Ultrasound Obstet Gynecol 2021; **57**: 681–686
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.23631.

Opinion

Benefits and potential harms of COVID-19 vaccination during pregnancy: evidence summary for patient counseling

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Historically, pregnant women have been excluded from the majority of drug and vaccine trials, a practice that has been criticized widely by the scientific community[1–3]. As a result, pregnant women are routinely denied beneficial, and sometimes potentially life-saving, therapeutic and preventive measures or receive them well after their non-pregnant peers. Data about safety and efficacy in pregnancy subsequently accumulate adventitiously as women receive the drug or vaccine before finding out that they are pregnant or become pregnant soon after receiving the therapy. In the absence of any significant adverse effects, eventually sufficient confidence is established (either as 'evidence of no harm' or, more frequently, as 'no evidence of harm') for a formal trial to be considered or, alternatively, the use of the intervention in pregnancy simply slips into routine practice.

This practice was repeated with the coronavirus disease 2019 (COVID-19) vaccines, with pregnant women being excluded from the initial trials. Only a small number of women who were unknowingly pregnant or became pregnant soon after vaccination were included and this cohort is currently being followed up as part of the original trials[4,5]. Due to lack of evidence around the safety of the COVID-19 vaccines in pregnancy, international societies have tended to take a cautious approach, recommending that vaccination of pregnant women should be evaluated on a case-by-case basis. The Society of Obstetricians and Gynaecologists of Canada and the International Federation of Gynecology and Obstetrics are notable exceptions as early endorsers of unrestricted COVID-19 vaccination in pregnancy[6,7]. In the UK, the Royal College of Obstetricians and Gynaecologists (RCOG) recommends that pregnant women at high risk for contracting COVID-19 and/or developing severe illness should be considered eligible for vaccination[8,9]; the criteria are under constant review and were recently updated on 24 February. The proposed risk factors are derived from literature relating specifically to pregnant women with COVID-19 or extrapolated from data on non-pregnant women with COVID-19, and consist primarily of chronic diseases or immunosuppressive conditions, as well as high risk of exposure to the virus (Table 1). It should be acknowledged that women may experience severe COVID-19 even in the absence of any of these risk factors[10]. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists has taken a stance similar to that of RCOG[11]. The American College of Obstetricians and Gynecologists recommends that COVID-19 vaccines should not be withheld from pregnant women who meet the criteria for vaccination based on the Advisory Committee on Immunization Practices recommended priority groups[12].

Here, we summarize the available evidence to support counseling of women contemplating COVID-19 vaccination during pregnancy.

Risks of COVID-19 in pregnancy and potential benefits of vaccination

Most pregnant women with COVID-19 will remain asymptomatic or have mild illness. Fortunately, severe disease and death are rare outcomes. In the UK, for example, the maternal mortality rate associated with COVID-19 is 2.2 per 100 000 maternities[13–16]. However, pregnant women hospitalized with COVID-19 are more likely to be admitted to the intensive care unit (ICU) compared to non-pregnant women with the infection, although it is unclear whether this represents more serious illness or a lower threshold for ICU admission[14]. According to a large systematic review[14], pregnant women with COVID-19 do not appear to be at higher risk of death compared to non-pregnant women with the disease. However, some studies from both high- and low-income settings have reported increased maternal mortality in pregnancies with COVID-19[15,17]. Summary findings should be contextualized if used during patient counseling. Compared with pregnant women without COVID-19, those with

symptomatic COVID-19 are at increased risk of adverse pregnancy outcomes, including admission to the ICU, iatrogenic preterm birth, pre-eclampsia-like symptoms, Cesarean section and death[13–15]. Existing data on the effect of COVID-19 on stillbirth are inconsistent, but it seems that stillbirth rates increased during the pandemic in low- to middle-income countries while there was no significant increase in high-income countries[18,19]. COVID-19 has additional indirect effects on maternal and fetal outcomes, such as increased maternal mental distress and intimate partner violence[19,20].

The risk of severe adverse outcomes (e.g. ICU admission, maternal death or stillbirth) in pregnant women with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is affected by individual and societal risk factors, and the availability and performance of healthcare in their setting[19]. Nevertheless, it seems reasonable to counsel pregnant women with obesity, advanced age or significant chronic conditions (Table 1) that they are at increased risk of severe COVID-19 and, therefore, more likely to benefit from vaccination in terms of protection from life-threatening disease (Table 2). Observational studies indicate that postnatal transmission of SARS-CoV-2 from the mother to her baby is rare, and continued breastfeeding appears to be safe[21–23]; still, the postnatal transmission risk will probably be even lower in vaccinated mothers. Other secondary adverse effects of COVID-19 include mother–infant separation in some settings and increased incidence of Cesarean section and iatrogenic preterm birth. The prevalence of these adverse effects is also likely to be reduced by vaccination, therefore, women should be counseled about the probable additional benefits of vaccination over and above protection from severe disease (Table 2). The presence of anti-SARS-CoV-2 IgG was reported in the neonate of a vaccinated mother[24], however, it is not yet possible to say what impact maternal vaccination will have on neonatal protection against infection after birth.

Available SARS-CoV-2 vaccines and their safety profiles

Four different types of COVID-19 vaccine are currently available (Table 3): mRNA, viral vector, inactivated virus and recombinant antigen. As yet, only three COVID-19 vaccines (two mRNA and one adenovirus vector-based) have been approved for emergency use by the US Food and Drug Administration (FDA), the European Medicines Agency (EMA) and the Medicines and Healthcare Products Regulatory Agency (MHRA), namely the mRNA-1273 (Moderna Therapeutics, Cambridge, MA, USA), BNT162b2 (BioNTech, Fosun Pharma, Pfizer, Mainz, Germany) and Ad26.COV2.S (Janssen Pharmaceutica, Beerse, Belgium) vaccines. The Oxford–AstraZeneca (AZD1222) viral vector vaccine has been approved by the EMA and is commonly used

Table 1 Groups of pregnant women with high risk for contracting coronavirus disease 2019 (COVID-19) or developing severe illness from COVID-19 to whom vaccination should be offered according to the Royal College of Obstetricians and Gynaecologists[9]

Risk factors for developing severe COVID-19	*Risk factors for contracting COVID-19*
Underlying medical conditions, such as immune conditions, diabetes, high blood pressure, heart disease or asthma	Patient or someone in their household is health or social care worker or works in care home
Overweight	Increased rate of COVID-19 infections in local community
Over 35 years of age	Frequent contact with people outside household
Third trimester of pregnancy (over 28 weeks)	Unable to comply with social distancing
	Crowded household
	Black, Asian or other minority ethnicity background

Table 2 Direct and indirect detrimental effects of coronavirus disease 2019 (COVID-19) on pregnant women and their babies, and potential effect of vaccination

Adverse effect	*Incidence*	*Mediator*	*Potential effect of vaccination*
Maternal ICU admission	Rare	COVID-19, direct	Prevention
Mechanical ventilation or ECMO	Rare	COVID-19, direct	Prevention
Maternal death	Rare	COVID-19, direct	Prevention
Iatrogenic preterm birth	Common	COVID-19, indirect	Reduction
Cesarean delivery	Common	COVID-19, indirect	Reduction
Stillbirth	Rare	Severe COVID-19, reduced healthcare access	Reduction
Increased mental distress scores	Common	Reduced healthcare access, pandemic or mitigation measures	Unknown
Mother–infant separation following delivery	Uncommon	Perceived risk of transmission	Reduction
Interruption of breastfeeding following delivery	Uncommon	Perceived risk of transmission or COVID-19 treatment incompatible with nursing	Reduction
Postnatal vertical transmission	Rare	COVID-19, direct	Reduction, prevention

ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.

in the UK. The two FDA-approved mRNA vaccines were shown to elicit a very strong immune response and protection against severe COVID-19[4,25]. Unpublished data from a study of the mRNA-1273 vaccine in pregnant rats identified no safety concerns regarding malformations or embryotoxicity[26]. The trials of both mRNA vaccines excluded pregnant women. Yet, initial reports from regulatory bodies, such as the EMA, show that a small number of women in these trials were pregnant at the time of vaccination; safety data from these pregnancies are still pending but, as yet, no significant adverse effects have been observed[27,28]. More recently, Dr Anthony Fauci, Chief Medical Advisor to the USA President, stated that more than 20 000 pregnant women have received the mRNA vaccine in the USA and to date there have been no concerning 'red flags'[29,30]. These as yet unpublished data illustrate that many pregnant women are willing to be vaccinated when their autonomy is respected and they have the opportunity to weigh their own personal risks and benefits. These preliminary safety data are reassuring and their publication is eagerly awaited.

Although mRNA vaccines have not previously been deployed on such a scale, they are not new. mRNA vaccines do not contain a live virus and do not use an adjuvant to increase vaccine efficacy. The mRNA in vaccines does not enter the cell nucleus and cannot alter the human genome. Animal studies have demonstrated the safety, efficacy and potential benefit of mRNA vaccines

Table 3 Available severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines with available phase-III trial results

SARS-CoV-2 vaccine	*Technology*	*Property*	*Direct safety data*	*Indirect safety data from vaccines using similar technology*	*Unknowns and theoretical safety concerns*
mRNA-1273	mRNA	Non-replicating	Tested on pregnant mice: no signs of embryonic, fetal or postnatal developmental problems	mRNA-based Zika virus vaccine used in pregnant mice showed no safety concerns	Transplacental passage of mRNA-containing lipids
BNT162b2	mRNA	Non-replicating	N/A	mRNA-based Zika virus vaccine used in pregnant mice showed no safety concerns	Transplacental passage of mRNA-containing lipids
AZD1222	Viral vector	Non-replicating	N/A	Adenovirus vector-based Zika virus vaccine used in pregnant mice showed no safety concerns	Safety of adenovirus vector
Ad26.COV2.S	Viral vector	Non-replicating	N/A	Adenovirus vector-based Zika virus vaccine used in pregnant mice showed no safety concerns	Safety of adenovirus vector
Gam-COVID-Vac	Viral vector	Non-replicating	N/A	Adenovirus vector-based Zika virus vaccine used in pregnant mice showed no safety concerns	Safety of adenovirus vector
BBIBP-CorV	Inactivated virus with aluminium hydroxide adjuvant	Non-replicating	N/A	Inactivated virus vaccines are considered safe during pregnancy; alum adjuvant has been used in vaccines that are considered safe during pregnancy (e.g. human papillomavirus and respiratory syncytial virus)	Safety of alum adjuvant
CoronaVac	Inactivated virus with aluminium hydroxide adjuvant	Non-replicating	N/A	Inactivated virus vaccines are considered safe during pregnancy; alum adjuvant has been used in vaccines that are considered safe during pregnancy (e.g. human papillomavirus and respiratory syncytial virus)	Safety of alum adjuvant
Novavax	Recombinant antigen with saponin-based adjuvant	Non-replicating	N/A	Recombinant vaccines are considered safe during pregnancy	Safety of saponin-based proprietary adjuvant

All listed vaccines have very high protection rates against serious and life-threatening SARS-CoV-2 infection. N/A, not available.

in pregnant women, benefits which may extend beyond simply protecting the mother from pathogens. Zika virus is a zoonotic pathogen, like coronavirus, and is capable of intrauterine infection. In 2017, Richner *et al.* reported on the efficacy of an mRNA vaccine against Zika virus in pregnant mice[31]. Following vaccination, pregnant mice were infected with live Zika virus; pups born to vaccinated dams showed no viral load in their brain tissue. Furthermore, the viral load was at or below the detection threshold in placental samples. The authors concluded that the mRNA vaccine was safe in pregnant mice and that it prevented vertical transmission of Zika virus. The principles of this vaccination technology should also apply to COVID-19 vaccines and provides generic reassurance around the use of mRNA vaccines in pregnancy. Furthermore, vaccination is likely to protect not only the pregnant woman but also the fetus/neonate. With regards to SARS-CoV-2 vaccines, a recent case report demonstrated transplacental transmission of antibodies against the spike protein following vaccination of the mother[24]. Efficient transplacental transfer of SARS-CoV-2 IgG antibodies was also shown in the majority of seropositive pregnant women after natural infection[32]. The presence of neutralizing antibodies in the fetal/neonatal circulation is potentially an added benefit of vaccination for the protection of the baby, in both fetal and neonatal life, against COVID-19.

Three adenovirus vector-based SARS-CoV-2 vaccines, AZD1222, Ad26.COV2.S and Gam-COVID-Vac (the latter also known as Sputnik V; Gamaleya Research Institute of Epidemiology and Microbiology, Moscow, Russia) have recently reported Phase-3 trial data showing high levels of efficacy against COVID-19, especially against severe disease and hospitalization[5,33,34]. As with the mRNA vaccines, there are limited data on the safety of adenovirus vector-based vaccines in pregnancy, though adenovirus vector-based Zika virus vaccines have been tested in pregnant mice without safety concerns[35]. These vaccines do not contain live virus and neither the SARS-CoV-2 spike protein nor the adenovirus vector replicates in humans and are eliminated from the tissues following injection.

Two inactivated virus vaccines from China (BBIBP-CorV (Beijing Institute of Biological Products, Beijing, China) and CoronaVac (Sinovac Life Sciences, Beijing, China)) and one from India (COVAXIN, Bharat Biotech, Hyderabad, India) are also commercially available, with varying efficacy rates for preventing symptomatic infection reported[36–40]. They have similarly high protection against severe COVID-19 and death as the mRNA vaccines. Inactivated virus vaccines are considered safe in pregnancy, though the aluminium hydroxide adjuvants used in these vaccines do not have a designated FDA safety category due to the lack of data[41,42]. However, alum adjuvants are used in many vaccines, including those for hepatitis B, DTaP (diphtheria, tetanus and pertussis) and human papillomavirus (HPV). Inadvertent vaccination with HPV vaccines during pregnancy has not been associated with any safety concerns[43]. A similar safety profile was observed with the respiratory syncytial virus vaccine, which also uses alum adjuvant[44].

One recombinant antigen vaccine (Novavax, Novavax, Inc., Gaithersburg, MD, USA) has shown high efficacy against symptomatic SARS-CoV-2 infection[45]. The antigens produced by recombinant technology are coupled with a saponin-based proprietary adjuvant in order to elicit an immune response. Recombinant vaccines are considered safe in pregnancy due to their non-replicating nature. However, the saponin-based proprietary adjuvant used in this vaccine lacks safety data in pregnant women.

Ongoing trials and pending safety data

Pregnancy trials of the BNT162b2 and Ad26.COV2.S vaccines are due to start soon. However, enrolment to prospective trials is threatened by the current global demand for vaccines, which will only increase with time. Worldwide, pregnant women are already choosing to be vaccinated against SARS-CoV-2 and safety data accumulating in official registries are likely to play a key role for expectant mothers considering vaccination. It is essential that countries establish national registries of pregnant women receiving the different types of SARS-CoV-2 vaccine as a matter of urgency; where possible, international registries should be developed[46,47]. Monitoring pregnancy, fetal and neonatal outcomes in vaccinated women and comparing them with those in unvaccinated pregnant women should be a priority.

Moreover, the ethics of enrolling pregnant women into placebo-controlled trials is increasingly questionable, at a time when more and more pregnant women, particularly those with risk factors for severe COVID-19, are already receiving the vaccine. SARS-CoV-2 vaccines are likely to deliver similar benefits to pregnant women as to non-pregnant individuals, and are likely to be safe. Withholding such a vaccine from prospective mothers who understand and accept the uncertainty of available preventive measures, while offering them enrolment into a placebo-controlled trial, might prove ethically challenging. Nevertheless, there are a number of advantages in recruiting pregnant women into trials in which they receive a licensed SARS-CoV-2 vaccine. This includes addressing questions around optimal timing of vaccination, number of doses, dose intervals and need for boosters in future pregnancies. In the meantime, animal studies should be rapidly undertaken to provide safety information about the current unknowns of SARS-CoV-2 vaccines, such as transplacental passage of mRNA-containing lipids or the safety of adjuvants and adenovirus vectors. There is an urgent need to focus and allocate more resources to research on SARS-CoV-2 vaccination in pregnancy while awaiting safety data from official registries.

Conclusions

Pregnant women should be provided with a balanced and clear assessment of their risk of COVID-19 in pregnancy, taking into account their individual circumstances, local

practices and available evidence from similar healthcare settings. In addition, they should be counseled with a balanced summary of the potential direct and indirect benefits of SARS-CoV-2 vaccines, while acknowledging the limited safety data. Whilst these vaccines have not yet been trialled in pregnancy, they are being offered to pregnant women with risk factors for severe COVID-19 during the national rollout of vaccine programs in the UK. These vaccines are also currently offered to pregnant women with a high risk of exposure to SARS-CoV-2, including health and care workers. In the UK, the MHRA is receiving regular feedback from the vaccination program and any concerns are met with appropriate action. So far, no safety concerns in vaccinated pregnant women have been reported in either the UK or the USA. We believe that COVID-19 vaccination should not be withheld from pregnant women who have received adequate counseling and understand the uncertainties, minimal potential harms and likely benefits of these vaccines. We also encourage further research to address current and future issues around SARS-CoV-2 vaccines in pregnancy.

REFERENCES

1. Heath PT, Le Doare K, Khalil A. Inclusion of pregnant women in COVID-19 vaccine development. *Lancet Infect Dis* 2020; **20**: 1007–1008.
2. Taylor MM, Kobeissi L, Kim C, Amin A, Thorson AE, Bellare NB, Brizuela V, Bonet M, Kara E, Thwin SS, Kuganantham H, Ali M, Oladapo OT, Broutet N. Inclusion of pregnant women in COVID-19 treatment trials: a review and global call to action. *Lancet Glob Health* 2021; **9**: e366–371.
3. Dashraath P, Nielsen-Saines K, Madhi SA, Baud D. COVID-19 vaccines and neglected pregnancy. *Lancet* 2020; **396**: e22.
4. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, Perez JL, Pérez Marc G, Moreira ED, Zerbini C, Bailey R, Swanson KA, Roychoudhury S, Koury K, Li P, Kalina WV, Cooper D, Frenck RW, Hammitt LL, Türeci Ö, Nell H, Schaefer A, Ünal S, Tresnan DB, Mather S, Dormitzer PR, Şahin U, Jansen KU, Gruber WC. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *NEJM* 2020; **383**: 2603–2615.
5. Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, Angus B, Baillie VL, Barnabas SL, Bhorat QE, Bibi S, Briner C, *et al*. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet* 2021; **397**: 99–111.
6. Society of Obstetricians and Gynaecologists of Canada. SOGC Statement on COVID-19 Vaccination in Pregnancy. 2021. https://sogc.org/common/Uploaded%20files/Latest%20News/SOGC_Statement_COVID-19_Vaccination_in_Pregnancy.pdf [Accessed March 13, 2021].
7. International Federation of Gynecology and Obstetrics. COVID-19 Vaccination for Pregnant and Breastfeeding Women. 2021. https://www.figo.org/sites/default/files/2021-03/FIGO%20Statement_COVID-19%20vaccination%20pregnant%20breastfeeding%20women_EN.pdf [Accessed March 13, 2021].
8. Royal College of Obstetricians & Gynaecologists. Updated advice on COVID-19 vaccination in pregnancy and women who are breastfeeding. 2021. https://www.rcog.org.uk/en/news/updated-advice-on-covid-19-vaccination-in-pregnancy-and-women-who-are-breastfeeding/ [Accessed February 14, 2021].
9. Royal College of Obstetricians and Gynaecologists. Merged information sheet and decision aid. 2021. https://www.rcog.org.uk/globalassets/documents/guidelines/2021-02-24-combined-info-sheet-and-decision-aid.pdf [Accessed March 13, 2021].
10. Barrantes JH, Ortoleva J, O'Neil ER, Suarez EE, Beth Larson S, Rali AS, Agerstrand C, Grazioli L, Chatterjee S, Anders M. Successful Treatment of Pregnant and Postpartum Women With Severe COVID-19 Associated Acute Respiratory Distress Syndrome With Extracorporeal Membrane Oxygenation. *ASAIO J* 2021; **67**: 132–136.
11. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists. COVID-19 Vaccination in Pregnant and Breastfeeding Women. 2021. https://ranzcog.edu.au/statements-guidelines/covid-19-statement/covid-19-vaccination-information [Accessed March 13, 2021].
12. American College of Obstetricians and Gynecologists. Vaccinating Pregnant and Lactating Patients Against COVID-19. 2021. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/12/vaccinating-pregnant-and-lactating-patients-against-covid-19 [Accessed February 14, 2021].
13. Khalil A, Kalafat E, Benlioglu C, O'Brien P, Morris E, Draycott T, Thangaratinam S, Le Doare K, Heath P, Ladhani S, von Dadelszen P, Magee LA. SARS-CoV-2 infection in pregnancy: A systematic review and meta-analysis of clinical features and pregnancy outcomes. *EClinicalMedicine* 2020; **25**: 10046.
14. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, Debenham L, Llavall AC, Dixit A, Zhou D, Balaji R, Lee SI, Qiu X, Yuan M, Coomar D, Sheikh J, Lawson H, Ansari K, van Wely M, van Leeuwen E, Kostova E, Kunst H, Khalil A, Tiberi S, Brizuela V, Broutet N, Kara E, Kim CR, Thorson A, Escuriet R, Oladapo OT, Mofenson L, Zamora J, Thangaratinam S. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ* 2020; **370**: m3320.
15. Zambrano LD, Ellington S, Strid P, Galang RR, Oduyebo T, Tong VT, Woodworth KR, Nahabedian JF, Azziz-Baumgartner E, Gilboa SM, Meaney-Delman D, CDC COVID-19 Response Pregnancy and Infant Linked Outcomes Team. Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-October 3, 2020. *MMWR Morb Mortal Wkly Rep* 2020; **69**: 1641–1647.
16. Jering KS, Claggett BL, Cunningham JW, Rosenthal N, Vardeny O, Greene MF, Solomon SD. Clinical Characteristics and Outcomes of Hospitalized Women Giving Birth With and Without COVID-19. *JAMA Intern Med* 2021. DOI: 10.1001/jamainternmed.2020.9241.
17. Martinez-Portilla RJ, Sotiriadis A, Chatzakis C, Torres-Torres J, Espino YSS, Sandoval-Mandujano K, Castro-Bernabe DA, Medina-Jimenez V, Monarrez-Martin JC, Figueras F, Poon LC. Pregnant women with SARS-CoV-2 infection are at higher risk of death and pneumonia: propensity score matched analysis of a nationwide prospective cohort (COV19Mx). *Ultrasound Obstet Gynecol* 2021; **57**: 224–231.
18. Khalil A, von Dadelszen P, Draycott T, Ugwumadu A, O'Brien P, Magee L. Change in the Incidence of Stillbirth and Preterm Delivery During the COVID-19 Pandemic. *JAMA* 2020; **324**: 705–706.
19. Chmielewska B, Barratt I, Townsend R, Kalafat E, van der Meulen J, Gurol-Urganci I, O'Brien P, Morris E, Draycott T, Thangaratinam S, Le Doare K, Ladhani S, von Dadelszen P, Magee L, Khalil A. Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis. *Lancet Glob Health* 2021. DOI: 10.1016/S2214-109X(21)00079-6.
20. Evans ML, Lindauer M, Farrell ME. A Pandemic within a Pandemic — Intimate Partner Violence during Covid-19. *NEJM* 2020; **383**: 2302–2304.
21. Walker KF, O'Donoghue K, Grace N, Dorling J, Comeau JL, Li W, Thornton JG. Maternal transmission of SARS-COV-2 to the neonate, and possible routes for such transmission: a systematic review and critical analysis. *BJOG* 2020; **127**: 1324–1336.
22. Salvatore CM, Han J-Y, Acker KP, Tiwari P, Jin J, Brandler M, Cangemi C, Gordon L, Parow A, DiPace J, DeLaMora P. Neonatal management and outcomes during the COVID-19 pandemic: an observation cohort study. *Lancet Child Adolesc Health* 2020; **4**: 721–727.
23. Centeno-Tablante E, Medina-Rivera M, Finkelstein JL, Rayco-Solon P, Garcia-Casal MN, Rogers L, Ghezzi-Kopel K, Ridwan P, Peña-Rosas JP, Mehta S. Transmission of SARS-CoV-2 through breast milk and breastfeeding: a living systematic review. *Ann N Y Acad Sci* 2021;**1484**: 32–54.
24. Gill L, Jones CW. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Antibodies in Neonatal Cord Blood After Vaccination in Pregnancy. *Obstet Gynecol* 2021. DOI: 10.1097/AOG.0000000000004367.
25. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, Diemert D, Spector SA, Rouphael N, Creech CB, McGettigan J, Khetan S, Segall N, Solis J, Brosz A, Fierro C, Schwartz H, Neuzil K, Corey L, Gilbert P, Janes H, Follmann D, Marovich M, Mascola J, Polakowski L, Ledgerwood J, Graham BS, Bennett H, Pajon R, Knightly C, Leav B, Deng W, Zhou H, Han S, Ivarsson M, Miller J, Zaks T. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *NEJM* 2020; **384**: 403–416.
26. FDA Briefing Document Moderna COVID-19 Vaccine. 2021. https://www.fda.gov/media/144434/download [Accessed February 14, 2021].
27. European Medicines Agency. Comirnaty: EPAR - Public assessment report. 2021. https://www.ema.europa.eu/en/documents/assessment-report/comirnaty-epar-public-assessment-report_en.pdf [Accessed February 14, 2021].
28. Male V. Are COVID-19 vaccines safe in pregnancy? *Nat Rev Immunol* 2021. DOI: 10.1038/s41577-021-00525-y.
29. Press Briefing by White House COVID-19 Response Team and Public Health Officials. 2021. https://www.whitehouse.gov/briefing-room/press-briefings/2021/02/10/press-briefing-by-white-house-covid-19-response-team-and-public-health-officials-3/ [Accessed March 12, 2021].
30. CDC National Center for Immunization & Respiratory Diseases. Advisory Committee on Immunization Practices (ACIP). COVID-19 vaccine safety update. 2021. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/05-covid-Shimabukuro.pdf [Accessed March 12, 2021].
31. Richner JM, Himansu S, Dowd KA, Butler SL, Salazar V, Fox JM, Julander JG, Tang WW, Shresta S, Pierson TC, Ciaramella G, Diamond MS. Modified mRNA Vaccines Protect against Zika Virus Infection. *Cell* 2017; **168**: 1114–1125.e10.
32. Flannery DD, Gouma S, Dhudasia MB, Mukhopadhyay S, Pfeifer MR, Woodford EC, Triebwasser JE, Gerber JS, Morris JS, Weirick ME, McAllister CM, Bolton MJ, Arevalo CP, Anderson EM, Goodwin EC, Hensley SE, Puopolo KM. Assessment of Maternal and Neonatal Cord Blood SARS-CoV-2 Antibodies and Placental Transfer Ratios. *JAMA Pediatr* 2021. DOI: 10.1001/jamapediatrics.2021.0038.
33. Logunov DY, Dolzhikova IV, Shcheblyakov DV, Tukhvatulin AI, Zubkova OV, Dzharullaeva AS, Kovyrshina AV, Lubenets NL, Grousova DM, Erokhova AS, Botikov AG, Izhaeva FM, Popova O, Ozharovskaya TA, Esmagambetov IB, Favorskaya IA, Zrelkin DI, Voronina DV, Shcherbinin DN, Semikhin AS, Simakova YV, Tokarskaya EA, Egorova DA, Shmarov MM, Nikitenko NA, Gushchin VA, Smolyarchuk EA, Zyryanov SK, Borisevich SV, Naroditsky BS, Gintsburg AL. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. *Lancet* 2021; **397**: 671–681.
34. Johnson & Johnson COVID-19 Vaccine Authorized by U.S. FDA For Emergency Use. Content Lab US. 2021. https://www.jnj.com/johnson-johnson-covid-19-vaccine-authorized-by-u-s-fda-for-emergency-usefirst-single-shot-vaccine-in-fight-against-global-pandemic [Accessed March 12, 2021].

35. Larocca RA, Mendes EA, Abbink P, Peterson RL, Martinot AJ, Iampietro MJ, Kang ZH, Aid M, Kirilova M, Jacob-Dolan C, Tostanoski L, Borducchi EN, De La Barrera RA, Barouch DH. Adenovirus Vector-Based Vaccines Confer Maternal-Fetal Protection against Zika Virus Challenge in Pregnant IFN-αβR−/− Mice. *Cell Host Microbe* 2019; **26**: 591–600.e4.
36. Xia S, Zhang Y, Wang Y, Wang H, Yang Y, Gao GF, Tan W, Wu G, Xu M, Lou Z, Huang W, Xu W, Huang B, Wang H, Wang W, Zhang W, Li N, Xie Z, Ding L, You W, Zhao Y, Yang X, Liu Y, Wang Q, Huang L, Yang Y, Xu G, Luo B, Wang W, Liu P, Guo W, Yang X. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomised, double-blind, placebo-controlled, phase 1/2 trial. *Lancet Infect Dis* 2021; **21**: 39–51.
37. Zhang Y, Zeng G, Pan H, Li C, Hu Y, Chu K, Han W, Chen Z, Tang R, Yin W, Chen X, Hu Y, Liu X, Jiang C, Li J, Yang M, Song Y, Wang X, Gao Q, Zhu F. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18-59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. *Lancet Infect Dis* 2021; **21**: 181–192.
38. The Official Portal of the UAE Government. Vaccines against COVID-19 in the UAE. 2021. https://u.ae/en/information-and-services/justice-safety-and-the-law/handling-the-covid-19-outbreak/vaccines-against-covid-19-in-the-uae [Accessed February 14, 2021].
39. Reuters. Turkish study revises down Sinovac COVID-19 vaccine efficacy to 83.5%. 2021. https://www.reuters.com/article/health-coronavirus-turkey-sinovac-int-idUSKBN2AV18P [Accessed March 14, 2021].
40. Bharat Biotech. *Bharat Biotech Announces Phase 3 Results of COVAXIN®: India's First COVID-19 Vaccine Demonstrates Interim Clinical Efficacy of 81%*. 2021. https://www.bharatbiotech.com/images/press/covaxin-phase3-efficacy-results.pdf [Accessed March 14, 2021].
41. Batista-Duharte A, Martínez DT, Carlos IZ. Efficacy and safety of immunological adjuvants. Where is the cut-off? *Biomed Pharmacother* 2018; **105**: 616–624.
42. Herberts C, Melgert B, van der Laan JW, Faas M. New adjuvanted vaccines in pregnancy: what is known about their safety?. *Expert Rev Vaccines* 2010; **9**:1411–1422.
43. Scheller NM, Pasternak B, Mølgaard-Nielsen D, Svanström H, Hviid A. Quadrivalent HPV Vaccination and the Risk of Adverse Pregnancy Outcomes. *NEJM* 2017; **376**: 1223–1233.
44. Madhi SA, Polack FP, Piedra PA, Munoz FM, Trenholme AA, Simões EAF, Swamy GK, Agrawal S, Ahmed K, August A, Baqui AH, Calvert A, Chen J, Cho I, Cotton MF, Cutland CL, Englund JA, Fix A, Gonik B, Hammitt L, Heath PT, de Jesus JN, Jones CE, Khalil A, Kimberlin DW, Libster R, Llapur CJ, Lucero M, Pérez Marc G, Marshall HS, Masenya MS, Martinón-Torres F, Meece JK, Nolan TM, Osman A, Perrett KP, Plested JS, Richmond PC, Snape MD, Shakib JH, Shinde V, Stoney T, Thomas DN, Tita AT, Varner MW, Vatish M, Vrbicky K, Wen J, Zaman K, Zar HJ, Glenn GM, Fries LF. Respiratory Syncytial Virus Vaccination during Pregnancy and Effects in Infants. *NEJM* 2020; **383**: 426–439.
45. Novavax Inc. Novavax COVID-19 Vaccine Demonstrates 89.3% Efficacy in UK Phase 3 Trial. 2021. https://ir.novavax.com/news-releases/news-release-details/novavax-covid-19-vaccine-demonstrates-893-efficacy-uk-phase-3 [Accessed February 14, 2021].
46. Public Health England. Inadvertent vaccination in pregnancy (VIP). 2021. https://www.gov.uk/guidance/vaccination-in-pregnancy-vip [Accessed March 13, 2021].
47. UKOSS. COVID-19 Vaccination in Pregnancy. 2021. https://www.npeu.ox.ac.uk/ukoss/current-surveillance/covid-19-vaccination-in-pregnancy [Accessed March 13, 2021].