

COVID19 & miscarriage or fetal loss



September 9th, 2021

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Materno-fetal and Obstetrics Research Unit
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Miscarriage / stillbirth

«DIRECT» EFFECT

- Virus reaches the placenta
- Multisystem inflammation



«INDIRECT» EFFECT

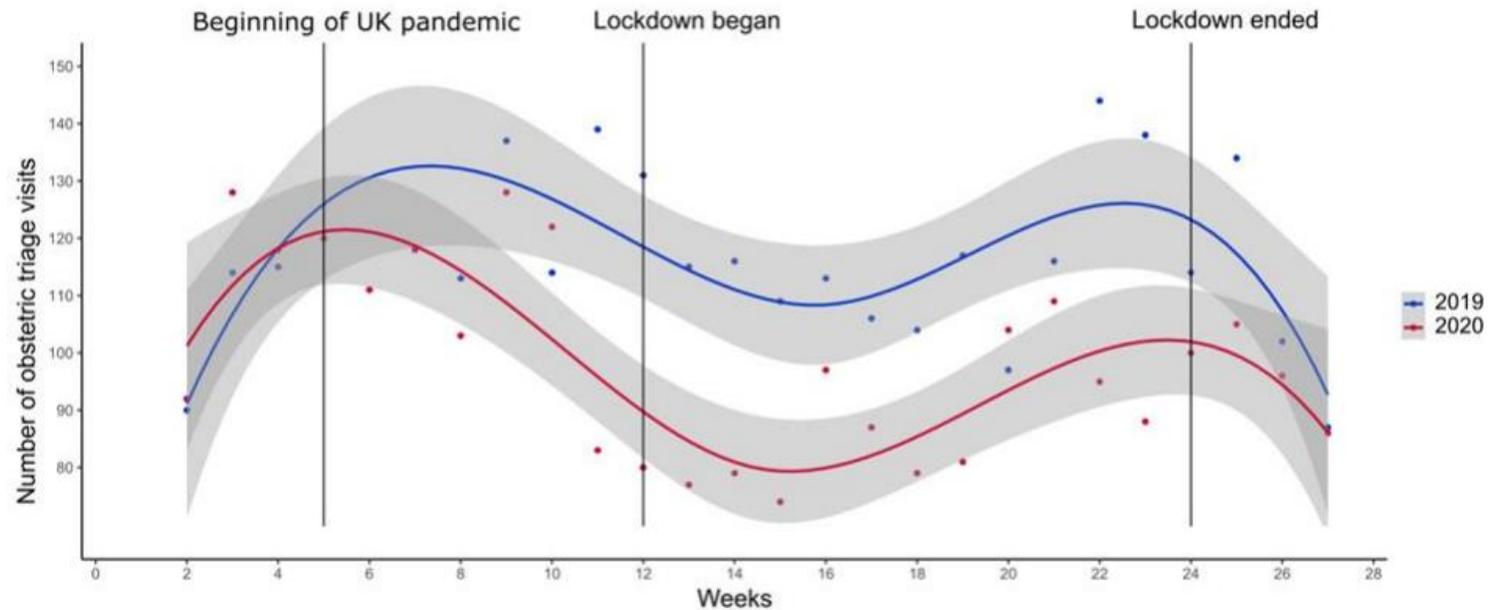
- Lack of surveillance
- Change in obstetrical practice
- Reluctance of pregnant women to attend hospital



COVID-19 & stillbirth

Khalil, JAMA, Jul 2020

Outcomes	Prepandemic period (n = 1681 births) ^a	Pandemic period (n = 1718 births) ^a	Difference (95% CI)	P value
Stillbirths, No./total No. (No. per 1000 births)	4/1681 (2.38)	16/1718 (9.31)	6.93 (1.83 to 12.0)	.01



Khalil, Lancet, Oct 2020



COVID-19 & stillbirth

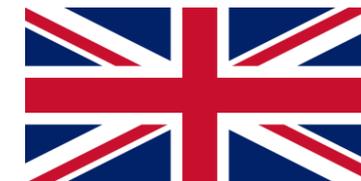


The screenshot shows the HSIB (Healthcare Safety Investigation Branch) website. The header includes the HSIB logo and the text 'HEALTHCARE SAFETY INVESTIGATION BRANCH'. Below the header is a navigation menu with links for 'Home', 'About us', 'Press office', 'For patients', 'For staff', and 'For organisations'. The main content area features a large, bold headline: 'Intrapartum stillbirth during COVID-19'.

Between April – June:

<u>2019</u>	=	24 stillbirth
<u>2020</u>	=	46 stillbirth

Journal Pre-proof



Maternal and perinatal outcomes of pregnant women with SARS-CoV-2 infection at the time of birth in England: national cohort study

Ipek GUROL-URGANCI, PhD, Jennifer E. JARDINE, MSc, Fran CARROLL, PhD, Tim DRAYCOTT, FRCOG, George DUNN, BA, Alissa FREMEAUX, MSc, Tina HARRIS, PhD, Jane HAWDON, PhD, Edward MORRIS, FRCOG, Patrick MULLER, MSc, Lara WAITE, MSc, Kirstin WEBSTER, MSc, Jan VAN DER MEULEN, PhD, Asma KHALIL,

	Pregnant women without SARS-CoV-2 infection		Pregnant women with laboratory-confirmed SARS-CoV-2 infection		Unadjusted OR (95% CI)	P value	Adjusted OR‡ (95% CI)	P value
	cases/births	%	cases/births	%				
Maternal data								
Fetal death	1140/338553	0.34	30/3527	0.85	2.54 (1.81,3.56)	<0.001	2.21 (1.58,3.11)	<0.001
Preterm birth	18572/322494	5.8	369/3047	12.1	2.25 (2.03,2.50)	<0.001	2.17 (1.96,2.42)	<0.001
Small for gestational age	17521/320188	5.5	191/3009	6.4	1.17 (1.00,1.37)	0.05	0.99 (0.84,1.16)	0.87
Preeclampsia/eclampsia	8591/338553	2.5	139/3527	3.9	1.58 (1.32,1.89)	<0.001	1.55 (1.29,1.85)	<0.001



COVID-19 & stillbirth



Article

Pregnancy Outcomes and SARS-CoV-2 Infection: The Spanish Obstetric Emergency Group Study

Sara Cruz Melguizo ¹, María Luisa de la Cruz Conty ^{2,*}, Paola Carmona Payán ³, Alejandra Abascal-Saiz ⁴,

- prospective observational study
- 78 Spanish centers
- 1347 PCR-positive / 1607 PCR-negative
- between February - November 2020
- Stillbirth →

Infected Cohort	Non-Infected Group	<i>p</i> -Value
1347	1607	
10 (0.7)	3 (0.2)	0.023 *

Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis

John Allotey, 

Table 1 | Outcomes in pregnant and recently pregnant women with coronavirus disease 2019 (covid-19)

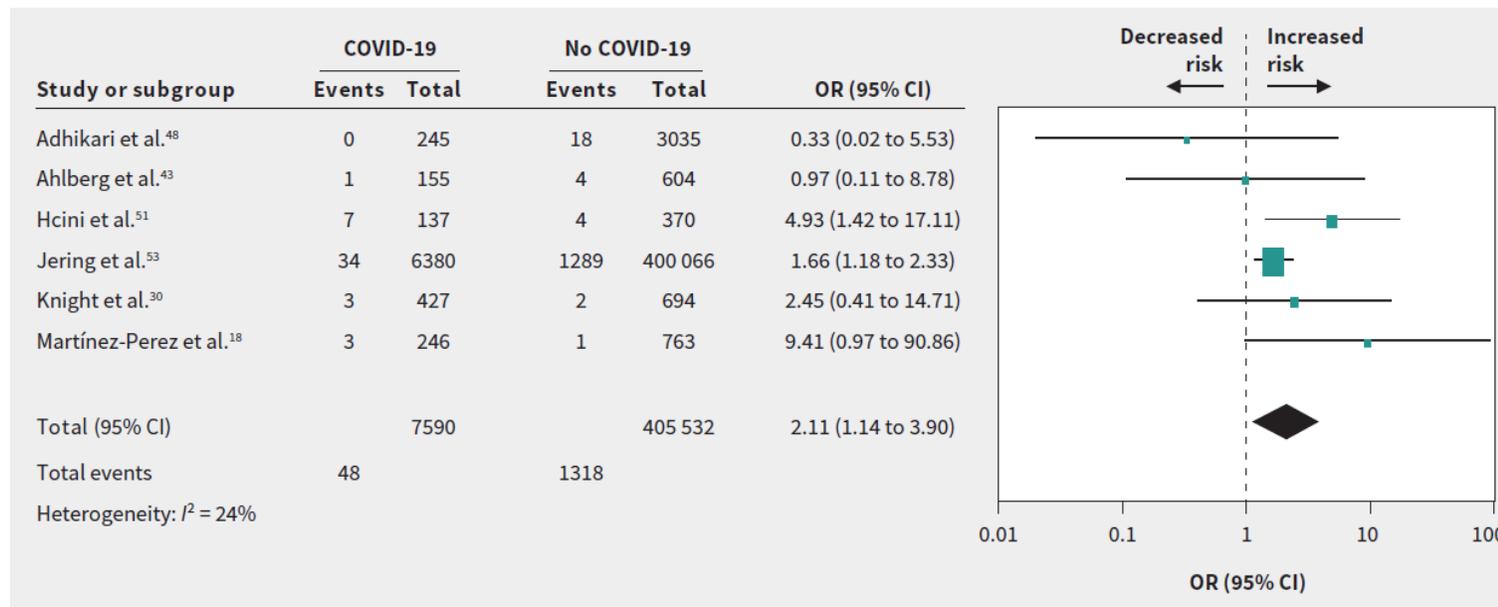
Outcomes	No of studies	Women (No with event/No in group (%))		Odds ratio (95% CI)
		Pregnant women with covid-19	Comparison group	
Stillbirth	9*	9/1039 (0.9)	26/4755 (0.5)	2.84 (1.25 to 6.45)

COVID-19 & stillbirth

The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis

Shu Qin Wei MD PhD, Marianne Bilodeau-Bertrand MSc, Shiliang Liu MB PhD, Nathalie Auger MD MSc

cmaj April 2021
BEST EVIDENCE • BEST PRACTICE • BEST RESULTS



Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis

Barbara Chmielewska, Imogen Barratt, Rosemary Townsend, Erkan Kalafat, Jan van der Meulen, Ipek Gurol-Urganci, Pat O'Brien, Edward Morris, Tim Draycott, Shakila Thangaratinam, Kirsty Le Doare, Shamez Ladhani, Peter von Dadelszen, Laura Magee, Asma Khalil

Lancet Glob Health 2021;

HIC subgroup

De Curtis et al, 2020 ⁴⁹	26	7755	10	9053	4.8%	3.04 (1.47-6.31)
Dell'Utri et al, 2020 ¹²	5	1126	1	1103	0.7%	4.92 (0.57-42.14)
Handley et al, 2021 ¹⁶	15	3007	32	5907	6.2%	0.92 (0.50-1.70)
Justman et al, 2020 ¹⁹	2	610	3	742	1.0%	0.81 (0.13-4.87)
McDonnell et al, 2020 ³⁰	6	2538	2	1262	1.2%	1.49 (0.30-7.41)
Meyer et al, 2020 ³¹	22	2594	22	2742	6.5%	1.06 (0.58-1.91)
Mor et al, 2020 ³²	6	1556	5	4564	2.1%	3.53 (1.08-11.58)
Stowe et al, 2021 ³⁷	543	131218	565	139745	18.3%	1.02 (0.91-1.15)
Subgroup total	625	150404	640	165118	40.9%	1.38 (0.94-2.02)

Heterogeneity: $\tau^2=0.1200$; $\chi^2=14.71$, $df=7$ ($p=0.04$); $I^2=52\%$

LMIC subgroup

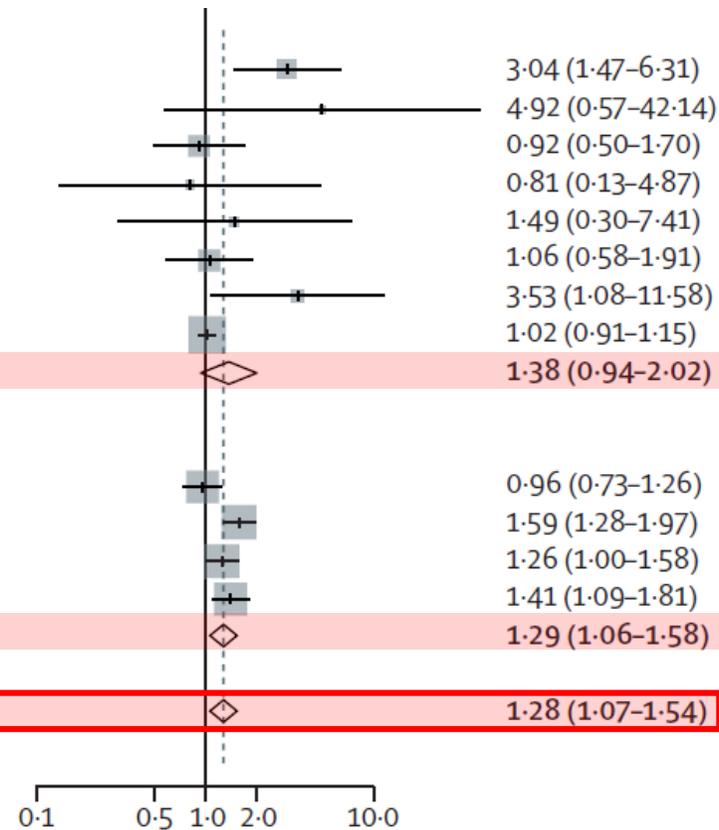
Caniglia et al, 2020 ⁴⁷	76	3589	183	8316	13.9%	0.96 (0.73-1.26)
Kc et al, 2020 ²¹	153	7165	179	13189	15.5%	1.59 (1.28-1.97)
Kumar et al, 2021 ²⁴	134	3610	183	6161	15.2%	1.26 (1.00-1.58)
Kumari et al, 2020 ²⁵	111	3527	140	6209	14.4%	1.41 (1.09-1.81)
Subgroup total	474	17891	685	33875	59.1%	1.29 (1.06-1.58)

Heterogeneity: $\tau^2=0.0272$; $\chi^2=8.42$, $df=3$ ($p=0.04$); $I^2=64\%$

Overall total 1099 168295 1325 198993 100.0% 1.28 (1.07-1.54)

Heterogeneity: $\tau^2=0.0445$; $\chi^2=29.48$, $df=11$ ($p<0.01$); $I^2=63\%$

Residual heterogeneity: $\tau^2=NA$; $\chi^2=23.14$, $df=10$ ($p=0.01$); $I^2=57\%$



+30%

COVID-19 and pregnancy

Other cases

Multisystem inflammatory syndrome in a neonate, temporally associated with prenatal exposure to SARS-CoV-2: a case report

Mahesh Kappanayil, Suma Balan, Sujata Alawani, Satish Mohanty, Sreelakshmi P Leeladharan, Sreja Gangadharan, Jessin P Jayashankar, Soumya Jagadeesan, Anil Kumar, Atul Gupta, Raman Krishna Kumar

Probable congenital SARS-CoV-2 infection in a neonate born to a woman with active SARS-CoV-2 infection

cmaj

Maksim Kirtsman MDCM, Yenge Diambomba MD, Susan M. Poutanen MD MPH, Ann K. Malinowski MD, Evangelia Vlachodimitropoulou MD PhD, W. Tony Parks MD, Laura Erdman MD PhD, Shaun K. Morris MD Prakesh S. Shah MD MSc

Gao et al. *Diagnostic Pathology* (2021) 16:8
<https://doi.org/10.1186/s13000-021-01067-6>

Diagnostic Pathology

CASE REPORT

Open Access

Placental pathology of the third trimester pregnant women from COVID-19



Severe Acute Respiratory Syndrome Coronavirus 2 Placental Infection and Inflammation Leading to Fetal Distress and Neonatal Multi-Organ Failure in an Asymptomatic Woman

Sam Schoenmakers,^{1,2} Pauline Snijder,² Robert M. Verdijk,² Thijs Kuiken,⁴ Sylvia S. M. Kamphuis,⁵ Laurens P. Koopman,⁶ Thomas B. Krasemann,⁶ Melek Rousian,¹ Michelle Broekhuizen,^{2,7} Eric A. P. Steegers,¹ Marion P. G. Koopmans,^{4,8} Pieter L. A. Fraaij,^{4,5} and Irwin K. M. Reiss²



ELSEVIER

Placenta

journal homepage: <http://www.elsevier.com/locate/placenta>

Review

SARS-CoV-2 placentitis: An uncommon complication of maternal COVID-19

Laura Linehan^{a,*}, Keelin O'Donoghue^a, Susan Dineen^b, Jessica White^b, John R. Higgins^c, Brendan Fitzgerald^b

nature
COMMUNICATIONS

ARTICLE

<https://doi.org/10.1038/s41467-020-17436-6> OPEN

Check for updates

Transplacental transmission of SARS-CoV-2 infection

Alexandre J. Vivanti^{1,8}, Christelle Vauloup-Fellous^{2,8}, Sophie Prevot³, Veronique Zupan⁴, Cecile Suffee⁵,

JAMA
Network | Open

Original Investigation | Obstetrics and Gynecology

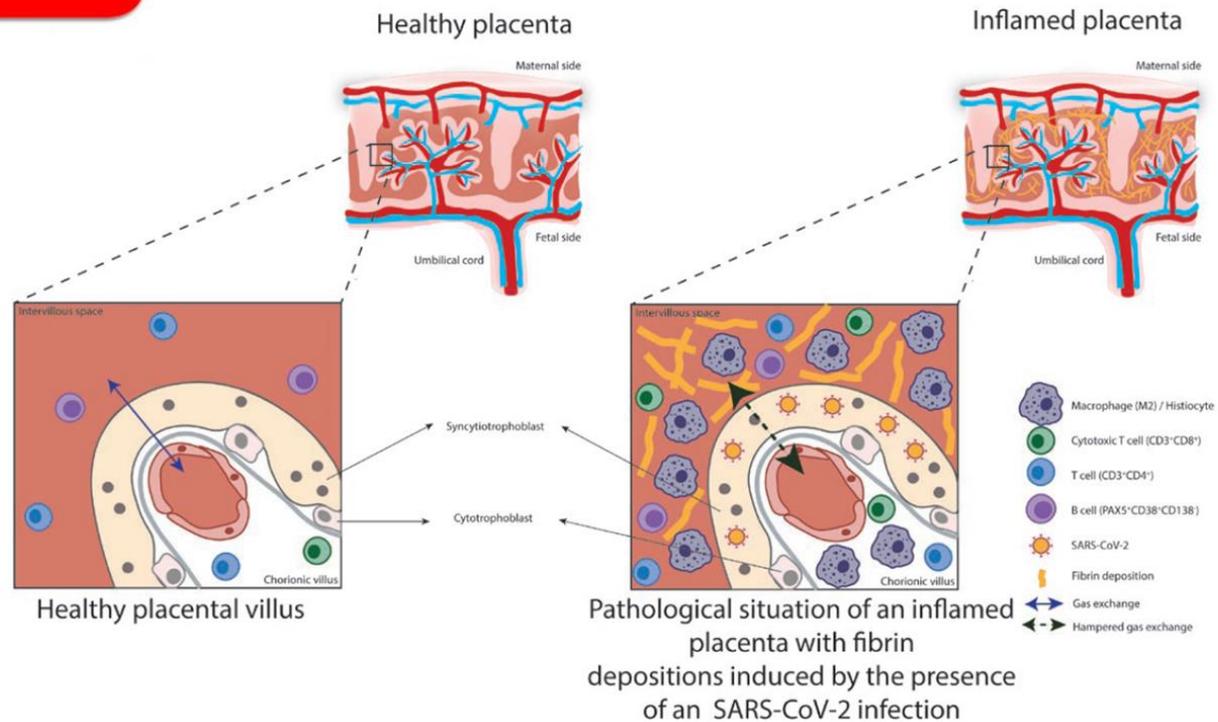
Assessment of Maternal and Neonatal SARS-CoV-2 Viral Load, Transplacental Antibody Transfer, and Placental Pathology in Pregnancies During the COVID-19 Pandemic

COVID-19 and pregnancy

Other cases

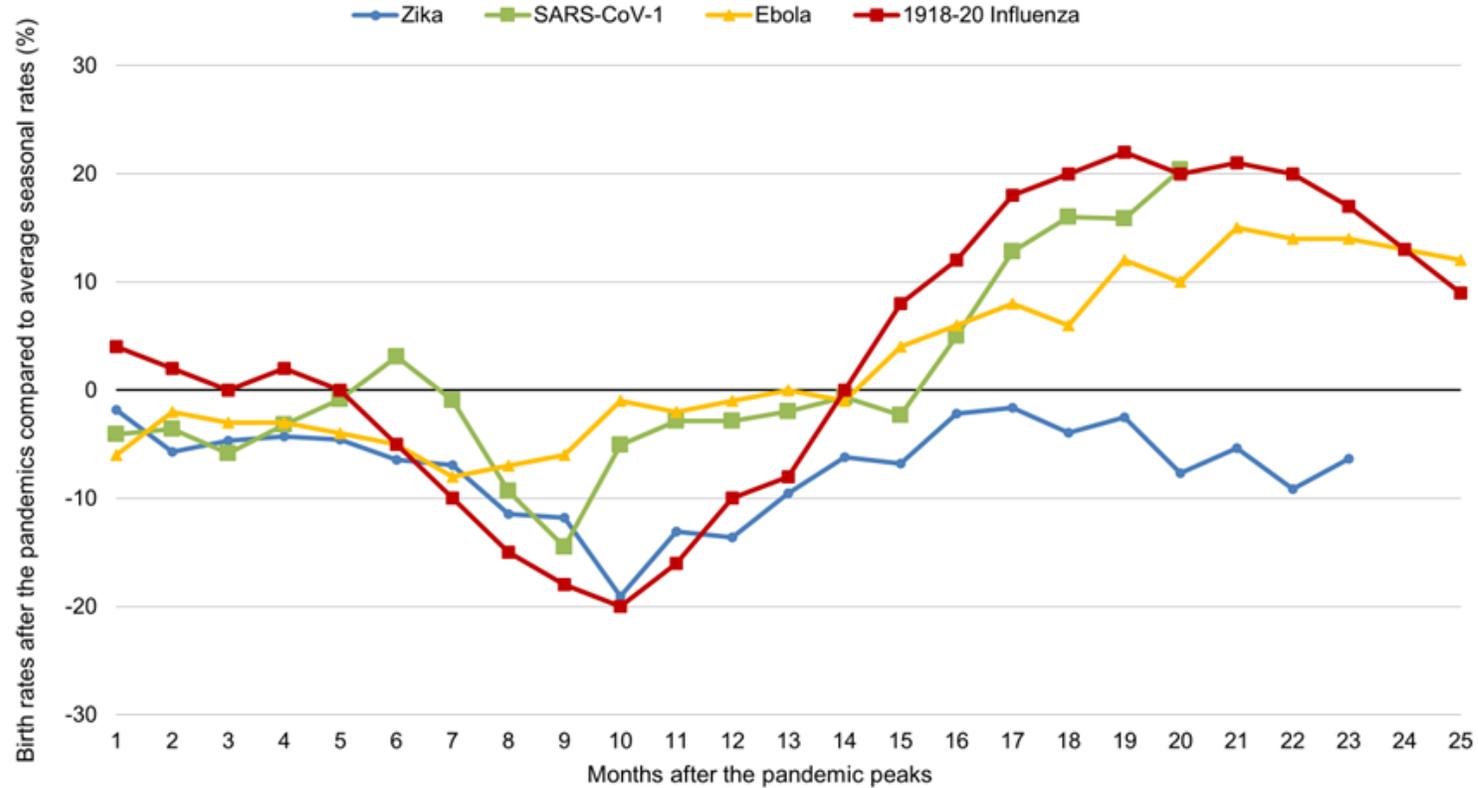


**1 week post-COVID
reduced fetal movements**



Potential Consequences of Sars-Cov-2 Pandemic on Birth Rates and Subsequent Demographics

Léo Pomar^{1*}, Agathe Contier¹, Jeffrey E Harris², Guillaume Favre¹, Karin Nielsen-Saines³ and David Baud¹



Protect pregnant women

www.thelancet.com Vol 396 September 5, 2020

COVID-19 vaccines and neglected pregnancy



Correspondence

THE LANCET

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Shabir A Madhi, *David Baud
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Published Online

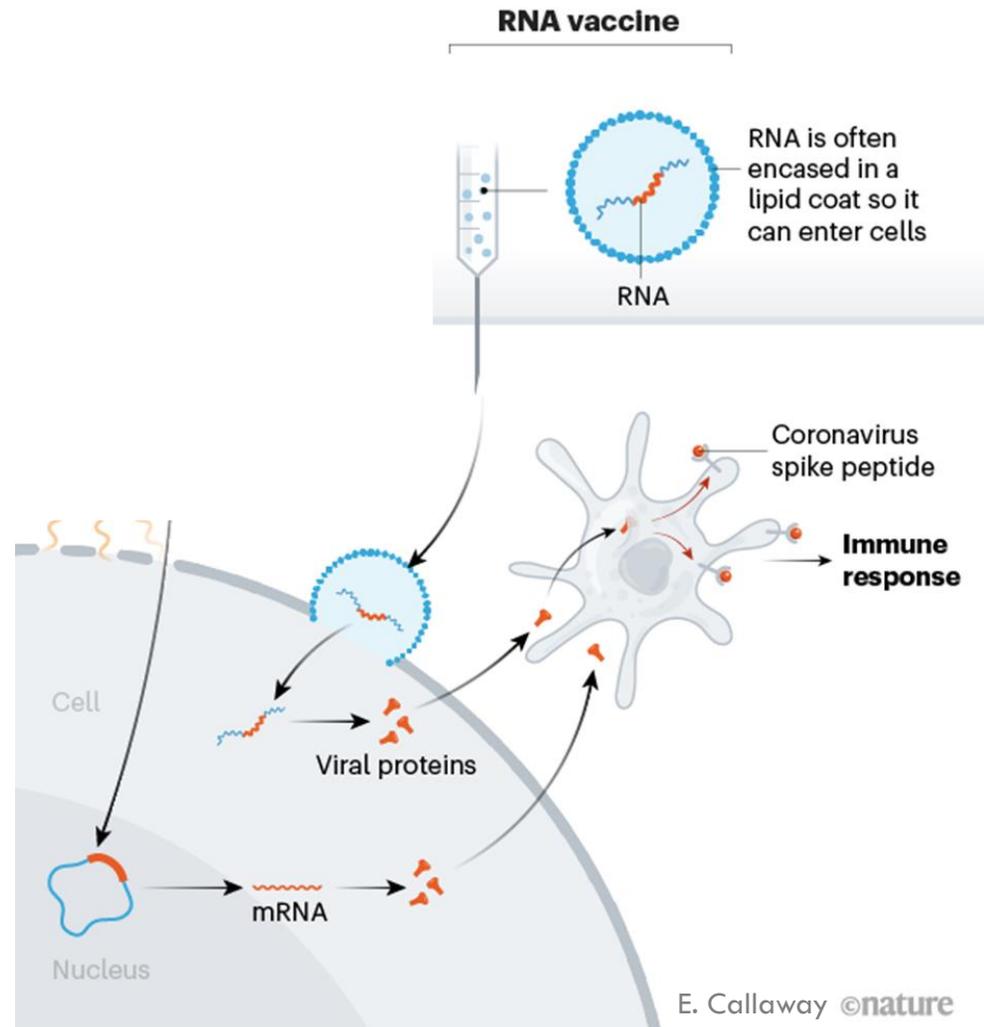


OFSP

BAG



mRNA vaccines



- Contain nothing expected to be harmful
- No live vaccine
- Do not enter nucleus, no adjuvant
- No adverse outcomes in PREGNANT animal studies

Are COVID-19 vaccines safe in pregnancy?

- Similar rates of pregnancies => no impact on fertility
- Similar rates of miscarriages

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

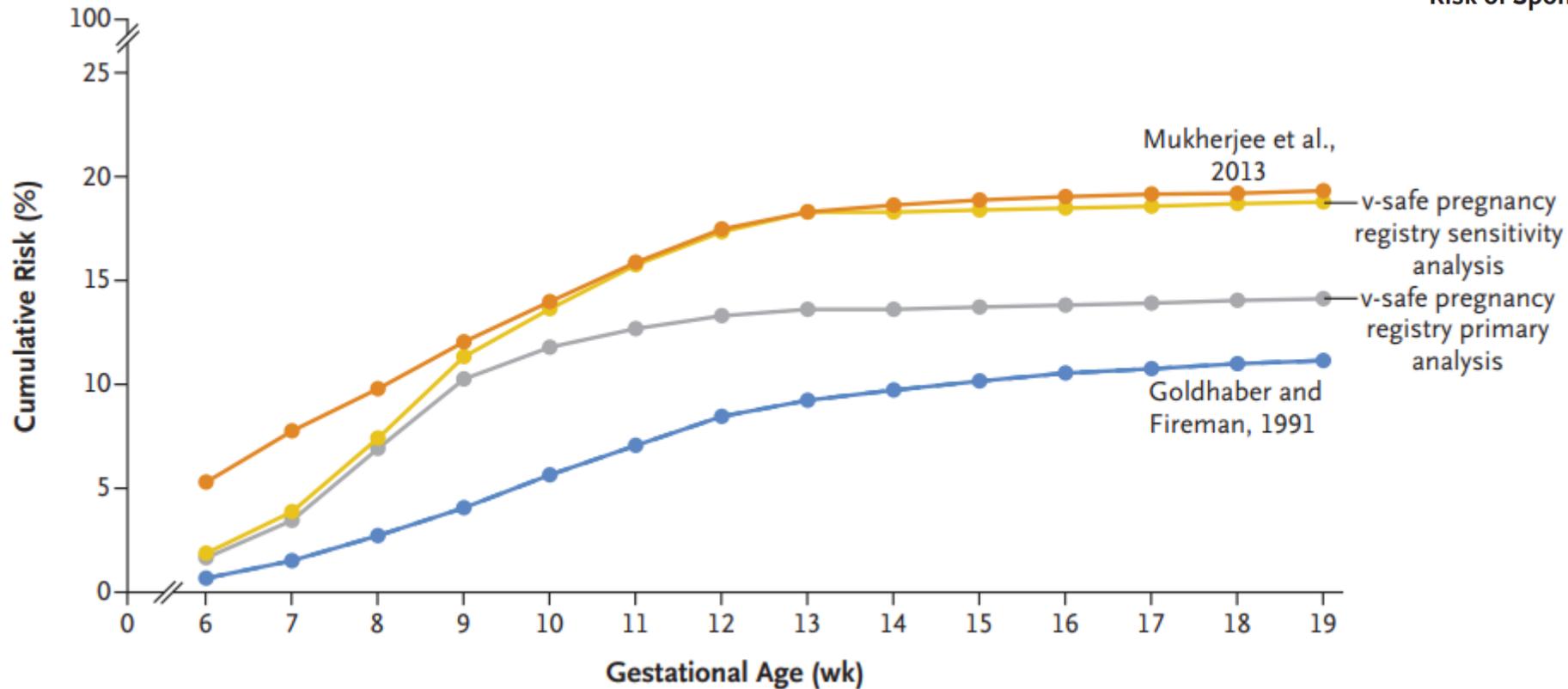
Vaccine type	Control group			Vaccinated group		
	Participants	Pregnancies	Miscarriages (rate)	Participants	Pregnancies	Miscarriages (rate)
Pfizer/BioNTech	18,846	12	1 (8%)	18,860	11	0 (0%)
Moderna	15,170	7	1 (14%)	15,181	6	0 (0%)
AstraZeneca	5,829	9	3 (33%)	5,807	12	2 (17%)

Are COVID-19 vaccines safe in pregnancy?

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Receipt of mRNA Covid-19 Vaccines and Risk of Spontaneous Abortion



Are COVID-19 vaccines safe in pregnancy?



The NEW ENGLAND
JOURNAL of MEDICINE

ORIGINAL ARTICLE

Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons

Tom T. Shimabukuro, M.D., Shin Y. Kim, M.P.H., Tanya R. Myers, Ph.D., Pedro L. Moro, M.D., Titilope Oduyebo, M.D., Lakshmi Panagiotakopoulos, M.D., Paige L. Marquez, M.S.P.H., Christine K. Olson, M.D., Ruiling Liu, Ph.D., Karen T. Chang, Ph.D., Sascha R. Ellington, Ph.D., Veronica K. Burkel, M.P.H., *et al.*, for the CDC v-safe COVID-19 Pregnancy Registry Team*

Table 4. Pregnancy Loss and Neonatal Outcomes in Published Studies and V-safe Pregnancy Registry Participants.

Participant-Reported Outcome	Published Incidence*	V-safe Pregnancy Registry†
	%	no./total no. (%)
Pregnancy loss among participants with a completed pregnancy		
Spontaneous abortion: <20 wk ¹⁵⁻¹⁷ ‡	Not applicable	104
Stillbirth: ≥ 20 wk ¹⁸⁻²⁰	<1	1/725 (0.1)§
Neonatal outcome among live-born infants		
Preterm birth: <37 wk ^{21,22}	8–15	60/636 (9.4)¶
Small size for gestational age ^{23,24}	3.5	23/724 (3.2)
Congenital anomalies ^{25**}	3	16/724 (2.2)
Neonatal death ²⁶ ††	<1	0/724



September 8, 2021

Spontaneous Abortion Following COVID-19 Vaccination During Pregnancy

Elyse O. Kharbanda, MD, MPH¹; Jacob Haapala, MPH¹; Malini DeSilva, MD, MPH¹; [et al](#)

	Spontaneous abortions		Ongoing pregnancy-periods ^a	
	No.	COVID-19 vaccine, No. (%)	No.	COVID-19 vaccine, No. (%)
All	250 944	20 139 (8.0)	13 160	1128 (8.6)

	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)

gynécologie suisse



AVANT LA VACCINATION			
Avez-vous été testée positive au SARS-CoV-2?	<input type="checkbox"/> OUI	<input type="checkbox"/> NON	<input type="checkbox"/> NE SAIT PAS
Si oui, quel test ?	<input type="checkbox"/> PCR nasopharyngée	<input type="checkbox"/> Test antigénique	<input type="checkbox"/> Sérologie <input type="checkbox"/> NE SAIT PAS
Date du test : (Jour/Mois/Année)		
Quels symptômes avez-vous présenté ?	<input type="checkbox"/> AUCUN SYMPTOME	<input type="checkbox"/> Fatigue	
	<input type="checkbox"/> Fièvre : <38 / 38-39 / >39 °C	<input type="checkbox"/> Céphalée / mal de tête	
	<input type="checkbox"/> Toux	<input type="checkbox"/> Nausées / vomissements	
	<input type="checkbox"/> Dyspnée / souffle court	<input type="checkbox"/> Glaires accompagnant la toux	
	<input type="checkbox"/> Mal de gorge	<input type="checkbox"/> Perte du goût / odorat	
	<input type="checkbox"/> Douleur musculaire	<input type="checkbox"/> Autres :	
Avez-vous été hospitalisée pour le COVID-19 ?	<input type="checkbox"/> OUI	Dans quel hôpital ?	Avez-vous reçu de l'oxygène ? <input type="checkbox"/> OUI <input type="checkbox"/> NON
VACCINATION - 1 ^{ère} injection			
Quel type de vaccin ?	<input type="checkbox"/> Moderna	<input type="checkbox"/> Comirnaty (Pfizer/BioNTech)	<input type="checkbox"/> Autre :
Date de la 1^{ère} dose (Jour/Mois/Année)		
• Site d'injection	<input type="checkbox"/> Bras droit	<input type="checkbox"/> Bras gauche	<input type="checkbox"/> Autre :
• Lieu de vaccination	<input type="checkbox"/> Gynécologue/Sage-femme (cabinet privé)		<input type="checkbox"/> Centre de vaccination
	<input type="checkbox"/> Gynécologue/Sage-femme (hôpital)		<input type="checkbox"/> Médecin généraliste
	<input type="checkbox"/> Programme de vaccination au travail		<input type="checkbox"/> Pharmacien
• Avez-vous pris des médicaments contre la fièvre le jour de la vaccination ? (Dafalgan, Ibuprofène...)	<input type="checkbox"/> OUI	<input type="checkbox"/> NON	<input type="checkbox"/> NE SAIT PAS
Réaction locale ?	<input type="checkbox"/> OUI	<input type="checkbox"/> NON	<input type="checkbox"/> NE SAIT PAS
• Si oui, quelle réaction locale ?	<input type="checkbox"/> Gonflement/Œdème	<input type="checkbox"/> Rougeur	<input type="checkbox"/> Douleur
	<input type="checkbox"/> Démangeaison	<input type="checkbox"/> Hématome	<input type="checkbox"/> Induration
• Quand ?	<input type="checkbox"/> les 7 premiers jours après 1 ^{ère} injection ?	<input type="checkbox"/> > 1 mois après la 1 ^{ère} injection	
	<input type="checkbox"/> 8 à 14 jours après 1 ^{ère} injection	<input type="checkbox"/> Ne sait pas	
	<input type="checkbox"/> 15 jours à 1 mois après 1 ^{ère} injection		
Réaction systémique ?	<input type="checkbox"/> OUI	<input type="checkbox"/> NON	<input type="checkbox"/> NE SAIT PAS
• Si oui, quelle réaction systémique ?	<input type="checkbox"/> Fatigue	<input type="checkbox"/> Fièvre (>= 38°C)	<input type="checkbox"/> Céphalées (mal de tête)
	<input type="checkbox"/> Frissons	<input type="checkbox"/> Vomissement	<input type="checkbox"/> Douleur musculaire
	<input type="checkbox"/> Nausées	<input type="checkbox"/> Douleur articulaire	
	<input type="checkbox"/> Diarrhée	<input type="checkbox"/> Malaise	<input type="checkbox"/> Autre :
• Quand ?	<input type="checkbox"/> les 7 premiers jours après 1 ^{ère} injection ?	<input type="checkbox"/> > 1 mois après la 1 ^{ère} injection	
	<input type="checkbox"/> 8 à 14 jours après 1 ^{ère} injection	<input type="checkbox"/> Ne sait pas	
	<input type="checkbox"/> 15 jours à 1 mois après 1 ^{ère} injection		
Effet secondaire SEVERE ?	<input type="checkbox"/> OUI	<input type="checkbox"/> NON	<input type="checkbox"/> NE SAIT PAS
• Si oui, quel évènement sévère ?	<input type="checkbox"/> Hospitalisation possiblement liée à la vaccination		
	<input type="checkbox"/> Admission maternelle aux soins intensifs		
	<input type="checkbox"/> Choc anaphylactique		
	<input type="checkbox"/> Autre évènement sévère :		
• Quand ?	<input type="checkbox"/> les 7 premiers jours après 1 ^{ère} injection ?	<input type="checkbox"/> > 1 mois après la 1 ^{ère} injection	
	<input type="checkbox"/> 8 à 14 jours après 1 ^{ère} injection	<input type="checkbox"/> Ne sait pas	
	<input type="checkbox"/> 15 jours à 1 mois après 1 ^{ère} injection		

COVID19 & miscarriage or fetal loss

- Probably not associated with **miscarriages**
- Probably associated with **stillbirth** (lack of surveillance)
- Vaccine (not associated with miscarriage)
- Register your cases **CO⁺VI-PREG**