Confirmed COVID-19 in neonates in Scotland

Protocol, April 2022

## Amendments

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| 09/06/2022 | As it was not possible to gain access to BPSU data for admitted babies with COVID-19 at this time, further detail on the admissions of neonates with confirmed COVID-19 will now be obtained from data sources held internally within PHS: the Scottish Birth Record and SMR01 hospital discharge records. |

## Background

* There have been relatively low infection rates in neonates, but these have noticeably increased in the Omicron period in the COPS data
* Neonates are generally not considered to be at high risk from COVID-19 infection, but some serious outcomes do occur
* This is necessarily an unvaccinated population
* WHO provide [guidelines](https://www.who.int/publications/i/item/WHO-2019-nCoV-mother-to-child-transmission-2021.1) on the identification of possible intra-uterine/intra-partum infections
* Very little population based information on neonatal infections has been published to date

## Questions

1. What is the overall rate of confirmed COVID-19 in neonates, and how has this changed over the duration of the pandemic to date?
2. How is the incidence of COVID-19 distributed across the neonatal period?
3. How does the rate of confirmed COVID-19 in neonates vary by maternal age, deprivation, and ethnicity, and neonatal sex and gestation at birth?
4. How does the rate of confirmed COVID-19 in neonates vary between babies born to women with, and without, confirmed COVID-19 infection at delivery (defined as a positive test in the 14 days prior to delivery, on the day of delivery, or on the day after delivery)?
5. What is the neonatal or paediatric in-patient admission rate among neonates with confirmed COVID-19, and how does this compare to background population rates?
6. What is the neonatal death rate among neonates with confirmed COVID-19, and how does this compare to background population rates?
7. What are the clinical characteristics of babies with confirmed COVID-19 and an associated admission (e.g. number/proportion treated with steroids, requiring respiratory support, length of stay, and discharge destination)?

## Timeline

Paper will be based on the April 2022 refresh of the COPS database. This will give us:

* Information on live births occurring up to the end March 2022 (NHS LBs)
* Information on SARS-CoV-2 PCR and LFD tests taken, and COVID-19 vaccinations delivered, up to the end March 2022
* Mostly complete information on maternal characteristics for pregnancies ending up to the end February 2022 (ANB, SMR02)
* Information on neonatal deaths occurring up to the end February 2022
* Data on hospital paediatric discharges (SMR01) mostly complete up to the end February 2022
* Data on neonatal care discharges (SBR) complete up to the end January 2022 for units in the four health boards with the most timely data (Fife, Tayside, GGC and Lanarkshire)

We will provide information on births/infections in March 2020 to January 2022 inclusive for most analyses. We will explore whether more recent data can be provided for some analyses (e.g. simple monthly infection rate), and conversely whether some analyses will need to be restricted to a curtailed time period to accommodate data lags (e.g. admission rate).

## Methods

***Study design:***

Descriptive study based on analysis of routine data, covering all Scotland from March 2020 onwards.

We will use a cross-sectional approach to calculating rates. For example, when calculating monthly neonatal infection rates, we will use confirmed neonatal infections during a particular month as the numerator, and live births during that month as the denominator. This means there is a slight mismatch between numerator and denominator, however it allows us to include the most recent data.

The alternative approach would be to use a cohort approach. When calculating monthly neonatal infection rates, this would involve identifying live births during a month (denominator) and following those babies up to see how many had confirmed infection during their neonatal period (numerator). This avoids the mismatch between numerator and denominator, however it precludes inclusion of the most recent data (due to the need to allow a follow up period), and can be affected by incomplete or inaccurate data linkage.

For neonates with confirmed COVID-19 and an associated admission, further details of the clinical characteristics of admitted babies will be obtained from hospital discharge records held within PHS. Detail on neonatal admissions will be taken from the Scottish Birth Record, and detail on paediatric admissions will be taken from SMR01 hospital discharge records.

***Data sources:***

The [COPS](https://www.ed.ac.uk/usher/research/projects/cops-study) cohort of pregnancies and live births, and the [BPSU](https://www.rcpch.ac.uk/work-we-do/bpsu/study-neonatal-complications-coronavirus-disease-covid-19) study of neonatal complications of coronavirus disease (COVID-19).

***Study population:***

All live births in Scotland from March 2020.

***Definition of confirmed neonatal infection:***

Confirmed neonatal infection is defined as a positive SARS-CoV-2 test indicating date of onset of infection at any point from birth to 27 days old inclusive.

Up to and including 5 Jan 2022, confirmed cases were identified by a positive SARS-CoV-2 viral PCR test result. From 6 Jan 2022 onwards, confirmed cases have been identified by a positive SARS-CoV-2 viral PCR test result or a positive LFD test result (unless the positive LFD result was followed by a negative viral PCR result within 48 hours).

For any individual baby, the specimen date of their first positive test result is taken as the date of onset of their first episode of COVID-19. Subsequent positive test results with specimen date within 90 days of a first positive result are discounted. Each baby can therefore only have one episode of COVID-19 during the neonatal period.

***Definition of COVID-19 associated admission:***

Admissions to neonatal or paediatric care where there has been a confirmed COVID-19 infection with date of onset of infection in the 7 days prior to admission or during admission, or where COVID-19 is listed as the main reason for admission.

To identify babies treated in postnatal wards, we will also explore whether babies with confirmed infection with date of onset on d0 (date of birth) should also be included, in particular if there is no subsequent negative test.

***Measures:***

* Overall infection numbers and rates over time
* Cumulative number of infections by date of onset (from d0 [date of birth] to d27) and total number of infections at 0-1 days old vs 2-27 days old
* Infection numbers and rates by maternal age, deprivation and ethnicity
* Infection numbers and rates by baby sex and gestation at birth
* Numbers and rates of infection by maternal COVID-19 infection status at delivery
* Numbers and rates of neonatal and paediatric admissions in neonates with COVID-19 and comparison background population numbers and rates
* Numbers and rates of neonatal deaths in neonates with COVID-19 and comparison background population numbers and rates
* Numbers of neonates with a COVID-19-associated admission whose highest level of care during a stay was ICU
* Numbers of neonates with a COVID-19-associated admission whose infection is likely to be nosocomial
* Numbers of neonates with a COVID-19-associated admission with a COVID-19 ICD10 code as a main diagnosis
* Length of stay for neonates with a COVID-19-associated admission