F-CRIN Network

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Innovative clinical research network in vaccinology

La vaccination maternelle : enjeux et bénéfices
Le suivi de cohortes de femmes enceintes

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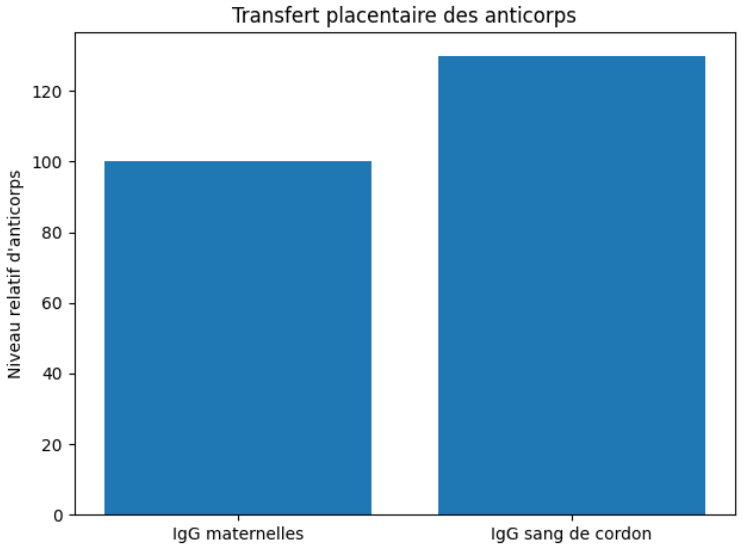
Pourquoi vacciner la femme enceinte?

- **Protéger femme enceinte**
- Vulnérabilité : modifications immunitaires et ventilatoires, risque accru de formes graves pour certaines infections (grippe, COVID)
- **Protéger fœtus, nouveau-né, jeune nourrisson**
- Vulnérabilité : immaturité système immunitaire < 6 mois.
- Transfert actif transplacentaire d'anticorps maternels (IgG)
- Protection durant les premiers mois de vie



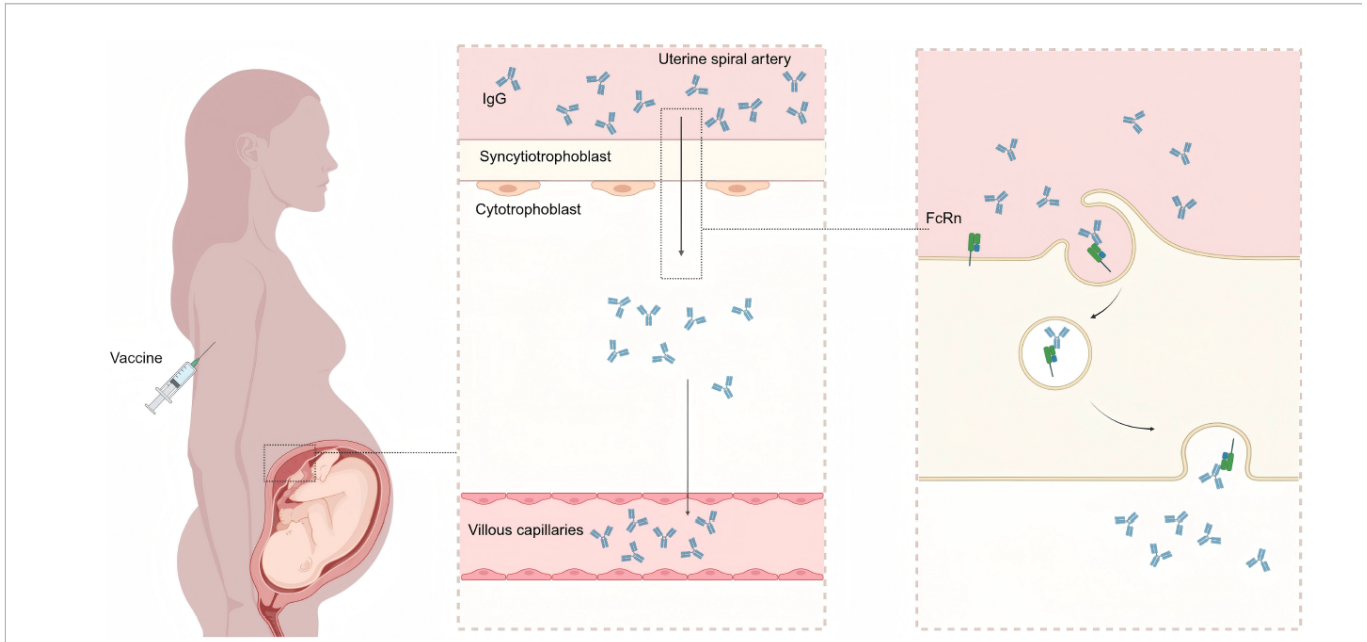
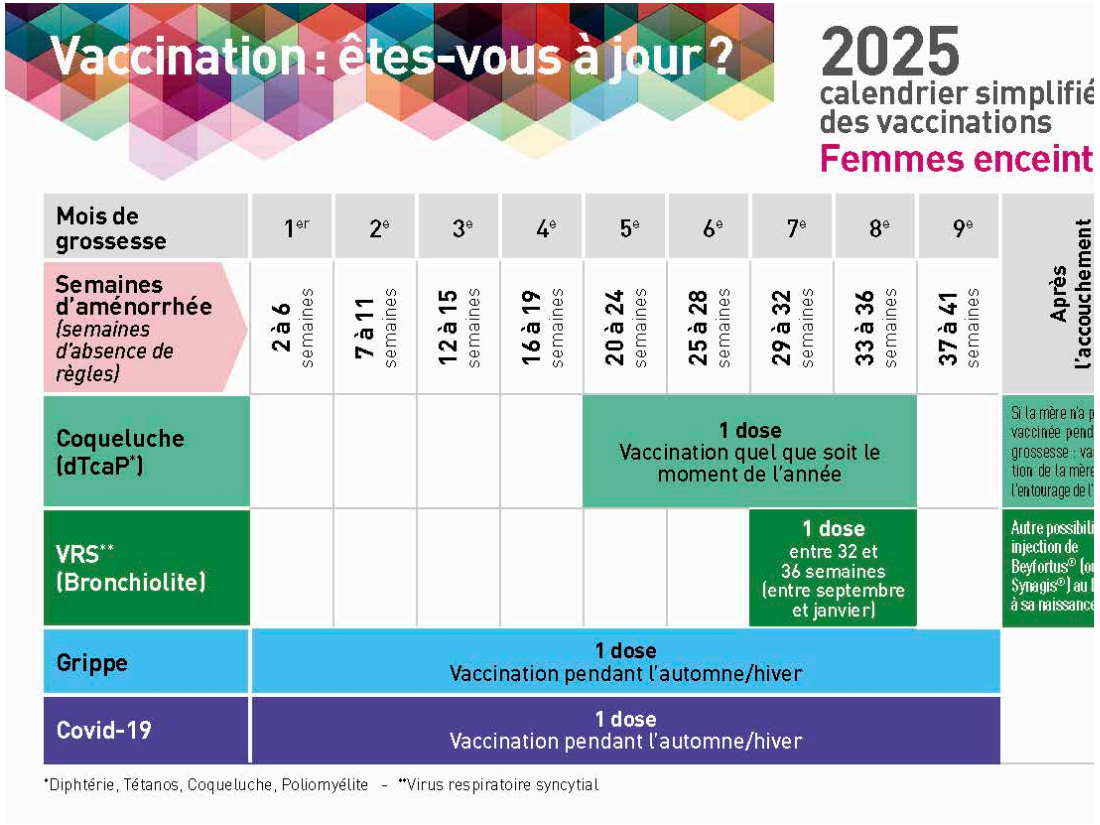


FIGURE 1
Mechanism of transplacental IgG transfer following maternal vaccination. Maternal IgG antibodies (produced postvaccination) bind to the fragment crystallizable neonatal receptor (FcRn) on placental trophoblast cells, undergo transcytosis across the syncytiotrophoblast layer, and are subsequently released into the fetal circulation. This figure was created with BioRender (https://biorender.com/).

Vaccinations recommandées actuellement en France

- **Coqueluche**
  - 20 - 36 SA
  - Protection nourrisson ++ via transfert anticorps maternels
  - *Amirthalingam G, et al. Effectiveness of maternal pertussis vaccination in England: an observational study. Lancet. 2014 Oct 25;384(9953):1521-8.*
- **Vaccinations saisonnalisées**
  - **Grippe :** double protection mère + enfant
  - **COVID-19 :**
    - Eviter formes sévères chez femme enceinte
    - Réduire risques accouchement prématuré, hypotrophie ou mort fœtale in utero



Mais la couverture vaccinale des femmes enceintes reste insuffisante !

- Coqueluche : 72% en 2024 (a augmenté suite à épidémie mortelle)
- Grippe : 30% en 2021
- Covid-19 : 70% début 2022 (inférieur à couverture femmes même âge)
- VRS : 27% saison 2024-2025

(Nirsevimab chez nouveau-nés : 80%)

Mais la couverture vaccinale des femmes enceintes reste insuffisante !

- Enquête nationale périnatale 2021 + enquête IPSOS 2022

  - Absence de proposition par professionnels de santé 40%
  - Peur d'effets défavorables pour le bébé 24%
  - Absence de crainte de la maladie (grippe) 22%
  - Méfiance envers les vaccins 22%
  - Peur d'effets défavorables pour la femme 16%
  - Conditions socio-économiques

Rôle des professionnels de santé +++

- Mais vaccination pas toujours proposée : absence de consultation dédiée, autres priorités, manque de motivation, manque de temps, oublis

https://www.ipsos.com/fr-fr/4-femmes-sur-10-se-font-vacciner-pendant-leur-grossesse

Rôle des professionnels de santé +++

Vaccination de la femme enceinte : quels sont les freins déclarés?

1 Professionnel de Santé sur 4

Estime que ses patientes enceintes vont refuser la vaccination et n'aborde donc pas avec elles le sujet de la vaccination maternelle

1 Professionnel de Santé sur 10

Estime que ce n'est pas son rôle de discuter, recommander ou prescrire un vaccin pendant la grossesse

1/3 est en attente d'informations complémentaires au sujet de la vaccination pendant la grossesse

1/4 se questionne sur l'innocuité des vaccins sur les nourrissons

6 Femmes enceintes sur 10 reçoivent une recommandation

5 Femmes enceintes sur 10 reçoivent une prescription

4 Femmes enceintes sur 10 reçoivent finalement une administration

https://www.ipsos.com/fr-fr/4-femmes-sur-10-se-font-vacciner-pendant-leur-grossesse

Quels déterminants de la vaccination pendant la grossesse?

Vaccine
Volume 41, Issue 49, 30 November 2023, Pages 7342-7347

Evaluation of intentions to get vaccinated against influenza, COVID 19, pertussis and to get a future vaccine against respiratory syncytial virus in pregnant women

Charlotte Cubizolles [a], Tiphaine Barjat [b c], Céline Chauleur [b c], Sébastien Bruel [a f], Elisabeth Botelho-Nevers [d e f g h], Amandine Gagneux-Brunon [d f g h]

Multivariate analysis of factors related to vaccine intention for influenza, Covid-19 and RSV (aOR: adjusted odd ratio, p: p-value, CI: confidence interval).

	Influenza		Covid-19		RSV		Pertussis	
	aOR (CI 95%)	**p**	**aOR (CI 95%)**	**p**	**aOR (CI 95%)**	**p**	**aOR (CI 95%)**	**p**
Age (for one year increase)	1.02 (0.92–1.12)	0.76	1 (0.92–1.08)	0.99	1 (0.99–1.01)	0.78		
Multiparous	1.21 (0.74–1.97)	0.44	1.02 (0.62–1.68)	0.94	1.47 (0.76–2.87)	0.25	1.4 (0.84–2.38)	0.2
5C Scale								
Confidence	**1.69 (1.09–2.61)**	**0.02**	**2.63 (1.7–4.07)**	**<0.005**	**1.92 (1.3–2.84)**	**<0.005**	1.25 (0.9–1.64)	0.19
Complacency	0.88 (0.57–1.37)	0.58	0.85 (0.61–1.2)	0.36	1.13 (0.81–1.58)	0.47	1.35 (0.99–1.84)	0.06
Constraints	1.37 (0.93–2.02)	0.11	1.11 (0.81–1.51)	0.52	0.87 (0.64–1.19)	0.398	0.84 (0.63–1.12)	0.23
Calculation	0.79 (0.58–1.09)	0.15	0.85 (0.66–1.1)	0.12	**0.76 (0.58–0.98)**	**0.038**	0.85 (0.67–1.08)	0.18
Collective responsibility	1.69 (0.91–3.14)	0.1	1.5 (0.90–2.49)	0.12	1.37 (0.84–2.23)	0.21	1.52 (0.98–2.37)	0.06
Education Status								
Primary/High School	Ref		Ref		Ref		Ref	
University degree or equivalent	0.91 (0.3–2.79)	0.88	0.75 (0.39–1.52)	0.76	0.50 (0.21–1.2)	0.12	0.75 (0.34–1.67)	0.49
Health care professional	**0.332 (0.13–0.88)**	**0.026**	0.76 (0.38–1.52)	0.44	0.98 (0.48–2.01)	0.97	0.8 (0.4–1.6)	0.52
Influenza vaccination	**13.5 (5.3–34.3)**	**<0.005**	1.95 (0.99–3.85)	0.055	1.35 (0.67–2.73)	0.40	**1.97 (1.1–3.84)**	**0.048**
Pertussis vaccination within the previous 5 years	0.79 (0.36–1.72)	0.56	0.97 (0.52–1.79)	0.91	**2.32 (1.26–4.27)**	**0.007**	**2.9 (1.6–5.18)**	**<0.005**
Antenatal care provider recommended a vaccine	**4.89 (2.24–10.7)**	**<0.005**	0.83 (0.44–1.55)	0.56	1.54 (0.82–2.88)	0.18	1.06 (0.47–2.4)	0.89
Knowledge score (for one point increase)	**1.56 (1.26–1.93)**	**<0.005**	1.059 (0.9–1.24)	0.49	**1.32 (1.11–1.57)**	**0.001**	1.15 (0.97–1.36)	0.11

*Pour accéder aux données sur le portail de la Cnam, il faut suivre la procédure standard HDH-CESREES-CNIL (sauf pour les organismes bénéficiant d'un accès permanant au titre de leurs missions indiquées dans la loi).
Source: CNIL,fr

Quels déterminants de la vaccination pendant la grossesse?

Influenza during pregnancy: Incidence, vaccination coverage and attitudes toward vaccination in the French web-based cohort G-GrippeNet

Paul Loubet[a,b,c], Caroline Guerrisi[a], Clément Turbelin[a], Béatrice Blondel[d], Odile Launay[b,c,d,e], Marc Bardou[f], François Goffinet[d,g], Vittoria Colizza[a], Thomas Hanslik[a], Solen Kernéis[b,c,d,*], the GGNET study group[1]

Crude and weighted influenza vaccination coverage by selected characteristics in the 2014/2015 G-GrippeNet cohort.

	Crude vaccination coverage %	Weighted vaccination coverage* %	p-value**
Total	39	26	
Age, years			$<10^{-3}$
20–29	36	16	
30–39	39	30	
40–49	54	82	
Educational Level			0.008
Under A-level	33	14	
A-level	21	13	
High School Level	41	41	
Occupation (if employed)			$<10^{-3}$
Professional	50	41	
Office work	33	27	
Other	9	20	
Parity			0.79
0	40	25	
≥1	39	29	
History of hospitalization during previous pregnancy			0.03
No	42	19	
Yes	48	50	
Chronic disease			0.08
No	40	24	
Yes	36	50	
BMI before pregnancy			0.27
<25	37	31	
>= 25	47	16	
Current smoker			$<10^{-3}$
Non smoker	40	40	
Smoker	27	2	
Vaccination Recommendation			$<10^{-3}$
No	18	8	
Yes	72	74	
Last season Vaccination			0.86
No	31	24	
Yes	69	28	

grippe covid net

Factors associated with influenza vaccine uptake in pregnant women from the 2014/2015 G-GrippeNet cohort (Final model of logistic regression).

	Weighted adjusted OR [95%CI]	Corrected OR* [95%CI]	p-value
Clinician recommendation			$<10^{-3}$
No	1	1	
Yes	19.0 [7.3–55.2]	7.8 [3.0–17.1]	
Smoking status			0.05
Yes	1	1	
No	7.0 [2.3–11.9]	2.1 [1.2–6.9]	

Quels déterminants de la vaccination pendant la grossesse? Covid-19

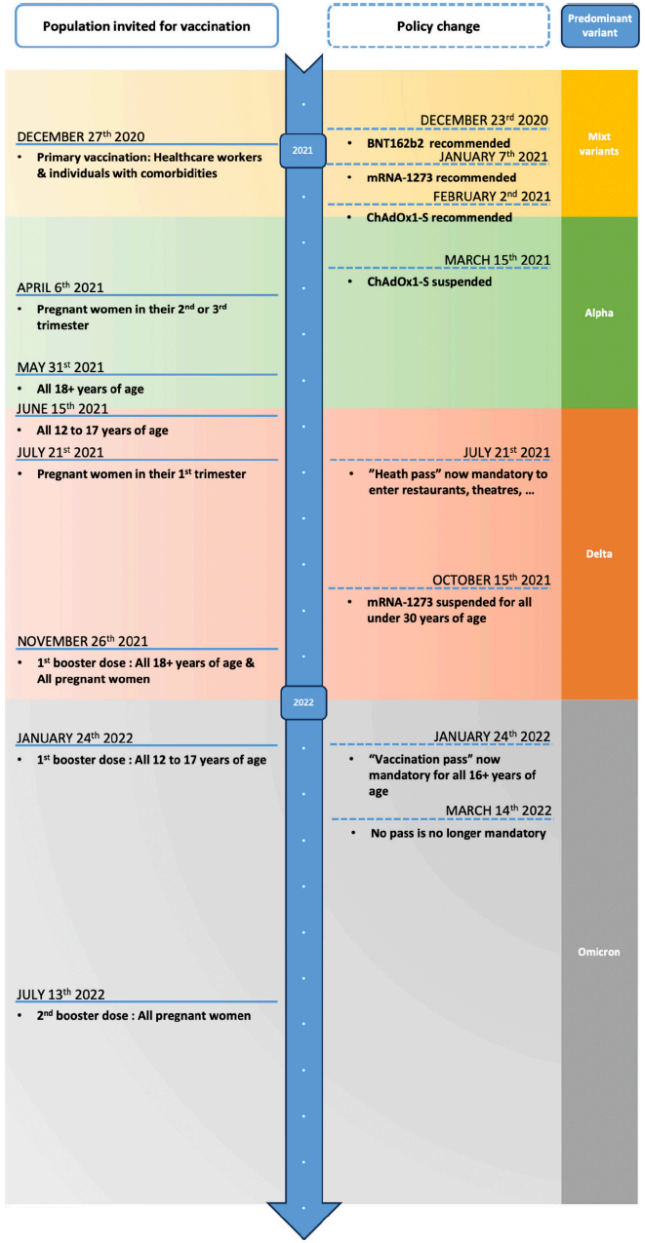


Table 1

Characteristics of women who received an initial dose of vaccine against COVID-19 during pregnancy or prior to conception and those who did not. Data for pregnant women who delivered in France after 20 weeks of gestation between April 1, 2021, and December 31, 2022.

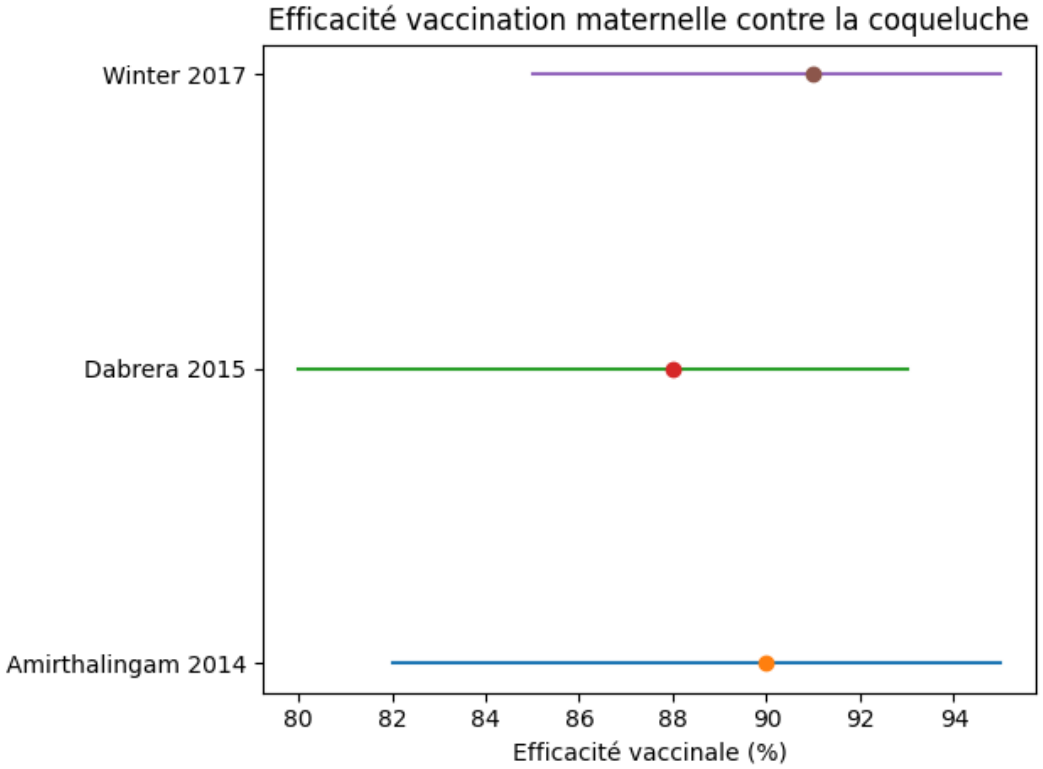
Characteristic	Vaccination status at delivery:		Odds Ratios[1]: Unvaccinated vs Vaccinated (Reference)			
			Crude association		Adjusted association[2]	
	Unvaccinated, *N* = 571,673 (48 %)	Vaccinated, *N* = 631,781 (52 %)	OR	95 % CI	OR	95 % CI
SOCIODEMOGRAPHIC						
Age class, N (%)						
<20	17,379 (64.3 %)	9654 (35.7 %)	2.30	2.24–2.36	1.87	1.81–1.92
20–24	85,359 (56.5 %)	65,832 (43.5 %)	1.66	1.64–1.68	1.67	1.65–1.70
25–29	178,049 (49.3 %)	182,802 (50.7 %)	1.24	1.23–1.25	1.31	1.29–1.32
30–34	180,472 (43.9 %)	230,402 (56.1 %)	Reference		Reference	
35–39	89,954 (43.5 %)	116,669 (56.5 %)	0.98	0.97–1.0	0.97	0.95–0.98
≥ 40	20,460 (43.6 %)	26,422 (56.4 %)	0.99	0.97–1.01	0.98	0.95–1.00
Beneficiary of the complementary health solidarity (C2S)						
No	479,145 (45.3 %)	578,262 (54.7 %)	Reference		Reference	
Yes	92,528 (63.4 %)	53,519 (36.6 %)	2.09	2.06–2.11	2.08	2.05–2.11
Social deprivation index quintiles						
Quintile 1 (Least deprived)	94,127 (39.5 %)	143,952 (60.5 %)	Reference		Reference	
Quintile 2	106,352 (44.8 %)	131,074 (55.2 %)	1.24	1.23–1.26	1.31	1.29–1.32
Quintile 3	108,041 (47.7 %)	118,514 (52.3 %)	1.39	1.38–1.41	1.48	1.46–1.50
Quintile 4	107,315 (49.1 %)	111,088 (50.9 %)	1.48	1.46–1.49	1.54	1.52–1.56
Quintile 5 (Most deprived)	118,654 (52.0 %)	109,624 (48.0 %)	1.66	1.64–1.67	1.63	1.61–1.66
Overseas departments	33,043 (72.8 %)	12,362 (27.2 %)	4.09	4.00–4.18	4.49	4.38–4.60
Unknown	4141 (44.5 %)	5167 (55.5 %)	1.23	1.18–1.28	1.24	1.18–1.30
Region						
Auvergne-Rhône-Alpes	68,210 (47.2 %)	76,236 (52.8 %)	Reference		Reference	
Bourgogne-Franche-Comté	20,876 (48.8 %)	21,926 (51.2 %)	1.06	1.04–1.09	1.01	0.99–1.04
Bretagne	21,508 (40.2 %)	31,976 (59.8 %)	0.75	0.74–0.77	0.69	0.67–0.70
Centre-Val de Loire	19,860 (46.2 %)	23,116 (53.8 %)	0.96	0.94–0.98	0.89	0.87–0.91
Overseas territories	846 (66.7 %)	423 (33.3 %)	2.24	1.99–2.51	2.56	2.25–2.92
Corse	2492 (56.7 %)	1905 (43.3 %)	1.46	1.38–1.55	1.71	1.59–1.83
Grand Est	42,454 (48.3 %)	45,405 (51.7 %)	1.05	1.03–1.06	1.05	1.03–1.07
Guadeloupe	5110 (81.7 %)	1141 (18.3 %)	5.01	4.69–5.34	6.08	5.67–6.52
Guyana	7386 (84.5 %)	1353 (15.5 %)	6.10	5.75–6.47	5.68	5.33–6.05
Hauts-de-France	47,061 (42.5 %)	63,644 (57.5 %)	0.83	0.81–0.84	0.68	0.66–0.69
Île-de-France	121,661 (45.7 %)	144,383 (54.3 %)	0.94	0.93–0.95	0.94	0.93–0.96
La Réunion	14,772 (65.0 %)	7963 (35.0 %)	2.07	2.01–2.13	1.92	1.85–1.98
Martinique	4628 (80.1 %)	1151 (19.9 %)	4.49	4.21–4.80	5.78	5.38–6.20
Normandie	23,513 (41.5 %)	33,084 (58.5 %)	0.79	0.78–0.81	0.68	0.67–0.70
Nouvelle-Aquitaine	40,575 (44.4 %)	50,723 (55.6 %)	0.89	0.88–0.91	0.85	0.84–0.87
Occitanie	50,474 (51.4 %)	47,667 (48.6 %)	1.18	1.16–1.20	1.19	1.17–1.21
Pays de la Loire	27,723 (41.4 %)	39,192 (58.6 %)	0.79	0.78–0.81	0.71	0.70–0.73
Provence-Alpes-Côte d'Azur	52,177 (56.5 %)	40,141 (43.5 %)	1.45	1.43–1.48	1.58	1.55–1.61

*Bernard, C., et al. (2025). Vaccine **53**: 127070.*

Vaccinations recommandées actuellement en France
Données de vie réelle

- Coqueluche études d'efficacité en population

Dabrera G. Clin Infect Dis. 2015 Feb 1;60(3):333-7.
Winter K. Clin Infect Dis. 2017 Jan 1;64(1):3-8.
Amirthalingam G, et al. Effectiveness of maternal pertussis vaccination in England: an observational study. Lancet. 2014 Oct 25;384(9953):1521-8.



Coqueluche études d'efficacité en population

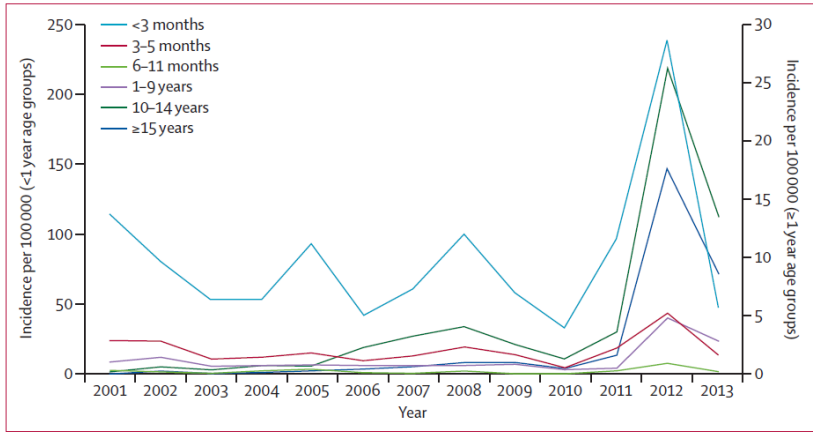


Figure 2: **Annual incidence of laboratory-confirmed cases of pertussis by age group**
Figure shows incidence from 2001 to 2013 in England only.

	2008	2009	2010	2011	2012	2013	% change 2013 vs 2012 (95% CI)	% change 2013 vs 2011 (95% CI)
<1 month	24 (3·4%)	16 (2·9%)	6 (2·0%)	16 (2·5%)	43 (0·7%)	10 (0·3%)	−77% (−90 to −53)	−38% (−75 to 46)
1 month	67 (9·5%)	43 (7·7%)	22 (7·2%)	57 (9·1%)	161 (2·7%)	37 (1·0%)	−77% (−84 to −67)	−35% (−58 to 0)
2 months	58 (8·3%)	29 (5·2%)	15 (4·9%)	45 (7·2%)	124 (2·1%)	25 (0·7%)	−80% (−87 to −69)	−44% (−67 to 7)
3–5 months	33 (4·7%)	20 (3·6%)	6 (2·0%)	21 (3·3%)	62 (1·0%)	22 (0·6%)	−65% (−79 to −41)	5% (−45 to 100)
6–11 months	8 (1·1%)	3 (0·5%)	3 (1·0%)	7 (1·1%)	22 (0·4%)	7 (0·2%)	−68% (−89 to −23)	0% (−70 to 234)
1–4 years	21 (3·0%)	19 (3·4%)	7 (2·3%)	10 (1·6%)	58 (1·0%)	41 (1·1%)	−29% (−54 to 7)	310% (102 to 818)
5–19 years	184 (26·2%)	121 (21·8%)	59 (19·4%)	124 (19·7%)	1128 (19·1%)	669 (17·6%)	−41% (−46 to −35)	440% (345 to 559)
≥20 years	307 (43·7%)	304 (54·8%)	186 (61·2%)	349 (55·5%)	4311 (73·0%)	2984 (78·6%)	−31% (−34 to −27)	755% (665 to 860)
Total number of cases	702	555	304	629	5909	3795	−36% (−38 to −33)	503% (454 to 557)
Reported deaths*	5 (CFR 3·4%)	1 (CFR 1·1%)	1 (CFR 2·3%)	3 (CFR 2·5%)	10 (CFR 3·0%)	2 (CFR 2·8%)	..	..

Table shows total number of laboratory-confirmed cases of pertussis in January to September (inclusive) for 2008–13 in England. Data are number of cases in each age group and percentage of total cases in that year. CFR refers to deaths as a percentage of all cases in infants younger than 3 months. CFR=case fatality rate. *Deaths reconciled from hospital admissions data, follow-up of laboratory-confirmed cases, and death certification.

Table 1: **Laboratory-confirmed cases by age group**

	2008	2009	2010	2011	2012	2013	% change 2013 vs 2012 (95% CI)	% change 2013 vs 2011 (95% CI)
<1 month	31 (9·2%)	24 (10·3%)	10 (8·3%)	25 (10·1%)	73 (11·3%)	18 (6·5%)	−75% (−86 to −58)	−28% (−73 to 37)
1 month	112 (33·1%)	80 (34·5%)	38 (31·4%)	99 (40·1%)	209 (32·3%)	68 (24·7%)	−67% (−76 to −57)	−31% (−50 to −6)
2 months	85 (25·1%)	47 (20·3%)	26 (21·5%)	59 (23·9%)	158 (24·4%)	54 (19·6%)	−66% (−75 to −53)	−8% (−38 to 35)
3–5 months	55 (16·3%)	44 (19·0%)	21 (17·4%)	26 (10·5%)	108 (16·7%)	54 (19·6%)	−50% (−65 to −30)	108% (28 to 246)
6–11 months	22 (6·5%)	10 (4·3%)	7 (5·8%)	11 (4·5%)	30 (4·6%)	11 (4·0%)	−63% (−83 to −25)	0% (−61 to 154)
1–4 years	18 (5·3%)	16 (6·9%)	9 (7·4%)	9 (3·6%)	29 (4·5%)	21 (7·6%)	−28% (−61 to 31)	133% (2 to 479)
5–19 years	11 (3·3%)	7 (3·0%)	5 (4·1%)	7 (2·8%)	23 (3·5%)	12 (4·4%)	−48% (−76 to 9)	71% (−38 to 414)
20+ years	4 (1·2%)	4 (1·7%)	5 (4·1%)	11 (4·5%)	18 (2·8%)	37 (13·5%)	106% (14 to 284)	236% (68 to 631)
Total	338	232	121	247	648	275	−58% (−63 to −37)	11% (−7 to 33)

Table shows total number of hospital admissions for pertussis in January to September (inclusive) for 2008–13 in England. Data are number of admissions in each age group and percentage of total pertussis admissions in that year.

Table 2: **Hospital admissions by age group**

Amirthalingam G, et al. Lancet. 2014 Oct 25;384(9953):1521-8.

Rôle des politiques sanitaires

- Inégalités sociales ++ :
  - Personnes milieux moins favorisés = les moins vaccinées
  - Aspects culturels, littératie en santé, adhésion normes

- Obstacles organisationnels

Rapport 25-05. Vaccination des femmes enceintes: répondre aux enjeux actuels – ANM 2025

Rôle des politiques sanitaires

Only **maternity ward A** offered vaccine + vaccination without charge at prenatal visits

Table 2. Determinants associated with vaccination: Multivariate analysis including maternity ward and social and demographic characteristics (N = 248).

Variables	Vaccinated women N = 48 n (%)	aOR	95% CI
Maternity ward			
B and C, n = 118	2 (1.7)	Ref.	-
A, n = 130	46 (35.4)	25.52	(5.76–113.10)
Geographic origin			
Other, n = 134	14 (10.4)	Ref.	-
Metropolitan France, n = 114	34 (29.8)	2.37	(1.03–5.46)
Number of children			
None, n = 97	27 (27.8)	Ref.	-
1, n = 66	10 (15.2)	0.80	(0.31–2.09)
≥ 2, n = 85	11 (13.1)	0.71	(0.27–1.91)
Twin pregnancy			
No, n = 239	44 (18.4)	Ref.	-
Yes, n = 9	4 (44.4)	3.39	(0.43–26.69)
Previous influenza vaccination*			
No, n = 195	27 (13.8)	Ref.	-
Yes, n = 51	21 (41.2)	3.13	(1.25–7.86)
Healthcare workers			
No, n = 222	38 (17.1)	Ref.	-
Yes, n = 26	10 (38.5)	0.60	(0.18–2.03)
Social-occupational category			
Company heads, managers, professionals, n = 66	24 (36.4)	Ref.	-
Intermediate professions, tradespeople, crafts workers and shopkeepers, office, sales, and service workers, n = 107	17 (15.9)	0.80	(0.33–1.95)
Farmers, blue-collar workers, unemployed, not in the labor force n = 75	7 (9.3)	0.71	(0.23–2.18)

Alessandrini, V., 2019. Does the availability of influenza vaccine at prenatal care visits and of immediate vaccination improve vaccination coverage of pregnant women? PLoS One 14, e0220705.

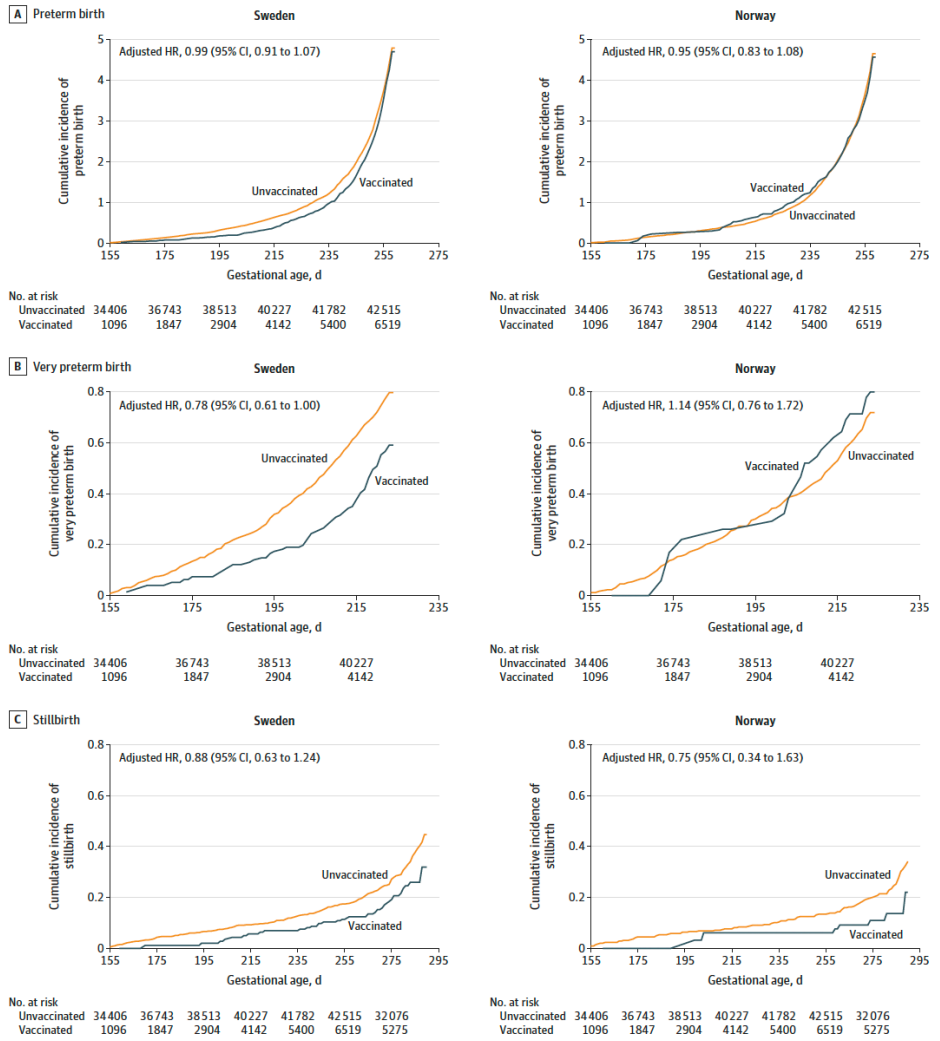
Les cohortes: Covipreg

Table 4
Neonatal outcomes for SARS-CoV-2-infected women (G1) and uninfected women (G2).

Variable	SARS-CoV-2 (-) G2 *N* = 1864	SARS-CoV-2 (+) G1 *N* = 310	OR	p*
Male sex	927/1852 (50.1 %)	120/217 (55.3 %)	1.23 [0.93;1.64]	0.14
Birthweight, g	3300 [3000;3620] (*N* = 1851)	3230 [2900;3500] (*N* = 217)	0.9995 [0.9993;0.998]	**<0.0001**
Birthweight, z-score	−0.3 [−0.9;0.4] (*N* = 1851)	−0.3 [−0.9;0.3] (*N* = 217)	0.98 [0.86;1.11]	0.78
5-min Apgar score >7	1785/1832 (97.4 %)	207/214 (96.7 %)	0.78 [0.37;1.91]	0.54
Resuscitation at birth	98/1837 (5.3 %)	29/215 (13.5 %)	2.77 [1.75;4.25]	**<0.0001**
Immediate neonatal transfer	129/1816 (7.1 %)	34/214 (15.9 %)	2.47 [1.62;3.68]	**<0.0001**
Infectious disease	31/1837 (1.7 %)	4/215 (1.9 %)	1.1 [0.33;2.82]	0.85
Respiratory disease	47/1837 (2.6 %)	14/215 (6.5 %)	2.65 [1.39;4.78]	**0.002**
Neurological disease	5/1836 (0.3 %)	3/215 (1.4 %)	5.18 [1.06;21.27]	**0.025**

* p-value of Wald test according to SARS-CoV-2 infection status; Group G2: Pregnant women with a negative serology at delivery and without a positive SARS-CoV-2 nasopharyngeal RT-PCR at any time during pregnancy; Group G1: Pregnant women with a positive SARS-CoV-2 nasopharyngeal RT-PCR between [14WG; 37WG[(symptomatic infection).

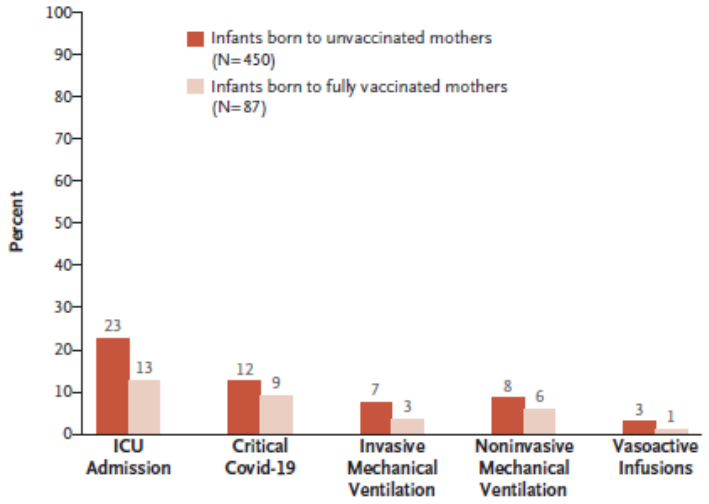
"Vivanti, A. J., et al. (2024). " J Gynecol Obstet Hum Reprod 53(6): 102764



CONCLUSIONS AND RELEVANCE In this population-based study conducted in Sweden and Norway, vaccination against SARS-CoV-2 during pregnancy, compared with no SARS-CoV-2 vaccination during pregnancy, was not significantly associated with an increased risk of adverse pregnancy outcomes. The majority of the vaccinations were with mRNA vaccines during the second and third trimesters of pregnancy, which should be considered in interpreting the findings.

Magnus, C et al. JAMA 2022, 327(15): 1469-77

Les études cas-contrôle: vaccin covid



Infants Born to Unvaccinated Mothers — no./total no. (%)	102/450 (23)	56/450 (12)	33/450 (7)	38/449 (8)	13/448 (3)
Infants Born to Fully Vaccinated Mothers — no./total no. (%)	11/87 (13)	8/87 (9)	3/87 (3)	5/87 (6)	1/87 (1)

Figure 2. Clinical Severity of Covid-19 as Indicated by Outcomes among Case Infants, According to Maternal Vaccination Status.

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Maternal Vaccination and Risk of Hospitalization for Covid-19 among Infants

N.B. Halasa, S.M. Olson, M.A. Staat, M.M. Newhams, A.M. Price, P.S. Pannaraj, J.A. Boom, L.C. Sahni, K. Chiotos, M.A. Cameron, K.E. Bline, C.V. Hobbs, A.B. Maddux, B.M. Coates, K.N. Michelson, S.M. Heidemann, K. Irby, R.A. Nofziger, E.H. Mack, L. Smallcomb, S.P. Schwartz, T.C. Walker, S.J. Gertz, J.E. Schuster, S. Kamidani, K.M. Tarquinio, S.S. Bhumbra, M. Maamari, J.R. Hume, H. Crandall, E.R. Levy, M.S. Zinter, T.T. Bradford, H.R. Flori, M.L. Cullimore, M. Kong, N.Z. Cvijanovich, S.M. Gilboa, K.N. Polen, A.P. Campbell, A.G. Randolph, and M.M. Patel, for the Overcoming Covid-19 Investigators*

Subgroup	Case Infants	Control Infants	Effectiveness of Maternal Vaccination
	no. of vaccinated mothers/total no. (%)		% (95% CI)
Overall effectiveness of maternal vaccination	87/537 (16)	147/512 (29)	52 (33 to 65)
Timing of vaccination			
During first 20 wk of pregnancy	46/496 (9)	62/427 (15)	38 (3 to 60)
After 20 wk of pregnancy	31/481 (6)	79/444 (18)	69 (50 to 80)
Delta-predominant period	14/181 (8)	61/216 (28)	80 (60 to 90)
Vaccinated during first 20 wk of pregnancy	8/175 (5)	22/177 (12)	68 (19 to 87)
Vaccinated after 20 wk of pregnancy	5/172 (3)	37/192 (19)	88 (68 to 96)
Omicron-predominant period	73/356 (21)	86/296 (29)	38 (8 to 58)
Vaccinated during first 20 wk of pregnancy	38/321 (12)	40/250 (16)	25 (−26 to 56)
Vaccinated after 20 wk of pregnancy	26/309 (8)	42/252 (17)	57 (25 to 75)
Type of hospital admission			
ICU	11/113 (10)	147/512 (29)	70 (42 to 85)
Non-ICU	76/424 (18)	147/512 (29)	47 (25 to 62)

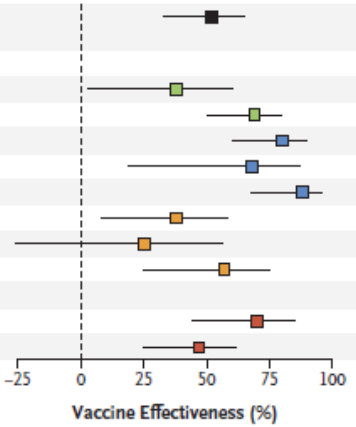


Figure 3. Effectiveness of Maternal Two-Dose mRNA Vaccination against Hospitalization for Covid-19 among Infants, Stratified According to Vaccination Timing, Variant, and Type of Admission.

Vaccinations recommandées actuellement en France
Le VRS

Virus respiratoire syncytial (VRS) depuis 2024

- Double protection mère + enfant (bronchiolite)
- Option alternative à injection nirsevimab chez nouveau-nés
- 32 - 36 SA

Qu'apportent les cohortes ?

Maternal and Neonatal Outcomes After Respiratory Syncytial Virus Prefusion F Protein Vaccination During Pregnancy

Analysis From the 2024–2025 Immunization Campaign in France

Amélie Gabet, PhD, Marion Bertrand, MSc, Marie-Joëlle Jabagi, PharmD, PhD, Epiphane Kolla, MD, PhD, Valérie Olié, PhD, and Mahmoud Zureik, MD, PhD

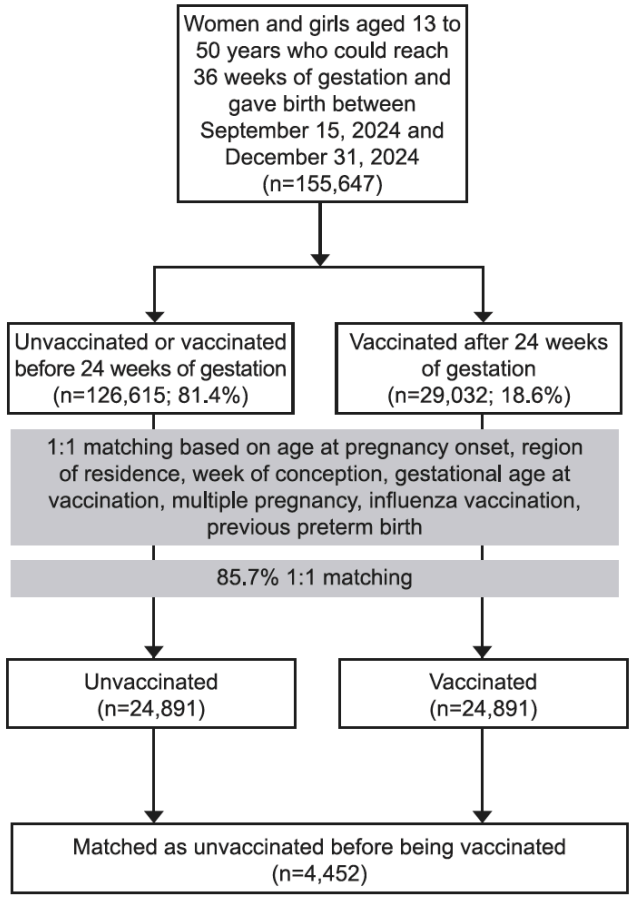


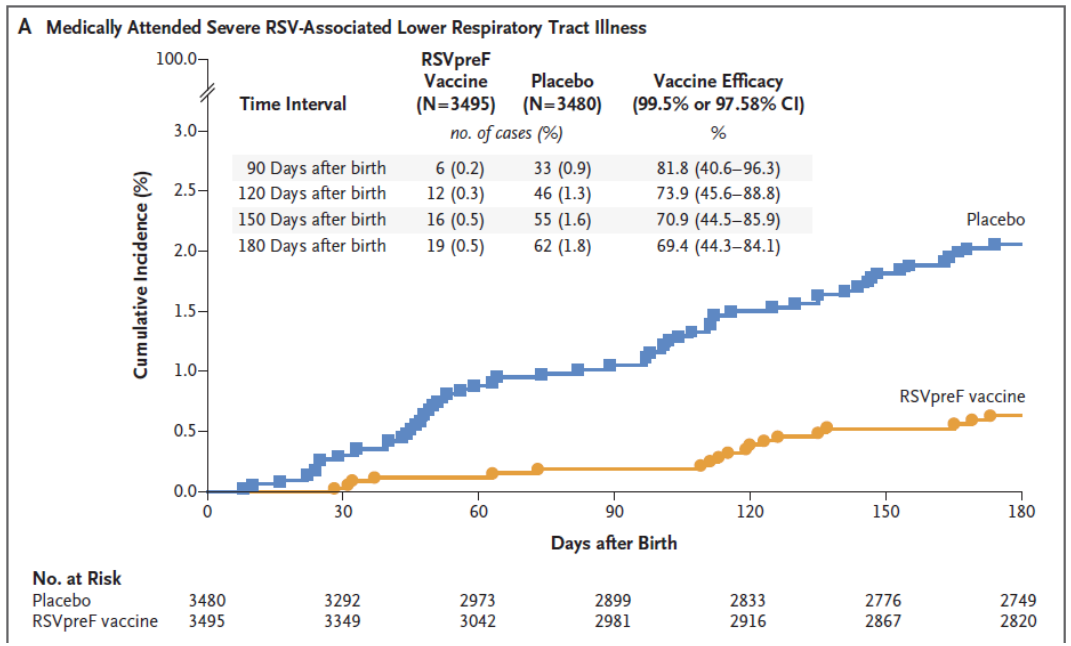
Table 2. Risk of Maternal and Fetal Outcomes in Women Who Received the Respiratory Syncytial Virus Prefusion F Protein Vaccine (n=24,891) Compared With Unvaccinated Women (n=24,891)

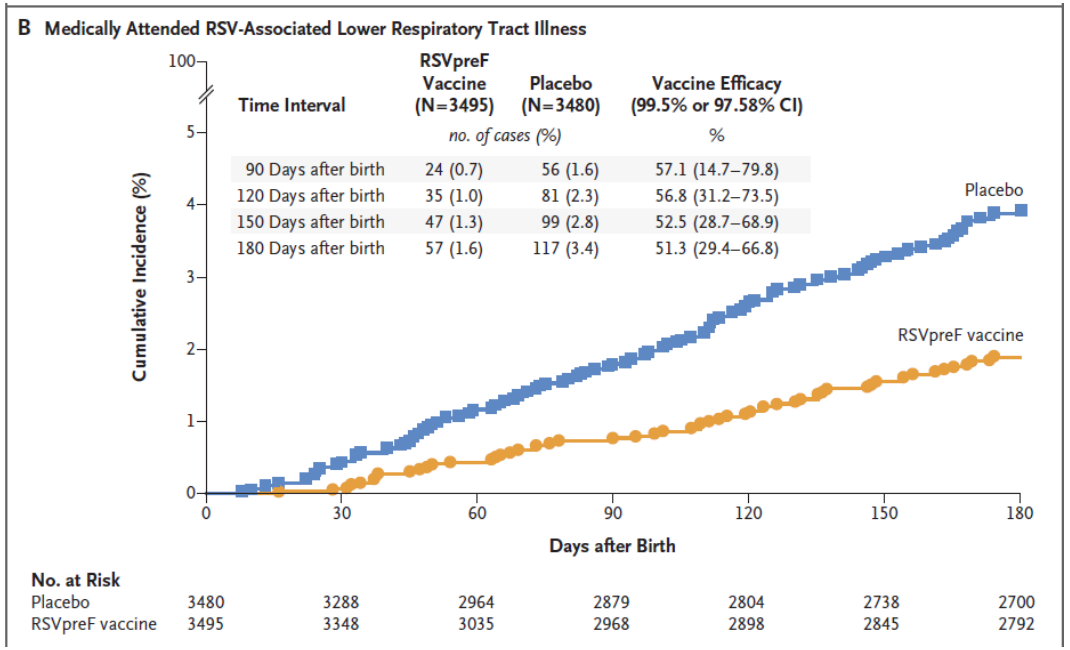
Outcome	RSVpreF Vaccination Events	Unvaccinated Events	Crude IRR (95% CI)	wIRR (95% CI)
Preterm birth*	951 (4.1)	986 (4.3)	0.96 (0.88–1.04)	0.97 (0.89–1.06)
Birth within the week	451 (1.8)	614 (2.5)	0.73 (0.66–0.82)	0.81 (0.72–0.90)
Birth within 2 wk	1,581 (6.4)	1,919 (7.7)	0.82 (0.77–0.87)	0.89 (0.84–0.94)
Birth within 3 wk	3,866 (15.5)	4,262 (17.1)	0.90 (0.87–0.93)	0.97 (0.93–1.00)
Stillbirth	24 (0.1)	33 (0.1)	0.72 (0.42–1.21)	0.77 (0.45–1.32)
Cesarean delivery	5,464 (22.0)	5,354 (21.5)	1.00 (0.97–1.04)	1.00 (0.96–1.03)
Emergency	3,516 (14.1)	3,398 (13.7)	1.02 (0.97–1.06)	0.99 (0.95–1.04)
Scheduled	1,946 (7.8)	1,954 (7.9)	0.98 (0.92–1.04)	1.00 (0.94–1.07)
SGA birth weight	2,774 (11.1)	2,728 (11.0)	1.00 (0.95–1.05)	1.01 (0.96–1.07)
Hemorrhage	1,976 (7.9)	1,894 (7.6)	1.03 (0.97–1.09)	1.03 (0.97–1.10)
Preeclampsia	267 (1.1)	255 (1.0)	1.02 (0.86–1.21)	1.02 (0.85–1.22)
MACE	9 (0.0)	15 (0.1)	0.59 (0.26–1.35)	0.60 (0.26–1.40)

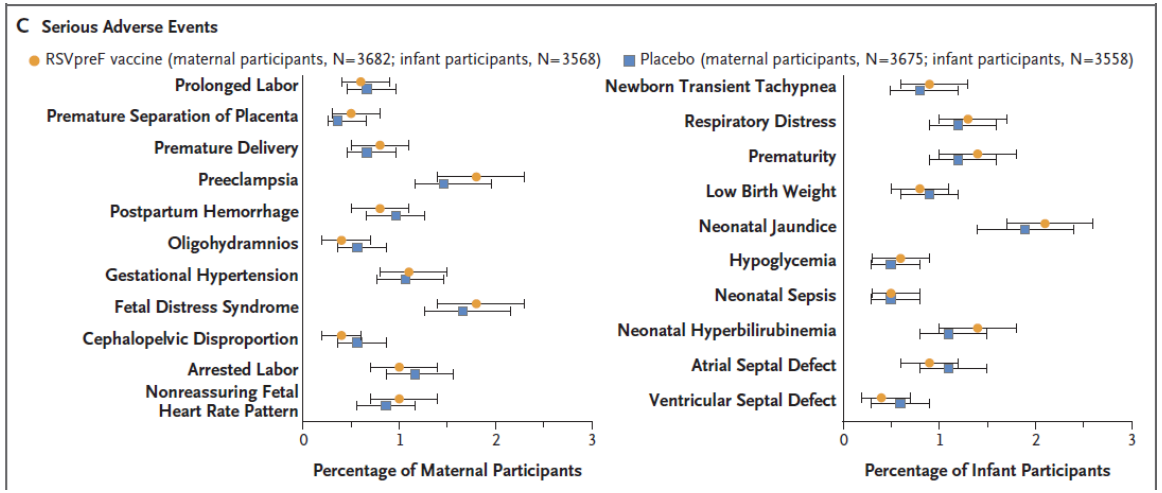
CONCLUSION: This large observational study found no major safety concerns associated with RSVpreF vaccination during pregnancy.

Gabet, A., et al. (2026). Obstet Gynecol 147(1): 118-126.

Vaccin VRS une efficacité démontrée







Kampmann, B., et al. N Engl J Med 388, 1451-1464.

Vaccin VRS efficacité en vie réelle

	Infants hospitalised for LRTD aged ≤6 months and tested for RSV		Maternal RSVpreF vaccination status during pregnancy	
	Case infants (RSV positive)	Control infants (RSV negative)	Received RSVpreF vaccine	Did not receive RSVpreF vaccine
Number of infants	286	219	160	345
Length of hospitalisation, days	7 (4–10)	5 (3–7)	5 (3–7)	6 (4–9)
Severe LRTD hospitalisation	142 (50%)	65 (30%)	53 (33%)	154 (45%)
Intensive care unit admission >4 h	69 (24%)	29 (13%)	23 (14%)	75 (22%)
In-hospital death	3 (1%)	0	0	3 (1%)

Data are mean (SD) or n (%), unless otherwise indicated. LRTD=lower respiratory tract disease. RSV=respiratory syncytial virus. RSVpreF=respiratory syncytial virus prefusion F vaccine.

Table 2: **Illness severity by infant case–control status and by maternal RSVpreF vaccination status during pregnancy**

	Case infants (RSV positive)		Control infants (RSV negative)		Crude odds ratio (95% CI)*	VE (95% CI)
	Mother received RSVpreF vaccine n/N (%)	Mother did not receive RSVpreF vaccine n/N (%)	Mother received RSVpreF vaccine n/N (%)	Mother did not receive RSVpreF vaccine n/N (%)		
RSV-associated LRTD leading to hospitalisation						
0 to ≤3 months (0 to ≤90 days)	39/201 (19%)	162/201 (81%)	82/145 (57%)	63/145 (43%)	0·18 (0·11–0·30)	78·6% (62·1–87·9)†
0 to ≤6 months (0 to ≤180 days)	51/286 (18%)	235/286 (82%)	109/219 (50%)	110/219 (50%)	0·21 (0·14–0·32)	71·3% (53·3–82·3)‡
RSV-associated severe LRTD leading to hospitalisation						
0 to ≤6 months (0 to ≤180 days)	22/142 (15%)	120/142 (85%)	31/65 (48%)	34/65 (52%)	0·19 (0·10–0·38)	76·9% (45·0–90·3)§

Data are n (%) unless stated otherwise. LRTD=lower respiratory tract disease; RSV=respiratory syncytial virus. RSVpreF=respiratory syncytial virus prefusion F vaccine. VE=vaccine effectiveness. *Crude OR calculated using multi-level logistic regression model with site-specific random effect. †VE calculated as (1–adjusted OR)x100, where the adjusted OR was generated using a multilevel logistic regression model with site-specific random effect, conception date, and calendar date of hospitalisation as natural cubic splines, inverse probability-of-treatment weights, and a fixed effect for infant sex (see appendix 2 p 8 for information on inverse probability-of-treatment weight methodology). ‡VE calculated as (1–adjusted OR)x100, where the adjusted OR was generated using a multilevel logistic regression model with site-specific random effect, conception date, calendar date of hospitalisation, and infant age at hospitalisation as natural cubic splines; and inverse probability-of-treatment weights. §VE calculated as (1–adjusted OR)×100, where the adjusted OR was generated using a multilevel logistic regression model with site-specific random effect, calendar date of hospitalisation and infant age at hospitalisation as natural cubic splines, inverse probability-of-treatment weights, and a fixed effect for complete exposure window.

Table 3: **Effectiveness of maternal RSVpreF vaccination during pregnancy against RSV-associated LRTD and severe LRTD leading to hospitalisation among infants from birth to 6 months of age**

Pérez Marc G, Vizzotti C, Fell D et al. The Lancet Infectious Diseases, 2025; 25, 1044-1054

Les essais cliniques

doi:10.1093/eurheartj/ehab103

Exclusion of pregnant and lactating women from COVID-19 vaccine trials: a missed opportunity

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In the midst of a devastating pandemic with high transmissibility and case fatality, the mRNA COVID-19 vaccine trials represent hope of an end to the global burden of COVID-19 infection, hospital utilization, and death. The efficacy and safety of the vaccines have been demonstrated in adults across a range of demographics, with the exception of those who are pregnant and lactating. This systematic exclusion—common in clinical trials—represents a missed opportunity to protect a group at risk of adverse outcomes in the setting of COVID-19 infection. It has special implications on the healthcare workforce, a majority of whom are women and at high risk of COVID-19 infection.

The exclusion of pregnant and lactating women from COVID-19 vaccine trials (*Text Box 1*) reflects a historic pattern of 'protection by exclusion', representing an instance in which the estimated effect of a therapy on mother and child will rely on anecdotal and delayed reports from healthcare settings rather than the monitored setting of a clinical trial.[2] This exclusion is not justified. For example, Pfizer and Moderna excluded pregnant and lactating women from their mRNA COVID-19 vaccine trials[3,4] with no biological evidence to suggest that the vaccines are teratogenic, and no plausibility that they are transmitted in breast milk. The mRNA vaccines rapidly degenerate after injection in muscle cells, and aside from the post-vaccination immune response that can cause a fever, there is no reason to assume, *a priori*, that harm will come to pregnant and lactating women enrolled in the trials.[4]

care workers in the USA alone are pregnant or immediately postpartum during vaccine implementing.[5] The dual risk posed by COVID-19 to pregnant healthcare professionals—increased workplace exposure and increased risk of adverse outcomes if infected[6]—makes it particularly concerning that the trials failed to include pregnant or lactating individuals. Furthermore, when healthcare workers are infected, they become sources of nosocomial spread thereby posing a risk to patients and to other healthcare workers.

The recommendations for use of the COVID-19 Pfizer and Moderna vaccine in pregnant and lactating women now range from avoidance of the vaccine—as recommended by the World Health Organization and some regulatory agencies—to reliance on recipients to make choices guided by their values or their clinicians' judgement.[5,7–9] Some regulatory bodies recommend against pregnancy in the weeks following the vaccine. The rationale for the recommendations of vaccine avoidance in pregnancy, pregnancy avoidance in weeks following vaccination, and decision-making regarding vaccination safety by clinicians in absence of clinical trial data is unclear.

Pregnancy and lactation are two distinct biological states that are often conflated in the eligibility criteria of clinical trials. Drugs that may have evidence of teratogenicity in biological studies may not be secreted in breast milk, and drugs secreted in breast milk with harmful effects to baby may not be teratogenic. The grouping of preg-

Et les essais cliniques ?

- Longtemps, femmes enceintes considérées comme **population vulnérable à exclure de la recherche**
- **Enjeux éthiques** : protection du fœtus, principe de précaution
- Nécessité démontrer **sécurité pour deux individus (mère + fœtus)**

- **Réticence patientes accrue :** perception risque ++, préférence vaccins déjà valides (cf Covid-19)
- **Réticence professionnels de santé :** risque médico-légal
- **Réticence industriels :** répercussions financières
- **Facteurs organisationnels**

Et les essais cliniques ?

- Sur ensemble essais cliniques *International Clinical Trials Registry Platform :*

Seuls 4% autorisent inclusion femmes enceintes

(*Clinical Trials Arena* 2026)

- **Seuls 6% des essais vaccinaux** entre 2018 et 2023

(Salloum et al. *Vaccine* 2023)

Un besoin spécifique d'essais cliniques chez la femme enceinte

- **Vaccin monovalent coqueluche**
  - Actuellement : uniquement vaccin quadrivalent DTPC
  - En cours évaluation pour Europe

- **Vaccin anti-VRS** : durée protection Ac ? Pour grossesses ultérieures ?

- **Combinaisons vaccinales ?** Grippe + Covid-19 + VRS ?

- **Vaccin Streptocoque B**

- **Vaccin HSV**

- **Vaccin CMV : l**a plus fréquente des infections materno-fœtales

Comment inciter la femme enceinte à participer ?

- Relation confiance+++
- Avis favorable des professionnels de santé habituels de la patiente (généraliste, gynécologue, sage-femme)
- Information sur gravité maladie potentiellement évitable
- Information sur données préliminaires vaccin

Initiatives nationales

PIPELINE-RSV-France

- CH Annecy
- Pierre Frange, Tristan Delory, Marc Lallemant
- Déterminer si vaccin maternel contre le VRS **Abrysvo associé au nirsevimab** est **plus efficace (test de supériorité)** que **nirsevimab**
- Pour prévenir **infections symptomatiques à VRS chez nourrissons au cours de leur première année de vie**

Prevention Strategy for RSV Infections in Infants in France (SPIRAV)

- APHP, Bénédicte COULM

- Evaluer l'adhésion des femmes enceintes à la stratégie actuelle de prévention de l'infection à VRS chez les nourrissons en France
- Stratégie le plus souvent choisie par les femmes ?
  - Vaccination maternelle Abrysvo®
  - Ou administration de nirsevimab (Beyfortus®) au nouveau-né
- Identifier les facteurs associés au choix de l'une ou l'autre stratégie, décrire principales raisons invoquées par les femmes pour accepter ou refuser ces stratégies de prévention

Le paradoxe gestationnel

- **Exclusion femmes enceintes** au moment essais cliniques initiaux
- Alors que femmes enceintes exposées aux maladies et aux agents infectieux, autant voire plus que la population générale

- => **Manque de données** sur efficacité et sécurité au moment introduction certains vaccins
- **Décisions cliniques basées sur extrapolations** ou données observationnelles post-marketing

- **Transfert du risque** de la recherche vers la pratique clinique

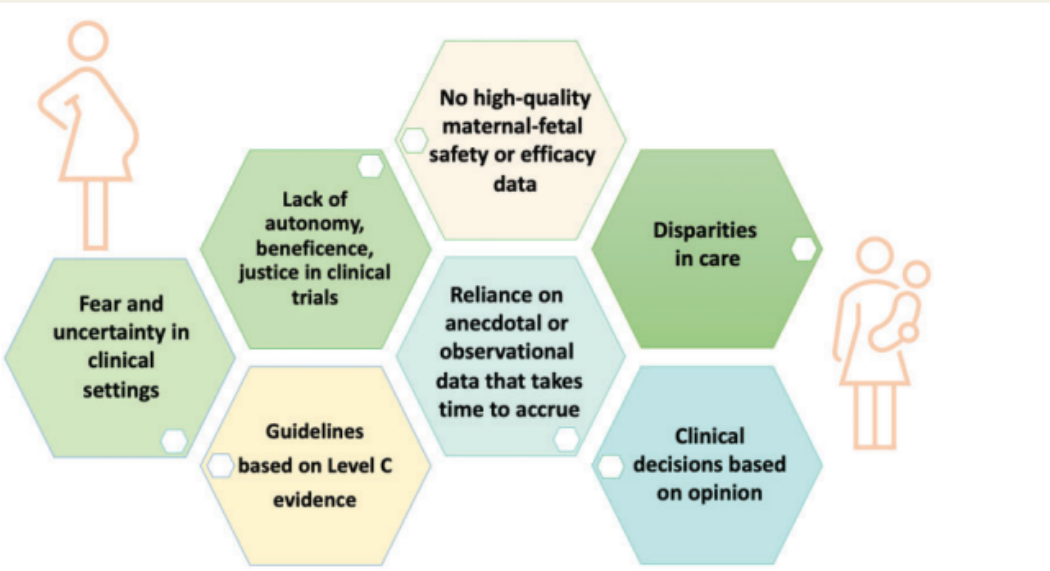

Figure 1 The risks posed by systematic exclusion of pregnant and lactating women from clinical trials.

Le paradoxe gestationnel

Editorial

The Last Therapeutic Orphan: The Pregnant Woman

The pregnant woman is perhaps the last true therapeutic orphan. Because of the ethical, medicolegal, and fetal safety concerns regarding pregnant women, few pharmacokinetic, pharmacodynamic, or clinical trials are conducted during pregnancy.

—Stika and Frederiksen (1)

Wisner. Am J Psychiatry 2012.

Pregnant women are still therapeutic orphans

Wisner et al. World Psychiatry 2020.

Thank You / Merci