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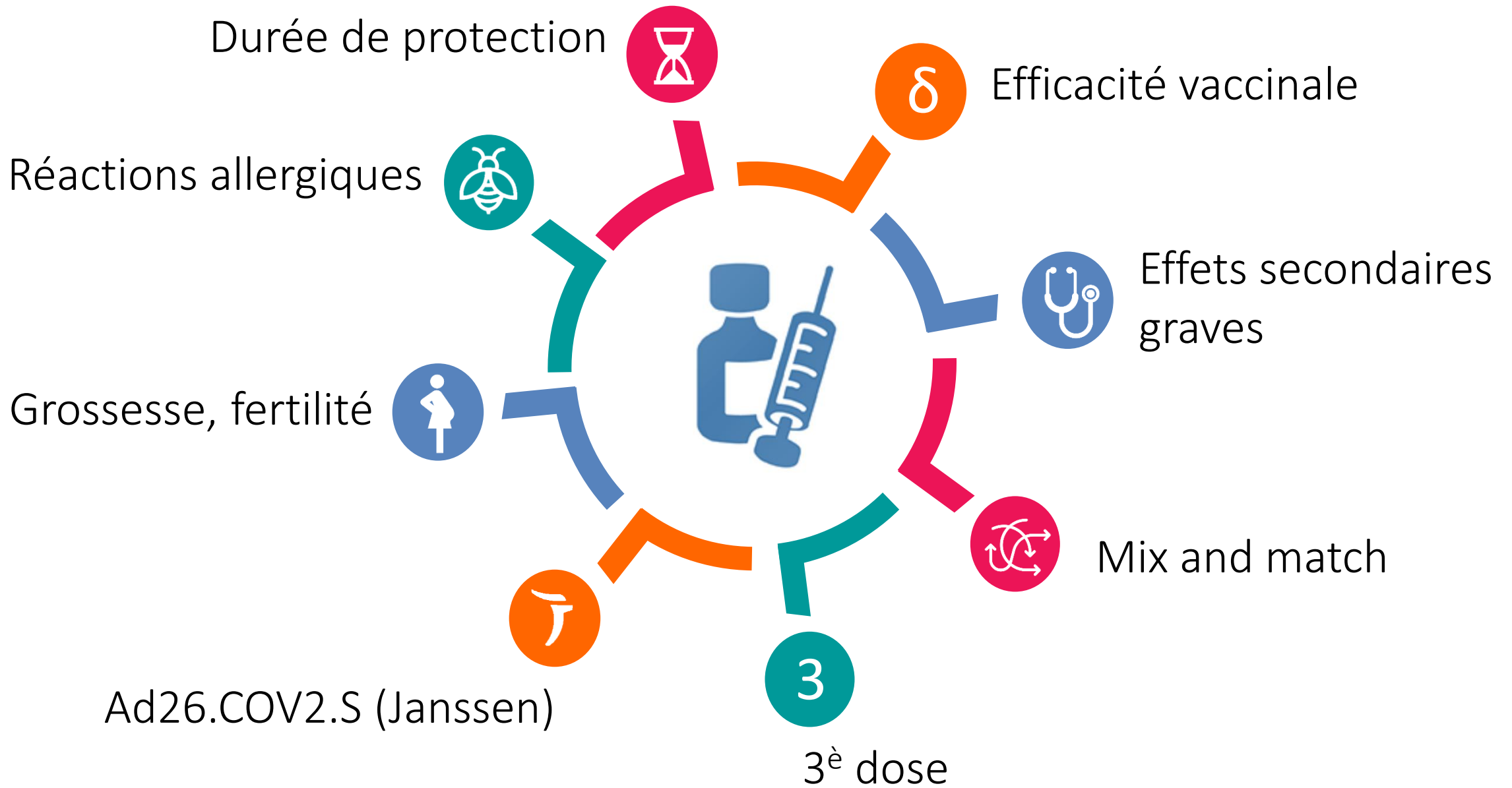
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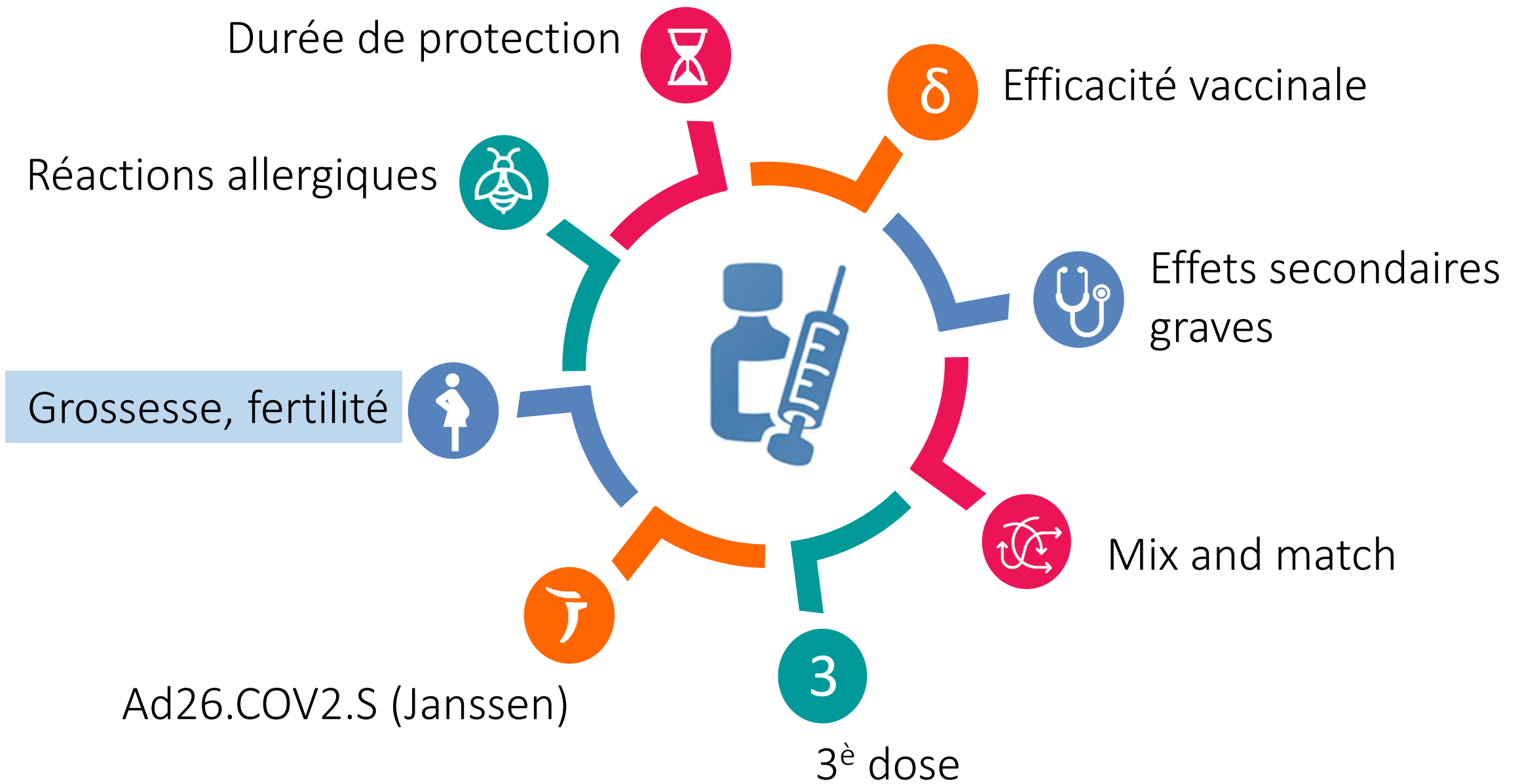
Où en sommes-nous avec la vaccination COVID-19 ?

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Policlinique Médecine Tropicale, Voyages et Vaccinations

Jeudi d'Unisanté – 23.09.2021







Fertilité

Chez la femme

Table 1 | Accidental pregnancies in trials for the COVID-19 vaccines approved in the United Kingdom

Vaccine type	Control group			Vaccinated group		
	Participants	Pregnancies	Miscarriages (rate)	Participants	Pregnancies	Miscarriages (rate)
Pfizer/BioNTech	18,846	12	1 (8%)	18,860	11	0 (0%)
Moderna	15,170	7	1 (14%)	15,181	6	0 (0%)
AstraZeneca	5,829	9	3 (33%)	5,807	12	2 (17%)

Male, Nature Reviews Immunology, 2021

Chez l'homme

Table. Change in Semen Analysis Parameters Before and After COVID-19 Vaccination

Parameter	Normal value	Median (IQR)		P value
		Baseline	Follow-up	
No. of participants		45	45	
Volume, mL	>1.5	2.2 (1.5-2.8)	2.7 (1.8-3.6)	.01
Sperm concentration, million/mL	>15	26 (19.5-34)	30 (21.5-40.5)	.02
Total motility, %	>40	58 (52.5-65)	65 (58-70)	.001
TMSC, million	>9	36 (18-51)	44 (27.5-98)	.001

Gonzales et al., JAMA, 2021



Sécurité de la vaccination chez la femme enceinte

- Effets secondaires locaux similaires à la population générale
- Possiblement légèrement moins d'effets secondaires systémiques

Shimabukuro et al, NEJM, 2021
Kachikis et al, JAMA 2021

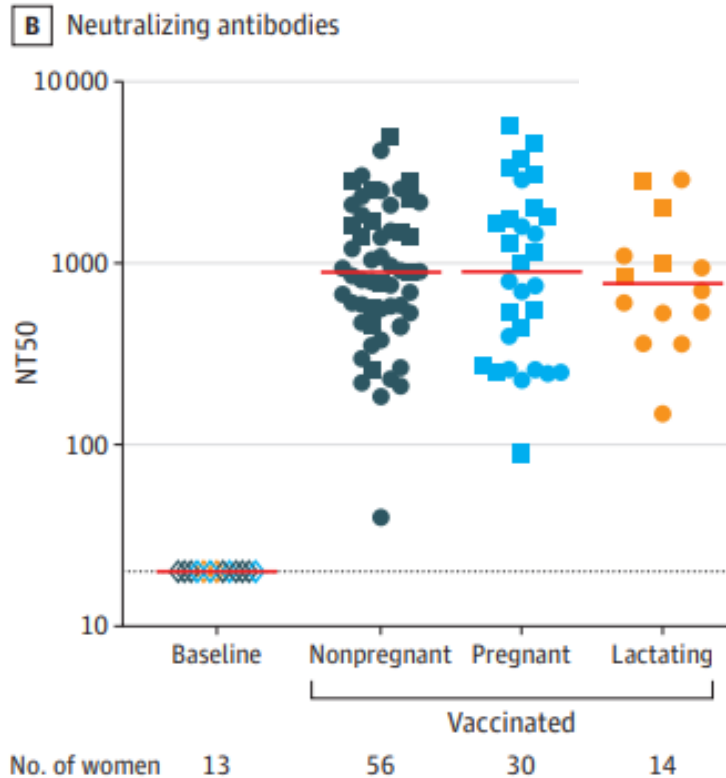
Table 2. Adjusted Odds Ratios for Receipt of COVID-19 Vaccine Within 28 Days Prior to a Spontaneous Abortion, December 15, 2020, Through June 28, 2021, Across 8 Vaccine Safety Datalink Sites and Among 264 104 Pregnancy-Periods^a

	Adjusted odds ratio (95% CI) ^b
Full population	1.02 (0.96-1.08)
By gestational age, wk	
6-8	0.94 (0.86-1.03)
9-13	1.07 (0.99-1.17)
14-19	1.08 (0.89-1.29)
By vaccine type ^c	
mRNA-1273 (Moderna)	1.03 (0.94-1.11)
BNT162b2 (Pfizer-BioNTech)	1.03 (0.95-1.11)

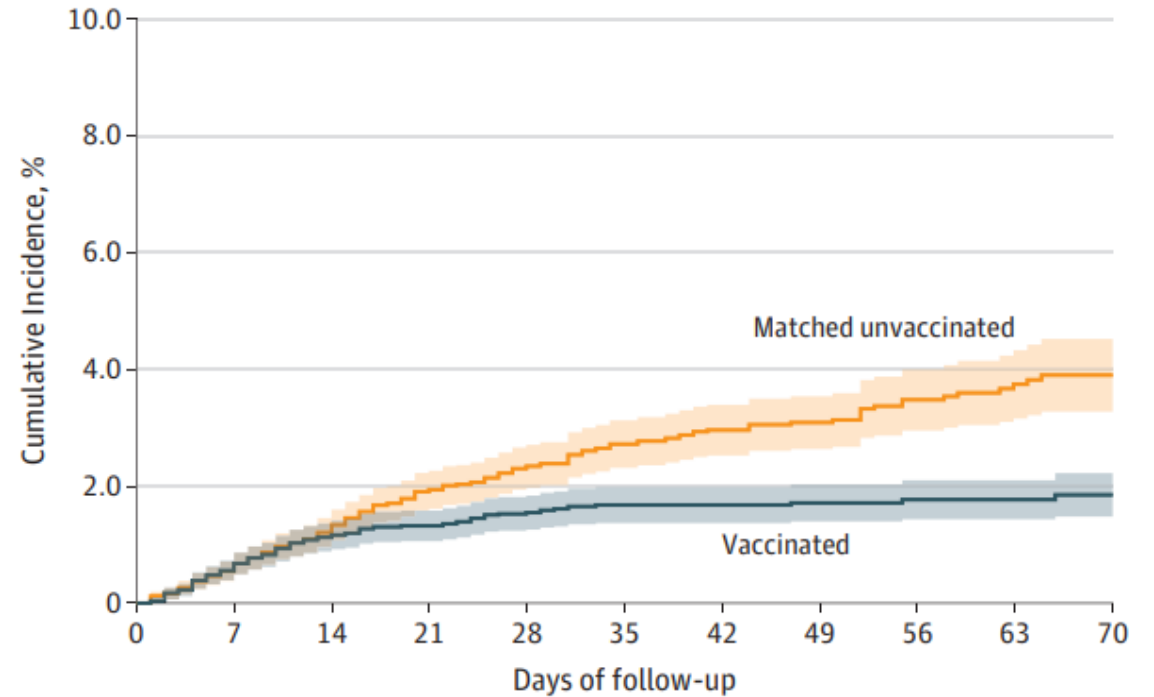
Kharbanda et al, JAMA 2021



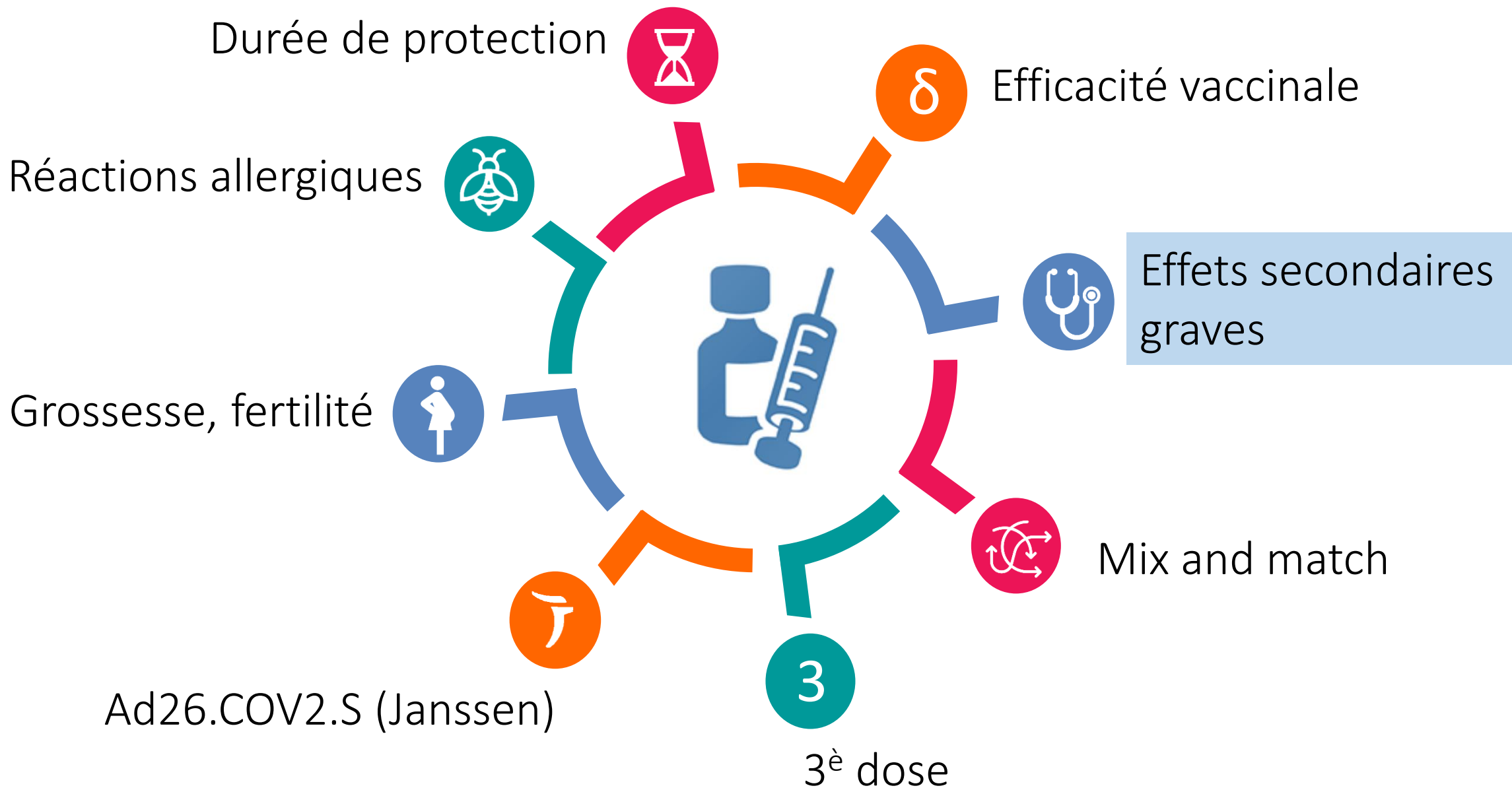
Immunogénicité et efficacité du vaccin chez la femme enceinte



Collier et al, JAMA, 2021



Goldshtein et al, JAMA, 2021





Effets secondaires graves

- Rares – non détectés dans les études de phase 3
- **Myocardites post-vaccinales :**
 - Estimation Swissmedic (juillet 2021) :
4.7 cas par million de doses administrées
 - Facteurs de risque :
 - Sexe masculin
 - Age < 30 ans
 - Deuxième dose



Myocardites

Sex/Benefits and harms from mRNA vaccination	No. per million vaccine doses administered in each age group (yrs) [†]				
	12-29	12-17	18-24	25-29	≥30
Male					
Benefit					
COVID-19 cases prevented [§]	11,000	5,700	12,100	15,200	15,300
Hospitalizations prevented	560	215	530	936	4,598
ICU admissions prevented	138	71	127	215	1,242
Deaths prevented	6	2	3	13	700
Harms					
Myocarditis cases expected [¶]	39-47	56-69	45-56	15-18	3-4

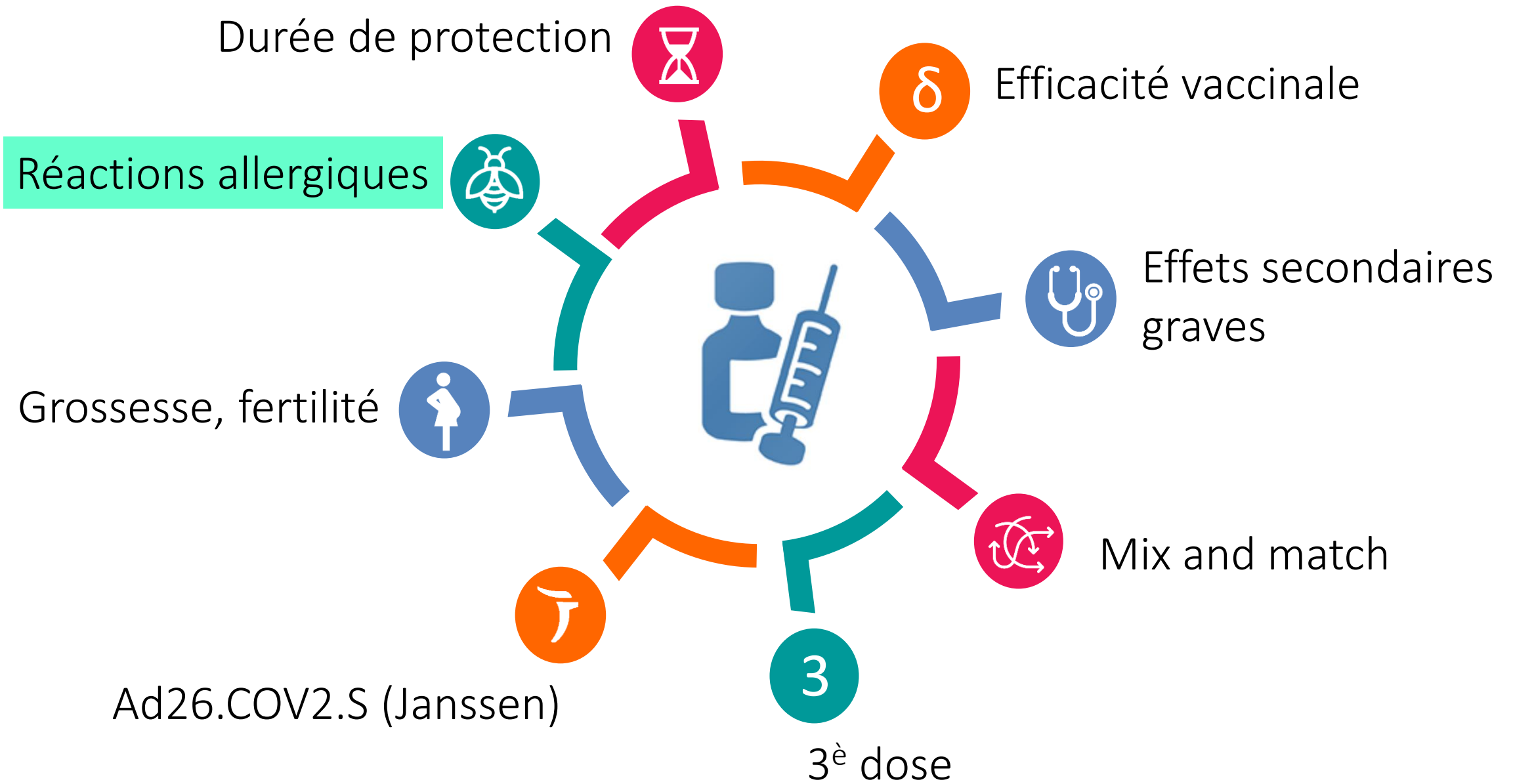
MMWR Morb Mortal Wkly
Rep 2021, June 2021



Autres effets secondaires graves

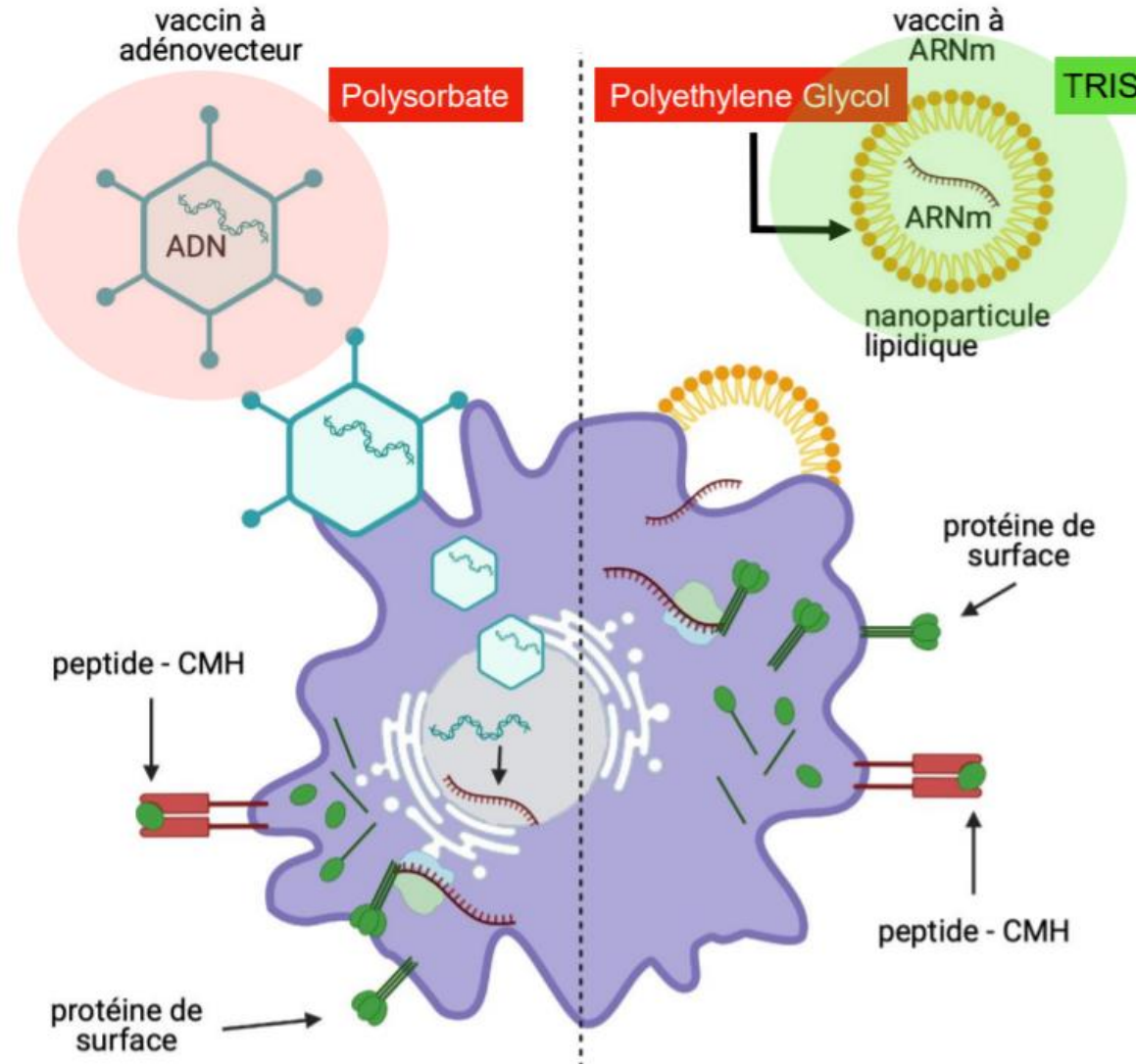
- Etude israélienne >1'000'000 de personnes vaccinées
- Risques significatifs :
 - Infection à VZV (15.8 évènements pour 100'000 personnes)
 - Appendicite (5 évènements pour 100'000 personnes)
- Pas d'augmentation de :
 - Evènements thrombo-emboliques
 - Accidents vasculaires cérébraux
 - Infarctus du myocarde

Barda et al, NEJM 2021



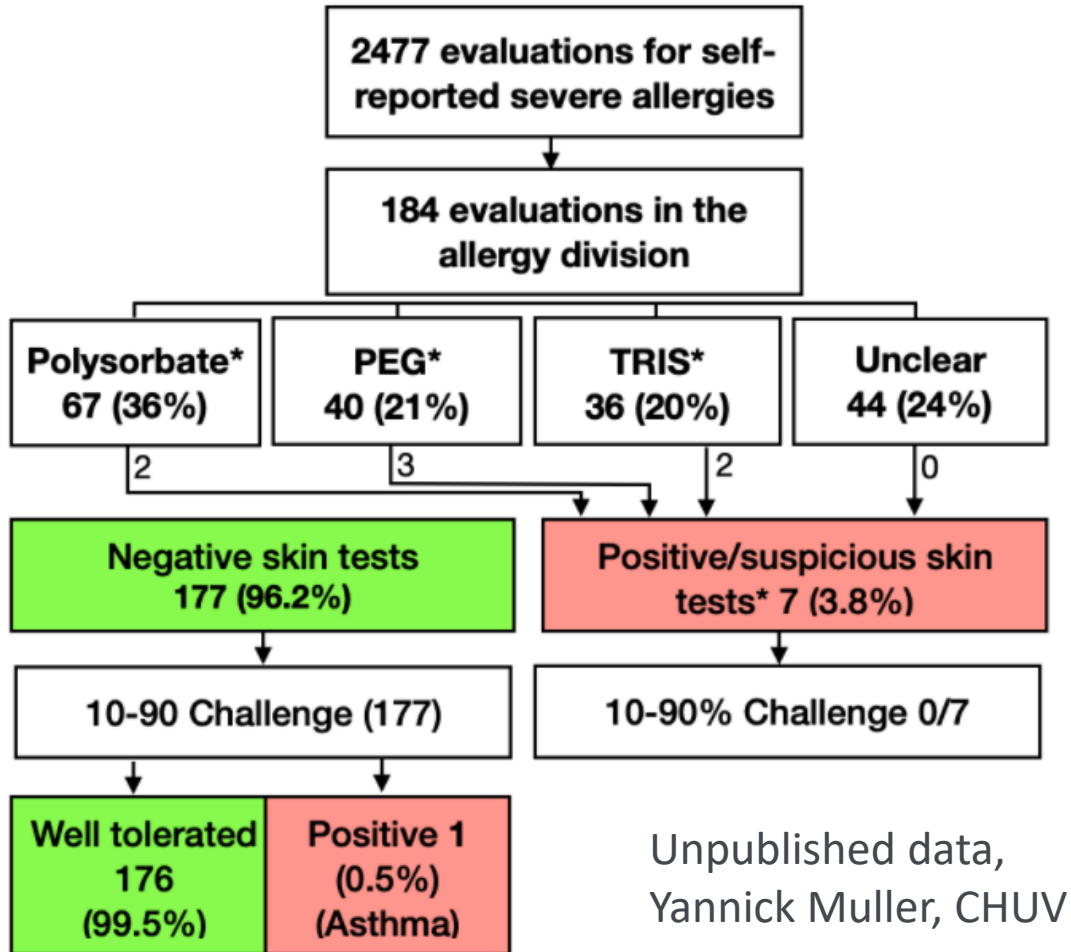


Réactions allergiques





Réactions allergiques



*12 patients with history of allergy to 2 different excipients

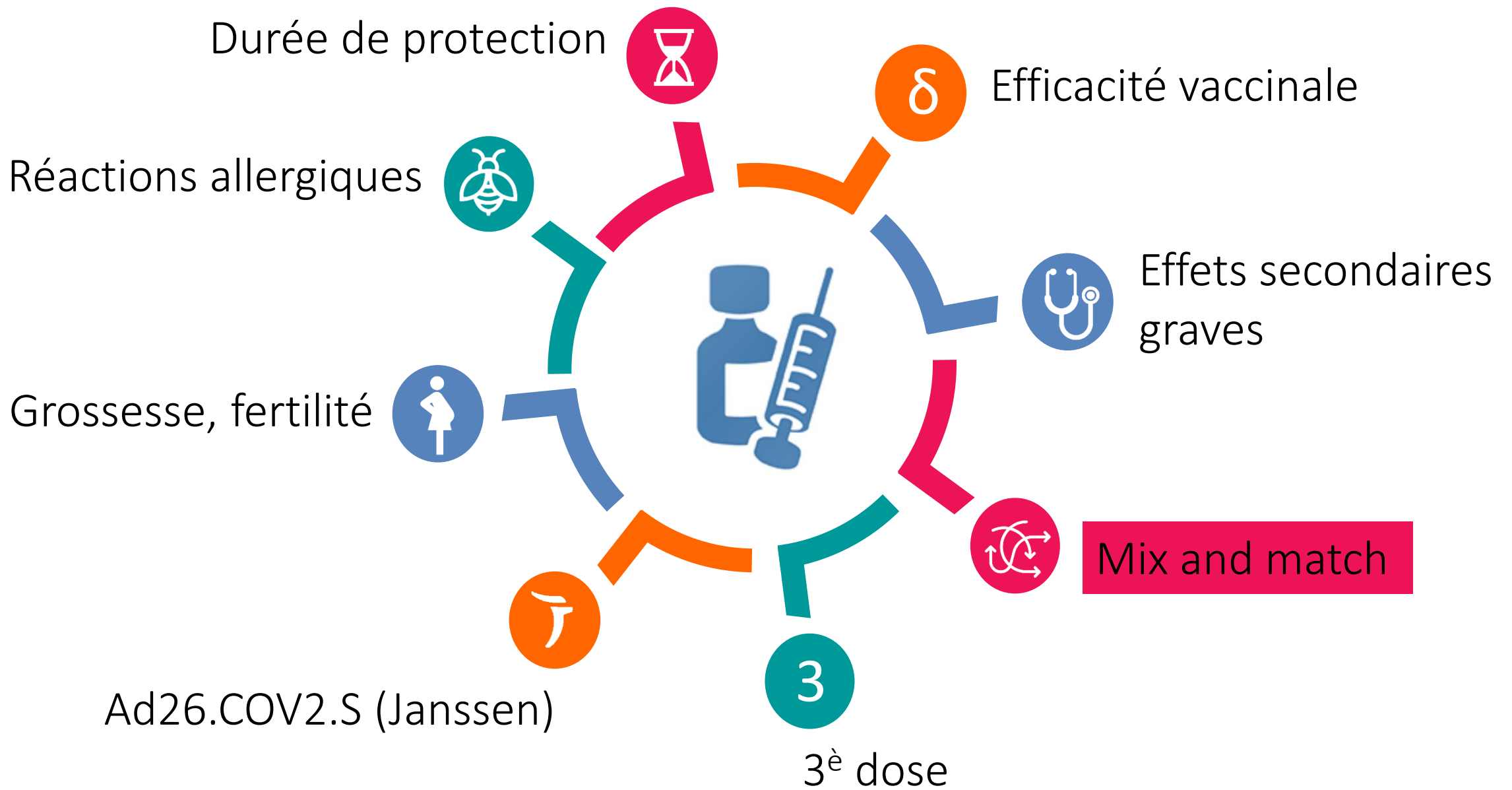
Risque d'anaphylaxie vaccins ARNm :
7.91 (95%CI 4.02-15.59) par million de doses

Greenhawt et al., The Journal of Allergy and Clinical Immunology, 2021

Risque d'anaphylaxie autres vaccins :
~ 1-10 évènements par million de doses

Dreskin et al., World Allergy Organ J, 2016

Unpublished data,
Yannick Muller, CHUV





Mix and match

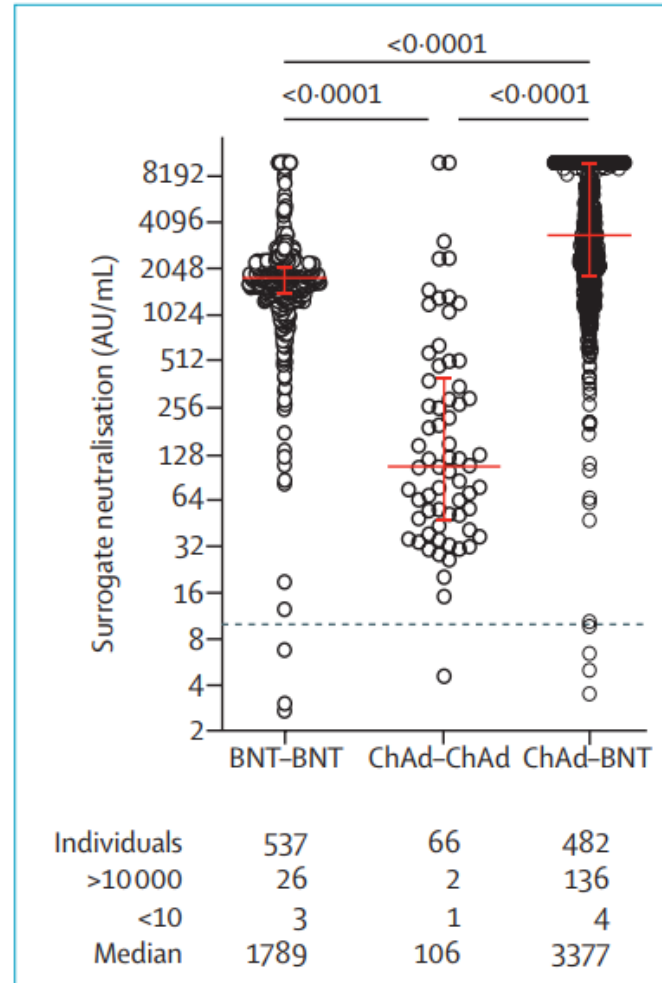


Figure: Comparison of surrogate neutralisation activity induced by homologous and heterologous COVID-19 vaccine regimens

Tenbusch and al., The Lancet infectious diseases, 2021

Durée de protection



Efficacité vaccinale



Effets secondaires graves



Mix and match



3^e dose



Réactions allergiques



Grossesse, fertilité



Ad26.COV2.S (Janssen)



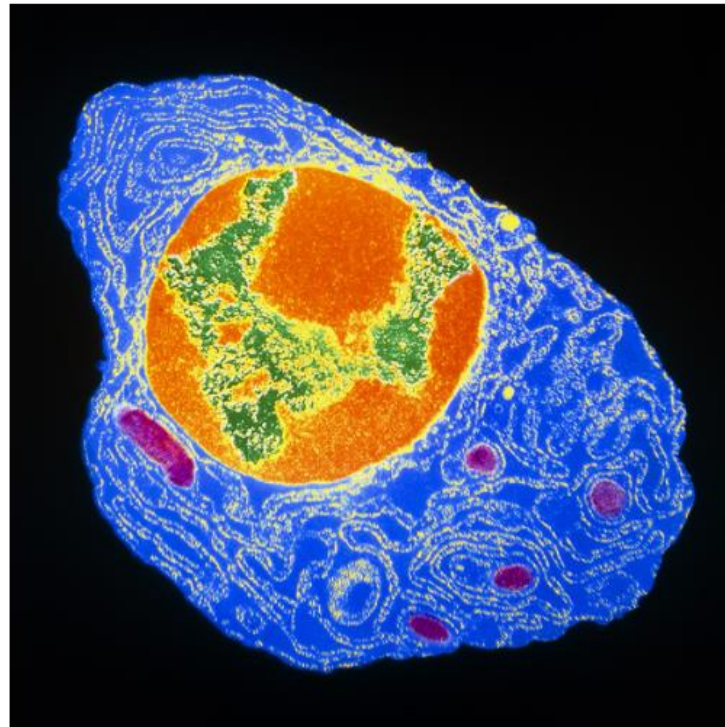
Durée de protection

NEWS | 26 May 2021 | Correction 27 May 2021

Had COVID? You'll probably make antibodies for a lifetime

People who recover from mild COVID-19 have bone-marrow cells that can churn out antibodies for decades, though viral variants could dampen some of the protection they offer.

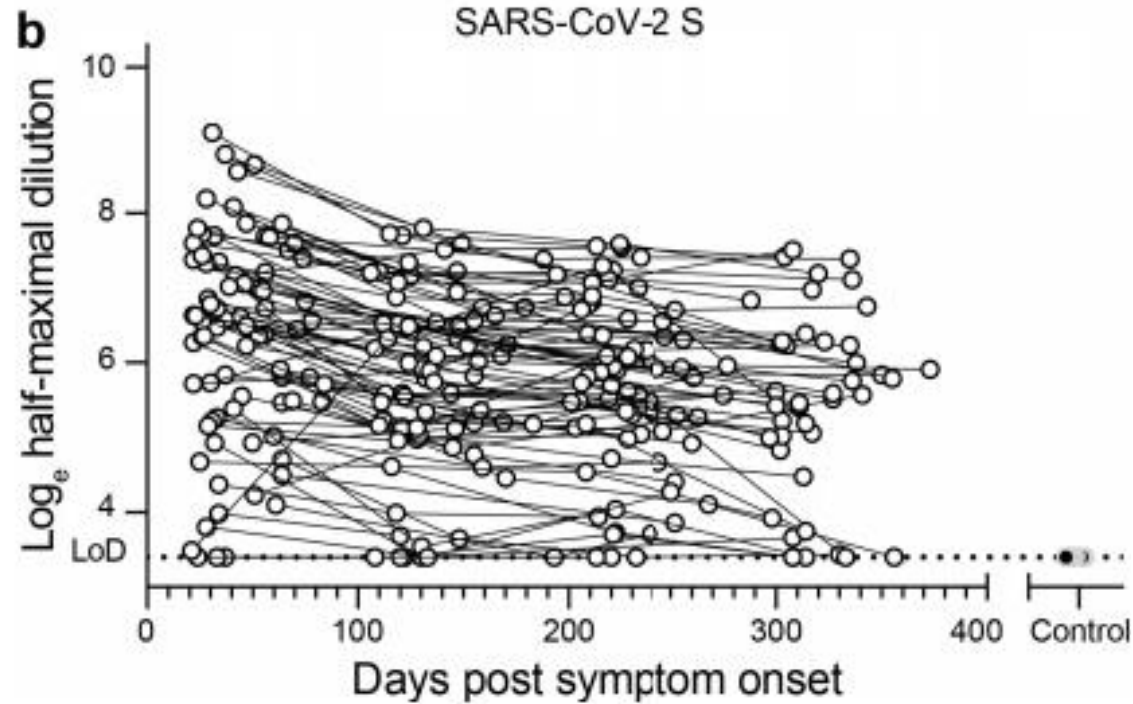
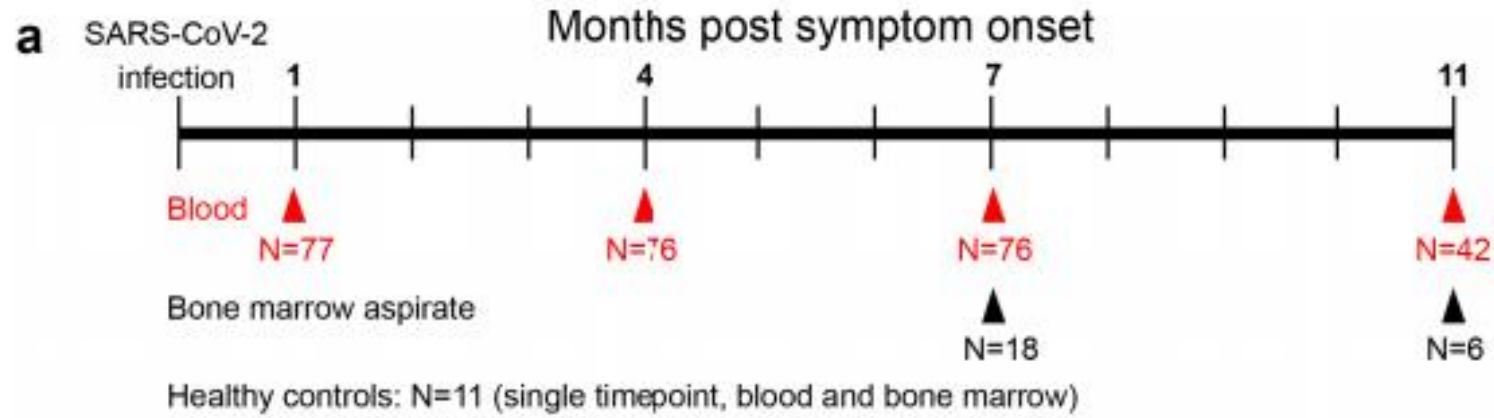
Ewen Callaway



A bone marrow plasma cell (artificially coloured). Such cells, which produce antibodies, linger for months in the bodies of people who have recovered from COVID-19. Credit: Dr Gopal Murti/Science Photo Library

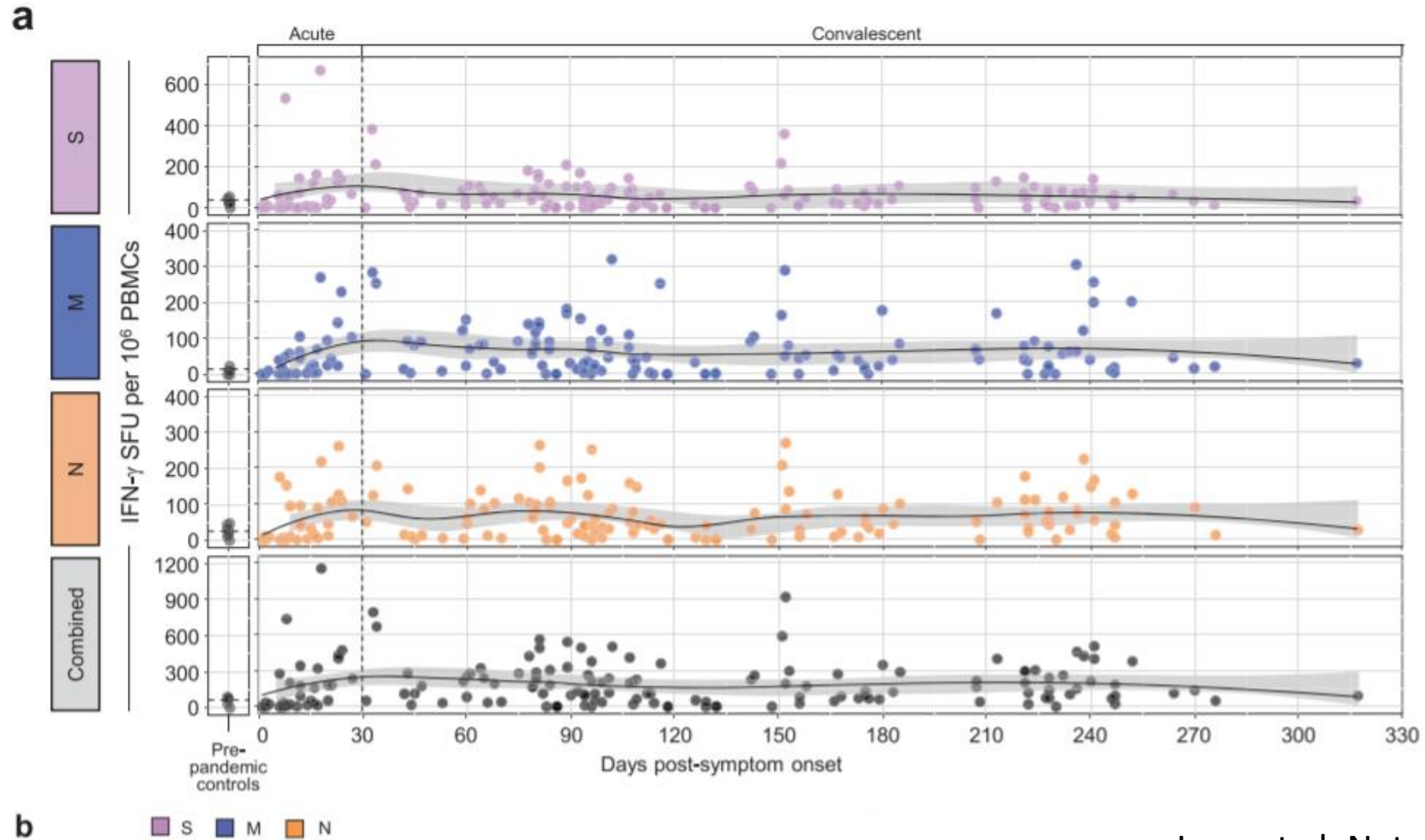


Durée anticorps





Persistence cellules T mémoire après infection naturelle (10 mois)

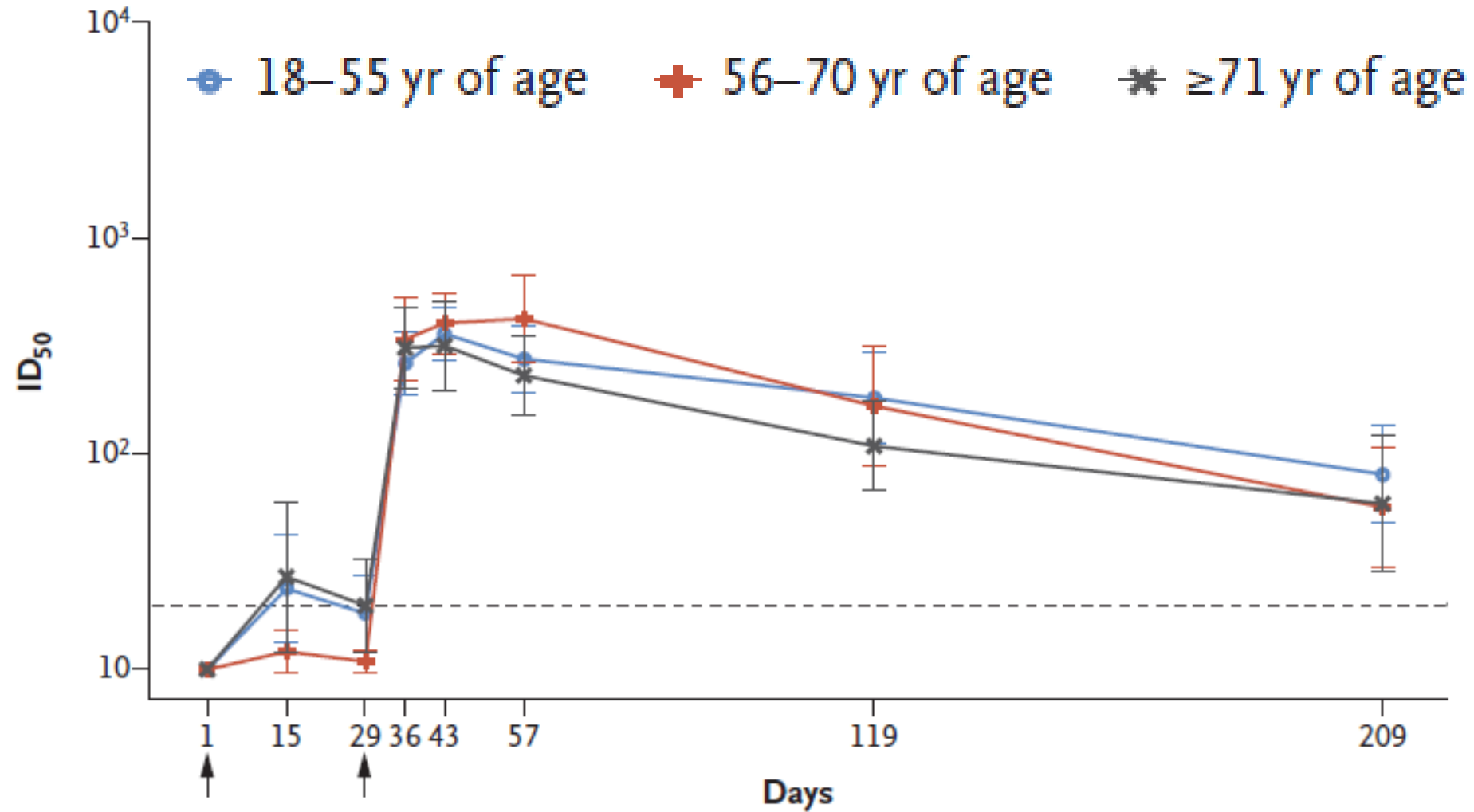


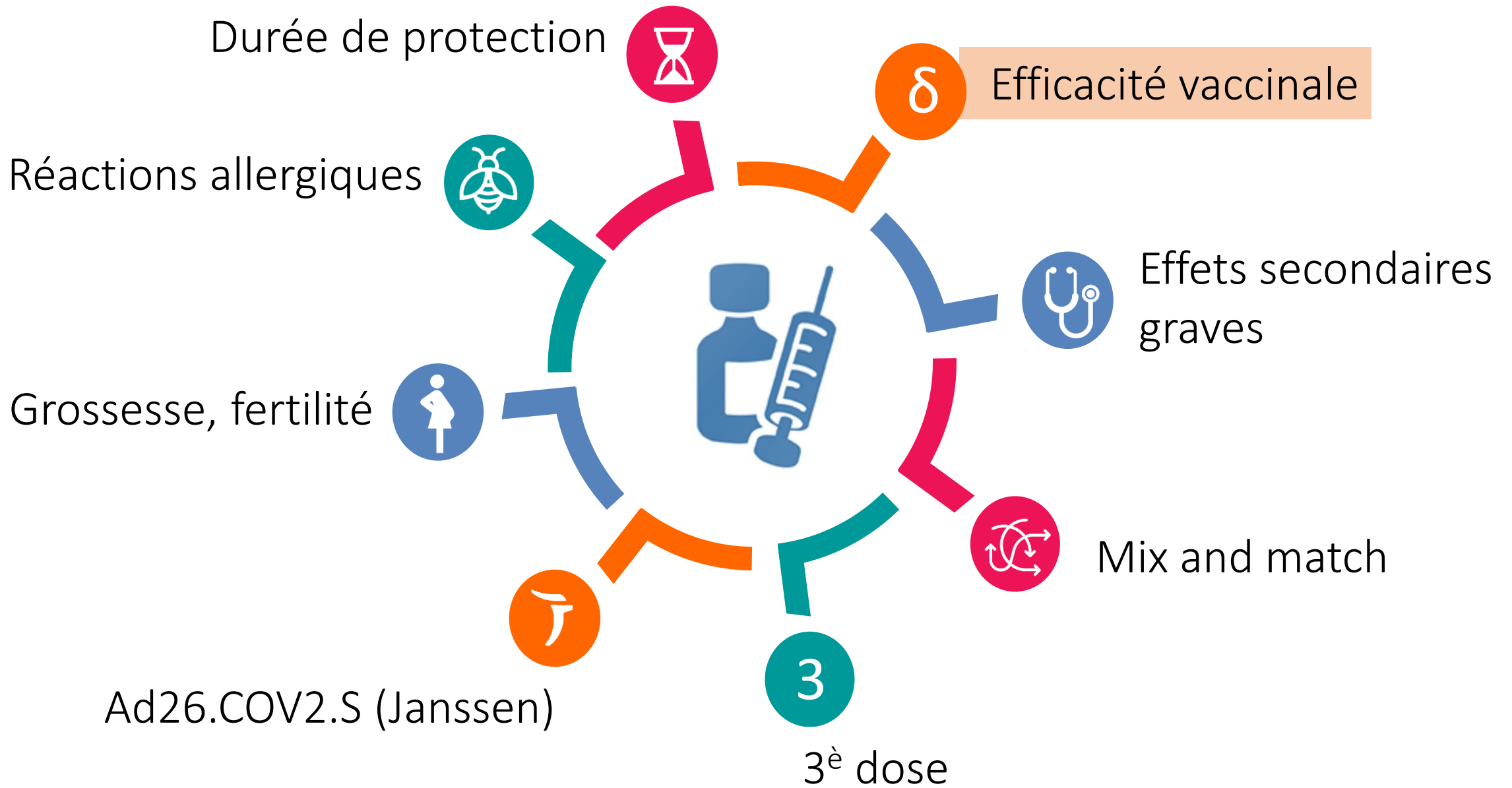
Jung et al, Nature communications, 2021



Durée Ac neutralisants -> 7 mois après vaccination

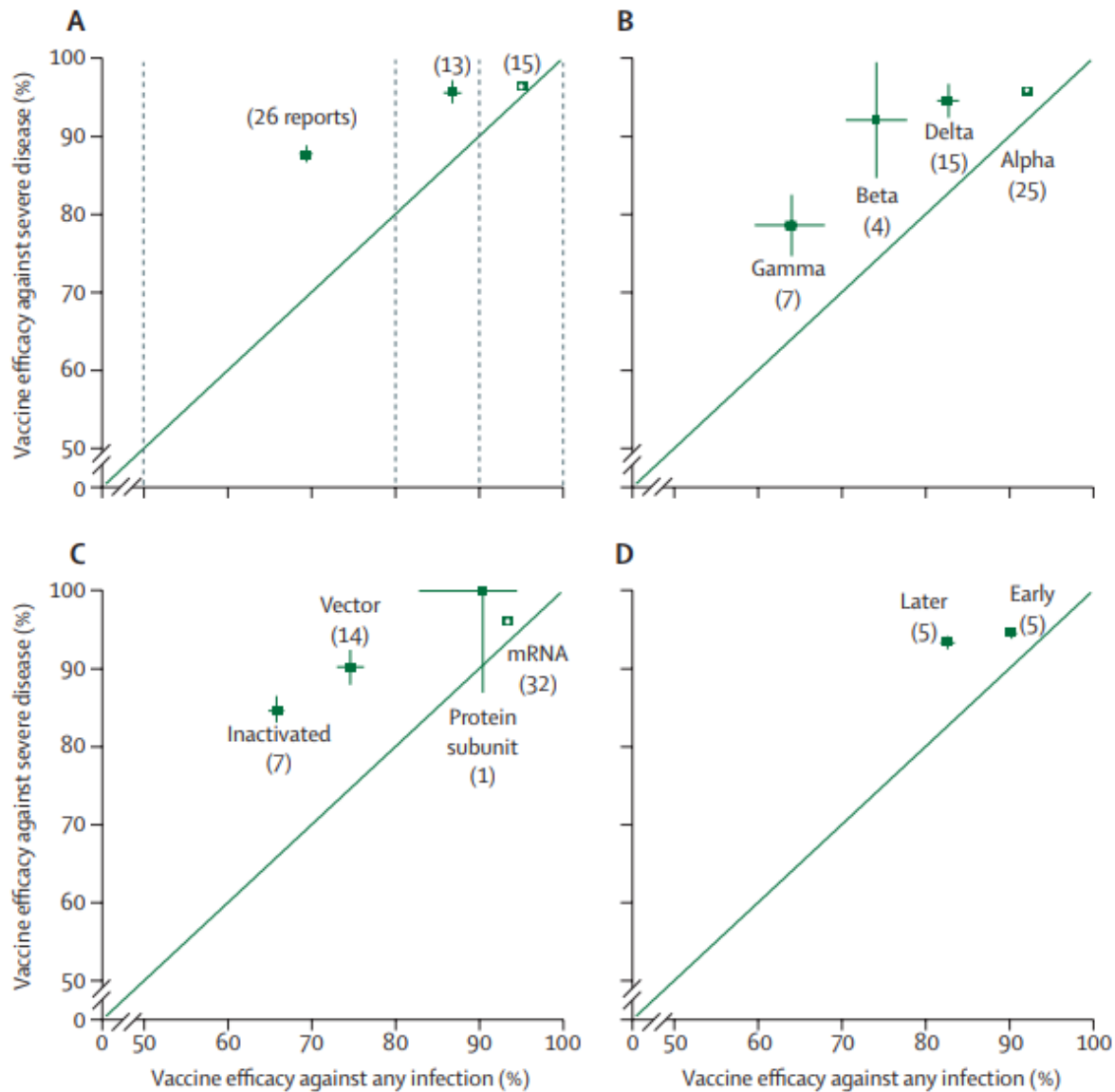
Pseudovirus Neutralization Assay



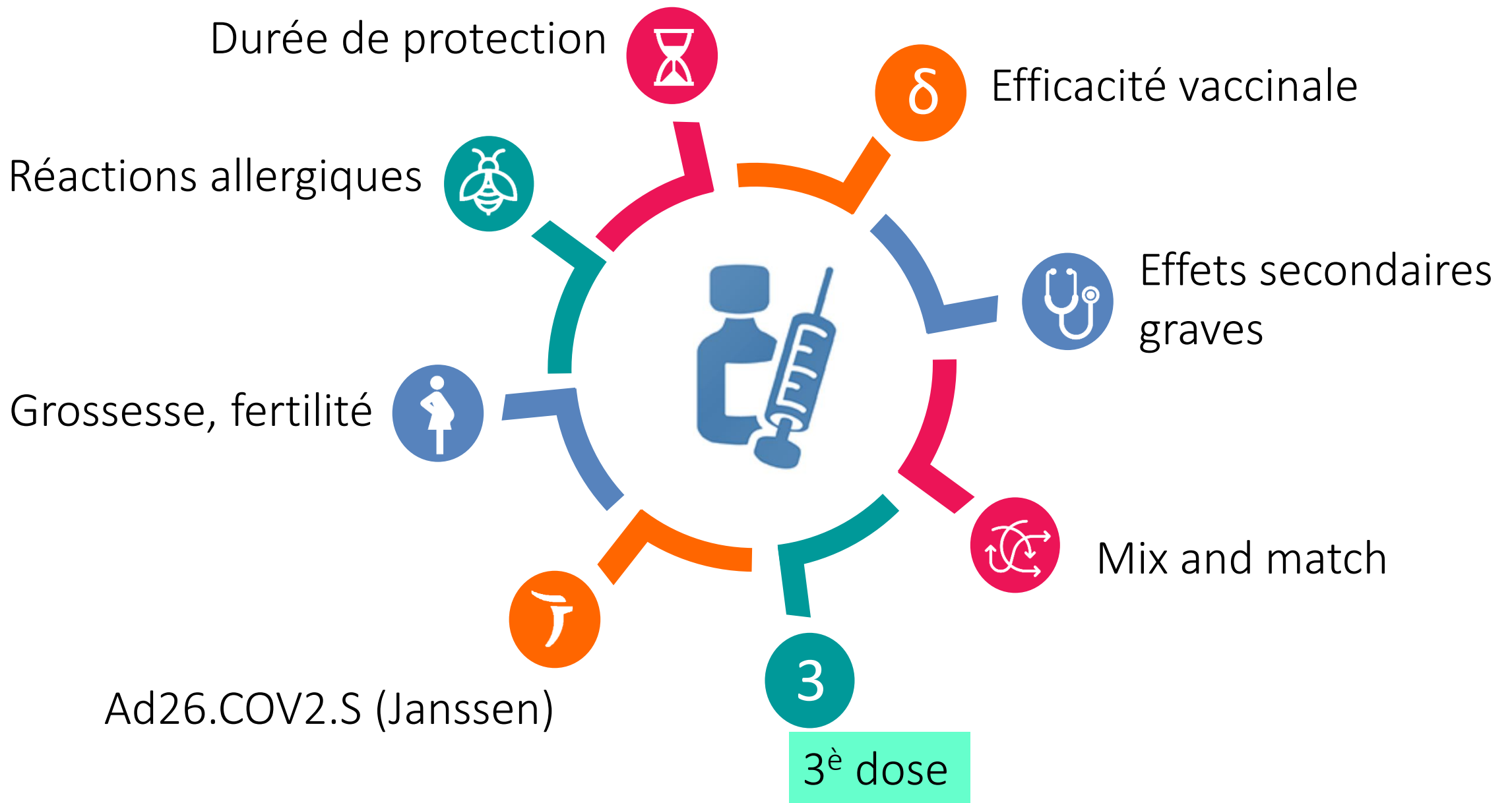




Effacité vaccinale



- Tous les vaccins sont efficaces contre maladie sévère, y compris contre le variant delta
- Les vaccins sont toujours plus efficaces contre maladie sévère que contre l'infection



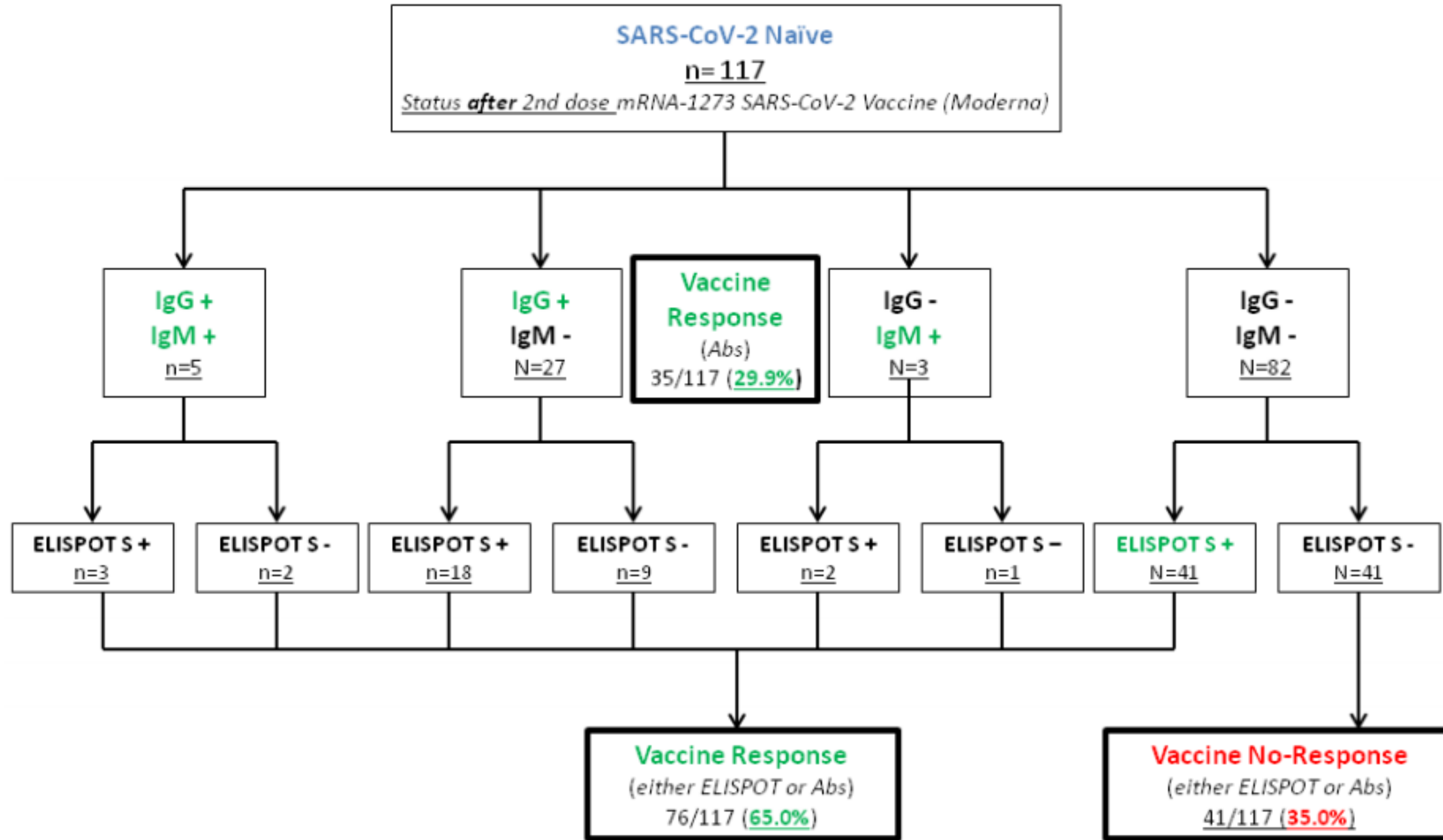
3 3^e dose

To boost or not to boost ?? No one is safe until everyone is safe

- Aucune évidence épidémiologique que la protection vaccinale diminue en Suisse
- Efficacité contre formes sévères maintenue
- Diminution des Ac avec tous les vaccins mais pas de rappels systématiques
- Efficacité des vaccins diminue mais nombreux biais (âge, exposition, nouveaux variants, changement comportement etc.)
- Pas de seuil de [] d'Ac (corrélée à une protection spécifique pour mRNA vaccines ('magic number'))
- Moratorium de l'OMS sur 2^e dose
- Donner une dose à toutes plutôt que 3 doses à qqun.e.s

3

Immunogenicité chez patients transplantés rénaux

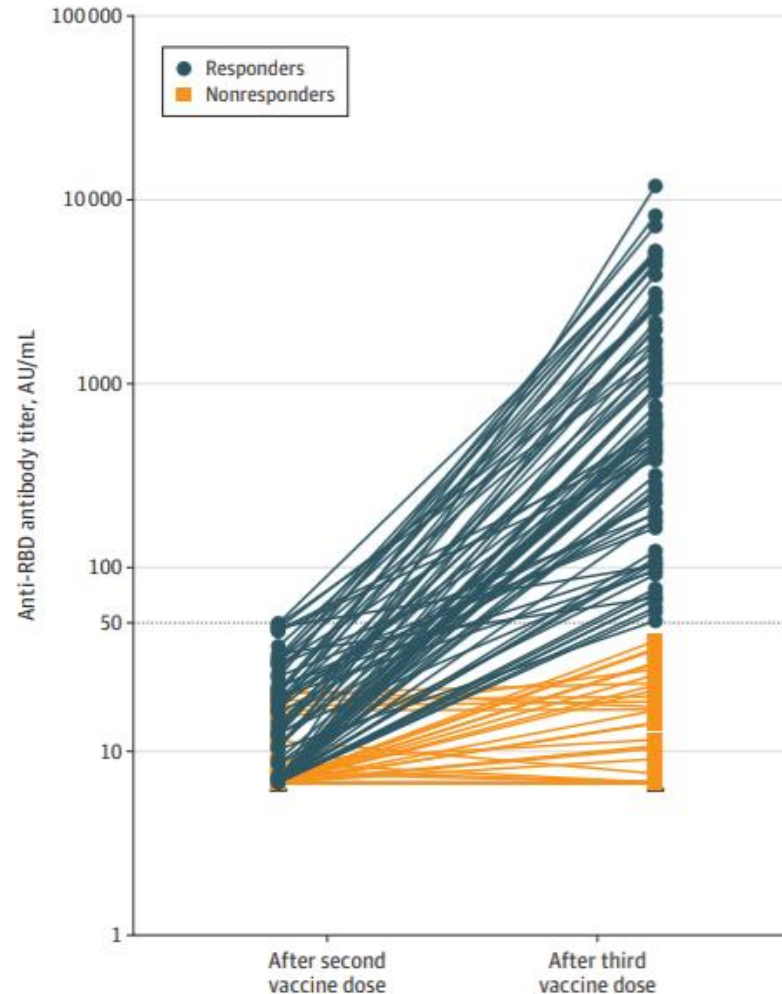


Half of those with no humoral responses had a cellular response

3

Effet 3^{ème} dose chez transplantés rénaux

Figure. Anti-Receptor-Binding Domain (RBD) IgG Antibody Titers Measured 28 Days After the Third Dose of mRNA-1273 SARS-CoV-2 Vaccine in 159 Kidney Transplant Recipients

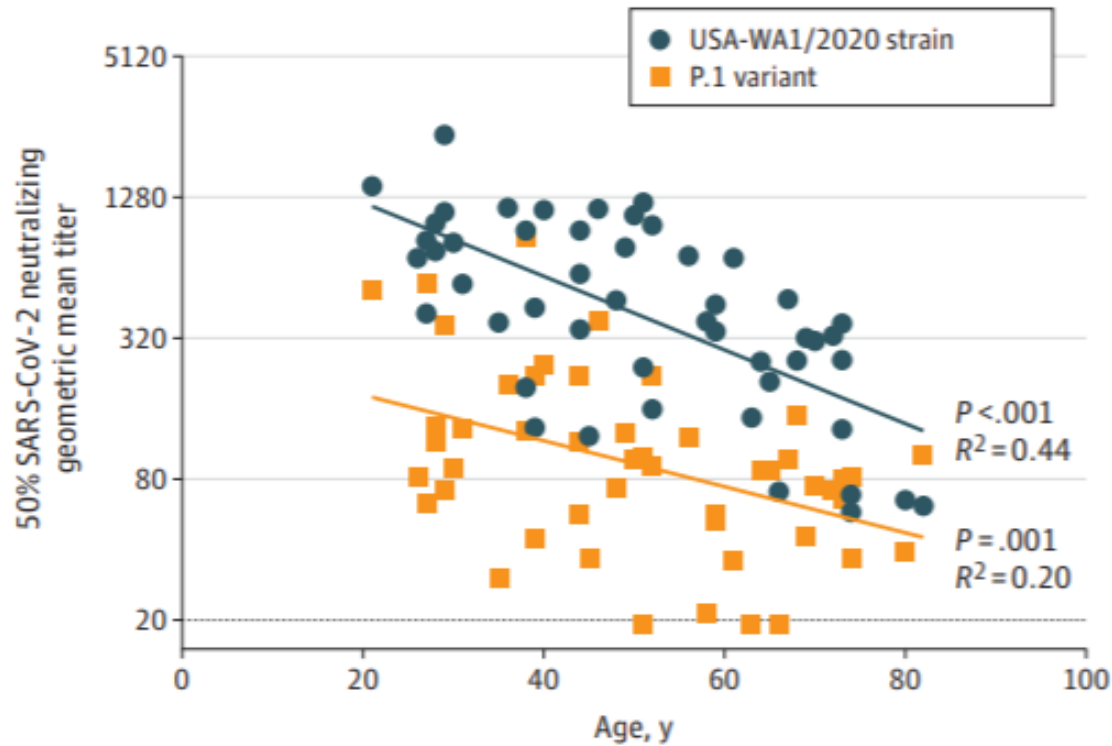


49% des non-répondeurs après 2 doses ont répondu à la 3^{ème} dose

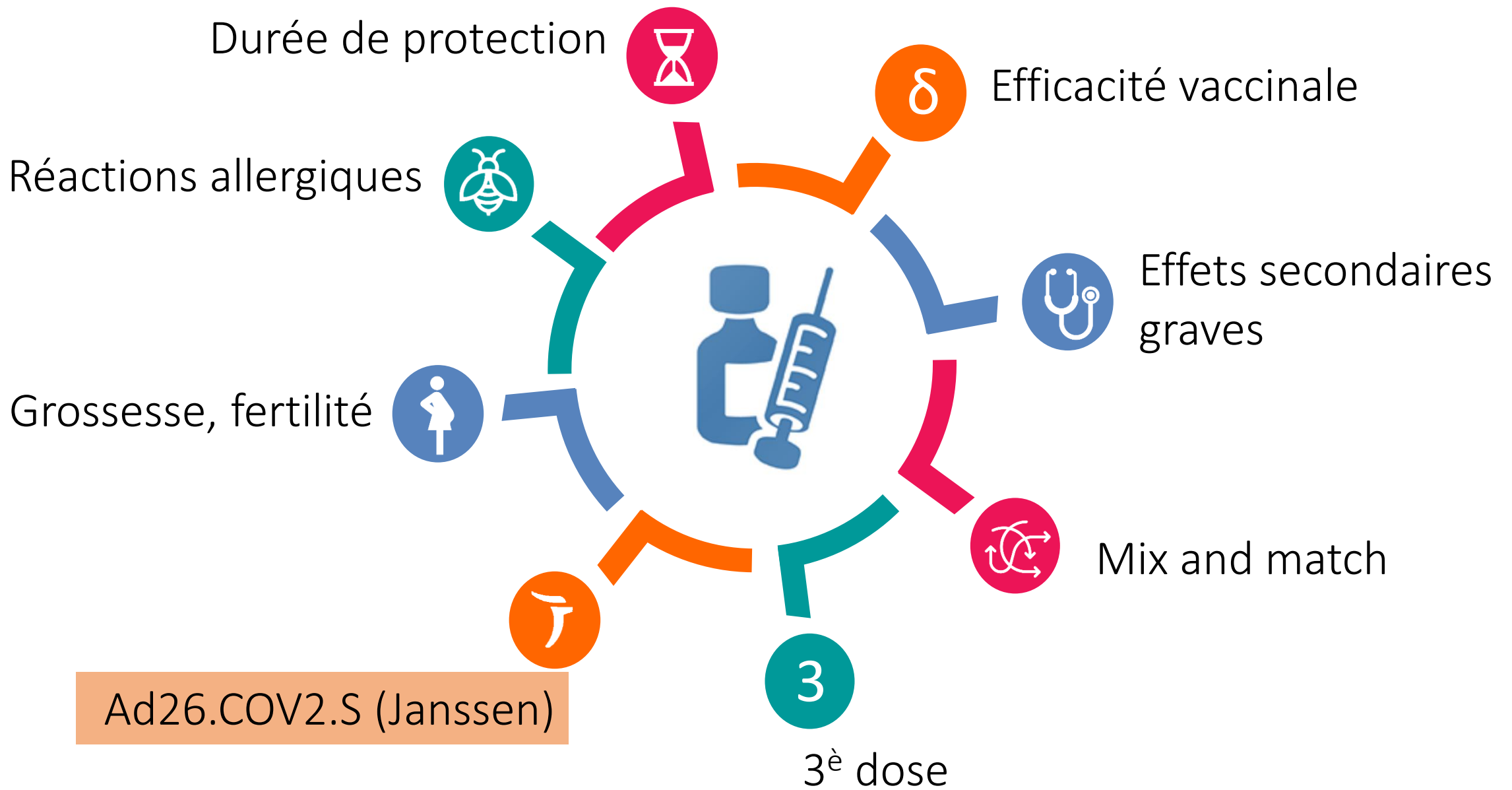
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Anticorps neutralisants en fonction âge

Figure 2. Neutralization of Live SARS-CoV-2 Clinical Isolates



Live virus neutralization of participant serum samples collected 14 days after the second vaccine dose. Neutralization experiments were performed with the USA-WA1/2020 strain and P.1 variant. Both show a significant negative association with participant age. The dotted line indicates the lower limit of quantification.





Ad26.COV2.S JNJ-78436735 [Johnson & Johnson (Janssen)]

Johnson & Johnson brings another effective Covid-19 vaccine to the arsenal – in a single dose

The level of protection, though, varied in different regions: 72 percent in the US, 66 percent in Latin America, and 57 percent in South Africa.

By Julia Belluz and Umair Irfan | Jan 29, 2021, 9:20am EST

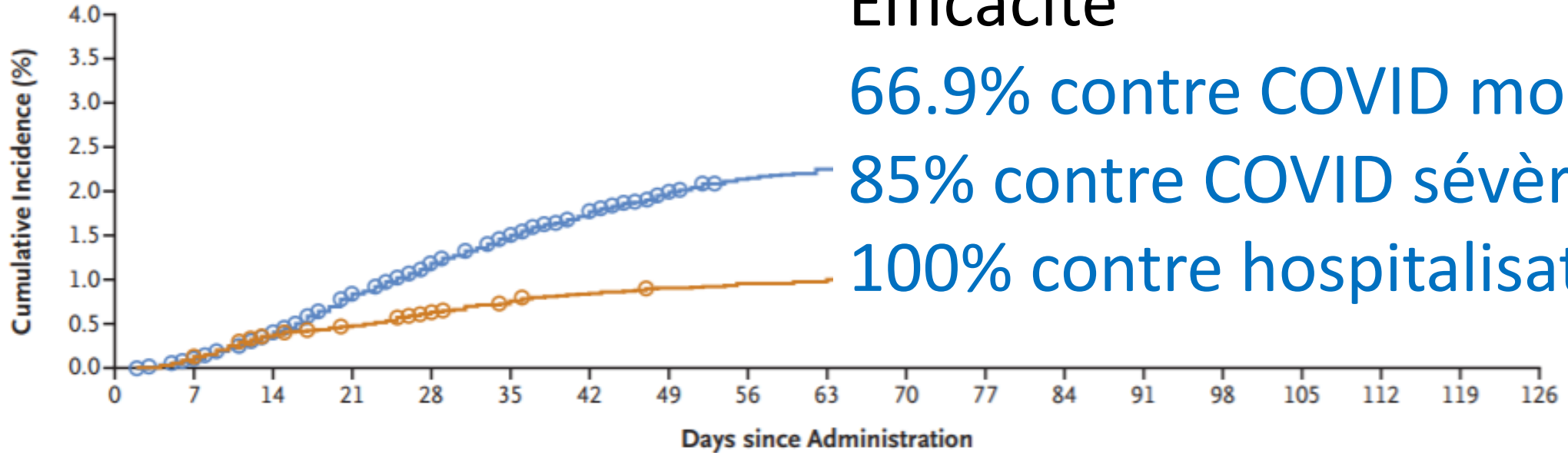
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Efficacité après 1 dose Ad26.COVS

A Moderate to Severe–Critical Cases of Covid-19



Efficacité

66.9% contre COVID modéré

85% contre COVID sévère

100% contre hospitalisations

No. at Risk

Placebo	19,822	19,804	19,745	19,652	19,579	19,488	18,411	14,814	10,823	7740	3876	1439	708	485	482	480	133	27	0
Ad26.COVS	19,744	19,725	19,669	19,642	19,612	19,578	18,541	14,909	10,930	7831	3998	1468	713	484	483	482	142	31	0

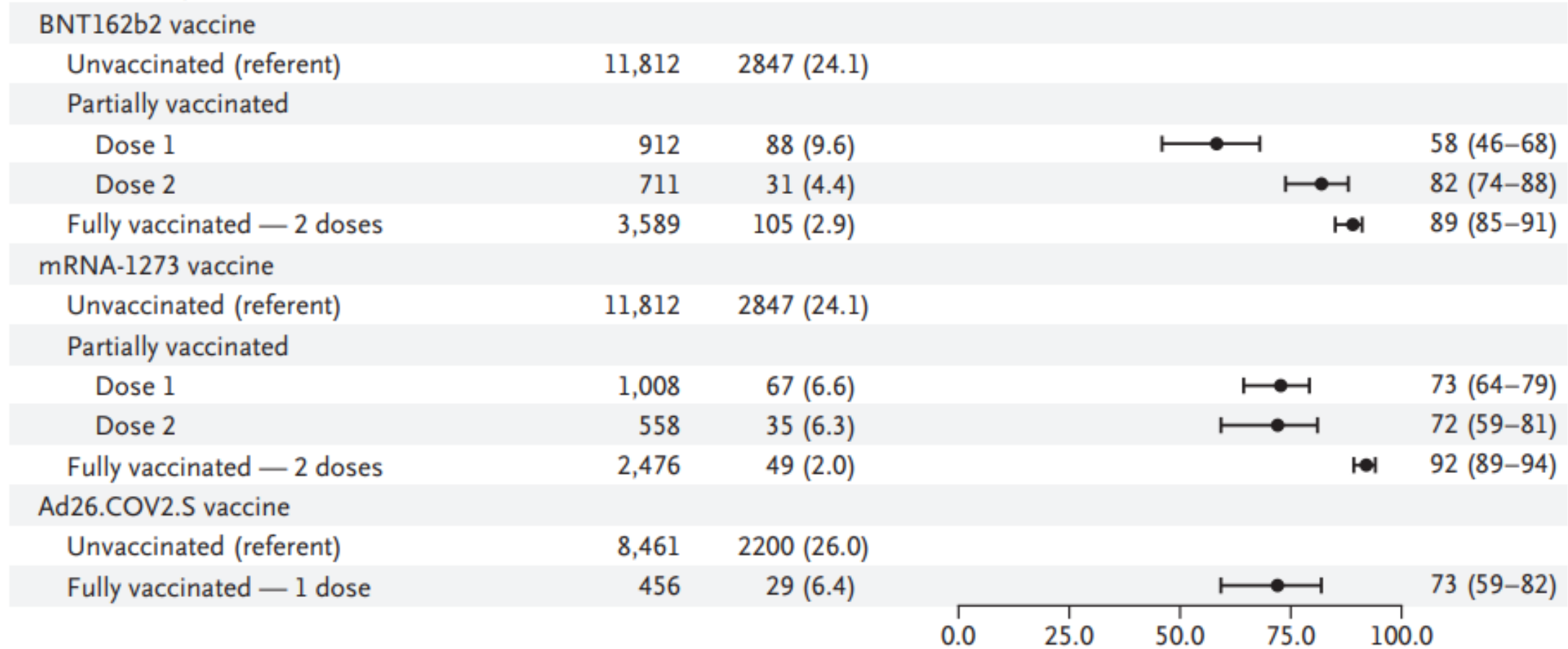
No. of Cases

Placebo	0	22	81	168	237	299	351	387	407	416	423	425	430	432	432	432	432	432	432
Ad26.COVS	0	27	76	96	126	151	168	178	184	188	189	191	191	192	193	193	193	193	193



Efficiency Pfizer et Moderna contre hosp. (>50 ans)

Effectiveness against emergency department or urgent care visit





Utilisation Ad26.COVS.S (Janssen)

- Personne avec contre-indication au vaccin mRNA
- 1'000'000 de personnes qui veulent autre chose que vaccin mRNA...
- A quand la 2^{ème} dose...

So... YOU'VE BEEN
EATING HOT DOGS
AND McCHICKENS
ALL YOUR LIFE

BUT DON'T WANT
THE VACCINE BECAUSE,
"YOU DON'T KNOW
WHAT'S IN IT?"