



MEETING REPORT — 13 April 2021

# COVAX: MATERNAL IMMUNIZATION WORKING GROUP WEBINAR

## CHALLENGES OF VACCINATING PREGNANT AND LACTATING WOMEN DURING THE COVID-19 PANDEMIC

# EXECUTIVE SUMMARY

On 13 April 2021, the COVAX Maternal Immunization Working Group, co-chaired by Ajoke Sobanjo ter-Meulen, MD and Flor Munoz, MD, held a virtual meeting on the challenges of vaccinating pregnant and lactating women during the COVID-19 pandemic.

## OVERVIEW: SESSION 1

The first session focused on data sources for informing policy and recommendations on COVID-19 vaccination in pregnant and lactating women. Drs Ibukun Abejirinde and Sami Gottlieb from the World Health Organization (WHO) provided details of the [WHO COVID-19 Pregnancy Longitudinal Cohort Study](#) which aims to assess whether SARS-CoV-2 infection in pregnancy increases the risk of adverse pregnancy outcomes; to estimate the risk of mother-to-child transmission of SARS-CoV-2; to describe viral presence and persistence of SARS-CoV-2 in bodily fluids; and to characterize the clinical course and disease spectrum of COVID-19 during pregnancy. The study will take place across 14 countries and aims to enroll 16,470 women by the end of 2022. Dr Gottlieb provided a summary of the varying vaccine policies for vaccination of pregnant women worldwide, from strong recommendation to prohibition. She highlighted that the WHO Pregnancy Cohort Study is being adapted to collect data on vaccination of pregnant women, including consideration of how roll-out of COVID-19 vaccines potentially affects the study protocol and how the study might be adapted to evaluate vaccine safety-related questions.

Dr Geeta Swamy from Duke University then provided an overview of COVID-19 Phase 3 clinical trial data, what we already know about COVID-19 vaccines in

pregnancy, and plans for COVID-19 vaccine studies in pregnant women. She presented a comparison between data on pregnancy and infant outcomes from women who have received COVID-19 vaccines during pregnancy and enrolled in the US Centers for Disease Control and Prevention (CDC) V-safe pregnancy registry, and background rates. In the absence of data from placebo-controlled trials, analysis of pregnancy and infant outcomes of women included in the V-safe pregnancy registries showed no safety concerns, specially noting similar pregnancy outcomes in vaccinated pregnant women compared to background rates of outcomes in unvaccinated pregnant women.

Dr Barney Graham from the National Institute of Allergy and Infectious Disease (NIAID) then provided background details on the structural biology of the SARS-CoV-2, and how it informed the design of currently authorized vaccines. He discussed details of the six vaccines currently being evaluated in the US and provided a detailed overview of construct type, current development stage, dates of emergency use authorization (EUA), where appropriate, developmental and reproductive toxicity (DART) study status, and current pregnancy/lactation exposure data.

A panel discussion then followed.

### The key points from Session 1 panel discussion were:

- COVID-19 recommendations for pregnant and lactating women are continually being revised as data become available.
- Data collected via the US V-safe pregnancy registry from pregnant women who have already

received a COVID-19 do not show any substantial differences in adverse pregnancy or infant outcomes compared with background rates, including among women who received a vaccine during the first trimester (Shimabukuro et al, *N Engl J Med.* 2021 Apr 21. doi: 10.1056/NEJMoa2104983; <https://www>.

[cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafepregnancyregistry.html](https://cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafepregnancyregistry.html)).

- A few clinical trials focusing on immunogenicity and safety in pregnant women have begun or are being planned (e.g. Pfizer, Janssen, Astra Zeneca vaccines), and the Pfizer study is also suitably powered to assess efficacy. The Pfizer study is placebo-controlled and is being conducted globally.
- Based on the known safety of the mRNA vaccines in the US, women who become pregnant after receiving the first dose of a two-dose vaccine schedule should be given the second dose as planned.
- Data on rare adverse events (e.g. thrombotic events following administration of adeno-vectored COVID-19 vaccine) are being assessed, and recommendations for pregnant and lactating women will likely follow regulatory bodies recommendations in non-pregnant adults. However, pregnancy is also a risk factor for thrombotic events, and should be considered when deciding on the optimal vaccine for pregnant women, where a choice is available.
- Communication about the risks of COVID-19 disease vs. the potential risks of vaccination is key to increase uptake, particularly in low- and middle-income countries (LMICs).
- There is a clear need for post-marketing (post-implementation) active surveillance globally. This effort could leverage existing systems such as pregnancy exposure registries for anti-retroviral drugs.
- Suggested immediate next steps for collection of safety data in LMICs are to create platforms to exchange information and methodologies for the assessment of vaccine safety in pregnancy; to develop safety surveillance systems that work across programs and integrate these into routine care; and to focus on cross-cutting collaborative projects and communications.

## OVERVIEW: SESSION 2

In the second session, case studies of COVID-19 vaccine rollout in four countries were presented, focusing on distribution, administration, and uptake in pregnant women. In the first country case study, Dr Denise Jamieson from Emory University School of Medicine provided an update on the COVID-19 vaccination experience in the US. She outlined the steps taken for COVID-19 vaccines to reach pregnant women in the US, and current recommendations from the American College of Gynecologists (ACOG) and the CDC Advisory Committee on Immunization Practices (ACIP) that pregnant and lactating women should be offered COVID-19 mRNA vaccines, while persons planning to become pregnant should complete the vaccination series prior to conception. She also further discussed the V-safe pregnancy registry data on pregnancy and neonatal outcomes in vaccinated women.

Dr Orna Diav-Citrin from the Israeli Teratology Information Service provided details of the COVID-19 vaccination experience in Israel. The Israeli advisory committee for COVID-19 vaccination recommends vaccination of women planning a pregnancy at increased risk for severe disease and lactating women, and advise that it should not be withheld from pregnant women, especially if they are exposed to COVID-19

patients at work. Dr Diav-Citrin outlined the position paper from the main professional organizations and presented data from each of the four official health insurance organizations indicating high vaccination rates in pregnant women over time. She concluded that the small, relatively young population of Israel, together with centralized systems, coordination between stakeholders, special funding for timely contraction of vaccines, and well-tailored outreach programs have contributed to Israel's rapid roll-out and acceptance of COVID-19 vaccines. A post-roll out safety surveillance system such as V-Safe however, is not in place.

Dr Asma Khalil, from St George's Hospital University of London provided information on the UK COVID-19 vaccine roll-out. She presented the results of a survey from the Royal College of Obstetricians and Gynecologists which identified the most common reasons for pregnant women accepting the vaccine as wanting to protect themselves, followed by their baby, their family and friends, and vulnerable people from COVID-19, and the most common reasons for declining were concerns that the vaccine could harm themselves or their baby, or they wanted to see more safety data in pregnancy first. The survey identified midwives, obstetricians, and general practitioners (GPs)

as the people pregnant women would most want to speak to about the benefits and risks of COVID-19 vaccination. In the UK, current recommendations state that pregnant women at high-risk of severe COVID-19 disease should be offered the vaccine. Dr Khalil then provided details of safety surveillance systems in the UK including the yellow card monitoring system, and a study evaluating pregnancy and infant outcomes compared with historical outcomes in a similar high-risk population. She concluded by discussing the thrombotic events observed after vaccination with the AstraZeneca adenovirus-vectored vaccine, and the UK benefits versus harms modelling has resulted in the vaccine being restricted to people  $\geq 30$  years of age, based on low exposure risk to COVID-19 vs. risk of thrombosis events post-vaccination.

Dr Narendra Kumar Arora presented the final case study of the COVID-19 vaccine experience in India. He provided background on the experience of maternal immunization in general in India, and highlighted that poor uptake is mainly rooted in misperceptions among treating physicians, rather than hesitancy in pregnant women themselves. Current guidelines in India do not recommend COVID-19 vaccination of pregnant and lactating women, however, the safety monitoring platform is ready. One positive to come out of the COVID-19 pandemic is the development of an elaborate safety surveillance system which can be easily adapted to include surveillance of pregnant women.

A second panel discussion then followed.

### **The key points from Session 2 panel discussion were:**

- Vaccine rollout in LMICs is limited by lack of vaccine supply. Where vaccines are available, limited information is available on whether such platforms are suitable for administration during pregnancy, resulting in restriction to the use of the vaccine which exclude pregnant women in the early phases of implementation.
- Removing pregnant women from frontline healthcare is an alternative option to vaccination adopted in some countries, but in many LMICs nearly all of this workforce are women of child-bearing age, therefore, this may not be a viable option.
- Recommendations about vaccination of pregnant and lactating women vary globally, and many countries do not recommend receipt of COVID-19 vaccines during pregnancy, due to lack of safety data.
- Safety surveillance in LMICs is hampered by the general lack of data on COVID-19 disease burden and information on background pregnancy/neonatal outcomes.
- Navigating risk perception is very challenging, particularly with the wealth of information (of varying accuracy) available in the media and on social media. Clear guidance from professional organizations can help women make informed decisions about whether to get vaccinated.
- Key priorities for research should include understanding what pregnant women need to know and from whom to make COVID-19 vaccines more acceptable and accessible; collection of specific data in pregnancy; and effective pharmacovigilance and harmonization of data collection.

# KEY FINDINGS AND NEXT STEPS

Key finding from both sessions and next steps are summarized below.

## Key Findings from the Webinar

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- There is no evidence to date of increased risk of severe COVID-19 in the 1st trimester of gestation, or of increased risk of adverse events (including miscarriages) following vaccination
- Active safety surveillance systems that include pregnant women are needed worldwide and can utilize existing platforms e.g. ART exposure registries
- More data are needed on the burden of COVID-19 and background rates of pregnancy outcomes in LMICs
- Consistent guidance from manufacturers, regulatory authorities, and the WHO on administration of COVID-19 vaccines in pregnancy and lactation is needed to reduce hesitancy and enable recommendations for vaccination in countries which currently prohibit receipt in pregnant and lactating women.
- Education of policy makers and healthcare providers, particularly in LMICs, is required to reduce misconceptions and enable access to vaccines for pregnant and lactating women.
- More research is needed on the safety of vaccines in pregnant women, and on the effects of COVID-19 in pregnancy, particularly in LMICs.
- Key priorities for research should include:
  1. Understanding what pregnant women need to know and from which trusted sources of information to make COVID-19 vaccines more acceptable and accessible;
  2. Collecting specific data on the burden of COVID-19 and the safety of COVID-19 vaccines in pregnancy; and
  3. Establishing effective pharmacovigilance and harmonization of data collection and data sharing

## Next Steps

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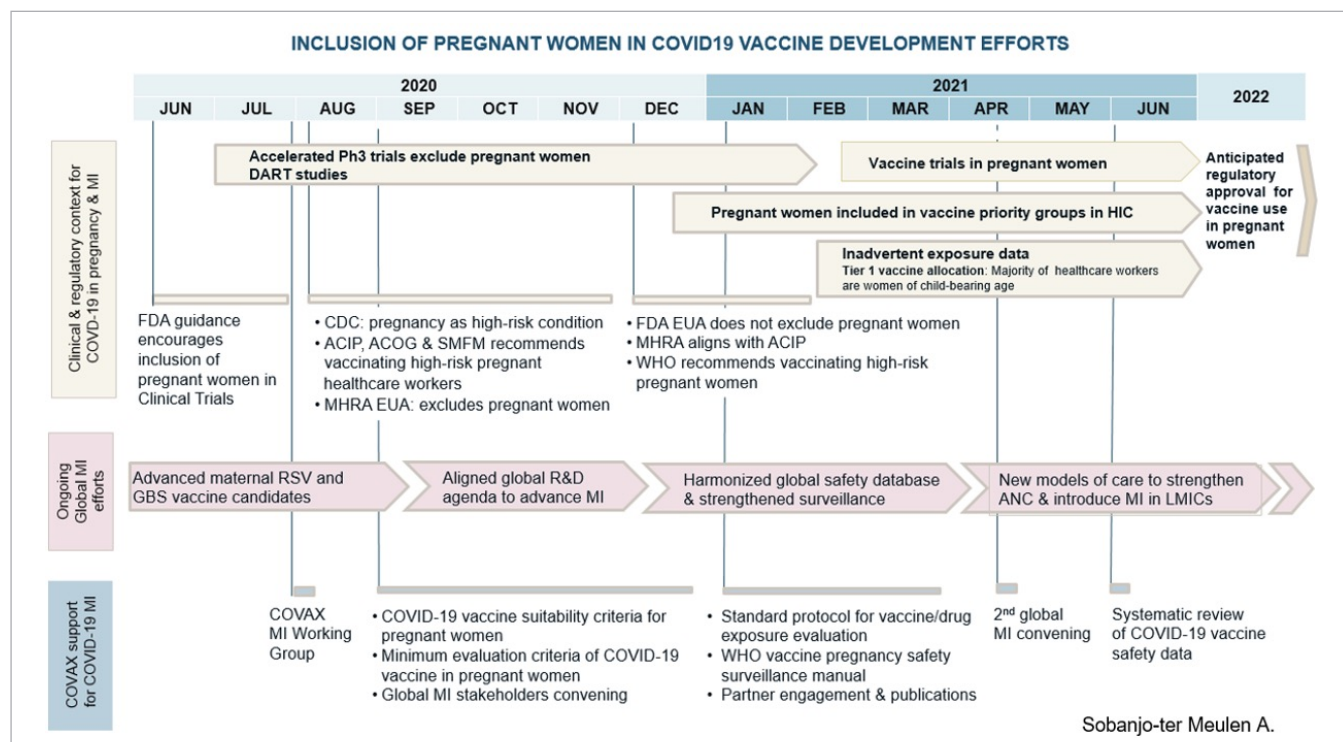
- There is a need to create cross-functional platforms and programs for the administration of vaccines to pregnant women. The stakeholders and path leading to the creation of such platforms and program must be defined.
- There is a need for the collection of post-vaccine exposure data to generate feedback which can be integrated into routine care.
- A vaccine manufacturer-centered roundtable on vaccination during pregnancy and the types of data which need to be collected to achieve the goal of inclusion of pregnant women in research and implementation of COVID-19 vaccines was considered beneficial, including worldwide representation with manufacturers of different types of vaccines.
- Ad-hoc discussions with relevant stakeholders of evolving situations (e.g. vaccine adverse events) were suggested to address communications. An immediate question to address is the occurrence of thrombosis thrombocytopenia events after adenoviral vectored vaccines, and their relevance in the context of vaccination of pregnant women.
- Targeted outreach to professional societies and other was considered a priority to engage health care providers globally in efficiently vaccinating pregnant women against COVID-19.
- Development of studies and surveillance systems to continue to address safety and effectiveness data needs in pregnant women remains a priority.

# MEETING SUMMARY

TIME (PDT)	SESSION	SPEAKER
8:00 am	Workshop Introduction	Ajoke Sobanjo-ter Meulen Flor Munoz
8:05 am	<b>Session 1 — Data sources for policy and recommendations</b>	
8:05 am	The WHO COVID-19 and Pregnancy Cohort Study: Opportunities and challenges in addressing important data gaps	Ibukun Abejirinde (WHO) Sami Gottlieb (WHO)
8:20 am	COVID-19 vaccine constructs and platforms suitable for pregnant women	Barney Graham (NIH)
8:35 am	Studies of COVID-19 vaccines in pregnancy — safety and efficacy — are RCT still feasible or necessary?	Geeta Swamy (Duke Medical Center; ACOG)
8:50 am	Q&A	
9:00 am	<b>Panel Discussion 1</b>	
	<i>Panelists:</i> <ol style="list-style-type: none"> <li>Alejandro Cravioto (WHO SAGE)</li> <li>Judy Absalon (Pfizer)</li> <li>Ushma Mehta (Cape Town University)</li> </ol>	<i>Moderator:</i> Ajoke Sobanjo-ter Meulen (BMGF) <i>Curator:</i> Chrissie Jones
9:30 am	Break (5 min)	
9:35 am	<b>Session 2 — COVID-19 vaccine distribution / administration / uptake in pregnant women</b>	
9:35 am	US Country case study 1	Denise Jamieson (Emory University)
9:45 am	Israel Country case study 2	Orna Diav-Citrin (Ministry of Health, Israel)
9:55 am	UK Country case study 3	Asma Khalil (St. George's University)
10:05 am	India Country case study 4	Narendra Arora (Inclen, Chair WHO COVID-19 vaccine pregnancy implementation/surveillance manual)
10:15 am	Q&A	
10:25 am	Break (5 min)	
10:30 am	<b>Panel Discussion 2</b>	
	<i>Panelists:</i> <ol style="list-style-type: none"> <li>Esperança Sevene (Ministry of Health, Mozambique)</li> <li>Ayoade Alakija (COVID-19 African Vaccine Delivery Alliance-AVDA)</li> <li>Heidi Larson (LSHTM Vaccine Confidence Project)</li> </ol>	<i>Moderator:</i> Flor Munoz <i>Curator:</i> Chrissie Jones
11:00 am	Concluding remarks	Ajoke Sobanjo-ter Meulen Flor Munoz

## SESSION 1: WELCOME AND INTRODUCTION

Dr Ajoke Sobanjo ter-Meulen welcomed all the attendees and provided a brief introduction to the meeting. Since the previous COVAX Maternal Immunization Working Group (MIWG) webinar in December 2020, a number of COVID-19 vaccines are now being administered under Emergency Use Authorizations (EUAs). Multiple maternal immunization workstreams across different organizations are currently working in parallel, including development of standardized protocols, and studies of disease burden, effectiveness, immunogenicity, and safety.



Dr Sobanjo ter-Meulen provided links to the latest reports from the COVAX MIWG group, including the December webinar report ([https://media.tghn.org/medialibrary/2021/02/2020\\_01\\_22\\_COVAX\\_Maternal\\_Immunization\\_Working\\_Group\\_Webinar\\_Report\\_final3.pdf](https://media.tghn.org/medialibrary/2021/02/2020_01_22_COVAX_Maternal_Immunization_Working_Group_Webinar_Report_final3.pdf)) and final version of the MIWG project report ([https://media.tghn.org/medialibrary/2021/04/12MAR2021\\_COVAX\\_MIWG\\_Project\\_report\\_final.pdf](https://media.tghn.org/medialibrary/2021/04/12MAR2021_COVAX_MIWG_Project_report_final.pdf)).

To date, over 60,000 pregnant women have received a COVID-19 vaccine in the US, with no apparent safety issues identified. However, while the rollout of COVID-19 vaccines has been broad and generally permissive to include pregnant women in high-income countries (HICs), pregnant women are mostly excluded from receipt of COVID-19 vaccines in low- and middle-income countries (LMICs), mainly due to lack of local

safety data. Despite these women often working in high exposure roles (e.g. frontline healthcare), they have generally not been included in COVAX vaccine dose requests. The Coalition for Epidemic Preparedness Innovations (CEPI) has identified the need to generate data on populations not included in Phase 3 trials, and have put out an active call for proposals (<https://cepi.net/get-involved/cfps/>) for studies in these areas, with the aim of supporting vaccine rollout in these populations and expanding access and capacity across LMICs. LMICs face a number of specific challenges in COVID-19 vaccine rollout and data collection, including lack of data on the burden of COVID-19 disease and pregnancy outcomes in general, limited capacity for pharmacovigilance monitoring or pregnancy registries, and limited choice of vaccines.

## WHO COVID-19 AND PREGNANCY LONGITUDINAL COHORT STUDY

Dr Ibukun Abejirinde, Consultant in Sexual and Reproductive Health and Research at the World Health Organization, provided some background on COVID-19 disease in pregnant and lactating women. In a recently updated living systematic review, the prevalence of SARS-CoV-2 infection or COVID-19 in pregnant women attending or admitted to hospital for any reason was 10%.<sup>1</sup> Overall, 10% of pregnant women with COVID-19 experienced severe disease, 4% required intensive care unit (ICU) admission, and 3% required mechanical ventilation.<sup>1</sup> Pregnant women were more likely than non-pregnant women of a similar age to have these complications of COVID-19. Pre-existing comorbidities, maternal age  $\geq 35$  years, high body mass index, and non-white ethnicity have been identified as risk factors for severe COVID-19 during pregnancy. Compared with pregnant women without COVID-19, pregnant women with COVID-19 have higher preterm birth rates and neonates requiring neonatal ICU admission. Differences have been observed between HICs and LMICs from a limited number of studies, with a significant increase in maternal mortality in LMICs compared to HICs.<sup>2</sup>

As part of the WHO "UNITY" studies (<https://tinyurl.com/unitymaternalneonatalprotocol>), the COVID-19

and Pregnancy Cohort Study aims to assess whether SARS-CoV-2 infection in pregnancy increases the risk of adverse outcomes; to estimate the risk of mother-to-child transmission of SARS-CoV-2; to describe viral presence and persistence in bodily fluids; and to characterize the clinical course and disease spectrum of COVID-19 during pregnancy. The study will follow women with and without confirmed SARS-CoV-2 infection during pregnancy until six weeks postpartum. Study outcomes will include maternal and pregnancy (e.g. miscarriage, preterm birth, maternal morbidity), perinatal (e.g. stillbirth, NICU admission), neonatal (e.g. infection, morbidity, mortality), postpartum (e.g. infection, bleeding, transmission of SARS-CoV-2), and COVID-19-specific outcomes (e.g. hospitalization, acute respiratory distress syndrome, maternal mortality).

The study is currently planned to take place at 56 sites across 14 countries, mostly LMICs, with the aim to enroll 16,470 pregnant women with almost 7000 women in the exposed (SARS-CoV-2-infected) group, between April/May 2021 and the end of 2022. Data analysis will include country-specific and pooled analyses supported by collaborating partners.

### Pregnancy cohort study countries

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- AMR: Argentina, Brazil, Chile
- AFR: Burkina Faso, Ghana, Kenya, Malawi
- EMR: Pakistan, IR Iran, Tunisia
- SEAR: Myanmar
- EUR: Spain, Georgia
- WPR: Philippines

56 sites  
14 countries

16,470 Women

April/May 2021

Enrollment end  
2022

Prelim. data  
Dec. 2021

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Twitter @HRPresearch



Dr Sami Gottlieb, Medical Officer in Sexual and Reproductive Health and Research at the World Health Organization then discussed COVID-19 vaccines and the WHO COVID-19 and Pregnancy Cohort Study, starting with a summary the rollout of COVID-19 vaccines to date. As of April 10, 2021, over 775 million doses had been administered, with campaigns started in 170 countries. However, vaccine policies for pregnant women vary worldwide, from strong recommendations in countries such as New Zealand and Ireland, to prohibition in Russia and several Asian, African, and South American countries. The variation in recommendations stems from the exclusion of pregnant women and thus lack of data on safety and efficacy from the initial clinic trials of COVID-19 vaccines. Interim recommendations have been based on considering the increased risk of severe disease in pregnancy, likely similar vaccine effectiveness, and the fact that the mechanisms of action and developmental and reproductive toxicology (DART) data in animals do not highlight any specific concerns for some of the vaccines (not available for all yet). However, more data on safety and effectiveness are needed to guide policy and reassure pregnant women and their care providers.

The WHO COVID-19 and Pregnancy Cohort Study is being adapted to collect data on vaccination of pregnant women and to consider how roll-out of COVID-19 vaccines potentially affects the study protocol and how the study might be adapted to evaluate vaccine-related questions. Such questions include: vaccine safety, immunogenicity and possibly vaccine effectiveness during pregnancy, vaccine coverage, and women's attitudes and beliefs related to COVID vaccination during pregnancy. In addition to collecting maternal and neonatal data following vaccination in

the prospective study, Dr Gottlieb mentioned the new pregnancy module in the WHO COVID-19 vaccine safety surveillance manual (soon to be released at: <https://www.who.int/publications/i/item/10665338400>) and highlighted the need for active and passive surveillance systems for assessment of adverse events following immunization (AEFIs), particularly during pregnancy. The WHO has also released guidance on best practice for evaluation of vaccine effectiveness ([https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccine\\_effectiveness-measurement-2021.1](https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccine_effectiveness-measurement-2021.1)), and cohort studies in pregnancy could be used for this purpose, although the type of analysis will depend on potential biases and vaccine coverage among pregnant women. One of the challenges for evaluation is that the WHO Pregnancy Cohort Study is using anti-spike protein serology tests to assign women to exposure groups, and most COVID-19 vaccines also elicit anti-spike protein antibody responses. Serology tests which include anti-nucleocapsid protein antibodies may help to distinguish previous natural infections from vaccine-acquired antibodies, although inactivated vaccines also elicit anti-nucleocapsid antibodies. Despite the challenges, the WHO COVID-19 and Pregnancy Cohort Study and similar studies offer opportunities to address crucial data gaps, particularly for LMICs. Further details of the WHO Pregnancy Cohort Study are available from <https://tinyurl.com/pregnancycohortstudy>.

## References

4. Allotey J, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*. 2020 Sep 1;370:m3320.
5. Chmielewska B, et al. Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis. *Lancet Glob Health*. 2021 Mar 31:S2214-109X(21)00079-6.

## COVID-19 VACCINES IN PREGNANCY: ARE RANDOMIZED CONTROLLED TRIALS STILL FEASIBLE, ETHICAL, OR NECESSARY?

Dr Geeta Swamy, Professor of Obstetrics and Gynecology at Duke University reiterated the increased risk of severe disease in pregnant women, and provided an update about what we already know about COVID-19 vaccines in pregnancy. Data are available from 22 pregnant women who were inadvertently exposed to COVID-19 vaccine in clinical trials (12, 6, and 4 for Pfizer, Moderna, and Janssen Phase 3 trials, respectively, to date), together with no concerns raised

from DART studies. Data in non-pregnant adults from the Phase 3 clinical trials of the mRNA vaccines demonstrated 94–95% efficacy following receipt of the second dose, and the single dose viral vector Janssen COVID-19 vaccine showed 67% efficacy against moderate/severe illness, and 93% efficacy against hospitalization 14 days after vaccination.<sup>1</sup> Mild side effects were reported for all three vaccines, with fever the least common solicited reaction:<sup>1</sup>

	Injection Site Reactions	Fatigue	Chills	Muscle Pain	Joint Pain	Headaches
<b>Moderna</b>	91.6%	68.5%	43.4%	59.6%	44.8%	63%
<b>Pfizer-BioNTech</b>	84.10%	62.90%	31.90%	38.30%	23.60%	55.10%
<b>Janssen Biotech Inc.</b>	48.6%	38.2%	N/A	33.2%	N/A	38.9%

*\*Fever was the least common side effect reported; see text above for data on frequency of fever*

Currently, the CDC's Advisory Committee on Immunization Practices (ACIP) and the American College of Obstetricians and Gynecologists (ACOG) recommend that COVID-19 vaccines should not be withheld from pregnant women and should be offered to lactating women.<sup>1</sup> While a conversation with a clinician may be helpful, it should not be required prior to vaccination, as this may cause unnecessary barriers to access. Pregnancy is listed as a high-risk condition for increased risk of severe illness, and hence in the US, pregnant women are included in stage 4 of vaccination prioritization, after healthcare workers, long-term care staff and residents, adults ≥65 years, and frontline essential workers. At the time of the meeting, 77,960 people had reported pregnancy in the V-safe post-vaccination health checker, and 4,218 had enrolled in the V-Safe COVID-19 vaccine pregnancy registry (<https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafepregnancyregistry.html>). In lieu of data from placebo-controlled trials, analysis of pregnancy and infant outcomes of women included in the V-safe pregnancy registries showed no substantial differences to background rates (see US country case study below).<sup>2,3</sup> Dr Swamy concluded with an update

on COVID-19 studies in pregnant women. Pfizer started a Phase 2/3 randomized controlled trial in pregnant women in Feb 2021 (NCT04754594) and Janssen have filed an observational study protocol (NCT04765384) but are not yet recruiting. The Centers for Disease Control and Prevention (CDC) Clinical Immunization Safety Assessment Group are also starting an observational study in April 2021 (NCT04826640), and National Institutes of Health (NIH) have a protocol in development, which is likely to be an observational study.







## References

1. The American College of Obstetricians and Gynecologists. Vaccinating Pregnant and Lactating Patients Against COVID-19. *Practice Advisory*, December 2020. <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/12/vaccinating-pregnant-and-lactating-patients-against-covid-19>
2. National Center for Immunization & Respiratory Diseases. COVID-19 vaccine safety update. Advisory Committee on Immunization Practices (ACIP) Meeting, March 1, 2021. <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/05-covid-Shimabukuro.pdf>
3. Shimabukuro TT, et al. Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. *N Engl J Med*. 2021 Apr 21. <https://doi:10.1056/NEJMoa2104983> (e-pub ahead of print).

## COVID-19 VACCINE CONSTRUCTS AND PLATFORMS SUITABLE FOR PREGNANT WOMEN

Dr Barney Graham, Deputy Director of the Vaccine Research Center at the National Institute of Allergy and Infectious Disease (NIAID) and NIH provided background on the structural biology of the COVID-19, and how it informed the design of currently authorized vaccines. The structure of the SARS-CoV-2 spike protein was determined in 2016 and a year later researchers managed to stabilize the protein in its prefusion conformation by substituting two proline amino acids at the top of the central helix (S-2P)! This inhibits rearrangement of the S2 fusion machinery and also improves expression levels in transfected cells, which is advantageous for gene-based delivery of vectors. The spike protein is the antigen used in most of the candidate vaccines worldwide and is used in all the vaccines being tested in US Phase 3 studies. mRNA vaccines use a modified nucleotide mRNA

which reduces TLR7, TLR3, and RIG1 signaling thereby reducing the type-I interferon production and inflammation relative to other mRNA approaches.<sup>2</sup> The Janssen vaccine uses an adenovirus 26 vector, which is a species type D adenovirus, whereas the AstraZeneca vector is a chimpanzee-derived species E type adenovirus. The Novavax protein-based vaccine uses a prefusion stabilized spike as a rosetted nanoparticle. All of these vaccines, with the exception of the AstraZeneca vaccine, use the S-2P stabilized version of the spike protein. Dr Graham then provided an overview of the six vaccines which are being evaluated in the US, including details of the construct type, current development stage, dates of EUA (where appropriate), DART study status, and current pregnancy/lactation exposure data:

						
<b>Platform / Design</b>	mRNA: encodes 2P-Spike SARS-CoV-2	mRNA: encodes 2P-Spike, TM	Replication incompetent Ad26; 2P-Spike; ΔF; TM	Replication incompetent ChAdOx1; Spike; ΔF; TM	BacV trimeric 2P-Spike, ΔF;TM + Matrix M	BacV trimeric 2P-Spike, ΔF + AS03
<b>Dose / Schedule</b>	2 doses 30 μg (0, 21 days)	2 doses 100 μg (0, 28 days)	1 dose 5 x 10 <sup>10</sup> vp	2 doses 5 x 10 <sup>10</sup> (0, 28 days)	2 doses 5 μg + Matrix M (0, 21 days)	5/15 μg + AS03 (0, 21 days)
<b>Current Status</b>	EUA Approved Dec-20	EUA Approved Dec-20	EUA Approved-Mar-21	Ph3 US / International Recruited	Ph3 US / International Recruited	Ph2
<b>DART</b>	Completed Dec-20	Completed Dec-20	Completed Jan-21	Started Nov-20	Completed Feb-21	Started Nov-20
<b>Current Pregnancy / Lactation Exposure</b>	23 exposed in Ph3 / approx. 30,000 by EUA	13 exposed in Ph3 / approx. 30,000 by EUA	1,613 exposed in Ph3 / 150 lactating women	NO; Platform tested in adults	Baculovirus Platform YES; Adjuvant tested in adults	Baculovirus Platform YES; Adjuvant in commercial vaccine (Pandemrix, Arepanrix)
<b>Upcoming Plans</b>	Observational Study in Pregnancy: TBC Pregnancy Registry	Observational Study in Pregnancy: TBC Pregnancy Registry	Platform proven safe for use in pregnancy	TBD	TBD	TBD
<b>Other sources of data</b>	<ul style="list-style-type: none"> <li>Spontaneous report to VAERS</li> <li>Enrollment / follow up of vaccinated pregnant women in V-Safe (about 78,000)</li> <li>CDC sponsored pregnancy registry (approx. 2000)</li> <li>Vaccine Safety Datalink epidemiological study on pregnancy/fetal outcomes</li> </ul>			<ul style="list-style-type: none"> <li>CDC sponsored observational study in pregnancy (CISA)</li> <li>CDC Birth Defects Study (BD-STEPS)</li> <li>DMID / VTEU Observational study in pregnancy and newborns (Immunity and safety)</li> </ul>		

Of the six vaccines, data from inadvertent exposure and receipt under EUA are available for Pfizer and Moderna vaccines, and 1,613 pregnant women and 150 lactating women have received the Janssen vaccine in a Phase 3 study. No data are available for the AstraZeneca, Sanofi/GSK, or Novavax vaccines, however, the AstraZeneca platform has been tested in non-pregnant adults, and data are available for subunit proteins made in the baculovirus platform in large maternal immunization studies, which forms the basis of the other two vaccines. While some vaccines/vaccine platforms may end up with preferential designation for use in women of child-

bearing age (e.g. due to very rare thrombotic events), the overall relative risk of severe disease from COVID-19 versus very rare vaccine side effects should be kept in mind where vaccine choice is not available.

### References

- Pallesen J, et al. Immunogenicity and structures of a rationally designed prefusion MERS-CoV spike antigen. *Proc Natl Acad Sci USA*. 2017 Aug 29;114(35):E7348-E7357.
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## Q&A SESSION

- ▶ **The question of data needs for robust assessment of different vaccines for pregnant and lactating women was posed in the context of evolving safety data which may impact recommendations.** Vaccine recommendations for pregnant women are likely to be in sync with CDC and FDA regulations, although as pregnant women are already at increased risk of thrombotic events, and platelet dysfunction is seen in hypertensive disorders of pregnancy, it may be the case that some vaccines receive a preferential designation for use in pregnant women. However, this remains to be determined. These events are very rare and the relative risk of the vaccine versus COVID-19 infection should be considered.
- ▶ **The second topic discussed was the impact of DART study findings on recommendations for COVID-19 vaccines during pregnancy.** While DART studies are focused on short-term outcomes, many people are asking questions about the long-term effects, despite vaccines not being known to cause long-term side effects. However, it remains difficult for physicians to provide clear evidence to patients based on the available data. Once more outcome data are available from pregnancy registries this should help diminish fears of potential long-term effects in pregnant women and guide revisions of recommendations.

## DISCUSSION

There then followed a panel discussion, moderated by Dr Ajoke Sobanjo-ter Meulen, with panelists Dr Alejandro Cravioto, Chair, WHO SAGE and Professor of Medicine at the Universidad Nacional Autónoma de México, Dr Judith Absalon, Senior Medical Director at Pfizer, and Dr Ushma Mehta, Senior Researcher at the University of Cape Town, South Africa.

### The main discussion points were:

- SAGE working group are evaluating recommendations of COVID-19 vaccines to pregnant and lactating women based on ever-evolving data. Initial recommendations were based on the limited safety data available at the time, and the type of vaccine construct used. The working group is currently focusing on the following three factors: 1. safety and any new adverse effects reported; 2. the impact on the vaccination on the mother and protection of the infant post-birth; 3. the impact of vaccination on antibody transfer in breast milk, which will provide information on how to use pediatric vaccines when they become available.
- Based on the known safety of the mRNA vaccines in the US, women who become pregnant after receiving the first dose of a two-dose vaccine schedule should be given the second dose as planned.
- Vaccination during the 1st trimester: there does not seem to be a higher likelihood of severe disease at any particular point during pregnancy. V-safe data shows no indication of any increases in miscarriages and no reason to expect any increased rates of malformations.
- Thrombotic events have not yet been reported for mRNA vaccines, but allergic reactions have, albeit they are infrequent.
- Key learnings from Pfizer's maternal immunization program:
  - Three programs ongoing: Group B Streptococcus, respiratory syncytial virus, and COVID-19.
  - Maternal immunization studies primarily focus on safety and planning and very different from other vaccine trials, as they also need to include infant outcomes.
  - Need background rates of maternal and infant outcomes to see if an event is more frequent after vaccination, although these data are often not available in LMICs.
  - Ongoing Phase 2/3 placebo-controlled COVID-19 vaccine study in pregnant women primarily focusing on safety and immunogenicity but is powered to assess efficacy based on attack rates. The study started in February once finalized DART data were available. Pfizer vaccine still seems to have high efficacy against SARS-CoV-2 variants. There are no current plans to specifically evaluate the efficacy of the vaccine against variants in pregnant women, but the study is being performed worldwide so will likely include participants who live in areas where variants are circulating.

- There is a clear need for post-marketing / post-implementation safety surveillance worldwide. The WHO has developed guideline on vaccine safety surveillance following maternal immunization (<https://cdn.who.int/media/docs/default-source/vaccine-safety/covid-vaccine-safety-in-pregnancypublicconsultation01apr2021.pdf>). Active and passive surveillance systems are in existence for routine vaccinations but these need to be adapted for maternal immunizations as pregnant women generally access different healthcare providers (e.g. antenatal and postnatal care).
- Passive surveillance systems exist globally but don't allow assessment of causality, so we ideally need active surveillance in LMICs too. These could utilize existing systems e.g. pregnancy exposure registries for anti-retroviral (ART) drugs. These registries can also provide useful data on concurrent control groups

in regions where no data on background rates of pregnancy and infant outcomes are available. Data from nested case control studies and linkage studies can also be used for these purposes.

- Communication about COVID-19 vaccines in LMICs is key to uptake.
- Suggested immediate next steps for collection of safety data in LMICs are to create platforms to exchange information and methodologies for the assessment of vaccine safety in pregnancy; to develop safety surveillance systems that work across programs and integrate these into routine care; and to focus on cross-cutting collaborative projects and communications.
- In most LMICs the regulatory agencies and immunization programs already work collaboratively on AEFI case reports.

## SESSION 2: COVID-19 VACCINE DISTRIBUTION, ADMINISTRATION, AND UPTAKE IN PREGNANT WOMEN

Four country case studies then followed detailing the experience and challenges of COVID-19 vaccination in pregnant and lactating women.

### COUNTRY CASE STUDY 1: US

Dr Denise Jamieson, Chair, Department of Obstetrics and Gynecology, James Robert McCord Professor at Emory University School of Medicine provided an update on the COVID-19 vaccination experience in the US. She outlined the steps required for COVID-19 vaccines to be able to reach pregnant women, including post-EUA guidance from appropriate professional organizations, such as ACOG and the Society for Maternal-Fetal Medicine (SMFM). Under Advisory Committee on Immunization Practices (ACIP)

recommendations for prioritization of vaccination, pregnant women are listed under Phase 1c recipients, as "persons aged 16–24 with high-risk conditions". ACOG recommended that pregnant and lactating women should be offered COVID-19 mRNA vaccines and that persons planning to become pregnant should complete the vaccination series prior to conception. Dr Jamieson also presented information on inadvertent exposure in clinical trials and analysis of the V-Safe data (also see presentation by Dr Geeta Swamy above).

### V-safe pregnancy registry outcomes of interest in COVID-19 vaccinated pregnant women as of February 18, 2021\*

Outcomes	Background rates*	V-safe pregnancy registry overall
<b>Pregnancy outcome</b>		
Miscarriage (<20 weeks)	26%	15% <sup>†</sup>
Stillbirth (≥ 20 weeks)	0.6%	1%
<b>Pregnancy complications</b>		
Gestational diabetes	7-14%	10%
Preeclampsia or gestational hypertension <sup>§</sup>	10-15%	15%
Eclampsia	0.27%	0%
Intrauterine growth restriction	3-7%	1%
<b>Neonatal</b>		
Preterm birth	10.1%	10%
Congenital anomalies <sup>‡</sup>	3%	4%
Small for gestational age <sup>^</sup>	3-7%	4%
Neonatal death	0.38%	0%

\* Sources listed on slide 33; <sup>†</sup> 93% of these were pregnancy losses <13 weeks of age; <sup>§</sup> Pre-eclampsia or gestational hypertension diagnosed during pregnancy and/or during delivery; <sup>‡</sup> Congenital anomalies (overall) diagnosed after delivery only; <sup>^</sup> Birthweight below the 10th percentile for gestational age and sex using INTERGROWTH-21st Century growth standards

## Reference

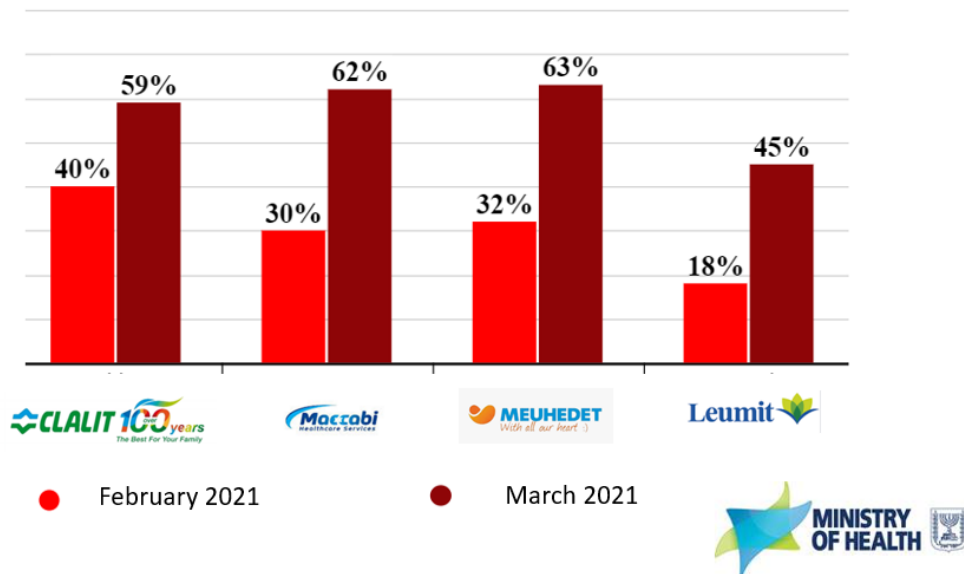
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## COUNTRY CASE STUDY 2: ISRAEL

Prof Orna Diav-Citrin, Chief Physician of the Israeli Teratology Information Service provided background on the population demographics in Israel, where approximately one third of the 9 million people are children. Israel has the highest fertility rate in HICs, with approximately 180,000 live births annually.<sup>1</sup> Membership of one of the four official health insurance organizations ("HMOs") is compulsory so data on vaccination rates are available from each of these four organizations. The Israeli advisory committee for COVID-19 vaccination recommends vaccination of women planning a pregnancy at increased risk for severe disease and lactating women, and advise that it should not be withheld from pregnant women, especially if they are exposed to COVID-19 patients at work. Dr Diav-Citrin outlined the position paper

from the main professional organizations, which states that, further to that already outlined, vaccination is recommended in the 2nd and 3rd trimester; women who conceive after the first dose should receive the 2nd dose as normal; women in the 1st trimester can choose to defer vaccination to the 2nd trimester; the use of antipyretics is recommended as fever is a potential adverse event; and a week interval between vaccination and amniocentesis is recommended to avoid adverse events which may be interpreted as amniocentesis complications.<sup>2</sup> She then presented data from the individual HMOs on the number of pregnant women who have received a COVID-19 vaccination. Across the HMOs, 45–63% of pregnant women had received a COVID-19 vaccine by March 2021, mostly in the 2nd and 3rd trimesters:

### Percentage of pregnant women vaccinated in February and March 2021



Data from the Ministry of Health on COVID-19 infection during pregnancy showed that of the 11,065 women with confirmed infection in pregnancy by 12th April 2021, 10.6% were hospitalized, 1.3% had severe COVID, and 5 died. These included women without pre-existing conditions. Negative media stories highlighting the risk to pregnant women and their fetuses and babies has resulted in increasing rates of vaccine uptake although circulation of misinformation about COVID-19 and vaccination remains an issue. Overall, the small, relatively young population, together with centralized systems, coordination between stakeholders, special funding for timely contraction of vaccines, and well-tailored outreach

programs have contributed to Israel's rapid roll-out of COVID-19 vaccines.<sup>3</sup>

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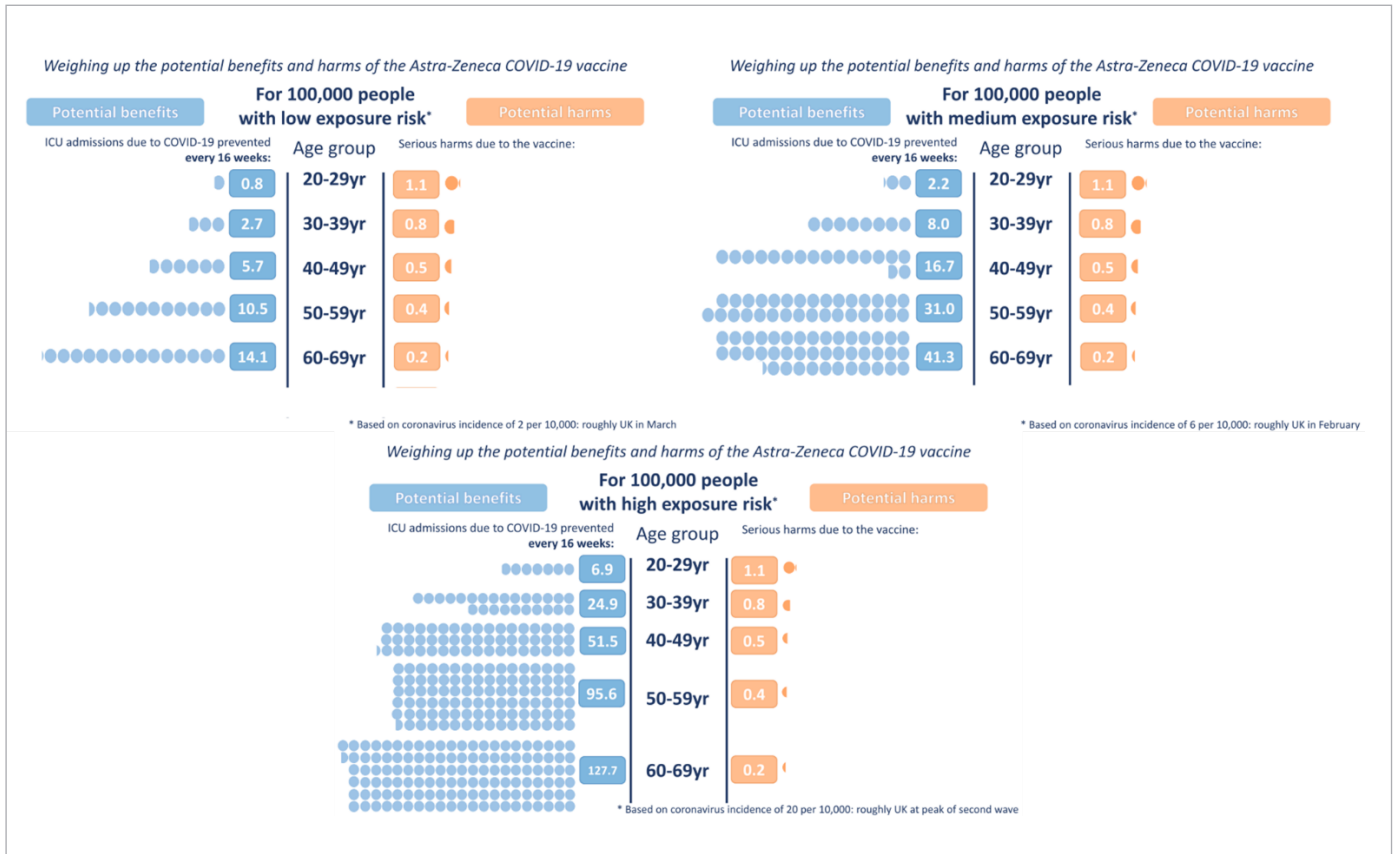
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2. Ministry of Health. Vaccinating Women who are Planning a Pregnancy, Pregnant or Breastfeeding with the COVID-19 Vaccine – Clarification. Available from: <https://www.gov.il/en/departments/news/28012021-03>
3. Rosen, B., Waitzberg, R. & Israeli, A. Israel's rapid rollout of vaccinations for COVID-19. *Isr J Health Policy Res* 2021; 10, 6

## COUNTRY CASE STUDY 3: UK

Dr Asma Khalil, Professor of Fetal Medicine at St George's Hospital University of London presented details COVID-19 vaccination in pregnant and lactating women in the UK. She began by presenting the results of a survey from the Royal College of Obstetricians and Gynecologists which investigated reasons for accepting or declining vaccination. The most common reasons for women accepting the vaccine were wanting to protect themselves, followed by their baby, their family and friends, and vulnerable people from COVID-19. The most common reasons for declining vaccination were concerns that the vaccine could harm themselves or their baby, or they wanted to see more safety data in pregnancy first. The survey also identified midwives, obstetricians, and general practitioners (GPs) as the people pregnant women would most want to speak to about the benefits and risks of COVID-19 vaccination. Currently, three COVID-19 vaccines (Pfizer, Moderna, and AstraZeneca) are available in the UK. The Joint Committee on Vaccination and Immunization (JCVI) advice on who should receive a COVID-19 vaccine in pregnancy has changed over time, but currently vaccination is recommended for pregnant women at high-risk of severe COVID-19 (e.g. comorbidities, high BMI, advanced maternal age, or are in the third trimester) or at high-risk of exposure (e.g. healthcare workers, crowded living conditions, etc). The same risk groups apply to lactating women. To help pregnant women decide whether to take a COVID-19 vaccine, a number of professional organizations have developed plain language resources which are freely available online (e.g. <https://www.rcog.org.uk/globalassets/>

[documents/guidelines/2021-02-24-combined-info-sheet-and-decision-aid.pdf](#)). While the JCVI advises that women do not need a pregnancy test before vaccination, women may wish to wait until the 2nd trimester to be vaccinated.<sup>1</sup> However, as pregnant women are at higher risk in the 3rd trimester, women may wish to be vaccinated earlier in their pregnancy. In terms of safety surveillance, the UK Obstetric Surveillance System (UKOSS) and UK Teratology Information Service (UKTIS) are researching the characteristics of pregnant women vaccinated in February and March 2021 and maternal/infant outcomes, with a historical comparison of outcomes to a group of women with similar high-risk characteristics. Other safety surveillance in place to monitor outcomes in vaccinated pregnant women include the Medicines and Healthcare products Regulatory Agency (MHRA) yellow card monitoring system and Public Health England's Inadvertent Vaccination in Pregnancy monitoring scheme. Dr Khalil then provided brief details of COVID-19 vaccine trials in pregnant women, including the Janssen HORIZON study, which is aiming to include 400 women, with about 50 from the UK, the Pfizer study, where 135 women will be enrolled in the UK, and a prospective cohort study in Scotland. Dr Khalil finished by discussing thrombosis and thrombocytopenia observed after vaccination with the AstraZeneca vaccine.<sup>2,3</sup> These are extremely rare conditions with no known risk factors. In the UK, benefits versus harms modelling has resulted in the vaccine being restricted to people ≥ 30 years of age, based on the current low exposure risk.





Women taking combined hormonal contraceptives should also continue taking these and may consider switching to a different contraceptive method if they want to not be at increased risk of thrombosis in the future.

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## COUNTRY CASE STUDY 4: INDIA

Dr Narendra Kumar Arora, Executive Director at the INCLEN Trust International, presented the final case study of the meeting. He began with the background of maternal immunization in India, with maternal tetanus vaccination introduced into the Universal Immunization Programme in 1983. COVID-19 vaccine acceptance among pregnant women and mothers of young children is very high in India (>80%), and considerably

higher than many HICs.<sup>1</sup> Despite a willingness to be vaccinated during pregnancy, uptake of other vaccines (e.g. influenza vaccine) during pregnancy is low. In a survey of 1000 pregnant women in North India,<sup>2</sup> none had been offered or received an influenza vaccine, with this poor uptake mainly rooted in misperceptions among treating physicians:

Perception	Likert score <sup>b</sup>				
	1	2	3	4	5
Vaccines cause unknown illness	0	20 (22.2)	56 (62.2)	14 (15.6)	0
Vaccines weaken immune system	0	2 (2.2)	39 (43.3)	49 (54.4)	0
Adverse effects are under-reported	2 (2.2)	64 (71.1)	24 (26.7)	0	0
Vaccine programs are motivated by profit	45 (50.0)	34 (37.8)	11 (12.2)	0	0
Vaccine programs are generally beneficial	55 (61.1)	35 (38.9)	0	0	0

**Perception of obstetricians toward influenza vaccination (n = 90)**  
**Likert scale: 1, strongly agree; 2, agree; 3, neither agree nor disagree; 4, disagree; 5, strongly disagree.**

In a mixed method study across three countries (Spain, Italy, and India),<sup>3</sup> the one of main drivers of maternal immunization decision making was political priority, together with mortality rates, cost, and disease burden. In order to assess background rates of pregnancy outcomes, a prospective surveillance study was performed across seven countries which included collection of vaccination status.<sup>4</sup> Although vaccination status was known for 92% of mothers, none of the cases assessed were classified to level 1 of diagnostic certainty, mostly due to lack of information on the timing or batch of vaccine. India has an integrated digital platform for monitoring distribution and safety of COVID-19 vaccines (Co-WIN). Current guidelines in India do not recommend COVID-19 vaccination of pregnant and lactating women, however, the safety monitoring platform is ready. One positive to come

out of the COVID-19 pandemic is the development of this elaborate surveillance system which can be easily adapted to include surveillance of pregnant women.

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1. Skjefte M, Ngirbabul M, Akeju O, et al. COVID-19 vaccine acceptance among pregnant women and mothers of young children: results of a survey in 16 countries. *Eur J Epidemiol.* 2021;36(2):197-211.
2. Koul PA, Bali NK, Ali S, Ahmad SJ, Bhat MA, Mir H, Akram S, Khan UH. Poor uptake of influenza vaccination in pregnancy in northern India. *Int J Gynaecol Obstet.* 2014 Dec;127(3):234-7.
3. Privor-Dumm L. Determinants of policy and uptake of national vaccine programs for pregnant women: results of mixed method study from Spain, Italy, and India. *Hum Vaccin Immunother.* 2021 May 4;17(5):1474-1482.
4. Anke Stuurman VE, et al, Global Vaccine Safety Multi Country collaboration project measuring risks of early childhood morbid conditions and assessing standardized methods. 2021.

## Q&A

- ▶ **The difference between V-safe and pregnancy registries was discussed.** V-safe is the voluntary surveillance system for anyone who has received a COVID-19 vaccine in the US (<http://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafe.html>). The system will ask the vaccine recipient if they are pregnant, and provide the opportunity to enroll in a pregnancy registries. There are substantially fewer pregnant women enrolled in the registry than in V-safe as this requires additional contact from someone at the CDC.
- ▶ **A discussion of safety surveillance findings from Israel then followed.** In over 50,000 women, no major adverse effects have been reported and Israel is primarily referencing the US safety surveillance through the comprehensive V-safe system.

## DISCUSSION

A panel discussion, moderated by Dr Flor Munoz, then followed with panelists Dr Esperança Sevens, Associate Professor of Clinical Pharmacology at Eduardo Mondlane University, Ayoada Alakija, Co-chair of the COVID-19 African Vaccine Delivery Alliance, and Dr Heidi Larson, Director and Founder of The Vaccine Confidence Project.

### The main points raised in the discussion were:

- Experience in Mozambique
  - As of March 30, 2021, Mozambique had cumulative COVID-19 totals of 67,446 cases and 772 deaths
  - As other countries, Mozambique started contacts with COVAX initiative and other bilateral initiatives in order to get vaccines to the country
  - Supply of vaccines under the COVAX scheme is limited as there are not enough vaccines for all countries to receive them at the same time, therefore Mozambique had to prioritize which groups would receive the first batch of vaccine – this included healthcare professionals, patients with co-morbidities, and older people
  - In LMICs, such as Mozambique, most healthcare professionals are women of childbearing age, however, pregnant women were not included in first group to be immunized as there was no information from clinical trials on safety and efficacy in this group at the time of the decision, it was unsure which vaccine would be delivered and whether it would be suitable for pregnant women, and the burden of disease in pregnant women was low at the time of the discussions.
  - Up to March 22, 2021, a total of 27 pregnant women were hospitalized with COVID-19, 2 of whom were admitted to ICU and 3 of whom died. While testing rates are low, even a correction factor of 100x still indicates low rates. Despite these low rates, vaccination remains important because of the potential of future waves and new variants
- A presidential decree was granted to remove pregnant women from frontline healthcare work to lower their risk
- The decision is being reconsidered for when the second batch of vaccine becomes available
- During the first phase, 82.5% of the 60,000 healthcare workers were vaccinated. Pregnant and lactating women, and people with active COVID-19 infection (or positive test within 14 days) were not eligible to receive the vaccine and are included in the 17.5% who were not vaccinated, unless they later received the vaccine
- Mozambique has received the AstraZeneca from COVAX and now needs to address hesitancy over safety and lack of vaccine confidence for the next round of the vaccination campaign
- The importance of vaccine equity was highlighted as without equity there is no confidence in receiving the vaccine.
- Currently in many LMICs we don't know the effects of COVID-19 vaccines as there are no vaccines available
- HICs have options for which vaccines to give to which population based on suitability and safety data. However, in general, the AstraZeneca vaccine is the only option available in LMICs, and the rollout pause

and restriction to older people in some HICs has led to mixed messaging and reduces confidence in vaccines.

- Pregnant and lactating women have been somewhat forgotten in development of COVID-19 vaccines, hence there are still only limited safety data available
- Taking pregnant and lactating women out of frontline healthcare is not an option for many countries, as women of child-bearing age make up nearly all of this workforce
- Burden of COVID-19 disease data on pregnant women is also lacking in LMICs. We don't yet know the effects of COVID-19 on pregnancy and gestation in general
- LMICs also have very little access to diagnostics and therapeutic options, and the seemingly low burden of disease may be due to lack of testing. For example, swabbing of bodies in Zambia at the end of 2020 indicated over a third were COVID-19 positive and yet Zambia reported very few cases of COVID-19
- More research and data are needed for pregnant and lactating women in general in LMICs, especially including other impacts of COVID-19, such as increases in teenage pregnancies during lockdowns
- In general, pregnant women are hyper-alert to risk and all the information provided via media and social

media channels make it hard for them to navigate the risks of COVID-19 and vaccination.

- In addition to scientific risk, other factors should be considered e.g. advice from religious leaders, political decisions, belief in the system and the importance of vaccination.
- Pregnant women in countries such as India are much more willing to have a vaccine in pregnancy than women in HICs, however, hesitancy among healthcare workers needs to be overcome to allow pregnant women to receive vaccines.
- The experience during the COVID-19 pandemic will determine people's trust and confidence in vaccines and the system for the future. If pregnant women feel left out and ignored, they will be less willing to engage in the future.
- Key priorities for research should include 1. understanding what pregnant women need to know and from which trusted sources of information to make COVID-19 vaccines more acceptable and accessible; 2. collecting of specific data on the burden of COVID-19 and the safety of COVID-19 vaccines in pregnancy; and 3. establishing effective pharmacovigilance and harmonization of data collection and data sharing

## MEETING CLOSE

Drs Ajoke Sobanjo ter-Meulen and Flor Munoz then thanked all the attendees and presenters and closed the meeting.

## APPENDIX

### Webinar Data

**Total number of registered attendees including speakers and organizers:** 361

**Total number of registered attendees excluding speakers and organizers:** 341

**Institutions attending:** 171\*

**Developers attending:** 50

*\*including funders, developers, regulators, universities and research centers*

### List of Attending Developers

Advaccine	Fiocruz	Oxford Vaccine Unit
Affinivax	IAVI	Pfizer, Inc.
Altimune	Icosavax, Inc.	Sanofi Pasteur
Astrazeneca	Immuno-Vax LLC	Seqirus, Inc.
Beijing Stemexcel Technology Co., Ltd	Indian Immunologicals Limited	Serum Institute of india Pvt. Ltd.
Bethesda Biologics Consulting, LLC	Inovio Pharmaceuticals Inc	Sinovac
Bharat Biotech International Limited	Instituto Butantan	SK Bioscience
Biological E Limited	International Vaccine Institute	Themis Bioscience
BioNet-Asia	Instituto Butantan	Vabiotech
BioNTech	J&J	Valneva
BIRAC	Janssen Vaccines	Vaxart
BravoVax	Jhpiego/JHSPH	Walvax Biotechnology Co., Ltd.
Cadila Healthcare Limited	Latham Biopharm Group	Zerun Bio
CanSino Biologics Inc.	Medigen Vaccine Biologics Corp.	Zydus
Clover Biopharma	Merck & Co., Inc.	
Codagenix Inc.	Moderna	
Curevac	Novavax	
EpiVax Therapeutics	Oswaldo Cruz Foundation	