

Maternal and perinatal outcomes of pregnant women with SARS-CoV-2 infection at the time of birth in England: national cohort study

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1 CONDENSATION

2 Among 342,080 births, we found that a positive SARS-CoV-2 test at the time of birth is
3 associated with increased rates of stillbirth, preterm birth, and other adverse maternal and
4 perinatal outcomes.

5

6 SHORT TITLE

7 Maternal and perinatal outcomes of pregnant women with SARS-CoV-2

8 AJOG AT A GLANCE

9

10 Why was this study conducted?

11 To determine the association between SARS-CoV-2 infection and maternal and perinatal
12 outcomes, in the context of universal screening of women giving birth in England.

13

14 What are the key findings?

15 Women who tested positive for SARS-CoV-2 at birth had increased rates of fetal death,
16 preterm birth, preeclampsia, emergency Cesarean delivery and other adverse maternal and
17 neonatal outcomes.

18

19 What does this study add to what is already known?

20 SARS-CoV-2 infection at the time of birth is associated with a higher rate of fetal death and
21 preterm birth, and other adverse maternal and neonatal outcomes. Observed increase in
22 rates of adverse neonatal outcomes was attributed to increased preterm birth.

23

24 **ABSTRACT**

25 **Objective:** The aim of this study was to determine the association between SARS-CoV-2
26 infection at the time of birth and maternal and perinatal outcomes.

27

28 **Methods:** This is a population-based cohort study in England. The inclusion criteria were
29 women with a recorded singleton birth between 29th May 2020 and 31st January 2021 in a
30 national database of hospital admissions. Maternal and perinatal outcomes were compared
31 between pregnant women with a laboratory-confirmed SARS-CoV-2 infection recorded in the
32 birth episode and those without. Study outcomes were fetal death at or beyond 24 weeks'
33 gestation (stillbirth), preterm birth (<37 weeks gestation), small for gestational age infant
34 (SGA; birthweight <10th centile), preeclampsia/eclampsia, induction of labor, mode of birth,
35 specialist neonatal care, composite neonatal adverse outcome indicator, maternal and
36 neonatal length of hospital stay following birth (3 days or more), 28-day neonatal and 42-day
37 maternal hospital readmission. Adjusted odds ratios (aOR) and their 95% confidence interval
38 (CI) for the association between SARS-CoV-2 infection status and outcomes were calculated
39 using logistic regression, adjusting for maternal age, ethnicity, parity, pre-existing diabetes,
40 pre-existing hypertension and socioeconomic deprivation measured using Index of Multiple
41 Deprivation 2019. Models were fitted with robust standard errors to account for hospital-level
42 clustering. The analysis of the neonatal outcomes was repeated for those born at term (≥ 37
43 weeks' gestation) since preterm birth has been reported to be more common in pregnant
44 women with SARS-CoV-2 infection.

45

46 **Results:** The analysis included 342,080 women, of whom 3,527 had laboratory-
47 confirmed SARS-CoV-2 infection. Laboratory-confirmed SARS-CoV-2 infection was more
48 common in women who were younger, of non-white ethnicity, primiparous, residing in the
49 most deprived areas, or had comorbidities. Fetal death (aOR, 2.21, 95% CI 1.58-3.11;
50 $P<0.001$) and preterm birth (aOR 2.17, 95% CI 1.96-2.42; $P<0.001$) occurred more
51 frequently in women with SARS-CoV-2 infection than those without. Risk of
52 preeclampsia/eclampsia (aOR 1.55, 95% CI 1.29-1.85; $P<0.001$), birth by emergency
53 Cesarean delivery (aOR 1.63, 95% CI 1.51-1.76; $P<0.001$) and prolonged admission
54 following birth (aOR 1.57, 95%CI 1.44-1.72; $P<0.001$) were significantly higher for women
55 with SARS-CoV-2 infection than those without. There were no significant differences in the
56 rate of other maternal outcomes.

57

58 Risk of neonatal adverse outcome (aOR 1.45, 95% CI 1.27-1.66; $P<0.001$), need for
59 specialist neonatal care (aOR 1.24, 95% CI 1.02-1.51; $P=0.03$), and prolonged neonatal

60 admission following birth (aOR 1.61, 95% CI 1.49-1.75; $P < 0.001$) were all significantly higher
61 for infants with mothers with laboratory-confirmed SARS-CoV-2 infection. When the analysis
62 was restricted to pregnancies delivered at term (≥ 37 weeks), there were no significant
63 differences in neonatal adverse outcome ($P = 0.78$), need for specialist neonatal care after
64 birth ($P = 0.22$) or neonatal readmission within four weeks of birth ($P = 0.05$). Neonates born at
65 term to mothers with laboratory-confirmed SARS-CoV-2 infection were more likely to have
66 prolonged admission following birth (21.1% compared to 14.6%, aOR 1.61, 95% CI 1.49-
67 1.75; $P < 0.001$).

68

69 **Conclusions:** SARS-CoV-2 infection at the time of birth is associated with higher rates of
70 fetal death, preterm birth, preeclampsia and emergency Cesarean delivery. There were no
71 additional adverse neonatal outcomes, other than those related to preterm delivery.
72 Pregnant women should be counseled regarding risks of SARS-COV-2 infection and should
73 be considered a priority for vaccination.

74

75 **Keywords:** COVID-19, pregnancy, birth, fetal death, stillbirth, preterm birth, obstetrics,
76 neonatal outcome, preeclampsia

77

78

79 INTRODUCTION

80 Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome
81 coronavirus 2 (SARS-CoV-2), has spread rapidly around the world since the first reported
82 case in late 2019. Studies from registries of pregnant women and single- or multicentre
83 cohorts have reported that pregnant women with COVID-19 are at greater risk than non-
84 pregnant women of childbearing age with COVID-19 of requiring intensive care unit (ICU)
85 support, severe morbidity and mortality.¹⁻³ Delivery may improve maternal condition in
86 women with severe COVID-19, leading to an observed increase in preterm birth and
87 neonatal unit admission for infants of infected mothers.^{1,4-6} In the general population,
88 advanced age, obesity, minority ethnic origin, socioeconomic deprivation and comorbidities
89 including diabetes and hypertensive disease are associated with higher risk of severe
90 disease, a pattern which is also seen in pregnant women.^{1,7} Neonatal SARS-CoV-2 infection
91 has not been associated with adverse outcomes for the newborn.⁸

92 A recent international registry study demonstrated an increase in adverse maternal and
93 neonatal outcomes for mothers infected with COVID-19 in pregnancy;⁴ and a study using
94 national data from Sweden demonstrated an increase in adverse neonatal outcomes for
95 infants born to women with SARS-CoV-2 infection, a finding largely mediated by increased
96 rates of preterm birth.⁹

97 We aimed to investigate maternal and perinatal outcomes of pregnant women with SARS-
98 CoV-2 infection in England using data available from routinely collected electronic healthcare
99 records.

100

101 MATERIALS AND METHODS

102 *Study design*

103 This study is a national population-based cohort study using Hospital Episode Statistics
104 (HES) data from 29th May 2020 to 31st January 2021. HES contains records of all inpatient

105 admissions to National Health Service (NHS) hospitals in England including data on patient
106 demographics (age, sex and ethnicity), the admission (date of admission and discharge) and
107 clinical information. On the 29th May 2020, the Royal College of Obstetricians and
108 Gynaecologists recommended universal screening of all women admitted to maternity
109 services with a PCR test, in line with recommendations from NHS England to test all hospital
110 admissions.^{10,11}

111 Diagnostic information is coded using the International Classification of Diseases, 10th
112 revision (ICD-10).¹² Operative procedures are described using the UK Office for Population
113 Censuses and Surveys classification, 4th revision (OPCS-4).¹³ Further details about the
114 labor and birth are captured in the episode record (e.g., gestational age, birthweight) in
115 supplementary data fields known as the HES 'maternity tail'. HES data is sufficiently
116 accurate to be used for research and managerial decision-making.¹⁴

117 *Cohort selection and outcome definitions*

118 The inclusion criteria were women who had a HES record of a singleton birth between 29th
119 May 2020 and 31st January 2021. HES includes births which occur in NHS hospitals and
120 hospital-associated community care in England. Only 0.3% of births in England in 2020
121 occurred in non-NHS organizations.¹⁵

122 A maternity episode was defined as any record that contained valid information about mode
123 of birth in either the procedure fields (OPCS-4 codes: R171 to R259) or the HES maternity
124 tail. Multiple births, which were excluded, were defined as maternity episodes with an ICD
125 code for a multiple birth (Z37.2–Z37.7) or strong evidence of a multiple birth in the maternity
126 tail (more than one distinct birthweight, birth order, and infant recorded in the same birth
127 episode). A neonatal episode was defined as any record that contained a newborn, defined
128 as being less than one day of age at episode onset. Maternal and neonatal episodes were
129 linked using encrypted versions of the mother's and infant's NHS number (a unique national
130 identifier for each individual NHS user, assigned at birth)¹⁶, available in the NHS Birth

131 Notifications data. These data also contained additional information on the birth such as
132 gestational age and birthweight.^{15,17}

133 A woman was classified as having laboratory-confirmed SARS-CoV-2 infection at the time of
134 birth if the ICD-10 code “COVID-19, virus identified” (U07.1) was recorded in the birth
135 episode.¹⁸ The test used to confirm infection in NHS hospital admissions is a nasal/throat
136 swab examined using PCR.¹¹

137 The study outcomes derived for the cohort identified by the maternity episode included fetal
138 death at or beyond 24 weeks’ gestation (stillbirth), preterm birth (less than 37 weeks,
139 liveborn or stillborn), small for gestational age at birth (SGA; defined as birthweight <10th
140 centile using UK-WHO paediatric growth charts¹⁹), maternal diagnosis with preeclampsia or
141 eclampsia, induction of labor, mode of birth (unassisted vaginal delivery, instrumental
142 vaginal delivery, elective Cesarean delivery and emergency Cesarean delivery), maternal
143 length of stay (three or more days) and 42-day readmission. The study outcomes derived for
144 the linked maternal-neonatal cohort included the provision of specialist neonatal care,
145 neonatal length of stay (three or more days), 28-day readmission and a composite neonatal
146 adverse outcome indicator (E-NAOI), which includes 16 diagnoses and 7 procedures and
147 has previously been validated in HES.²⁰ The definitions and coding of all study outcomes are
148 specified in Supplementary Table 1. This dataset does not contain sufficient information to
149 distinguish between antepartum and intrapartum fetal death (stillbirth); in England in 2018
150 (the latest date for which this information is available), nine in every ten stillbirths were
151 antepartum.²¹

152 Maternal age was grouped into five-year periods, with women under 20 and over 40 years
153 being aggregated into single categories. Parity was defined using records of previous births
154 through a ‘look-back’ approach in HES, and handled in three categories: primiparous,
155 multiparous without previous Cesarean delivery, and multiparous with previous Cesarean
156 delivery.^{22,23} Maternal ethnicity was coded using the Office for National Statistics
157 categorization system from the 2001 Census and collapsed into four groups: White, South

158 Asian, Black, and Other Stated. Information about pre-existing diabetes and hypertension
159 was available in the diagnosis codes attached to the birth episode, with women assumed not
160 to have the condition if the code was not present. Index of Multiple Deprivation 2019 (IMD)
161 provides an overall measure of multiple deprivation derived from information about income,
162 education, employment, crime, and the living environment. IMD rankings of 32,844 “Lower
163 Super Output Areas”, with typically 1,500 inhabitants, were used to categorize women into
164 five socioeconomic groups.²⁴

165 *Statistical analysis*

166 Characteristics of women in the cohort with and without laboratory-confirmed SARS-CoV-2
167 infection at the time of birth were tabulated. Rates of maternal and perinatal outcomes were
168 calculated in women with and without laboratory-confirmed SARS-CoV-2 infection at the
169 time of birth. Adjusted odds ratios (aOR) and their 95% confidence interval (CI) for the
170 association between SARS-CoV-2 infection status and outcomes were calculated using
171 logistic regression, adjusting for maternal age, ethnicity, parity, pre-existing diabetes, pre-
172 existing hypertension and socioeconomic deprivation measured using IMD. Models were
173 fitted with robust standard errors to account for hospital-level clustering. The analysis of the
174 neonatal outcomes was repeated for those born at term (at or beyond 37 weeks’ gestation)
175 since preterm birth has been reported to be more common in pregnant women with SARS-
176 CoV-2 infection.

177 Data were complete for all variables except maternal ethnicity (89.1% complete) and IMD
178 (99.4% complete). For regression analyses, missing values of ethnicity and IMD were
179 imputed using chained equations to generate 10 datasets; estimates from these datasets
180 were pooled using Rubin’s rules.²⁵ Stata 16 was used for all analyses. A P value of less than
181 0.05 was assumed to represent statistical significance.

182 *Ethical approval*

183 This study used data collected to evaluate service provision and performance and therefore
184 was exempt from ethical review by the NHS Health Research Authority. The use of personal
185 data without individual consent was approved by the NHS Health Research Authority
186 (16/CAG/0058).

187

188 **RESULTS**

189 The analysis included 342,080 women with singleton pregnancy who gave birth in England
190 between 29th May 2020 and 31st January 2021, of whom 3,527 (10.3 per 1000) were
191 recorded as having laboratory-confirmed SARS-CoV-2 infection (Figure 1, Table 1).
192 Laboratory-confirmed SARS-CoV-2 infection was more likely in younger women, women
193 from non-white ethnicity, those with pre-existing diabetes, pre-existing hypertension and
194 women residing in the most socioeconomically deprived areas (Table 1).

195 Table 2 shows that fetal death was significantly more common in women with laboratory-
196 confirmed SARS-CoV-2 infection at the time of birth (30/3,527 or 8.5 per 1000) than in those
197 without (1,140/338,553 or 3.4 per 1000; aOR, 2.21, 95% CI 1.58-3.11; $P < 0.001$). There was
198 also a significant increase in the risk of preterm birth (5.8% in women without laboratory-
199 confirmed SARS-CoV-2 infection; 12.1% in those with, aOR 2.17, 95% CI 1.96-2.42;
200 $P < 0.001$). Women with laboratory-confirmed SARS-CoV-2 infection were at increased risk
201 of preeclampsia/eclampsia (3.9% compared to 2.5%, aOR 1.55, 95% CI 1.29-1.85; $P < 0.001$)
202 and emergency Cesarean delivery (27.6% compared to 18.5%, aOR 1.63, 95% CI 1.51-
203 1.76; $P < 0.001$), with a corresponding reduction in the rate of spontaneous vaginal delivery
204 (49.2% compared to 54.6% in women without laboratory-confirmed SARS-CoV-2 infection,
205 aOR 0.80, 95% CI 0.75 to 0.86). Rates of elective Cesarean delivery (10.8% compared to
206 13.8%, aOR 0.81, 95% CI 0.71-0.91; $P < 0.001$) were lower in women with laboratory-
207 confirmed SARS-CoV-2 infection than in those without. Following birth, women with SARS-
208 CoV-2 infection were at increased risk of hospital admission lasting three days or more

209 (25.8% compared to 17.0%, aOR 1.57, 95% CI 1.44-1.72; $P < 0.001$) and readmission within
210 six weeks after birth (4.3% compared to 3.1%, aOR 1.39, 95% CI 1.10-1.76; $P = 0.01$) than
211 those without. No significant differences were seen in the rates of SGA ($P = 0.87$), induction
212 of labor ($P = 0.40$) or instrumental vaginal delivery ($P = 0.20$).

213 Of the 342,080 maternity records, 330,057 (96.5%) were linked to the neonatal record
214 (Figure 1). Risk of neonatal adverse outcome (aOR 1.45, 95% CI 1.27-1.66; $P < 0.001$), need
215 for specialist neonatal care (aOR 1.24, 95% CI 1.02-1.51; $P = 0.03$), and prolonged neonatal
216 admission following birth (aOR 1.61, 95% CI 1.49-1.75; $P < 0.001$) were all significantly higher
217 for infants with mothers with laboratory-confirmed SARS-CoV-2 infection compared to those
218 without (Table 2). When the analysis was restricted to pregnancies delivered at term (≥ 37
219 weeks), there were no significant differences in neonatal adverse outcome ($P = 0.78$), need
220 for specialist neonatal care after birth ($P = 0.22$) or neonatal readmission within four weeks of
221 birth ($P = 0.05$) (Table 2). Term infants born to mothers with laboratory-confirmed SARS-CoV-
222 2 infection had prolonged admission following birth (21.1% compared to 14.6%, aOR 1.61,
223 95% CI 1.49-1.75; $P < 0.001$) (Table 2).

224

225 **COMMENT**

226 *Principal findings*

227 In this population-based study of women giving birth to a singleton infant in England in 2020-
228 2021, we report that women with a record of laboratory-confirmed SARS-CoV-2 infection at
229 the time of birth were more than twice as likely as women without SARS-CoV-2 infection to
230 have fetal death or preterm birth. Women with SARS-CoV-2 infection were also more likely
231 to have preeclampsia and to give birth by emergency Cesarean delivery. Both women and
232 their neonates were more likely to have prolonged hospital stay of three days or more, and
233 mothers were more likely to be readmitted to hospital in the postnatal period. There was no
234 significant difference in rates of induction of labor, instrumental vaginal delivery or SGA

235 between women who did and did not have SARS-CoV-2 infection at the time of birth. The
236 composite neonatal adverse outcome and specialist neonatal care were significantly higher
237 in pregnancies with SARS-CoV-2 infection at the time of birth. However, when the analysis
238 was restricted to term deliveries, neonatal outcomes were similar for those born to mothers
239 with and without SARS-CoV-2 infection.

240 *Results in the Context of What is Known*

241 Our findings concur with those of an ongoing living systematic review which estimates the
242 pooled association between COVID-19 and fetal death at OR 2.84 (95% CI 1.25 to 6.45);¹
243 with a more recent multinational case-control study which reports an association between
244 COVID-19 and a composite neonatal adverse outcome of RR 2.14 (95% CI 1.66 to 2.75⁴);
245 and with a recent population level study reporting an increase in adverse neonatal outcomes
246 for infants born to women with COVID-19 infection.⁹ However, the systematic review is
247 limited by the size and number of studies available, with only nine women experiencing a
248 stillbirth in the COVID-19 group of the pooled dataset;¹ and the case-control study was
249 unable to report on fetal death alone, instead incorporating it into an adverse outcome
250 including intrauterine or neonatal death, prolonged neonatal stay, or severe neonatal
251 morbidity.⁴ In the population-level study, as in our study, almost all of the association
252 between maternal COVID-19 infection and adverse neonatal outcome was explained by
253 increased risk of preterm birth.⁹ In our study we were not able to stratify preterm birth into
254 spontaneous and indicated/iatrogenic (where birth is initiated by the clinician); other studies
255 have suggested that the increase in preterm birth is due to indicated delivery to improve
256 maternal condition.¹

257 The key potential bias in our study comes from misclassification of the exposure; this could
258 be caused by selective testing (whether the chance of a woman having been tested for
259 SARS-CoV-2 was dependent on her pregnancy outcome), selective recording (whether the
260 chance of a woman who tested positive had that result recorded in HES was dependent on

261 her pregnancy outcome) or missed cases (women who had SARS-CoV-2 infection but were
262 not recorded as such).

263 It is unlikely that either selective testing or recording fully explain our results. First,
264 throughout the pandemic there was a statutory requirement to report cases of SARS-CoV-2
265 infection in healthcare settings.²⁶ Second, the laboratory-confirmed SARS-CoV-2 infection
266 rate of 1.96% between 1st October 2020 and 31st January 2021 (when national data is
267 available and could be compared) which we observed in all women giving birth in this period
268 is very close to the SARS-CoV-2 infection rate of 1.74% (and within the credible intervals of
269 1.53% to 1.98%) reported for people between 25 and 35 years old by the Office for National
270 Statistics (ONS) for the period 3rd October 2020 to 22nd January 2021 based on a routine
271 national survey of households;²⁷ this provides evidence that universal testing of maternity
272 admissions was fully implemented during this period.²⁸ The slightly higher rate may be
273 attributed to women of childbearing age likely to be living with children and to be required to
274 leave the house to interact with healthcare providers.²⁹

275 These results provide further evidence that SARS-CoV-2 infection increases the risk of fetal
276 death. The potential mechanisms may be pregnancy-specific, including placental disease
277 with reports of abnormal inflammation of the placenta in association with maternal COVID-
278 19.^{30,31} However, the association may also be a more generic consequence of severe
279 maternal illness in pregnancy, given that women who become seriously unwell with other
280 illnesses are known to be at higher risk of perinatal morbidity and mortality.³²

281 Our findings related to the characteristics of women infected with SARS-CoV-2, and
282 associations with other complications including preeclampsia, preterm birth, Cesarean
283 delivery and adverse neonatal outcomes concur with other studies in the UK and
284 internationally.^{1,4} Our results regarding length of stay and maternal readmissions are novel,
285 but also relate to the context of care in England, where much of postnatal maternity care is
286 provided in the community.²⁸

287

288 *Clinical and research implications*

289 The finding that women with a recorded SARS-CoV-2 infection at the time of birth may have
290 an increased risk of fetal death and other adverse maternal and perinatal outcomes concurs
291 with a recent international case-control study⁴ and will be of particular concern to pregnant
292 women and healthcare professionals. The overall numbers of fetal deaths are too small to
293 impact the overall national rate of stillbirth in the UK, as seen in provisional national reports
294 for 2020.³³ It is therefore important to carefully contextualise these findings when counselling
295 pregnant women.

296 However, this finding should prompt reflection on the treatment of pregnant women infected
297 with SARS-CoV-2, as well as the relative risks and benefits of vaccination. For pregnant
298 women who test positive for SARS-CoV-2 in the later stages of pregnancy, care should
299 consider the wellbeing of the baby. At term, acknowledgement of the increased risk of fetal
300 death may prompt discussion of the potential risks of ongoing expectant management of
301 pregnancy, and consideration of an earlier planned birth.

302 For women earlier in pregnancy, our findings may change the risk-benefit analysis for
303 vaccination. At present, data on the safety and efficacy of COVID-19 vaccination in
304 pregnancy are limited due to the exclusion of pregnant women in clinical trials,³⁴ although
305 trials are now underway to address this urgent need. This has motivated widespread
306 hesitancy about recommendation of vaccination to all pregnant women, with governments
307 and professional organizations initially recommending offering vaccination to pregnant
308 women at high risk of either occupational exposure or severe disease³⁵ and pregnant
309 women reluctant to take up a vaccine offer.³⁶ In the USA and Israel, where vaccination has
310 been recommended to those at higher risk, initial data provide a positive signal of safety and
311 efficacy in pregnant women.³⁷⁻³⁹ Further evidence of a link between SARS-CoV-2 infection

312 and an increased risk of fetal death may motivate prioritization of, and encourage pregnant
313 women to access, vaccination.

314

315 *Strengths and limitations*

316 The main strengths of this study are its large size and representative nature, covering almost
317 the entire population of births in England during the time period. The use of HES data to
318 understand maternity outcomes is well established and offers rich information about
319 individual women to allow for adjustment for individual risk.²³

320 The principal exposure of SARS-CoV-2 infection is defined using an ICD-10 code recorded if
321 the woman had a laboratory-confirmed infection. The use of ICD-10 codes in this way to
322 understand differences between admissions with and without SARS-CoV-2 infection has
323 been established elsewhere.^{9,40}

324 The use of administrative data including diagnostic and procedure codes to establish
325 exposures and outcomes (including in our study pre-eclampsia, neonatal adverse outcome,
326 and SARS-CoV-2 status) has inherent limitations as the primary purpose of data recording is
327 for payment rather than clinical research; known limitations include under-recording and
328 misclassification.⁴¹ This may particularly affect pre-eclampsia where there is variation in
329 diagnostic criteria and thresholds; gestational hypertension may be conflated with pre-
330 eclampsia.⁴²

331 While in our study we were able to adjust for many potential confounders, we had no
332 information on the severity of COVID-19 illness or maternal body mass index (BMI) in our
333 dataset. Maternal obesity is a risk factor for both severe COVID-19 and fetal death.^{1,43} It is
334 therefore possible that the observed association could be partially accounted for by
335 differences between groups of women.

336 Our results should be strictly interpreted as being related to the result of a test for SARS-
337 CoV-2 at the time of birth, rather than to any infection which occurred during pregnancy. This
338 is an important feature given that some of the observations in women who tested positive for
339 SARS-CoV-2, especially the increases in risk of stillbirth and preterm birth in women with a
340 positive test, may be partly explained by variations in the rate of SARS-CoV-2 infection
341 according to gestational age. This is different from other studies which seek to understand
342 effects on women who are infected with SARS-CoV-2 at any point during their pregnancy,
343 and from studies which assess population risks of fetal death measuring both direct and
344 indirect effects.⁴⁴⁻⁴⁶

345 *Conclusions*

346 Our results demonstrate that women who have laboratory-confirmed infection with SARS-
347 CoV-2 at the time of birth have higher rates of fetal death and preterm birth, preeclampsia
348 and emergency Cesarean delivery, as well as prolonged maternal and neonatal admission
349 following birth, compared to those without SARS-CoV-2 infection. There were no additional
350 adverse neonatal outcomes, other than those related to preterm delivery. These findings
351 should guide the counselling of pregnant women about risks of SARS-COV-2 infection
352 during pregnancy and indicate that pregnant women should be prioritized for vaccination.

353

354

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356

357 *Author contributions:* IGU, JJ, JvdM, AK conceived and designed the study. IGU performed
358 the analysis. All authors interpreted the data. JJ wrote the first draft of the manuscript with
359 supervision from JvdM and AK. IGU and JJ had full access to all the data in the study and
360 take responsibility for the integrity of the data and the accuracy of the data analysis. All
361 authors revised the paper critically for important intellectual content and provided final
362 approval of the submitted manuscript.

363

Journal Pre-proof

364 **Table 1.** Characteristics and study outcomes of women included in the study

	Pregnant women without laboratory-confirmed SARS-CoV-2 infection at the time of birth n (%)	Pregnant women with laboratory-confirmed SARS-CoV-2 infection at the time of birth n (%)	P-value (Chi2 test)
Number of births	338553 (100)	3527 (100)	
Maternal age in years			<0.001
≤19	8907 (2.6)	94 (2.7)	
20-24	44755 (13.2)	581 (16.5)	
25-29	93051 (27.5)	1040 (29.5)	
30-34	114639 (33.9)	1079 (30.6)	
35-39	62451 (18.5)	587 (16.6)	
40+	14750 (4.4)	146 (4.1)	
Maternal ethnicity*			<0.001
White	230202 (76.3)	1857 (58.5)	
South Asian	36834 (12.2)	768 (24.2)	
Black	13998 (4.6)	251 (7.9)	
Other	20546 (6.8)	298 (9.4)	
Obstetric history			0.13
Primiparous	142289 (42.0)	1514 (42.9)	
Multiparous with no previous CS [†]	156269 (46.2)	1634 (46.3)	
Multiparous with previous CS [†]	39995 (11.8)	379 (10.8)	
Pre-existing diabetes	3112 (0.9)	58 (1.6)	<0.001
Pre-existing hypertension	2624 (0.8)	44 (1.3)	0.002
Index of Multiple Deprivation*			<0.001
1= least deprived	50814 (15.1)	342 (9.8)	
2	57892 (17.2)	413 (11.8)	
3	65104 (19.3)	602 (17.2)	
4	75159 (22.3)	874 (25.0)	
5 = most deprived	87703 (26.1)	1265 (36.2)	
* ethnicity missing in 37326 (10.9%) of records, IMD missing in 1912 (0.6%) of records; % may not add to 100 due to rounding. [†] Cesarean section			

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Table 2. Comparison of study outcomes between pregnant women with and without laboratory-confirmed SARS-CoV-2 infection (ICD-10 U07.1) at the time of birth

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	Pregnant women without SARS-CoV-2 infection		Pregnant women with laboratory-confirmed SARS-CoV-2 infection		Unadjusted OR (95% CI)	P value	Adjusted OR‡ (95% CI)	P value
	cases/births	%	cases/births	%				
Maternal data								
Fetal death	1140/338553	0.34	30/3527	0.85	2.54 (1.81,3.56)	<0.001	2.21 (1.58,3.11)	<0.001
Preterm birth	18572/322494	5.8	369/3047	12.1	2.25 (2.03,2.50)	<0.001	2.17 (1.96,2.42)	<0.001
Small for gestational age	17521/320188	5.5	191/3009	6.4	1.17 (1.00,1.37)	0.05	0.99 (0.84,1.16)	0.87
Preeclampsia/eclampsia	8591/338553	2.5	139/3527	3.9	1.58 (1.32,1.89)	<0.001	1.55 (1.29,1.85)	<0.001
Induction of labor	96651/236822	40.8	940/2382	39.5	0.95 (0.82,1.08)	0.42	0.95 (0.83,1.08)	0.40
Elective Cesarean delivery	46843/338553	13.8	380/3527	10.8	0.75 (0.67,0.85)	<0.001	0.81 (0.71,0.91)	<0.001
Emergency Cesarean delivery	62479/338553	18.5	975/3527	27.6	1.69 (1.56,1.83)	<0.001	1.63 (1.51,1.76)	<0.001
Instrumental vaginal delivery	43393/338553	12.9	422/3527	12.0	0.92 (0.83,1.03)	0.14	0.93 (0.82,1.04)	0.20
Unassisted delivery	184989/338553	54.6	1734/3527	49.2	0.80 (0.75,0.86)	<0.001	0.76 (0.70,0.82)	<0.001
Maternal length of stay (3+days)	55529/326248	17.0	857/3321	25.8	1.70 (1.55,1.85)	<0.001	1.57 (1.44,1.72)	<0.001
Maternal readmission (42-day)	8660/281178	3.1	78/1818	4.3	1.41 (1.11,1.78)	0.004	1.39 (1.10,1.76)	0.01
Maternal-neonatal linked data								
Neonatal adverse outcome indicator (ENAOI)†	16501/318073	5.2	222/2922	7.6	1.50 (1.32,1.72)	<0.001	1.45 (1.27,1.66)	<0.001
Specialist neonatal care	35032/326901	10.7	432/3156	13.7	1.32 (1.04,1.67)	0.02	1.24 (1.02,1.51)	0.03
Neonatal length of stay (3+days)	58410/324665	18.0	857/3104	27.6	1.74 (1.62,1.87)	<0.001	1.61 (1.49,1.75)	<0.001
Neonatal readmission (28-day)	14259/277804	5.1	126/2058	6.1	1.21 (1.01,1.44)	0.04	1.18 (0.98,1.41)	0.08
Maternal-neonatal linked data of deliveries at term (≥ 37 weeks)								
Neonatal adverse outcome indicator (ENAOI)†	9970/298099	3.3	89/2542	3.5	1.05 (0.85,1.29)	0.45	1.03 (0.84,1.27)	0.78
Specialist neonatal care	28002/299456	9.4	294/2555	11.5	1.26 (0.92,1.73)	0.15	1.18 (0.90,1.55)	0.22
Neonatal length of stay (3+days)	43390/297805	14.6	534/2530	21.1	1.56 (1.42,1.74)	<0.001	1.61 (1.49,1.75)	<0.001
Neonatal readmission (28-day)	12749/262437	4.9	106/1802	5.9	1.22 (1.02,1.47)	0.03	1.20 (1.00,1.45)	0.05

†Composite outcome. Birth with any of: birthweight<1500g, gestational age under 32 completed weeks, neonatal death within 28 days, respiratory distress syndrome (RDS), seizure, intraventricular haemorrhage (grade 3 or 4), cerebral infarction, periventricular leukomalacia, birth trauma (intracranial haemorrhage paralysis due to brachial plexus injury, skull or long bone fracture), hypoxic ischaemic encephalopathy, necrotising enterocolitis, sepsis/septicaemia, pneumonia, respiratory disease (respiratory failure, primary atelectasis, chronic respiratory disease originating in the perinatal

period, bacterial meningitis, resuscitation (intubation/chest compression), mechanical ventilation/continuous positive airway pressure/high flow nasal oxygen, central venous or arterial catheter, pneumothorax requiring intracostal catheter, any intravenous fluids, any body cavity surgical procedure, therapeutic hypothermia
‡Adjusted for maternal age, ethnicity, socioeconomic deprivation measured by IMD, parity, previous Cesarean delivery, diabetes and hypertension

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Supplementary Table 1. Definitions of study outcomes and their coding in Hospital Episode Statistics (HES)

Outcome	Numerator / coding	Denominator / coding
Using maternal data:		
Stillbirth (fetal death)	Defined using ICD10 code (Z37.1) OR birth status field (birstat_1=2,3,4) in maternity tail for providers with over 95% data completeness. In the UK stillbirth is defined as birth without signs of life occurring at or after 24+0 completed gestational weeks, based on estimated due date calculated using universally offered ultrasound scan at 11-13 weeks' gestation.	All singleton births This dataset does not contain sufficient information to distinguish between antepartum and intrapartum stillbirth; in England in 2018 (the latest date for which this information is available), nine in every ten stillbirths were antepartum. ¹
Preterm birth	Defined using gestational age field in HES maternity tail (gestat_1<37)	All singleton births, excluding records missing information on gestational age
Small-for-gestational age	Defined as less than the 10 th birthweight centile using the WHO-UK charts. ² Birthweight centiles are calculated using birthweight (birweit_1), gestational age (gestat_1), sex of baby (sexbaby_1) fields in maternity tail	All singleton births, excluding records missing information on gestational age, birthweight or sex of baby
Preeclampsia/eclampsia	Defined using the ICD-10 codes O14 (preeclampsia) and O15 (eclampsia).	All singleton births
Induction of labor	Defined using the delivery onset field (delonset=3,4,5) from the maternity tail. Failed induction (ICD-10 code O61) is also included in the numerator as this represents intention to treat.	All singleton births, excluding elective Cesarean section; and records missing information on delivery onset
Elective Cesarean delivery	ELC is defined using OPCS code R17	All singleton births
Emergency Cesarean delivery	EMCS is defined using OPCS codes R18/R25.1	All singleton births
Instrumental delivery	Instrumental birth is defined using OPCS codes R21/R22	All singleton births
Unassisted delivery	Unassisted birth is defined using OPCS code R23/R24	All singleton births
Maternal length of stay post birth (3 or more days)	Length of stay is defined as the number of days between date of discharge and date of admission for the birth episode.	All singleton births with non-missing date of discharge information and date of delivery before 28 th January 2021 (to allow for 3-day follow up)
Maternal readmission (42-days)	Maternal readmission is defined as unplanned, overnight readmission to hospital within 42 days of giving birth, excluding those accompanying an unwell baby. Mothers readmitted with the following admission method codes: 21, 22, 23, 24, 28, 2A, 2B, 2D, 31, 32, 82, 83	All singleton births with non-missing date of discharge information and date of delivery before 19 th December 2020 (to allow for six-week follow up). Women who died before discharge or were not discharged within 42 days of delivery were excluded.

¹ Draper ES, Gallimore ID, Smith LK, Fenton AC, Kurinczuk JJ, Smith PW, Bobby T, Manktelow BN, on behalf of the MBRRACE-UK Collaboration. MBRRACE-UK Perinatal Mortality Surveillance Report, UK Perinatal Deaths for Births from January to December 2018. Leicester: The Infant Mortality and Morbidity Studies, Department of Health Sciences, University of Leicester. 2020.

² Cole TJ, Williams AF, Wright CM. Revised birth centiles for weight, length and head circumference in the UK-WHO growth charts. *Ann Hum Biol.* 2010;38(1):7-11. doi:10.3109/03014460.2011.544139

Outcome	Numerator / coding	Denominator / coding
Using maternal-neonatal linked data:		
Neonatal specialist care	Neonatal specialist care is defined using the "neocare" variable in HES, and includes values 1=Special care: care given in a special nursery, transitional care ward or postnatal ward, which provides care and treatment exceeding normal routine care; 2 = Level 2 intensive care (high dependency intensive care); and 3 = Level 1 intensive care (maximal intensive care)	All singleton, term births with non-missing information on neonatal specialist care
Neonatal adverse outcome indicator (ENAOI)	ENAOI is defined as births with any of the following outcomes: birthweight<1500g, gestational age under 32 completed weeks, neonatal death within 28 days, respiratory distress syndrome (RDS), seizure, intraventricular haemorrhage (grade 3 or 4), cerebral infarction, periventricular leukomalacia, birth trauma (intracranial haemorrhage paralysis due to brachial plexus injury, skull or long bone fracture), hypoxic ischaemic encephalopathy, necrotising enterocolitis, sepsis/septicaemia, pneumonia, respiratory disease (respiratory failure, primary atelectasis, chronic respiratory disease originating in the perinatal period, bacterial meningitis, resuscitation (intubation/chest compression), mechanical ventilation/CPAP/high flow nasal oxygen, central venous or arterial catheter, pneumothorax requiring intracostal catheter, any intravenous fluids, any body cavity surgical procedure, therapeutic hypothermia. Coding of these diagnoses and procedures can be found in Knight et al 2018, Supplementary Table 1.	All liveborn singleton term births with non-missing information on gestational age and birthweight
Neonatal length of stay post birth (3 or more days)	Length of stay is defined as the number of days between date of discharge and date of admission for the birth episode.	All singleton births with non-missing date of discharge information and date of birth before 28 th January 2021 (to allow for 3-day follow up)
Neonatal readmission (28-days)	Neonatal readmission is defined as unplanned, overnight readmission to hospital within 28 days of birth, excluding those accompanying an unwell mother. Babies readmitted with the following admission method codes: 21, 22, 23, 24, 28, 2A, 2B, 2D, 31, 32, 82, 83 within 28 days of birth.	All singleton neonates with non-missing date of discharge information and date of birth before 3 rd January 2021 (to allow for four-week follow up). Babies who died before discharge or were not discharged within 28 days of birth were excluded.

FIGURE LEGEND

Figure 1. Study flowchart

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REFERENCES

1. Allotey J, Stallings E, Bonet M, 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. doi:10.1136/bmj.m3320
2. DeBolt CA, Bianco A, Limaye MA, et al. Pregnant women with severe or critical COVID-19 have increased composite morbidity compared to non-pregnant matched controls. *Am J Obstet Gynecol*. Published online 2020. doi:10.1016/j.ajog.2020.11.022
3. Hantoushzadeh S, Shamsirsaz AA, Aleyasin A, et al. Maternal death due to COVID-19. *Am J Obstet Gynecol*. 2020;223(1):109.e1-109.e16. doi:10.1016/j.ajog.2020.04.030
4. Villar J, Ariff S, Gunier RB, et al. Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection. *Jama Pediatr*. 2021;175(8). doi:10.1001/jamapediatrics.2021.1050
5. Vousden N, Bunch K, Morris E, 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). Published online n.d. doi:10.1101/2021.01.04.21249195
6. Mullins E, Hudak ML, Banerjee J, et al. Pregnancy and neonatal outcomes of COVID-19: co-reporting of common outcomes from PAN-COVID and AAP SONPM registries. *Ultrasound Obst Gyn*. Published online 2021. doi:10.1002/uog.23619
7. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature*. Published online 2020:1-7. doi:10.1038/s41586-020-2521-4
8. Gale C, Quigley MA, Placzek A, 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 Heal*. Published online 2020. doi:10.1016/s2352-4642(20)30342-4
9. Norman M, Navér L, Söderling J, et al. Association of Maternal SARS-CoV-2 Infection in Pregnancy With Neonatal Outcomes. *Jama*. 2021;325(20). doi:10.1001/jama.2021.5775
10. RCOG. Principles for the testing and triage of women seeking maternity care in hospital settings, during the COVID-19 pandemic. Published May 29, 2020. Accessed March 21, 2021. <https://www.rcog.org.uk/globalassets/documents/guidelines/2020-05-29-principles-for-the-testing-and-triage-of-women-seeking-maternity-care-in-hospital-settings-during-the-covid-19-pandemic.pdf>
11. Public Health England. Healthcare associated COVID-19 infections: further action. Published May 30, 2020. Accessed March 24, 2021.

<https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/06/Healthcare-associated-COVID-19-infections--further-action-24-June-2020.pdf>

12. World Health Organization. International Statistical Classification of Diseases and Related Health Problems 10th Revision. Published 2016.

<https://icd.who.int/browse10/2016/en>

13. OPCS Classification of Interventions and Procedures (OPCS-4). Accessed March 1, 2021.

https://www.datadictionary.nhs.uk/web_site_content/supporting_information/clinical_coding/opcs_classification_of_interventions_and_procedures.asp

14. Burns EM, Rigby E, Mamidanna R, et al. Systematic review of discharge coding accuracy. *J Public Health*. 2012;34(1):138-148. doi:10.1093/pubmed/fdr054

15. Provisional births in England and Wales - Office for National Statistics. Published 2021. Accessed March 21, 2021.

<https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/articles/provisionalbirthsinenglandandwales/2020#:~:text=Based%20on%20birth%20notification%20data,most%20recent%20peak%20in%202012.>

16. NHS Digital. What is an NHS number? Accessed April 28, 2021.

<https://www.nhs.uk/using-the-nhs/about-the-nhs/what-is-an-nhs-number/>

17. NHS Digital. Birth notification service. Accessed May 1, 2021.

<https://digital.nhs.uk/services/birth-notification-service>

18. World Health Organization. Emergency use ICD codes for COVID-19 disease outbreak. Accessed March 21, 2021. <https://www.who.int/standards/classifications/classification-of-diseases/emergency-use-icd-codes-for-covid-19-disease-outbreak>

19. Cole TJ, Williams AF, Wright CM. Revised birth centiles for weight, length and head circumference in the UK-WHO growth charts. *Ann Hum Biol*. 2010;38(1):7-11. doi:10.3109/03014460.2011.544139

20. Knight HE, Oddie SJ, Harron KL, et al. Establishing a composite neonatal adverse outcome indicator using English hospital administrative data. *Archives Dis Child - Fetal Neonatal Ed*. Published online 2018:fetalneonatal-2018-315147. doi:10.1136/archdischild-2018-315147

21. Draper ES, Gallimore ID, Smith LK, et al. *MBRRACE-UK Perinatal Mortality Surveillance Report, UK Perinatal Deaths for Births from January to December 2018.*; 2020. https://www.npeu.ox.ac.uk/assets/downloads/mbrance-uk/reports/perinatal-surveillance-report-2018/MBRRACE-UK_Perinatal_Surveillance_Report_2018_-_final_v2.pdf

22. Cromwell DA, Knight HE, Gurol-Urganci I. Parity derived for pregnant women using historical administrative hospital data: Accuracy varied among patient groups. *J Clin Epidemiol*. 2014;67(5):578-585. doi:10.1016/j.jclinepi.2013.10.011

23. Knight H, Gurol- Urganci I, Meulen J, et al. Vaginal birth after caesarean section: a cohort study investigating factors associated with its uptake and success. *Bjog Int J Obstetrics Gynaecol.* 2014;121(2):183-192. doi:10.1111/1471-0528.12508
24. Department for Community and Local Government. *The English Indices of Deprivation 2015 Statistical Release.*; 2015. <https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015>
25. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med.* 2011;30(4):377-399. doi:10.1002/sim.4067
26. COVID-19: infection prevention and control. Published n.d. Accessed March 24, 2021. <https://www.gov.uk/government/publications/wuhan-novel-coronavirus-infection-prevention-and-control>
27. Coronavirus (COVID-19) infections in the community in England - Office for National Statistics. Published n.d. Accessed March 26, 2021. <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/coronaviruscovid19infectionsinthecommunityinengland>
28. RCOG COVID-19 Guidance Cell. Coronavirus infection in pregnancy. Version 13. Published Feb 19, 2021. <https://www.rcog.org.uk/en/guidelines-research-services/guidelines/coronavirus-pregnancy/>
29. Forbes H, Morton CE, Bacon S, et al. Association between living with children and outcomes from covid-19: OpenSAFELY cohort study of 12 million adults in England. *Bmj.* 2021;372:n628. doi:10.1136/bmj.n628
30. Schwartz DA, Baldewijns M, Benachi A, et al. Chronic Histiocytic Intervillositis with Trophoblast Necrosis are Risk Factors Associated with Placental Infection from Coronavirus Disease 2019 (COVID-19) and Intrauterine Maternal-Fetal Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Transmission in Liveborn and Stillborn Infants. *Arch Pathol Lab Med.* Published online 2020. doi:10.5858/arpa.2020-0771-sa
31. Patberg ET, Adams T, Rekawek P, et al. Coronavirus disease 2019 infection and placental histopathology in women delivering at term. *Am J Obstet Gynecol.* 2021;224(4):382.e1-382.e18. doi:10.1016/j.ajog.2020.10.020
32. Mengistu TS, Turner JM, Flatley C, Fox J, Kumar S. The Impact of Severe Maternal Morbidity on Perinatal Outcomes in High Income Countries: Systematic Review and Meta-Analysis. *J Clin Medicine.* 2020;9(7):2035. doi:10.3390/jcm9072035
33. Shimabukuro TT, Kim SY, Myers TR, et al., on behalf of the CDC v-safe COVID-19 Pregnancy Registry Team. Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. *N Engl J Med* 2021;Apr 21
34. Dashraath P, Nielsen-Saines K, Madhi SA, Baud D. COVID-19 vaccines and neglected pregnancy. *Lancet.* 2020;396(10252):e22. doi:10.1016/s0140-6736(20)31822-5

35. Kalafat E, O'Brien P, Heath PT, et al. Benefits and potential harms of COVID- 19 vaccination during pregnancy: evidence summary for patient counseling. *Ultrasound Obst Gyn*. Published online 2021. doi:10.1002/uog.23631
36. Battarbee AN, Stockwell MS, Varner M, et al. Attitudes toward COVID-19 illness and COVID-19 vaccination among pregnant women: a cross-sectional multicenter study during August-December 2020. *Medrxiv*. Published online 2021:2021.03.26.21254402. doi:10.1101/2021.03.26.21254402
37. Gray KJ, Bordt EA, Atyeo C, et al. COVID-19 vaccine response in pregnant and lactating women: a cohort study. *Am J Obstet Gynecol*. Published online 2021. doi:10.1016/j.ajog.2021.03.023
38. Shimabukuro TT, Kim SY, Myers TR, et al. Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. *New Engl J Med*. Published online 2021. doi:10.1056/nejmoa2104983
39. Perl SH, Uzan-Yulzari A, Klainer H, et al. SARS-CoV-2–Specific Antibodies in Breast Milk After COVID-19 Vaccination of Breastfeeding Women. *Jama*. 2021;325(19). doi:10.1001/jama.2021.5782
40. Jones SJ, Mason N, Palser T, Swift S, Petrilli CM, Horwitz LI. Trends in Risk-Adjusted 28-Day Mortality Rates for Patients Hospitalized with COVID-19 in England. *Journal of Hospital Medicine*. Published online February 5, 2021. doi:10.12788/jhm.3599
41. Coster CD, Quan H, Finlayson A, et al. Identifying priorities in methodological research using ICD-9-CM and ICD-10 administrative data: report from an international consortium. *BMC Health Serv Res*. 2006;6(1):77. doi:10.1186/1472-6963-6-77
42. Stepan H, Hund M, Andrzejek T. Combining Biomarkers to Predict Pregnancy Complications and Redefine Preeclampsia. *Hypertension*. 2020;75(4):918-926. doi:10.1161/hypertensionaha.119.13763
43. Chu SY, Kim SY, Lau J, et al. Maternal obesity and risk of stillbirth: a metaanalysis. *Am J Obstet Gynecol*. 2007;197(3):223-228. doi:10.1016/j.ajog.2007.03.027
44. Pasternak B, Neovius M, Söderling J, et al. Preterm Birth and Stillbirth During the COVID-19 Pandemic in Sweden: A Nationwide Cohort Study. *Ann Intern Med*. Published online 2021. doi:10.7326/m20-6367
45. Handley SC, Mullin AM, Elovitz MA, et al. Changes in Preterm Birth Phenotypes and Stillbirth at 2 Philadelphia Hospitals During the SARS-CoV-2 Pandemic, March-June 2020. *Jama*. 2021;325(1):87-89. doi:10.1001/jama.2020.20991
46. Khalil A, Dadelszen P von, Draycott T, Ugwumadu A, O'Brien P, Magee L. Change in the Incidence of Stillbirth and Preterm Delivery During the COVID-19 Pandemic. *Jama*. 2020;324(7). doi:10.1001/jama.2020.12746

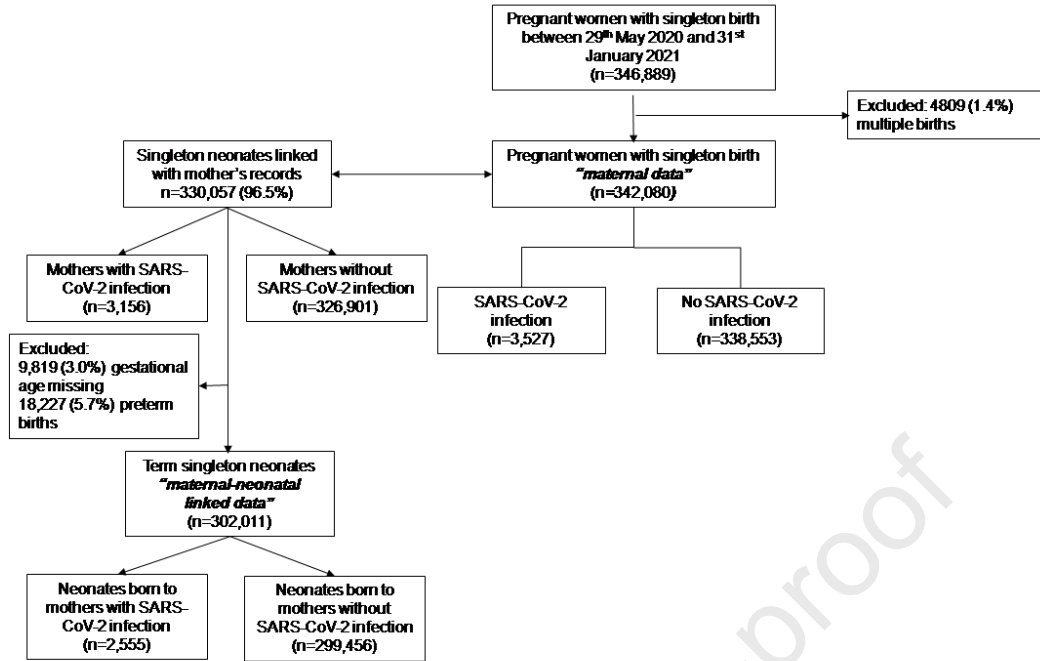


Figure 1