



## Coronavirus (COVID-19) Infection in Pregnancy

Information for healthcare professionals

Version 14: Published Wednesday 25 August











## Quick reference summary of acute COVID-19 management in pregnancy

Quick reference only, see section 6 for further detail.

- Assess admit, or discharge with clear advice about symptom deterioration and specific contact details.
- Oxygen to maintain saturations above 94%, escalating with e.g. nasal prongs, masks, CPAP, IPPV, ECMO
- No antibiotics unless additional bacterial infection suspected.
- LMWH for VTE prophylaxis
- Steroids if oxygen is needed (e.g. oral prednisolone 40 mg once daily or IV hydrocortisone 80 mg twice daily, with intramuscular dexamethasone 6 mg twice daily for four doses followed by oral prednisolone as below if fetal lung maturity is also required).
- MDT review is escalation required? Does birth need expediting?
- Strongly consider tocilizumab (400 mg/600 mg/800 mg single IV infusion depending on weight) if C-reactive protein at or above 75 mg/l or in ICU.
- Strongly consider REGEN-COV monoclonal antibodies (8 g single IV infusion) in those with no SARS-CoV-2 antibodies.

Remdesivir should only be considered for those who are not improving or who are deteriorating.

Azithromycin, hydroxychloroquine and lopinavir/ritonavir have been shown to be ineffective and should not be offered.

#### **Contents**

	Executive summary	4–8
	Summary of updates	9
ı	Purpose and scope	10–23
2	COVID-19 vaccination in pregnancy	24–32
3	Antenatal care during the COVID-19 pandemic	33–43
4	Venous thromboembolism prevention	44–46
5	Labour and birth during the COVID-19 pandemic	47–57
6	Managing clinical deterioration during the COVID-19 pandemic	58–67
7	Postnatal care	68–72
8	Acknowledgements	73–74
9	Appendix 1: Summary of previous updates	75–90
10	Appendix II: Development methods of this guidance	91
11	Appendix III: Summary of key studies on maternal and pregnancy outcomes	92–101
12	Appendix IV: Example of a telephone triage tool for symptomatic women with suspected or confirmed COVID-19	102
13	Appendix V: Example of a maternity escalation plan for women with suspected or confirmed COVID-19	103
14	References	104–122





## **Executive summary**

#### **Executive summary**

#### COVID-19 and pregnancy

- Pregnant women appear no more or less likely to contract SARS-CoV-2 than the general population, and more than two-thirds of identified pregnant women have no symptoms. The most common symptoms of COVID-19 in pregnant women are cough and fever.
- There is growing evidence that pregnant women may be at increased risk of severe illness from COVID-19 compared with non-pregnant women, particularly in the third trimester. The overall risk of death remains very low.
- Risk factors associated both with being infected and hospitalised with COVID-19 include ethnic minority backgrounds, having a BMI above 25 kg/m², having a prepregnancy co-morbidity, (e.g. diabetes or hypertension), a maternal age of 35 years or older, living in increased socioeconomic deprivation and working in healthcare or other public-facing occupations.
- The delta variant seems to be associated with more severe disease: 1:10 symptomatic women admitted to hospital with alpha variant needed admission to intensive care whereas this is 1:7 for symptomatic women with the delta variant.
- There is no reported increase in congenital anomalies incidence because of COVID-19 infection. Vertical transmission is rare.
- Maternal COVID-19 infection is associated with an approximately doubled risk of stillbirth and may be associated with an increased incidence of small-for-gestational-age babies. The preterm birth rate in women with symptomatic COVID-19 appears to be two to three times higher than the background rate; these are primarily iatrogenic preterm births.
- Higher rates of perinatal mental health disorders have been reported during the pandemic, including anxiety and depression.

#### Vaccination

- Vaccination in pregnancy against COVID-19 is strongly recommended and should be offered at the same time as the rest of the population based on age and clinical risk.
- More than 200 000 women in the UK and USA have had a COVID-19 vaccine in pregnancy with no concerning safety signals. There is excellent real-world evidence of vaccine efficacy with 98% of women admitted to hospital and getting severe infection having not had the vaccine.
- COVID-19 vaccines can be given at any time in pregnancy, and preference is to offer the Pfizer-BioNTech or Moderna vaccines.

- Pregnant women receiving a COVID-19 vaccine show similar patterns of reporting for common minor adverse effects to non-pregnant people. The rare syndrome of vaccine-induced thrombosis and thrombocytopenia (VITT) has been reported after the Oxford-AstraZeneca and the Janssen vaccines. It is an idiosyncratic reaction not associated with any of the usual venous thromboembolism risk factors. There is no evidence that pregnant or postpartum women are at higher risk of VITT.
- Breastfeeding women can receive a COVID-19 vaccine without having to stop breastfeeding. There is no evidence to suggest that COVID-19 vaccines affect fertility. Women planning a pregnancy or fertility treatment can receive a COVID-19 vaccine and do not need to delay conception.

#### Antenatal care

- The National Institute for Health and Care Excellence recommended schedule of antenatal care should be offered in full wherever possible.
- Healthcare providers should be aware of the increased risk of domestic abuse in pregnancy, which has escalated during the pandemic.
- There is evidence that the pandemic has resulted in a greater level of anxiety and other mental health problems in pregnant women compared the overall population. Women should be asked about their mental health at every contact.

#### Venous thromboembolism

- All pregnant women admitted with confirmed or suspected COVID-19 should be
  offered prophylactic low molecular weight heparin, unless birth is expected within
  12 hours or there is significant risk of haemorrhage. The dose may need to be
  individualised for women with severe complications of COVID-19.
- All pregnant women who have been hospitalised and have had confirmed COVID-19, or those up to 6 weeks postpartum, should be offered thromboprophylaxis for 10 days following hospital discharge. A longer duration of thromboprophylaxis should be considered for women with persistent morbidity.

#### Labour and birth

- In women with symptomatic COVID-19, there may be an increased risk of fetal compromise in active labour and caesarean birth. Women with symptomatic suspected or confirmed COVID-19 should be advised to labour and give birth in an obstetric unit with continuous electronic fetal monitoring. This is not required for asymptomatic infection.
- Senior obstetric and medical input for a woman with severe or critical COVID-19 should be sought, particularly for decision making about birth.

- The level of personal protective equipment (PPE) required by healthcare professionals caring for a woman with COVID-19 who is undergoing a caesarean birth should be determined by the risk of her requiring intubation for a general anaesthetic.
- Water birth is not contraindicated for women who are asymptomatic of COVID-19, providing adequate PPE can be worn by those providing care. Women with symptomatic COVID-19 should not labour or birth in water.

#### Clinical deterioration

- Chest imaging is essential for the evaluation of an unwell woman with COVID-19. It should be performed when indicated, and not delayed because of radiation exposure concerns.
- A woman's care should be escalated urgently if signs of decompensation develop. These signs include: increasing oxygen requirements or fraction of inspired oxygen (FiO<sub>2</sub>) above 35%, increasing respiratory rate above 25 breaths/minutes or a rapidly rising respiratory rate despite oxygen therapy, a reduction in urine output, acute kidney injury or drowsiness.
- For unwell pregnant women in the third trimester, an individualised assessment should be undertaken by a multidiscliplinary team to decide if maternal stabilisation is required before delivery can be undertaken safely. Following this, decisions concerning emergency caesarean birth or induction of labour should be prioritised, either to facilitate maternal resuscitation (including the need for prone positioning) or because of concerns regarding fetal health.
- COVID-19 can be associated with thrombocytopenia. When aspirin has been prescribed as prophylaxis for pre-eclampsia, it should be discontinued for the duration of the infection as this may increase the bleeding risk in women with thrombocytopenia.
- Oxygen should be titrated to ensure saturations of 94–98% using escalation through nasal cannula, face mask, venturi mask, non-rebreather mask, non-invasive positive airway pressure (e.g. continuous positive airway pressure [CPAP]), intubation and Intermittent positive-pressure ventilation (IPPV), and extracorporeal membrane oxygenation (ECMO) as appropriate.
- Caution should be applied to fluid balance and intravenous (IV) fluid management. Hourly fluid input/output charts should be recorded in women with moderate to severe symptoms of COVID-19, aiming to maintain a neutral fluid balance in labour. When required, boluses in volumes of 250–500 ml may be employed.
- Corticosteroid therapy should be given for 10 days or up to discharge, whichever is sooner, for women who are unwell with COVID-19 and requiring oxygen or ventilatory support. If steroids are not indicated for fetal lung maturity, treatment should be with oral prednisolone 40 mg once a day, or IV hydrocortisone 80 mg

twice daily, for 10 days or until discharge, whichever is sooner. If steroids are indicated for fetal lung maturity, prescribe intramuscular dexamethasone 6 mg every 12 hours for four doses, then oral prednisolone 40 mg once a day, or IV hydrocortisone 80 mg twice daily, to complete a total of 10 days or until discharge, whichever is sooner.

- Tocilizumab (interleukin-6 receptor antagonist) has been shown to improve outcomes, including survival, in hospitalised patients with hypoxia and evidence of systemic inflammation (C-reactive protein at or above 75 mg/l).
- Remdesivir should only be considered in pregnant women with COVID-19 who are not improving or who are deteriorating. Hydroxychloroquine, lopinavir/ritonavir and azithromycin should not be used as they are ineffective for treating COVID-19 infection.

#### Postnatal care

- National guidelines for routine postnatal care should be followed.
- Women should be informed that COVID-19 infection is not a contraindication to breastfeeding.

### **COVID-19 Infection and Pregnancy guideline**

#### Summary of updates

Version	Date	Summary of changes	
14.0	30/07/2021	<b>Throughout</b> Comprehensive editorial review resulting in rewording and minor changes, some of which made to align with new RCOG style guidance.	
14.0	30/07/2021	<b>Throughout</b> New evidence added to most sections to support or update existing conclusions or advice.	
14.0	30/07/2021	New Quick reference summary of acute COVID-19 management in pregnancy	
14.0	30/07/2021	New Executive summary added, replacing Appendix II in v13.	
14.0	30/07/2021	Sections 1.2, 1.4.2 and 1.5 update of epidemiology and risk factors including evidence about severity of disease in pregnancy with the delta variant.	
14.0	30/07/2021	New Section 2 COVID-19 Vaccination in pregnancy added, replacing section 1.4 in v13 (Vaccination against COVID-19). Inclusion of vaccination guidance, addition of Janssen vaccine, recommendation for vaccine at all stages of pregnancy and an increased emphasis on the importance of vaccination overall given the increased safety and efficacy data.	
14.0	30/07/2021	Section 6 overall update, including addition of monoclonal antibodies, emphasis on ECMO and proning, and advice about remdesivir, safety netting and saturation monitoring.	
14.0	30/07/2021	Appendix III, Table I updated with new studies.  Table 2 (summary of key studies relevant for the effect of COVID-19 on maternal outcomes) added, along with meta-analyses of studies.	



## I. Purpose and scope

#### I. Purpose and scope

This document aims to provide guidance to healthcare professionals who care for pregnant women during the COVID-19 pandemic. It is not intended to replace existing clinical guidelines, but to act as a supplement with additional advice on how to implement standard practice during this time.

The advice in this document is provided as a resource for UK healthcare professionals based on a combination of available evidence, good practice and expert consensus opinion. The guidance may also be relevant to other healthcare systems but may need to be adapted for the local environment. The priorities are:

- (i) The reduction of transmission of SARS-CoV-2 to pregnant women, their family members and healthcare workers.
- (ii) The provision of safe, personalised and woman-centred care during pregnancy, birth and the early postnatal period, during the COVID-19 pandemic.
- (iii) The provision of safe, personalised and woman-centred care to pregnant and postnatal women with suspected or confirmed COVID-19.

This guidance is under regular review and updated as new information and evidence emerges. Owing to the changing prevalence of COVID-19 infections in the UK, changes in care should be proportionate to the background prevalence at a given time. Decision-making around care and discussions about risks and benefits will depend on the background prevalence of the COVID-19 viral infection and the vaccination status of the woman. Updated advice and information will be published in the **Coronavirus (COVID-19)**, **pregnancy and women's health section** of the Royal College of Obstetricians and Gynaecologists (RCOG) website.

Information for pregnant women and their families is available in question and answer format, with accompanying videos in some cases, on the RCOG and Royal College of Midwives (RCM) COVID-19 hubs.

This guidance uses the terms 'woman' or 'mother' throughout, and 'female' where this has been specifically stated in the published study. These should be taken to include people who do not identify as women but are pregnant or have given birth.

#### 1.1 Identification and assessment of evidence

This guidance has been developed by a multidisciplinary group using the best available evidence retrieved by weekly literature reviews undertaken by a member of the RCOG Library team.

Owing to the relatively recent emergence of COVID-19 and the rapidly evolving nature of the pandemic, highest quality evidence is lacking. Using a conventional grading system for guideline development, such as SIGN, many of the studies would be classed as level 3 or 4 (non-analytical studies, e.g. case series/reports), with a few studies being classed as level 2 (systematic reviews of cohort studies). Much of the advice based on this evidence would therefore be graded D, and in some cases, graded as good practice points based on expert opinion. Furthermore, where randomised trials have been undertaken, such as to investigate therapeutic interventions in severe COVID-19, most of the trial participants were not pregnant. Healthcare providers, women and their families are advised to be aware of the low-quality evidence on which the advice is given when using this guidance to assist decision making.

For a more detailed description of the methods used to develop this guidance please see Appendix II.

#### 1.2 Epidemiology

SARS-CoV-2 is the strain of coronavirus which causes COVID-19. It was first identified in Wuhan City, China, towards the end of 2019.<sup>2</sup> Other human coronavirus (HCoV) infections include HCoV 229E, NL63, OC43 and HKU1, which usually cause mild to moderate upper respiratory tract illnesses like the common cold, Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV).<sup>3</sup>

The diagnosis of COVID-19 can be made based on symptoms and known exposure, or simply from a positive test for SARS-CoV-2 even in the absence of any symptoms. COVID-19 can therefore be symptomatic or asymptomatic.

As with all viruses, mutations can occur leading to the development of new strains. To date four of the new strains of the COVID-19 virus are of concern and have been termed the alpha, beta, gamma and delta variants. These variants have significant characteristics which may include increased transmissibility or more severe disease. The delta variant is significantly more transmissible than other variants. As of June 2021, the delta variant has been the most prevalent variant in the UK and has been found in over 90% of COVID test samples. The delta variant seems to be associated with more severe disease; 1:10 symptomatic women admitted to hospital with alpha variant needed admission to intensive care whereas this is 1:7 for symptomatic women with the delta variant.

The World Health Organization (WHO) publishes a <u>weekly international situation report</u> with an additional <u>Situation Dashboard</u> to provide information for individual countries. The total number of confirmed cases in the UK is published by the Department of Health and Social Care (DHSC), and is available in a <u>visual dashboard</u>.

For the most up-to-date advice please refer to health protection agency websites: for **England**, **Wales**, **Scotland** and **Northern Ireland**. Public Health England (PHE) and Public Health Scotland (PHS) have been cited throughout this document; specific guidance from the other areas of the UK will be updated as they become available.

#### 1.3 Transmission

Most global cases of COVID-19 have evidence of human-to-human transmission. This virus can be readily isolated from respiratory droplets or secretions, faeces and fomites (objects). Transmission of the virus is known to occur most often through close contact with an infected person or, probably uncommonly, from contaminated surfaces. With regard to vertical transmission (transmission from woman to her baby antenatally or intrapartum), evidence now suggests that if vertical transmission does occur, it is rare. If it does occur, it appears to not be affected by mode of birth, delayed cord clamping, skin-to-skin contact, method of feeding or whether the woman and baby stay together (rooming in).<sup>4–9,84</sup>

There is, however, evidence of transplacental transmission of antibodies against COVID-19 following maternal infection. Several studies, <sup>187–190</sup> have demonstrated the presence of immunoglobulin G (IgG) umbilical cord blood samples suggesting that passive immunity might be transferred to the neonate. IgG levels in cord blood have been reported to be higher with longer intervals between maternal infection and delivery. <sup>187,190</sup> The duration of IgG antibody presence and whether this truly confers passive immunity is unknown. <sup>187,190</sup>

#### 1.4 Effect of COVID-19 on pregnant women

#### 1.4.1 Symptoms of COVID-19 in pregnant women

#### Key findings

- Pregnant women do not appear more likely to contract the infection than the general population.
- The majority of pregnant women who are infected with SARS-CoV-2 are asymptomatic.
- Most symptomatic women experience only mild or moderate cold/flu-like symptoms.
- The main symptoms of COVID-19 are cough, fever, sore throat, dyspnoea, myalgia, loss of sense of taste and diarrhoea.

Pregnant women do not appear more likely to contract the infection than the general population.<sup>10</sup>

The majority of pregnant women who are infected with SARS-CoV-2 will be asymptomatic: the PregCOV-19 Living Systematic Review<sup>149</sup> reporting on universal screening in pregnancy found an estimated 73% (95% Cl 62–82) of women were asymptomatic, while another study<sup>11</sup> from the USA reported that 86% of women who were admitted in labour and who tested positive for SARS-CoV-2 were asymptomatic.

Most symptomatic women experience only mild or moderate cold/flu-like symptoms.<sup>12</sup> The PregCOV-19 systematic review<sup>149</sup> has so far included over 64 000 pregnant women worldwide with suspected or confirmed COVID-19 (reported prior to 29 November 2020). In this review the overall rate of COVID-19 diagnosis in pregnant and recently pregnant women attending or admitted to hospital for any reason was 10%. The most common symptoms of COVID-19 in pregnant women were cough (41%) and fever (40%). Less frequent symptoms were dyspnoea (14%), myalgia (15%), loss of sense of taste (11%) and diarrhoea (6%). Pregnant women with COVID-19 were less likely to have fever or myalgia than non-pregnant women of the same age. The PRIORITY (Pregnancy CoRonavirus Outcomes RegIsTry) study,<sup>13</sup> an ongoing prospective cohort study of pregnant women from the USA, found the most prevalent first symptoms in infected women were cough (20%), sore throat (16%), myalgia (12%) and fever (12%). In this group of 594 symptomatic women, one-quarter had persistent symptoms 8 or more weeks after onset.

At present, it is unclear whether pregnancy will impact on the proportion of women who develop prolonged signs and symptoms after an acute SARS-CoV-2 infection, (so-called 'long COVID' or post COVID-19 condition). NICE has produced a rapid guideline outlining the care of individuals who develop long-term effects of COVID-19. 14,149

#### 1.4.2 Severe illness with COVID-19 in pregnant women

#### Key findings

- More than two-thirds of pregnant women with COVID-19 are asymptomatic.
- Compared to non-pregnant with COVID-19, pregnant women with COVID-19:
  - have higher rates of intensive care unit (ICU) admission; this may reflect a lower threshold for admission to ICU, rather than more severe disease.
  - have higher needs for ventilation and extracorporeal membrane oxygenation (ECMO).
  - who require hospitalisation have overall worse maternal outcomes, including an increased risk of death, although the risk of death remains very low (the UK maternal mortality rate from COVID-19 is 2.4/100 000 maternities).
- Pregnant women may be at increased risk of complications in the third trimester when compared to earlier in pregnancy.

#### 1.4.2.1 Frequency of severe illness in pregnant women

COVID-19 ranges from asymptomatic infection, through to mild disease (no evidence of pneumonia or hypoxia), moderate disease (viral pneumonia), severe disease (severe pneumonia, e.g. with SpO<sub>2</sub> below 90% on room air) and critical disease (Acute Respiratory

Distress Syndrome [ARDS], sepsis, septic shock, or complications such pulmonary embolism or acute coronary syndrome).

Severe illness, such as that requiring ICU admission, is relatively uncommon in women of reproductive age, but can occur. During the initial wave of the pandemic, there were case reports and case series of women with severe COVID-19 infection at the time of birth who received ventilation and ECMO, 15 and of maternal death. 16 In the PregCOV-19 Living Systematic Review Consortium analysis, 149 0.02% (95% CI 0.00–0.42%) of pregnant women with confirmed COVID-19 were recorded as having died of any cause, and 0.2% (95% CI 0.0–0.7%) of pregnant women with COVID-19 required ECMO. A large USA study 153 published in January 2021 compared outcomes for pregnant women with and without COVID-19 from April—November 2020, drawing the information retrospectively from a database that covers about 20% of the American population. Data were available for 406 446 women hospitalised for childbirth, 6380 (1.6%) of whom had COVID-19. In-hospital maternal death was rare, but rates were significantly higher for women with COVID-19 (141/100 000 women, 95% CI 65–268) than for women without COVID-19 (5/100 000 women, 95% CI 3.1–7.7).

A study was published in February 2021 with the results from two large COVID-19 in pregnancy registries. 156 The PAN-COVID registry recorded suspected or confirmed COVID-19 at any stage in pregnancy (in the UK and ten other countries), and the AAP SONPM registry recorded maternal COVID-19 around the time of birth (from 14 days before to 3 days after birth). Maternal mortality was uncommon in both registries: it occurred in 3/651 (0.46%) of women with confirmed COVID-19 in the PAN-COVID registry, and in 5/2398 women with COVID-19 (0.21%) in the AAP SONPM registry. For the UK data (PAN-COVID), the mortality rate may be inflated by under-reporting of women with asymptomatic or mild COVID-19 in pregnancy. The authors of this study have postulated that only 10% of maternal COVID-19 infections were detected as cases, and the true infection fatality rate would therefore be ten times lower (i.e. 0.046%, which is close to the estimate of 0.03% for men and women aged 15-44 years in the UK REACT2 study). 17 Nonetheless, these maternal mortality rates are higher than previously recorded maternal mortality rates in these populations – for example, the maternal deaths from the AAP SONPM registry equate to a perinatal maternal mortality rate of 167/100 000 (for women who have COVID-19 around the time of birth), compared with a pre-COVID rate of 17.3/100 000 in the USA. Moreover, COVID-19 was listed as the cause of death for all the maternal deaths in these registries where cause of death was known.

The UK Obstetric Surveillance System (UKOSS) published its first report<sup>98</sup> on pregnant women admitted to hospital with confirmed COVID-19 in the UK on 8 June 2020, and an updated report<sup>18</sup> was published 5 May 2021. This second report covers the period from 1 March—31 August 2020. During that time, 1148 hospitalised women had COVID-19 in pregnancy. Most (63%) of women were symptomatic with COVID-19; however, this includes many women from the initial wave of the pandemic, when testing was only performed for symptomatic individuals. As testing for SARS-CoV-2 has become more routinely offered on admission to labour ward, the proportion of asymptomatic women is likely to have increased. Of the 1148 hospitalised pregnant women, 63 (5%) required critical care. During this time,

eight women with symptomatic COVID-19 died in hospital. Two of the deaths were not related to COVID-19, and six deaths were, giving a maternal mortality rate of 2.2 hospitalised women per 100 000 maternities (95% CI 0.9–4.3). MBRRACE-UK Confidential Enquiries into Maternal Deaths published their second report on SARS-CoV-2 related maternal deaths that occured between 1 June 2020 and 31 March 2021. MBRRACE methodology reviews the deaths of women that occur during pregnancy and up to 6 weeks after pregnancy, and the deaths of women that occur 6 weeks to 1 year after pregnancy. The estimated SARS-CoV-2 associated maternal mortality rate for this MBRRACE rapid review period is 2.4 per 100 000 (95% CI 1.3-4.0)

Severe illness appears to be more common in later pregnancy. In the UKOSS study, <sup>18</sup> most women were hospitalised in the third trimester or peripartum (bearing in mind that admission at term to give birth will contribute to this distribution). Symptomatic COVID-19 was principally diagnosed in the third trimester: 83% of symptomatic women were diagnosed at or beyond 28 weeks, with 52% diagnosed at or beyond 37 weeks. The reason for hospital admission was known for a subset of pregnant women in the UKOSS study. For asymptomatic women, the reason for admission was principally to give birth (68%). For symptomatic women, the reasons for admission were roughly a third for symptomatic COVID-19, a third to give birth, and a third for other reasons.

The UK Intensive Care National Audit and Research Centre (ICNARC) has released two reports of patients admitted to intensive care with COVID-19. The first report <sup>19</sup> covered the start of 2020 up until 31 August 2020. During that time, a total of 70 women who were either currently or recently (within 6 weeks) pregnant were admitted to intensive care, representing 8.9% of all the 785 pregnant and non-pregnant women admitted aged 16–49 years. The second ICNARC report <sup>152</sup> included the period from 1 September 2020–31 May 2021. During this period, a further 320 women who were either currently or recently (within 6 weeks) pregnant were admitted to intensive care, corresponding to 13.9% of the 2309 women admitted aged 16–49 years. For context, the conception rate in the UK in 2018 was 75.4/1000 women aged 15–44 years, suggesting that the percentage of women pregnant at any one time in the UK is less than 7.5%. <sup>20</sup> It is important to note that the threshold for admitting a pregnant woman to intensive care is likely to be lower than for a non-pregnant woman: a higher rate of intensive care admission for pregnant women does not therefore necessarily mean a higher burden of severe disease.

A preprint publication written as a collaboration between the International Severe Acute Respiratory and Emerging Infection Coronavirus (ISARIC4C), Clinical characteristic consortium, UKOSS and the Covid-19 Clinical Information Network (Co-CIN) was presented to the Scientific Advisory Group for Emergencies on 25 March 2021. <sup>226</sup> The three sources of data used for this analysis were ISARIC4C/CO-CIN, UKOSS and MBRRACE-UK Confidential Enquiry into Maternal Deaths. Between 1 March 2020 and 28 February 2021, 5479 pregnant women with confirmed SARS-CoV-2 infection were admitted across the UK. Maternal deaths in this period were also included in the study. Data so far suggest that maternal mortality has increased during the pandemic. UK maternal mortality is estimated to be 20% higher than in previous recent years (12/100 000 maternities compared to 10/100 000) the rise in maternal

death is not all attributed to COVID-19. Twenty-four women with SARS-CoV-2 infection were reported to MBRRACE-UK;<sup>235</sup> 20 during pregnancy or in the immediate postpartum period (up to 6 weeks postnatal) and four during the extended postpartum period (up to 1 year). Nineteen deaths were because of COVID-related respiratory or thrombotic disease. Of note, in the same time period, the Office for National Statistics reported 319 deaths of women aged 20–39 in England and Wales with COVID-19 mentioned on the death certificate.

#### 1.4.2.2 Data from studies comparing severity of COVID-19 in pregnant and non-pregnant women

It was not clear early in the pandemic whether pregnancy itself was a risk factor for severe illness from COVID-19. There is now growing evidence that pregnant women may be at increased risk of severe illness from COVID-19 compared with non-pregnant women, particularly in the third trimester. The most consistent signal of increased severity of COVID-19 in pregnancy is an increase in ICU admissions for pregnant women. However, ICU admission rates must be interpreted with caution, as the threshold for ICU admission for a pregnant woman may be lower than for a non-pregnant woman. Moreover, there are currently no robust data from the UK comparing pregnant and non-pregnant women with COVID-19. Part of the UKOSS/ISARIC/CO-CIN investigation<sup>226</sup> compared pregnant women with males and non-pregnant females aged 20–39 years. To summarise pregnant females were less likely to require oxygen, non-invasive and invasive ventilation, were less likely to be admitted to ICU and were more likely to be discharged alive, rather than die or be admitted to ongoing care compared with males and non-pregnant females. The studies in this section are from countries with different healthcare systems, populations and different baseline maternal risks, and should therefore be interpreted with caution from a UK perspective.

Intensive care admission is likely to be more common in pregnant women with COVID-19 than in non-pregnant women with COVID-19 of the same age. The PregCOV-19 Living Systematic Review Consortium analysis <sup>149</sup> concluded that pregnant women are more likely than non-pregnant women to be admitted to intensive care (OR 2.13, 95% CI 1.53–2.95) and require invasive ventilation (OR 2.95, 95% CI 2.28–2.94). This finding was based overwhelmingly on a single study <sup>22</sup> published by the US Centers for Disease Control and Prevention (CDC); in this study two major limitations of the results were acknowledged. The first was that admissions for indications related to pregnancy and those for COVID-19 could not be distinguished. The second was that pregnancy status was missing for three-quarters of the women of reproductive age; a pregnancy rate of 9% was identified – higher than the expected 5%. This could account for significant bias in the results.

Since the last update of that systematic review, a small number of studies from the USA and Mexico have also pointed to increased illness severity from COVID-19 in pregnant women compared to non-pregnant women. The US CDC published an updated study  $^{158}$  in November 2020, based on surveillance of COVID-19 cases in the USA from January—October 2020. This study addressed some of the limitations of their earlier work quoted above, although missing data might still have led to bias (e.g. pregnancy status was missing for more than half the cases reported to the CDC). This report compared pregnant women with symptomatic COVID-19 (n = 23 434) to non-pregnant women of reproductive age with symptomatic COVID-19

(n = 386 028). The pregnancy rate in this study was 5.7%, close to the expected value, and by focussing on symptomatic women, this study was less likely to be biased by women being admitted principally for obstetric reasons. This large study found that pregnant women were more likely be admitted to ICU (adjusted risk ratio [aRR] 3.0, 95% CI 2.6–3.4), to receive invasive ventilation (aRR 2.9, 95% CI 2.2–3.8), ECMO (aRR 2.4, 95% CI 1.5–4.0), and to die (1.5/1000 versus 1.2/1000 cases; aRR 1.7, 95% CI 1.2–2.4).

A large case—control study<sup>155</sup> from Mexico compared 5183 pregnant women with symptomatic COVID-19 with 5183 matched non-pregnant controls. The data were taken from a prospective cohort of people of any age with clinically suspected SARS-CoV-2 infection who were admitted to one of 475 monitoring hospitals in Mexico. This data therefore suffers from some of the same limitations as the CDC data above, with some outcomes missing for large numbers of individuals. For example, information on ICU admission was only available for one-fifth of pregnant women. Pregnant women had higher odds of death (OR 1.84, 95% CI 1.30—2.61), pneumonia (OR 1.99, 95% CI 1.81—2.19) and ICU admission (OR 2.25, 95% CI 1.86—2.71), but similar odds of intubation (OR 0.93, 95% CI 0.70—1.25).

A smaller study<sup>151</sup> from the New York area also found higher ICU admission rates for pregnant women with COVID-19: 38 pregnant women admitted to hospital with severe or critical COVID-19 were compared to 94 non-pregnant women with severe or critical COVID-19. Pregnant women were only included in this study if they were admitted for treatment of COVID-19 (and not for any obstetric reason). Pregnant women were more likely to be admitted to ICU (39.5% versus 17.0%, P < 0.01; adjusted OR 5.2, 95% CI 1.5–17.5). This was despite the fact that the control group had higher rates of comorbidities (hypertension, diabetes, obesity) and was slightly older. A similar study<sup>150</sup> from France during the initial wave of the pandemic compared the clinical outcomes of 83 pregnant women (above 20 weeks of gestation) with COVID-19 to 107 non-pregnant women with COVID-19, after matching the two groups using a propensity score. Pregnant women were at higher risk for ICU admission than non-pregnant women (11.08% versus 2.38%, P = 0.024), for needing hospital admission because of COVID-19 respiratory decompensation (58.21% versus 17.4%), for the need for oxygen therapy (36.04% versus 17.24%, P = 0.006), and for endotracheal intubation (10.16% versus 1.67%, P = 0.022).

Another study<sup>157</sup> from the US, published in January 2021, compared 22 pregnant women with symptomatic COVID-19 to 240 non-pregnant controls. This study found that pregnant women were more likely than non-pregnant controls to have severe COVID-19, based on two different measures of disease severity (adjusted relative risk [RR] for severe COVID-19 was 3.59 [95% CI 1.49–7.01] for one measure of severity, and 5.65 [95% CI 1.36–17.31] for the other measure of severity). Finally, a study<sup>154</sup> from the Washington State COVID-19 in Pregnancy Collaborative, published at the end of January 2021, found a higher mortality rate for pregnant women with COVID-19 than for non-pregnant controls. This study analysed data on 240 women who tested positive for COVID-19 in pregnancy. Of these, 24 women (10%) were admitted to hospital specifically for COVID-19-related respiratory concerns; this is approximately three times the hospitalisation rate with COVID-19 compared to all adults aged 20–39 years in Washington state (RR 3.5, 95% CI 2.3–5.3). There were three maternal deaths

directly attributed to COVID-19, giving a maternal mortality rate of 1250/100 000 pregnancies (95% CI 257–3653) and a COVID-19 case fatality in pregnancy that was 13.6 times (95% CI 2.7–43.6) higher than for all adults aged 20–39 years. This study also highlighted the increased risk of severe COVID-19 in the third trimester: of the 24 women who were admitted unwell with COVID-19, the median gestation was 32<sup>+4</sup> weeks of gestation (interquartile range [IQR] 26–36<sup>+1</sup> weeks of gestation).

Taken together, these studies point to a possibly increased risk of severe disease from COVID-19 for pregnant women compared to non-pregnant women with COVID-19. However, the most consistent finding was of increased ICU admission rates for pregnant women, and this may in part be explained by a lower threshold for ICU admission in pregnancy in general.

Studies on the risk of severe disease from COVID-19 in pregnancy are summarised in Appendix IV, Table 2.

The care of pregnant women with severe COVID-19 is covered in section 6 of this guidance.

#### 1.5 Risk factors for hospital admission with COVID-19 infection in pregnancy

#### Key findings

- Risk factors that appear to be associated both with being infected and being admitted to hospital with COVID-19 include:
  - o Black, Asian or other minority ethnic background.
  - having a BMI of 30 kg/m<sup>2</sup> or more.
  - pre-pregnancy co-morbidity, such as pre-existing diabetes and chronic hypertension.
  - o maternal age 35 years or older. 98,149
  - o living in areas or households of increased socioeconomic deprivation (data not specific to pregnancy).<sup>101</sup>
- In addition to these, the risk of becoming infected with SARS-CoV-2 is higher in individuals who are more exposed, for example, those working in healthcare or other public-facing occupations.

In the PregCOV-19 Living Systematic Review,<sup>149</sup> the maternal risk factors associated with severe COVID-19 were: age 35 years and older, OR 1.83 (95% CI 1.27–2.63); for BMI 30 kg/m<sup>2</sup> and above, OR 2.37 (95% CI 1.83–3.07); for chronic hypertension, OR 2.0 (95% CI 1.14–3.48); and for pre-existing diabetes, OR 2.12 (95% CI 1.62–2.78).

The UKOSS/ISARIC/CO-CIN study in the UK described the characteristics of 5479 pregnant women with confirmed SARS-CoV-2. The estimated the incidence of pregnant women admitted to hospital with SARS-CoV-2 aged 35 and older was 8.93/1000 maternities (95% CI 8.49–9.39), pregnant women with a BMI above 30 kg/m² 10.18/1000 maternities (95% CI 9.70–10.68) and pregnant women of Black, Asian or other minority ethnic background 18.06/1000 maternities (95% CI 17.12-19.04), 18.83/1000 maternities (95% CI 17.36–20.42) and 8.17/1000 maternities (95% CI 7.35–9.07) respectively.<sup>226</sup>

The association between Black, Asian and minority ethnic background and severe COVID-19 in pregnancy echoes findings from before the pandemic which showed women of Black, Asian and minority ethnic background had higher morbidity and mortality in pregnancy than white women. For example, the MBRRACE-UK report of the Confidential Enquiry into Maternal Death and Morbidity 2016–2018,<sup>24</sup> showed there remains a more than four-fold difference in mortality rates among women from Black ethnic backgrounds and an almost two-fold difference among women from Asian backgrounds compared to white women.

The association between Black, Asian and minority ethnic background and severe COVID-19 or death from COVID-19 is not confined to pregnant women. In the UK, 13% of the total population identify as being from a Black, Asian and minority ethnic background, but 30% of all individuals admitted to UK critical care for COVID-19 were from Black, Asian and minority ethnic backgrounds, and individuals from Black, Asian and minority ethnic backgrounds were more likely to die from COVID-19. The case of COVID-19, it has been postulated that this association may be related to health inequalities or socioeconomic factors; however, further research is needed. Ed. 26,98

Another possible contributing factor to the observed association between severe illness and Black, Asian and minority ethnic background is vitamin D deficiency.<sup>27</sup> UK advice recommends vitamin D supplementation to all pregnant women and individuals of Black, Asian and minority ethnic background, regardless of the COVID-19 pandemic.<sup>28,29</sup>

#### 1.6 Effect of COVID-19 on pregnancy

#### Key findings

- Symptomatic maternal COVID-19 is associated with an increased likelihood of iatrogenic preterm birth.
- COVID-19 may be associated with an increased incidence of small-for-gestational-age babies.
- It seems likely that neonatal morbidity for babies born to mothers with COVID-19 infection is linked to preterm birth rather than the COVID-19 infections itself.
- While stillbirth remains a rare outcome, maternal COVID-19 infection is associated with an increased risk of stillbirth.

Preterm birth is associated with perinatal mortality, but also with long term morbidity.<sup>23</sup> It is the single biggest cause of neonatal morbidity and mortality in the UK, with about 7% of babies in the UK born preterm. 100 The preterm birth rate in women with symptomatic COVID-19 appears to be two to three times higher than this background rate. The PregCOV-19 Living Systematic Review<sup>149</sup> estimated the risk of preterm birth at approximately 17%. Most of these preterm births (94%) were iatrogenic. In the initial UKOSS study, 98 the median gestational age at birth was 38 weeks of gestation (IQR 36-39 weeks of gestation). Of the women who gave birth, 27% had preterm births: 47% of these were iatrogenic for maternal compromise and 15% were iatrogenic for fetal compromise. The updated UKOSS study<sup>18</sup> confirmed that preterm birth was more likely for women with COVID-19: 19% of women with symptomatic COVID-19 and 9% of women with asymptomatic COVID-19 gave birth before 37 weeks of gestation. Compared with a historical cohort of pregnant women without SARS-CoV-2, pregnant women with symptomatic COVID-19 were more likely to give birth before 32 weeks of gestation (adjusted OR [aOR] 3.98, 95% CI 1.48-10.70) and before 37 weeks of gestation (aOR 1.87, 95% CI 1.23–2.85). Newer studies<sup>81,170,219</sup> confirm the increased risk of preterm birth with symptomatic maternal COVID-19 infection. The care of women at risk of iatrogenic preterm birth is addressed in section 5.2. Pregnant women with asymptomatic COVID-19 were not, however, at increased risk of preterm birth.

The results of two large COVID-19 in pregnancy registries<sup>156</sup> found the number of small-for-gestational age neonates was comparable to historical and contemporaneous UK and USA data; however, growth restriction is considered a theoretical possibility in pregnancies complicated by COVID-19 as two-thirds of pregnancies with SARS were affected by fetal growth restriction (FGR).<sup>12,31,30</sup> Furthermore, a published systematic review of 42 studies<sup>219</sup> reported an increased risk of low birth weight (OR 1.89 95% CI 1.14–3.12) associated with maternal COVID-19 infection, and a large multinational study<sup>180</sup> also reported a higher low birth weight rate (RR 1.58 95% CI 1.29–1.94) among women with COVID-19 infection. This newer evidence adds to the previously theorised risks that maternal COVID-19 infection poses to fetal growth as seen in pregnancies with SARS.

For babies born to women with COVID-19, the overall outcomes are positive, with over 95% of newborns included in the PregCOV-19 Living Systematic Review<sup>149</sup> reported as being born in good condition. A large study<sup>5</sup> from the USA also reported reassuring neonatal outcomes during the pandemic. Of 1481 births overall, 116 (8%) women (giving birth to 120 neonates) tested positive for SARS-CoV-2. All 120 neonates were tested at 24 hours of life and none were positive for SARS-CoV-2. Of 79 neonates who had a repeat SARS-CoV-2 polymerase chain reaction test at age 5–7 days (66% follow-up rate), all tested negative; 72 neonates were also tested at 14 days old and again, none were positive. None of the neonates had signs of COVID-19. A national level cohort study in Sweden<sup>222</sup> reported small increases in measures of neonatal morbidity for neonates born to mothers with COVID-19 infection, including admission to neonatal unit and respiratory distress syndrome, but no differences in neonatal length of stay or mortality. In the updated UKOSS study,<sup>18</sup> 19% of babies born in the UK to women with symptomatic SARS-CoV-2 infection, were admitted to the neonatal unit. These admissions may, in part, represent the policy of the maternity unit rather than concerns about wellbeing of the neonate.

However, a national level study in England<sup>170</sup> also reported no difference in measures of neonatal morbidity including admission to neonatal unit or readmission when restricting the analysis to babies born at term. This is indicative that reports of neonatal morbidity for babies born to mothers with COVID-19 infection is likely to be linked to morbidity associated with preterm birth.

Despite over 100 million confirmed COVID-19 infections worldwide, there has been no reported increase in the incidence of congenital anomalies.

Findings from an earlier publication of the PregCOV-19 Living Systematic Review were that stillbirth and neonatal death rates were not raised for women with COVID-19. The updated review, <sup>149</sup> however, reported that compared with pregnant and recently pregnant women without the disease, pregnant women with COVID-19 were at higher risk of stillbirth (OR 2.84, 95% CI 1.25–6.45). It is important to note that the overall number of stillbirths was small. The updated UKOSS report <sup>18</sup> found no significant difference in the risk of stillbirth or neonatal death for any symptom status of SARS-CoV-2 infection compared to the historical cohort of pregnant women over a 6-month period. Although the number of stillbirths or neonatal deaths that occurred in the groups of pregnant women with symptomatic (n = 5) or asymptomatic (n = 4) SARS-CoV-2 were higher than the historical cohort (n = 2), this difference did not reach statistical significance.

More recently published studies and systematic reviews have reported an increased risk of stillbirth associated with maternal COVID-19 infection. 180,170,219 A large study in England, 170 reported a statistically significant two-fold increase in stillbirth for women with a laboratory confirmed SARS-COV-2 infection at the time of birth (OR 2.21 95% CI 1.58-3.11). This study was unable to differentiate between severity of COVID-19 disease in the cohort, and was not able to quantify risk of stillbirth based on historical COVID-19 infection at any other time during pregnancy. In addition, a multinational study 180 covering 18 countries also reported a two-fold increase in a composite measure of severe perinatal morbidity and mortality, which included intrauterine fetal death, and an increase in risk of this measure as severity of COVID-19 symptoms increased. A systematic review of 42 studies<sup>219</sup> also reported a two-fold increase in stillbirth (OR 2.11) associated with maternal COVID-19 infection. While substantial evidence for causality of the observed increased stillbirth risk is lacking, studies have suggested impairment of placental function from COVID-19 infection as a plausible mechanism, and therefore the fetal wellbeing of women with COVID-19 infection should be cared for accordingly (see section 3.4). A nationwide study in the USA<sup>221</sup> reported no increase in the risk of fetal loss prior to 20 weeks of gestation because of COVID-19 infection. However, further evidence on COVID-19 infection in early pregnancy is currently lacking.

Maternal COVID-19 is also associated with an increased rate of caesarean birth. From the initial UKOSS study, 98 59% of women had caesarean births; approximately half of these were because of maternal or fetal compromise. The remainder were for obstetric reasons (e.g. progress in labour, previous caesarean birth) or maternal request (6%). Of the women having a caesarean birth, 20% required general anaesthesia (GA). Approximately two-thirds of the women who had GA were intubated for maternal respiratory compromise, and the remaining

third was to facilitate urgent birth. The updated UKOSS data<sup>159</sup> confirmed this trend, with a 49% caesarean birth rate for women with symptomatic COVID-19 versus 29% for a historical control group from 2018 (before COVID-19).

## 1.7 Effect of service modifications during the COVID-19 pandemic on maternal and perinatal experience and outcomes

#### Key findings

During the first wave of the COVID-19 pandemic in 2020, changes were made to the provision of maternity services with the aim of reducing nosocomial transmission. This included reduced antenatal and postnatal appointments, adopting of remote consultation methods, restricted access to midwifery-led birth settings or home birth, and changed methods of screening for FGR and gestational diabetes. These service changes impacted on the experience of women and their families, potentially increasing barriers to care and exacerbating adverse mental health outcomes. The full consequences of these changes have yet to be determined.

During the first wave of the COVID-19 pandemic in 2020, changes were made to the provision of maternity services with the aim of reducing nosocomial transmission, the unintended consequences of which have yet to be determined.

In the UK, two survey studies have demonstrated that during April 2020, the majority of units reduced antenatal and postnatal appointments, adopted remote consultation methods, restricted access to midwifery-led birth settings or home birth, and changed methods of screening for FGR and gestational diabetes.<sup>32,33</sup> These service changes impacted on the experience of women and their families. An online questionnaire survey<sup>34</sup> of 1451 pregnant or recently pregnant women in the UK found that the majority felt there were barriers to accessing maternity care while anxieties were expressed about changes to antenatal, intrapartum and postnatal services.<sup>13</sup>

Meta-analyses and systematic reviews<sup>35,36</sup> have found higher rates of perinatal mental health disorders during the pandemic, including anxiety and depression. Some of these impacts may be attributed to modifications to maternity services. The MBRRACE-UK rapid report<sup>21</sup> highlighted two instances where women died by suicide, where referrals to perinatal mental health teams were refused or delayed because of restrictions related to COVID-19.



# 2. COVID-19 vaccination in pregnancy

#### 2. COVID-19 vaccination in pregnancy

This section aims to summarise, in a format useful for maternity care, the evidence presented in existing COVID-19 vaccination guidance from the PHE/DHSC Green Book<sup>191</sup> as well as leaflets and information from PHE and the NHS.

#### 2.1 Background on COVID-19 vaccines available in the UK

#### Key findings

COVID-19 vaccine background (in non-pregnant population):

- The phase 3 trials of the four currently-approved vaccines assessed protection against COVID-19 after two doses in three, and after a single dose in one.
- The Pfizer-BioNTech vaccine has an efficacy of 95% (95% CI 90.0–97.9%) against symptomatic COVID-19. 192
- The Oxford-AstraZeneca vaccine has an efficacy of 66.7% (95%CI 57.4–74.0%) against symptomatic COVID-19.193
- The Moderna vaccine has an efficacy of 94.1% (95% CI 89.3–96.8%). 194
- The Janssen vaccine has an efficacy of 66.1% (95% CI 55.0–74.8%). 196
- Real-world monitoring has confirmed that one dose of the Pfizer-BioNTech or Oxford-AstraZeneca vaccines confers about 60% protection against symptomatic COVID-19.[?]
- Vaccination with two doses of the Pfizer-BioNTech or Oxford-AstraZeneca vaccines are effective against symptomatic disease secondary to infection by the delta variant. 185,186

#### 2.1.1 Available vaccines in the UK and their mechanisms of action

As of June 2021, four COVID-19 vaccines are approved for use in the UK: the Pfizer-BioNTech vaccine, the Oxford-AstraZeneca vaccine, the Moderna vaccine and the Janssen vaccine. The MHRA approved the Pfizer-BioNTech vaccine in the UK on 2 December 2020, the Oxford-AstraZeneca vaccine on 30 December 2020, the Moderna vaccine on 8 January 2021 and the Janssen vaccine on 28 May 2021.

The Pfizer-BioNTech and Moderna vaccines are messenger RNA (mRNA) vaccines in which mRNA encoding SARS-CoV-2 spike protein is introduced into the person when they are vaccinated via a lipid nanoparticle coat. The mRNA does not go into the nucleus of the host cell, so it remains separate from the host DNA. The host cell produces the spike protein, as for the Oxford-AstraZeneca and Janssen vaccines below, and this protein elicits a protective

immune response. The mRNA from the vaccine is broken down by the host cell within a few days. [9]

The Oxford-AstraZeneca and Janssen vaccines are viral-vector vaccines in which DNA encoding the SARS-CoV-2 spike protein is introduced into the person when they are vaccinated using a modified adenovirus vector. The adenovirus vector has been modified so that it cannot replicate, and the spike protein is not expressed on the adenovirus itself.

Rather, the adenovirus vector serves only to deliver the spike DNA into the host cell. The host cell then produces the spike protein, and this elicits a protective immune response.

#### 2.1.2 Vaccine safety

The adverse effect profiles of the four available vaccines were similar in their phase 3 trials. Most participants in the trials had a minor local reaction (pain, redness or swelling at the injection site). Mild systemic adverse effects like fatigue, headache or myalgia were also common; these were typically short-lived (less than a few days). About 10–20% of participants had a fever after vaccination. In general, adverse events are more common after the first dose than the second dose for the Oxford-AstraZeneca vaccine and more common after the second dose than the first dose for the Pfizer-BioNTech and Moderna vaccines.

These vaccines have continued to be monitored for safety after their authorisation, and an association has emerged between the Oxford-AstraZeneca vaccine and rare cases of serious thrombosis in the context of thrombocytopenia (see 2.3.2.1 below). There have also been very rare reports of myocarditis and pericarditis following vaccination with Pfizer-BioNTech and Moderna vaccines. 197

#### 2.2 Eligibility for the vaccine in pregnancy

#### Key findings

- Vaccination against COVID-19 is strongly recommended. It should be offered to pregnant women at the same time as the rest of the population, based on age and clinical risk.
- Pregnant women should be offered the Pfizer-BioNTech or Moderna vaccines unless they have already had one dose of the Oxford-AstraZeneca vaccine, in which case they should complete the course with Oxford-AstraZeneca.

The eligibility criteria are based on recommendations from the Joint Committee on Vaccination and Immunisation (JCVI).<sup>37</sup> The choice of vaccine is based on the recommendations from the Green Book<sup>191</sup> and reflects the fact that most of the safety data regarding vaccination in pregnancy comes from the USA where pregnant women were usually offered the Pfizer-BioNTech or Moderna vaccines.

#### 2.3 Potential fetal and maternal effects

More than 200 000 women in UK and US have had a COVID-19 vaccine in pregnancy with no concerning safety signals. 198,229,230

Pregnant women were not included in the large randomised controlled trials testing the safety and adverse effect profiles of the COVID-19 vaccines. However, as of 7 June 2021, over 120 000 pregnant women from diverse ethnic backgrounds in the USA have received either a Pfizer-BioNTech or Moderna vaccine, with no evidence of harm being identified. <sup>198</sup> In general, there are no known risks from giving inactivated or recombinant vaccines in pregnancy, or while breastfeeding, <sup>199</sup> and there is therefore no reason to suppose that the adverse effects from these COVID-19 vaccines should be different for pregnant women compared to non-pregnant women.

#### 2.3.1 Maternal effects

#### 2.3.1.1 Common minor adverse effects

Minor and short-lived adverse effects such as soreness at the injection site, headache and fatigue are common in the general population after a COVID-19 vaccine. A report<sup>200</sup> on the first 35 000 pregnant women to receive a COVID-19 vaccine in the USA showed similar patterns of reporting for common minor adverse effects. Systemic features such as fever appeared more commonly in non-pregnant women, but pregnant women did report nausea and vomiting more frequently after the second dose of the Pfizer-BioNTech and Moderna vaccines.<sup>200</sup> Smaller observational studies<sup>201,202</sup> have also reached similar conclusions showing no significant difference between pregnant and non-pregnant women in their symptoms post vaccination, and a reduced incidence of systemic features such as fever in pregnant women.

#### 2.3.1.2 Vaccine-induced thrombosis and thrombocytopenia (VITT)

The rare syndrome of vaccine-induced thrombosis and thrombocytopenia (VITT) has been reported after the Oxford-AstraZeneca vaccine; it has also been reported after the Janssen vaccine. VITT is an unpredictable idiosyncratic vaccine reaction (not dissimilar to heparin-induced thrombocytopenia and thrombosis associated with heparin therapy) and it is not associated with any of the usual venous thromboembolism (VTE) risk factors. It has been described as presenting 5–28 days after the first dose, particularly in adults younger than 50 years old. Although pregnancy increases the risk of coagulopathy there is no evidence that pregnant or postpartum women are at higher risk of VITT than non-pregnant women. 191,204

The risk of VITT is therefore extremely low with a first dose of the Oxford-AstraZeneca vaccine (approximately 1:100 000),<sup>241</sup> and even lower with a second dose for those who were well after the first dose. The UK government has advised that individuals younger than 40 years old should be offered an alternative vaccine to the Oxford-AstraZeneca vaccine based on the risk/benefit ratio for this age group. There is no known risk of VITT with the Pfizer-BioNTech and Moderna vaccines.

#### 2.3.2 Fetal effects

Pregnancy outcomes following mRNA vaccination (Pfizer-BioNTech and Moderna) appear similar to comparator groups prior to the onset of COVID-19. The most common adverse outcomes among 724 livebirths in the study by Shimabukuro et al. 200 were preterm birth (9.4%), small-for-gestational-age (3.2%) and major congenital anomalies (2.2%) – all consistent with published rates. None of the mothers whose babies were born with congenital anomalies had received the COVID-19 vaccine in the first trimester or the periconception period.

Preliminary findings from the USA<sup>200</sup> have not identified any safety problems with regards to maternal and neonatal risks. Spontaneous miscarriage occurred at similar rate in women who received a COVID-19 vaccine as those who are unvaccinated (104/827, 12.6%), with 92.3% of these miscarriages occurring in the first trimester.

#### 2.3.2. I Antibody transfer

#### Key findings

- SARS-CoV-2 antibodies in neonatal cord blood and in breast milk have been found following COVID-19 infection in pregnancy, and it may therefore be that passive immunity is conferred.
- Vaccine-elicited antibodies have also been found in infant cord blood and breast milk following the administration of the COVID-19 vaccine. The degree of protection these antibodies confer to the neonate, however, is not known.

Studies  $^{188,205}$  have demonstrated the presence of SARS-CoV-2 antibodies in neonatal cord blood and in breast milk produced in response to COVID-19 infection in pregnancy. These findings suggest the development of passive immunity in the neonate. In one of these studies  $^{188}$  87% of neonates (n = 83) had IgG conferred in cord blood following COVID-19 infection in pregnancy. Furthermore, the other cohort study  $^{205}$  of 2312 lactating women in the Netherlands reported that 23.1% of women had IgA antibodies in their breast milk, which remain present for 10 months following infection in pregnancy.

Similar findings have been reported following the administration of the COVID-19 vaccine. Two cohort studies <sup>199,200</sup> of over 100 women established the presence of vaccine-elicited antibodies in infant cord blood and breast milk. Both studies were conducted in the USA and utilised Pfizer-BioNTech or Moderna vaccines. There is some suggestion that timing of vaccination in pregnancy or during lactation may have an effect on the level of passive immunity conferred to the neonate, and two studies <sup>200,205</sup> found that production of IgG antibodies and their subsequent transfer were improved following a second dose of either vaccine. Similar to natural infection, IgA titres appear to remain stable for several weeks following vaccination, with mRNA vaccines suggesting continual transference of antibodies during lactation. <sup>206</sup> The degree of protection these antibodies confer to the neonate, however, is not yet known.

## 2.4 Recommended vaccine timing in relation to stage of pregnancy or breastfeeding

#### 2.4. I Timing of vaccination in pregnancy

#### Key findings

- COVID-19 vaccines can be given at any time in pregnancy.
- Breastfeeding women can receive a COVID-19 vaccine; there is no need to stop breastfeeding to have the vaccine.
- There is no evidence to suggest that COVID-19 vaccines affect fertility. Women planning a pregnancy or fertility treatment can also receive a COVID-19 vaccine and do not need to delay conception.

There is no robust evidence to guide the timing of vaccination in pregnancy: the advice above is based on expert opinion rather than experimental data.

The COVID-19 vaccines are considered to be safe and effective. Pregnant women are more likely to become seriously unwell when compared to non-pregnant women and have a higher risk of their baby being born prematurely if they develop COVID-19 in their third trimester (after 28 weeks of gestation). As far as possible, women should be offered both doses before giving birth, or before entering the third trimester, bearing in mind that it takes time for immunity to develop and protection is higher after the second dose of the vaccine. Women who had a first dose of vaccine before becoming pregnant should complete the course with the same vaccine (including if their first dose was with the Oxford-AstraZeneca vaccine). [9]

#### 2.4.2 Timing in the postpartum period

Women in the immediate postpartum period should be offered vaccination in line with the general (non-pregnant) population.<sup>191</sup>

#### 2.4.3 Timing with breastfeeding

The JCVI advice<sup>37</sup> published on 30 December 2020 stated there is no known risk in giving available COVID-19 vaccines to breastfeeding women. Breastfeeding women should be offered vaccination at the time when they become eligible (as for the general non-pregnant population). Although there are a lack of safety data for the available vaccines relating to breastfeeding, there is no plausible mechanism by which any vaccine ingredient could pass to a breastfeed baby through breast milk. Women should, therefore, not stop breastfeeding in order to be vaccinated against COVID-19.

#### 2.4.4 Timing for women who are planning a pregnancy/undergoing fertility treatment

There is no evidence to suggest that COVID-19 vaccines affect fertility, and there is no biologically plausible mechanism by which current vaccines could cause any impact on women's fertility. The JCVI advises that women do not need a pregnancy test before vaccination, and that women planning a pregnancy do not need to delay pregnancy after vaccination. Animal studies of the Pfizer-BioNTech and Moderna vaccines showed that administering these vaccines in rats had no effect on fertility. Preliminary animal studies also showed no effect on fertility from the Oxford-AstraZeneca vaccine. The theory that immunity to the spike protein could lead to fertility problems is not supported by evidence. Most people who contract COVID-19 will develop antibody to the spike protein and there is no evidence of fertility problems in people who have already had COVID-19. The British Fertility Society and Association of Reproductive and Clinical Scientists of advise people of reproductive age to have a COVID-19 vaccine, including those individuals who are trying to get pregnant or planning a pregnancy in the future. Furthermore, they advise that women can have the COVID-19 vaccine during fertility treatment, and that there is no need to delay fertility treatment after receiving a COVID-19 vaccine.

#### 2.5 How should women be counselled

#### Key findings

- Pregnant women should be supported to come to an informed decision about vaccination.
- There is excellent real-world evidence of vaccine efficacy, with 98% of women admitted to hospital and developing severe infection having not had the vaccine.
- An informed decision-making process should cover the options for timing of vaccination, the benefits and risks of vaccination, and the risks of declining vaccination.
- The **RCOG Information sheet and decision aid** can be used to aid counselling.

It is a pregnant woman's choice to have a vaccination against COVID-19. If a pregnant woman is undecided whether to get the COVID-19 vaccine, the role of the healthcare provider is to enable the pregnant woman to make her decision through an informed shared decision-making process. It is not necessary to show evidence of this discussion prior to the pregnant women receiving their vaccination (as is the case for the general population presenting for COVID-19 vaccination).

A pregnant woman should have the opportunity to read or view reliable information about COVID-19 vaccine in pregnancy, for example from the NHS, PHE or the RCOG. An informed decision-making process involves supporting a pregnant woman to understand the options available (including the risks and benefits of those options) and to make a decision based on the evidence and her personal preference.<sup>211,212</sup>

#### Counselling may cover the following points:

#### 1. The options available to the pregnant woman:

- To receive vaccination against COVID-19 now.
- To decline the vaccine, with the option of having it in future (either later in her pregnancy, or after the birth of her baby) once more information about the vaccine is available.
- To decline to have the vaccine altogether; this is a woman's individual choice.

#### 2. The benefits of vaccination:

- Reduction in severe disease for a pregnant woman.
- Potential reduction in the risk of preterm birth associated with COVID-19.
- Potential reduction in transmission of COVID-19 to vulnerable household members.
- Potential reduction in the risk of stillbirth associated with COVID-19.
- Potential protection of the newborn from COVID-19 by passive antibody transfer.

#### 3. The risks of vaccination (see section 2.3 for further detail):

- Minor local reaction (pain, redness or swelling at the injection site). There is excellent real-world evidence of vaccine efficacy, with 98% of women admitted to hospital and getting severe infection having not had the vaccine. <sup>228</sup>
- Mild systemic adverse effects like fatigue, headache or myalgia, typically short-lived (less than a few days).
- Thrombotic adverse events following use of the Oxford-AstraZeneca or Janssen vaccines are extremely rare.
- There has been no evidence to suggest fetal harm following vaccination against COVID-19, and fetal harm is considered to be extremely unlikely based on evidence from other non-live vaccines. Risk of fetal harm cannot be precisely estimated until large scale studies of vaccination in pregnancy have been completed.

#### 4. The risks from COVID-19 if the pregnant woman declines vaccination:

• The risks from COVID-19 to mother and fetus are covered in detail in section I of this guideline, and are summarised below:

#### o Maternal risks:

- Most women with COVID-19 in pregnancy will have no symptoms. However, some women will develop critical illness from COVID-19.

- The risk of severe illness from COVID-19 is higher for pregnant women than for non-pregnant women, particularly in the third trimester.
- There is consistent evidence that pregnant women are more likely to be admitted to an intensive care unit than non-pregnant women with COVID-19.

#### • Fetal risks:

- Symptomatic maternal COVID-19 is associated with a two to three times greater risk of preterm birth.
- Although the overall risk of stillbirth is small, the risk is approximately doubled with SARS-CoV-2 infection. 149,170
- These risks should be personalised to each individual pregnant woman:
  - Risk of exposure because of occupation: for example (and not limited to) healthcare and social workers, public-facing roles and education settings.
  - Risk of severe illness: medical conditions (hypertension, diabetes), body mass index above 30 kg/m².

#### 2.6 Research on COVID-19 vaccines in pregnant women

There is ongoing research on COVID-19 vaccines in pregnant women, addressing aspects of immunity, safety, different vaccines and optimal schedules for protecting women. More information can be found on the RCOG website. These include a randomised controlled trial funded by Pfizer<sup>213</sup> being conducted worldwide, including several UK National Institute for Health Research sites, in which pregnant women are being randomly assigned to receive either the Pfizer-BioNTech vaccine or a placebo. Those who receive the placebo during the trial will then be offered the vaccine once they give birth to ensure all participants have the opportunity of being vaccinated. The HORIZON I study is also being planned by Janssen, <sup>214</sup> in which all participants will receive the Janssen vaccine (no one will receive a placebo). Finally, there is the PregCOV-19LSR pragmatic trial<sup>215</sup> in which pregnant women are receiving different vaccines on different schedules, depending on their gestational age at enrolment. The aim is to identify the most effective schedule in order to protect pregnant women, as well as other aspects such as whether or not vaccines improve immunity conferred by breast milk.



# 3. Antenatal care during the COIVD-19 pandemic

#### 3. Antenatal care during the COVID-19 pandemic

#### 3.1 What are the considerations for organisation of antenatal care?

- Women should be advised to continue their routine antenatal care, although it may be modified, unless they meet self-isolation criteria for individuals or households (including social bubbles) with suspected or confirmed COVID-19.
- Service modifications are required to enable social distancing measures and where possible good ventilation, to reduce the risk of transmission between women, staff and other clinic/hospital visitors, and to provide care to women who are self-isolating for suspected or confirmed COVID-19 for whom a hospital attendance is essential.
- The National Institute for Health and Care Excellence (NICE) recommended schedule of antenatal care should be offered in full wherever possible. Ideally and where safe, these appointments should be offered in-person, particularly to those from Black, Asian and other minority ethnic communities, those with communication difficulties or those living with medical, social or psychological conditions that put them at higher risk of complications, or adverse outcomes, during pregnancy.
- Maternity staff should be aware that for some women with hearing or communication difficulties, mask wearing may prevent lip reading.
- Basic assessments such as blood pressure and urine testing, and assessment of fundal height in women not receiving serial fetal growth ultrasound scans, are still required.
   Trusts and health boards should plan local strategies to ensure women are able to receive this monitoring, even where antenatal care is provided remotely.
  - o If it is considered more appropriate for appointments to be conducted remotely, for example during periods of 'local lockdown', units should employ teleconferencing or videoconferencing consultations. The limitations of remote consultation methods should be recognised, including being aware that some women will not have sufficient internet access on their mobile devices or other computer hardware.
  - o It should be acknowledged that remote appointments, particularly by telephone, may cause new challenges in relationship-building between women and healthcare professionals, especially among socially vulnerable groups, women for whom English is not their first language or women who are hearing impaired.
  - Healthcare professionals should be aware that the women may have unvoiced concerns regarding their care if they have less contact in person.
  - Healthcare professionals should be aware that women may not have the privacy within their home to disclose private, personal and sensitive information. Efforts should be made at in-person appointments, such as ultrasound scans, to discuss sensitive issues such as domestic violence,

sexual and psychological abuse, psychiatric illness and recreational drug

- When in-person appointments are required (e.g. for blood tests, maternal examination or ultrasound scans) these should be arranged alongside other in-person maternity appointments to limit repeated clinic attendance.
- Appropriate screening for diabetes in pregnancy should still be provided, following NICE guidance as far as possible, with awareness that modifications to screening protocols are associated with a reduction in the detection of cases of gestational diabetes.
- Particular consideration should be given to pregnant women who have comorbidities which make them clinically vulnerable to the effects of COVID-19. Shared waiting areas should be avoided.
- If women who are in this group attend hospital, where possible, they should be cared for in single rooms.
- Women should be able to notify the unit regarding non-attendance owing to self isolation for COVID-19 using standard telephone numbers already available to them.
  - There should be a system in place to effectively identify, support and follow up women who have missed appointments.
  - Units should appoint a named midwife or consultant to coordinate care for women unable to attend appointments owing to self-isolation or a positive test. Missed appointments should be reviewed and either rescheduled if an in-person review is necessary or converted to a virtual appointment.
- For women receiving antenatal care across different sites, units must ensure that there are clear pathways for communication via handheld notes, electronic records and correspondence to general practitioners.
- Open access to day assessment and maternity triage services should be maintained. Women should be actively encouraged to attend if they have concerns about their or their baby's wellbeing.
- Continuity of care should be maintained wherever possible, particularly for women from vulnerable groups who may also be at greater risk from COVID-19.
- Healthcare providers should be aware of specific changes to services which have been suggested through regularly updated subspecialty service guidance available via the **RCOG website**.

#### Summary of evidence and rationale for guidance

Antenatal and postnatal care should be regarded as essential and women encouraged to attend, while observing social distancing and infection prevention measures, as recommended by the <u>UK Government</u>. Studies<sup>38,39</sup> in the UK and internationally have shown that women who do not attend antenatal services are at increased risk of maternal death, stillbirth and other adverse perinatal outcomes. NICE guidance<sup>40</sup> on antenatal care, including the schedule of antenatal appointments recommended for women with uncomplicated pregnancies, is well established in the UK.

The UK Government has published a <u>list of conditions</u> that make an individual extremely vulnerable to the severe effects of COVID-19, along with guidance on how best to protect these individuals.

A small study<sup>41</sup> in Massachusetts, USA, conducted in spring 2020 (early in the pandemic) showed that there was no relationship between the number of in-person antenatal visits and the risk of developing COVID-19 for pregnant women, suggesting that nosocomial transmission could be minimised. No similar evidence exists for the UK.

Another small survey study<sup>42</sup> from the USA found that the offer of remote appointments to pregnant women at high risk of obstetric complications reduced the rate at which women 'did not attend' their appointments, and that 86.9% of women were satisfied with the care received. As discussed earlier, the majority of pregnant or recently pregnant women who participated in an online questionnaire survey<sup>45</sup> felt there were barriers to accessing maternity care while anxieties were expressed about changes to antenatal services including remote consultations.

NHS England<sup>43</sup> and NHS Scotland/Scottish Perinatal Network<sup>237</sup> have issued guidance on the adoption of remote consultations in secondary care in order to minimise hospital visits.<sup>44</sup> Data directly comparing telephone/video appointments with in-person appointments are not available; until these are, healthcare providers should follow locally agreed guidelines for antenatal care provision.

During the pandemic, modifications to the NICE recommendation to screen for gestational diabetes were suggested to reduce the risk of pregnant women being infected with SARSCoV-2 during hospital visits. 46 While the number of cases of COVID-19 avoided using this strategy is unknown, evidence has quantified the reduction in diagnoses of gestational diabetes. 47-49 The rationale for the modified testing strategy is described in the Appendix of the RCOG document <u>Guidance for maternal medicine services in the coronavirus</u> (COVID-19) pandemic.

The use of personal protective equipment (PPE) and facemasks in particular can lead to difficulties in communication, especially for women with hearing loss.<sup>50</sup> Masks block lip movements and facial expressions and muffle the high frequency portions of sound. Various strategies to improve communication with women of the deaf community have been suggested and can be found on the **Royal National Institute for Deaf People** website.

The care of pregnant women with complex healthcare needs is challenging during a pandemic. To support healthcare providers caring for these women, the following guidance documents to assist maternity units with changes to antenatal and postnatal care were developed and can be found on the **RCOG** and **RCM** websites.

- Guidance for antenatal and postnatal services in the evolving coronavirus (COVID-19) pandemic.
- <u>Guidance for antenatal screening and ultrasound in pregnancy during the coronavirus (COVID-19) pandemic.</u>
- Guidance for maternal medicine in the coronavirus (COVID-19) pandemic (Version 2.5).
- RCM professional clinical briefings:
  - o RCM Professional briefing on <u>providing safe and effective virtual</u> <u>consultations</u>.
  - o RCM Professional briefing on domestic abuse during the pandemic.
  - o RCM Professional briefing on <u>public health care during the pandemic</u>, <u>including smoking cessation support</u>.
  - RCM Professional briefing on antenatal care for women <u>with</u> and <u>without</u> COVID-19.

## 3.2 What are the considerations for antenatal appointments and advice for pregnant women?

- Evidence suggests that individuals from a Black, Asian or minority ethnic background, including pregnant women from these groups, are at higher risk of developing severe complications of COVID-19. Therefore, it is advised that:
  - Healthcare providers should discuss these risks with women of Black, Asian or minority ethnic background in a sensitive manner.
  - Women of Black, Asian or minority ethnic background are encouraged to seek advice without delay if they are concerned about their health.
  - Healthcare providers should be aware of this increased risk, and have a lower threshold to review, admit and consider multidisciplinary escalation of symptoms in women of BAME background.
  - When reorganising services, maternity units should be particularly cognisant of evidence that individuals from a Black, Asian or minority ethnic background are at particular risk of developing severe and life-threatening COVID-19 disease.

- Healthcare professionals should proactively advise all pregnant women to contact emergency antenatal services if they have any concern about their or their baby's wellbeing.
- Carbon monoxide (CO) testing of all pregnant women should be undertaken, where it is safe to do so.
- Women should continue to take folic acid and vitamin D supplements in line with national recommendations.
- Women should be advised that influenza vaccination is still safe at all gestations of pregnancy and is recommended to protect both the woman and baby from the adverse effects of becoming seriously ill with flu during pregnancy.
- Pregnant women will continue to need at least as much support, advice, care and guidance in relation to pregnancy, childbirth and early parenthood as before the pandemic, especially socially vulnerable women (with risk factors including poverty, homelessness, substance misuse, being an asylum seeker, experiencing domestic abuse and mental health problems).
  - Midwifery, obstetric and support staff should remain aware of the support needs for all women, acknowledging local and national restrictions on visitors and accompanying persons may affect the amount of support women require.
- Healthcare providers should be aware of the increased risk of domestic abuse in pregnancy, which has escalated during the pandemic. Women should be encouraged to share any concerns at every opportunity and be provided with advice and support on how to access the appropriate services if required.
- Healthcare providers should maintain in-person appointments with women when there are safeguarding concerns, in order to provide extra support.
- There is evidence the pandemic has resulted in a greater level of anxiety and other mental health problems in pregnant women than in the overall population. Women should be asked about their mental health at every contact. Women who require further support should be signposted to resources and local services, which may be provided by virtual means. These include:
  - o <u>Sources of self-help for anxiety and stress</u>.
  - o Self-referral to local IAPT (Improving Access to Psychological Therapies) services in England. In Scotland, advice is available from <a href="Parentclub">Parentclub</a> and <a href="Parentclub">NHS</a>
    <a href="Inform">Inform</a>. Further information is available from the <a href="RCM">RCM</a> and <a href="Royal College of Psychiatrists">Royal College of Psychiatrists</a> websites.

- Women who express concern about their mental health or 'red flag' symptoms, such as suicidal thoughts or sudden mood changes, or where their families express these concerns on their behalf, should be supported to access urgent care either through appropriate signposting or, when required in severe cases, by immediate referral.
- Services should establish triage processes to ensure that women with mental health concerns can be appropriately assessed.

The appropriate use of PPE is to protect healthcare workers, women and their families by functioning as a physical barrier to the transmission of infectious particles present in bodily fluids. Units should follow the regularly updated **public health guidance** issued jointly by the DHSC, Public Health Wales, Public Health Agency (PHA) Northern Ireland, Health Protection Scotland/National Services Scotland, PHE and NHS England (published by PHE on their behalf), and review this in collaboration with their local guidance and infection control teams. There are also clear guidelines on PPE from the **RCM**.

The UK Government has issued guidelines on the use of face coverings within enclosed spaces in England; these are applicable to women attending outpatient maternity appointments (including scans) and to hospital visitors.<sup>32</sup> **Scotland**, **Northern Ireland** and **Wales** have issued similar guidance.

Before this pandemic, there was already extensive evidence of the inequality of experience and outcomes for women from Black, Asian or minority ethnic backgrounds giving birth in the UK.<sup>24,51,52</sup> The increased risks of COVID-19 among individuals of Black, Asian or minority ethnic background are likely to result from a number of factors such as socioeconomic disadvantage, and the fact that they are more likely to work in key worker roles, including health and social care. Women of Black, Asian or minority ethnic background who are living with socioeconomic deprivation and/or in crowded conditions, those who were born outside the UK and whose first language is not English, and those with a high BMI and/or underlying medical conditions appear to be at particularly high risk.

The RCOG Race Equality Taskforce has launched a joint campaign with <u>FiveXMore</u> that aims to help communication with women of Black, Asian or minority ethnic background, with five easy to remember steps.

There is currently an absence of accurate information about the additional risk of smoking and severe COVID-19 infection.<sup>53</sup> A scientific brief from the WHO<sup>60</sup> on smoking and COVID-19, concludes that smoking is associated with increased severity of disease and death in hospitalised COVID-19 patients. The <u>UK National Centre for Smoking Cessation and Training</u> have advised maternity units to resume carbon monoxide testing on all pregnant women, where it is safe to do so. A <u>risk assessment</u> must be undertaken prior to CO testing including a well ventilated room and being able to maintain a 2 metre distance between the woman and healthcare professionals. Recommendations on smoking screening and cessation support are based on previous evidence on the effectiveness of these interventions.

Pregnancy is a risk factor for hospital admission with influenza.<sup>54</sup> Influenza vaccination is safe and effective for pregnant women, who are always included in the annual NHS flu campaign.<sup>55</sup> It is possible to be co-infected with influenza and SARS-CoV-2.<sup>56</sup> The impact of co-infection is not known. In addition, influenza symptoms are difficult to distinguish from COVID-19 symptoms.

Isolation, bereavement, financial difficulties, insecurity and inability to access support systems are all widely recognised risk factors for mental ill health and are expected to affect individuals more than usual during the pandemic.<sup>57</sup> Access to mental health services has also been constrained and delays to accessing care were evident in two maternal deaths by suicide that occurred during the spring of 2020.<sup>21</sup>

This pandemic has resulted in an increased level of anxiety and other mental health problems in the general population. This has had a larger impact on women than on men. There is increasing evidence that this is likely to be even greater for pregnant women, as pregnancy represents a period of additional uncertainty. Specifically, these anxieties are likely to revolve around: a) COVID-19 itself, b) the impact of social isolation resulting in reduced support from wider family and friends, c) the potential of reduced household finances and d) major changes in antenatal and other NHS care, including some appointments being changed from in person to telephone contact. Meta-analyses and systematic reviews have found higher rates of perinatal mental health disorders during the pandemic, including anxiety and depression.

The <u>Royal College of Psychiatrists</u>, in collaboration with NHS England and NHS Improvement, have developed recommendations on mental wellbeing during the COVID-19 pandemic.

The coronavirus pandemic has increased the incidence of domestic abuse. Additional advice regarding support for victims of domestic abuse during the pandemic is available from the **UK government**. In addition, **Women's Aid**, **Save Lives** and **Refuge** have updated guidance for people experiencing domestic abuse during the COVID-19 outbreak.

## 3.3 How should women with suspected or confirmed COVID-19 needing hospital attendance or advice be cared for?

#### Advice

For women who telephone maternity services:

• If women report symptoms attributed to COVID-19 on the phone to maternity services, consider differential diagnoses for fever, cough or shortness of breath. This includes, but is not limited to urinary tract infection, chorioamnionitis and pulmonary embolism.

- If women have symptoms suggestive of COVID-19, they should be advised to self-refer to national services for SARS-CoV-2 testing.
- Maternity units should develop triage tools to assess the severity of illness for women who telephone with suspected or confirmed COVID-19. This should include an assessment of symptoms, clinical and social risk factors and escalation pathways. This should include 'safety netting advice' about the risks of deterioration and when to seek urgent medical attention

For women with possible or confirmed COVID-19, for whom hospital attendance is required or who self-present (this includes women who live with an individual who has possible or confirmed COVID-19):

These women should be advised to attend via private transport where possible.

- If an ambulance is required, the call handler should be alerted if the woman, or a member of her household, is symptomatic of COVID-19.
- Women should be advised to alert a member of maternity staff by mobile telephone on arrival at the hospital entrance prior to entering any of the buildings.
- Women should be met at the maternity unit or hospital entrance by staff wearing appropriate PPE to provide the woman with a fluid-resistant surgical mask.
- Staff providing care should wear appropriate PPE as per UK health protection guidance.
- Women should be cared for within isolation rooms from which all non-essential items have be removed prior to the woman's arrival (this includes other rooms in which the woman spends time during her hospital attendance [e.g. scan rooms when bedside scans are not appropriate]).
- Women should immediately be escorted to an isolation room or cohort bay/ward, suitable for the majority of care during their hospital visit or stay.
  - o Isolation rooms or ward bays should ideally have a defined area for staff to put on and remove PPE, and suitable bathroom facilities.
- The woman's facemask should not be removed until she is isolated in a suitable room or cohort bay.
- Only essential staff should enter the isolation room or bay.
- Visitors to isolation rooms or cohort bays/ward should be kept to a minimum and follow local hospital visitor policies.
- All clinical areas must be cleaned following use, according to specific COVID-19 UK wide **public health guidance**.

Maternity units should develop triage tools to assess the severity of illness for women who telephone with suspected or confirmed COVID-19. An example developed by clinicians in Guy's and St Thomas' NHS Foundation Trust is provided in Appendix V.Triage tools should include an assessment of symptoms, clinical and social risk factors and escalation pathways. This should include 'safety netting advice' about the risks of deterioration and when to seek urgent medical attention.

Availability of resources, provision of services, building/unit configuration and local prevalence of COVID-19 will vary across geographical regions, and will determine how women requiring hospital admission with confirmed or suspected COVID-19 are cared for Advice on care in isolation rooms and COVID-19 cohort bays is available from PHE, having been issued on behalf of the four nations of the UK.<sup>68</sup>This advice may change frequently and it is vital that healthcare providers stay abreast of the latest developments.

As above, units should follow the regularly updated advice on PPE, in conjunction with guidance from the RCM and their local guidance and infection control teams.<sup>68,69</sup> Guidance on cleaning clinical areas used to provide care to women with suspected or confirmed COVID-19 is available from PHE.<sup>68</sup>

## 3.4 What are the considerations for antenatal care for women who have recovered from COVID-19?

- For women who have recovered from COVID-19 with mild, moderate or no symptoms, without requiring admission to hospital, antenatal care should remain unchanged following a period of self-isolation.
- Services should ensure that women who have missed antenatal appointments because of self-isolation are seen as early as is practical after the period of self-isolation ends.
- For women who have recovered from a period of serious or critical illness with COVID-19 requiring admission to hospital for supportive therapy, ongoing antenatal care should be planned together with a consultant obstetrician prior to hospital discharge.
- Women who have been seriously or critically unwell from COVID-19 should be offered an ultrasound scan to assess the fetal biometry approximately 14 days following recovery from their illness, unless there is a pre-existing clinical reason for an earlier scan.

To date, there is an absence of evidence to guide the care for women recovering from mild or moderate symptoms of COVID-19. Women who have recovered should be encouraged to attend antenatal appointments in line with advice statements outlined above.

New studies from different nations have suggested an association between COVID-19 infection and stillbirth (see section 1.6).<sup>170,180,219</sup> While substantial evidence of causality for an association between stillbirth and COVID-19 infection is lacking, there is a growing body of evidence describing the effect of COVID-19 infection on the placenta and possible associated mechanisms for poor pregnancy outcomes.

Placental histopathology studies<sup>70,71,216</sup> have found that abnormalities, including fetal vascular malperfusion and villitis of unknown aetiology, are more frequent among COVID-19 cases than controls. One study found evidence of an increased immunological response for women infected with SARS-CoV-2 at term without evidence of active infection at the placental site.<sup>217</sup> Placental inflammation is associated with poor pregnancy and fetal outcomes,<sup>218</sup> and therefore these findings provide a hypothesis to explain the associated poorer fetal outcomes experienced by women with COVID-19 infection. Studies that have reported increased risk of developing hypertension in pregnancy following COVID-19 infection adds to the narrative of placental involvement,<sup>220</sup> and therefore confirm that women recovering from severe infection with COVID-19 should be monitored accordingly.

A systematic review concluded that in comparison to mild COVID-19 infection, severe COVID-19 infection is associated with a significant increase in risk of having a baby of low birth weight (OR 1.89).<sup>219</sup> However, a histopathology study which examined placentas of women with asymptomatic or mild COVID-19 infection reported no differences in outcomes (including birthweight) compared to COVID-19 negative controls.<sup>216</sup> This is suggestive that as severity of COVID-19 infection increases the risk for compromised fetal growth and wellbeing are impaired. In addition it is known that two-thirds of pregnancies with SARS were affected by FGR. Ultrasound to assess fetal biometry and placental function for women who have been seriously or critically unwell from COVID-19 should be undertaken and this approach has been adopted internationally.<sup>30,72</sup>

Guidance on fetal growth surveillance following COVID-19 was developed along with NHS England and NHS Improvement <u>Saving Babies' Lives Care Bundle Appendix G</u>. This recommends a single fetal growth ultrasound scan a minimum of 14 days following resolution of acute COVID-19 illness that required hospitalisation.



# 4. Venous thromboembolism prevention

## 4. Venous thromboembolism prevention

- Women who are self-isolating at home should stay hydrated and mobile.
- Women should have a VTE risk assessment performed during their pregnancy in line with RCOG Green-top Guideline No. 37a. Infection with SARS-CoV-2 should be considered a transient risk factor and trigger reassessment.
- Where normally indicated, thromboprophylaxis should still be offered and administered as prescribed during the COVID-19 pandemic.
- If healthcare professionals are concerned about the risk of VTE during a period of self-isolation, a clinical VTE risk assessment (in person or by virtual means) should be performed, and thromboprophylaxis considered and prescribed on an individual basis.
- Local procedures should be followed to ensure women are supplied with low molecular weight heparin (LMWH), particularly where they cannot attend hospital during periods of self-isolation.
- Thromboprophylaxis initiated for pregnant women who are self-isolating should be continued until they have recovered from the acute illness (between 7 and 14 days). Advice should be sought from a clinician with expertise in VTE for women with ongoing morbidity and limited mobility.
- All pregnant women admitted with confirmed or suspected COVID-19 should be offered prophylactic LMWH, unless birth is expected within 12 hours or there is significant risk of haemorrhage.
- For women with severe complications of COVID-19, the appropriate dosing regimen of LMWH should be discussed with a multidisciplinary team (MDT), including a senior obstetrician or clinician with expertise in managing VTE in pregnancy.
- All pregnant women who have been hospitalised and have had confirmed COVID-19 should be offered thromboprophylaxis for 10 days following hospital discharge.
   A longer duration of thromboprophylaxis should be considered for women with persistent morbidity.
- If women are admitted with confirmed or suspected COVID-19 within 6 weeks postpartum, they should be offered thromboprophylaxis for the duration of their admission and for at least 10 days after discharge. Consideration should be given to extending this until 6 weeks postpartum for women with significant ongoing morbidity.

Pregnancy is a hypercoagulable state.<sup>73</sup> The existing RCOG Green-top Guidelines No. 37a<sup>76</sup> and 37b<sup>77</sup> on VTE prevention and management should continue to support decision making during the COVID-19 pandemic.VTE risk assessment in the context of the COVID-19 pandemic should consider both the hypercoagulable state associated with the infection, as well as the increased risk that may come from self-isolation.

Evidence<sup>74,75</sup> indicates that individuals admitted to hospital with moderate and severe COVID-19 are also hypercoagulable. Infection with SARS-CoV-2 is likely to be associated with an increased risk of maternal VTE. This is likely to be multifactorial, including the reduced mobility resulting from self-isolation at home or hospital admission, and other associated obstetric or maternal morbidities. Consequently, the cumulative risk is difficult to quantify. In the MBRRACE rapid report<sup>78</sup> one women died from a confirmed thromboembolic event and a second woman experienced a sudden deterioration that may be attributed to a thromboembolic event.

Pregnant women, and women who have recently given birth, who have tested positive for SARS-CoV-2 are recommended to self-isolate at home even if they are asymptomatic – this may impact on their mobility which will alter further their VTE risk assessment.

The statements above were developed following expert consensus discussion to determine what increased risk COVID-19 may pose to pregnant women.VTE prevention for an unwell woman with COVID-19 is considered in section 6.2.





# 5. Labour and birth during the COVID-19 pandemic

## 5. Labour and birth during the COVID-19 pandemic

Women admitted to hospital, including maternity units, should be offered testing for SARS-CoV-2 on admission. This includes women admitted for intrapartum care.

## 5.1 What are the considerations for labour and birth in asymptomatic women who test or have tested positive for SARS-CoV-2?

#### Advice

- Low risk women who test positive for SARS-CoV-2 within 10 days prior to birth who are asymptomatic and wish to give birth at home or in a midwifery-led unit, should have an informed discussion around place of birth with their clinician.
- For asymptomatic women who test positive for SARS-CoV-2 on admission, continuous electronic fetal monitoring (CEFM) during labour using cardiotocography (CTG) is not recommended solely because of a positive test.
  - Fetal monitoring options should be discussed with the woman, acknowledging the current uncertainties in women who are asymptomatic with a positive test for SARS-CoV-2.
  - Women who test positive for SARS-CoV-2 should be offered delayed cord clamping and skin-to-skin contact with their baby in line with usual practice.

#### Summary of evidence and rationale for guidance

NHS England and NHS Scotland have recommended that women (and their support partners in NHS England) should be offered testing for SARS-CoV-2 when they are admitted to maternity units to give birth.

While fetal compromise in women who are symptomatic of COVID-19 has been reported by some case series, <sup>79,80</sup> it is reassuring that measures of fetal compromise at birth for asymptomatic women who test positive for SARS-CoV-2 are not reported to differ from women who test negative.

The need for CEFM for asymptomatic women who test positive for SARS-CoV-2 but who are otherwise low risk for labour (e.g. CEFM would not otherwise be indicated by NICE Clinical Guideline [CG190] on *Intrapartum care for healthy women and babies*<sup>82</sup>) is an area of clinical uncertainty because of the lack of robust evidence. It is, therefore, important that asymptomatic women of low obstetric risk should continue to have the risks and benefits of CEFM discussed with them on a holistic basis.

There is no evidence<sup>83,84</sup> that the practice of delayed cord clamping and skin-to-skin contact between mother and baby increases the transmission of SARS-CoV-2 to the neonate. The well documented benefits of these practices should be discussed with the woman to make an informed choice and implemented in line with pre-pandemic practice. In the absence of other evidence, NICE CG190 should be followed.<sup>82</sup>

## 5.2 How should a woman with suspected or confirmed COVID-19 be cared for in labour if they are symptomatic?

- Women with mild COVID-19 symptoms can be encouraged to remain at home (self-isolating) in early (latent phase) labour consistent with routine care.
- If there are no concerns regarding the health of either the woman or baby, women who attend the maternity unit and would usually be advised to return home until labour is more established can still be advised to do so, unless private transport is not available.
  - Women should be provided with the usual advice regarding signs and symptoms of labour, but also be informed about symptoms that might suggest deterioration related to COVID-19 and be advised to call back if concerned.
- Advice on PPE is available in section 5.8.
- Women with symptomatic suspected or confirmed COVID-19 should be advised to labour and give birth in an obstetric unit.
- On admission, a full maternal and fetal assessment should be undertaken, including:
  - Assessment of the severity of COVID-19 symptoms by the most senior available clinician.
  - Maternal observations including temperature, respiratory rate and oxygen saturation.
  - Confirmation of the onset of labour, as per standard care.
  - CEFM using CTG.
- The following members of the MDT should be informed of the woman's admission: consultant obstetrician, consultant anaesthetist, midwife-in-charge, consultant neonatologist, neonatal nurse-in-charge and the infection control team. Other members of the team may include an obstetric physician or respiratory physician.
- Standard hourly maternal observations and assessment should be performed (as per the recommendations in NICE CG190, *Intrapartum care for healthy women and babies*), with the addition of hourly oxygen saturation monitoring. Oxygen therapy should be titrated to aim for saturation above 94%.

- CEFM should be offered to women with symptomatic suspected or confirmed COVID-19 during labour and vaginal birth.
- Maternal infection with SARS-CoV-2 is in itself not a contraindication to performing a fetal blood sample or using fetal scalp electrodes.
- The number of staff members entering the room should be minimised, and units should develop a local policy specifying essential personnel for emergency scenarios.
- Women with symptomatic suspected or confirmed COVID-19 should be offered delayed cord clamping and skin-to-skin contact with their baby, if the condition of the woman and infant allows.

NHS England has produced clinical guidance<sup>85</sup> on the temporary reorganisation of intrapartum maternity care during the coronavirus pandemic and a framework has been published in Scotland.<sup>86</sup>

COVID-19 infection and control guidance issued by PHE, on behalf of the four nations of the UK, gives advice about avoiding disease transmission.<sup>80</sup> WHO has produced guidance on clinical management of COVID-19.<sup>87</sup>

In women with symptomatic COVID-19, there may be an increased risk of fetal compromise in active labour.<sup>79,80,88,89</sup> In addition, it is reported<sup>90</sup> that women with symptomatic COVID-19 have an increased risk of caesarean birth, which further supports the guidance to give birth in an obstetric unit where timely access to emergency care is available.

While further data is required in women with symptomatic confirmed or suspected COVID-19, it appears prudent to use CEFM, as would usually be recommended for maternal systemic infection.

There is no evidence<sup>83,84</sup> that the practice of delayed cord clamping and skin-to-skin contact between woman and baby increases the transmission of SARS-CoV-2 to the neonate.

## 5.3 What are the considerations for labour and birth for women who have recovered from COVID-19?

#### Advice

• For women who have recovered from antenatal COVID-19 without requiring admission to hospital, and who have completed self-isolation in line with public health guidance, there should be no change to planned care during labour and birth.

- For women who have recovered following a hospital admission for serious or critical COVID-19 illness needing supportive therapy, healthcare professionals should discuss and plan place of birth with the woman. While making a personalised assessment, consideration should be given to both the growth of the fetus and the woman's choices.
- Healthcare professionals should ensure that any growth ultrasound scan undertaken following a period of severe illness has been reviewed. If the interval between resolution of illness and presentation for birth has been insufficient to allow for a growth scan, the implications of this should be considered in the assessment and care plan.
- When participating in informed discussions with women about fetal monitoring, healthcare professionals should acknowledge evidence of fetal distress is based on small numbers of babies born to women symptomatic of COVID-19, and theoretical risks extrapolated from pregnancies affected by FGR in women with other coronaviruses.

There is an absence of evidence for this situation. The above is based on expert consensus.

## 5.4 What are the considerations for birth partners during the COVID-19 pandemic?

- Women should be supported and encouraged to have a birth partner present with them during active labour and birth if they wish to do so.
- Birth partners who are symptomatic, or in a period of self-isolation for confirmed SARS-CoV-2 infection, should remain in self-isolation at home and not attend the hospital.
- NHS England recommends efforts should be made to utilise the available testing capacity to test both the woman and her birth partner to mitigate infection risk where resources allow.
- Local level risk assessments should be made for each maternity service space (for example shared wards) to identify if there are elevated risks of SARS-CoV-2 transmission from the presence of a birth partner.
- On attendance at the maternity unit, all birth partners should be asked whether they have experienced any symptoms suggestive of COVID-19 in the preceding 10 days, e.g. fever, acute persistent cough, changes in or loss of sense of smell (anosmia) or taste.

- o If they have had symptoms within the last 10 days, the birth partner should leave the maternity unit immediately and self-isolate at home, unless they have had a negative test result for SARS-CoV-2 since the onset of symptoms.
- o If they have had a fever within the last 48 hours, birth partners should leave the maternity unit immediately and self-isolate at home, regardless of their test result.
- Birth partners, not otherwise advised to be self-isolating, should be allowed to stay with the woman through labour and birth, unless the birth occurs under general anaesthetic. Further guidance about access to maternity services for a birth partner and other supportive adults has been published by the NHS and should be followed as far as possible.
- Birth partners should wear a face covering unless exempt, remain by the woman's bedside, be advised not to walk around the ward/hospital and should wash their hands frequently.
- Restrictions on visitors should follow local hospital policy.
- Trusts and health boards should prioritise the birth partners of women who require continuous support, such as women with disabilities, communication challenges or complex medical, mental health or social factors.

Having a trusted birth partner present throughout labour is known to make a significant difference to the safety and wellbeing of women in childbirth. <sup>91–93</sup> The pandemic has affected the levels of perinatal stress experienced by pregnant women, as well as feelings of fear and loneliness in relation to their birth experience. <sup>94,95</sup> A supportive birth partner is a recognised protective factor for the emotional wellbeing and birth experiences of women. UK-wide PHE guidance, local hospital infection control and visitor policies should be adhered to. <sup>96,97</sup> The NHS has produced guidance to support the access of birth partners and other supportive adults to maternity services in England and Scotland.

## 5.5 What informed discussions should take place with women regarding timing and mode of birth during the COVID-19 pandemic?

#### Advice

• Clinicians should discuss mode of birth during the COVID-19 pandemic with the woman and her family. Consideration should be given to her preferences and any obstetric or fetal indications for intervention.

- A personalised assessment should take place to determine whether it is beneficial overall to delay a planned caesarean birth or induction of labour (IOL), and any associated appointments, for women who are self-isolating because of suspected COVID-19 in themselves or in a household contact.
  - Consider the urgency of the birth and the risk of infectious transmission to other women, healthcare workers and, postnatally, to her baby.
  - If a planned caesarean birth or IOL cannot be delayed, follow the advice for services providing care to women admitted with suspected or confirmed COVID-19.
- Women with worsening symptoms, or who are becoming exhausted, should be
  offered personalised information so they can make an informed decision about
  expediting birth.
- Senior obstetric and medical input for a woman with severe or critical COVID-19 should be sought, particularly for decision making about birth. Consider whether the benefits of an urgent caesarean birth outweigh any risks to the woman.
- The advice in section 5.8 on PPE for caesarean birth should be followed.
- Women and their families should be informed that donning PPE for emergency caesarean births is time-consuming but essential, and this may impact on the time it takes to assist in the birth of the baby. Consider this during decision making and, where possible, discuss during birth planning.

There is no evidence to favour one mode of birth over another in women with COVID-19. In the earlier UKOSS study, <sup>98</sup> 12 (5%) babies tested positive for SARS-CoV-2 infection; six within the first 12 hours (two were born by unassisted vaginal birth and four by caesarean birth) and six after 12 hours (two born vaginally and four by caesarean birth). <sup>98</sup>The rate of neonatal COVID-19 infection is no greater when babies are born vaginally, breastfed or stay with their mother after birth. <sup>99–101</sup>

Donning PPE is expected to lengthen the decision to birth interval because of the additional action required before commencing surgery, however, there is no evidence of this within the UK setting. A single centre cohort study<sup>102</sup> demonstrated a possible longer time to birth in urgent caesarean births for women with suspected or confirmed COVID-19 (25.5 minutes [95% CI 17.5–31.75] versus 18.0 minutes [95% CI 10.0–26.25]; P = 0.113]). This did not reach statistical significance, which may be explained by the study sample size which was not chosen to power for the outcome. Simulation training has been proposed as a way of improving the response to obstetric emergencies during the COVID-19 pandemic, including donning and doffing of PPE. <sup>103</sup>

#### 5.6 What are the considerations for water birth?

#### Advice

- Water birth is not contraindicated for women who are asymptomatic of COVID-19 and presumed or confirmed SARS-CoV-2 swab negative, providing adequate PPE can be worn by those providing care.
- Women with symptomatic COVID-19 who have a cough, fever or feel unwell, should not labour and birth in water.
- Asymptomatic women who have tested positive for SARS-CoV-2 should be advised there is inadequate evidence about the risk of transmission of the virus in water.
- Healthcare providers should be aware that the integrity of PPE, such as a facemask, could be compromised when it becomes wet.

#### Summary of evidence and rationale for guidance

Labour and birth in water may confer benefits to women at low risk of complications during birth. Women report<sup>104</sup> that restrictions to access water birth are a concern during the pandemic, and therefore in the absence of contraindication to water birth, this option should be available. Care providers should discuss with women the lack of evidence on this topic in the context of the COVID-19 pandemic in order to facilitate informed decision making.

The RCM<sup>227</sup> notes that in relation to women who are asymptomatic of COVID-19, but test positive for SARS-CoV-2, there is inadequate evidence about the risk of transmission of the virus in water. There is evidence that SARS-CoV-2 RNA may be present in faeces, but no evidence to support that this has resulted in faecal—oral spread. <sup>105,106</sup> There is, therefore, insufficient evidence for or against the use of water in labour or birth for asymptomatic women and staff caring for them. The RCM does note that healthcare providers should be aware that the integrity of PPE, such as a face mask, could be compromised when it becomes wet.

It is recommended that women with pyrexia should not labour or birth in water.<sup>82</sup> Women with a cough or breathing difficulties, or those who feel unwell, should be closely monitored for their oxygen saturations and other vital signs and may require oxygen support. This care is better provided out of water to enable more effective monitoring and rapid access to emergency care.

### 5.7 What are the specific considerations for labour analgesia or anaesthesia

#### Advice

• Entonox (50% nitrous oxide and 50% oxygen) can be safely offered with a standard single-patient microbiological filter.

• The option of epidural analgesia should be discussed with women with suspected or confirmed COVID-19 when they are in early labour so they can make informed decisions regarding use or type of labour analgesia. Women should be informed that the use of epidural analgesia may avoid the need for GA in some cases, and the associated additional risks in this scenario.

#### Summary of evidence and rationale for guidance

Advice published on the considerations for <u>labour analgesia or anaesthesia</u> is based on expert opinion following consultation with the Obstetric Anaesthetists Association (OAA).

There is no evidence that the use of Entonox is an aerosol-generating procedure (AGP). There is no evidence that epidural or spinal analgesia or anaesthesia is contraindicated in the presence of coronaviruses.<sup>107</sup>

Intubation, required for GA, is an AGP. This significantly increases the risk of transmission of SARS-CoV-2 to attending staff. <sup>108</sup>

UK case studies<sup>109</sup> reported significantly lower rates of GA for caesarean births (down from 7.7% to 3.7%), as well as lower rates of conversion from neuraxial to GA during the initial wave of the SARS-CoV-2 infection in 2020. Recommendations for anaesthetic decision making made by the OAA are thought to have been influential in the decline in GA rate. This supports the guidance that clinicians should facilitate fully informed discussions regarding choice of analgesia early in labour for women with suspected or confirmed COVID-19.

## 5.8 What personal protective equipment is recommended when caring for women during labour and birth?

- Healthcare professionals should follow national recommendations on the use of PPE in clinical settings.
- Owing to the differing levels of PPE required for caesarean birth, a multidisciplinary discussion should be held about the likelihood of a woman requiring a GA.
- For caesarean births where GA is planned from the outset all staff in theatre should wear PPE, including an FFP3 mask and visor. PPE should be donned prior to commencing the GA.
- Local standard operating procedures should be developed to determine the type of PPE required in cases where GA is not planned from the outset, but neuraxial anaesthesia for caesarean birth either cannot be sited or is ineffective.

The appropriate use of PPE is to protect healthcare workers, women and their families by functioning as a physical barrier to the transmission of infectious particles present in bodily fluids. General advice from PHE, issued on behalf of the four nations of the UK, on type and specification of <u>PPE</u> is available. The <u>RCM</u> and the <u>OAA</u> have provided specific advice on the type and specification of PPE for maternity care and obstetric anaesthesia.

The level of PPE required by healthcare professionals caring for a woman with COVID-19 who is undergoing a caesarean birth should be determined on the basis of the risk of her requiring a GA, which would require intubation and is, therefore, an AGP.<sup>110</sup>

The provision of neuraxial anaesthesia (spinal, epidural or combined spinal epidural [CSE]) is not an AGP.

The chance of requiring conversion to a GA during a caesarean birth commenced under neuraxial anaesthesia is small, but this chance increases with the urgency of caesarean birth. In situations where there are risk factors that make conversion to a GA more likely, the decision on what type of PPE to wear should be based on the individual circumstances. If the risk of requiring conversion to a GA is considered significant (e.g. in a category I caesarean birth), the theatre team should wear PPE appropriate to a GA in readiness.

A retrospective analysis<sup>109</sup> of anaesthetic practices for caesarean births in maternity units in the north-west of England during the initial wave of the COVID-19 pandemic, found a reduction in GA rates (from 7.7% before the pandemic to 3.7% during). Further there was a reduction in conversion rates from neuraxial to GA (from 1.7% to 0.8%). The key factors identified for these reductions included anaesthetic decision-making, recommendations from anaesthetic guidelines and the increased presence of on-site anaesthetic consultants. This is encouraging but should be interpreted with some caution as the authors did not report neonatal outcomes.

## 5.9 How should obstetric theatres be managed during the COVID-19 pandemic?

- Elective obstetric procedures, such as caesarean birth or cervical cerclage, for women with suspected or confirmed COVID-19, should ideally be scheduled at the end of the operating list.
- Emergency procedures for women with suspected or confirmed COVID-19 should be conducted in a second obstetric theatre where available, allowing time for a full postoperative theatre clean as per national health protection guidance.
- The number of staff in the operating theatre should be kept to a minimum and all colleagues should wear appropriate PPE.

- Anaesthetic care for women with suspected or confirmed COVID-19 should be provided with reference to guidance from the Royal College of Anaesthetists (RCoA)/OAA/Faculty of Intensive Care Medicine/Intensive Care Society/Association of Anaesthetists.
- Operating theatre checklists should be used to aid closed loop communication as the wearing of PPE compromises communication.

The advice above is based on UK government advice on infection prevention and control,<sup>96</sup> and guidance from the RCoA, OAA,Faculty of Intensive Care Medicine, the Intensive Care Society and the Association of Anaesthetists.<sup>110</sup>

The use of PPE causes communication difficulties in operating theatre settings, <sup>111</sup> including obstetric theatres. <sup>110</sup> It is proposed that operating theatre checklists should be employed to improve communication in operating theatres.

## 5.10 What are the considerations for bereavement care during the COVID-19 pandemic?

Summary of evidence and rationale for guidance

#### Advice

- Maternity services should ensure that bereavement care remains of a high standard during the COVID-19 pandemic, with continued provision of appropriate intrapartum and postnatal care, including all appropriate investigations and postnatal appointments.
- Women should be supported and encouraged to have a support person accompany them to all care episodes related to a pregnancy loss if they wish.

Sands and the RCM have provided further guidance on bereavement care during the pandemic in their briefing **Bereavement Care in Maternity Services During COVID-19 pandemic. Sands** has also produced information for bereaved families about care during the pandemic.



# 6. Managing clinical deterioration of COVID-19

### 6. Managing clinical deterioration of COVID-19

6.1 How should a pregnant woman requiring hospital admission with symptoms suggestive of COVID-19 be investigated?

- Pregnant and postpartum women presenting with COVID-19 should be investigated and treated the same as non-pregnant women unless there is a clear reason not to do so.
- The decision for admission or for self-directed care at home depends on the overall clinical picture. Care at home should include clear 'safety netting advice' and in some instances this may involve home monitoring of oxygen saturation levels.
- Women presenting with a fever, should be cared for in line with RCOG Green-top Guideline No. 64a *Bacterial Sepsis in Pregnancy*. Testing for SARS-CoV-2 should be offered in addition to blood cultures.
- While pyrexia may suggest COVID-19, clinicians should not assume that all pyrexia is because of COVID-19. The possibility of bacterial infection should be considered and a full sepsis screen performed in line with the <a href="UK Sepsis Trust Sepsis Screening and Action Tool">UK Sepsis Trust Sepsis Screening and Action Tool</a> and intravenous (IV) antibiotics administered when appropriate.
- Bacterial (rather than viral) infection should be considered if the white blood cell count is raised (lymphocytes are usually low with COVID-19) and antibiotics should be commenced.
- Radiographic investigations should be performed as for the non-pregnant adult; this includes chest X-ray and computerised tomography (CT) of the chest. Chest imaging is essential for the evaluation of an unwell woman with COVID-19 and should be performed when indicated, and not delayed because of concerns of possible maternal and fetal exposure to radiation, as maternal wellbeing is paramount.
- A diagnosis of pulmonary embolism or heart failure should be considered for women presenting with chest pain, worsening hypoxia or a respiratory rate above 20 breaths/minute (particularly if there is a sudden increase in oxygen requirements), or in women whose breathlessness persists or worsens after expected recovery from COVID-19. Additional tests to investigate for possible differential diagnoses, including electrocardiogram, echocardiogram, CT pulmonary angiogram, ventilation perfusion lung scan, should be considered.
- Ferritin and C-reactive protein are usually raised in COVID-19. D-Dimer is also usually raised and is therefore not useful to assess VTE.
- Disseminated intravascular coagulation can also occur, with prolonged prothrombin time and activated partial thromboplastin time, and low fibrinogen levels.

The clinical symptoms of COVID-19 overlap with those of a variety of other clinical conditions. Healthcare providers should consider all differential diagnoses for women who present with a fever in pregnancy and follow the advice and guidance of the RCOG Green-top Guideline No. 64a.<sup>112</sup>

Several studies<sup>113</sup> have shown decreased lymphocyte counts in the general population affected by COVID-19. One systematic review<sup>114</sup> noted decreased lymphocyte counts in pregnant women.

'Safety netting' describes what symptom deterioration to look out for and the specific actions to take if this occurs. Pulse oximetry may be offered as part of this process, or used in some situations, for home monitoring of oxygen saturation. An example of safety netting might include the points below, and further advice is available from the NHS.<sup>231,232,233</sup>

- Ring your GP/local out-of-hours service/labour ward (the advice should be clear and specific to each local service) as soon as possible if you slowly start feeling more unwell or more breathless, or are having difficulty breathing when getting up to go to the toilet or similar, or you sense that something is wrong (e.g. general weakness, extreme tiredness, loss of appetite, reduced urine output, unable to care for yourself), or if you use a pulse oximeter and your blood oxygen level is 94% or 93%.
- Attend your nearest A&E or call 999 immediately, if you are unable to complete short sentences when at rest because of breathlessness, or your breathing suddenly worsens within an hour, or you have blue lips or a blue face, or you feel cold sweaty and pale, or collapse or faint, or become agitated, confused or very drowsy, or you use a pulse oximeter and it measures 92% or less.
- If using a pulse oximeter, caution should be observed for women with darker skin tones as pulse oximeters may overestimate the oxygen saturation.<sup>234</sup>

# 6.2 How should a pregnant, or recently pregnant, woman with suspected or confirmed COVID-19 who is clinically deteriorating be cared for?

#### Advice

#### Organisation and principles of care

- Obstetricians should be familiar with and follow local guidelines for the initial investigation and care of women presenting with possible COVID-19.
- Women with suspected COVID-19 should be treated as if positive until test results are available.

- The priority for medical care should be to stabilise the woman's condition with standard therapies.
- An urgent MDT meeting should be arranged for any unwell woman with suspected or confirmed COVID-19. This includes women who are requiring oxygen to maintain saturations between 94% and 98%, women with a respiratory rate above 20 breaths/ minute and women with a heart rate greater than 110 beats/minute. This should ideally involve senior decision makers and may include: a consultant obstetrician, consultant anaesthetist, midwife-in-charge, consultant neonatologist, neonatal nurse-in-charge, intensivist responsible for obstetric care, an obstetric physician, a respiratory physician and the infection control team. The discussion should be shared with the woman, and her family if she chooses. The following should be considered:
  - Key priorities for medical care of the woman and her baby, and her birth preferences.
  - The most appropriate location of care (e.g. intensive care unit, 'COVID bays', specific COVID-19 wards, isolation room in infectious disease ward or other suitable isolation room) and lead specialty.
  - Concerns among the team regarding special considerations in pregnancy, including the health of the baby.
- A consultant in obstetrics and gynaecology should review all pregnant and recently pregnant women with suspected or confirmed COVID-19 who are in hospital at least daily, particularly if they are admitted to a bed outside of the maternity unit.
- If appropriate, a designated team member should be responsible for regularly updating the woman's family about her health, and that of the baby.

#### Observations and investigations

- Clinicians should monitor both the absolute values and trends of the hourly observations, including heart rate, respiratory rate and oxygen saturation.
- Clinicians should be aware that young, fit women can compensate for deterioration in respiratory function and are able to maintain normal oxygen saturations until sudden decompensation.
- Units should have an escalation plan for the care of pregnant and postnatal women with COVID-19.
- A woman's care should be escalated urgently if any of the following signs of decompensation develop:
  - o increasing oxygen requirements or fraction of inspired oxygen (FiO<sub>2</sub>) above 35%.

- o increasing respiratory rate despite oxygen therapy of, or above, 25 breaths/ minutes or a rapidly rising respiratory rate,
- o reduction in urine output when this is being monitored,
- acute kidney injury (serum creatinine levels above 77 μmol/l in women with no pre-existing renal disease),
- o drowsiness, even if the oxygen saturations are normal.
- The possibility of myocardial injury should be considered, as the symptoms are similar to those of respiratory complications of COVID-19.
- The appropriateness and frequency of fetal heart rate monitoring should be considered on an individual basis, accounting for the gestational age and the maternal condition.

#### Planning for the birth of the baby

- For pregnant women in the third trimester who are unwell, an individualised assessment should be undertaken by the MDT to decide whether emergency caesarean birth or IOL should be performed, either to facilitate maternal resuscitation (including the need for prone positioning) or because of concerns regarding fetal health.
- If maternal stabilisation is required before delivery can be undertaken safely, this is the priority, as it is in other maternity emergencies.
- If urgent intervention for birth is indicated for fetal reasons, then birth should be expedited as for usual obstetric indications, as long as the maternal condition is stable.
- When iatrogenic preterm birth is required, the administration of antenatal corticosteroids to promote fetal lung maturation and magnesium sulfate for fetal neuroprotection, should be considered by the MDT. Urgent intervention for birth should not be delayed for their administration.

#### Summary of evidence and rationale for guidance

A useful summary on supportive care for adults diagnosed with COVID-19 has been published by the WHO.<sup>115</sup> Specific guidance on the care of patients with COVID-19 who are admitted to critical care has been published by NICE and SIGN.<sup>116,117</sup>

Hospitals should have escalation guidelines for the care of pregnant and postnatal women with COVID-19. An example of a maternity escalation plan from Guy's and St Thomas' NHS Foundation Trust is given in Appendix VI.

As discussed in section 4, infection with SARS-CoV-2 requiring admission to hospital is associated with an increased risk of VTE. All pregnant and recently pregnant women should be assessed for risk of VTE and prescribed thromboprophylaxis with LMWH unless there is a contraindication. The dose of LMWH should be considered on an individual basis and discussed with the MDT. There is currently not enough evidence of the benefits and risks of therapeutic dose anticoagulation applicable to pregnant women who may require imminent operative birth, to recommend therapeutic anticoagulation routinely in the absence of suspected or proven VTE.

While most patients with severe COVID-19 infection will have normal or even high platelet counts, COVID-19 can be associated with thrombocytopenia. When aspirin has been prescribed as prophylaxis for pre-eclampsia, it should be discontinued for the duration of the infection as this may increase the bleeding risk in women with thrombocytopenia. Women who take LMWH thromboprophylaxis during pregnancy should discontinue this if their platelet count falls below  $50 \times 10^9$ /L and their care should be discussed with a haematologist.

Myocardial injury and its complications were observed in 11% of all patients who died in Italy up to 4 June 2020,<sup>79</sup> and studies of cardiac biomarkers also support evidence of myocardial injury.<sup>165</sup> Early involvement of multidisciplinary colleagues to investigate for potential myocardial injury is essential if this is suspected.<sup>120</sup> Further details of investigation and management is available in the NICE rapid guideline on diagnosing myocardial injury in patients with suspected or confirmed COVID-19.<sup>120</sup>

Increased rates of iatrogenic preterm birth are associated with severe COVID-19 infection in pregnancy (sections 1.4.3 and 1.6). Antenatal corticosteroids are well established as being beneficial in preterm labour, or if iatrogenic preterm birth is anticipated. <sup>100</sup> Magnesium sulfate therapy is recommended for neuroprotection of the neonate, and should be offered to women up to 29<sup>+6</sup> weeks of gestation and considered up to 33<sup>+6</sup> weeks of gestation. <sup>100</sup> The administration of steroids and magnesium sulfate to women who are severely unwell with COVID-19 should be considered by an MDT.

For non-specialist anaesthetists and physicians involved in the care of pregnant women with COVID-19 and other medical conditions, useful information is available from the RCoA guideline Care of the critically ill woman in childbirth; enhanced maternal care and the Royal College of Physicians' Acute care toolkit 15: Managing acute medical problems in pregnancy. 122,123

Prone positioning of patients with moderate to severe acute respiratory distress syndrome (ARDS) can improve respiratory function and has been recommended for the care of patients with COVID-19.<sup>115</sup> There is little evidence on the use of prone positioning in pregnancy, and guidance from the Intensive Care Society in the UK<sup>124</sup> advises that it is relatively contraindicated in the second and third trimesters of pregnancy. However, a review article<sup>125</sup> on prone positioning for pregnant women who are unwell with COVID-19 provides advice, guidance and an algorithm on how this can be undertaken successfully in the second and early third trimesters.

## 6.3 What therapies should be offered to pregnant, or recently pregnant, women with COVID-19?

- If there is clinical uncertainty about whether to offer a therapy to a pregnant woman, advice should be sought through maternal medicine networks.
- Oxygen should be titrated to target saturations to 94–98%. Using escalation through nasal cannula, face mask, venturi mask, non-rebreather mask, non-invasive positive airway pressure (e.g. CPAP), intubation and IPPV, and ECMO as appropriate. Referrals to the NHS ECMO service should be made for pregnant women or women postpregnancy using the same criteria as for other adult patients i.e. if worsening severe respiratory failure despite appropriate conventional ventilatory support, or for women in whom lung-protective ventilation cannot be achieved because of the severity of hypoxaemia or hypercapnia, or significant air-leak (e.g, barotrauma or bronchopleural fistula).
- Proning should be strongly considered. Although evidence is limited there are reports that this is feasible (with appropriate padding) up to at least 28 weeks of gestation.
- Caution should be applied to IV fluid management:
  - Hourly fluid input/output charts should be used to monitor fluid balance in women with moderate to severe symptoms of COVID-19.
  - The aim should be to maintain a neutral fluid balance in labour.
  - When required, boluses in volumes of 250–500 ml should be employed and an assessment for fluid overload made before proceeding with further fluid resuscitation.
- Antibiotics should be commenced at presentation if there is clinical suspicion of bacterial infection or sepsis, with an early review and rationalisation of antibiotics if COVID-19 is confirmed. Even when COVID-19 is confirmed, clinicians should remain open to the possibility of another coexisting condition. There should be no delay in the administration of therapy that would usually be given in maternity care (e.g. IV antibiotics in woman with fever and prolonged rupture of membranes).
- All pregnant women should be assessed for risk of VTE and prescribed thromboprophylaxis with LMWH unless there is a contraindication (see section 4). The dose of LMWH should be considered on an individual basis and discussed with the MDT. Therapeutic doses of LMWH should be employed when VTE is suspected until objective testing can be undertaken.

- Thrombocytopenia may be associated with severe COVID-19. For women with thrombocytopenia (platelets less than 50 × 10<sup>9</sup>/L) aspirin and LMWH thromboprophylaxis should be discontinued and haematology advice sought. The use of mechanical aids (such as intermittent pneumatic compression) should be used if LMWH therapy is contraindicated or paused secondary to thrombocytopenia.
- Corticosteroid therapy should be given for 10 days or up to discharge, whichever is sooner, for women who are unwell with COVID-19 and requiring oxygen supplementation or ventilatory support. One suggested steroid regimen is:
  - o If steroids are not indicated for fetal lung maturity, oral prednisolone 40 mg once a day, or IV hydrocortisone 80 mg twice daily, for 10 days or until discharge, whichever is sooner.
  - o If steroids are indicated for fetal lung maturity, intramuscular dexamethasone 6 mg every 12 hours for four doses, immediately followed by oral prednisolone 40 mg once a day, or IV hydrocortisone 80 mg twice daily, to complete a total of 10 days or until discharge, whichever is sooner.
- The interleukin-6 receptor antagonist (anti-IL6) Tocilizumab has been shown to improve outcomes, including survival, in hospitalised patients with hypoxia (oxygen saturation below 92% on air or requiring oxygen therapy) and evidence of systemic inflammation (C-reactive protein at or above 75 mg/l). Although data for the use of tocilizumab in pregnancy in this situation are limited, there is currently no evidence that tocilizumab is teratogenic or fetotoxic. For women meeting the criteria above (hypoxic with systemic inflammation), the use of tocilizumab should be strongly considered. It is recommended that any decision to treat with anti-IL6 agents should be taken by an MDT, including obstetric and infection specialists, and given if the benefits outweigh the risks.
- Strongly consider REGEN-COV2 (casirivimab and imdevimab) monoclonal antibodies (8 g single IV infusion) in pregnant and breastfeeding women treatment if they are symptomatic, hospitalised with COVID-19 infection, and have no SARS-CoV-2 antibodies (note: currently seeking UK licence).
- Remdesivir may be considered in pregnant women with COVID-19 as described below if a woman is not improving or if there is deterioration. Clinicians should be aware that the fetal risk profile of remdesivir is largely unknown.
- Other therapies are being investigated for the management of COVID-19, and pregnant women should be offered the opportunity to enrol in clinical trials (such as the RECOVERY trial) for which they are eligible.
- Hydroxychloroquine, lopinavir / ritonavir and azithromycin have been shown to be ineffective in treating COVID-19 infection and should not be used for this purpose.

Adequate early oxygen therapy is essential.<sup>164</sup> There is evidence that ECMO is either not being considered or being inappropriately discounted<sup>164</sup> and there is now a UK NHS consensus statement for COVID-19 patients on the criteria for considering, and referring to, an ECMO centre.<sup>163</sup>

There is no evidence to guide prophylactic LMWH dosing in obstetric patients, i.e. whether to prescribe the usual prophylactic dose, a higher prophylactic dose or a therapeutic dose. There is some evidence to guide dosing in other groups of patients, <sup>239,240</sup> which may not translate to an obstetric population, and this is also summarised in the NICE COVID-19 rapid guideline: managing COVID-19.<sup>238</sup>

The interim results of the RECOVERY trial demonstrated a significant reduction in 28-day mortality for individuals with COVID-19 requiring oxygen who were given corticosteroid therapy (age-adjusted rate ratio 0.83, 95% CI 0.75–0.93; P < 0.001). <sup>126</sup> The RECOVERY trial protocol for pregnancy recommends oral prednisolone 40 mg once daily, and, in women unable to take oral medicine, IV hydrocortisone 80 mg twice daily instead of dexamethasone treatment. <sup>21,127,128</sup> Unlike dexamethasone, prednisolone and hydrocortisone are extensively metabolised in the placenta with minimal transfer to the fetus.

While the neonatal benefits of antenatal corticosteroids (betamethasone and dexamethasone) are well-established when administered to women at risk of imminent preterm birth (NICE NG25), 100 exposure to repetitive doses of steroids is associated with adverse neonatal outcomes. 129 It is, therefore, recommended that if corticosteroids are not indicated for fetal lung maturity, oral prednisolone 40 mg once a day, or IV hydrocortisone 80 mg twice daily, should be administered for 10 days or up to discharge, whichever is sooner. If steroids are indicated for fetal lung maturity, intramuscular dexamethasone 6 mg every 12 hours for four doses, then oral prednisolone 40 mg once a day, or IV hydrocortisone 80 mg twice daily, should be given for 10 days or up to discharge, whichever is sooner.

Anti-IL6 agents, tocilizumab and sarilumab, have been investigated <sup>132</sup> on adult patients with COVID-19, administered within 24 hours of commencing organ support in an intensive care unit. It was reported that anti-IL6 agents decreased hospital mortality and reduced progression to intubation, extracorporeal membrane oxygenation, or death. Another study investigating tocilizumab in unwell patients with COVID-19 did not show these favourable outcomes <sup>133</sup> and a need for caution in the use of tocilizumab in unwell patients with COVID-19 has been proposed. <sup>134</sup> Encouragingly, results from the RECOVERY trial investigating the use of tocilizumab in patients admitted to hospital with COVID-19 have shown that tocilizumab improved survival and other clinical outcomes in patients with hypoxia and systemic inflammation (C-reactive protein at or above 75 mg/l). <sup>126</sup> These benefits were seen regardless of the level of respiratory support. Drug registries <sup>136,137</sup> on the use of tocilizumab in pregnancy have limited numbers but show no evidence of harm. Tocilizumab is excreted in very low levels in breast milk. <sup>138</sup> Any decision to treat pregnant or postnatal women with anti-IL6 agents should be taken by an MDT and, when feasible, in discussion with the woman.

A preliminary report of an RCT in which 9785 patients hospitalised with COVID-19 were randomly allocated to receive usual care or usual care plus monoclonal antibodies to the SARS-CoV-2 spike protein on the surface of cells (REGEN-COV, casirivimab and imdevimab) has been published.  $^{162}$  Of these patients, 3153 (32%) were seronegative for SARS-CoV-2, 5272 (54%) seropositive and 1360 (14%) patients had an unknown baseline antibody status. In the seronegative patients, 396 (24%) of 1633 patients allocated to REGEN-COV and 451 (30%) of 1520 patients allocated to usual care died within 28 days (rate ratio 0.80; 95% CI 0.70–0.91; P = 0.0010). By contrast, no such benefit was seen for patients who were anti-SARS-CoV-2 antibody positive at randomisation. While only 25 women recruited to the study were pregnant, there is no reason to suppose that the effect of monoclonal antibodies in pregnancy would be different from those who are not pregnant.

Data on safety of monoclonal antibodies in pregnancy has previous been evaluated in a variety of cohort and registry studies indicating that exposure in pregnancy is not associated with an increased risk for adverse pregnancy outcomes when compared to unexposed pregnancies with the same underlying medical diseases. <sup>160</sup> This is supported by a consensus report on immunosuppressives and biologics during pregnancy and lactation, with no evidence of elevated adverse pregnancy outcomes or malformation risks <sup>161</sup> and by small observational series' of Tocilizumab in pregnant women with COVID-19. <sup>166</sup> Some monoclonal antibodies are transported across the placenta (and may also enter breast milk) but as casirivimab and imdevimab (also called REGN 10933 and REGN 10987) do not have any human targets, such exposure should not be associated with risk of harm.

The interim results of the WHO Solidarity trial<sup>130</sup> have reported that the antiviral agent remdesivir had little or no effect on overall mortality, initiation of ventilation and duration of hospital stay, in hospitalised patients with COVID-19. Since the safety of remdesivir in pregnancy is largely unknown, consider these two criteria when making decisions about its use in pregnant women with COVID-19:

- consider on an individual basis for those who are stable but not improving,
- consider more strongly in those who are deteriorating.

In breastfeeding women with COVID-19, the use of remdesivir should be restricted to women where benefit has been reported (hospitalised patients requiring oxygen therapy, especially early in disease course, and not in patients who are mechanically ventilated).<sup>131</sup> Any decision to treat with remdesivir should be taken by an MDT and, when feasible, in discussion with the woman.

Pregnant women can be enrolled in the RECOVERY trial. <sup>126</sup> Where therapies or participation in trials are offered, they should also be considered for and offered to pregnant women.





# 7. Postnatal care

### 7. Postnatal care

Routine postnatal care for women in accordance with national guidelines and the <u>RCOG</u> guidance for maternity service organisation in areas of high-risk prevalence/local lockdown during the <u>COVID-19 pandemic</u> should be followed. As prevalence subsides, strategies will be needed to ensure that previous evidence-based services put on hold or amended are reinstated.

## 7.1 How should neonatal care for the baby be provided during the COVID-19 pandemic?

#### Advice

- Women and their healthy babies should remain together in the immediate postpartum period, if they do not otherwise require maternal critical care or additional neonatal care.
- Women with suspected or confirmed COVID-19 should remain with their baby and be supported to practise skin-to-skin/kangaroo care, if the newborn does not require additional medical care at this time.
- Adopt a precautionary approach for a woman who has suspected or confirmed COVID-19 and whose baby needs to be cared for in the neonatal unit, to minimise any risk of women-to-infant or women-to-staff transmission; at the same time, involve parents in decisions, mitigating potential problems for the baby's health and wellbeing and for breastfeeding, bonding and attachment.
- Women who test positive for SARS-CoV-2 during their maternity admission, but who are not unwell with COVID-19 need only self isolate for 7 days.
- Women should be supported to make an informed decision about how they feed their baby. Women who choose to breastfeed should be supported to do so, even if they have probable or confirmed COVID-19.
- Babies born to SARS-CoV-2-positive women should be cared for as per guidance from the <u>Royal College of Paediatrics and Child Health (RCPCH)</u>/British Association of Perinatal Medicine (BAPM).
- Specific guidance on neonatal resuscitation during the COVID-19 pandemic is available from the **Resuscitation Council**.

#### Summary of evidence and rationale for recommendation

There are limited data to guide the neonatal care of babies of women who tested positive for SARS-CoV-2 in the third trimester.<sup>139</sup> A prospective cohort study<sup>140</sup> in the UK investigating SARS-CoV-2 infection in the first 28 days of life found neonatal infection is uncommon (66 babies with confirmed SARS-CoV-2 infection [incidence 5.6/10 000 livebirths, 95% CI 4.3–7.1], of whom 28 [42%] had severe neonatal SARS-CoV-2 infection [incidence 2.4/10 000 livebirths, 95% CI 4.3–7.1]

95% CI 1.6—3.4]), and infection with neonatal admission following birth to a woman with perinatal SARS-CoV-2 infection was unlikely; consequently, this study supported guidance to avoid separation of woman and baby.

The RCPCH/BAPM and the RCM have provided separate guidance on this topic, <sup>141,142</sup> with accompanying FAQs produced by **BAPM**, as well as various COVID-19 resources on newborn life support from the **Resuscitation Council**.

## 7.2 What should women and families be advised regarding infant feeding during the COVID-19 pandemic?

- Breastfeeding should be recommended to all women in line with usual guidance.
- Individualised support, advice and guidance on breastfeeding should be offered to all women who wish to breastfeed. Remote support for breastfeeding should be signposted to all women.
- Women and their families should be informed that infection with COVID-19 is not a contraindication to breastfeeding.
- Women and their families should be supported to make a fully informed choice on how to feed their baby. The potential risks and benefits of feeding the baby in close proximity to individuals with suspected or confirmed COVID-19 should be discussed.
- When a woman is not well enough to care for her own infant or where direct breastfeeding is not possible, the woman should be supported to express her breast milk by hand or using a breast pump, and/or offer access to donor breast milk. Formula feeding is entirely acceptable if this is the mother's choice.
- The following **RCPCH/BAPM** precautions should be taken to limit viral spread to the baby:
  - Wash hands before touching the baby, breast pump or bottles.
  - Avoid coughing or sneezing on the baby while feeding.
  - Consider wearing a face covering or fluid-resistant facemask while feeding or caring for the baby.
- Babies should not wear masks or other face coverings as they may risk suffocation.
- When women are expressing breast milk in hospital, a dedicated breast pump should be used.
  - Adhere to recommendations for pump cleaning after each use

- Adhere strictly to sterilisation guidance for babies who are bottle-fed with formula or expressed milk.
- Consider asking someone who is well to feed the baby.

The long term well-established benefits of breastfeeding are highly likely to outweigh any potential risks of transmission of the virus through breast milk. A systematic review found that in 24 cases breast milk tested negative for COVID-19; however, given the small number of cases, this evidence should be interpreted with caution. A cohort study demonstrated both skin-to-skin and breastfeeding are not associated with increased neonatal infection with SARS-CoV-2. Similar findings exist in smaller studies which supports the guidance. More recently, studies have reported presence of antibodies in breast milk from previous COVID-19 infection as well as COVID vaccination. This suggests a mechanism of passive immunity from breastfeeding mothers to their babies.

In light of the evidence to date, <sup>143</sup> the benefits of breastfeeding outweigh any potential risks of transmission of the virus through breast milk, and this is a view supported by the UNICEF UK Baby Friendly Initiative, which has been widely implemented in the UK. <sup>144</sup>

The main risk of breastfeeding is the close contact between the baby and the woman, who is likely to share infective respiratory droplets.

Specific recommendations on minimising the risk of COVID-19 transmission when feeding babies has been developed by the RCPCH/BAPM and RCM.<sup>141,142</sup>The <u>NHS</u> has general guidance on sterilising bottles in order to protect babies against infections.

Face coverings are not appropriate for babies. The UK government advice for using face coverings is directed towards adults and children aged 11 and over. 147

## 7.3 What are the considerations for postnatal care for women and babies following admission with COVID-19?

#### General advice

- Postnatal care should be provided as per NICE NG 194 Postnatal care.
- Following childbirth, effective contraception should be discussed with and offered to all women prior to discharge from maternity services.

#### Advice

• When a woman with COVID-19 has given birth, all members of her household are recommended to self-isolate at home for 10 days.

- Women and their families should be advised about safe sleeping and a smoke-free environment, along with provision of clear advice about careful hand hygiene and infection control measures when caring for and feeding the baby.
- Families should be guided on how to identify signs of illness in their newborn or worsening of the woman's symptoms, and should be provided with appropriate contact details if they have concerns or questions about their baby's wellbeing. **NHS**leaflets, providing this information, are also available.
- Women should be advised that if they or their babies require readmission for postnatal obstetric or neonatal care during a period of self-isolation for suspected or confirmed COVID-19 they should telephone their local unit ahead of arrival.
- Women who have recently given birth and test positive for COVID-19 should receive all recommended advice, guidance and support in relation to their postnatal physical and mental health and wellbeing and care of their newborn baby. This includes necessary in-person assessments using appropriate PPE.
- In-person home or clinic appointments should be offered to allow an overall assessment of the physical and psychological health and wellbeing of the woman and her baby.
- In some areas, and where appropriate, some postnatal care will need to be via telephone or video link because of local infection rates and staff absence, but considerations should be made upon individual circumstances. This should be discussed with women and families.
- All pregnant women who have been hospitalised and have had confirmed COVID-19 should be offered thromboprophylaxis for 10 days following hospital discharge.
   A longer duration of thromboprophylaxis should be considered for women with persistent morbidity.

The RCPCH has published guidance on the neonatal care of babies born to women with COVID-19.<sup>141</sup> The advice for households to isolate for 10 days after the birth of a baby born to a woman who is infected and admitted with SARS-CoV-2 is to ensure a full period of isolation in case of incubation of the virus in the baby. In women who are asymptomatic but have tested positive for the virus, 7 days isolation is required before visiting the neonatal unit. These advice statements have been extrapolated from the RCPCH guidance and expert consensus opinion.

Guidance on the provision of contraception by maternity services after childbirth during the COVID-19 pandemic has been produced jointly by the Faculty of Sexual and Reproductive Health, the RCOG and the RCM.

Recommendations on postnatal care should be maintained as per the NICE NG194 Postnatal care. 148

## Acknowledgements

#### RCOG COVID-19 guidance cell is comprised of:

Dr Edward Morris (President, RCOG), Professor Tim Draycott (Vice President for Clinical Quality, RCOG), Dr Pat O'Brien (Vice President for Membership, RCOG), Dr Brian Magowan (COVID Guidance Development Lead), Dr Mary Ross-Davie (Director for Scotland, RCM), Dr Corinne Love (Senior Medical Officer, Obstetrics, the Scottish Government), Dr Sayaka Okano (Honorary Clinical Fellow, RCOG), Dr Michael Shea (Honorary Clinical Fellow, RCOG), Lara Waite (Clinical Midwifery Fellow, RCOG), Dr Ayisha Ashmore (Clinical Fellow, RCOG), Dr Amar Karia (Clinical Obstetric Fellow, RCOG), Louise Thomas (Head of Quality Improvement, RCOG), Emma Gilgunn-Jones (Director of Media and PR, RCOG), Jenny Priest (Director of Policy and Public Affairs, RCOG), Hannah Gurney (Media and PR Manager, RCOG), Daniel Wolstenholme (Director of Clinical Quality, RCOG), Farrah Pradhan (Interim Business Manager, RCOG), Michelle Sadler (Guidance Editorial Manager, RCOG), Sarah Miles (Guidance Editorial Manager, RCOG) and Sophie Cooper (Business Coordinator, RCOG).

We also wish to acknowledge the contributions of colleagues from the RCOG Digital, External Affairs and Clinical Quality teams.

We wish to acknowledge the contributions of the following current and previous members of the RCOG/RCM vaccination subgroup:

Dr Pat O'Brien, Dr Mary Ross Davie, Professor Lucy Chappell, Dr Edward Morris, Dr Ayisha Ashmore, Professor Adam Balen, Dr Helen Campbell, Sophie Cooper, Dr Catherine Coyle, Dr Christine Ekechi, Emma Gilgunn-Jones, Hannah Gurney, Professor Paul Heath, Dr Ken Hodson, Miss Fatima Husain, Sarah James, Karen Jewell, Dr Jennifer Jardine, Professor Chrissie Jones, Dr Amar Karia, Professor Marian Knight, Dr Alison Little, Clare Livingstone, Dr Corinne Love, Dr Sarah Mee, Dr Janet Nooney, Dr Heather Payne, Jenny Priest, Charlie Podschies, Dr Luke Richardson, Dr Mike Shea, Mr Nigel Simpson, Dr Judith Standing, Dr Victoria Tzortziou-Brown.

#### The following external experts contributed to the guidance:

Dr Matthew Jolly and Dr Misha Moore at NHS England, Professor Beverley Hunt, Professor Catherine Nelson-Piercy, Professor Rezan Abdulkadir, Dr Peter MacCallum, Dr Louise Bowles and Dr Shohreh Beski, Dr Margaret Blott, Dr Arlene Wise, Professor Lucy Chappell, Dr Anita Banerjee, Dr Guy Glover and staff at Guy's and St Thomas' NHS Foundation Trust, Professor Marian Knight at the University of Oxford, Dr Alison Wright and Rebecca Wilson-Crellin at NHS England and Improvement, Katie De Freitas-Merchant at the Maternal and Neonatal Safety Improvement Programme, Professor Russell Viner and Dr David Evans on behalf of the Royal College of Paediatrics and Child Health, Dr Fiona Donald and Dr Nuala Lucas on behalf of the Obstetric Anaesthetists Association and Royal College of Anaesthetists, Dr Giles Berrisford on behalf of the Royal College of Psychiatrists, Professor Asma Khalil, Dr Lucy Mackillop, Dr Charlotte Frise, Dr Toni Hazell, Dr Ed Mullins, Emma Crookes and Shaista Gohir on behalf of the RCOG Women's Network, Dr Benjamin Black, Zeenath Uddin, Mr Kim Hinshaw from the British Maternal & Fetal Medicine Society, Professor Donald Peebles from University College Hospitals NHS Foundation Trust, Professor Justin Clarke from the British Society for Gynaecological Endoscopy, Jaki Lambert at the Scottish Government, Dr Fiona Donald on behalf of the Royal College of Anaesthetists and Dr Nuala Lucas from the Obstetric Anaesthetists Association, Louise Page from the British Intrapartum Care Society, Dr Jennifer Jardine, Dr Chrissie Jones at the University of Southampton, Dr Peter MacCallum at Barts and the London School of Medicine and Dentistry, Queen Mary University of London, Dr Helen Mactier on behalf of the British Association of Perinatal Medicine and members of the RCOG Guidelines Committee.

These individuals were, but are not currently, members of the guidance cell and have contributed to earlier versions of this document:

Dr Jennifer Jardine (Clinical Fellow, RCOG), Dr Sophie Relph (Clinical Fellow, RCOG), Dr Andrew Thomson (COVID Guidance Development Lead, RCOG), Dr Jahnavi Daru (Honorary Clinical Fellow, RCOG), Dr Christine Ekechi (Honorary Clinical Fellow, RCOG), Dr Gemma Goodyear (Clinical Fellow, RCOG), Dr Anushka Tirlapur (Honorary Clinical Fellow, RCOG), Anita Powell (Senior Director for Clinical Quality, RCOG), Gemma Thurston (Business Manager, RCOG), Stephen Hall (Political Advisor to the President, RCOG) and Gozde Zorlu (Media and PR Manager, RCOG).



# Appendices

## Appendix I: Summary of previous updates

Version	Date	Summary of changes	
2	13/03/2020	I.2: At the time of writing, Public Health Wales are aligning with Public Health England on case definitions, assessment, infection prevention and control and testing. We will update this guidance if this changes	
2	13/03/2020	<b>2.2:</b> Updated to reflect PHE and health protection advice as per 13.03.20, in particular to use online symptom checkers and to treat all individuals with symptoms as possibly having COVID-19.	
2	13/03/2020	<b>3.2:</b> Sentence on who to test updated to reflect advice to test women with symptoms suggestive of COVID-19 who require admission	
2	13/03/2020	<b>3.6.4 and 3.6.5:</b> Updated to suggest considering delay of elective caesarean birth or induction for women with symptoms suggestive of COVID-19 as well as those with confirmed COVID-19.	
2	13/03/2020	<b>3.8:</b> Infant feeding modified from recommendation to wear a face mask to try and avoid coughing or sneezing on the baby, and consider wearing face mask where available.	
2	13/03/2020	<b>4:</b> New section added for antenatal care for pregnant women following self-isolation for symptoms suggestive of COVID-19.	
2	13/03/2020	5 (new). New section - Advice for pregnant healthcare professionals.	
2	13/03/2020	Appendix I: Flow chart amended to reflect modified PHE guidance.	
2	13/03/2020	References: 19: NHS Staff Council Statement on Covid-19 2020 [Available from: <a href="https://www.nhsemployers.org/-/media/Employers/Documents/">https://www.nhsemployers.org/-/media/Employers/Documents/</a> Pay-and-reward/NHS-Staff-CouncilGuidance-for-Covid-19-Feb-20.  pdf?la=en&hash=70C909DA995280B9FAE4BF6AF291F4340890445C] accessed 12 March 2020.	
3	17/03/2020	2: Advice for Health Professionals to share with Pregnant Women updated to reflect current guidelines.	
3	17/03/2020	3: New section added on Advice for all midwifery and obstetric services.	
3	17/03/2020	4.1: General advice to services providing care to pregnant women updated to reflect advice from chief medical officer on 16/3/20	
3	17/03/2020	4.1: Advice on cleaning ultrasound equipment added, and reference added.	
3	17/03/2020	<b>4.5:</b> Linked to new national guidance on the actions required when a COVID-19 case was not diagnosed on admission	
3	17/03/2020	<b>4.6.2:</b> Recommendations added: There is evidence of household clustering and household co-infection. Asymptomatic birth partners should be treated as possibly infected and asked to wear a mask and wash their hands frequently. If symptomatic, birth partners should remain in isolation and not attend the unit. The use of birthing pools in hospital should be avoided in suspected or confirmed cases, given evidence of transmission in faeces and the inability to use adequate protection equipment for healthcare staff during water birth.	
3	17/03/2020	<b>4.6.2:</b> Advice about Entonox changed to There is no evidence that the use of Entonox is an aerosol-prone procedure Entonox should be used with a single-patient microbiological filter. This is standard issue throughout maternity units in the UK	
3	17/03/2020	<b>4.6.4:</b> Anaesthetic management for women with symptoms or confirmed COVID-19, which was previously in this guidance, has been removed and external links provided	

3	17/03/2020	<b>4.7.1:</b> Statement inserted 'Chest imaging, especially CT chest, is essential for the evaluation of the unwell patient with COVID-19 and should be performed when indicated and not delayed due to fetal concerns.'	
	17/02/2020	indicated and not delayed due to fetal concerns.'	
3	17/03/2020	<b>Updated</b> to reflect current public health guidance on self-isolation and social distancing.	
3	17/03/2020	<b>4.7.1:</b> Advice on neonatal management and testing has been removed. Please refer to RCPCH guidance.	
3	17/03/2020	<b>6:</b> Advice for healthcare professionals updated in line with Chief Medical Officer statement on Monday 16 March.	
4	21/03/2020	6: Section on 'Occupational health advice for employers and pregnant women during the COVID-19 pandemic' added, replacing the previous section 6 on 'Information for Healthcare Professionals'. Section includes specific recommendations for healthcare professionals.	
4	21/03/2020	<b>I.3-1.4:</b> Additional information added on the susceptibility of pregnant women to COVID-19 infection.	
4	21/03/2020	2: Additional information on social distancing for pregnant women added, particularly specifying stringent adherence to recommendations for women >28 weeks gestation	
4	21/03/2020	<b>4.7:</b> New section added on specific recommendations for PPE during labour and birth.	
4	21/03/2020	I: Addition of information and links for the UKOSS reporting system.	
4	21/03/2020	All: General proofread and editorial changes	
4	21/03/2020	<b>6:</b> Page 36 title changed to 'Occupational health advice for employers and pregnant women during the COVID-19 pandemic	
4.1	26/03/2020	Chapter 6: 'Occupational health advice for employees and pregnant women during the COVID-19 pandemic' has been removed from this general guidance on pregnancy and COVID-19 infection, and published as a separate document given the distinct audience for the occupational health advice.	
4.1	26/03/2020	4.7.3: On Personal Protective Equipment updated in line with NHS England guidance	
5	28/03/2020	1.3: Section updated to include new evidence on possible vertical transmission	
5	28/03/2020	<b>2.2:</b> Sentence added on the major new measures announced by government for pregnant women with co-existing significant congenital or acquired heart disease.	
5	28/03/2020	2.3: Section updated to emphasise the need to attend maternity care.	
5	28/03/2020	3: General advice for antenatal care extended to include considerations for vulnerable women. Section also added on general advice regarding intrapartum services.	
5	28/03/2020	<b>3.1:</b> Specific advice added regarding the cessation of carbon monoxide monitoring in pregnancy, following advice from the National Centre for Smoking Cessation and Training.	
5	28/03/2020	<b>4:</b> Scotland specific links to Health Protection Scotland removed after confirmation from the Scottish government that National links from gov.uk should be used.	
5	28/03/2020	<b>4.3.6:</b> Scotland specific links to Health Protection Scotland removed after confirmation from the Scottish government that National links from gov.uk should be used	
5	28/03/2020	<b>4.7.3</b> and <b>4.76</b> : Advice on PPE considerations for caesarean birth and general advice for obstetric theatres moved to new section 'Specific peri-operative advice for pregnant women with suspected/confirmed COVID-19 requiring surgical intervention'.	

5	28/03/2020	<b>4.8.1:</b> Reference made to new guidance published by NICE on the management of patients with COVID-19 in critical care.		
5	28/03/2020	<b>4.8.1:</b> Additional recommendations made for the management of women admitted during pregnancy with suspected/confirmed COVID-19.		
5	28/03/2020	<b>4.9.2:</b> Section edited to make infant feeding recommendations to any caregiver, not just to the mother		
5	28/03/2020	<b>4.10:</b> New section on 'Specific peri-operative advice for pregnant women with suspected/confirmed COVID-19 requiring surgical intervention'.		
5	28/03/2020	<b>5.1:</b> Correction of an error in the title to clarify that this section refers to the care of women recovering from suspected (not confirmed) COVID-19 for which hospitalisation was not required.		
6	03/04/2020	<b>Throughout:</b> References to the new RCOG guidance on (I) antenatal and postnatal services (2) antenatal screening (3) fetal medicine services (4) maternal medicine services and (5) self-monitoring of blood pressure, have been added throughout the document.		
6	03/04/2020	1.2: New resources signposted on current UK and international disease incidence		
6	03/04/2020	I.4: Sentence reporting that there are 'no reported maternal deaths from COVID-19' removed because there was recently a possible maternal death reported in tabloid media. There is not any robust evidence to amend this statement or report confidently in the guideline.		
6	03/04/2020	<b>3.2</b> : Addition of new advice on screening birth partners for recent possible symptoms of COVID-19 when they attend the maternity unit. In addition, suggestion of information to give the birth partner about what is expected of them whilst they are in the hospital, to assist staff in reducing the risk of infection transmission and to assist with communication when birth partners accompany women into operating theatres		
6	03/04/2020	3.4: Moved to section 3.2.		
6	03/04/2020	3.5: New section on maternal mental wellbeing during the pandemic.		
6	03/04/2020	<b>4.1</b> The previous section 4.2 was repetitive of section 3.1 and so has been removed. Sections 4.2 onwards have been re-numbered.		
6	03/04/2020	<b>4.3:</b> Inclusion of the PHE case definition for COVID-19 testing, rather than referring readers to this through the link		
6	03/04/2020	<b>4.9:</b> Updates to advice on PPE for caesarean birth, to ensure that these are consistent with new PHE advice.		
7	09/04/2020	I.4: Update to data from ICNARC and inclusion of a report of 43 pregnant women with COVID-19 from New York		
7	09/04/2020	I.4: New comment on risk of venous thromboembolism from COVID-19.		
7	09/04/2020	<b>2.3:</b> Advice for pregnant women added – if they are advised to attend a face-to face antenatal appointment, this is because the appointment is important and the benefit of attending is perceived to be greater than the possible risk of infection with COVID-19 caused by leaving home. Added also emphasised advice to contact maternity services if concerns during pregnancy.		
7	09/04/2020	<b>3.1:</b> New section of reducing the risk to women of new infection caused by attending maternity settings. All other subsections in section 3 have been renumbered		
7	09/04/2020	3.2: New comment on visitor restrictions in maternity settings.		
		3.2: List of risk factors which contribute to mental ill health in pregnant women,		
7	09/04/2020	and acknowledgement of the risk of increasing domestic violence with policy for social distancing, moved to section 3.6 on maternal mental wellbeing		

7	09/04/2020	<b>4.2:</b> Section 4.2 renamed 'Women with unconfirmed COVID-19 but symptoms suggestive of possible infection' to allow for inclusion of new recommendations on women who call the maternity unit with possible COVID-19 infection (not just attend in person).	
7	09/04/2020	<b>4.2:</b> Additional recommendations made to consider usual differential diagnoses in women who call the maternity unit to report a new fever/cough/respiratory symptoms.	
7	09/04/2020	<b>4.3.1:</b> New subsection added on the care of pregnant women who are self-isolating at home with suspected COVID-19.	
7	09/04/2020	<b>4.4:</b> Changed to subsection 4.3.3 (subsequent subsections re-numbered).	
7	09/04/2020	<b>4.6.1:</b> New recommendations re. prophylactic low molecular weight heparin to reduce risk of venous thromboembolism with COVID-19 infection in pregnancy, and to consider pulmonary embolism if women with COVID-19 suddenly deteriorate	
7	09/04/2020	<b>4.7.2:</b> Statement on calling neonatal team early to inform them of imminent birth of a baby to a woman with COVID-19 moved to section 4.5, because it applies to all cases of COVID-19, not just in women with severe disease.	
8	17/04/2020	I: New paragraph on the quality of the available evidence and resultant classification of the advice.	
8	17/04/2020	I.4: New evidence included on the risk of COVID-19 in the woman, including a case series of pregnant women attending two maternity units in New York, who were screened for COVID-19 on arrival, the inclusion of the first report of maternal death directly attributed to COVID-19 in scientific literature and an update to the ICNARC data.	
8	17/04/2020	<b>4.2, 4.5.2 &amp; 4.6.2:</b> Restructured, including some new subtitles to organise and break up the text	
8	17/04/2020	<b>4.3.1:</b> Renamed 'risk of venous thromboembolism'.	
8	17/04/2020	<b>4.6:</b> Section restructured for clarity.	
8	17/04/2020	<b>4.7</b> and <b>4.8</b> : Re-ordered the two sections within the text so that considerations for birth are written before considerations for neonatal and postnatal care.	
8	17/04/2020	<b>5.3:</b> Section re-structured. Also includes clarification that the recommendation for 10 days postnatal LMWH is regardless of mode of birth.	
8	17/04/2020	Appendix 2: Table of previous updates moved to appendix 3	
8	17/04/2020	Appendix 3: New information on considerations when caring for women with suspected/confirmed COVID-19 during labour and birth	
9	13/05/2020	I: Aims updated to include: The provision of safe, woman-centred care to women who are pregnant, give birth or are in the early postnatal period during the COVID-19 pandemic.	
9	13/05/2020	I: Findings of UKOSS data included in the summaries on viral transmission, effects on the woman and effects on the fetus/neonate. Where this supersedes existing references because of higher quality research or larger numbers, it has been used to replace it.	
9	13/05/2020	<b>I.3:</b> Updated information on possibility of vertical transmission to state that there are serious limitations to the available evidence.	
9	13/05/2020	I.4: Updated with emerging evidence on increased risk from COVID-19 to individuals with black, Asian and minority ethnic (BAME) background.	
9	13/05/2020	2: Information to share with pregnant women and their families has been removed from the guidance. All this information is also available in the RCOG information for pregnant women and their families in the COVID-19 hub. All subsequent sections have been renumbered.	
		sabsequent sections have been renambered.	

9	13/05/2020	3.2 (Now 2.2): Statement and recommendations added: Emerging evidence suggests that individuals of black and minority ethnic (BAME) background may be at higher risk of developing severe complications of COVID-19. This may equally apply to pregnant women. We therefore advise: Women of BAME background should be opportunistically advised that they may be at higher risk of complications of COVID-19, and advised to seek help early if they are concerned about their health.  Clinicians should be aware of this increased risk, and have a lower threshold to review, admit and consider multidisciplinary escalation in women of BAME background.	
9	13/05/2020	<b>2.2:</b> Removed statement that further guidance on remote consultations will be published soon, and provided reference to RCM/RCOG guidance on antenatal and postnatal care	
9	13/05/2020	<b>2.3:</b> Changed the statement that units should consider reducing provision of induction of labour for indications that are not 'strictly necessary', to units should consider reducing induction of labour where this is not 'medically indicated'.	
9	13/05/2020	<b>3.3 (Now 2.3):</b> Reference to NHS England 'Clinical guide for the temporary reorganisation of intrapartum maternity care during the coronavirus pandemic' added.	
9	13/05/2020	<b>3.3 (Now 2.3):</b> Statement added: 'Care should be taken to maintain safe services which continue to offer women support and choice as far as possible at this time. In particular, women should continue to be encouraged to contact their maternity unit with concerns about their or their baby's wellbeing. Justification should be provided for any service rationalisation required.'	
9	13/05/2020	3.3 (Now 2.3): Statement added: 'When reorganising services, maternity units should be particularly cognisant of emerging evidence that black, Asian and minority ethnic group (BAME) individuals are at particular risk of developing severe and life-threatening COVID-19. There is already extensive evidence on the inequality of experience and outcomes for BAME women during pregnancy and birth in the UK. Particular consideration should be given to the experience of women of BAME background and of lower socioeconomic status, when evaluating the potential or actual impact of any service change.'	
9	13/05/2020	<b>4.6 (Now 3.6):</b> Recommendation to be aware that myocardial injury is common among individuals with COVID-19, and reference added to NICE Guidance on diagnosis of myocardial injury in patients with suspected or confirmed COVID-19.	
9	13/05/2020	<b>4.8.1 (Now 3.8.1):</b> Reference added to Resuscitation Council guidance on neonatal life support during the COVID-19 pandemic.	
9	13/05/2020	<b>4.5.2 (Now 3.5.2):</b> Care in labour: Risk of venous thromboembolism. Clarification added that all women with suspected or confirmed COVID-19 should be discharged with 10 days' supply of prophylactic LMWH	
9	13/05/2020	<b>4.4 (Now 3.4):</b> Women who develop new symptoms of COVID-19 during admission: Statement added that prophylaxis for venous thromboembolism should be considered and prescribed unless contraindicated.	
9	13/05/2020	<b>4.6 (Now 3.6):</b> Title change from 'Additional considerations in women with moderate/ severe symptoms' to 'Women with suspected or confirmed COVID-19 and moderate/severe symptoms', to reflect that this includes information relevant to pregnant women admitted with COVID-19 outside of obstetric services.	

9	13/05/2020	4.6 (Now 3.6): Recommendation added: 'Prophylaxis for venous thromboembolism should be prescribed during admission unless contraindicated. At the time of discharge from hospital following a period of care for confirmed COVID-19 infection, all women should be prescribed at least 10 days of prophylactic LMWH.'This is consistent with recommendations already made elsewhere in previous versions of this document.
9	13/05/2020	<b>4.6 (Now 3.6):</b> Changed statement 'Consider bacterial infection if the white blood cell count is raised (lymphocytes usually normal or low with COVID-19) and commence antibiotics' to 'Bacterial infection is an important differential diagnosis to COVID-19 infection. We advise blood cultures and a low threshold for antibiotics at presentation, with early review and rationalisation of antibiotics if COVID-19 is confirmed.'

## Version 10

The following Version 10 summary of changes includes an additional column to reflect significant restructure changes between version 9 and 10 of this guidance.

Date	Summary of chang version 10	es from version 9 to	
	Subject	Section content from v9	Location in v10
04/06/2020	Introduction		Now incorporates the following sections from v9:  Purpose and scope  Identification and assessment of evidence  Epidemiology  Transmission  Effect of COVID-19 on pregnant women  Risk factors for hospital admission with COVID-19  Effect of COVID-19 on the fetus
04/06/2020	Antenatal care during the COVID-19 pandemic	2.2. General advice regarding the continued provision of antenatal and postnatal services	2.1 What are the considerations for organisation of antenatal care during the COVID-19 pandemic?
04/06/2020	Antenatal care during the COVID-19 pandemic	2.3 General advice regarding possible service modifications during COVID-19	2.2 What are the considerations for antenatal appointments?
04/06/2020	Antenatal care during the COVID-19 pandemic	2.6 Smoking cessation and carbon monoxide monitoring in pregnancy	2.3 What are the considerations for antenatal appointments?
04/06/2020	Antenatal care during the COVID-19 pandemic	2.5 Maternal mental wellbeing	2.2 What are the considerations for antenatal appointments?
04/06/2020	Antenatal care during the COVID-19 pandemic	3.1 General advice for services providing care to pregnant women with suspected or confirmed COVID-19, where hospital attendance is necessary	2.3 How should women with suspected or confirmed COVID-19 needing hospital attendance or advice be cared for?

04/06/2020	Antenatal care during the COVID-19 pandemic	<b>3.2</b> Women with unconfirmed COVID-19 but symptoms suggestive of possible infection	2.3 How should women with suspected or confirmed COVID-19 needing hospital attendance or advice be cared for?
04/06/2020	Antenatal care during the COVID-19 pandemic	3.3.3 Attendance for unscheduled/urgent antenatal care in women with suspected or confirmed COVID-19	2.3 How should women with suspected or confirmed COVID-19 needing hospital attendance or advice be cared for?
04/06/2020	Antenatal care during the COVID-19 pandemic	<b>4.1</b> Antenatal care for pregnant women following self-isolation for symptoms suggestive of COVID-19	2.4 What are the considerations for antenatal care for women who have recovered from COVID-19?
04/06/2020	Antenatal care during the COVID-19 pandemic	<b>4.2</b> Antenatal care for pregnant women following hospitalisation for confirmed COVID-19 illness	2.4 What are the considerations for antenatal care for women who have recovered from COVID-19?
04/06/2020	Venous thromboembolism prevention	<b>3.3.1</b> Risk of venous thromboembolism	3.1 How should prevention of venous thromboembolism during the COVID-19 pandemic be addressed?
04/06/2020	Venous thromboembolism prevention	3.4 Women who develop new symptoms of COVID-19 during admission (antenatal, intrapartum or postnatal) Sentence on thromboprophylaxis	<b>3.1</b> How should prevention of venous thromboembolism during the COVID-19 pandemic be addressed?
04/06/2020	Labour and birth	<b>2.4</b> General advice regarding intrapartum services	<b>4.4</b> What about birth partners during the COVID-19 pandemic?
04/06/2020	Labour and birth	Not in version 9	New section in version 10:4.1 What are the considerations for labour and birth in asymptomatic women who test or have tested positive for SARS-CoV-2?
04/06/2020	Labour and birth	3.5 Women attending for intrapartum care with suspected or confirmed COVID-19	<ul> <li>4.2 How should a woman with suspected/confirmed COVID-19 be looked after in labour if they are symptomatic?</li> <li>4.5 What informed discussions should take place with women regarding timing and mode of birth during the COVID-19 pandemic?</li> <li>4.6 What are the specific considerations for labour analgesia or anaesthesia?</li> </ul>

04/06/2020	Labour and birth	3.7 Specific perioperative advice for healthcare professionals caring for pregnant women with suspected/confirmed COVID-19 who require surgical intervention	<ul><li>4.8 How should obstetric theatres be managed during the COVID-19 pandemic?</li><li>4.7 What personal protective equipment is recommended when caring for women during labour and birth?</li></ul>
04/06/2020	Postnatal	3.8 Neonatal care	<ul><li>6.1 How should neonatal care for the baby be provided during the COVID-19 pandemic?</li><li>6.2 What should parents/carers be advised regarding infant feeding during the COVID-19 pandemic?</li></ul>
04/06/2020	Postnatal	<b>4.3</b> Postnatal care for pregnant women immediately following hospitalisation for confirmed COVID-19 illness	6.3 What are the considerations for postnatal care for women and babies following admission with COVID-19?

Version	Date	Summary of changes	
10.1	19/06/2020	I.I: Removal of 'MERS, Middle East Respiratory Syndrome' from the literature search strategy since it has not resulted in any new references since the first search.	
10.1	19/06/2020	I.4: UKOSS reference changed to the published article in The BMJ.	
10.1	19/06/2020	2.2: Advice on face masks changed to reflect national guidance from NHS England.	
10.1	19/06/2020	<b>4.4:</b> Advice on number of visitors and/or birth partners for hospital inpatients changed to reflect national guidance from NHS England	
10.1	19/06/2020	<b>5.2:</b> Advice for women who are clinically deteriorating modified to include government recommendations based on the interim results of the RECOVERY trial.	
10.1	19/06/2020	<b>6.2:</b> Specified that babies should not be advised to wear face masks because of the risk of suffocation.	
11	24/07/2020	I.I: Updated methodology about search strategies and the review process.	
П	24/07/2020	1.3: Updated evidence that there is a low rate of vertical transmission and possible transplacental transmission.	
П	24/07/2020	<b>I.4:</b> Updated evidence that pregnant women are not necessarily more susceptible to SARS-CoV-2 than the general population	
11	24/07/2020	<b>1.5:</b> Updated evidence identifying the risk factors of Black, Asian and minority ethnicity (BAME), obesity and comorbidities in pregnant women admitted with COVID-19.	
П	24/07/2020	1.6: Updated evidence on possible fetal growth restriction associated with COVID-19.	

Ш	24/07/2020	2.1: Updated advice:	
		<ul> <li>Units should employ teleconferencing and videoconferencing where possible and consider which appointments can be most appropriately conducted remotely, especially in areas of local lockdown to minimise hospital attendance.</li> <li>Particular consideration should be given to pregnant women who are 'shielding' or have been 'shielding'. Shared waiting areas should be avoided.</li> <li>Units should appoint a named midwife or consultant to coordinate care for women forced to miss appointments due to self-isolation or a positive test.</li> <li>Missed appointments should be reviewed and either rescheduled if a face-to-face</li> </ul>	
		review is necessary or converted to a remote appointment.  Evidence added on the possible increased incidence of stillbirths in women without symptoms suggestive of COVID-19 in the pandemic compared to prepandemic periods.	
11	24/07/2020	2.2: Updated advice:	
		<ul> <li>Evidence suggests that individuals of BAME background are at higher risk of developing severe complications of COVID-19. This also applies for pregnant women. We therefore advise that: <ul> <li>Women of BAME background should be advised that they may be at higher risk of complications of COVID-19; and encouraged to seek advice without delay if they are concerned about their health.</li> <li>Clinicians should maintain face-to-face appointments with women when there are safeguarding concerns in order to provide extra support.</li> <li>It is recommended that women should continue to take folic acid and vitamin D supplements as per national recommendations.</li> <li>If women or their families express concerns about their mental health or 'red flag' symptoms such as suicidal thoughts or sudden mood changes they should be supported to access urgent care by healthcare providers signposting or referring appropriately.</li> </ul> </li> </ul>	
11	24/07/2020	2.3: Amended advice:  Visitors to isolation rooms or ward cohort bays should be kept to a minimum and follow local hospital visitor policies.	
11	24/07/2020	<ul> <li>4.1: Amended advice:</li> <li>For asymptomatic women who test positive for SARS-CoV-2 on admission, continuous electronic fetal monitoring (CEFM) during labour using cardiotocography (CTG) is not recommended solely for this reason, and should only be used if it is required for another reason (e.g. previous caesarean birth).</li> <li>o Fetal monitoring options should be discussed with the woman, acknowledging the current uncertainties in the care of women who are asymptomatic with a positive test for SARS-CoV-2.</li> </ul>	

11	24/07/2020	4.2: Additional advice:
		There are no contraindications to performing a fetal blood sample or using
		fetal scalp electrodes.
		Advice on waterbirths has been revised and moved to (new) section 4.6.
11	24/07/2020	4.3: Amended advice:
		Informed discussions with women about fetal monitoring should
		acknowledge that evidence of fetal distress is based on small numbers
		of babies born to women symptomatic of COVID-19 and theoretical risks extrapolated from pregnancies affected by fetal growth restriction in
		women with other coronaviruses.
11	24/07/2020	4.4: Amended advice:
		If birth partners are symptomatic or in a period of self-isolation for
		confirmed SARS-CoV-2 infection, they should remain in self-isolation at
		home and not attend the unit.
		Advice removed: on birth partners being asked to remain by the woman's
		bedside and not to walk around the ward/hospital.
11	24/07/2020	4.5: Amended advice:
		Women and their families should be aware that donning PPE for
		emergency caesarean births is time-consuming but essential, and that
		this may impact on the time it takes to assist in the birth of the baby and
		potentially result in an adverse outcome. This should be taken into account
		during decision-making and ideally discussed during birth planning.
		Removed advice on the use of birthing pools in hospital for women with
		suspected or confirmed cases of COVID-19.
		Updated evidence about vertical transmission and data about donning PPE.
11	24/07/2020	<b>4.6:</b> New section on 'What are the considerations regarding waterbirth?'
Ш	24/07/2020	4.8: Amended advice:
		Healthcare professionals are advised to follow national recommendations
		on the use of personal protective equipment in clinical settings.
П	24/07/2020	4.10: New section 'What are the considerations for bereavement care during the
		COVID-19 pandemic?'
11	24/07/2020	5.1: Amended advice:
		Women should be offered testing for COVID-19 if they meet the inpatient or
		community PHE criteria.

П	24/07/2020	5.2: Updated advice:
		<ul> <li>A designated team member should be responsible for regularly updating the woman's family about her progress, utilising interpreting services where necessary.</li> <li>Thrombocytopenia is associated with severe COVID-19. For women with thrombocytopenia (platelets &lt;50 x 10<sup>9</sup>/L) stop aspirin prophylaxis and thromboprophylaxis and seek haematology advice.</li> <li>Consider using mechanical aids (such as intermittent calf compressors) if thromboprophylaxis is paused secondary to thrombocytopenia</li> <li>Consider the use of antiviral medications, such as remdesivir, that have been shown to be potentially beneficial in COVID-19.</li> <li>If there is clinical uncertainty in whether to offer a therapy to a pregnant woman, seek advice through maternal medicine networks.</li> </ul>
11	24/07/2020	6.1: Added advice:
		<ul> <li>Women with suspected or confirmed COVID-19 should be supported and enabled to remain together with their babies when the woman is well enough, and to practice skin-to-skin/kangaroo care, if the newborn baby does not require additional medical care at this time.</li> <li>For a woman who has suspected or confirmed COVID-19 and whose baby needs to be cared for on the neonatal unit, a precautionary approach should be adopted to minimise any risk of women-to-infant transmission; at the same time, steps should be taken to involve parents in decisions, mitigating potential problems for the baby's health and well-being and for breastfeeding and attachment.</li> <li>Women who have suspected, probable or confirmed COVID-19 should be enabled and supported to breastfeed, if this is what they choose.</li> </ul>
11	24/07/2020	<ul> <li>6.2: Title amended to: What should women and families be advised regarding infant feeding during the COVID-19 pandemic?</li> <li>Added advice</li> <li>Breastfeeding is recommended for all women and newborn infants.</li> <li>Support, advice and guidance on breastfeeding should be provided to all women who choose to breastfeed</li> <li>When a woman is not well enough to care for her own infant or where direct breastfeeding is not possible, she should be supported to express her breastmilk by hand expression or by pump, and/or be offered access to donor breast milk.</li> </ul>

Ш	24/07/2020	6.3: Added advice:
		<ul> <li>New mothers with COVID-19 still require all recommended advice, guidance and support in relation to their postnatal physical and mental health and wellbeing and care of their newborn.</li> <li>Postnatal care should be provided as per national guidance. Face-to face home or clinic appointments are required to provide physical checks and the offer of screening, including any wound examinations from caesarean births/assisted births, the newborn blood spot test and checking the weight of the baby. In some areas, and where appropriate, some postnatal care will need to be via virtual appointments using telephone or video link due to local infection rates and staff absence but considerations need to be made upon individual circumstances. This needs to be communicated to women and families.</li> </ul>
12	14/10/2020	Throughout: Comprehensive editorial review resulting in rewording and minor changes which do not affect meaning. Any changes to meaning and recommendations are detailed elsewhere in this table of changes
12	14/10/2020	I.2-I.7 Summary of evidence: Comprehensively updated and rewritten to incorporate changes to evidence base, in particular the MBRRACE Rapid Report and recent systematic reviews
12	14/10/2020	<ul> <li>2.1 Antenatal care</li> <li>Recommendations added:</li> <li>The NICE recommended schedule of antenatal care should be offered in full wherever possible. These appointments should be offered in-person as far as possible, with particular attention to those from BAME communities or those living with medical, social or psychological conditions that make them higher risk.</li> <li>Appropriate screening for diabetes in pregnancy should be provided, following NICE guidance as far as possible, with awareness that changes in screening provision may be associated with a reduction in the detection of milder cases of gestational diabetes.</li> <li>Open access for pregnant women to day assessment and triage services should be maintained. Women should be actively encouraged to attend if they have concerns about their or their baby's wellbeing.</li> <li>Continuity of carer should be maintained wherever possible, particularly where this is offered to women from vulnerable groups who may also be at greater risk from COVID-19.</li> </ul>
12	14/10/2020	<b>2.2</b> Title changed for 'what are the considerations for antenatal appointments?' to 'what are the considerations for antenatal appointments and advice for pregnant women?'

12	14/10/2020	2.2 Recommendations added
		Women should be advised that vaccination against influenza is safe at all gestations of pregnancy and is recommended to protect both the woman and baby from the adverse effects of becoming seriously ill with flu during pregnancy. During the COVID-19 pandemic, it is particularly important that pregnant women take up the influenza vaccine to reduce their risk of contracting flu.
		Appointments where physical examination is not required and where there are no additional risk factors are most appropriate to be conducted by virtual means.
		Services should establish triage processes to ensure that women with mental health concerns can be appropriately assessed.
		Recommendations removed
		Virtual consultations should be encouraged where appropriate to minimise contact in person, however traditional in-person appointments may be more effective, especially when interpreters are required.
		Supporting statement updated with evidence from MBRRACE UK Rapid Report and survey studies regarding modifications to care during the pandemic.
12	14/10/2020	3.1 Thromboembolism. Supporting statement updated with reference to MBRRACE rapid report.
12	14/10/2020	<b>4.1 Labour and birth.</b> Recommendations updated to reflect national policy change to 10 days isolation following a positive test for COVID-19.

12	14/10/2020	4.4 Birth partners. Recommendations revised to:						
		<ul> <li>On attendance at the maternity unit, all birth partners should be asked whether they have experienced any symptoms suggestive of COVID-19 in the preceding 14 days, e.g. fever, acute persistent cough, changes in or loss of sense of smell (anosmia) or taste.</li> <li>o If they have had symptoms within the last 10 days, they should be asked to leave the maternity unit immediately and self-isolate at home, unless they have had a negative test result for coronavirus since symptom onset</li> <li>o If they have had a fever within the last 48 hours, they should be asked to leave the maternity unit immediately and self-isolate at home, regardless of their test result.</li> <li>o Guidance about testing of women and their birth partners is discussed in the RCOG document Principles for the testing and triage of women seeking maternity care in hospital settings, during the COVID-19 pandemic.</li> </ul>						
		Asymptomatic birth partners, not otherwise advised to be self-isolating, should be permitted to stay with the woman throughout labour and birth, unless the birth occurs under general anaesthetic. Further guidance about access to maternity services for birth partners and other supportive adults has been published by the NHS, and should be followed as far as possible.						
12	14/10/2020	<b>4.6 Water birth.</b> Supporting statement updated to reflect evidence review by the UK Infection Prevention and Control Cell.						
12	14/10/2020	<b>6.3 Postnatal care.</b> Recommendation revised to clarify that postnatal women who have tested positive for COVID-19, while required to isolate along with their households for 14 days, should still receive necessary in-person postnatal care.						
13	18/02/2021	<b>Throughout:</b> Comprehensive editorial review resulting in rewording and minor changes.						
13	18/02/2021	<b>Throughout:</b> New evidence added to most sections to support or update existing conclusions or advice.						
13	18/02/2021	I.4 New section added: Vaccination against COVID-19.						
13	18/02/2021	I.5: Comprehensively updated including new evidence, key findings, new sections on the frequency of severe illness in pregnant women, data from the UK comparing pregnant and non-pregnant women, data from international studies comparing pregnant and non-pregnant women and insertion of tables in appendix summarising studies.						
13	18/02/2021	<b>Sections 2 and 6 updated: t</b> o signpost to guidance documents to assist maternity units with changes to antenatal and postnatal care.						
13	18/02/2021	New appendices added and updated to reflect changes to document.						

## Appendix II: Development method of this guidance

The development methods have evolved over the lifetime of this guidance. This version of the guidance was developed by a multidisciplinary group of authors listed in acknowledgments. Specific sections of the guidance were contributed by subject experts also listed in Acknowledgments.

Weekly literature reviews are generated using the following search terms, MESH headings and associated synonyms: pregnancy, coronavirus, SARS, severe acute respiratory syndrome, infant, newborn and breastfeeding. The search results are published weekly on the RCOG website. Populations of interest include pregnant women, those recently given birth, partners, neonates. Studies of other populations are included where necessary, in order to understand population risk, asymptomatic carriage of coronavirus and antibody results where we believe these findings can be extrapolated to pregnant women. The retrieved evidence is reviewed by clinically trained members of the guidance team for inclusion. The criteria for including evidence has evolved as the evidence base has matured. For each section of the guidance, the best available evidence is included. The guidance also includes reference to 'grey' literature such as registry studies, reports from national organisations and non-peer reviewed content. Where there is a need to change practice and where published alternatives are not available, 'preprints' are discussed within the core guidance team and considered for inclusion.

For this guidance, good practice points are based on expert consensus of the multidisciplinary guidance group comprising healthcare providers across a variety of disciplines reviewing the available evidence and from their own expertise and experience within clinical practice. Appreciating the paucity of high-quality evidence in this area, this guidance is reviewed regularly to ensure the advice remains up-to-date and relevant.

While this document has not been subject to an open peer review or formal stakeholder consultation process, specific individuals and groups were asked to review its content prior to publication. These are listed in Acknowledgments and include a wide range of external stakeholders including lay representatives, other Royal Colleges and professional associations and representatives from the governments across England and the devolved nations. Feedback on this guidance sent to the dedicated COVID-19 inbox is also considered.

No external funding was received in order to develop this guidance.

### Appendix III: Summary of key studies on maternal and pregnancy outcomes

### Key studies summary on the effect of COVID-19 on pregnancy and maternal outcomes

Tables I and 2 give details of the key studies on which sections I.5.2 and I.5.3 are based. The largest study is the PregCOV-I9 systematic review. <sup>149</sup> Thirteen publications already included in that systematic review are not listed individually; only the PregCOV-I9 systematic review and studies that were published since that review are shown in these tables. Forest plots from an unpublished meta-analysis of the publications listed in tables I and 2 are included below. Updated June 2021. Case series with less than 20 cases have been excluded.

Table I: Summary of key studies relevant for the effect of COVID-19 on pregnancy outcomes

Study	Country	Population		Effect of COVID-19 on	pregnancy	
Allotey et al 2020 <sup>149</sup>	30 countries	COVID-19	Control	COVID-19	Control	aOR
PregCOV-19 Systematic Review (updated 29/11/20)		Approx 1000 pregnant women with COVID-19	Approx 5000 pregnant women without COVID-19	12.4% Preterm (147/1184) 0.9% Stillbirth (9/1039)	7.8% Preterm (572/7365) 0.5% Stillbirth (26/4755)	1.47 (1.14–1.91) 2.84 (1.25–6.45)
Vousden et al 2021 159	UK	COVID-19	Control  Historical control of	Overall   15.6% preterm (15.6/1003)	Control  9% preterm hirth (63/70)	)
UKOSS update		1148 pregnant women with COVID-19 hospitalised for any reason (722 symptomatic)	Historical control of 694 pregnant women from 2018	15.6% preterm (156/1003)  1.1% stillbirth (11/1019)  Symptomatic COVID  19% preterm birth (76% iatrogenic) (120/623)  49% caesarean section  Asymptomatic COVID  9% preterm birth (36/380)  40% caesarean section	9% preterm birth (63/702) 0.3% stillbirth (2/705) 29% caesarean section	

Jering et al 2021 153	USA	COVID-19	Control	COVID-19	Control	aOR (95%CI)
		6380 pregnant women with	400 066 pregnant women without	7.2% preterm birth (322)	5.8% preterm (16137)	1.17 (1.06–1.29)
		COVID	COVID	28.9% caesarean section 8.8% preeclampsia	27.5% caesarean	1.07 (1.02–1.13)
				0.5% stillbirth (34)	6.8% pre-eclampsia	1.21 (1.11–1.33)
					0.3% stillbirth (1289)	
Crovetto et al 2021 <sup>169</sup>	Barcelona, Spain	COVID-19	Control	COVID-19	Control	Risk difference
		317 pregnant women with	1908 pregnant women without	13.6% pregnancy complication	14% preg complication	-0.4% (-4.1–4.1)
		COVID-19 (detected by	COVID-19	11.4% preterm (20/176)	7.2% preterm (81/1128)	4.2% (-0.03–9.9)
		antibody or PCR)		0.6% perinatal death (1/178)	0.5% perinatal death (6/1160)	0.1% (-0.7–2.7)
				Symptomatic COVID	Control	
				16.9% preterm birth (12/71)	7.2% preterm birth (81/1128)	
				19.2% intrapartum fetal distress	9.1% intrapartum fetal distress	
Molenaar 2021 176	NY, USA	COVID-19 (not acute)	Control	COVID-19	Control	aOR
			591 women who	7.6% preterm (8)	6.3% Preterm (37)	1.08 (0.46- 2.54)
		105 women who were seropositive for SARS-COV-2	were seronegative for SARS-CoV-2 and PCR negative at	8.6% SGA (9)	7.3% SGA (43)	1.19 (0.53– 2.65)
		but PCR negative at delivery	delivery			

Metz et al 2021 <sup>175</sup>	USA	split by severity:		Severe/critical COVID 41.8% preterm birth	Asymptomatic COVID  I 1.9% preterm birth	aRR (95% CI) 3.53 (2.42–5.14)
Savirón-Cornudella et al 2021 <sup>177</sup>	Spain	65 pregnant with COVID (by Ab or PCR), all asymptomatic or mild infection	Control  1146 pregnant women without COVID-19	COVID-19 0% stillbirth (0)	Control 0.2% stillbirth (2)	P-value 0.944
Abedzadeh- Kalahroudi 2021 <sup>167</sup>	Iran	COVID-19  56 women with COVID-19	94 pregnant women with COVID-19	COVID-19 16.1% fetal distress 34.5% preterm (19) 3.6% perinatal death (2)	Control 4.3% fetal distress 12.8% preterm (12) 0% perinatal death (0)	RR 3.84 (1.24–11.90) 2.70 (1.42–5.14) 8.48 (0.41–173.53)
Trahan 2021 <sup>179</sup>	Canada	COVID-19 45 pregnant women with COVID-19	Control  225 pregnant women without COVID-19	COVID-19 16% preterm (7)	Control 9% preterm (21)	P = 0.28
Zgutka 2021 <sup>173</sup>	NY, USA	62 pregnant women with COVID-19	Control  124 pregnant women without COVID-19	COVID-19 18.3% preterm (11)	Control 8.1% preterm (10)	P = 0.04

Katz 2021 172	USA	COVID-19	Control	COVID-19	Control	aOR (95%CI)
		490 pregnant women with	964 pregnant women without COVID-19	14.8% preterm (73)	10.2% preterm (98)	1.47 (1.03–2.09)
		COVID-19 (176 (35.95) symptomatic)	Without COVID-17	Symptomatic		2.08 (1.29–3.36)
Martinez-Perez 2021 <sup>174</sup>	Spain	COVID-19	Control	COVID-19	Control	aOR or P
		246 pregnant women with	763 pregnant women without COVID-19	13.8% preterm (34)	6.7% preterm (51)	2.12 (1.32–3.36)
		COVID-19	William Covid 17	1.2% stillbirth (3)	0.1% stillbirth (1)	P = 0.047
Hcini 2021 171	French Guiana	COVID-19	Control	COVID-19	Control	RR
		137 pregnant women with	370 pregnant women without COVID-19	5.1% stillbirth (7)	1.1% stillbirth (4)	4.7 (1.4–15.9)
		COVID-19		0.8% preterm < 34 weeks (1)	3.4% preterm < 34 weeks (12)	RR not given
Villar 2021 180	18 countries	COVID-19	Control	COVID-19	Control	RR
		706 pregnant women with	1424 pregnant women without	22.5% preterm (159)	13.6% preterm (194)	1.59 (1.30–1.94)
		COVID-19	COVID-19	17% severe perinatal morbidity and mortality index (120)	7.9% severe perinatal morbidity and mortality index (113)	2.14 (1.66–2.75)
Adhikari 2020 <sup>168</sup>	USA	COVID-19	Control	COVID-19	Control	RR
		252 pregnant women with COVID-19	3122 pregnant women without COVID-19	I I% preterm (27) 0% stillbirth (0)	11% preterm (328) 0.6% stillbirth (18)	1.02 (0.70–1.48) 0.33 (0.02–5.48)

Soto-Torres 2021 178		COVID-19	Control	COVID-19	Control	OR
		106 pregnant women with COVID-19	103 pregnant women without COVID-19	20.8% preterm (£35/40) (22/106)	8.8% preterm (£35/40) (9/103)	2.37 (1.14–4.91)
Gurol-Urganci 2021 170	UK	COVID-19	Control	COVID-19	Control	aOR
		3527 pregnant women with	338 553 pregnant women without	12.1% preterm	5.8% preterm	2.17 (1.96–2.42)
		COVID-19	COVID-19	0.85% stillbirth	0.34% stillbirth	2.21 (1.58–3.11)

Table 2: Summary of key studies relevant for the effect of COVID-19 on maternal outcomes

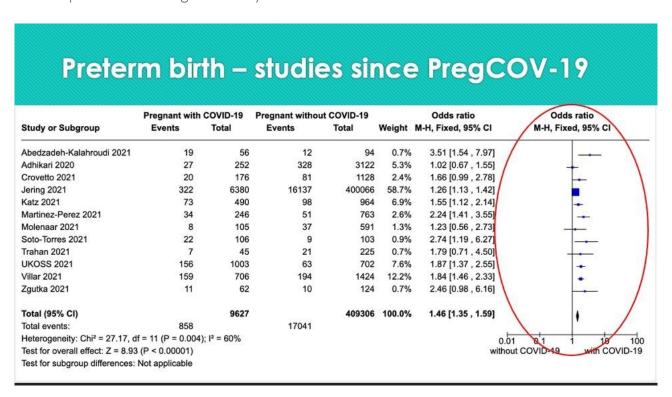
Study	Country	Population		Effect of COVID-19 on p	regnant women	
Allotey et al. 2020 <sup>149</sup>	30 countries	Pregnant	Not pregnant	Pregnant	Not pregnant	Adjusted OR
PregCOV-19 Systematic Review (updated 29/11/20)		34 047 pregnant women with COVID-19	567 075 non- pregnant women with COVID-19	<ul><li>1.8% ICU (616)</li><li>0.6% ventilation (270)</li></ul>	<ul><li>1.7% ICU (9568)</li><li>0.6% ventilation (3280)</li></ul>	<ul><li>2.13 (1.54–2.95)</li><li>2.59 (2.28–2.94)</li></ul>
Zambrano et al. 2020 <sup>158</sup> CDC Report	USA	Pregnant  23 434 pregnant women with symptomatic COVID-19	Not pregnant  386 028 non- pregnant women aged 15-44 with symptomatic COVID-19	Pregnant  1.05% ICU 0.29% invasive ventilation 0.07% ECMO 0.15% death	Not pregnant  Output  Output  Not pregnant  Output  Not pregnant  Output  Not pregnant  Not pregnant	Risk ratio (95% Cl)  • aRR 3.0 (2.6–3.4)  • aRR 2.9(2.2–3.8)  • aRR 2.4(1.5–4.0)  • aRR 1.7(1.2–2.40)
Martinez-Portilla et al 2020 <sup>155</sup>	Mexico	Pregnant  5183 pregnant women with symptomatic COVID-19 admitted to hospital	Not pregnant  5183 matched non-pregnant women aged 15-49 with symptomatic COVID-19	Pregnant  1.5% death  13% ICU  8.1% intubated	Not pregnant  • 0.8% death  • 7.4% ICU  • 8.6% intubated	• OR 1.84 (1.30– 2.61) • 2.25(1.86–2.71) • 0.93(0.70–1.25)

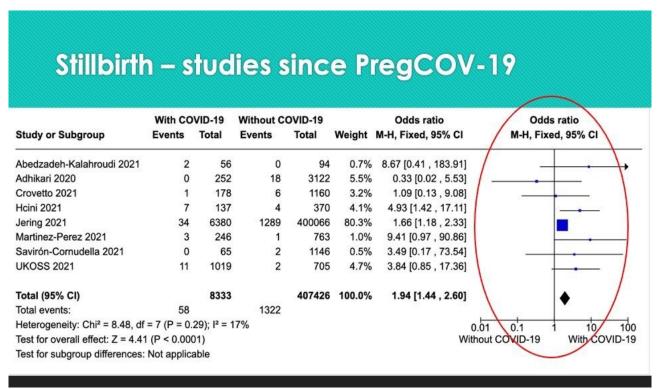
DeBolt et al 2020 <sup>151</sup>	USA	Pregnant	Not pregnant	Pregnant	Not pregnant	aOR (95% CI)
		38 pregnant women with severe or critical COVID-19	94 non-pregnant women aged 23–50 with severe or critical COVID-19	<ul><li>39.5% ICU</li><li>26.3% invasive ventilation</li></ul>	<ul><li>17% ICU</li><li>10.6% invasive ventilation</li></ul>	• 5.2 (1.5–17.5) • 3.3 (0.5–21.1)
Badr et al 2020 <sup>150</sup>	France	Pregnant	Not pregnant	Pregnant	Not pregnant	
		83 pregnant women (320 weeks) with COVID-19	107 non-pregnant women of reproductive age with COVID-19	11.08% ICU     10.16% invasive     ventilation	<ul><li>2.38% ICU</li><li>1.67% invasive ventilati</li></ul>	ion
Oakes et al 2021 157	USA	Pregnant:	Not pregnant:	Pregnant	Not pregnant	Relative risk (95% Cl)
		22 pregnant women with symptomatic COVID-19	240 non-pregnant women aged 13–45 with symptomatic COVID-19	<ul> <li>31.8% severe COVID (NCPERET criteria)</li> <li>13.6% severe COVID (WHOOSCI criteria)</li> </ul>	<ul><li>7.1% severe COVID (NCPERET criteria)</li><li>2.5% severe COVID (WHOOSCI criteria)</li></ul>	• aRR 3.59(1.49– 7.01) • aRR 5.65 (1.36– 17.31)
Lokken et al 2021 154	USA	Pregnant	Not pregnant	Pregnant	Not pregnant	Relative risk (95% CI)
		240 women with COVID-19	34 902 adults (male and female) aged 20–39	<ul><li>10% hospitalisation for COVID-19</li><li>1.25% death</li></ul>	<ul><li>2.8% hospitalisation for COVID-19</li><li>0.091% death</li></ul>	• RR 3.5 (2.3–5.3) • RR 13.6 (2.7–43.6)
Artymuk el 2021 181	Siberia, Russia	Pregnant	Not pregnant	Pregnant	Not pregnant	,
		8485 women with COVID-19	General population (496-170)	<ul> <li>5933 per 100 000 incidence</li> <li>3.57% ICU</li> <li>0.48% mechanical ventilation</li> </ul>	<ul> <li>1960 per 100 000 incidence</li> <li>2.24% ICU</li> <li>1.05% mechanical ventilation</li> </ul>	
Behrens 2021 182	USA	Pregnant	Not pregnant	Pregnant	Not pregnant	
		43 women with COVID	1265 women with COVID aged 16–51	• 0% deaths (0)	• 3% deaths (39 deaths)	

Vizheh 2021 184	Iran	Pregnant	Not pregnant	Pregnant	Not pregnant	P value
		, 0	234 non-pregnant women with COVID	9.1% ICU (10) 5.5% death (6)	• 8.1% ICU (18) • 5.1% death (12)	<ul><li> P = 0.76</li><li> P = 0.80</li></ul>
Qeaden 2021 183		Pregnant	Not pregnant	Pregnant	Not pregnant	P value
		1609 pregnant women with COVID-19	20 884 non pregnant women with COVID, aged 18–44	<ul><li>1.6% ventilation (26)</li><li>0.2% death (4)</li></ul>	<ul><li>1.9% ventilation (396)</li><li>0.5% death (100)</li></ul>	<ul><li> P = 0.48</li><li> P= 0.26</li></ul>

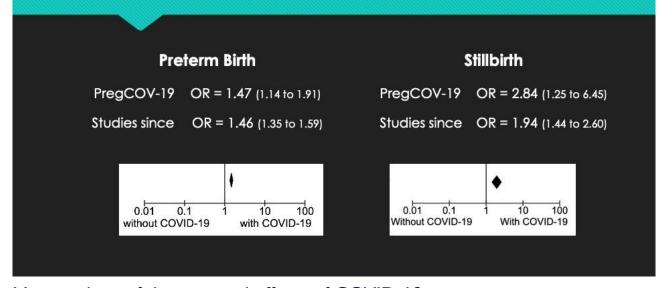
### Meta-analysis of the effect of COVID-19 on pregnancy outcomes

Meta-analysis of the effects of COVID-19 on pregnancy outcomes (preterm birth, stillbirth) was performed using data from the studies in Table I (above) published since the last update of the PregCOV-19 systematic review, using the online Cochrane Revman software (Shea et al, unpublished). The results of this meta-analysis are compared with the results of the latest online update of the PregCOV-19 systematic review from 29 November 2020.



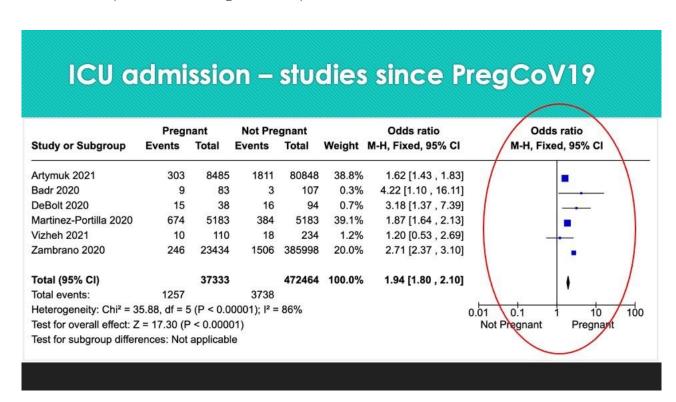


## Pregnancy outcomes for pregnant women with vs without COVID-19



### Meta-analysis of the maternal effects of COVID-19

Meta-analysis of the maternal effects of COVID-19 (ICU admission, mechanical ventilation, and death) was performed using data from the studies in Table 2 (above) published since the last update of the PregCOV-19 systematic review, using the online Cochrane Revman software (Shea et al, unpublished). The results of this meta-analysis are compared with the results of the latest online update of the PregCOV-19 systematic review from 29 November 2020. 149



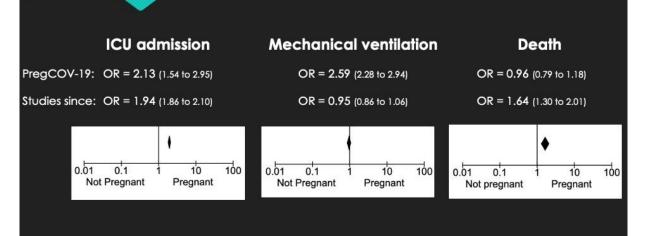
## Mechanical ventilation – studies since PregCov19

	Pregr	nant	Not Pre	gnant		Odds ratio	Odds ratio
Study or Subgroup	<b>Events</b>	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Artymuk 2021	41	8485	845	80476	23.6%	0.46 [0.33 , 0.63]	
Badr 2020	8	83	2	107	0.2%	5.60 [1.16 , 27.12]	
DeBolt 2020	10	38	10	94	0.6%	3.00 [1.13 , 7.96]	
Martinez-Portilla 2020	420	5183	446	5183	60.2%	0.94 [0.81, 1.08]	
Qeaden 2021	26	1609	396	20884	8.2%	0.85 [0.57, 1.27]	I -I
Zambrano 2020	65	23434	425	386028	7.1%	2.52 [1.94 , 3.28]	-
Total (95% CI)		38832		492772	100.0%	0.95 [0.86 , 1.06]	\ \ \
Total events:	570		2124				\
Heterogeneity: Chi <sup>2</sup> = 8	4.78, df = 5	(P < 0.0	0001); I <sup>2</sup> =	94%			0.01 0.1 1 10 10
Test for overall effect: Z = 0.87 (P = 0.39)							Not Pregnant Pregnant
Test for subgroup differ	ences: Not	applicabl	е				

## Death – studies since PregCOV-19

	Pregr	nant	Not Pre	gnant		Odds ratio	Odds ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Behrens 2021	0	43	39	1265	2.6%	0.36 [0.02 , 5.90]	
Lokken 2021	3	240	32	34902	0.4%	13.79 [4.19 , 45.35]	/
Martinez-Portilla 2020	78	5183	41	5183	39.7%	1.92 [1.31, 2.80]	<b> </b>
Qeaden 2021	4	1609	100	20884	14.0%	0.52 [0.19, 1.41]	
Vizheh 2021	6	110	12	234	7.1%	1.07 [0.39, 2.92]	
Zambrano 2020	35	23434	463	567075	36.1%	1.83 [1.30 , 2.58]	-
Total (95% CI)		30619		629543	100.0%	1.64 [1.30 , 2.07]	\
Total events:	126		687				\
Heterogeneity: Chi <sup>2</sup> = 2	0.27, df = 5	6 (P = 0.0)	01); I <sup>2</sup> = 75	5%			0.01 0.1 1 10 10
Test for overall effect: Z = 4.18 (P < 0.0001)							Not pregnant Pregnant
Test for subgroup differ	ences: Not	applicabl	e				

## Maternal Risks: pregnant vs non-pregnant women with COVID-19



# Appendix IV: Example of a telephone triage tool for symptomatic women with suspected or confirmed COVID-19

(adapted from Guy's and St Thomas' NHS Foundation Trust)

### Assess severity of illness:

- Shortness of breath/difficulty breathing
- Difficulty completing short sentences without needing to stop/gasp for air
- Coughing blood
- Pain or pressure in chest (other than with coughing)
- Unable to keep liquids down
- Less responsive than normal or becoming confused while talking

### **Symptoms**

present

.....

RECOMMEND ATTENDANCE FOR MATERNITY ASSESSMENT

### None of these symptoms



#### Assess clinical and social risks:

- Age >35 years old, BMI >30 kg/m<sup>2</sup>
- Women of the Black, Asian or other minority ethnic community
- Consider VTE risk assessment and score
- Medical co-morbidities: diabetes, hypertension, asthma/respiratory disease, HIV, heart disease, immunosuppression, chronic kidney disease
- Obstetric factors: at risk of fetal growth restriction, suspected preterm labour, reduced fetal movements
- Social factors: language barriers, safeguarding concerns, mental health issues, poor social support, domestic violence

#### No risk factors



Advise to self-isolate and arrange a COVID-19 test (if not yet done) in line with national guidance:

- Inform named consultant and midwifery team
- Safety net to call back if symptoms worsen

Risk

factors

present

.....

DISCUSS WITH
CONSULTANT ABOUT
POSSIBLE NEED FOR
ADMISSION

# Appendix V: Example of a maternity escalation plan for women with suspected or confirmed COVID-19

(adapted from Guy's and St Thomas' NHS Foundation Trust)

Category	Clinical criteria for oxygenation	Suggested actions	Other considerations for viable fetus			
Green	SpO2 94%-98%	Ensure no obstetric or medical concerns				
	Room air and RR ≤ 20	Discharge for self-isolation in line with national guidance				
Yellow	Target SpO <sub>2</sub> 94%– 98% on ≥ FiO <sub>2</sub> 28% and/or RR ≥ 21	Increase oxygen flow rate to maintain SaO2 94%–98%  Assessment by obstetric registrar In-patient care Inform maternity escalation team:  Obstetric consultant  Obstetric anaesthetist  On-call medical team  Give oral prednisolone 40 mg for	Assess fetal wellbeing Consider fetal monitoring Discuss timing of birth Depending on the gestational age:  Consider steroids for fetal lungs  Consider magnesium sulfate for neuroprotection if considering birth of the baby			
Amber	Target SpO <sub>2</sub> 94%– 98% on ≥ FiO <sub>2</sub> 35% and/or RR ≥ 25	Increase oxygen flow rate to maintain SaO <sub>2</sub> 94%–98%  Consider 15l/min O <sub>2</sub> via non-rebreathe mask  Refer to ITU team  Urgent review by the maternity escalation team  Consider awake proning position when feasible/high flow oxygen in critical care setting only	Discuss the risks and benefits of emergency caesarean birth  Depending on the gestational age:  Consider steroids for fetal lungs  Consider magnesium sulfate for neuroprotection if considering birth			
Red	SpO2 < 94% on 151/min O2 via non- rebreathe mask	Urgent review by ITU team  Urgent attendance by the maternity escalation team  Consider awake proning position when feasible/high flow oxygen in critical care setting only	Discuss the risks and benefits of emergency caesarean birth  Depending on the gestational age:  Consider steroids for fetal lungs  Consider magnesium sulfate for neuroprotection if considering birth			
Peri-arrest		Call 2222 – adult cardiac arrest tea neonatal crash team	m, obstetric crash team and			





## References

## **References**

- 1. Scottish Intercollegiate Guidelines Network. Implementation Support. 2019; Website
- 2. World Health Organization. Coronavirus disease (COVID-2019) situation reports. 2020; Website
- 3. Centers for Disease Control and Prevention. Human Coronavirus Types. 2020; Website
- 4. Walker KF, O'Donoghue K, Grace N, Dorling J, Comeau JL, 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(11):1324-1336
- 5. Salvatore CM, Han J-Y, Acker KP, Tiwari P, Jin J, Brandler M, et al. Neonatal management and outcomes during the COVID-19 pandemic: an observation cohort study. *The Lancet. Child & adolescent health* 2020;4(10):721-727
- 6. Dumitriu D, Emeruwa UN, Hanft E, Liao GV, Ludwig E, Walzer L, et al. Outcomes of Neonates Born to Mothers With Severe Acute Respiratory Syndrome Coronavirus 2 Infection at a Large Medical Center in New York City. JAMA pediatrics 2021;175(2):157-167
- 7. Jimenez IM, Lopez RS, Garcia Rosas E, Rodriguez de la Torre I, Montes Garcia J, de la Cruz Conty ML, et al. Umbilical cord clamping and skin-to-skin contact in deliveries from women positive for SARS-CoV-2: a prospective observational study. *BJOG* 2021; 128(5):908-915
- 8. Ronchi A, Pietrasanta C, Zavattoni M, Saruggia M, Schena F, Sinelli MT, et al. Evaluation of Rooming-in Practice for Neonates Born to Mothers With Severe Acute Respiratory Syndrome Coronavirus 2 Infection in Italy. *JAMA pediatrics* 2021;175(3):260-266
- 9. World Health Organization. Scientific Brief: Definition and categorization of the timing of mother-to-child transmission of SARS- CoV-2. 2021; Website
- 10. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ* 2020;369:m1985
- 11. Reale SC, Lumbreras-Marquez MI, King CH, Burns SL, Fields KG, Diouf K, et al. Patient characteristics associated with SARS-CoV-2 infection in parturients admitted for labour and delivery in Massachusetts during the spring 2020 surge: A prospective cohort study. *Paediatr Perinat Epidemiol* 2021;35(1):24-33
- 12. Public Health England. COVID-19: investigation and initial clinical management of possible cases. 2020; Website
- 13. Afshar Y, Gaw SL, Flaherman VJ, Chambers BD, Krakow D, Berghella V, et al. Clinical Presentation of Coronavirus Disease 2019 (COVID-19) in Pregnant and Recently Pregnant People. *Obstet Gynecol* 2020;136(6):1117-1125

- 14. National Institute for Health and Care Excellence. COVID-19 Rapid Guideline: Managing the Long-Term Effects of COVID-19. NICE guideline [NG188]. 2020; Website
- 15. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. *Acta Obstet Gynecol Scand* 2020;99(7):823-829
- 16. Nakamura-Pereira M, Betina Andreucci C, de Oliveira Menezes M, Knobel R, Takemoto MLS . Worldwide maternal deaths due to COVID-19: A brief review. *Int J Gynaecol Obstet* 2020;151(1):148-150
- 17. Ward H, Atchison C, Ainslie KE, Elliot J, Okell L, Redd R, et al. Antibody prevalence for SARS-CoV-2 following the peak of the pandemic in England: REACT2 study in 100,000 adults. medRxiv 2020; Website
- 18. Vousden N, Bunch K, Morris E, Simpson N, Gale C, O'Brien P, et al. The incidence, characteristics and outcomes of pregnant women hospitalized with symptomatic and asymptomatic SARS-CoV-2 infection in the UK from March to September 2020: a national cohort study using the UK Obstetric Surveillance System (UKOSS). *PLoS One* 2021;16(5):e0251123
- 19. Intensive Care National Audit Research Centre (ICNARC). Report on COVID-19 in critical care. 2020; Website
- 20. Office for National Statistics. Conceptions in England and Wales: 2018. 2020; Website
- 21. MBRRACE-UK. Saving Lives, Improving Mothers' Care Rapid report: Learning from SARS-CoV2-related and associated maternal deaths in the UK. March-May 2020. 2021; Website
- 22. Ellington S, Strid P, Tong VT, Woodworth K, Galang RR, Zambrano LD, et al. Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status United States, January 22—June 7, 2020. MMWR Morbidity and Mortality Weekly Report 2020; Website
- 23. D'Onofrio BM, Class QA, Rickert ME, Larsson H, Långström N, Lichtenstein P. Preterm birth and mortality and morbidity: a population-based quasi-experimental study. JAMA Psychiatry 2013;70(11):1231-40
- 24. Knight M, Bunch K, Tufnell D. Saving Lives, Improving Mothers' Care Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2016-18. 2020; Website
- 25. Office for National Statistics. Coronavirus (COVID-19) related deaths by ethnic group, England and Wales: 2 March to 28 July 2020. 2021; Website
- 26. Khunti K, Singh AK, Pareek M, Hanif W. Is ethnicity linked to incidence or outcomes of covid-19? *BMJ* 2020;369:m1548
- 27. Liu N, Sun J, Wang X, Zhang T, Zhao M, Li H. Low vitamin D status is associated with coronavirus disease 2019 outcomes: a systematic review and meta-analysis. International journal of infectious diseases. *Int J Infect Dis* 2021;104:58-64

- 28. NHS. Vitamin D. 2017; Website
- 29. NHS. Vitamins, supplements and nutrition in pregnancy. 2020; Website
- 30. Swartz DA, Graham AL. Potential Maternal and Infant Outcomes from (Wuhan) Coronavirus 2019-nCoV Infecting Pregnant Women: Lessons from SARS, MERS, and Other Human Coronavirus Infections. *Virus*es 2020;12(2):194
- 31. Alserehi H, Wali G, Alshukairi A, Alraddadi B. Impact of Middle East Respiratory Syndrome coronavirus (MERS-CoV) on pregnancy and perinatal outcome. *BMC infectious diseases* 2016;16:105
- 32. Rimmer MP, Al Wattar BH. Provision of obstetrics and gynaecology services during the COVID-19 pandemic: a survey of junior doctors in the UK National Health Service. *BJOG* 2020;127(9):1123-1128
- 33. Jardine J, Relph S, Magee LA, von Dadelszen P, Morris E, Ross-Davie M, et al. Maternity services in the UK during the coronavirus disease 2019 pandemic: a national survey of modifications to standard care. *BJOG* 2021;128(5):880-8891
- 34. Karavadra B, Stockl A, Prosser-Snelling E, Simpson P, Morris E. Women's perceptions of COVID-19 and their healthcare experiences: a qualitative thematic analysis of a national survey of pregnant women in the United Kingdom. *BMC Pregnancy and Childbirth* 2020;20(1):600
- 35. Yan H, Ding Y, Guo W. Mental Health of Pregnant and Postpartum Women During the Coronavirus Disease 2019 Pandemic: A Systematic Review and Meta-Analysis. *Frontiers Psychol* 2020;11:617001
- 36. Fan SI, Guan J, Cao LI, Wang M, Zhao H, Chen L, et al. Psychological effects caused by COVID-19 pandemic on pregnant women: A systematic review with meta-analysis. *Asian J Psychiatr* 2021;56:102533
- 37. Joint Committee on Vaccination and Immunisation. Advice on priority groups for COVID-19 vaccination. 2020; Website
- 38. Dowswell T, Carroli G, Duley L, Gates S, Gülmezoglu AM, Khan-Neelofur D, et al.: Alternative versus standard packages of antenatal care for low-risk pregnancy. The Cochrane Database Syst Rev 2015;(7):CD000934
- 39. MBRRACE-UK: Saving Lives, Improving Mothers' Care. Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2014-16. 2018; Website
- 40. National Institute for Health and Care Excellence. *Antenatal Care for Uncomplicated Pregnancies*. NICE Clinical Guideline 62 [CG62]. 2008; Website
- 41. Reale SC, Fields KG, Lumbreras-Marquez MI, King CH, Burns SL, Huybrechts KF, et al. Association Between Number of In-Person Health Care Visits and SARS-CoV-2 Infection in Obstetrical Patients. *JAMA* 2020;324(12):1210-1212

- 42. Jeganathan S, Prasannan L, Blitz MJ, Vohra N, Rochelson B, Meirowitz N. Adherence and acceptability of telehealth appointments for high-risk obstetrical patients during the coronavirus disease 2019 pandemic. *Am J Obstet Gynecol MFM* 2020;2(4):100233
- 43. NHS England and NHS Improvement : Clinical guide for the management of remote consultations and remote working in secondary care during the coronavirus pandemic. 2020; Website
- 44. Peahl AF, Smith RD, Moniz MH. Prenatal care redesign: creating flexible maternity care models through virtual care. *Am J Obstet Gynecol* 2020;223(3):389.e1-389.e10
- 45. Karavandra B, Stockl A, Prosser-Snelling E. Women's perceptions of COVID-19 and their healthcare experiences: a qualitative thematic analysis of a national survey of pregnant women in the United Kingdom. *BMC Pregnancy Childbirth* 2020; 20(1):600
- 46. National Institute for Health and Care Excellence. Diabetes in pregnancy: management from preconception to the postnatal period. NICE guideline 3 [NG3]. 2015; Website
- 47. van-de-l'Isle Y, Steer PJ, Watt Coote I, Cauldwell M. Impact of changes to national UK Guidance on testing for gestational diabetes screening during a pandemic: a single-centre observational study. *BJOG* 2021;128(5):917-920
- 48. McIntyre HD, Gibbons KS, Ma RCW, Tam WH, Sacks DA, Lowe J, et al. Testing for gestational diabetes during the COVID-19 pandemic. An evaluation of proposed protocols for the United Kingdom, Canada and Australia. *Diabetes Res Clin Pract* 2020;167:108353
- 49. Meek CL, Lindsay RS, Scott EM, Aiken CE, Myers J, Reynolds RM, et al. Approaches to screening for hyperglycaemia in pregnant women during and after the COVID-19 pandemic. *Diabet Med* 2021;38(1):e1438
- 50. Chodosh J, Weinstein BE, Blustein J. Face masks can be devastating for people with hearing loss. *BMJ* 2020;370:m2683
- 51. Henderson J, Gao H, Redshaw M. Experiencing maternity care: the care received and perceptions of women from different ethnic groups. *BMC Pregnancy Childbirth* 2013;13:196
- 52. Raleigh VS, Hussey D, Seccombe I, Hallt K. Ethnic and social inequalities in women's experience of maternity care in England: results of a national survey. *J R Soc Med* 2010;103(5):188-98
- 53. Vardavas CI, Nikitara K : COVID-19 and smoking: A systematic review of the evidence. *Tob Induc Dis* 2020;18:20
- 54. Mertz D, Geraci J, Winkup J, Gessner BD, Ortiz JR, Loeb M. Pregnancy as a risk factor for severe outcomes from influenza virus infection: A systematic review and meta-analysis of observational studies. *Vaccine* 2017;35(4):521-528
- 55. Quach THT, Mallis NA, Cordero JF. Influenza Vaccine Efficacy and Effectiveness in Pregnant Women: Systematic Review and Meta- analysis. *Matern Child Health J* 2020;24(2):229-240

- 56. Cuadrado-Payán E, Montagud-Marrahi E, Torres-Elorza M, Bodro M, Blasco M, Poch E, et al. SARS-CoV-2 and influenza virus co- infection. *Lancet* 2020;395(10236):e84
- 57. Corbett GA, Milne SJ, Hehir MP, Lindow SW, O'connell MP. Health anxiety and behavioural changes of pregnant women during the COVID-19 pandemic. *Eur J Obstet Gynecol Reprod Biol* 2020;249:96-97
- 58. Wu Y, Zhang C, Liu H, Duan C, Li C, Fan J, et al. Perinatal depressive and anxiety symptoms of pregnant women during the coronavirus disease 2019 outbreak in China. *Am J Obstet Gynecol* 2020;223(2):240.e1-240.e9
- 59. Banks J, Xu X.The mental health effects of the first two months of lockdown and social distancing during the Covid-19 pandemic in the UK. <u>Website</u>
- 60. World Health Organization. Scientific Brief: Smoking and COVID-19. 2020; Website
- 61. Banks J, Xu X. Institute for Fiscal Studies Working Paper W20/16 The mental health effects of the first two months of lockdown and social distancing during the Covid-19 pandemic in the UK 2020. 2020; Website
- 62. Etheridge B, Spantig L. Institute for Social and Economic Research ISER Working Paper Series 2020-08. The gender gap in mental well-being during the Covid-19 outbreak: evidence from the UK. 2020; Website
- 63. Saccone G, Florio A, Aiello F, Venturella R, De Angelis MC, Locci M, et al. Psychological impact of coronavirus disease 2019 in pregnant women. *Am J Obstet Gynecol* 2020;223(2):293-295
- 64. Lebel C, MacKinnon A, Bagshawe M, Tomfohr-Madsen L, Giesbrecht G. Elevated depression and anxiety symptoms among pregnant individuals during the COVID-19 pandemic. J Affect Dis 2020;277 5-13
- 65. Royal College of Midwives. Domestic Abuse. 2020; Website
- 66. Fraser E, VAWG Helpdesk. Impact of COVID-19 Pandemic on Violence against Women and Girls. VAWG Helpdesk Research Report No. 284. 2020; Website
- 67. Roesch E, Amin A, Gupta J, García-Moreno C. Violence against women during covid-19 pandemic restrictions. *BMJ* 2020;369:m1712
- 68. Public Health England. COVID-19: Guidance for maintaining services within health and care settings. Infection prevention and control recommendations. 2021; <u>Website</u>
- 69. Royal College of Midwives. Personal Protective Equipment: Know your Rights. 2020; Website
- 70. Patberg ET, Adams T, Rekawek P, Vahanian SA, Akerman M, Hernandez A, et al. Coronavirus disease 2019 infection and placental histopathology in women delivering at term. *Am | Obstet Gynecol* 2021;224(4):382.e1-382.e18

- 71. Sharps MC, Hayes DJL, Lee S, Zou Z, Brady CA, Almoghrabi Y, et al. A structured review of placental morphology and histopathological lesions associated with SARS-CoV-2 infection. *Placenta* 2020;101:13-29
- 72. Abu-Rustum RS, Akolekar R. ISUOG Consensus Statement on organization of routine and specialist obstetric ultrasound services in the context of COVID-19. *Ultrasound Obstet Gynecol* 2020; 55(6):863-870
- 73. Bremme KA: Haemostatic changes in pregnancy. Best Pract Res Clin Haematol 2003;16(2):153-68
- 74. Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggin E, et al. COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-Up: JACC State-of-the-Art Review. J Am Coll Cardiol 2020;75(23):2950-2973
- 75. D'Souza R, Malhamé I, Teshler L, Acharya G, Hunt BJ, McLintock C. A critical review of the pathophysiology of thrombotic complications and clinical practice recommendations for thromboprophylaxis in pregnant patients with COVID-19. Acta Obstet Gynecol Scand 2020;99(9):1110-1120
- 76. Royal College of Obstetricians and Gynaecologists. Reducing the Risk of Venous Thromboembolism during Pregnancy and the Puerperium. Green-top Guideline No. 37a. 2015; Website
- 77. Royal College of Obstetricians and Gynaecologists. *Thrombosis and Embolism during Pregnancy and the Puerperium: Acute Management.* Green-top Guideline No. 37b. 2015; Website
- 78. Freedman RL, Lucas DN. MBRRACE-UK: saving lives, improving mothers' care implications for anaesthetists. *Int | Obstet Anesth* 2015;24(2):161-73
- 79. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet* 2020;395(10226):809-815
- 80. Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr* 2020;9(1):51-60
- 81. Cruz-Lemini M, Ferriols Perez E, de la Cruz Conty ML, Caño Aguilar A, Encinas Pardilla MB, Prats Rodríguez P, et al. Obstetric Outcomes of SARS-CoV-2 Infection in Asymptomatic Pregnant Women. *Virus*es 2021;13(1):112
- 82. National Institute for Health and Care Excellence: Intrapartum Care for healthy women and babies. NICE Clinical Guideline 190 [CG190]. Updated 21 February 2017. 2014; Website
- 83. Mejía Jiménez I, Salvador López R, García Rosas E, Rodriguez de la Torre I, Montes García J, de la Cruz Conty ML, et al. Umbilical cord clamping and skin-to-skin contact in deliveries from women positive for SARS-CoV-2: a prospective observational study. *BJOG* 2021;128(5):908-915

- 84. Sánchez-Luna M, Fernández Colomer B, de Alba Romero C, Alarcón Allen A, Baña Souto A, Camba Longueira F, et al. Neonates Born to Mothers With COVID-19: Data From the Spanish Society of Neonatology Registry. *Pediatrics* 2021;147(2): e2020015065
- 85. NHS. Clinical guide for the temporary reorganisation of intrapartum maternity care during the coronavirus pandemic. 2020; Website
- 86. Scottish Government. Coronavirus (COVID-19): delivering maternity and neonatal services update December 2020. 2020; Website
- 87. World Health Organization. COVID-19 Clinical management: living guidance. 2021; Website
- 88. Zimmermann P, Curtis N. COVID-19 in Children, Pregnancy and Neonates: A Review of Epidemiologic and Clinical Features. *Pediatr Infect Dis J* 2020;39(6):469-477
- 89. Yang Z, Wang M, Zhu Z, Liu YI. Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review. *J Matern Fetal Neonatal Med* 2020;1-4
- 90. Vouga M, Favre G, Martinez Perez O. Maternal and Obstetrical Outcomes in a Cohort of Pregnant Women Tested for SARS-CoV-2: Interim Results of the COVI-Preg International Registry. 2020; Journal
- 91. Bohren MA, Hofmeyr G, Sakala C. Continuous support for women during childbirth. *Cochrane Database Syst Rev* 2017;7(7):CD003766
- 92. Bohren MA, Berger BO, Munthe-Kaas H, Tunçalp Ö. Perceptions and experiences of labour companionship: a qualitative evidence synthesis. *Cochrane Database Syst Rev* 2019;3 CD012449
- 93. Shakibazadeh E, Namadian M, Bohren MA, Vogel JP, Rashidian A, Nogueira Pileggi V, et al. Respectful care during childbirth in health facilities globally: a qualitative evidence synthesis. *BJOG* 2018;125(8):932-942
- 94. Ravaldi C, Wilson A, Ricca V, Homer C, Vannacci A. Pregnant women voice their concerns and birth expectations during the COVID-19 pandemic in Italy. *Women Birth* 2021;34(4):335-343
- 95. Hui PW, Ma G, Seto MTY, Cheung KW. Effect of COVID-19 on delivery plans and postnatal depression scores of pregnant women. *Hong Kong Med J* 2021;27(2):113-117
- 96. Public Health England. COVID-19: infection prevention and control (IPC). Updated I June 2021. 2020; Website
- 97. NHS England and NHS Improvement. Visiting healthcare inpatient settings during the COVID-19 pandemic. Updated 23 March 2021. 2020; Website
- 98. Knight M, Bunch K, Vousden N, Morris E, Simpson N, Gale C, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. *BMJ* 2020;369:m2107

- 99. Walker KF, O'Donoghue K, Grace N, Dorling J, Comeau JL, Li W, et al. Maternal transmission of SARS-COV-2 to the neonate, and possible routes for such transmission: a systematic review and critical analysis. *BJOG* 2020;127(11):1324-1336
- 100. National Institute for Health and Care Excellence. *Preterm labour and birth*. NICE guideline [NG25]. Updated 2 August 2019. 2015; Website
- 101. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature* 2020;584(7821):430-436
- 102. Cuerva MJ, Carbonell M, Martín Palumbo G, Lopez Magallon S, De La Calle M, Bartha JL. Personal Protective Equipment during the COVID-19 pandemic and operative time in cesarean section: retrospective cohort study. *J Matern Fetal Neonatal Med* 2020;1-4
- 103. Lowe B, De Araujo V, Haughton H, Schweitzer J, Brazil V: Preparing maternity for COVID-19: A translational simulation approach. *Aust N Z J Obstet Gynaecol* 2020;60(4):628-632
- 104. Karavadra B, Stockl A, Prosser-Snelling E, Simpson P, Morris E. Women's perceptions of COVID-19 and their healthcare experiences: a qualitative thematic analysis of a national survey of pregnant women in the United Kingdom. *BMC Pregnancy Childbirth* 2020;20(1):600
- 105. Amirian ES. Potential fecal transmission of SARS-CoV-2: Current evidence and implications for public health. *Int J Infect Dis* 2020;95 363-370
- 106. Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, et al. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. *JAMA* 2020;323(18):1843-1844
- 107. Morau E, Bouvet L, Keita H, Vial F, Bonnet MP, Bonnin M, et al. Anaesthesia and intensive care in obstetrics during the COVID-19 pandemic. *Anaesth Crit Care Pain Med* 2020;39(3):345-349
- 108. Public Health England. 6. COVID-19 infection prevention and control guidance: aerosol generating procedures procedures that create a higher risk of respiratory infection transmission. 2021; Website
- 109. Bhatia K, Columb M, Bewlay A, Eccles J, Hulgur M, Jayan N, et al. The effect of COVID-19 on general anaesthesia rates for caesarean section. A cross-sectional analysis of six hospitals in the north-west of England. *Anaesthesia* 2021;76(3):312-319
- 110. Royal College of Anaesthetists, Obstetric Anaesthetists' Association, Association of Anaesthetists, Intensive Care Society, The Faculty of Intensive Care Medicine. Management of pregnant women with known or suspected COVID-19. 2020; Website
- III. Hampton T, Crunkhorn R, Lowe N, Bhat J, Hogg E, Afifi W, et al.: The negative impact of wearing personal protective equipment on communication during coronavirus disease 2019. *J Laryngol Otol* 2020; 134(7):577-581
- 112. Royal College of Obstetricians and Gynaecologists. *Bacterial sepsis in pregnancy*. Greentop Guideline No. 64a. 2012; Website

- 113. Yang H, Hu B, Zhan S, Yang L-Y, Xiong G. Effects of Severe Acute Respiratory Syndrome Coronavirus 2 Infection on Pregnant Women and Their Infants. *Arch Pathol Lab Med* 2020;144(10):1217-1222
- 114. Shi Ll, Wang Y, Yang H, Duan G, Wang Y: Laboratory Abnormalities in Pregnant Women with Novel Coronavirus Disease 2019. Am J Perinatol 2020;37(10):1070-1073
- 115. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. 2020; Website
- 116. National Institute for Health and Care Excellence. COVID-19 rapid guideline: critical care in adults. NICE guideline 159 [NG159]. Updated 12 February 2021. 2020; Website
- 117. Scottish Intercollegiate Guidelines Network. COVID-19 position statement: Maternal critical care provision. 2020; Website
- 118. Lippi G, Plebani M, Henry BM.Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. *Clin Chim Acta* 2020;506 145-148
- 119. Gavillet M, Rolnik DL, Hoffman MK, Panchaud A, Baud D. Should we stop aspirin prophylaxis in pregnant women diagnosed with COVID-19? *Ultrasound Obstet Gynecol* 2020;55(6):843-844
- 120. National Institute for Health and Care Excellence. *COVID-19 rapid guideline: acute myocardial injury.* NICE guideline 171 [NG171]. 2020; Website
- 121. McIntosh JJ. Corticosteroid Guidance for Pregnancy during COVID-19 Pandemic. Am J Perinatol 2020;37(8):809-812
- 122. Royal College of Anaesthetists. Care of the critically ill woman in childbirth; enhanced maternal care. 2018; Website
- 123. Royal College of Physicians. Acute care toolkit 15: Managing acute medical problems in pregnancy. 2019; Website
- 124. Intensive Care Society. Prone Positioning in Adult Critical Care. 2020; Website
- 125. Tolcher MC, McKinney JR, Eppes CS, Muigai D, Shamshirsaz A, Guntupalli KK, et al. Prone Positioning for Pregnant Women With Hypoxemia Due to Coronavirus Disease 2019 (COVID-19). *Obstet Gynecol* 2020;136(2):259-261
- 126. The RECOVERY Collaborative Group. Dexamethasone in Hospitalized Patients with Covid-19. New Engl J Med 2021;384(8):693-704
- 127. ClinicalTrials.gov. Randomised Evaluation of COVID-19 Therapy (RECOVERY). 2020; Website
- 128. Saad AF, Chappell L, Saade GR, Pacheco LD. Corticosteroids in the Management of Pregnant Patients With Coronavirus Disease (COVID-19). *Obstet Gynecol* 2020;136(4):823-826
- 129. Thevathasan I, Said JM. Controversies in antenatal corticosteroid treatment. *Prenat Diagn* 2020;40(9):1138-1149

- 130. Pan H, Peto R, Henao-Restrepo A-M, Preziosi M-P, Sathiyamoorthy V, Abdool Karim Q, et al. Repurposed Antiviral Drugs for Covid-19 Interim WHO Solidarity Trial Results. *N Engl J Med* 2021;384(6):497-511
- 131. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, et al. Remdesivir for the Treatment of Covid-19 Final Report. N Engl J Med 2020;383(19):1813-1826
- 132. Gordon AC, Mouncey PR, Al-Beidh F: Interleukin-6 Receptor Antagonists in Critically III Patients with Covid-19 Preliminary report. medRxiv 2021; Journal
- 133. Veiga VC, Prats JAGG, Farias DLC, Rosa RG, Dourado LK, Zampieri FG, et al. Effect of tocilizumab on clinical outcomes at 15 days in patients with severe or critical coronavirus disease 2019: randomised controlled trial. *BMJ* 2021;372:n84
- 134. McCreary EK, Meyer NJ. Covid-19 controversies: the tocilizumab chapter. *BMJ* 2021;372:n244
- 135. Horby PW, Pessoa-Amorim G, Peto L. RECOVERY Collaborative Group. Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): preliminary results of a randomised, controlled, open-label, platform trial. *medRxiv* 2021; **Website**
- 136. Hoeltzenbein M, Beck E, Rajwanshi R, Gøtestam Skorpen C, Berber E, Schaefer C, et al. Tocilizumab use in pregnancy: Analysis of a global safety database including data from clinical trials and post-marketing data. Semin Arthritis Rheum 2016;46(2):238-245
- 137. Nakajima K, Watanabe O, Mochizuki M, Nakasone A, Ishizuka N, Murashima A. Pregnancy outcomes after exposure to tocilizumab: A retrospective analysis of 61 patients in Japan. *Mod Rheumatol* 2016;26(5):667-71
- 138. Saito J, Yakuwa N, Kaneko K, Takai C, Goto M, Nakajima K, et al. Tocilizumab during pregnancy and lactation: drug levels in maternal serum, cord blood, breast milk and infant serum. *Rheumatol* 2019;58(8):1505-1507
- 139. Stuebe A. Should Infants Be Separated from Mothers with COVID-19? First, Do No Harm. *Breastfeed Med* 2020;15(5):351-352
- 140. Gale C, Quigley MA, Placzek A, Knight M, Ladhani S, Draper ES, et al. Characteristics and outcomes of neonatal SARS-CoV-2 infection in the UK: a prospective national cohort study using active surveillance. *Lancet Child Adolesc Health* 2021;5(2):113-121
- 141. Royal College of Paediatrics and Child Health. COVID-19 guidance for paediatric services. 2020; <u>Website</u>
- 142. Royal College of Midwives. Optimising mother-baby contact and infant feeding in a pandemic. Rapid review Version 2. 2020; Website
- 143. Williams J, Namazova-Baranova L, Weber M, Vural M, Mestrovic J, Carrasco-Sanz A, et al. The Importance of Continuing Breastfeeding during Coronavirus Disease-2019: In Support of the World Health Organization Statement on Breastfeeding during the Pandemic. *J Pediatr* 2020;223 234-236

- 144. UNICEF Baby Friendly Initiative. Statements on supporting infant feeding during the coronavirus (Covid-19) outbreak. 2021; Website
- 145. World Health Organization. Breastfeeding and COVID-19. 2020; Website
- 146. Martins-Filho PR, Santos VS, Santos HP.To breastfeed or not to breastfeed? Lack of evidence on the presence of SARS-CoV-2 in breastmilk of pregnant women with COVID-19. Rev Panam Salud Publica 2020;44:e59
- 147. UK Government Department of Health and Social Care: Public advised to cover faces in enclosed spaces. 2020; <u>Website</u>
- 148. National Institute for Health and Care Excellence. *Postnatal care*. NICE guideline 194 [NG194]. 2021; Website
- 149. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, 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;370:m3320
- 150. Badr DA, Mattern J, Carlin A, Cordier A-G, Maillart E, El Hachem L, et al. Are clinical outcomes worse for pregnant women at ≥20 weeks' gestation infected with coronavirus disease 2019? A multicenter case-control study with propensity score matching. Am J Obstet Gynecol 2020;223(5):764-768
- 151. DeBolt CA, Bianco A, Limaye MA, Silverstein J, Penfield CA, Roman AS, et al. Pregnant women with severe or critical coronavirus disease 2019 have increased composite morbidity compared with nonpregnant matched controls. *Am J Obstet Gynecol* 2020;224(5):510.e1-510.e12
- 152. Intensive Care National Audit Research Centre (ICNARC): ICNARC report on COVID-19 in critical care: England, Wales and Northern Ireland 15 January 2021. 2021; Website
- 153. Jering KS, Claggett BL, Cunningham JW, Rosenthal N, Vardeny O, Greene MF, et al. Clinical Characteristics and Outcomes of Hospitalized Women Giving Birth With and Without COVID-19. JAMA Intern Med 2021; 181(5):714-717
- 154. Lokken EM, Huebner EM, Taylor GG, Hendrickson S, Vanderhoeven J, Kachikis A, et al. Disease severity, pregnancy outcomes, and maternal deaths among pregnant patients with severe acute respiratory syndrome coronavirus 2 infection in Washington State. Am J Obstet Gynecol 2021;225(1):77.e1-77.e14
- Martinez-Portilla RJ, Sotiriadis A, Chatzakis C, Torres-Torres J, Espino Y Sosa S, Sandoval-Mandujano K, et al. 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 Obstetrics Gynecol* 2021;57(2):224-231
- 156. Mullins E, Hudak ML, Banerjee J, Getzlaff T, Townson J, Barnette K, et al. Pregnancy and neonatal outcomes of COVID-19: coreporting of common outcomes from PAN-COVID and AAP-SONPM registries. *Ultrasound Obstetrics Gynecol* 2021;57(4):573-581

- 157. Oakes MC, Kernberg AS, Carter EB, Foeller ME, Palanisamy A, Raghuraman N, et al. Pregnancy as a risk factor for severe coronavirus disease 2019 using standardized clinical criteria. *Am | Obstet Gynecol MFM* 2021;3(3):100319
- I 58. Zambrano LD, Ellington S, Strid P, Galang RR, Oduyebo T, Tong VT, et al. 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 (44):1641-1647
- 159. Vousden N, Bunch K, Morris E, Simpson N, Gale C, O'Brien P, et al. The incidence, characteristics and outcomes of pregnant women hospitalized with symptomatic and asymptomatic SARS-CoV-2 infection in the UK from March to September 2020: A national cohort study using the UK Obstetric Surveillance System (UKOSS). *PloS one* 2021;16(5):e0251123
- 160. Chambers CD, Johnson DL, Xu R, Luo Y, Lopez-Jimenez J, Adam MP, et al. Birth outcomes in women who have taken adalimumab in pregnancy: A prospective cohort study. *PloS one* 2019;14(10):e0223603
- 161. Puchner A, Gröchenig HP, Sautner J, Helmy-Bader Y, Juch H, Reinisch S, et al. Immunosuppressives and biologics during pregnancy and lactation: A consensus report issued by the Austrian Societies of Gastroenterology and Hepatology and Rheumatology and Rehabilitation. Wien Klin Wochenschr 2019;131(1-2):29-44
- 162. RECOVERY Collaborative Group, Horby PW, Mafham M, Peto L. Casirivimab and imdevimab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *medRxiv* 2021; **Journal**
- 163. Camporota L, Meadows C, Ledot S, Scott I, Harvey C, Garcia M, et al. Consensus on the referral and admission of patients with severe respiratory failure to the NHS ECMO service. *Lancet Respir Med* 2021;9(2):e16-e17
- 164. Knight M, Bunch K, MBRRACE-UK: Saving Lives, Improving Mothers' Care. Rapid report 2021: Learning from SARS-CoV-2-related and associated maternal deaths in the UK June 2020-March 2021. Oxford, National Perinatal Epidemiology Unit, University of Oxford 2021; Website
- 165. Pachtman Shetty SL, Meirowitz N, Blitz MJ, Gadomski T, Weinberg CR. Myocardial injury associated with coronavirus disease 2019 in pregnancy. *Am J Obstet Gynecol* 2021;224(2):229-232
- 166. Jiménez-Lozano I, Caro-Teller JM, Fernández-Hidalgo N, Miarons M, Frick MA, Batllori Badia E, et al. Safety of tocilizumab in COVID-19 pregnant women and their newborn: A retrospective study. *J Clin Pharm Ther* 2021;46(4):1062-1070
- 167. Abedzadeh-Kalahroudi M, Sehat M, Vahedpour Z, Talebian P. Maternal and neonatal outcomes of pregnant patients with COVID-19: A prospective cohort study. *Int J Gynaecol Obstet* 2021;153(3):449-456

- 168. Adhikari EH, Moreno W, Zofkie AC, MacDonald L, McIntire DD, Collins RRJ, et al. Pregnancy Outcomes Among Women With and Without Severe Acute Respiratory Syndrome Coronavirus 2 Infection. *JAMA Netw Open* 2020;3(11):e2029256
- 169. Crovetto F, Crispi F, Llurba E, Pascal R, Larroya M, Trilla C, et al. Impact of SARS-CoV-2 Infection on Pregnancy Outcomes: A Population-Based Study. *Clin Infect Dis* 2021 [epub ahead of print]
- 170. Gurol-Urganci I, Jardine JE, Carroll F, Draycott T, Dunn G, Fremeaux A, et al. Maternal and perinatal outcomes of pregnant women with SARS-CoV-2 infection at the time of birth in England: national cohort study. *Am J Obstet Gynecol* 2021; S0002-9378(21)00565-2
- 171. Hcini N, Maamri F, Picone O, Carod J-F, Lambert V, Mathieu M, et al. Maternal, fetal and neonatal outcomes of large series of SARS-CoV-2 positive pregnancies in peripartum period: A single-center prospective comparative study. Eur J Obstet Gynecol Reprod Biol 2021;257 11-18
- 172. Katz D, Bateman BT, Kjaer K, Turner DP, Spence NZ, Habib AS, et al. The Society for Obstetric Anesthesia and Perinatology (SOAP) COVID-19 Registry: An analysis of outcomes among pregnant women delivering during the initial SARS-CoV-2 outbreak in the United States. *Anesth Analg* 2021; 133(2):462-473
- 173. Zgutka K, Prasanth K, Pinero-Bernardo S, Lew LQ, Cervellione K, Rhythm R, et al. Infant outcomes and maternal COVID-19 status at delivery. *J Perinat Med* 2021;49(6):691-696
- 174. Martinez-Perez O, Prats Rodriguez P, Muner Hernandez M, Encinas Pardilla MB, Perez Perez N, Vila Hernandez MR, et al. The association between SARS-CoV-2 infection and preterm delivery: a prospective study with a multivariable analysis. *BMC Pregnancy Childbirth* 2021;21(1):273
- 175. Metz TD, Clifton RG, Hughes BL, Sandoval G, Saade GR, Grobman WA, et al. Disease Severity and Perinatal Outcomes of Pregnant Patients With Coronavirus Disease 2019 (COVID-19). Obstet Gynecol 2021;137(4):571-580
- 176. Molenaar N, Rommel A-S, de Witte L, Dolan S, Lieb W, Ibroci E, et al. Seroprevalence of SARS-CoV-2 during pregnancy and associated outcomes: results from an ongoing prospective cohort study, New York City. *MedRXiv* 2021; **Journal**
- 177. Savirón-Cornudella R, Villalba A, Esteban LM, Tajada M, Rodríguez-Solanilla B, Andeyro-Garcia M, et al. Screening of severe acute respiratory syndrome coronavirus-2 infection during labor and delivery using polymerase chain reaction and immunoglobulin testing. *Life Sci* 2021;271:119200
- 178. Soto-Torres E, Hernandez-Andrade E, Huntley E, Mendez-Figueroa H, Blackwell S. Ultrasound and Doppler findings in pregnant SARS-CoV-2 positive women. *Ultrasound Obstet Gynecol* 2021;58(1):111-120
- 179. Trahan M-J, Malhamé I, O'Farrell P, Mitric C, Desilets J, Bastrash M-P, et al. Obstetrical and Newborn Outcomes Among Patients With SARS-CoV-2 During Pregnancy. *J Obstet Gynaecol Can* 2021;43(7):888-892.e1

- 180. Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, et al. Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection: The INTERCOVID Multinational Cohort Study. *JAMA Pediatr* 2021; 175(8):817-826
- 181. Artymuk NV, Belokrinitskaya TE, Filippov OS, Frolova NI, Surina MN. Perinatal outcomes in pregnant women with COVID-19 in Siberia and the Russian Far East. *J Matern Fetal Neonatal Med* 2021;1-4
- 182. Behrens E, Warrior S, Thomas J, Pombar X, Gezer S, Venugopal P, et al. Thrombosis and Mortality in Pregnant Patients with COVID-19. *Blood* 2020;136(Suppl 1):8-9
- 183. Qeadan F, Mensah NA, Tingey B, Stanford JB. The risk of clinical complications and death among pregnant women with COVID-19 in the Cerner COVID-19 cohort: a retrospective analysis. *BMC Pregnancy Childbirth* 2021;21(1):305
- 184. Vizheh M, Muhidin S, Aghajani F, Maleki Z, Bagheri F, Hosamirudsari H, et al. Characteristics and outcomes of COVID-19 pneumonia in pregnancy compared with infected nonpregnant women. *Int J Gynaecol Obstet* 2021;153(3):462-468
- 185. Bernal JL, Andrews N, Gower C, Gallagher E, Simmons R, Thelwall S, et al.: Effectiveness of COVID-19 vaccines against the B.I.617.2 variant. *medRxiv* 2021; **Website**
- 186. Abu-Raddad LJ, Chemaitelly H, Butt AA. Effectiveness of the BNT162b2 Covid-19 Vaccine against the B.I.I.7 and B.I.35 | Variants. N Engl | Med 2021;385(2):187-189
- 187. Song D, Prahl M, Gaw SL, Narasimhan S, Rai D, Huang A, et al. Passive and active immunity in infants born to mothers with SARS- CoV-2 infection during pregnancy: Prospective cohort study. *medRxiv* 2021; **Journal**
- 188. Flannery DD, Gouma S, Dhudasia MB, Mukhopadhyay S, Pfeifer MR, Woodford EC, et al. Assessment of Maternal and Neonatal Cord Blood SARS-CoV-2 Antibodies and Placental Transfer Ratios. *JAMA Pediatr* 2021;175(6):594-600
- 189. Kubiak JM, Murphy EA, Yee J, Cagino KA, Friedlander RL, Glynn SM, et al. Severe acute respiratory syndrome coronavirus 2 serology levels in pregnant women and their neonates. *Am J Obstet Gynecol* 2021;225(1):73.e1-73.e7
- 190. Rathberger K, Häusler S, Wellmann S, Weigl M, Langhammer F, Bazzano MV, et al.: SARS-CoV-2 in pregnancy and possible transfer of immunity: assessment of peripartal maternal and neonatal antibody levels and a longitudinal follow-up. *J Perinat Med* 2021;49(6):702-708
- 191. Public Health England. COVID-19: the green book, chapter 14a. Coronavirus (COVID-19) vaccination information for public health professionals. Updated 30 July 2021. 2020; Website
- 192. Polack FP,Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *N Engl J Med* 2020;383(27):2603-2615

- 193. Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, 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(10269):99-111
- 194. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med* 2021;384(5):403-416
- 195. Sadoff J, Gray G, Vandebosch AN, Cárdenas V, Shukarev G, Grinsztejn B, et al. Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19. *N Engl J Med* 2021;384(23):2187-2201
- 196. Lopez Bernal J, Panagiotopoulos N, Byers C.Transmission dynamics of COVID-19 in household and community settings in the United Kingdom. *medRxiv* 2020; **Journal**
- 197. Centers for Disease Control and Prevention. Myocarditis and Pericarditis Following mRNA COVID-19 Vaccination. Updated May 2021. 2021; Website
- 198. Centers for Disease Control and Prevention. V-safe COVID-19 Vaccine Pregnancy Registry. 2021; Website
- 199. Kroger A, Plotkin S: Vaccines (General Immunisation Practices). 6th Edition, Saunders 2012
- 200. Shimabukuro TT, Kim SY, Myers TR, Moro PL, Oduyebo T, Panagiotakopoulos L, et al. Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. *N Engl J Med* 2021;384(24):2273-2282
- 201. Collier A-RY, McMahan K, Yu J, Tostanoski LH, Aguayo R, Ansel J, et al. Immunogenicity of COVID-19 mRNA Vaccines in Pregnant and Lactating Women. *JAMA* 2021;325(23):2370-2380
- 202. Gray KJ, Bordt EA, Atyeo C, Deriso E, Akinwunmi B, Young N, et al. Coronavirus disease 2019 vaccine response in pregnant and lactating women: a cohort study. Am J Obstet Gynecol 2021;S0002-9378(21)00187-3
- 203. World Health Organization. Statement of the COVID-19 subcommittee of the WHO Global Advisory Committee on Vaccine Safety (GACVS) on safety signals related to the Johnson & Johnson/Janssen COVID-19 vaccine. 2021; Website
- 204. UK Government Department of Health and Social Care. Use of the AstraZeneca COVID-19 (AZD1222) vaccine: updated JCVI statement, 7 May 2021. 2021; Website
- 205. Juncker HG, Romijn M, Loth VN, Ruhé EJM, Bakker S, Kleinendorst S, et al. Antibodies Against SARS-CoV-2 in Human Milk: Milk Conversion Rates in the Netherlands. *J Hum Lact* 2021 [epub ahead of print].
- 206. Golan Y, Prahl M, Cassidy A, Wu AHB, Jigmeddagva U, Lin CY et al. Immune response during lactation after anti-SARS-CoV2 mRNA vaccine. *medRxiv* 2021; Website
- 207. Medicines & Healthcare products Regulatory Agency. Information for Healthcare Professionals on COVID-19 Vaccine Pfizer/ BioNTech (Regulation 174). 2021; Website

- 208. Medicines & Healthcare products Regulatory Agency. Summary of Product Characteristics for COVID-19 Vaccine Moderna. 2021; Website
- 209. Medicines & Healthcare products Regulatory Agency. Information for Healthcare Professionals on COVID-19 Vaccine AstraZeneca (Regulation 174). 2021; Website
- 210. British Fertility Society/Association of Reproductive and Clinical Scientists. BFS & ARCS Covid-19 Vaccines & Fertility updated FAQs. 2021; Website
- 211. NHS England and NHS Improvement. Shared Decision Making Summary Guide. February 2019; Website
- 212. National Institute for Health and Care Excellence. Shared decision making. NICE guideline 197 [NG197]. 2021; Website
- 213. ClinicalTrials.gov. Study to Evaluate the Safety, Tolerability, and Immunogenicity of SARS CoV-2 RNA Vaccine Candidate (BNT162b2) Against COVID-19 in Healthy Pregnant Women 18 Years of Age and Older. 2021; Website
- 214. ClinicalTrials.gov. A Study of Ad26.COV2.S in Healthy Pregnant Participants (COVID-19) (HORIZON 1). 2021; Website
- 215. St George's Vaccine Institute: Preg-Cov-trial. 2021; Website
- 216. Jaiswal N, Puri M, Agarwal K, Singh S, Yadav R, Tiwary N, et al. COVID-19 as an independent risk factor for subclinical placental dysfunction. *Eur J Obstet Gynecol Reprod Biol* 2021;259 7-11
- 217. Lu-Culligan A, Chavan AR, Vijayakumar P, Irshaid L, Courchaine EM, Milano KM, et al. Maternal respiratory SARS-CoV-2 infection in pregnancy is associated with a robust inflammatory response at the maternal-fetal interface. *Med (NY)* 2021;2(5):591-610. e10
- 218. Nadeau-Vallée M, Obari D, Palacios J, Brien M-È, Duval C, Chemtob S, et al. Sterile inflammation and pregnancy complications: a review. *Reproduction* 2016;152(6):R277-R292
- 219. Wei SQ, Bilodeau-Bertrand M, Liu S, Auger N.: The impact of COVID-19 on pregnancy outcomes: a systematic review and meta- analysis. *CMA*/ 2021;193(16):E540-E548
- 220. Rosenbloom JI, Raghuraman N, Carter EB, Kelly JC. Coronavirus disease 2019 infection and hypertensive disorders of pregnancy. *Am J Obstetr Gynecol* 2021;224(6):623-624
- 221. Jacoby VL, Murtha A, Afshar Y, Gaw S, Asiodu I, Tolosa J, et al. Risk of Pregnancy Loss Prior to 20 weeks Gestation with COVID-19. *Am J Obstetr Gynecol* 2021 [epub ahead of print]
- 222. Norman M, Navér L, Söderling J, Ahlberg M, Hervius Askling H, Aronsson B, et al. Association of Maternal SARS-CoV-2 Infection in Pregnancy With Neonatal Outcomes. //AMA 2021;325(20):2076-2086

- 223. Golan Y, Prahl M, Cassidy A, Wu ABH, Jigmeddagva U, Lin C, et al. Immune response during lactation after anti-SARS-CoV2 mRNA vaccine. *medRxiv* 2021; **Journal**
- 224. Fox A, Marino J, Amanat F, Krammer F, Hahn-Holbrook J, Zolla-Pazner S, et al. Robust and Specific Secretory IgA Against SARS- CoV-2 Detected in Human Milk. *iScience* 2020;23(11):101735
- 225. Fox A, Marino J, Amanat F, Oguntuyo K, Hahn-Holbrook J, Lee B, et al. The Spike-specific IgA in milk commonly-elicited after SARS-Cov-2 infection is concurrent with a robust secretory antibody response, exhibits neutralization potency strongly correlated with IgA binding, and is highly durable over time. *medRxiv* 2021; **Journal**
- 226. Knight M, Ramakrishnan R, Bunch K, ISARIC4C Consortium, UK Obstetric Surveillance System (UKOSS) and COVID-19 Clinical Information Network (CO-CIN). Females in hospital with SARS-CoV-2 infection, the association with pregnancy and pregnancy outcomes: A UKOSS/ISARIC/CO-CIN investigation. 2021; Website
- 227. Royal College of Midwives. RCM Clinical Briefing Sheet Waterbirth during the COVID-19 pandemic. June 2021; Website
- 228. Vousden N, Ramakrishnan R, Bunch K: Impact of SARS-CoV-2 variant on the severity of maternal infection and perinatal outcomes: Data from the UK Obstetric Surveillance System national cohort. *medRxiv* 2021 **Journal**
- 229. Public Health England. Health chiefs encourage more pregnant women to get their COVID-19 vaccine. 2021; Website
- 230. Public Health Scotland. Covid-19 statistical report (Scotland). 2021; Website
- 231. NHS. Suspected coronavirus (COVID-19): Important information to keep you safe while isolating at home. 2021; Website
- 232. NHS. How to look after yourself at home if you have coronavirus (COVID-19). 2021; Website
- 233. NHS. Pregnancy and coronavirus (COVID-19). 2021; Website
- 234. Sjoding MW, Dickson RP, Iwashyna TJ, Gay SE, Valley TS. Racial Bias in Pulse Oximetry Measurement. *N Engl | Med* 2020;383(25):2477-2478
- 235. Knight M, Bunch K, Cairns A, Cantwell R, Cox P, Kenyon S, et al. Saving Lives, Improving Mothers' Care Rapid Report 2021: Learning from SARS-CoV-2-related and associated maternal deaths in the UK June 2020- March 2021. Oxford: National Perinatal Epidemiology Unit, University of Oxford 2021. 2021; Website
- 236. Public Health England: SARS-CoV-2 variants of concern and variants under investigation in England Technical briefing 20. 2021; **Website**
- 237. NHS Scotland, Scottish Perinatal Network. NHS Near Me. Website
- 238. National Institute for Health and Care Excellence. *COVID-19 rapid guideline: managing COVID-19*. NICE guideline 191 [NG191]. 2021; Website

- 239. REMAP-CAP, ACTIV-4a, ATTACC Investigators, Lawler PR, Goligher EC, Berger JS, et al. Therapeutic Anticoagulation with Heparin in Noncritically III Patients with Covid-19. *N Engl J Med* 2021 [epub ahead of print]
- 240. REMAP-CAP, ACTIV-4a, ATTACC Investigators, Goligher EC, Bradbury CA, McVerry BJ, et al. Therapeutic Anticoagulation with Heparin in Critically III Patients with Covid-19. *N Engl J Med* 2021 [epub ahead of print]
- 241. Cines DB, Bussel JB. SARS-CoV-2 Vaccine-Induced Immune Thrombotic Thrombocytopenia. N Engl | Med 2021;384(23):2254-2256