NISEC 1 meeting

Oxford

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Preg-CoV study

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Preg-CoV

1. background and aim
2. design and recruitment
3. preliminary results
4. challenges
5. study potential

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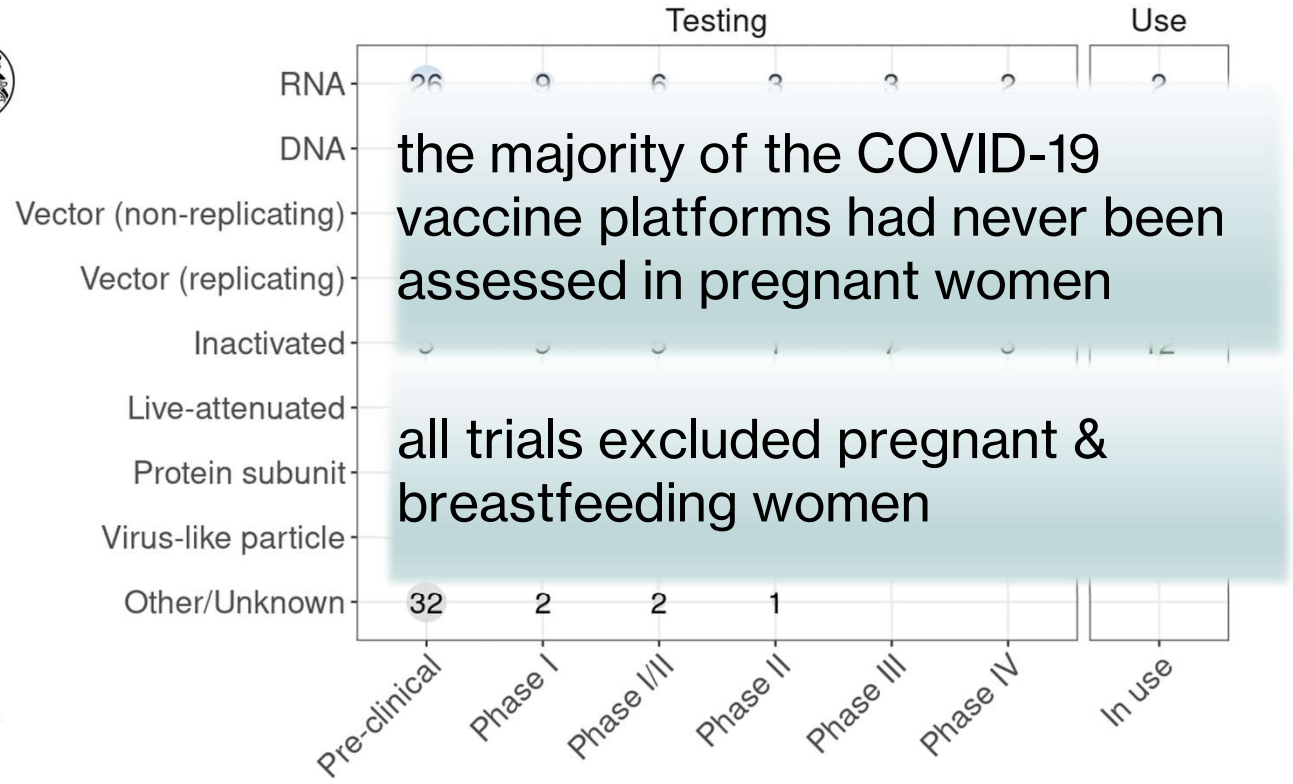
COVID-19 vaccination in pregnant women



the majority of the COVID-19 vaccine platforms had never been assessed in pregnant women

all trials excluded pregnant & breastfeeding women

Maternal COVID-19 vaccination

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

From: Are COVID-19 vaccines safe in pregnancy?

Vaccine type	Control group			Vaccinated group			Ref.
	Participants	Pregnancies	Miscarriages (rate)	Participants	Pregnancies	Miscarriages (rate)	
Pfizer/BioNTech	18,846	12	1 (8%)	18,860	11	0 (0%)	4
Moderna	15,170	7	1 (14%)	15,181	6	0 (0%)	5
AstraZeneca	5,829	9	3 (33%)	5,807	12	2 (17%)	6

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Other information needed

- no clinical trial data available
- ongoing observational research, addressing a range of important aspects regarding safety and immunity
- further data required:

optimal dosing intervals for immunisation during pregnancy to protect mothers & babies

reactogenicity & safety of all available COVID-19 vaccines in pregnant women

need for and reactogenicity of **additional doses** with each pregnancy

Co-administration with other routine vaccines...

fractional doses of COVID-19 vaccines in pregnant women

- it is important that such data are gathered in a **systematic and controlled manner**

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Maternal COVID-19 vaccine trials

Trials involving pregnant women

Show 20 entries

Phase	Vaccine	Platform	N	Age (years)	N doses	Rand.	Design	Location
Phase II	BNT162/mRNA-1273/ChAdOx1-S/NVX-CoV2373	RNA/Vector (non-replicating)/Protein subunit	800	18–45 (pregnant)	2	Yes	Single-blind	UK
Phase II	Janssen Ad26.COV2.S	Vector (non-replicating)	400	18–45 (pregnant)	1 or 2	Yes	Open-label	USA, Brazil, South Africa
Phase II/III	BioNTech BNT162 (b2)	RNA	343	≥18 (pregnant)	2	Yes	Observer-blind	USA, Brazil, South Africa, others
Phase IV	BNT162/Ad26.COV2.S/mRNA-1273/ChAdOx1-S	RNA/Vector (non-replicating)	100	18–64 (pregnant)	2	Not specified	Open-label	Netherlands
Phase IV	BNT162/mRNA-1273	RNA	15	≥18 (pregnant/lactating)	2	No	Open-label	Belgium

Showing 1 to 5 of 5 entries

Preg-CoV Study

- Network of maternal recruiting centres
- Adaptive platform design to assess:
  - **immunogenicity and reactogenicity** of different schedules of approved COVID-19 vaccines
  - **new vaccines** as they are approved
  - **new questions** of relevance to the UK vaccine programme, as required

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Objectives

1. To determine whether the **immune response**, in COVID-19 seronegative participants, to immunisation with COVID-19 vaccines according to **“long”** dosing intervals is superior to that observed following immunisation according to **“short”** dosing intervals.
2. To evaluate the **reactogenicity** of COVID-19 vaccines, when given as 1- or 2-dose vaccination regimens, in pregnant participants.

*To determine whether the immune response to booster immunisation during pregnancy with COVID-19 vaccines at **fractional dosing** is non-inferior to standard COVID-19 vaccine dosing.*

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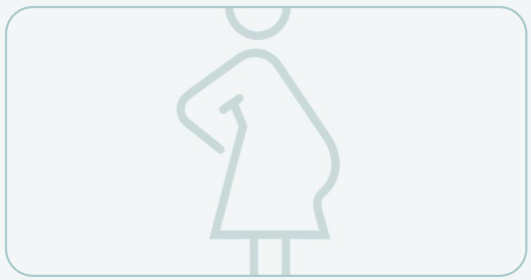
Study design



Recruitment

1. leaflets and posters
2. institutional websites,
3. social media
4. press release
5. face-to-face, clinics
6. NIHR Vaccine registry

Intervention

1. Short vs long interval
2. Short vs long interval
3. 1-dose in pregnancy
4. 2nd or 3rd dose
5. Observational sub-study
6. Fractional/coadministration

Follow up

1. Safety
2. Blood samples
3. Colostrum / breastmilk
4. Infant follow-up to 12mo

Up to 5 visits pre-delivery

Up to 3 visits post-delivery

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Visit schedule- example cohort 1

Visit Number	Screening + V1	V2	V3	V4	V5	V6	V7	V8[A]	V9	V10	V11	V12
Study Day	**0**	**14**	**28-42**	**56-84**	**84-112**	**112-140[¥]**	**DELIVERY**	**0-7 after delivery**	**12-16 after delivery**	**28-42 OR 70-84 after delivery**	**182 after delivery**	**364 after delivery**
Location	Trial site	Telephone	Trial site	Trial site	Trial site	Trial site	Delivery site	Visit ONLY if BM sub-study (Home/ trial site)[A]	Telephone (Home/ trial site if in BM sub-study)	Home/ Trial site	Telephone	Home/ Trial site
Main activities	Consent Screening Examination E-diary set-up	Review	Review	Review	Review	Review	Review	Review[A]	Review	Review	Review	Review Baby assessment
Blood tests	Maternal		Maternal	Maternal	Maternal	Maternal	Cord Blood* Maternal			Maternal Baby		Maternal
Breast milk (BM) collection (optional)								Colostrum*	Breast milk*			
Short Interval Boost	Covid-19		Covid-19	Pertussis								
Long Interval Boost	Covid-19		Pertussis	Covid-19								

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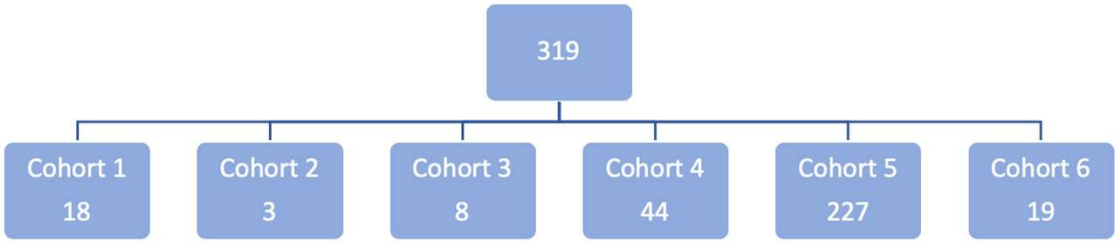
Recruitment

Total enrolled

Cohorts



Cohort 1- 2 vaccines, blinded to vaccine and dose interval

Cohort 2- 2 vaccines, blinded to vaccine only

Cohort 3- 1 vaccine (first dose), blinded to vaccine

Cohort 4- 1 vaccine (second or booster dose)

Cohort 5- observational arm (received 1 or more vaccines during pregnancy)

Cohort 6- fractional dose and pertussis co-administration sub-study

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Preliminary results
Reactogenicity

- Solicited Local and Systemic Adverse Events after vaccinations
- Similar range of adverse events across vaccines and doses
- Tenderness > fatigue > muscle ache > headache
- Few reports of fever after 2nd dose
- Overall mild or moderate in severity
- Majority day 0-2
- Overall, more AE noted in Moderna than Pfizer recipients for 1st, 2nd and 3rd doses, most marked for tenderness

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Preliminary results
Immunogenicity

- There was no evidence of an impact of the interval between the last two doses of COVID-19 vaccines on antibody concentrations in women at any time point during or after pregnancy
- There was no evidence of an effect of pregnancy trimester at the time of last maternal COVID-19 vaccination on infant antibody responses
- Placental transfer of maternally-derived anti-SARS-CoV-2 IgG antibodies following COVID-19 vaccination during pregnancy is positively correlated with maternal antibody levels at delivery
- Infant antibodies decay over the first 3 months of life; the implication of this with regard to clinical protection requires further study

Preg-CoV further work

- Outcome at 12 months
- Immunogenicity at 12 months
- SARS-CoV-2 antibodies in breast milk
- Data on symptomatic events

Preg-CoV challenges

Recruitment	Changing policies	Logistics
Vaccine hesitancy Anxiety	Vaccine implementation- fewer eligible participants, addition of observation arm Policy change in interval- amendments to keep in line with national policy	Multiple study visits- in addition to multiple routine visits Cord blood samples – out of hours Breastmilk samples

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Preg-CoV potential

- Established network of recruiting maternity centres
  - Vaccines studies
  - Surveillance studies
- ‘Protocol template’ can be adapted to incorporate other licensed vaccines and new vaccines
  - Coadministration with pertussis and Influenza
  - RSV
  - GBS

Acknowledgement

- St. George's Vaccine Institute team
- Preg-CoV Study sites
- Study collaborators
- Study participants

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Preg-CoV Evaluating COVID-19 Vaccines in Pregnancy

UK Health Security Agency

NISEC

oxford vaccine group

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