

## STANDPUNT

### COVID-19 en zwangerschap, bevalling en kraambed



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#### INITIATIEF

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### **Looptijd**

Dit standpunt is geldig vanaf 14 mei 2020.

Dit standpunt kan worden bijgewerkt en/of gewijzigd op basis van nieuwe informatie. De meest actuele versie is de versie die staat op de website van de Federatie Medisch Specialisten.

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# 1 Samenstelling van de werkgroep

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## 2 Korte inleiding

Eind 2019 werd COVID-19, het ziektebeeld veroorzaakt door het SARS-CoV-2 virus voor het eerst gediagnosticeerd in Wuhan, China. Inmiddels heeft het virus zich wereldwijd verspreid.

5 In Nederland is het aantal patiënten sinds eind februari 2020, en het aantal ziekenhuis opnamen sinds halverwege maart, sterk gestegen.

In dit document worden adviezen gegeven over:

10 \* Antenatale controles bij vrouwen die COVID-19 hebben (doorgemaakt) tijdens de zwangerschap

\* Verloskundig beleid tijdens de bevalling bij vrouwen met COVID-19

\* Borstvoeding en verzorging bij COVID-19

15 Voor het opstellen van dit document is gebruik gemaakt van beschikbare wetenschappelijke publicaties en de ervaringen binnen en buiten het ziekenhuis met de behandeling van SARS-CoV-2 besmette patiënten.

20 Het document is ter consultatie voorgelegd aan de volgende wetenschappelijke verenigingen en beroepsorganisaties: NVOG, KNOV, NVA, NVK, Patiëntenfederatie Nederland, Stichting Zelfbewust Zwanger, Stichting Kind en Ziekenhuis, RIVM, NVMM, BO Geboortezorg, NBVK, V&VN, NFU, NVZ, STU.

### 25 **Definities:**

De werkgroep hanteert de volgende definities (*conform de Leidraad persoonlijke bescherming in de poliklinische setting vanwege SARS-CoV-2 Versie 1.0 – 290420*):

30 *Asymptomatische COVID-patiënt*: een persoon waarbij de SARS-CoV-2 RT-PCR positief is, maar die op geen enkel moment aantoonbare symptomen ontwikkelt.

*Presymptomatische COVID-patiënt*: een besmet persoon in de 1-2 dagen direct voordat symptomen duidelijk worden, het virus reeds uitgescheiden wordt.

35 De asymptomatisch en presymptomatisch patiënten worden samengenomen als *subklinische COVID-patiënten*.

40 De meest voorkomende symptomen van COVID-19 zijn: koorts, vermoeidheid, droge hoest, spierpijn, neusverkoudheid (verstopte neus en loopneus), keelpijn en (minder vaak) diarree. Onder *patiënten met COVID-19* verstaat de werkgroep mensen die één of meer van deze symptomen hebben en een positieve SARS-CoV-2 RT-PCR test.

Voor de ernst van de ziekte wordt de volgende indeling aangehouden (Wu Z, 2020):

- 45 • Mild – ie. non-pneumonia and mild pneumonia
- Severe – ie. dyspnea, respiratory frequency  $\geq 30$ /min, blood oxygen saturation  $\leq 93\%$ , partial pressure of arterial oxygen to fraction of inspired oxygen ratio  $< 300$ , and/or lung infiltrates  $> 50\%$  within 24 to 48 hours
- 50 • Critical – ie. septic shock, respiratory failure, and/or multiple organ failure

### 3 Literatuur samenvatting

#### Uitgangsvragen:

1. Leidt COVID-19 in de zwangerschap tot meer zwangerschapscomplicaties zoals pre-eclampsie, intra-uteriene groeivertraging en vroeggeboorte?
2. Zijn er complicaties van COVID-19, met name pulmonale complicaties, die ernstiger zijn bij zwangere vrouwen dan bij niet-zwangere vrouwen (en bij mannen)?
3. Leidt COVID-19 tijdens de zwangerschap tot meer complicaties bij de bevalling?
4. Wanneer moet een vrouw met COVID-19 en (P)PROM bevallen?
5. Welke aanpassingen zijn nodig voor vrouwen met COVID-19 om borstvoeding te geven en het risico op besmetting te voorkomen? Wat is het risico van besmetting tijdens de voeding en verzorging van de pasgeborene? Mogen zij huid op huid contact hebben?

15

#### Clinical questions:

1. Do SARS-CoV-2 infections in pregnant women lead to more pregnancy complications like preeclampsia, fetal growth restriction and preterm birth?
2. Which complications are more prevalent among pregnant women with SARS-CoV-2 infections than in non-pregnant women (and men)?
3. Do SARS-CoV-2 infections in pregnant women lead to more complications during delivery?
4. When should pregnant women with COVID-19 after (P)PROM be delivered?
5. What precautions do women with SARS-CoV-2 infections need to take to breastfeed their newborn while minimizing the risk of transmission? What is the risk of transmission of the virus during nursing? Is skin to skin contact allowed?

#### 30 Search and select

The databases PubMed and Embase (via Embase.com) were searched with relevant search terms until 20 April, 2020. The detailed search strategy is depicted below. The initial search also included MERS and SARS. However, based on the results of the rapid review by Mullins et al.(2020), showing that the consequences of SARS-CoV-2 for pregnant women were not comparable to those of MERS and SARS, these papers were not considered further. The systematic literature search (limited to COVID-19) initially resulted in 126 hits. The search was updated on a weekly basis and further supplemented with 219 hits, resulting in a total of 345 hits. During the updating process, other information sources such as Google Scholar, the preprint source medRxiv, and the database of the World Health Organization were searched in addition to the conventional databases. Studies were selected based on the following criteria: any reports of original clinical data concerning pregnant women with COVID-19. Forty-five articles were selected, 14 of which were excluded. The reasons for exclusion are presented in the table 'Excluded papers with reasons' below. One additional paper was found by searching the references of the review articles. This resulted in the inclusion of 32 papers reporting original data.

#### Results

Thirty-two papers were included in the analysis of the literature. From the identified papers information was extracted regarding all five clinical questions, so no distinction was made between papers identified by the four initial search strategies. Important study characteristics are summarized in Table 1 and results are summarized in Tables 2 - 5.

50

## Summary of the literature

### Description of studies

5 Thirty-two papers were included, 22 from China, two from the USA, and one from Korea, Honduras, Turkey, Sweden, Italy, Peru, Australia and Iran each. Fifteen were case reports, and 17 were case series, the number of cases varying from 2 to 42, median 9. Assuming that there were no duplicate descriptions of patients in the included papers, these papers report the clinical data of 251 pregnant women and 156 neonates. The majority of the reported cases were admitted in the last trimester of pregnancy, and delivery was mostly by  
10 Caesarean section (CS). The indications for the CS were often not reported.

### Results

15 The sparse information in the literature did not give any indication of an increased risk of pregnancy complications apart from the symptoms of the disease which may lead to fetal distress due to hypoxia, nor of an increased risk of pulmonary complications in pregnant women (Table 2).

The sparse information in the literature did not give any indication of an increased risk of complications during delivery, apart from the symptoms of the disease which may lead to fetal distress due to hypoxia (Table 3).

20 There was virtually no information in the literature about (P)PROM (Table 4).

In 12 women breast milk samples were tested for the presence of the virus, and in all cases the tests were negative (Table 5).

## 25 **4 Pregnancy in women with COVID-19: more complications of COVID-19 and/or more pregnancy complications?**

1. Do SARS-CoV-2 infections in pregnant women lead to more pregnancy complications like preeclampsia, fetal growth restriction and preterm birth?
- 30 2. Which complications are more prevalent among pregnant women with SARS-CoV-2 infections than in non-pregnant women (and men)?

### **Considerations**

#### 35 Pros and cons of the intervention and the quality of evidence

Of the 251 pregnant women currently described in the included literature, three women were diagnosed with preeclampsia, nine with gestational hypertension, nine with spontaneous preterm birth and 18 with gestational diabetes (Table 2).

40 Although not all studies made a clear distinction in spontaneous versus induced or iatrogenic preterm births, it seems that pregnant women with COVID-19 more frequently underwent a preterm CS (<37 weeks) due to their worsening maternal condition, but this was rarely before 32 weeks.

45 One case of stillbirth at 34 weeks' gestational age was described in a patient with a severe ARDS and multi-organ disease caused by COVID-19 (Liu Y, 2020). Although there is a risk of underreporting due to the non-structural data collection and low level of evidence of the selected articles (only retrospective case-reports or case series with small numbers), there is no evidence that the pregnancy complications preeclampsia, fetal growth restriction and

preterm birth are more frequent in women with COVID-19 compared to healthy pregnant women.

5 Furthermore, due to the short follow-up period of COVID-19 so far and the fact that most of the women presented in the third stage of pregnancy and delivered shortly after the diagnosis or were diagnosed postpartum, nothing can be concluded yet about the possible effects of SARS-CoV-2 infections during early pregnancy on the prevalence of preeclampsia and fetal growth restriction later in pregnancy.

10 Based on the sparse information from the 251 women described in the included literature, we hypothesize that SARS-CoV-2 infection does not lead to a more severe course of the disease in pregnancy. In the case series of Breslin et al. (New York) 9% of the SARS-COV-2 positive pregnant women had severe disease and 5% critical disease as defined by Wu et al. This is comparable with the disease severity in the non-pregnant adult population (Breslin, 15 2020).

20 From other respiratory viruses (Influenza, SARS Cov1, MERS) it is known that these infections may have a higher risk of respiratory failure during pregnancy (particularly in the third trimester). This may be caused by reduced lung volume and the changed cardiopulmonary status of pregnant women. However, for SARS-CoV-2 infections the limited data do not show so far an increased risk for severe lung problems in pregnant women compared to the non-pregnant population.

#### Values and preferences of patients (and if applicable their caretakers)

25 Women experiencing possible symptoms of COVID-19 during pregnancy may be worried about the effects of the disease on themselves and their fetuses. For both midwifery-led care and hospital-led care it is important to take this into account and to inform them that based on the above mentioned (limited) data there is no evidence to assume that SARS-CoV-2 infection during pregnancy leads to a higher prevalence of preeclampsia, fetal growth 30 restriction and/or preterm birth. So far, women with only mild symptoms and no need for oxygen treatment (mild disease) can be reassured that it is safe to continue care as usual during their pregnancies. Attention has to be paid to the fact that the long-term effects on the fetus (especially from an infection in the 1<sup>st</sup> or 2<sup>nd</sup> trimester) are not known yet.

#### 35 Costs

Not applicable to this item.

#### Acceptability, feasibility and implementation

40 Not applicable to this item.

### **Recommendations**

#### Rationale of the recommendation: weighting of arguments for and against the intervention

45 No reliable answer can be given on the prevalence of preeclampsia, fetal growth restriction and preterm birth in SARS-CoV-2 infected pregnant women. Based on a low level of evidence, COVID-19 seems not to increase the risk of preeclampsia, fetal growth restriction and spontaneous preterm birth. More structural data and longer follow-up of COVID-19 patients with an ongoing pregnancy is needed to have a final answer on this this question 50 and also on the effects of an infection in the 1<sup>st</sup> or 2<sup>nd</sup> trimester.



For severe or critical cases it is not known whether a period of maternal hypoxemia with need for oxygen has an effect on the fetal growth. Because this is not known yet, we consider that in these cases (but not for the mild cases) fetal growth should be monitored in the 3<sup>rd</sup> trimester of pregnancy. Furthermore, for severe or critical cases follow-up of the ongoing pregnancy in the hospital is recommended.

5

Recent data show that thrombosis and pulmonary embolism plays an important role in severe and critical cases of SARS-CoV-2 infections (Tang 2020, Klok 2020, Cui 2020). As pregnancy is characterized by a state of hypercoagulability, theoretically there might be an increased risk for venous thromboembolism (VTE) in pregnant women with SARS-CoV-2 infections. The Dutch guideline recommends to treat all hospitalized patients with COVID-19 with low molecular weight heparin (LMWH) (*Leidraad COVID-19 coagulopathie, 14 april 2020*).

10

*So far, there is no evidence to assume that SARS-CoV-2 infection during pregnancy leads to a higher prevalence of preeclampsia, fetal growth restriction and/or spontaneous preterm birth.*

*Based on the hypothesis that severe or critical cases of SARS-CoV-2 infection in pregnant women might have an effect on fetal growth, we recommend monitoring of fetal growth in the third trimester of pregnancy (at least two ultrasound scans starting at 28 weeks of gestation with a 2 weeks interval; if reassuring with a longer interval thereafter).*

*According to recent guidelines it is advisable to treat all patients admitted because of COVID-19 disease with LMWH, this is recommended for pregnant women as well.*

*We recommend for pregnant women after a severe or critical SARS-CoV-2 infection to continue prenatal care in hospital.*

15

*Tot nu toe is er geen bewijs om aan te nemen dat infectie met SARS-CoV-2 tijdens de zwangerschap leidt tot meer pre-eclampsie, foetale groeivertraging en/of spontane vroeggeboorte.*

*Ernstige of kritische SARS-CoV-2 infectie bij zwangere vrouwen zou een effect kunnen hebben op de foetale groei. Daarom adviseren wij om de foetale groei in het derde trimester van de zwangerschap te bewaken met tenminste 2 echo's vanaf 28 weken zwangerschapsduur met een interval van 2 weken; indien de uitslag niet verontrustend is vervolgens met langere tussenpozen.*

*In overeenstemming met het recente advies om alle patiënten die zijn opgenomen vanwege COVID-19 te behandelen met LMWH, wordt dit ook voor zwangere vrouwen aangeraden.*

*Na een ernstige of kritische SARS-CoV-2 infectie bij een zwangere vrouw bevelen wij aan om de prenatale zorg in het ziekenhuis te laten plaatsvinden.*

*So far, there is no evidence to assume that SARS-CoV-2 infection during pregnancy has a more severe course compared to the non-pregnant population.*

*Pregnant women with mild COVID-19 should receive care as usual, and referral from first to second or third line care is not necessary.*

*It is recommended that in cases of severe respiratory failure in pregnant women due to COVID-19, therapy and management should be undertaken in a multidisciplinary team (critical care physician and/or anesthesiologist, obstetrician and neonatologist). Depending on the severity and the gestational age the woman should be referred to a tertiary care center.*

*Tot nu toe is er geen bewijs om aan te nemen dat infectie met SARS-CoV-2 in de zwangerschap ernstiger verloopt dan bij de niet-zwangere populatie.*

*Zwangere vrouwen met milde COVID-19 moeten behandeld worden zoals gebruikelijk, en verwijzing vanuit de eerste naar de tweede of derde lijn is niet nodig.*

*In geval van ernstig respiratoir falen door COVID-19 bij een zwangere vrouw wordt behandeling en beleid door een multidisciplinair team (intensivist en/of anesthesioloog, obstetricus en neonatoloog) aanbevolen. Afhankelijk van de ernst van de ziekte en de zwangerschapsduur dient de vrouw naar een derdelijns centrum te worden verwezen.*

5

## **5 Labour in women with COVID-19: more delivery complications?**

- 10 3. Do SARS-CoV-2 infections in pregnant women lead to more complications during delivery?

### **Considerations**

- 15 Pros and cons of the intervention and the quality of evidence

The vast majority of the SARS-CoV-2 infected women reported in the included literature who delivered, had a cesarean section (Table 3). The study with most of the vaginal deliveries was

the only study from Italy (Ferrazzi, 2020). Twenty-four of the 42 COVID-19 patients delivered vaginally in this study. Most other studies were in Chinese patients with a high percentage of CS. Indications for CS were not always mentioned (Table 3). In mild cases of COVID-19 induction of labor or waiting for the spontaneous onset of labor are feasible options. Fetal distress caused by hypoxemia was described in 15 cases.

Values and preferences of patients (and if applicable their caretakers)  
 Women with (suspicion of) COVID-19 need information about the optimal place for delivery, whether their risk of labour complications is increased, and what may be different due to COVID-19 during labour.

Costs  
 Not applicable to this item.

Acceptability, feasibility and implementation  
 Not applicable to this item.

**20 Recommendations**

Rationale of the recommendation: weighting of arguments for and against the intervention

Based on the currently available data (mostly Chinese reports) most women delivered by a CS. However, taking into account that in general the percentage of CS is twice as high in China (41.3 %) and Italy (38%) compared to the Netherlands (17%) (Macfarlane 2014, Boerma 2018), the described high percentage of CS in COVID-19 patients is presumably not comparable to our setting. Only in severe COVID-19 cases during pregnancy (severe cases defined as: hospital admittance with oxygen therapy or artificial ventilation) it is likely that a women has a higher chance for a CS on either maternal or fetal indication (fetal distress possibly caused by maternal hypoxemia seems to occur more frequently in severe cases of COVID-19). To detect a potential deteriorating clinical condition of the mother, the MEOWS-score (Modified Early Obstetric Warning Score) (Figure) might be of assistance during labour. This may be especially helpful for women with COVID-19 delivering in midwifery-led care and at home.

| Score               | 3   | 2      | 1          | 0            | 1                 | 2                | 3           |
|---------------------|-----|--------|------------|--------------|-------------------|------------------|-------------|
| Temperature         |     | <35 °c | 35-35.9 °c | 36-37.4 °c   | 37.5-37.9 °c      | 38.0-38.9 °c     | ≥39 °c      |
| Systolic BP         | ≤69 | 70-79  | 80-89      | 90-139       | 140-149           | 150-159          | ≥160        |
| Diastolic BP        |     |        | ≤49        | 50-89        | 90-99             | 100-109          | ≥110        |
| Pulse               |     | <40    | 40-49      | 50-99        | 100-109           | 110-129          | ≥130        |
| Respiratory Rate    | ≤10 |        |            | 11-19        | 20-24             | 25-29            | ≥30         |
| AVPU                |     |        |            | Alert        | Responds to Voice | Responds to Pain | Unconscious |
| Urine output mLs/hr | <10 | <30    |            | Not Measured |                   |                  |             |

*In midwifery-led care (1<sup>st</sup> line) and at home we advise additional monitoring of respiratory rate during labour to assess the clinical condition of women with mild COVID-19. A MEWS score could be used for this purpose, with a cut-off of  $\geq 3$  for referral to hospital-led care.*

*During hospital deliveries (2<sup>nd</sup> or 3<sup>rd</sup> line), there is no reason to monitor women with mild COVID-19 more closely during labour. Care as usual with regular maternal and fetal monitoring is advised.*

*In cases of severe respiratory distress, supportive management should be similar to that in non-pregnant patients (mother always comes first).*

*Tijdens de bevalling van een vrouw met milde COVID-19 onder leiding van een verloskundige (eerste lijn, thuis of poliklinisch) adviseren wij om de ademhalingsfrequentie extra in de gaten te houden om de klinische conditie van de vrouw te bewaken. Hiertoe kan een MEWS score worden gebruikt; bij een score  $\geq 3$  wordt verwijzing naar het ziekenhuis geadviseerd.*

*Bij een ziekenhuisbevalling (tweede of derde lijn) is er bij milde COVID-19 geen reden voor intensievere bewaking, maar is de gebruikelijke zorg met regelmatige maternale en foetale bewaking voldoende.*

*Bied bij ernstige ademhalingsproblemen van de barende vrouw hetzelfde ondersteunende beleid als bij niet-zwangere patiënten (moeder op de eerste plaats).*

## 5 **6 (P)PROM in pregnant women with COVID-19**

4. When should pregnant women with COVID-19 after (P)PROM be delivered?

### 10 **Considerations**

#### Pros and cons of the intervention and the quality of evidence

15 There is no valuable literature regarding the clinical course of (P)PROM during SARS-CoV-2 infection (only 9 cases have been described in literature). Since this is too little information to formulate specific recommendations, the working group has the opinion to follow the identical protocol as for women without COVID-19 in case of (P)PROM. It is well known that (P)PROM increases the risk of intrauterine infection, and this should therefore be monitored. Furthermore, maternal deterioration can be a reason to terminate pregnancy.

#### 20 Values and preferences of patients (and if applicable their caretakers)

5 If SARS-CoV-2 positive women with (P)PROM would be immediately induced instead of watchful waiting, this would have consequences for mother and child after birth. Depending on the gestational age at (P)PROM, there is a chance that the child will be admitted to the neonatal ward because of prematurity. Since SARS-CoV-2 positive parents are not allowed on the neonatal ward, this would mean in some hospitals that parents and child will be separated after birth.

#### Costs

10 Not applicable to this item.

#### Acceptability, feasibility and implementation

15 Since the advice is to follow standard protocol, acceptability, feasibility and implementation are not applicable.

### Recommendations

*The working group recommends to follow standard protocols in case of (P)PROM. No specific advice can be given on the timing of delivery after (P)PROM in women with COVID-19.*

*The advice to deliver should be made based on the clinical condition (maternal as well as fetal).*

*If there are any signs of intrauterine infection, we strongly advise to terminate the pregnancy.*

20

*De werkgroep adviseert bij (P)PROM de standaard protocollen te volgen. Er kan geen specifiek advies worden gegeven over de timing van de bevalling na (P)PROM bij vrouwen met COVID-19.*

*Het advies om het kind geboren te laten worden, wordt gegeven op basis van de klinische conditie van moeder en foetus.*

*Als er tekenen zijn van intra-uteriene infectie adviseren wij dringend om de zwangerschap te beëindigen.*

25

## 7 Nursing of the neonate

5. What precautions do women with SARS-CoV-2 infections need to take to breastfeed their newborn while minimizing the risk of transmission? What is the risk of transmission of the virus during nursing? Is skin to skin contact allowed?

### Considerations

#### Pros and cons of the intervention and the quality of evidence

- 10 Literature regarding breastfeeding during maternal SARS-CoV-2 infection is sparse and therefore the evidence grade is low. Breastmilk samples of 12 SARS-CoV-2 positive mothers have been tested for the presence of the virus, all samples were negative. Therefore, so far, there is no reason to assume that the virus is transmitted from mother to child through breastmilk. Furthermore, breastfeeding has beneficial effects, such as the transmission of maternal antibodies and stimulates bonding between mother and baby. However, since there is an increased risk of horizontal transmission during direct contact between a symptomatic SARS-CoV-2 positive mother and her child, it is essential to apply additional hygiene measures during breastfeeding. However, these hygiene measures apply for all contact moments with the child, and thus also for formula feeding. It could be considered to pump breastmilk and leave the feeding of the baby to a SARS-CoV-2 negative person. However, this also reduces the (skin-to-skin) contact between mother and baby, which is beneficial for bonding. According to the World Health Organization, asymptomatic patients (definition according to 'Leidraad persoonlijke bescherming in de poliklinische setting vanwege SARS-CoV-2 Versie 1.0 – 290420': a person with a positive SARS-CoV-2 RT-PCR test, who does not develop demonstrable symptoms at any moment) are much less infectious than symptomatic patients, and do not contribute to the spread of the disease. Therefore, extra protective measures do not seem necessary in cases of an asymptomatic infection, or after a patient does not have symptoms for more than 24 hours.
- 30 It is important, especially for care-givers and parents, to realize that a neonate may develop COVID-19 up to 14 days after the mother has become free of symptoms (see NVK guideline: Beleid bij neonaat en zwangere bij verdenking COVID-19, 17 april 2020). This means that care-givers visiting families at home should be protected during the entire quarantine period of 14 days.

35

#### Values and preferences of patients (and if applicable their caretakers)

- 40 It is understandable that women who are keen to breastfeed their child want to do this also in case of a SARS-CoV-2 infection. These women should be well informed about the possible risks of transmission and how to minimize these risks. The possibility of horizontal transmission cannot be fully prevented, but proper hygiene measures lower this risk. Furthermore, similar risks and advices apply to formula feeding and other contact moments (e.g. cuddling, diaper changes), and to the partner. In case of a partner with COVID-19, similar measures apply to nursing of the baby by the partner. The infection could be transmitted both to his/her partner and the neonate.

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#### Costs

The advice to wear a surgical mask during feeding increases the costs. However, the same advice applies to formula feeding.

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#### Acceptability, feasibility and implementation

It should be considered whether it is feasible to supply surgical masks to symptomatic mothers with COVID-19 for all contact moments with their child, since these masks are sparse.

5

### Recommendations

*Neonates who are born to symptomatic mothers with COVID-19 can be breastfed, provided that additional protective measures are applied to minimize the risk of horizontal transmission. It should be explained that horizontal transmission cannot be prevented completely.*

*Women with COVID-19 should be instructed about proper hand hygiene and how to use a surgical mask during contact moments such as feeding of their neonate, and use a new mask each time.*

*Similar hygiene measures should be taken in case of formula feeding and other contact moments, such as cuddling. This recommendation not only applies to the mother, but also to the other parent.*

*These hygiene measures need to be applied until the mother has been free of symptoms for 24 hours.*

10

*Een pasgeborene van een symptomatische moeder met COVID-19 kan borstvoeding krijgen, mits er aanvullende beschermende maatregelen worden toegepast om het risico van besmetting te minimaliseren. Aan de moeder moet worden uitgelegd dat besmetting niet 100% kan worden voorkomen.*

*Een moeder met COVID-19 dient instructies te krijgen over handhygiëne en hoe een chirurgisch masker te gebruiken tijdens contactmomenten zoals het voeden. Dat masker moet iedere keer vervangen worden.*

*Dezelfde hygiënische maatregelen worden aanbevolen bij het geven van flesvoeding en bij andere contactmomenten zoals knuffelen. Deze aanbevelingen gelden evenzeer voor de andere ouder.*

*Deze hygiënische maatregelen worden toegepast tot beëindiging van de besmettelijk periode ( zie Leidraad Niet meer besmettelijk na COVID-19 infectie FMS).*

## 8 Literature

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## 9 Tables

**Table 1.** Papers reporting on cases of pregnant women with COVID-19 – search date 20 April 2020

| <b>first author, year (journal)</b>     | <b>place</b>  | <b>time</b>                 | <b>number of women / neonates</b>                   | <b>consecutive patients?</b>   | <b>gestational age at entry</b>                  | <b>gestational age at delivery</b>               | <b>information about (1 or more of the following)</b><br><b>1. pregnancy complications</b><br><b>2. complications of labour</b><br><b>3.(P)PROM</b><br><b>4. breastfeeding</b> |
|---|---|-----------------------------|---|--|--|--|--|
| Alzamora (Am J Perinatol)               | British American Hospital, Lima, Peru                                       | March 29, 2020              | 1/1   | NA   | 33   | 33   | 1, 2   |
| Breslin (Am J Obstet Gynecol MFM)       | Columbia University Irving Medical Center and Allen Hospital (New York, NY) | March 13 to 27, 2020        | 31 of 43 women who tested positive were symptomatic | yes; all pregnant women who tested positive in this period were included | not extractable for symptomatic women separately | not extractable for symptomatic women separately | 1, 3   |
| Chen H (Lancet)                         | Zhongnan Hospital of Wuhan University, Wuhan, China,                        | from Jan 20 to Jan 31, 2020 | 9 /9  | not clear  | 36 – 39 weeks                                    | not reported                                     | 1, 2, 4  |
| Chen R (Canadian Journal of Anesthesia) | Renmin hospital of Wuhan University, China                                  | 30 Jan – 23 Feb 2020        | 17  | Not clear  | Not reported                                     | 3 < 37 weeks, 14 > 37 weeks                      | 1, 2   |

|   |  |  |       |   |               |   |        |
|---|--|--|-------|---|---------------|---|--------|
| Chen S<br>(Zhonghua<br>Bing Li Xue Za<br>Zhi)                       | Union<br>Hospital,<br>Tongji Medical<br>College,<br>Huazhong<br>University,<br>Wuhan, China  | Placental<br>tissue<br>received on<br>4 Feb 2020     | 3/3   | Not reported  | 35-39 weeks   | 35-39 weeks   | 1, 2   |
| Chen S, Liao E<br>and Shao Y<br>(Journal of<br>Medical<br>Virology) | Maternal and<br>Child Hospital<br>of Hubei<br>Province,<br>Tongji Medical<br>College,<br>Huazhong<br>University of<br>Science and<br>Technology,<br>Wuhan, China | between<br>January 20<br>and<br>February 10,<br>2020 | 5/5   | 'all 5 cases of<br>pregnant<br>women with<br>COVID-19'                              | 38 – 41 weeks | 38 – 41 weeks   | 1, 2   |
| Chen Y<br>(Front<br>Pediatr)  | Tongji<br>Hospital,<br>Wuhan, China  | Not<br>reported                                      | 4/4   | Not clear (only<br>live born<br>neonates<br>included)                               | Not reported  | >37   | 1,2    |
| Fan<br>(Clin Infect<br>Dis)   | Renmin<br>Hospital,<br>Wuhan, China  | Jan 2020   | 2/2   | no  | 36-37         | 36+5-39   | 1,2,4  |
| Ferrazzi E<br>(Pre Print<br>SSRN)                                   | 12 northern<br>Italian centres   | 1-20 March<br>2020                                   | 42/42 | Yes ('few<br>might have<br>slipped<br>through this<br>network and<br>not reported') | Not reported  | term: n =30<br>34-37 wk: n =7<br><34 wk: n = 4<br>Missing: n =1 | 1,2, 4 |
| Gidlöf  | Stockholm<br>South General   | Not<br>reported                                      | 1 / 2 | NA  | 36+2          | 36+2  | 1,2,4  |

|  |   |                       |                              |           |             |              |         |
|--|---|-----------------------|------------------------------|-----------|-------------|--------------|---------|
| (Acta Obstet Gynecol Scand)                      | Hospital, Sweden  |                       |                              |           |             |              |         |
| Iqbal (NEJM)                                     | Washington DC, USA  | Not reported          | 1/1                          | NA        | 39          | 39+          | 2,4     |
| Kalafat (UOG)                                    | Ankara, Turkey  | March 2020            | 1/1                          | NA        | 35+3        | 36+          | 1,2,4   |
| Khan (Infection Control & Hospital Epidemiology) | Renmin Hospital, Wuhan China                                | Jan 28 – Mar 1 2020   | 3/3                          | Not clear | 34+6-39+1   | 34+6-39+1    | 2       |
| Lee (Korean J of Anesthesiol)                    | Daegu Fatima Hospital, South Korea                          | Feb 2020              | 1/1                          | NA        | 36+2        | 37+6         | 1,2     |
| Li N (Clin Infect Dis)                           | Hubei Provincial Maternal and Child Health Center, Wuhan    | Jan 24 – Feb 29, 2020 | 16/17 (confirmed cases only) | yes       | 33+6-40+4   | Mean 38      | 1,2,3   |
| Li Y (Emerg Infect Dis)                          | Zhejiang University, Hangzhou, China                        | 6 Feb 2020            | 1/1                          | NA        | 35 weeks    | 35 weeks     | 1, 2, 4 |
| Liao (Balkan Medical Journal)                    | Chongqing University Three Gorges Hospital, Chongqing China | Feb 2020              | 1/1                          | NA        | 35+1        | 35+3         | 1,2     |
| Liu D (AJR)                                      | Union Hospital,   | 20 Jan – 10 Feb 2020  | 15/11                        | yes       | 12-38 weeks | Not reported | 1, 2    |

|                                   |  |                                  |  |           |              |  |         |
|-----------------------------------|--|----------------------------------|--|-----------|--------------|--|---------|
|                                   | Tongji Medical College, Huazhong University, Wuhan, China.                   |                                  |  |           |              |  |         |
| Liu H (Journal of Infection)      | Xinhua hospital and Maternal and Child Health hospital Hubei, China          | Jan 27-feb 14 2020               | 41/? (no information about neonates)     | No        | 22-40+5      | Not reported                           | 1       |
| Liu W (Front Med)                 | Tongji Hospital, Huazhong University of science and technology, Wuhan, China | 2 – 5 Feb 2020                   | 3/3                                      | yes       | 37-40 weeks  | 38-40 weeks                            | 1, 2, 4 |
| Liu Y (J Infect)                  | hospitals outside of Wuhan   | From Dec 8, 2020 to Feb 25, 2020 | 13/9 (3 ongoing pregnancy, 1 stillbirth) | not clear | 25-38+ weeks | not reported, 6 preterm, all >32 weeks | 1,2,3   |
| Lowe (Aust N Z J Obstet Gynaecol) | Gold Coast University Hospital (GCUH), Southport, Australia                  | not reported                     | 1/1                                      | NA        | 40+0         | 40+3                                   | 2, 4    |
| Wang S (Clin Infect Dis)          | Tongji Hospital, Wuhan, China.   | Feb 1, 2020                      | 1/1                                      | NA        | 40           | 40                                     | 1,2,4   |
| Wang X                            | The Affiliated Infectious  | Feb 2, 2020                      | 1/1                                      | NA        | 30           | 30+6                                   | 1,2,3,4 |

|   |   |                       |                             |     |              |          |       |
|---|---|-----------------------|-----------------------------|-----|--------------|----------|-------|
| (Clin Infect Dis)                                 | Hospital of Soochow University, Suzhou, China.      |                       |                             |     |              |          |       |
| Wen (J Microbiol Immunol Infect)                  | Qingdao, Shandong, China                            | Jan 21 2020           | 1/0                         | NA  | 30           | NA       | 1     |
| Xia (Pediatric Pulmonology)                       | Wuhan Red Cross Hospital, Wuhan, China              | Jan 20, 2020          | 1/1                         | NA  | 36+5         | 37+2     | 1,2,3 |
| Yu (Lancet Infect Dis)                            | Tongji Hospital, Wuhan, China                       | Jan 1 – Feb 8, 2020   | 7/7                         | yes | 37-41+2      | 37-41    | 1,2   |
| Zamaniyan (Prenat Diagn)                          | Imam Khomeini Hospital, Sari, Iran                  | March 7, 2020         | 1/1                         | NA  | 32           | 32       | 1, 2  |
| Zambrano (Travel Medicine and Infectious Disease) | Hospital Escuela of Tegucigalpa, Honduras           | March 2020            | 1/1                         | NA  | 31           | 32       | 1,2   |
| Zhang (Zhonghua Fu Chan Ke Za Zhi)                | Eastern Hospital Wuhan University People's Hospital | Jan 30 – feb 17, 2020 | 16/10 (6 ongoing pregnancy) | yes | not reported | 35+5 -41 | 2,4   |
| Zhang, B (Chest)                                  | Xiaolan People's Hospital of                        | Feb 2020              | 1/1                         | NA  | 35+2         |          | 1,2   |

|                            |                         |                         |              |    |              |       |       |
|----------------------------|-------------------------|-------------------------|--------------|----|--------------|-------|-------|
|                            | Zhongshan,<br>China     |                         |              |    |              |       |       |
| Zhu<br>(Transl<br>Pediatr) | 5 hospitals in<br>Hubei | Jan 20 – feb<br>5, 2020 | 9/10 (twins) | no | not reported | 31-39 | 1,2,3 |

NA: not applicable



**Table 2.** Information about pregnancy complications in women with COVID-19

| First author | number of women | number with pregnancy complications                | types of pregnancy complications  | Maternal comorbidity (not pregnancy-related)   |
|--------------|-----------------|--|---|--|
| Alzamora     | 1               | 1  | need for mechanical ventilation because of COVID-19 pneumonia   |  |
| Breslin      | 43              | 4 (not clearly reported)                           | 29 initially symptomatic patients:<br>20 presented with COVID-symptoms, 9 with obstetric complaints;<br>1 case of 34-week preterm labor,<br>1 case of term prelabor rupture of membranes<br><br>14 initially asymptomatic patients:<br>2 (initial obstetrical indication for induction of labour) postpartum ICU admission to the ICU due to complications including respiratory distress | not reported   |
| Chen H       | 9               | 6  | 1 pre-existent pre-eclampsia<br>1 pre-existent gestational hypertension<br>2 PROM<br>2 fetal distress<br>Outcomes favourable in all mothers and neonates  | 1 influenza  |
| Chen R       | 17              | Unclear if complications are in different patients | 5 anemia<br>1 hypertension<br>1 diabetes<br>Outcomes favourable in all mothers and neonates   | 5 anemia<br>1 hypertension<br>1 diabetes<br>Not reported if this was pregnancy-related |
| Chen S       | 3               | 3  | 2 placenta praevia<br>1 placental abruption<br>Outcomes favourable in all mothers and neonates  | Not reported   |

|                                 |    |                      |  |   |
|---------------------------------|----|----------------------|--|---|
| Chen S,<br>Liao E and<br>Shao Y | 5  | 3                    | 2 gestational diabetes<br>1 preeclampsia   | none ('all were physically fit and conceived naturally')  |
| Chen Y                          | 4  | 1                    | Placenta praevia   | 1 cholecystitis   |
| Fan                             | 2  | 1                    | Vaginal bleeding third trimester   | none  |
| Ferrazzi E                      | 42 | Not clearly reported | 6 preterm elective CS (2 <34 wk)<br>5 spontaneous preterm birth (1 <34 wk)<br>6 gestational diabetes   | Not reported  |
| Gidlöf                          | 1  | 1                    | PE, gestational diabetes   | Not reported  |
| Kalafat                         | 1  | 0                    |  | thalassemia   |
| Lee                             | 1  | 0                    | none   | none  |
| Li N                            | 16 | 11                   | 3 gestational diabetes<br>1 PE<br>1 PROM<br>3 gestational hypertension<br>1 sinus tachycardia<br>2 hypothyroidism<br>3 premature birth (2 (P)PROM, 1 placental bleeding)<br>2 fetal distress | N=2: Chronic hypertension, PCOS and Hep B (not clearly reported which were in the same patient) |
| Li Y                            | 1  | 1                    | Fetal distress   | Not reported  |
| Liao                            | 1  | 1                    | Fetal distress   | Not reported  |
| Liu D                           | 15 | 2                    | 1 placenta previa<br>1 gestational diabetes<br>Outcomes favourable in all mothers and neonates (4 still pregnant)  | 1 thalassemia<br>1 history of mitral and tricuspid valve replacement                            |
| Liu H                           | 41 | 8                    | 4 gestational diabetes<br>3 gestational hypertension   | 1 hepatitis B   |
| Liu W                           | 3  | 3                    | 1 Fetal distress<br>1 scar uterus + placenta accrete<br>1 gestational diabetes<br>Outcomes favourable in all mothers and neonates  | 1 hypothyroidism and epiglottic cysts   |

|           |    |   |   |   |
|-----------|----|---|---|---|
| Liu Y     | 13 | 6 | 6 preterm labour (between 32 and 36 weeks)<br>1 stillbirth at 34 weeks GA (in patient with severe ARDS and MODS)<br>1 PROM<br>3 fetal distress<br>Favourable outcome mothers and neonates, except for 1 severe case (see above) | None of the patients had underlying medical disease |
| Wang S    | 1  | 1 | 1 vaginal blood loss, abdominal pain and fever<br>Favourable outcome mother and neonate   | hypothyroidism                                      |
| Wang X    | 1  | 1 | 1 fetal distress<br>Favourable outcome mother and neonate   | no  |
| Wen       | 1  | 0 |   |   |
| Xia       | 1  | 1 | 1 fetal distress<br>Favourable outcome mother and neonate   | not reported  |
| Yu        | 7  | 0 |   | 3 scar uterus, 1 hypothyroidism, 1 PCOS             |
| Zamaniyan | 1  | 1 | very ill during pregnancy, but no mention of mechanical ventilation   | history of controlled hypothyroidism                |
| Zambrano  | 1  | 1 | Gestational hypertension, fetus with a multicystic kidney   | hypothyroidism                                      |
| Zhang, B  | 1  | 1 | Fetal endouterine asphyxia  | Not reported  |
| Zhu       | 9  | 7 | 6 fetal distress<br>3 PROM<br>1 placenta praevia<br>1 oligohydramnios<br>1 polyhydramnios<br>1 vaginal bleeding third trimester   | no  |

**Table 3.** Information about labour complications in women with COVID-19

| First author              | number of women / neonates | mode of delivery (Caesarean section (CS) or vaginal delivery (VD)) | labour complications   |
|---------------------------|----------------------------|--|--|
| Alzamora                  | 1/1                        | CS   | Maternal indication (respiratory distress)   |
| Breslin                   | 2/2                        | Both CS  | Indications: failed induction and arrest of descent. 1 woman had extensive blood loss during CS. No neonatal complications or signs of vertical transmission. Postpartum both mothers admitted to ICU, 1 b/o need for endotracheal intubation and 1 b/o uncontrollable hypertension. |
| Chen H                    | 9 / 9                      | All CS   | indications for CS: 1 elevated liver enzymes, 1 history of CS, 1 preeclampsia, 2 fetal distress, 2 PROM, 1 history of stillbirth and 1 mature pneumonia  |
| Chen R                    | 17 / 17                    | All CS (3 emergency, 14 scheduled)                                 | indications for CS not reported.<br>3 premature births, no neonatal complications.   |
| Chen S                    | 3 / 3                      | All CS   | Indications for CS: 1 complete placenta praevia, 1 placenta praevia and scar uterus, 1 placental abruption. 1 infant had low birth weight (but born at 35w)  |
| Chen S, Liao E and Shao Y | 5                          | 3 vaginal, 2 CS  | 1 emergency CS due to fetal tachycardia, 1 elective CS due to gestational diabetes   |
| Chen Y                    | 4/4                        | 3 CS, 1 VD   | Indication for CS not clearly reported   |
| Fan                       | 2/2                        | Both CS  | CS because of maternal illness (persistent fever and pneumonia) 1 neonate did develop mild pneumonia (but SARS-CoV-2 neg). Both mothers and neonates had good outcomes.  |
| Ferrazzi E                | 42/42                      | 24 VD<br>18 CS   | 10 CS because of worsening dyspnea or COVID related symptoms<br>8 indication unrelated tot COVID   |
| Gidlöf                    | 1/2                        | CS (uncomplicated)   | Indication for CS: severe preeclampsia   |
| Iqbal                     | 1/1                        | Uncomplicated VD   |  |
| Kalafat                   | 1/1                        | CS   | Indication for CS: to relieve pressure of maternal lungs   |
| Khan                      | 3/3                        | All uncomplicated VD   |  |
| Lee                       | 1/1                        | CS   | Indication for CS: obstructed labor (cephalopelvic disproportion)  |
| Li N                      | 16/17                      | 14 CS, 2 VD  | Indication for CS: COVID pneumonia. There were 3 preterm births, and 3 babies with low birth weight.   |

|           |              |   |   |
|-----------|--------------|---|---|
|           |              |   | This study compared outcomes with a matched non-COVID group: increased incidence of preterm birth and low birth weight. No differences in gestational age, APGAR and fetal distress. There were no cases of neonatal asphyxia and/or death. 3 neonates were tested: all negative. |
| Li Y      | 1 / 1        | Emergency CS  | Indication fetal distress. No other complications   |
| Liao      | 1/1          | CS  | Indication for CS: fetal distress   |
| Liu D     | 15 /11       | 10 CS, 1 VD, 4 still pregnant                           | Indications for CS not reported, no neonatal complications.   |
| Liu W     | 3 / 3        | 2 CS, 1 VD  | 1 meconium stained fluids   |
| Liu Y     | 13 / 10      | 10 CS (3 patients ongoing pregnancy)                    | 1 stillbirth (preterm CS, severe maternal ARDS and MODS)<br>1 (P)PROM (preterm CS)<br>3 fetal distress (of which 1 preterm CS)<br>3 preterm CS (reason not mentioned)<br>2 term CS (reason not mentioned)<br>All preterm deliveries >32 weeks                                     |
| Lowe      | 1/1          | rotational vacuum delivery for non-reassuring fetal CTG | none  |
| Wang S    | 1 / 1        | CS  | Emergency CS because of vaginal blood loss, abdominal pain and maternal fever. Meconium-stained amniotic fluid  |
| Wang X    | 1 / 1        | CS  | CS because of severe maternal pneumonia and fetal distress  |
| Xia       | 1 / 1        | CS  | CS because of severe maternal pneumonia and fetal distress  |
| Yu        | 7/7          | All CS  | Indications not clearly reported  |
| Zamaniyan | 1/1          | CS  | Maternal indication (respiratory distress)  |
| Zambrano  | 1/1          | Spontaneous preterm VD                                  |   |
| Zhang     | 16 /10       | 10 CS (6 patients ongoing pregnancy)                    | Indications for CS not clearly reported   |
| Zhang, B  | 1/1          | CS  | Indication for CS: severe maternal ARDS and multiple organ dysfunction syndrome. Newborn died of endouterine asphyxia. Mother recovered.  |
| Zhu       | 9 /10 (twin) | 7 CS, 2 VD  | 6 fetal distress<br>3 PROM  |

**Table 4.** Information about (P)PROM in women with COVID-19

| <b>First author</b> | <b>number of women</b>            | <b>number with (P)PROM</b> | <b>information about clinical course</b>                                  |
|---------------------|-----------------------------------|----------------------------|---|
| Breslin             | 29 initially symptomatic patients | 1 term PROM                | Not reported  |
| Chen H              | 9                                 | 2                          | PROM at 36+2 and 39+4 days, both had CS, healthy neonate                  |
| Li N                | 16                                | 2-3 (not clearly stated)   | Not reported  |
| Liu Y               | 13                                | 1                          | Illness onset at 34 weeks. (P)PROM with CS. Healthy neonate transmission. |
| Wang X              | 1                                 | 0                          |   |
| Xia                 | 1                                 | 0                          |   |
| Zhu                 | 9                                 | 3                          | Not clearly reported  |

**Table 5.** Information about COVID-19 and breast feeding

| <b>First author</b> | <b>number of women</b> | <b>number of women with information about breast feeding</b> | <b>information about breast feeding</b>   |
|---------------------|------------------------|--|---|
| Chen H              | 9                      | 6  | all 6 breast milk samples were negative   |
| Fan                 | 2                      | 1  | Breast milk samples were negative   |
| Ferrazzi E          | 42                     | 11   | 11 neonates received breastfeeding if mother was asymptomatic/pauci-symptomatic. With a mask and frequent hand cleaning. Two neonates were breastfed without mask (maternal cases with post partum diagnosis) and had positive tests for COVID-19 infection at day one and three. |
| Gidlöf              | 1                      | 1  | Both babies were breast fed, milk samples were negative   |
| Iqbal               | 1                      | 1  | Neonate received breast milk, not tested for SARS-CoV-2   |
| Kalafat             | 1                      | 1  | Neonate is breast fed, milk sample negative   |
| Li Y                | 1                      | 1  | Breast milk samples were negative   |
| Liu W               | 3                      | 2  | Breast milk samples were negative   |
| Lowe                | 1                      | 1  | breast feeding with surgical mask; neonate healthy  |
| Wang S              | 1                      | 1  | no breast feeding was started   |
| Wang X              | 1                      | 1  | no breast feeding was started   |
| Zhang               | 16                     | 16   | 'breast feeding could be started at least 14 days after isolation'  |

## Excluded papers with reasons

| First author | reason for exclusion  |
|--------------|---|
| Chen D       | Opinion-based recommendations for practice; no data   |
| Mullins      | rapid review, no original data  |
| Rasmussen    | educational paper, no original data   |
| Chen L       | retrospective report of 118 pregnant women with COVID-19 identified in 50 hospitals in Wuhan city between December 8, 2019 and March 20, 2020; not possible to identify possible duplicate reports  |
| Di Mascio    | SR of CoV infections including MERS and SARS in pregnancy; no original data   |
| Gajbhiye     | SR; no original data  |
| Li L         | update on 4 of 15 earlier reported cases (Liu D); no relevant additional information  |
| Liu W        | case series of 19 neonates admitted to Tongji Hospital from January 31 to February 29, 2020, born to SARS-CoV-2 infected mothers; not possible to identify possible duplicate reports   |
| Sutton       | screening study in pregnant women; no information about course of disease in symptomatic pregnant women   |
| Wei          | retrospective report of 17 pregnant and 32 non-pregnant women admitted to Tongji Hospital, Tongji Medical College of Huazhong University of Science and Technology, Wuhan, Hubei, China between January 19 and March 2, 2020; not possible to identify possible duplicate reports                   |
| Yang H       | retrospective report of 55 suspected pregnant patients who were admitted to Maternal and Child Health Hospital of Hubei Province, Tongji Medical College, Huazhong University of Science and Technology, from January 20th to March 23th, 2020; not possible to identify possible duplicate reports |
| Yang J       | retrospective report of 18 patients with COVID-19 in the 3rd trimester admitted to Renmin Hospital of Wuhan University between January 30 and March 1, 2020; not possible to identify possible duplicate reports  |
| Yang P       | case series of 7 newborns delivered by SARS-CoV-2 infected pregnant women in Zhongnan Hospital of Wuhan University between January 20 and January 29, 2020; not possible to identify possible duplicate reports   |
| Yin          | retrospective comparison of 31 pregnant and 35 non-pregnant women admitted to Wuhan Union and Tongji hospitals of Huazhong University of Science and Technology between January 28 and February 28, 2020; not possible to identify possible duplicate reports                                       |



## 10 Literature search strategy

|   |  |
|---|--|
| <p>Background:</p> <p>The NVOG formulated several questions regarding COVID-19. Five of these were labeled as urgent/high priority.</p> <p>Since literature about COVID-19 was limited, every initial COVID-19 search was supplemented with a broader search including SARS and MERS. These results were collected separately and could be consulted if desirable.</p>  |  |
| <p>Questions:</p> <ol style="list-style-type: none"> <li>1. Do COVID-19 infections in pregnant women lead to more pregnancy complications like preeclampsia, fetal growth restriction and preterm birth?</li> <li>2. Which complications are more prevalent among pregnant women with COVID-19 infections than in non-pregnant women and men?</li> <li>3. Do COVID-19 infections in pregnant women lead to more complications during delivery?</li> <li>4. When should pregnant women with COVID-19 infections after (P)PROM be delivered?</li> <li>5. Is it safe by women with COVID-19 infections to give their newborns breast feeding?</li> </ol>   |  |
| <p>Initial database(s): Embase, PubMed<br/>           Later complemented with: Medrxiv, Google Scholar and WHO</p>  | <p>Initial search date: 25-3-2020<br/>           Last updated: 20-4-2020</p> |
| <p>Information specialist: Miriam van der Maten</p>   |  |
| <p>Further remarks:</p> <ul style="list-style-type: none"> <li>• Questions 1 and 2 are covered using: (pregnancy OR pregnancy complications) <b>AND</b> (COVID19 OR COVID19/MERS/SARS/SARI)</li> <li>• Question 3 is covered using: (labor/delivery OR labor complications) <b>AND</b> (COVID19 OR COVID19/MERS/SARS/SARI)</li> <li>• Question 4 is covered using: (P)PROM <b>AND</b> (COVID19 OR COVID19/MERS/SARS/SARI)</li> <li>• Question 5 is covered using: (breastfeeding) <b>AND</b> (COVID19 OR COVID19/MERS/SARS/SARI)</li> </ul> <p>When the combination of a question-specific search block and the COVID19/MERS/SARS/SARI block resulted in a large number of hits, the set of results was divided into different study designs (SR, RCT, observational studies or other). Standardized filters were applied as normally used by the knowledge institute.</p> <p>E-mail alerts were created for every question to monitor new literature on a daily basis.</p> <p>The most recent information (preprints, non peer-reviewed sources e.g.) regarding this topic did not always appear in the conventional databases. Hence, other information sources were consulted along the way.</p> |  |

### Initial search results

|   | COVID 19   | COVID19/MERS/SARS/SARI |
|---|------------|------------------------|
| <i>Question 1 and 2 (pregnancy complications)</i> | 61         | 305                    |
| <i>Question 3 (labor)</i>                         | 93         | 559                    |
| <i>Question 4 ((P)PROM)</i>                       | 0          | 6                      |
| <i>Question 5 (breastfeeding)</i>                 | 2          | 20                     |
| <b>Total</b>                                      | <b>126</b> |                        |

### Results since last update (20-4-2020)

|  | COVID 19 |
|--|----------|
|  |          |

**Search justification**

| Database | Searched terms  |
|----------|---|
| Embase   | <p><b><u>COVID19:</u></b><br/> (2019ncov:ti,ab,kw OR '2019 ncov':ti,ab,kw OR 'novel coronavirus*':ti,ab,kw OR 'novel corona virus*':ti,ab,kw OR ((coronavirus*':ti,ab,kw OR 'corona virus*':ti,ab,kw OR 'pneumonia virus*':ti,ab,kw OR cov:ti,ab,kw OR ncov:ti,ab,kw) AND (outbreak:ti,ab,kw OR wuhan:ti,ab,kw)) OR covid19:ti,ab,kw OR 'covid 19':ti,ab,kw OR ((coronavirus*':ti,ab,kw OR 'corona virus*':ti,ab,kw) AND 2019:ti,ab,kw) OR 'sars cov 2':ti,ab,kw OR sars2:ti,ab,kw OR 'new coronavirus*':ti,ab,kw OR 'new corona virus*':ti,ab,kw OR 'ncov 2019':ti,ab,kw OR 'sars coronavirus 2':ti,ab,kw OR 'sars corona virus 2':ti,ab,kw OR 'severe acute respiratory syndrome cov 2':ti,ab,kw OR 'severe acute respiratory syndrome cov2':ti,ab,kw) AND [2019-2020]/py</p> <p><b><u>MERS/SARS/COVID19/SARI</u></b><br/> 2019ncov:ti,ab,kw OR '2019 ncov':ti,ab,kw OR 'novel coronavirus*':ti,ab,kw OR 'novel corona virus*':ti,ab,kw OR ((coronavirus*':ti,ab,kw OR 'corona virus*':ti,ab,kw OR 'pneumonia virus*':ti,ab,kw OR cov:ti,ab,kw OR ncov:ti,ab,kw) AND (outbreak:ti,ab,kw OR wuhan:ti,ab,kw)) OR covid19:ti,ab,kw OR 'covid 19':ti,ab,kw OR ((coronavirus*':ti,ab,kw OR 'corona virus*':ti,ab,kw) AND 2019:ti,ab,kw) OR sars*:ti,ab,kw OR 'new coronavirus*':ti,ab,kw OR 'new corona virus*':ti,ab,kw OR 'ncov 2019':ti,ab,kw OR 'sars corona virus 2':ti,ab,kw OR 'severe acute respiratory syndrome cov 2':ti,ab,kw OR 'severe acute respiratory syndrome':ti,ab,kw OR 'severe acute respiratory syndrome'/exp OR 'sars-related coronavirus'/exp OR 'sars-like cov':ti,ab,kw OR 'sars-like coronavirus':ti,ab,kw OR 'sars-related cov':ti,ab,kw OR 'sars-related coronavirus':ti,ab,kw OR 'sarsr-cov':ti,ab,kw OR 'severe acute respiratory syndrome-like coronavirus':ti,ab,kw OR 'severe acute respiratory syndrome-related coronavirus':ti,ab,kw OR 'sars coronavirus'/exp OR 'hcov-sars':ti,ab,kw OR 'human sars coronavirus':ti,ab,kw OR 'sars cov':ti,ab,kw OR 'sars associated coronavirus':ti,ab,kw OR 'sars coronavirus':ti,ab,kw OR 'sars virus':ti,ab,kw OR 'sars-cov':ti,ab,kw OR 'sars-associated coronavirus':ti,ab,kw OR 'severe acute respiratory syndrome coronavirus':ti,ab,kw OR 'severe acute respiratory syndrome virus':ti,ab,kw OR 'middle east respiratory syndrome coronavirus'/exp OR 'mers coronavir*':ti,ab,kw OR 'mers vir*':ti,ab,kw OR 'mers-cov':ti,ab,kw OR 'middle east respiratory syndrome coronavir*':ti,ab,kw OR 'severe acute respiratory infection*':ti,ab,kw</p> <p><b><u>Pregnancy and pregnancy complications:</u></b><br/> 'pregnancy'/exp OR 'pregnant woman'/exp OR 'prepregnancy care'/exp OR pregnan*:ti,ab,kw OR gravidit*:ti,ab,kw OR gestation*:ti,ab,kw OR placentat*:ti,ab,kw OR prepregnan*:ti,ab,kw OR conception*:ti,ab,kw OR preconception*:ti,ab,kw<br/> <b>OR</b><br/> 'pregnancy disorder'/exp OR (pregnan* NEAR/3 (complicat* OR disorder* OR disease*)):ti,ab,kw<br/> <b>OR</b><br/> 'premature labor'/exp OR (((labo*r OR delivery OR parturition OR birth OR childbirth) NEAR/3 (premature OR preterm OR 'pre term' OR early OR prior)):ti,ab,kw)<br/> <b>OR</b><br/> 'abortion'/exp OR abort*:ti,ab,kw<br/> <b>OR</b><br/> 'eclampsia and preeclampsia'/exp OR 'hells syndrome'/exp OR eclamp*:ti,ab,kw OR preeclamp*:ti,ab,kw OR 'pre-eclamp*':ti,ab,kw OR preclamp*:ti,ab,kw OR hellp:ti,ab,kw OR 'h\$emolysis elevated liver enzymes and low platelet*':ti,ab,kw<br/> <b>OR</b><br/> 'intrauterine growth retardation'/exp OR iugr:ti,ab,kw OR ((restrict* OR retard* OR disorder) NEAR/2 growth NEAR/2 (fetal OR foetal OR fetus OR foetus OR intrauterine OR 'intra uterine' OR 'in utero' OR prenatal)):ti,ab,kw</p> |

|         |   |
|---------|---|
|         | <p><b>OR</b><br/>'fetus disease'/exp OR ((fetal OR foetal OR fetus OR foetus) NEAR/3 (abnormalit* OR anomal* OR disease* OR disorder* OR complicat*)):ti,ab,kw OR fetopath*:ti,ab,kw OR foetopath*:ti,ab,kw</p> <p><b>Labor:</b><br/>'obstetric delivery'/exp OR 'labor complication'/exp OR (labo*r OR delivery OR parturition* OR birth* OR childbirth*):ti,ab,kw</p> <p><b>(P)PROM:</b><br/>'premature fetus membrane rupture'/exp OR prom:ti,ab,kw OR pprom:ti,ab,kw OR ((premature OR preterm OR prelabo*r) NEAR/3 ('rupture of membrane*')):ti,ab,kw</p> <p><b>Breast feeding:</b><br/>'breast feeding'/exp OR (breastfeeding OR 'breast* feeding'):ti,ab,kw</p>  |
| Pubmed  | <p><b>COVID19</b><br/>((coronavirus*[tiab] OR corona virus*[tiab] OR pneumonia virus*[tiab] OR cov[tiab] OR ncov[tiab]) AND (outbreak[tiab] OR wuhan[tiab])) OR covid19[tiab] OR "covid 19"[tiab] OR ((coronavirus*[tiab] OR corona virus*[tiab]) AND 2019[tiab]) OR "sars cov 2"[tiab] OR sars2[tiab] OR new coronavirus*[tiab] OR new corona virus*[tiab] OR "ncov 2019"[tiab] OR "sars coronavirus 2"[tiab] OR "sars corona virus 2"[tiab] OR "severe acute respiratory syndrome cov 2"[tiab] OR "severe acute respiratory syndrome cov2"[tiab]<br/>Filters: Publication date from 2019/11/01</p> <p><b>MERS/SARS/COVID19/SARI</b><br/>"Severe Acute Respiratory Syndrome"[Mesh] OR "SARS Virus"[Mesh] OR "COVID-19"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR 2019ncov[tiab] OR 2019 ncov[tiab] OR novel coronavirus*[tiab] OR novel corona virus*[tiab] OR ((coronavirus*[tiab] OR corona virus*[tiab] OR pneumonia virus*[tiab] OR cov[tiab] OR ncov[tiab]) AND (outbreak[tiab] OR wuhan[tiab])) OR covid19[tiab] OR covid 19[tiab] OR ((coronavirus*[tiab] OR corona virus*[tiab]) AND 2019[tiab]) OR sars*[tiab] OR new coronavirus*[tiab] OR new corona virus*[tiab] OR ncov 2019[tiab] OR "sars corona virus"[tiab] OR "sars-like cov"[tiab] OR "sars-like coronavirus"[tiab] OR sars-related cov[tiab] OR sars-related coronavirus[tiab] OR sarsr-cov[tiab] OR "severe acute respiratory syndrome-like coronavirus"[tiab] OR "severe acute respiratory syndrome-related coronavirus[tiab] OR hcov-sars[tiab] OR human sars coronavirus[tiab] OR sars cov[tiab] OR sars associated coronavirus"[tiab] OR sars coronavirus[tiab] OR sars virus[tiab] OR sars-cov[tiab] OR sars-associated coronavirus[tiab] OR severe acute respiratory syndrome coronavirus[tiab] OR severe acute respiratory syndrome virus[tiab] OR mers coronavir*[tiab] OR mers vir*[tiab] OR mers-cov[tiab] OR middle east respiratory syndrome coronavir*[tiab] OR severe acute respiratory infection*[tiab]</p> <p><b>Pregnancy and pregnancy complications:</b><br/>((((("Pregnancy"[Mesh] OR "Pregnant Women"[Mesh] OR "Preconception Care"[Mesh] OR pregnan*[tiab] OR gravidit*[tiab] OR gestation*[tiab] OR placenta*[tiab] OR prepregnan*[tiab] OR conception*[tiab] OR preconception*[tiab]) OR ("Pregnancy Complications"[Mesh] OR (pregnan* AND (complicat* OR disorder* OR disease*))[tiab])) OR ("Obstetric Labor, Premature"[Mesh] OR ((labor OR labour OR delivery OR parturition OR birth OR childbirth) AND (premature OR preterm OR 'pre term' OR early OR prior))[tiab])) OR ("Abortion, Spontaneous"[Mesh] OR abort*[tiab])) OR ("Hypertension, Pregnancy-Induced"[Mesh] OR eclamp*[tiab] OR preeclamp*[tiab] OR 'pre-eclamp*[tiab] OR preclamp*[tiab] OR hellp[tiab] OR 'hemolysis elevated liver enzymes and low platelet*'[tiab] OR 'haemolysis elevated liver enzymes and low platelet*'[tiab])) OR ("Fetal Growth Retardation"[Mesh] OR iugr[tiab] OR ((restrict* OR retard* OR disorder) AND growth AND (fetal OR foetal OR fetus OR foetus OR intrauterine OR 'intra uterine' OR 'in utero' OR prenatal))[tiab])) OR ("Fetal Diseases"[Mesh] OR ((fetal OR foetal OR fetus OR foetus) AND (abnormalit* OR anomal* OR disease* OR disorder* OR complicat*))[tiab] OR fetopath*[tiab] OR foetopath*[tiab])</p> <p><b>Labor:</b><br/>"Labor, Obstetric"[Mesh] OR "Obstetric Labor Complications"[Mesh] OR (labor OR labour OR delivery OR parturition* OR birth* OR childbirth*))[tiab]</p> <p><b>(P)PROM:</b><br/>"Fetal Membranes, Premature Rupture"[Mesh] OR prom[tiab] OR pprom[tiab] OR ((premature OR preterm OR prelabor OR prelabour) AND ('rupture of membrane*'))[tiab]</p> <p><b>Breast feeding:</b><br/>"Breast Feeding"[Mesh] OR (breastfeeding OR 'breast* feeding')[tiab]</p> |
| Filters | <p><b>EMBASE</b><br/><i>Sytematische reviews</i></p>  |

('meta analysis'/de OR cochrane:ab OR embase:ab OR psycinfo:ab OR cinahl:ab OR medline:ab OR ((systematic NEAR/1 (review OR overview)):ab,ti) OR ((meta NEAR/1 analy\*):ab,ti) OR metaanalys\*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de)

RCT's

'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random\*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo\*:ab,ti

Observational research

'major clinical study'/de OR 'clinical study'/de OR 'case control study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'cohort analysis'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti)

**PubMed**

Systematic reviews

((review[tiab] OR "Review"[Publication Type] OR "Meta-Analysis as Topic"[Mesh] OR meta-analysis[tiab] OR "Meta-Analysis "[Publication Type]) NOT ("Letter"[Publication Type] OR "Editorial"[Publication Type] OR "Comment"[Publication Type])) NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))

RCT

((random\*[tiab] AND (controlled[tiab] OR control[tiab] OR placebo[tiab] OR versus[tiab] OR vs[tiab] OR group[tiab] OR groups[tiab] OR comparison[tiab] OR compared[tiab] OR arm[tiab] OR arms[tiab] OR crossover[tiab] OR cross-over[tiab]) AND (trial[tiab] OR study[tiab])) OR ((single[tiab] OR double[tiab] OR triple[tiab]) AND (masked[tiab] OR blind\*[tiab])))

Observational research

"Epidemiologic Studies"[Mesh] OR cohort[tiab] OR (case[tiab] AND (control[tiab] OR controll\*[tiab] OR comparison[tiab] OR referent[tiab])) OR risk[tiab] OR causation[tiab] OR causal[tiab] OR "odds ratio"[tiab] OR etiol\*[tiab] OR aetiol\*[tiab] OR "natural history"[tiab] OR predict\*[tiab] OR prognos\*[tiab] OR outcome[tiab] OR course[tiab] OR retrospect\*[tiab]