Effects of the SARS-CoV-2 pandemic on perinatal activity in Yorkshire and the Humber region during 2020: an interrupted time series analysis

Andrei Scott Morgan, Charlotte Bradford, Hilary Farrow, Elizabeth S Draper, Cath Harrison

ABSTRACT
Objective To assess the impact of public health measures taken during the COVID-19 pandemic on perinatal health indicators.

Design Interrupted time series analysis comparing periods of the pandemic with the previous 5 years.


Main outcome measures Relative risk (RR) of stillbirth, extreme preterm (EPT, <27 weeks’ gestational age) delivery, hypoxic ischaemic encephalopathy (HIE) and meconium aspiration syndrome (MAS), antenatal transfer for threatened EPT delivery and postnatal transfer for EPT birth, HIE or MAS.

Results Stillbirths fell from 3.7/1000 deliveries prepandemic to 2.9/1000 afterwards; EPT births decreased from 2.5/1000 to 1.8/1000 live births. Following adjustment, during the first lockdown there were decreased antenatal transfers (RR 0.74, 95% CI 0.57 to 0.94) with non-statistically significant increases overall stillbirth (RR 1.08, 95% CI 0.78 to 1.51) and decreased EPT admissions (RR 0.88, 95% CI 0.60 to 1.29). Over the entire pandemic period, antenatal transfer (RR 0.64, 95% CI 0.55 to 0.76) and EPT birth (RR 0.73, 95% CI 0.56 to 0.94) decreased; stillbirths showed non-statistically significant increases overall (RR 1.21, 95% CI 0.98 to 1.49) but with increasing trend through the pandemic (RR 1.11, 95% CI 1.00 to 1.22). No changes were seen for HIE, MAS, postnatal transfers or in subgroup analyses by ethnicity.

Conclusions Lower rates of antenatal transfer and extreme preterm birth were identified, alongside an apparent increase in stillbirth over time. The findings provide evidence that effects on perinatal activity related to the pandemic changed over time.

BACKGROUND
The appearance of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) led to extensive public health measures being taken around the world. Although SARS-CoV-2 did not appear to affect neonates or young children seriously, the societal impact of measures taken to contain spread led to substantial changes in behaviour, with increased home-working, manual workers in non-essential jobs furloughed and widespread fear about attending hospitals.

Early reports suggested there were decreased numbers of extremely preterm (EPT) babies live born, with a possible increase in stillbirths. Subsequent studies added weight to these suggestions, with a systematic review finding increased stillbirths (predominantly in low-income and middle-income countries) and a tendency towards decreased preterm birth (particularly in high-income countries). Most studies included compared the first few months following the implementation of public health measures with similar time periods in previous years; few published studies include longer time periods or take into account potential variation over time unrelated to the pandemic.

WHAT IS ALREADY KNOWN ON THIS TOPIC
⇒ Previous studies suggest there were decreased extremely preterm births during the first few months following the institution of pandemic public health measures in 2020.
⇒ Differences in the impact of the pandemic have been noted according to ethnicity.
⇒ The impact of the pandemic on antenatal or neonatal transfer and on morbidities in term-born infants is currently unclear.

WHAT THIS STUDY ADDS
⇒ During the pandemic, decreased rates of extremely preterm admission were accompanied by decreased rates of antenatal transfer for threatened preterm labour.
⇒ There were no differences in rates of hypoxic ischaemic encephalopathy, meconium aspiration syndrome or in postnatal emergency transfers.
⇒ No differences were identified by ethnicity, but there was an increase in the proportions of missing data during the pandemic.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND/OR POLICY
⇒ Public health measures are likely to have immediate and delayed effects; these should both be considered when developing policy to deal with unforeseen events.
⇒ In times of increased health service pressures, maintenance of high-quality data collection is critical for understanding differential effects on populations (eg, by ethnicity).
⇒ Future studies should investigate how perinatal activity changed over the course of the pandemic, including consideration of delayed impacts from public health interventions.

We sought to explore the impact of the pandemic and related public health measures on timing and place of birth by examining perinatal health indicators in a region of England taking into consideration underlying time trends. We examined antenatal transfer for EPT delivery and, as stillbirths may occur at term gestations, the term neonatal morbidities of meconium aspiration syndrome (MAS) and hypoxic ischaemic encephalopathy (HIE) as well as EPT birth and stillbirth. We also examined postnatal transfers for these conditions.

**METHODS**

**Data collection**

Data were collected on a weekly basis using statistical weeks (starting on Mondays) for the years 2015–2020; the first week began 29 December 2014 and the last week the 28 December 2020. The years 2015 and 2020 had 53 weeks, all others had 52 weeks.

**Obstetric data**

Stillbirth data are routinely collected by hospitals in the UK for inclusion in the national audit Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK, but delayed returns mean that data are not immediately available. Instead, the 13 National Health Service Trusts (including 16 acute hospitals) in the Yorkshire and the Humber region providing maternity services were contacted individually and asked to provide aggregated data on the total number of stillbirths, live births and of women delivering in their Trust, broken down by ethnicity using Office for National Statistics (ONS) categorisations. Weekly data were required for 2020. For historical data (2015–2019), some hospitals were unable to provide weekly data hence we accepted monthly or quarterly data; these were averaged over the intervening time periods to provide weekly estimates.

**Transport and neonatal data**

All hospitals in Yorkshire and the Humber region collect neonatal data for clinical care purposes using the BadgerNet system with real-time reporting available on a network-wide basis. Data were obtained for admissions of EPT (<27 weeks of gestational age (GA)) and for babies ≥36 weeks’ GA with HIE (defined as treatment with active hypothermia within 48 hours of birth) or MAS (defined as receiving inhaled nitric oxide treatment within 5 days of birth).

The Embrace Transport Service, which coordinates all antenatal and postnatal transfers, maintains a database of activity. We obtained data for transfers of women with threatened EPT delivery with singleton pregnancies of <27 weeks’ GA or multiple pregnancies of <28 weeks’ GA, in line with national recommendations.

Neonatal but not transport data were also available using the same ethnicity categorisations as the obstetric data.

**Exposure**

The primary exposure for this study was time, divided into the following periods:

1. Prepandemic period (all weeks prior to the implementation of public health measures in England, from the beginning of the study until the week beginning 16 March 2020).
2. The initial period of public health measures, or ‘first lockdown’, from 23 March to 14 June 2020.
3. The time between national lockdowns, when fewer restrictions were in place, from 15 June until the beginning of the second lockdown.
4. From the start of the second lockdown, for which the first complete week commenced 9 November 2020, until the end of the year.

**Outcomes**

We studied the rates of antenatal transfer (per 1000 women delivering), stillbirth (per 1000 births) and EPT, HIE and MAS transfers and admissions to neonatal intensive care (all per 1000 live births).

**Ethnicity**

Ethnicities were recategorised from standard ONS classification to white ethnicities combined.

**Missing data**

Data were imputed using the Kalman smoothing algorithm from the R package ‘imputeTS’.

**Sensitivity analyses**

All analyses were repeated using the available data only. Main analyses were also repeated using negative binomial regression models.

**RESULTS**

Complete obstetric data were obtained for 2017, 2018 and 2019; one Trust only moved to an electronic data collection system in April 2016 and could not provide data prior to this, another changed systems during 2015 and could not retrieve data from the old system and another experienced downtime during which no records were computerised. Antenatal and postnatal transfer...

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**Table 1 Ethnic categories**

<table>
<thead>
<tr>
<th>Category</th>
<th>ONS classifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian</td>
<td>Indian, Pakistani, Bangladeshi, other Asian, Chinese</td>
</tr>
<tr>
<td>Black</td>
<td>Black Caribbean, black African, black other</td>
</tr>
<tr>
<td>Mixed</td>
<td>Mixed white-black Caribbean, mixed white-black African, mixed white Asian, mixed other</td>
</tr>
<tr>
<td>Other</td>
<td>Any other, not known</td>
</tr>
<tr>
<td>White</td>
<td>White British, white Irish, white other</td>
</tr>
</tbody>
</table>

ONS, Office for National Statistics.
Table 2 Descriptive data (means (SD)) for perinatal activity indicators in Yorkshire and the Humber, 2015–2020

<table>
<thead>
<tr>
<th></th>
<th>Prepandemic</th>
<th>Lockdown 1</th>
<th>Between lockdown 1 and 2</th>
<th>Lockdown 2</th>
<th>Entire pandemic period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of women</td>
<td>1161.4 (56.9)</td>
<td>1074.3 (33.2)</td>
<td>1103.2 (30.4)</td>
<td>1006.2 (60.9)</td>
<td>1075.8 (52.7)</td>
</tr>
<tr>
<td>Number of deliveries</td>
<td>1192.8 (58.9)</td>
<td>1090.7 (35.0)</td>
<td>1117.0 (32.6)</td>
<td>1016.7 (60.0)</td>
<td>1089.8 (54.4)</td>
</tr>
<tr>
<td>Number of live births</td>
<td>1187.4 (58.3)</td>
<td>1086.6 (34.7)</td>
<td>1112.8 (31.9)</td>
<td>1011.8 (59.4)</td>
<td>1085.4 (54.2)</td>
</tr>
<tr>
<td>Number of stillbirths</td>
<td>4.9 (2.1)</td>
<td>3.6 (2.5)</td>
<td>3.7 (1.7)</td>
<td>3.5 (2.2)</td>
<td>3.6 (2.0)</td>
</tr>
<tr>
<td>Number of antenatal transfers</td>
<td>8.1 (3.1)</td>
<td>6.2 (2.8)</td>
<td>5.9 (2.7)</td>
<td>3.0 (2.3)</td>
<td>5.4 (2.9)</td>
</tr>
<tr>
<td>EPT admissions</td>
<td>3.1 (2.0)</td>
<td>2.8 (1.8)</td>
<td>1.9 (1.5)</td>
<td>2.6 (2.2)</td>
<td>2.3 (1.7)</td>
</tr>
<tr>
<td>HIE admissions</td>
<td>1.6 (1.3)</td>
<td>1.4 (0.9)</td>
<td>1.6 (1.2)</td>
<td>1.1 (1.1)</td>
<td>1.4 (1.1)</td>
</tr>
<tr>
<td>MAS admissions</td>
<td>0.7 (0.9)</td>
<td>0.6 (0.8)</td>
<td>1.0 (0.9)</td>
<td>0.5 (0.9)</td>
<td>0.8 (0.9)</td>
</tr>
<tr>
<td>EPT transfers</td>
<td>1.0 (0.9)</td>
<td>1.3 (1.1)</td>
<td>0.6 (0.7)</td>
<td>0.9 (1.1)</td>
<td>0.9 (0.9)</td>
</tr>
<tr>
<td>HIE transfers</td>
<td>0.6 (0.8)</td>
<td>0.6 (0.7)</td>
<td>0.7 (0.7)</td>
<td>0.2 (0.5)</td>
<td>0.6 (0.7)</td>
</tr>
<tr>
<td>MAS transfers</td>
<td>0.6 (0.9)</td>
<td>0.6 (0.7)</td>
<td>0.7 (0.9)</td>
<td>0.2 (0.7)</td>
<td>0.6 (0.8)</td>
</tr>
</tbody>
</table>

Prepandemic: 29 December 2014 to 22 March 2020; lockdown 1: 23 March 2020 to 14 June 2020; between lockdown 1 and 2: 15 June 2020 to 8 November 2020; lockdown 2: 9 November 2020 to 3 January 2021; entire pandemic period: 23 March 2020 to 3 January 2021; antenatal transfers: number of women transferred as <27 weeks’ GA, or <28 weeks’ GA if multiple pregnancy; EPT, extremely preterm (<27 weeks of GA); GA, gestational age; HIE, hypoxic ischemic encephalopathy (defined as babies 36+ weeks’ GA who received active cooling within 48 hours of delivery); MAS, meconium aspiration syndrome (defined as babies 36+ weeks’ GA who received inhaled nitric oxide within 5 days of delivery).

Sensitivity analyses
Analyses of complete data were consistent with the main results (online supplemental tables S7 and S8). Models using negative binomial regression (online supplemental table S9) were also very similar.

DISCUSSION
In this population-based analysis comparing indicators of perinatal activity during the pandemic with the preceding 5 years, we identified decreased rates of antenatal transfers for women with threatened EPT delivery alongside decreased rates of admission to neonatal intensive care for babies born EPT. We did not identify any changes in the rates for babies with HIE or MAS, or with postnatal transfers, nor were any changes seen in rates of stillbirth although there was a suggestion these increased across the study period.

Strengths and limitations
We employed an interrupted time series regression methodology; this has been infrequently used in previous studies examining the impact of the COVID-19 pandemic on perinatal outcomes, but is necessary to ensure underlying trends are appropriately accounted for. We also used population-level data from a defined geographical area that were obtained from all NHS Trusts providing maternity care within the region. There were potentially some limitations. Data were collected retrospectively and some Trusts could only provide historical data at monthly or quarterly intervals, hence these data were averaged over the intervening time. This may have reduced week-to-week variability among the historic data. We do not believe this had a major influence on the results: most hospitals provided weekly data, and marked weekly variability remained, as seen in figure 1. Furthermore, the pandemic periods we studied were all 8 weeks or longer, with comparisons made against the trend of data from the entire historic period rather than just a comparable week in preceding years. There were also a small amount of missing data: this amounted to fewer than 5% overall and was accounted for using imputation. Additionally, complete data analysis gave consistent results. A further point is that we did not directly model a lag period. This is consistent with previous literature and is based on the assumption that public health measures taken during the pandemic had an

data were complete other than information relating to postnatal transfer of extremely preterm babies in 2015.

In the prepandemic period, there was a mean of 1161.4 (SD 56.9) women giving birth to a mean 1192.8 (SD 58.8) babies (1187.4 (SD 58.3) live borns) per week. This decreased during the pandemic, with the lowest numbers seen during the period of the second lockdown (table 2). Means for all outcomes were lower during the pandemic period, other than the mean number of HIE admissions during the period between lockdowns which was similar to before the pandemic. There was evidence of a decrease over time in the number of women delivering with a strong seasonal component as well as in the number of babies delivered and live born (figure 1).

The mean proportion of women delivering who self-identified as white decreased over time (table 3). This was primarily related to an increase in women classified as other, although the proportion of women who were classified as Asian also increased in the pandemic period.

Stillbirths fell from 3.7/1000 deliveries prepandemic to 2.9/1000 afterwards; EPT births decreased from 2.5/1000 to 1.8/1000 live births. Following adjustment, during the first lockdown there were decreased antenatal transfers (RR 0.74, 95% CI 0.57 to 0.94) with non-statistically significant increased stillbirth (RR 1.08, 95% CI 0.78 to 1.51) and decreased EPT admissions (RR 0.88, 95% CI 0.60 to 1.28). Over the entire COVID-19 period, antenatal transfer (RR 0.64, 95% CI 0.55 to 0.76) and EPT birth (RR 0.73, 95% CI 0.56 to 0.94) decreased; stillbirths showed non-statistically significant increases overall (RR 1.21, 95% CI 0.98 to 1.49) but with increasing trend through the pandemic (RR 1.11, 95% CI 1.00 to 1.22). No changes were seen for HIE, MAS or postnatal transfers. Full results are shown in table 4.

Analyses by ethnicity
No meaningful differences were seen among Asian or black women. EPT admissions decreased for those classified as white across the different periods of the pandemic (RR 0.80, 95% CI 0.67 to 0.95), although the change for the whole period combined was not significant (RR 0.73, 95% CI 0.52 to 1.02). Among those in the other category, across the whole of the pandemic both EPT admissions (RR 0.56, 95% CI 0.35 to 0.90) and admissions for HIE (RR 0.37, 95% CI 0.18 to 0.78) decreased. Full details are in online supplemental tables S1 to S6.
Figure 1  Time series for perinatal indicators from Yorkshire and the Humber region, 2015–2020. Solid black lines indicate the trend over time, taking into consideration seasonal variation; dashed black lines indicate trends additionally taking into account the different periods of the pandemic which are separated by vertical dotted lines. Pre-pandemic: 29 December 2014 to 22 March 2020; L1: lockdown 1, from 23 March 2020 to 14 June 2020; L2: between lockdowns 1 and 2, from 15 June 2020 to 8 November 2020; L2: lockdown 2, from 9 November 2020 to 3 January 2021.
immediate effect—or, at least, that effects occurred within the weekly intervals used in this study. An alternative hypothesis is that public health measures had a delayed impact, for example, with decreased provision of antenatal care being associated with increased stillbirths were not identified in England during the first lockdown.11 Our results potentially support this, as the RR for stillbirth was higher at later points during the study period and coincided with a decreased rate of antenatal transfer during the second lockdown. We were unable to disaggregate the gestational age of stillbirths as we did not have access to individual level data. The interplay between EPT birth and stillbirth at these gestations could not therefore be examined directly, nor could we examine balances between late pregnancy losses, delayed presentation (resulting in HIE or MAS) and delivery of a healthy baby at term. We were also limited in our examination of ethnicity to categories defined in official statistics. These do not capture the fact that over 20% of the region’s foreign-born inhabitants are from Eastern Europe,12 thus may have different outcomes from other women classified as white who were born and raised in England.

Interpretation
The finding of decreased EPT admissions is consistent with other studies4 as well as with anecdotal reports suggesting there were decreased EPT births during the pandemic, and may be related to biological mechanisms such as decreased physical stress for pregnant women or decreased exposure to viral infections. That antenatal transfers for threatened EPT delivery also decreased is coherent: decreases in EPT births are most likely due to decreased spontaneous deliveries, thus likely preceded by fewer women with threatened EPT labour—hence fewer women requiring transfer. Indeed, this is the first study that we know of examining both antenatal and postnatal transfers within a defined geographical region. The findings, particularly for antenatal transfer, are likely to be similar for other parts of the UK with similar transfer policies, and suggest the pandemic had an important impact on where women delivered that may not be sustained in the future. As noted above and demonstrated in figure 1, the stillbirth rate appeared to increase through the study period, corresponding with decreasing antenatal transfers. This might be related to women having less contact with antenatal services than previously, thus being less aware of when to attend hospital.

Ethnicity is frequently identified as important in analyses relating to the pandemic.13 We did not find evidence of a difference between ethnic groups, but numbers per week were low and, as a majority of women were classified as white, there was probably insufficient power to detect differential effects across groups. The one notable result was the finding of decreased HIE admissions among non-whites, primarily due to a markedly lower rate in the other category. This category included women for whom ethnicity was unknown, and increased substantially during the pandemic, hence the result may simply be due to misclassification.

Generalisability
Yorkshire and the Humber includes approximately 10% of England’s population (between 5 and 5.5 million inhabitants) with major urban conglomerations as well as more rural areas. Around 10% of the population were foreign-born in 2017,14 and 20% of births are to black and minority ethnic mothers.14 There are some differences from elsewhere, notably poorer child health indicators than the average for England.14 Despite this, the region is probably representative of England in terms of population attitudes and behaviours.

Although not all studies have found differences in perinatal outcomes,15 16 consistency with some studies suggests our results are true. Moreover, it is likely that other factors explain differences in findings: the outcomes studied are relatively uncommon, hence requiring studies with large baseline populations, yet behavioural effects from public health measures are likely to be more localised and to vary between geographical regions.12 Our data are interesting because we included the

Table 4 Rate ratios (RR), adjusted for trend over time and seasonal variation, for perinatal activity indicators during the periods of the COVID-19 pandemic compared with the previous 5 years

<table>
<thead>
<tr>
<th></th>
<th>Lockdown 1</th>
<th>Between lockdown 1 and 2</th>
<th>Lockdown 2</th>
<th>P value (trend)</th>
<th>Entire pandemic period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td>Stillbirths</td>
<td>1.08 (0.78 to 1.51)</td>
<td>1.26 (0.97 to 1.65)</td>
<td>1.29 (0.87 to 1.93)</td>
<td>0.050</td>
<td>1.21 (0.98 to 1.49)</td>
</tr>
<tr>
<td>Antenatal transfers</td>
<td>0.74 (0.57 to 0.94)</td>
<td>0.70 (0.57 to 0.86)</td>
<td>0.37 (0.24 to 0.56)</td>
<td>&lt;0.001</td>
<td>0.64 (0.55 to 0.76)</td>
</tr>
<tr>
<td>EPT admissions</td>
<td>0.88 (0.60 to 1.28)</td>
<td>0.60 (0.42 to 0.85)</td>
<td>0.81 (0.51 to 1.28)</td>
<td>0.015</td>
<td>0.73 (0.56 to 0.94)</td>
</tr>
<tr>
<td>HIE admissions</td>
<td>0.85 (0.50 to 1.45)</td>
<td>0.81 (0.54 to 1.22)</td>
<td>0.68 (0.34 to 1.38)</td>
<td>0.159</td>
<td>0.80 (0.57 to 1.11)</td>
</tr>
<tr>
<td>MAS admissions</td>
<td>0.79 (0.35 to 1.80)</td>
<td>1.41 (0.81 to 2.45)</td>
<td>1.00 (0.35 to 2.85)</td>
<td>0.434</td>
<td>1.15 (0.71 to 1.84)</td>
</tr>
<tr>
<td>EPT transfers</td>
<td>1.37 (0.77 to 2.44)</td>
<td>0.61 (0.32 to 1.15)</td>
<td>0.86 (0.39 to 1.93)</td>
<td>0.324</td>
<td>0.90 (0.59 to 1.37)</td>
</tr>
<tr>
<td>HIE transfers</td>
<td>1.04 (0.45 to 2.40)</td>
<td>0.94 (0.50 to 1.78)</td>
<td>0.36 (0.09 to 1.51)</td>
<td>0.302</td>
<td>0.84 (0.50 to 1.44)</td>
</tr>
<tr>
<td>MAS transfers</td>
<td>0.92 (0.40 to 2.12)</td>
<td>1.28 (0.67 to 2.44)</td>
<td>0.62 (0.14 to 2.62)</td>
<td>0.926</td>
<td>1.05 (0.61 to 1.79)</td>
</tr>
</tbody>
</table>


EPT, extreme preterm (27 weeks of GA); GA, gestational age; HIE, hypoxic ischaemic encephalopathy (defined as babies 36+ weeks’ GA who received active cooling within 48 hours of delivery); MAS, meconium aspiration syndrome (defined as babies 36+ weeks’ GA who received inhaled nitric oxide within 5 days of delivery).
whole of 2020 as well as considering different periods of the pandemic. Other studies published recently have also included longer time periods, although the way epochs are defined varies. The fact we identified substantial differences between epochs is notable, and highlights that impacts from pandemic public health measures are complex, potentially with both short-term and long-term repercussions.

Conclusion
In a population-based interrupted time series analysis, following implementation of public health measures for the COVID-19 pandemic in Yorkshire and the Humber, we identified lower rates of antenatal transfer and EPT birth, with an apparent increase in stillbirth over time. No differences were identified in the rates of HIE, MAS or postnatal transfer, nor were important differences identified in non-white ethnic groups. Our findings also provide evidence that effects on perinatal activity changed over the course of the pandemic.

Author affiliations
1Obstetrical, Perinatal and Pediatric Epidemiology Research Team (EPOPE), Centre de Recherche en Épidémiologie et Statistiques (CRESS), Université Paris Cité, INSERM, Hôpitaux Universitaires de Paris, Paris, France
2Elizabeth Garrett Anderson Institute for Women’s Health, University College London, London, UK
3Department of Neonatology, Port-Royal Maternity, Paris, France
4Yorkshire & Humber Neonatal Operational Delivery Network, Sheffield, UK
5Yorkshire & Humber Maternity Clinical Network, NHS England and NHS Yorkshire & Humber Neonatal Operational Delivery Network, Sheffield, UK
6Department of Health Sciences, University of Leicester, Leicester, UK
7Embrace Transport Service, Sheffield Children’s Hospital NHS Foundation Trust, Barnsley, UK
8Department of Neonatology, Leeds Teaching Hospitals NHS Trust, Leeds, UK

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Contributors
ASM and CH conceived the study, ASM and ESD were involved in developing the methodology, ASM, CH, CB and HF were involved in data collection; ASM and CB were responsible for data curation, and ASM conducted the data analysis, drafted the initial manuscript and coordinated revisions. All authors were involved in reviewing and approving the final manuscript. ASM is the guarantor for the study.

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Competing interests
None declared.

Patient consent for publication
Not applicable.

Ethics approval
No patient identifiable information was used in this study, with all data aggregated across the region, hence formal ethical approval was not required. The project was approved in advance by the Yorkshire & Humber Neonatal Operational Delivery Network Executive Management Group meeting (1 September 2020), and by Yorkshire & Humber Maternity Network (via the weekly Heads of Maternity meeting, 9 October 2020).

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Data availability statement
Data are available on reasonable request.

Supplemental material
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ORCID iDs
Andrei Scott Morgan http://orcid.org/0000-0003-4143-1977
Elizabeth S Draper http://orcid.org/0000-0001-9340-8176

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