The Impact of the Coronavirus Pandemic on Perinatal Activity

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Introduction

This paper describes the early stages of an investigation into the impact of the coronavirus pandemic on perinatal health indicators in a region of England, and is based on a presentation given at the online Radical Statistics Conference 2020.

The research project was informed by two studies carried out during the first half of 2020, early in the pandemic. A Danish study demonstrated decreased extremely preterm (below 28 weeks of gestational age) births, which the authors hypothesised was due to decreased infectious triggers for extremely preterm births or women being in less stressful environments or working fewer hours, again leading to decreased triggers for extremely preterm births.[1] Another study from London found there was an increase in stillbirths.[2] The suggestion here was that potentially women were more scared to go to hospital because of the risk of getting COVID and were thus not presenting in time for appropriate treatment during preterm labour or other birthing difficulties, hence leading to more babies dying at home prior to delivery.

There was also anecdotal evidence in perinatal communities of fewer *in utero* and postnatal transfers occuring during the period of the lockdown, and that neonatal units were not as busy as before the pandemic. This was additional to the fact that many paediatric intensive care units had been converted into adult care units during the pandemic. Combined, these factors led to us wanting to investigate the impact of SARS-CoV-2 and related public health measures, specifically the lockdown, on a broader range of perinatal heath indicators using a more robust methodology. The purpose of the project was therefore to answer the following specific questions:

• In a geographically defined population, in relation to previously (e.g., last 5 years), have there been changes in:

- birth rates (live births, stillbirths, preterm births),
- \circ birth-related morbidity, or
- place of birth and associated perinatal transport activity (i.e., antenatal and postnatal transfers

.... during the "first wave"² of the pandemic and the associated lockdown? And do any of these factors differ by ethnicity?

Background

The Yorkshire and Humber region (Figure 1) is located in northeast England, with an approximate population of 5.5 million people (as of 2018). The region is further split into 5 sub-regions, of which West Yorkshire and South Yorkshire are the most populous with the main urban locations. North Yorkshire is less populous, but there are greater numbers of people residing around the Humber River between Lincolnshire and East Riding of Yorkshire.

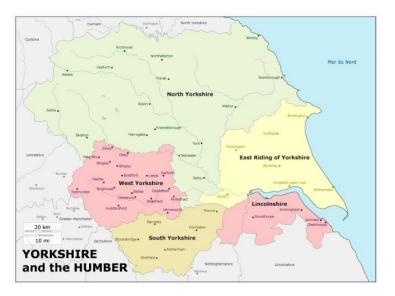


Figure 1: Map of Yorkshire and the Humber Region

Compared to the rest of England, the overall population of Yorkshire and Humber is older, less ethnically diverse and has a poorer life expectancy. There is a higher proportion of children living in lower income households in the region and also a higher infant mortality rate in the region.[3]

² Defined as between Weeks 13 – 25 (March 23rd to June 15th 2020)

Data Sources

Various sources were potentially available for the data we desired. For the maternity data, a 2016 report had proposed the creation of a Maternity Services Dashboard that "aims to bring together maternity information from a range of different sources. It supports the aim of the Maternity Transformation Programme in implementing the Better Births report".[4] This led to the subsequent creation of the Maternity Services Data Set in 2018. However, both resources were established within the 5-year window of this study, resulting in incomplete data sets. They also lacked the level of granularity required for this study and so could not be used.

Another potential source on birth data was *Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK* (MBRRACE-UK) which gathers data on stillbirths and perinatal deaths in the UK. However, MBRRACE-UK's data is only made publicly available after publication. The most recent data published was from 2018 hence, with 2020 data being unavailable, this source could not be used either.

Instead, the required birth data had to be collected by approaching hospitals directly.

We were more fortunate with the remaining data. The *Embrace Transport Service* is a specialised inter-hospital transport service that transfers newborn and critically ill children in Yorkshire and the Humber region, and performs approximately 180 transfers per month, of which 75% are neonatal transfers. Embrace covers all 13 NHS Trusts, including 16 hospitals, in the region. These range from hospitals providing Level 1 care (the lowest intensity or lowest dependency, expecting mainly healthy births) to "Level 3" (the highest-level care for the sickest and most premature babies). There are 4 Level 3 hospitals in the Yorkshire and Humber region. Embrace also arranges antenatal, or *in utero*, transfers for women with threatened preterm labour. Transport data were therefore able to be provided by Embrace Transport Service andm through collaboration with the Yorkshire & Humber Neonatal network we were also able to obtain the neonatal data used in this study.

Data variables

The collected obstetric data included the number of women delivering and the number of babies delivered, disaggregated into live births and stillbirths. From Embrace, data were collected on antenatal (*in utero*) transfers and neonatal transfers for babies born below 27 weeks of gestational age (GA). Neonatal network data were collected on the number of births below 27 weeks' GA, as well as the number of babies born with Hypoxic Ischaemic Encephalopathy (HIE) and those born with Meconium Aspiration Syndrome (MAS). Because of problems associated with the coding of these diagnoses, babies born with HIE were defined as those above 36 weeks' GA who were treated with active hypothermia following delivery, and babies with MAS were as those born above 36 weeks' GA treated with inhaled nitric oxide.

Table 1: Obstetric data provided by each NHS Trust through to February 2021

NHS Trust	Historic data	2020 data		
A	Х	\checkmark		
В	\checkmark	\checkmark		
С	\checkmark	\checkmark		
D	\checkmark	\checkmark		
E	Х	Part		
F	\checkmark	Part		
G	Х	Part		
Н	\checkmark	\checkmark		
Ι	\checkmark	\checkmark		
J	\checkmark	\checkmark		
K	No ethnicity breakdown			
L	No ethnicity breakdown			
М	Wrong dates			

Unfortunately, due to staffing problems related to the pandemic, there were delays in receiving the data from Embrace on neonatal transfers and also with the some of the neonatal network data. Hence, these data could not be included in the study. There were also significant challenges in collecting the obstetric data. Data were initially requested from all hospitals up to Week 40, but several Trusts were slow to provide historical data or data disaggregated by ethnicity. Due to these difficulties, the data collection period was extended to allow all Trusts to supply data, and we decided to include all data through to the end of 2020. A detailed breakdown of the obstetric data provided by the time of the RadStats conference in February 2021 can be seen in Table 1.

Missing Birth Data

Figure 2 shows a different representation of the missing data. The light grey areas represent data that were available, with the black areas representing the missing data. The headings at the top of the chart lists each variable that was being collected. The first 3 variables listed are the hospital name, week number and date the week began on, which were available for all data observations. The data towards the top of the chart is the historical data where each thisck black "line" is a Hospital Trust that has not yet provided complete data for the relevant variables over all 5 years. There were also some missing data for 2020: this can be seen at the bottom of the chart (the thin black lines) where additional data were not provided for the time period after the study was extended (i.e. from week 40 until the end of 2020). Overall, approximately 63% of the data we hoped to collect were available, with around 37% of the data currently missing.

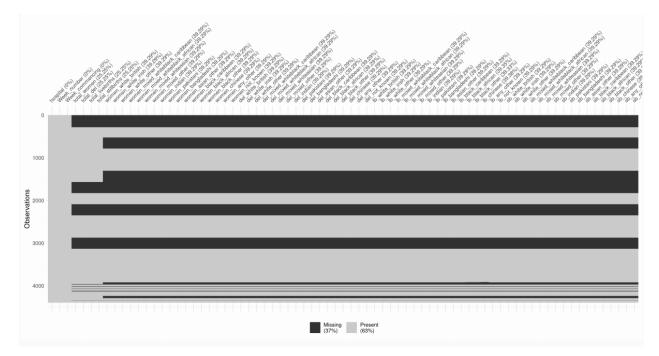
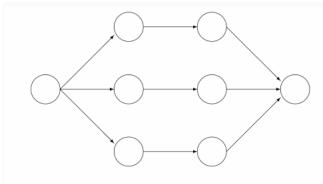


Figure 2: Missing Birth Data

Dealing with missing data

To address this problem of missing data, one option is to use multiple imputation. Imputation is defined as "the process of replacing missing data with substituted values"[5] where statistical methods allow for the estimation of the missing data based on the data available in the data set. Multiple imputation uses multiple data sets and then averages the results across those data sets to create a singular pooled result according to Rubin's rules, as shown in Figure 3.



Incomplete data Imputed data Analysis results Pooled result

Figure 3: The principles of Multiple Imputation (adapted from

This method is based on various assumptions of the pattern of missingness (Figure 4). Data that are "Missing Completely At Random" (MCAR) have no pattern to the missing data, and thus require no further work for unbiased results. Data that are "Missing At Random" (MAR) have a pattern to the missingness, but this pattern can be explained by other existing data. Finally, data that are "Missing Not At Random" (MNAR) have a pattern, but there are no additional data that explain is, hence leading to biased results.

MNAR v MAR v MCAR

Pattern?	Data explains pattern? Yes No			
Yes	MAR	MNAR		
No	—	MCAR		

Figure 4: Patterns of Missingness

Returning to the data...

The missing data shown in Figure 2 have a pattern, thus suggesting that the missing data problem could be addressed with multiple imputation. Unfortunately, when multiple imputation was used, although all observations in the data set were completed for all variables, when the data were examined they were clearly erroneous. An example is shown in Figure 5 which indicates higher numbers of stillbirths for the periods when there were most missing data - i.e. before 2020, and for the last weeks of 2020 (after week 40). We know that they are erroneous as the data for weeks 1-40 during 2020 were the complete data collected from NHS Trusts, and this includes a period of time when there should have been no differences from previously as the full implications of the pandemic and associated public health measures had not yet commenced. A similar pattern was also seen across all the other variables that had missing data imputed, including the number of women delivering per week, the number of deliveries (total births) per week, and the number of live births per week. The interpretation therefore was that the imputed data were inaccurate and should not be used.

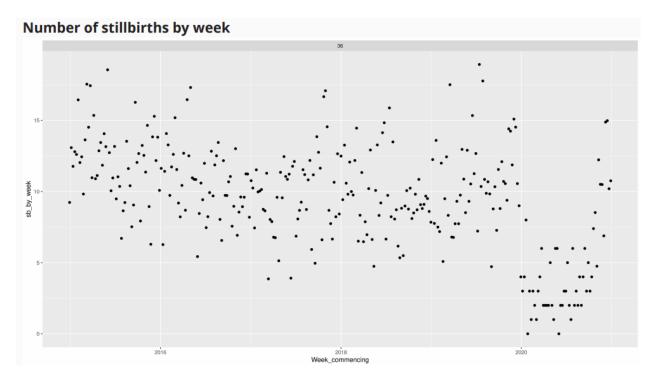


Figure 5: Number of stillbirths per week

Looking Only at 2020 Data

In order to avoid using the inaccurate imputed data, we decided to look only at the reported data from 2020 to see if there was a pattern in the number of stillbirths. As demonstrated in Figure 6, the number of stillbirths per week ranges from 0 to 8, most often being between 2 and 6, and was relatively constant throughout the period for which data were available.

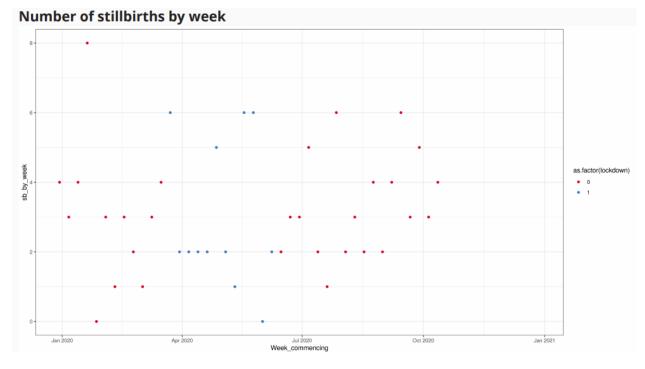
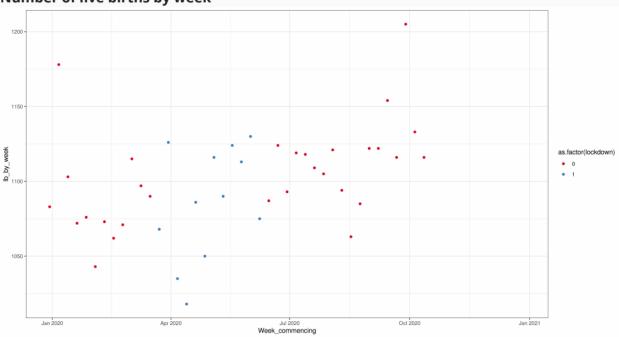
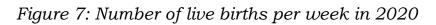


Figure 6: Number of stillbirths per week in 2020; results during the lockdown are shown in blue.

Figure 6 also indicates that the number of stillbirths occurring during the lockdown (Weeks 13 - 25) were not different from the number of stillbirths before or after this period. A similar pattern is shown in Figures 7 and 8, showing that the numbers of live births and deliveries (total births) per week during the lockdown were also consistent with the trends before and after the lockdown.



Number of live births by week



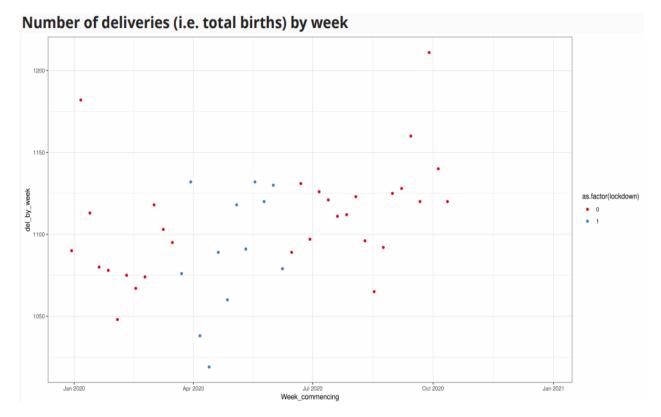
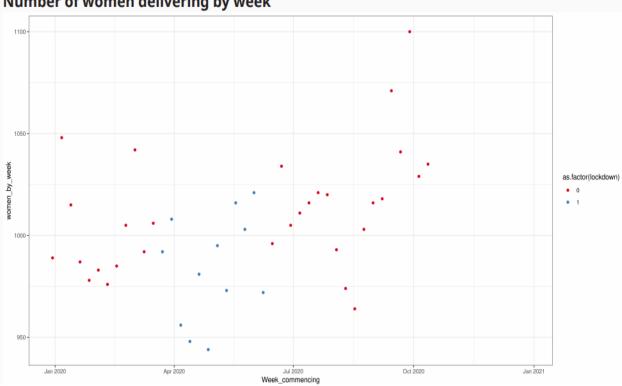


Figure 8: Number of deliveries (total births) per week in 2020

In contrast, the number of women delivering per week, seen in Figure 9, suggests there may have been some fluctuations during the lockdown, but this was not statistically significant.



Number of women delivering by week

Figure 9: Number of women delivering per week in 2020

Answering the original questions

There were no obvious changes seen in the number of women delivering or in the number of live stillbirths occurring during the period of lockdown. However, the original questions also related to the morbidities and to the location of these births. Table 2 shows the average number of admissions per week over the past 5 years, including data specifically for the admissions that took place between Weeks 13 -25 and Weeks 26 - 40. The data for the whole year and for Weeks 13 -25 demonstrate that there is no real difference between the admissions rate for 2020 compared to the rates for the 5 preceding years. However, the admissions rate of 1.88 between Weeks 26 - 40 in 2020 indicates that there was potentially a decrease in the admissions rate after the lockdown ended when compared with the same time period in previous years. However, this datapoint should be taken in context, as there may

have already been a downward trend in births during these weeks, as evidenced by the rate of 3.44 admissions per week in 2017 falling to 2.25 in 2019.

Table 2: Average hospital admissions for extreme preterm births per week

Admissions / week	2015	2016	2017	2018	2019	2020
Whole year	2.94	3.21	3.04	3.38	3.12	2.58*
Weeks 13-25	2.69	3.08	2.62	3.69	3.77	2.62
Weeks 26-40	2.44	3.13	3.44	2.69	2.25	1.88

* 2020 to week 40 only; lockdown occurred from weeks 13 to 25

Comparing Findings to Other Studies

These data do not lead us to conclude that there have been any changes in perinatal care caused by the Coronavirus pandemic or associated lockdowns. There are several caveats to this conclusion, however, especially when comparing it to other studies. Both of the previously mentioned studies had potential issues, with both being susceptible to selection biases or random error. In particular, only one extremely preterm child was included in the Danish study during the period of the pandemic, and they only included data on neonatal admissions, meaning that the data may have been biased as it did not include any data on births or deaths in the delivery room or any deliveries that were not admitted to hospital. The second study only included data from a single hospital, which also may be biased as it does not tell us if more mothers went to this particular hospital during the lockdown thus resulting in more stillbirths there, and consequently may not be reflective of an increase in stillbirths across the population. Furthermore, neither study took into consideration possible changes over time that were happening prior to the pandemic (e.g. a natural decrease in the birth rate).

Various other studies have also been conducted on perinatal activity. A study in Ireland found a decrease in the number of Extremely Low Birth Weight (ELBW) and Very Low Birth Weight (VLBW) live births, but these data were collected in a single region with a population of 473,000 and

had extremely wide confidence intervals, hence may not be representative of a larger population.[6] Another study conducted in California found that there was no change in preterm live births using routine data.[7] Another study using routine data across England also found no change in the rate of stillbirths.[8] A Swedish study using register data found no change in preterm delivery or in stillbirths [9] and a study in Spain using regional hospital data also found no changes in preterm delivery or in stillbirths.[10] A full list of studies has been collected on the website <u>https://ripe-tomato.org</u> ³

Further Research

To further this research, full data sets from all hospitals need to be obtained and multiple imputation should be avoided to replace missing data. There may be more power if this study is conducted with a longer time-series – i.e. covering the full 5 years which have been requested – as well as with a more complete data set from 2020. This then leads to the question of which time periods should be included: for example, the first lockdown, post-lockdown over the summer, the second lockdown period – or a combination of all three; or if simply a pre- and post-pandemic cut-off should be established as of March 2020.

Another further research step could be to create an "adverse outcome" indicator based on the hypothesis that there were increased adverse outcomes for perinatal asphyxia, meconium aspiration, stillbirths, and preterm births. However, the direction of the change for each of these categories may not be the same, and is not necessarily clear without having additional information about gestational age (which was not being collected). Further research also needs to be conducted on the place of birth and if there was a change in the location that women were delivering as evidenced by antenatal and postnatal transfer data.

Conclusion

From this study, we can conclude that at the present time there is no evidence of a link between SARS-CoV-2 and the public health measures established in response to the pandemic and perinatal health in general. However, there are likely behavioural changes caused by these health measures that are subtle and have different local effects, meaning that

³ <u>https://ripe-tomato.org/2020/10/08/indirect-effects-of-the-covid-19-pandemic-on-pregnancy/</u>

they may be difficult to notice in larger data sets. As more data are collected, more definitive results and conclusions can be drawn. That being said, it will clearly take time before some of these questions can be answered and there is a possibility that some of these questions may never be answered.

We can however take more general learning points: these include that both proper data cleaning and a full understanding of the data are very important to be able to decipher what is going on in a specific context. Another learning point is that data collection is difficult, even in countries with good data systems such as the UK; data collection is also hampered by the fact that much of the available data are siloed (i.e. contained in different, incompatible locations), and these silos therefore hinder knowledge. There needs to be more work done to ensure data are open and accessible for analysis.

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Acknowledgements

Dr. Cath Harrison, Chair of the UK Neonatal Transport Group, Chair of the UK Neonatal Transport Group

Professor Elizabeth S. Draper, Professor of Perinatal and Paediatric Epidemiology, The Infant Mortality and Morbidity Studies (University of Leicester)

Charlotte Bradford, Senior Information Manager (Yorkshire & Humber Neonatal ODN)

Hilary Farrow, Quality Improvement Manager (Y&H Maternity Clinical Network, NHS England and NHS Improvement – North East and Yorkshire)