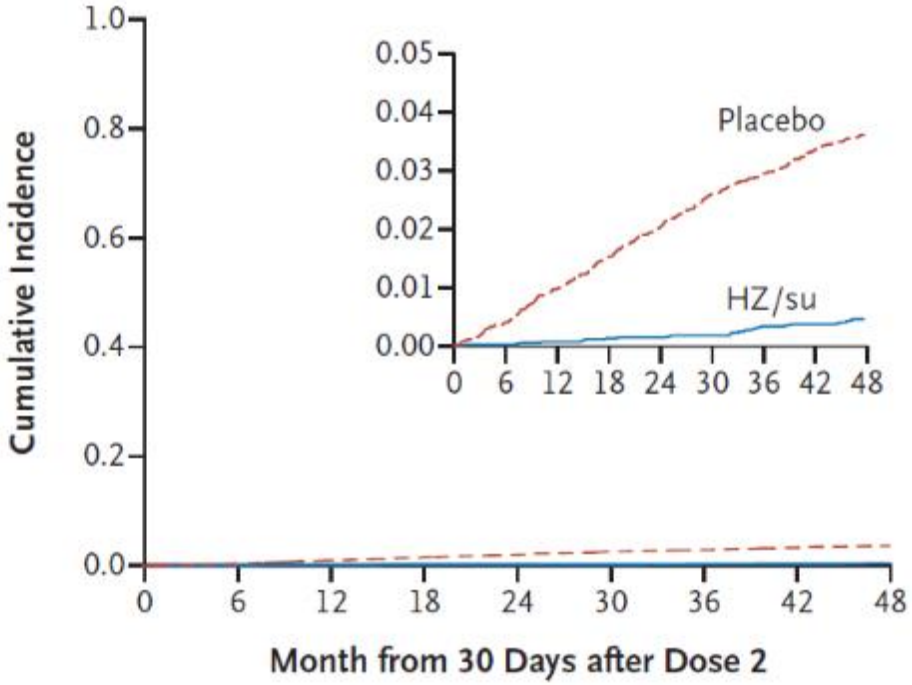
ESTABLISHED IN 1812 SEPTEMBER 15, 2016 VOL. 375 NO. 11

Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older

A.L. Cunningham, H. Lal, M. Kovac, R. Chlibek, S.-J. Hwang, J. Díez-Domingo, O. Godeaux, M.J. Levin, J.E. McElhaney, J. Puig-Barberà, C. Vanden Abeele, T. Vesikari, D. Watanabe, T. Zahaf, A. Ahonen, E. Athan, J.F. Barba-Gomez, L. Campora, F. de Looze, H.J. Downey, W. Ghesquiere, I. Gorfinkel, T. Korhonen, E. Leung, S.A. McNeil, L. Oostvogels, L. Rombo, J. Smetana, L. Weckx, W. Yeo, and T.C. Heineman, for the ZOE-70 Study Group*

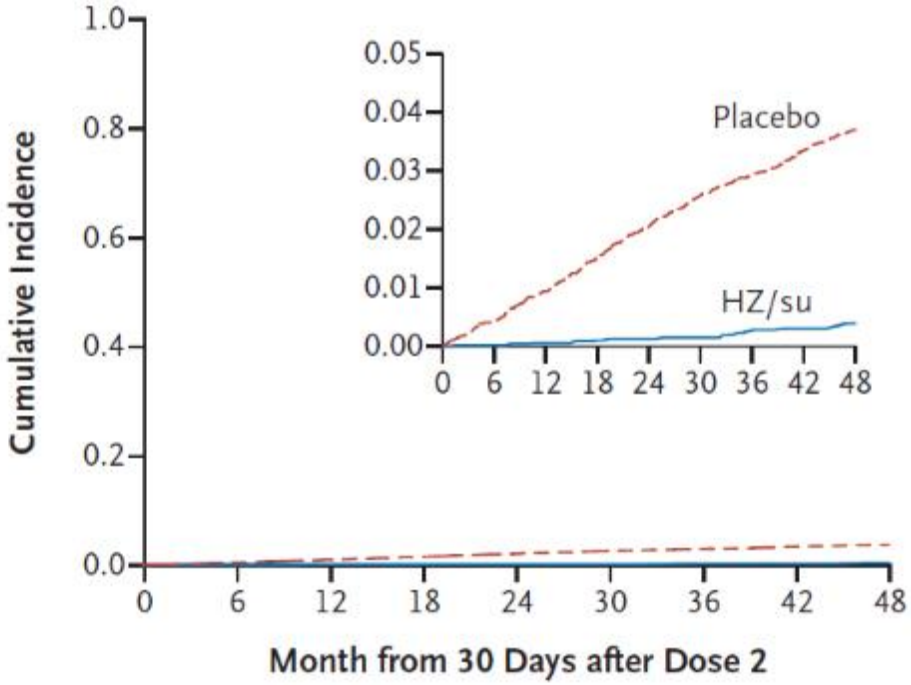
Zona

C Total Vaccinated Cohort in ZOE-70



No. at Risk									
HZ/su	6950	6696	6634	6496	6409	6254	6146	5966	4326
Placebo	6950	6717	6592	6410	6280	6101	5969	5780	4164
Cumulative No. of Cases									
HZ/su	0	2	5	9	10	12	22	24	29
Placebo	0	28	66	100	134	170	192	216	232

D Total Vaccinated Cohort in ZOE-50 and ZOE-70

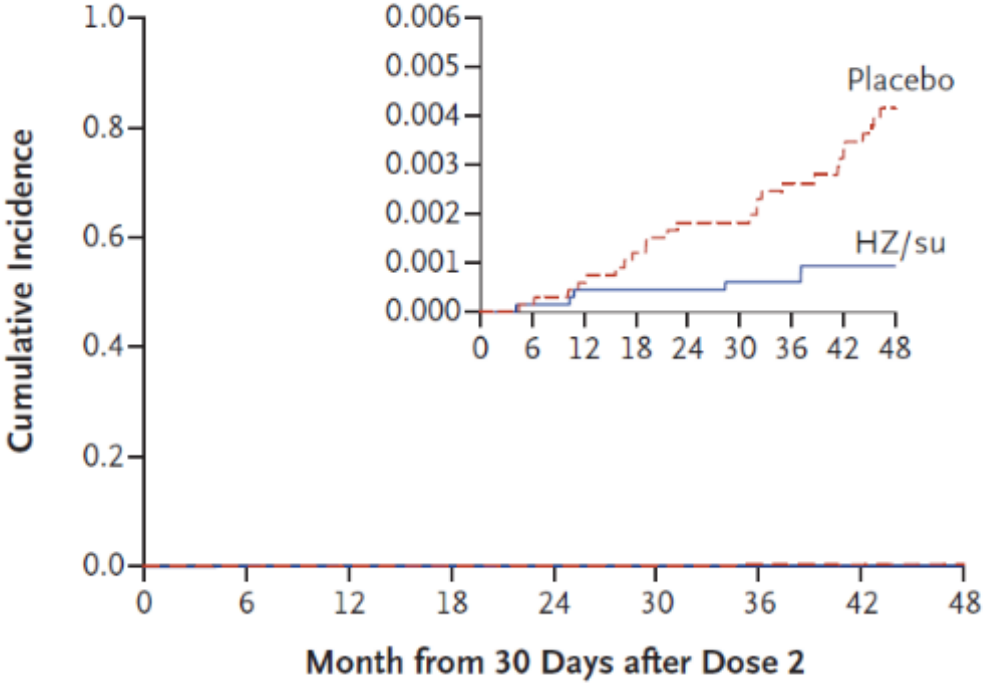


No. at Risk									
HZ/su	8758	8436	8355	8177	8066	7865	7732	7499	5376
Placebo	8773	8463	8310	8077	7910	7693	7521	7276	5188
Cumulative No. of Cases									
HZ/su	0	2	5	9	11	13	23	25	31
Placebo	0	39	81	128	173	215	244	275	300

Figure 2. Risk of Development of Herpes Zoster after Vaccination.

Algies post-zostériennes

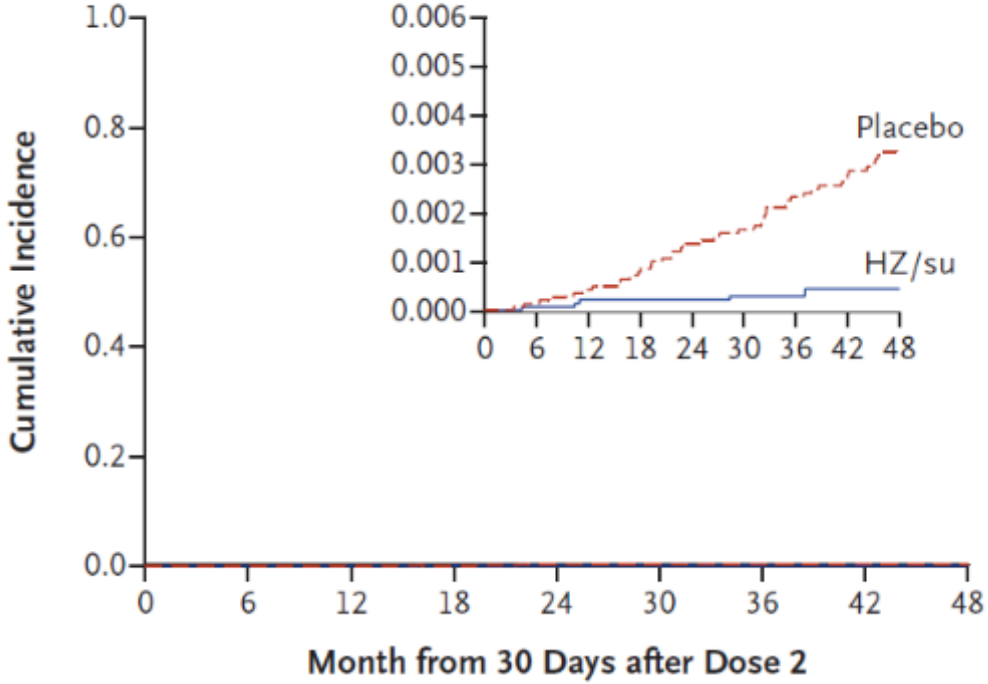
C Participants ≥70 Yr of Age in the Total Vaccinated Cohort



No. at Risk									
HZ/su	8758	8437	8357	8183	8074	7874	7751	7518	5393
Placebo	8773	8500	8386	8192	8061	7878	7725	7502	5361

Cumulative No. of Cases									
HZ/su	0	1	3	3	3	4	4	6	6
Placebo	0	1	4	9	15	18	23	26	34

D Participants ≥50 Yr of Age in the Total Vaccinated Cohort



No. at Risk									
HZ/su	14,645	14,168	14,038	13,789	13,655	13,393	13,230	12,885	10,308
Placebo	14,660	14,250	14,104	13,817	13,659	13,432	13,241	12,902	10,292

Cumulative No. of Cases									
HZ/su	0	1	3	3	3	4	4	6	6
Placebo	0	2	6	11	19	23	32	37	45

Figure 3. Risk of Development of Postherpetic Neuralgia after Vaccination in the Pooled Population.

Open Forum Infectious Diseases

BRIEF REPORT

Shingrix : Taux d'anticorps après 5 à 10 ans

Long-term Protection Against Herpes Zoster by the Adjuvanted Recombinant Zoster Vaccine: Interim Efficacy, Immunogenicity, and Safety Results up to 10 Years After Initial Vaccination

Ana Strezova,[1] Javier Diez-Domingo,[2] Kamal Al Shawafi,[3] Juan Carlos Tinoco,[4] Meng Shi,[5] Paola Pirrotta,[6] and Agnes Mwakingwe-Omari[5] on behalf of the Zoster-049 Study Group[a]

[1]GSK, Rixensart, Belgium, [2]FISABIO Fundación para el Fomento Investigación Sanitaria y Biomédica de la Comunitat Valenciana, Valencia, Spain, [3]Modis, Belgium c/o GSK, Wavre, Belgium, [4]Hospital General de Durango, Durango, Mexico, [5]GSK, Rockville, Maryland, USA, and [6]GSK, Wavre, Belgium

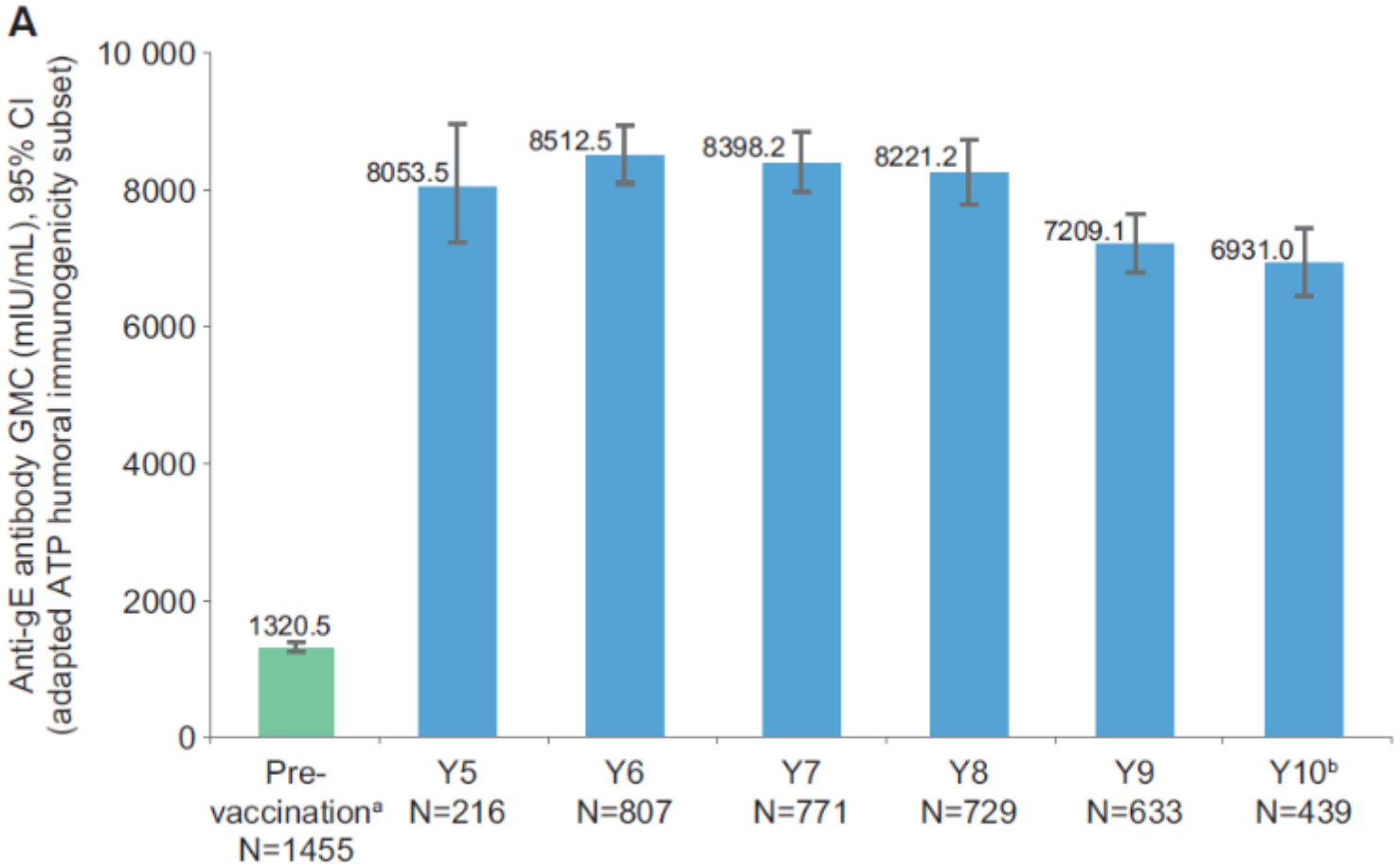


Table 1. Vaccine Efficacy in the ZOE-50/70 Studies and ZOE-LTFU After at Least 4 Additional Years of Follow-up (mTVC)

	RZV				Historical Control[a]/Placebo Group in ZOE-50/70[b]					
	N	n	Sum of Follow-up Years	Incidence (per 1000 py)	N	n	Sum of Follow-up Years	Incidence (per 1000 py)	Vaccine Efficacy (95% CI), %	*P* value
Vaccine efficacy in ZOE-LTFU – primary objective (up to the data lock point for the second interim analysis in ZOE-LTFU)										
Overall[a]	7277	52	32 673.8	1.6	7277	283	32 673.8	8.7	81.6 (75.2–86.6)	*P* < .0001
Vaccine efficacy from 1 month post–dose 2 – secondary objective (up to the data lock point for the second interim analysis in ZOE-LTFU)										
Overall[a]	13 881	84	85 796.7	1.0	13 881	765	85 796.7	8.9	89.0 (85.6–91.3)	*P* < .0001
Year 1[b]	13 881	3	13 744.5	0.2	14 035	130	13 823.3	9.4	97.7 (93.1–99.5)	*P* < .0001
Year 2[b]	13 569	10	13 415.6	0.7	13 564	136	13 332.5	10.2	92.7 (86.2–96.6)	*P* < .0001
Year 3[b]	13 185	9	13 016.1	0.7	13 074	116	12 834.0	9.0	92.4 (85.0–96.6)	*P* < .0001
Year 4[b]	12 757	10	12 946.7	0.8	12 517	95	12 637.4	7.5	89.8 (80.3–95.2)	*P* < .0001
Gap between ZOE-50/70 and ZOE-LTFU										
Year 6[a]	7277	7	7210.2	1.0	7277	61	7210.2	8.5	88.5 (74.9–95.6)	*P* < .0001
Year 7[a]	7100	10	6995.8	1.4	7100	60	6995.8	8.6	83.3 (67.2–92.4)	*P* < .0001
Year 8[a]	6878	9	6762.9	1.3	6878	57	6762.9	8.4	84.2 (67.9–93.1)	*P* < .0001
Year 9[a]	6648	15	6487.6	2.3	6648	55	6487.6	8.5	72.7 (51.0–85.7)	*P* < .0001
Year 10[a,c]	6258	11	4869.1	2.3	6258	41	4869.1	8.4	73.2 (46.9–87.6)	*P* < .0001

Shingrix : recommandations à venir

- Vaccination des sujets après 50 ans
- Vaccination des immunodéprimés

- 2 doses séparées de 2 mois

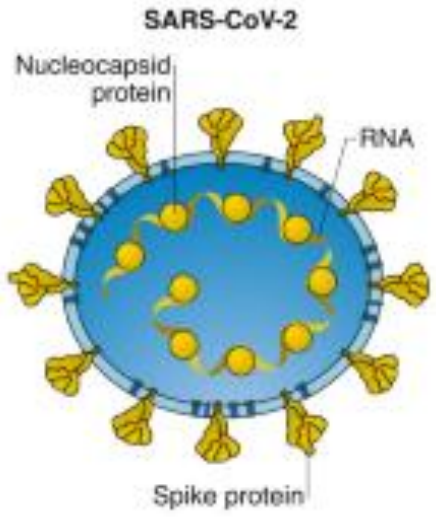
Vaccins à ARN

Portrait-robot d'un vaccin

- De l'« information antigénique »
  - Qui deviendra la cible de la réponse immune
    - Pour susciter de la réponse humorale
    - Pour susciter une réponse cellulaire
  - Multiple / chaotique : virus mort
  - Multiple / rationalisé : protéines purifiées
  - Unique : protéine (ou sucre capsulaire) ou séquence génétique codant pour la protéine
  - Dont le ciblage est efficace

- Un mode de délivrance
  - Physique (injection, inhalation, absorption …)
  - Moléculaire (comment l'Ag rencontre-t-il le SI ?)

- Un signal d'activation
  - Reproduisant l'activation secondaire à la détection d'un pathogène
  - Permettant d'éviter l'instauration d'une tolérance vis-à-vis de l'antigène vaccinal
  - Permettant de polariser la réponse immune vers la forme la plus adaptée
  - Soit il faut un adjuvant, soit le dispositif vaccinal est lui-même activateur (vaccin vivant …)
    - Adjuvants : aluminium … et nombreuses recherche autour des ligands de TLR


SARS-CoV-2
Nucleocapsid protein
RNA
Spike protein

comment

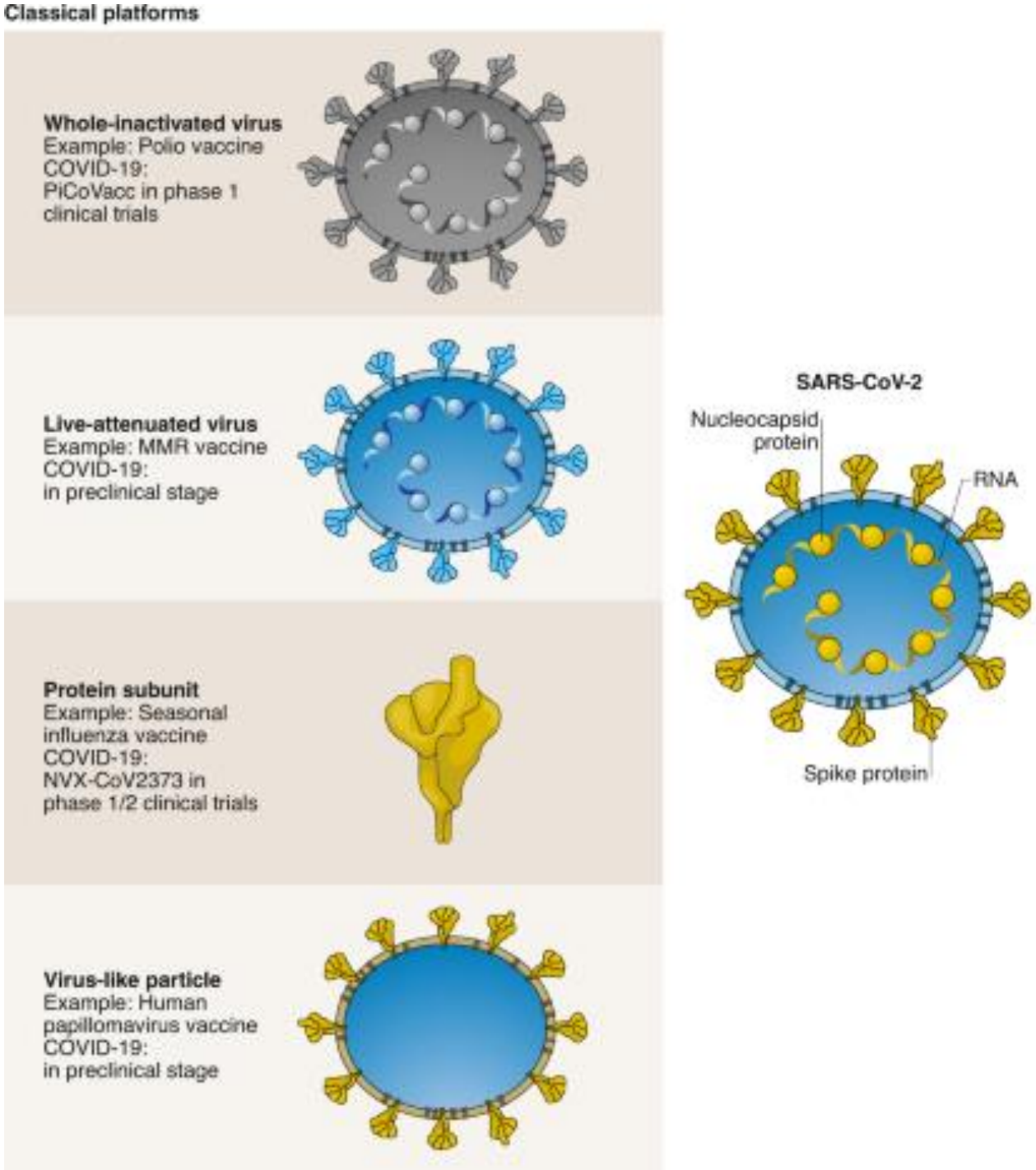
Check for updates

2020

Next-generation vaccine platforms for COVID-19

Consensus among experts is that only an effective COVID-19 vaccine will end the pandemic. This Comment focuses on how this pandemic has accelerated the development of vaccine platforms distinct from classical vaccines; these novel platforms may also increase the response time when new viruses emerge in the future.

Debby van Riel and Emmie de Wit



comment

Check for updates

2020

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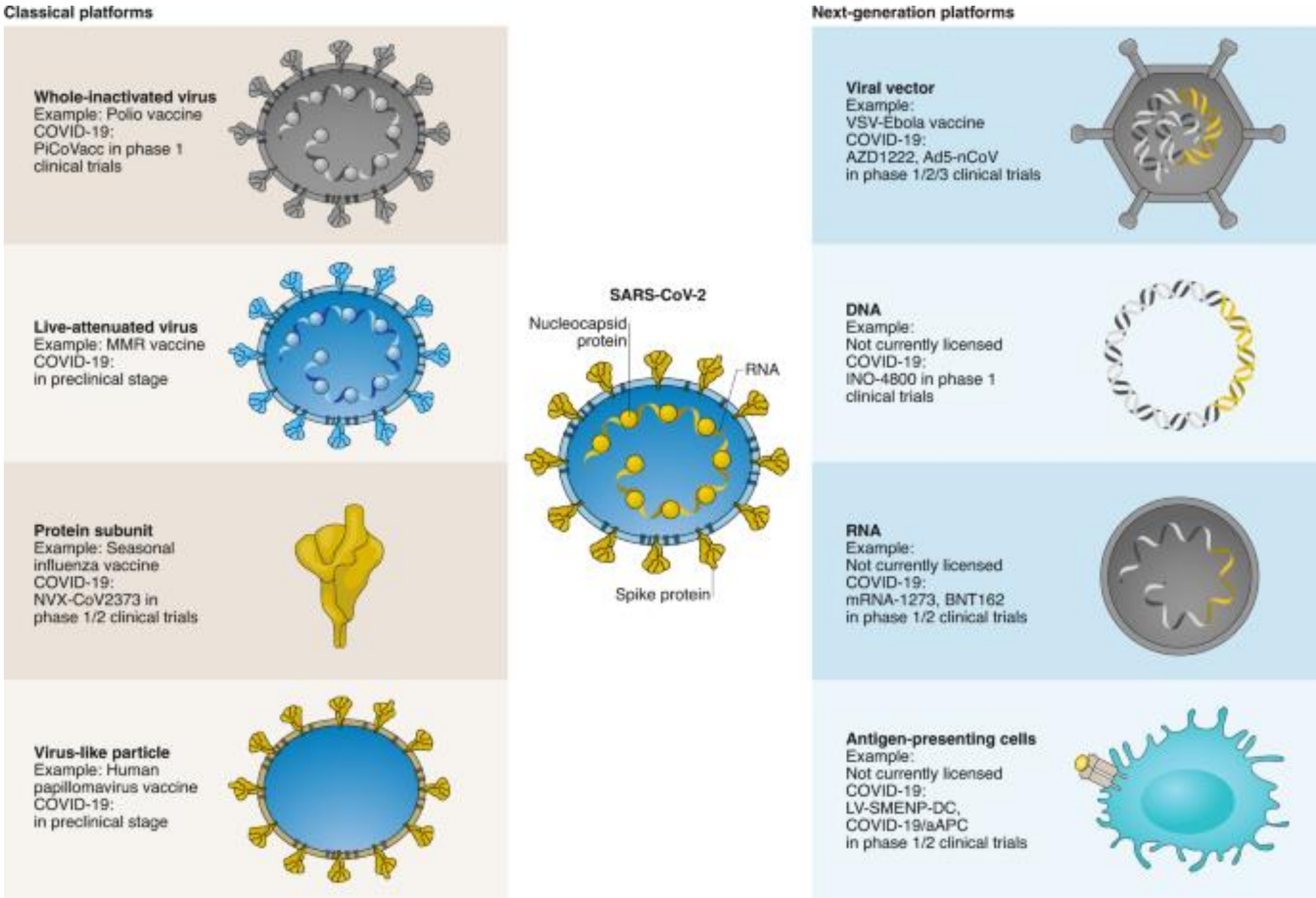


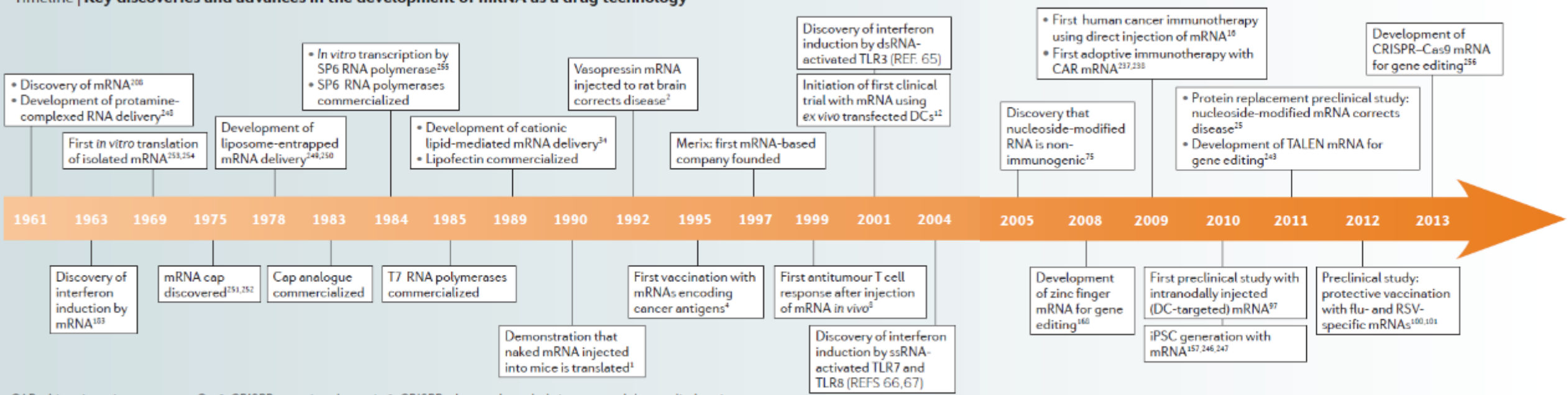
mRNA-based therapeutics — developing a new class of drugs

Ugur Sahin[1,2], Katalin Karikó[2,3] and Özlem Türeci[1]

2014

La découverte de l'ARN puis son développement comme outil pour faire synthétiser des protéines voire des antigène vaccinaux est une longue histoire : on n'avait pas attendu la Covid …

Timeline | **Key discoveries and advances in the development of mRNA as a drug technology**

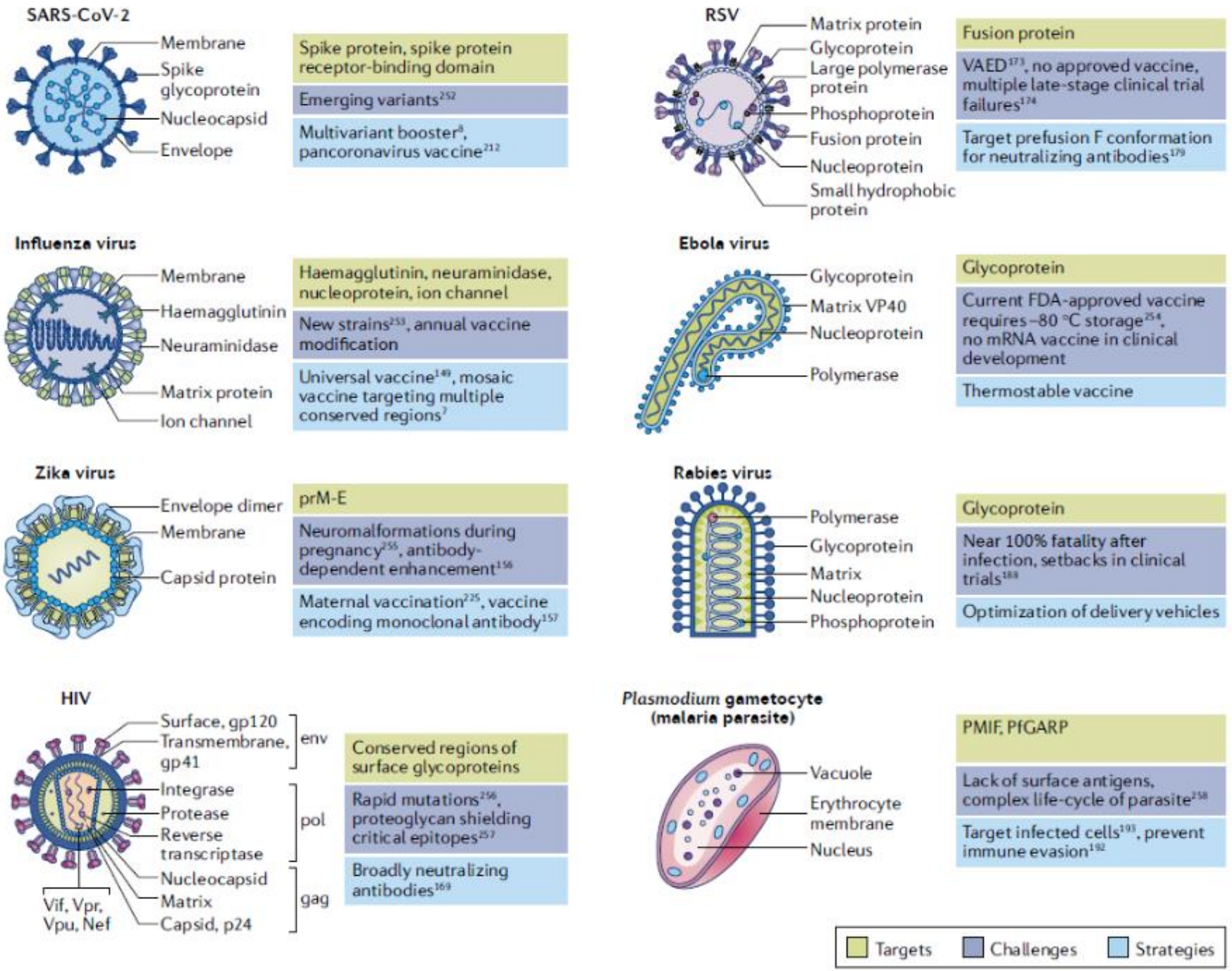


CAR, chimeric antigen receptor; Cas9, CRISPR-associated protein 9; CRISPR, clustered regularly interspaced short palindromic repeat; DC, dendritic cell; dsRNA, double-stranded RNA; iPSC, induced pluripotent stem cell; RSV, respiratory syncytial virus; ssRNA, single-stranded RNA; TALEN, transcription activator-like effector nuclease; TLR, Toll-like receptor.

mRNA vaccines for infectious diseases: principles, delivery and clinical translation

Namit Chaudhary[1], Drew Weissman[2] and Kathryn A. Whitehead[1,3]

De nombreux projets vaccinaux basés sur l'ARNm existaient avant la Covid-19



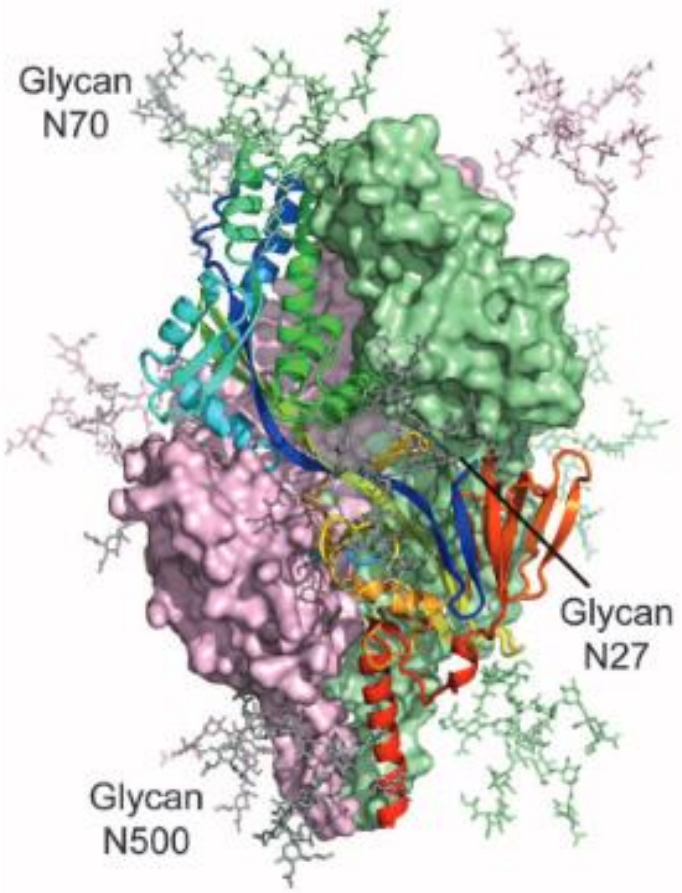
VRS

2013

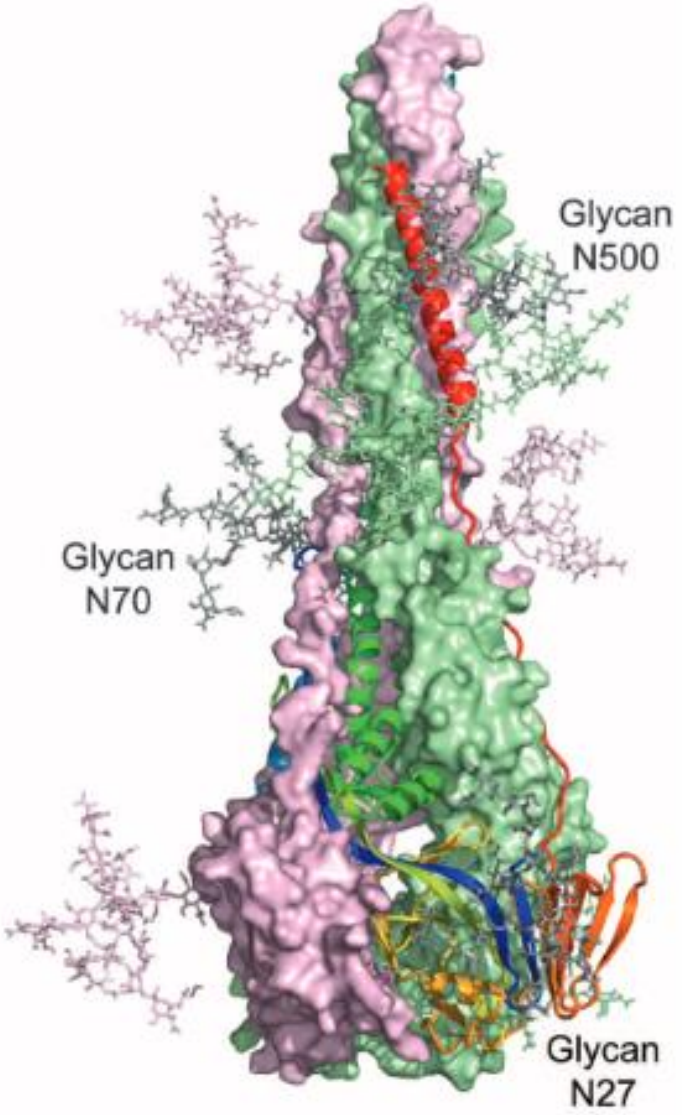
Structure of RSV Fusion Glycoprotein Trimer Bound to a Prefusion-Specific Neutralizing Antibody

Jason S. McLellan,[1*] Man Chen,[1] Sherman Leung,[1] Kevin W. Graepel,[1] Xiulian Du,[1] Yongping Yang,[1] Tongqing Zhou,[1] Ulrich Baxa,[2] Etsuko Yasuda,[3] Tim Beaumont,[3] Azad Kumar,[1] Kayvon Modjarrad,[1] Zizheng Zheng,[4] Min Zhao,[4] Ningshao Xia,[4] Peter D. Kwong,[1*] Barney S. Graham[1]

La conformation de la protéine de fusion F utilisée comme antigène vaccinal est cruciale : les anticorps neutralisants sont principalement obtenus avec la forme préfusion.



Prefusion F trimer



Postfusion F trimer

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2021, VOL. 17, NO. 5, 1248–1261
https://doi.org/10.1080/21645515.2020.1829899

Taylor & Francis
Taylor & Francis Group

RESEARCH PAPER

Check for updates

A phase 1, randomized, placebo-controlled study to evaluate the safety and immunogenicity of an mRNA-based RSV prefusion F protein vaccine in healthy younger and older adults

Antonios O. Aliprantis[a], Christine A. Shaw[b], Paul Griffin[c,d,e], Nicholas Farinola[f], Radha A. Railkar[a], Xin Cao[a], Wen Liu[a], Jeffrey R. Sachs[a], Christine J. Swenson[a], Heather Lee[b], Kara S. Cox[a], Daniel S. Spellman[a], Colleen J. Winstead[a], Igor Smolenov[b], Eseng Lai[a], Tal Zaks[b], Amy S. Espeseth[a], and Lori Panther[b]

[a]Merck & Co., Inc., Kenilworth, NJ, USA; [b]Moderna, Inc., Cambridge, MA, USA; [c]QPharm, Herston, Australia; [d]The University of Queensland, Brisbane, Australia; [e]Mater Research Raymond Terrace, South Brisbane, Australia; [f]CMAX, Adelaide, Australia

Un vaccin ARNm codant pour cette protéine de fusion stabilisée en conformation « pré-fusion » déclenche chez l'humain des Ac neutralisants.

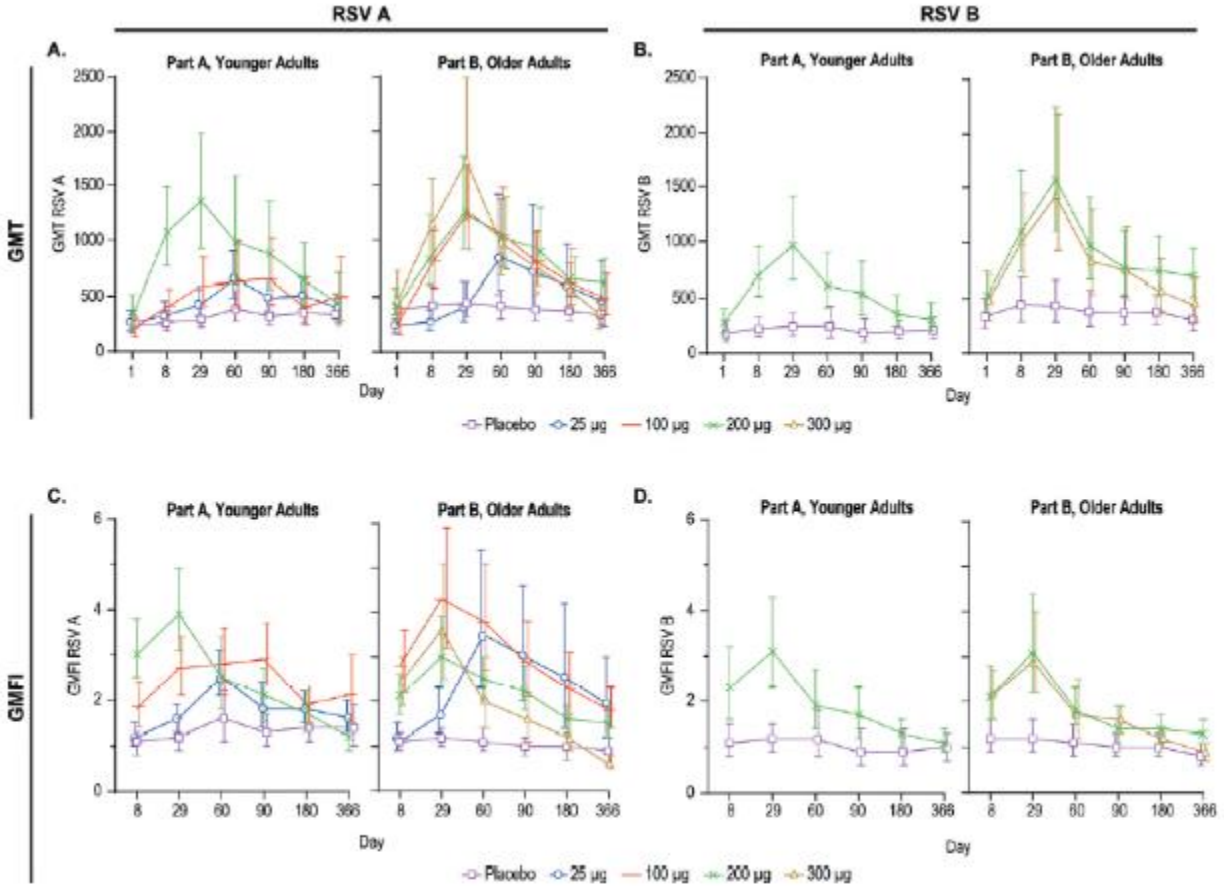


Figure 5. Serum Neutralization Titers against RSV A and RSV B. Serum neutralization GMTs for RSV A (Panel A) and RSV B (Panel B), and GMFIs for RSV A (Panel C) and RSV B (Panel D) by time. Per-protocol population is shown. Error bars represent the 95% confidence intervals.

Clinical Trial > N Engl J Med. 2023 Feb 16;388(7):595-608. doi: 10.1056/NEJMoa2209604.

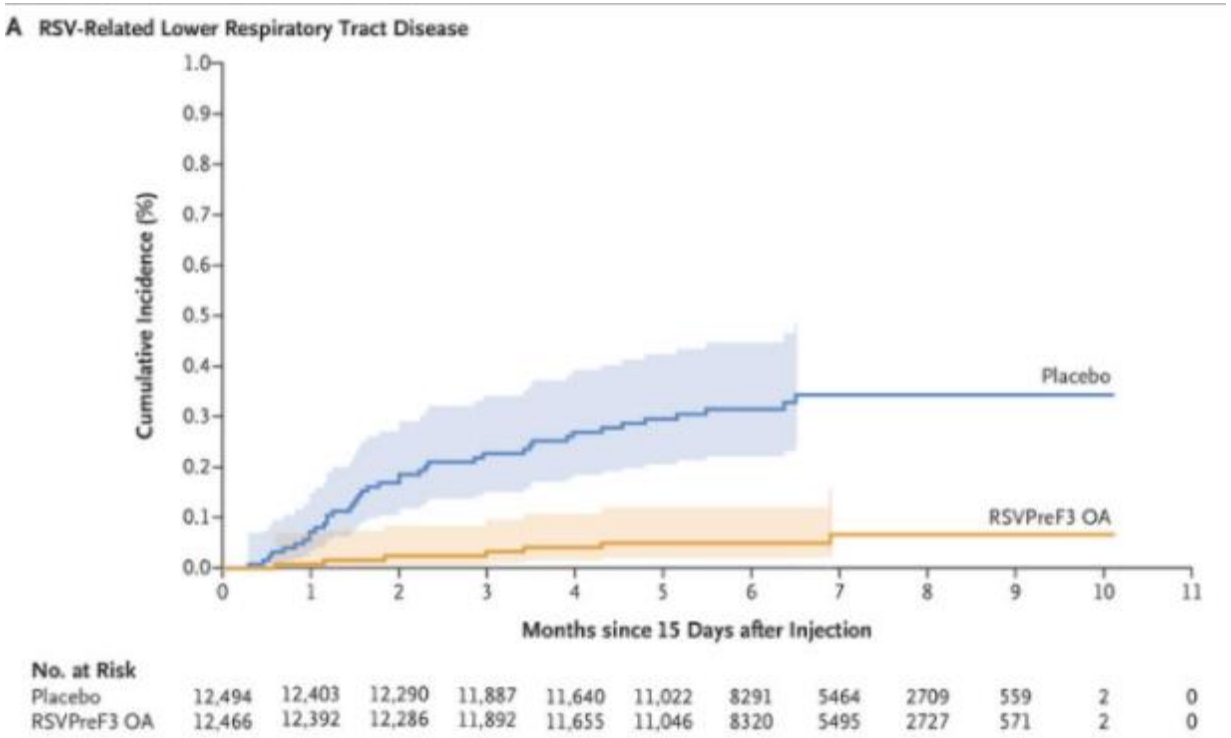
FULL TEXT LINKS

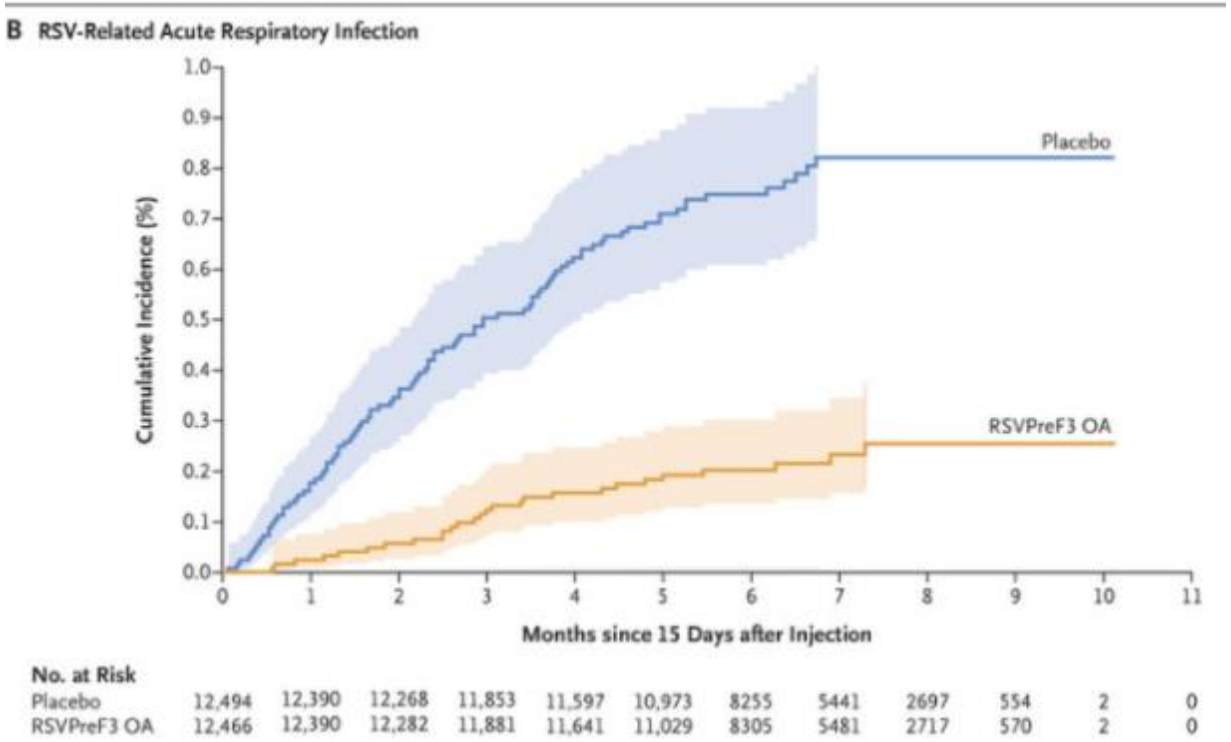
NEJM FULL TEXT

2023

Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults

Alberto Papi [1], Michael G Ison [1], Joanne M Langley [1], Dong-Gun Lee [1], Isabel Leroux-Roels [1], Federico Martinon-Torres [1], Tino F Schwarz [1], Richard N van Zyl-Smit [1], Laura Campora [1], Nancy Dezutter [1], Nathalie de Schrevel [1], Laurence Fissette [1], Marie-Pierre David [1], Marie Van der Wielen [1], Lusine Kostanyan [1], Veronica Hulstrøm [1]; AReSVi-006 Study Group





FDA NEWS RELEASE

FDA Approves First Respiratory Syncytial Virus (RSV) Vaccine

Arexvy Approved for Individuals 60 Years of Age and Older

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For Immediate Release: May 03, 2023

Today, the U.S. Food and Drug Administration approved Arexvy, the first respiratory syncytial virus (RSV) vaccine approved for use in the United States. Arexvy is approved for the prevention of lower respiratory tract disease caused by RSV in individuals 60 years of age and older.

Probable « vague » de vaccins VRS à venir

- ARN et protéine adjuvantée
- Pour les enfants à risques
- Pour les adultes à risque
- Pour les sujets âgés

Autres réflexions en cours

- Vacciner les nourrissons contre les méningocoques ACWY et non seulement C
- Faire un rappel méningocoque aux adolescents
- Élargir l'âge du rattrapage de la vaccination HPV pour tous et toutes jusqu'à 26 ans inclus
- Obligation vaccinale Rougeole pour les soignants nés après 1980