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## Investigation and management of serum sodium after subarachnoid haemorrhage (SaSH)

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## COVER PAGE

**Title:** Indirect effects of the COVID-19 pandemic on paediatric healthcare use and severe disease: a retrospective national cohort study

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## **Abstract**

**Objectives** To determine the indirect consequences of the COVID-19 pandemic on paediatric healthcare utilisation and severe disease at a national level following lockdown on March 23, 2020.

**Design** National retrospective cohort study.

**Setting** Emergency childhood primary and secondary care providers across Scotland; two national Paediatric Intensive Care Units (PICUs); statutory death records.

**Participants** 273,455 unscheduled primary care attendances; 462,437 emergency department attendances; 54,076 emergency hospital admissions; 413 PICU unplanned emergency admissions requiring invasive mechanical ventilation; and 415 deaths during the lockdown study period and equivalent dates in previous years.

**Main outcome measures** Rates of emergency care consultations, attendances and admissions; clinical severity scores on presentation to PICU; rates and causes of childhood death. For all datasets, rates during the lockdown period were compared to mean or aggregated rates for the equivalent dates in 2016-19.

**Results** The rates of emergency presentations to primary and secondary care fell during lockdown in comparison to previous years. Emergency PICU admissions for children requiring invasive mechanical ventilation also fell as a proportion of cases for the entire population, with an odds ratio of 0.52 for likelihood of admission during lockdown (95% CI 0.37-0.73), compared to the equivalent period in previous years. Clinical severity scores did not suggest children were presenting with more advanced disease. The greatest reduction in PICU admissions was for diseases of the respiratory system; those for injury, poisoning or other external causes were equivalent to previous years. Mortality during lockdown did not change significantly compared to 2016-19.

**Conclusions** National lockdown led a reduction in paediatric emergency care utilisation, without associated evidence of severe harm.

### **What is already known on this topic?**

- In different settings the COVID-19 pandemic has been shown to lead to a reduction in paediatric emergency department attendances and Paediatric Intensive Care Unit (PICU) admissions for respiratory causes.
- The pandemic has also led to concerns amongst clinicians about delayed care-seeking for serious paediatric conditions, and a possible increase in non-accidental injuries.
- The overall effects of the pandemic on national emergency healthcare utilisation in primary, secondary and critical care, and how this has impacted on severe paediatric disease, have yet to be quantified.

### **What this study adds?**

- We found a reduction in paediatric emergency care utilisation rates at a national level associated with lockdown.
- This reduction is likely to be due to a combination of changes in healthcare seeking behaviour, and a fall in the overall burden of paediatric infectious disease.
- These measures did not appear to have been associated with evidence of severe harm to children in Scotland, as evidenced by severity scores on presentation to PICU or overall mortality.

## **Main text**

### **Introduction**

The global impact of the coronavirus (SARS-CoV-2) pandemic has been extensive with over 30 million confirmed cases of COVID-19 and 1 million deaths globally as of October 2020.<sup>1</sup> The first case of SARS-CoV-2 in Scotland was identified on March 1, 2020,<sup>2</sup> with evidence of sustained community transmission ten days later.<sup>3</sup> With a rising number of cases across the United Kingdom (UK), a UK-wide lockdown was implemented on March 23, 2020 (Figure 1A). This included a number of non-pharmacological interventions (NPIs), such as widespread closures of school/nurseries, leisure centres, indoor play spaces and non-essential workplaces, as well as promotion of home working, hand washing and wearing of face coverings.<sup>3,4</sup> Phased easing of lockdown measures by the Scottish Government began on May 29, 2020; pupils returned to schools on August 12, 2020 (Figure 1B).<sup>3</sup>

Despite a significant direct impact of SARS-CoV-2 on adult mortality and morbidity, the paediatric population appear to have been relatively protected during the first wave of the pandemic, with a low number of reported infections, hospitalization rates and mortality.<sup>5</sup> Public Health Scotland (PHS) and National Records of Scotland (NRS) data shows that by the end of August 2020 in the 0-14 age range there had been 345 confirmed SARS-CoV-2 positive cases, 43 hospital admissions,<sup>6</sup> and no deaths.<sup>7</sup>

Whilst severe disease directly associated with acute SARS-CoV-2 infection in children is rare,<sup>5</sup> the health consequences of NPIs, widespread societal lockdown, and possible changes in caregiver healthcare seeking behaviour on children have not been fully quantified. A reduction in asthma exacerbations<sup>8</sup> and PICU admissions for respiratory conditions have been seen,<sup>9</sup> with both presentations commonly being triggered by respiratory viruses. Paediatric Emergency

Department (ED) attendance rates in the Republic of Ireland were reduced during the lockdown period compared to previous years.<sup>10</sup> Other case series have shown delays in care-seeking behaviour<sup>11</sup> and an increase in non-accidental injuries during lockdown,<sup>12</sup> suggesting that there may be risks associated with decreased availability of healthcare and lower levels of surveillance from health, education and social care workers during this period. Our study used complete national datasets to quantify the indirect effects of the COVID-19 pandemic on emergency paediatric health care utilisation rates and paediatric morbidity and mortality in Scotland during the lockdown period.

## **Methods**

### ***Data sources and data collection***

The overall design was a retrospective, population-based analysis of all emergency paediatric healthcare utilisation. We examined unscheduled primary care and emergency department attendances, emergency hospital admissions, emergency paediatric intensive care (PICU) admissions requiring invasive mechanical ventilation, and paediatric mortality for all children in Scotland. Disclosure controlled, aggregate count data of relevant healthcare utilisation events (apart from PICU admissions) was provided by Public Health Scotland (PHS). The data used is publicly available upon request, with no ethical permissions required. Emergency hospital admissions data are derived from the Rapid Preliminary Inpatient Data (RAPID) dataset.<sup>13</sup>

Data from the two PICUs in Scotland were collected, the Royal Hospital for Children (NHS Greater Glasgow and Clyde) and the Royal Hospital for Children and Young People (NHS Lothian), representing the entire PICU service provision for Scotland and complete national data for children requiring critical care. Data on unplanned, emergency admissions requiring

invasive mechanical ventilation were collected. Analysis was performed as part of a service evaluation program and in concordance with both NHS Greater Glasgow and Clyde and NHS Lothian Quality Improvement policies ethical approval is not required. PICU data was collected in an electronic clinical information system (CIS) MetaVision® provided by iMDsoft® and in the Paediatric Intensive Care Audit Network (PICANet) database.<sup>14</sup> National Records of Scotland provided detailed childhood mortality data, stratified by age group (0-4 and 5-14 years), and by cause of death classified by ICD-10 code. A number of deaths for 2019 and 2020 had not yet been reached final coding stage and therefore were documented as a “Not yet classified”. National data on mid-year population estimates by age group were referenced from a National Records of Scotland (NRS) dataset.<sup>15</sup>

### ***Study design***

#### ***Calculation of population at risk***

The paediatric population was calculated by taking the number of children within each age category from the mid-year population estimates from NRS for each year. For the year 2020 to date, the population at risk was estimated by taking the mid-year population estimates for years 0-13 for 2019, equating to ages 1-14 in 2020. To estimate the mid-year population of infants aged <1 in 2020, the ratio of the number of births in weeks 1-12 in 2020 to those in the equivalent period in 2019 was calculated and applied to the mid-year population for age group <1 year in 2019.

#### ***Study outcomes***

Data for healthcare utilisation and mortality rates were examined for all children living in Scotland aged 0-14 years of age. Rates of health care use, including unscheduled primary care and emergency department attendance, and emergency hospital admissions were analysed.



Healthcare utilisation rates from the period March 23 to August 9, 2020 (epidemiological weeks 13-32, corresponding to the start of lockdown, and the re-opening of schools) were compared to the mean of the equivalent period in previous years, calculated as a rate per 100,000 children at risk. Unscheduled primary care (including telephone consultations) and emergency department attendances were available from January 1, 2016, onwards. Emergency hospital admission rates were obtained from the RAPID dataset for years 2018-20. Attendance and admission rates in all settings were calculated by referencing the same epidemiological weeks for previous years.

Data referencing diagnosis codes for PICU admissions were available until June 30, 2020. The rate of admissions for the period March 23 to June 30, 2020 was compared to the equivalent epidemiological weeks in 2016-19. Admission diagnoses were classified according to ICD-11 diagnostic codes.<sup>16</sup> Illness severity at presentation to PICU was determined by reference to the Paediatric Index of Mortality 2 (PIM2R) Score,<sup>17</sup> a score calculated for purposes of submission to PICANet using a recalibration dating to 2016 (PIM2R 2016).<sup>18</sup> As PICU admissions occur up to the age of 16 years, the population at risk used for calculations was that of children aged 0-15 years. Childhood mortality data, categorised by age groups 0-4 and 5-14 years, was available for epidemiological weeks 13-30 in 2020 (March 23 to July 31) and the equivalent periods in 2016-19 for comparison. Codes for the cause of death were categorised by ICD-10 code.<sup>19</sup> Mortality rates were normalised by the total population at risk as described above.

### ***Statistical analysis***

Statistical analysis was conducted using R,<sup>20</sup> v3.4.1 and Graphpad Prism 6.04 (La Jolla California). For unscheduled primary care consultations, ED attendances and emergency admissions, geometric means with 95% confidence intervals (CIs) were used to compare

epidemiological weeks 5-32 (February 2 to August 9, 2020) with equivalent weeks in 2016-19. Two-sided Fisher's exact tests with an alpha value of 0.05 were used to compare events in the lockdown period to previous years (epidemiological weeks 13-32, equating to March 23 to August 9, 2020). PICU admissions were analysed using geometric means with 95% CIs used to compare admissions by month (February to June, 2020) to equivalent months in 2016-19. A Fisher's exact test was used to compare the number of admissions (March 23 to June 30, 2020) compared to admissions during equivalent weeks in 2016-19. A Kolmogorov-Smirnov test was used to compare mean severity score on presentation to PICU. Childhood mortality rates from epidemiological weeks 13-30 (March 23 to July 26, 2020) were compared to the equivalent periods in 2016-19. A z-score was calculated for childhood deaths and PICU admissions by category in 2020, by subtracting the 2016-19 mean from the value for 2020 and by dividing the difference by the standard deviation. P-values were calculated using the `pnorm` function in R.<sup>20</sup> All scripts and data used for the analysis are published on GitLab ([https://git.ecdf.ed.ac.uk/twillia2/indirect\\_effects\\_covid-19\\_open\\_data](https://git.ecdf.ed.ac.uk/twillia2/indirect_effects_covid-19_open_data)). This study is reported in accordance with the STROBE statement.<sup>21</sup>

## **Results**

### ***Reduction in primary care out of hours consultations and emergency department attendances***

The onset of lockdown on the March 23, 2020 (occurring one day after the end of epidemiological week 12, Figure 1A) until the end of the study period was associated with an almost two-thirds reduction in the number of unscheduled primary care attendances (OR 0.36, 95% CI 0.35-0.37,  $p < 0.001$ ) when compared to epidemiological weeks 13 to 32 in 2016-19 (Figure 2A). For the same period, there was a reduction in emergency department attendances compared to previous years (OR 0.49, 95% CI 0.48-0.49,  $p < 0.001$ ) (Figure 2B).

### ***Reduction in emergency hospital admissions for medical but not surgical diagnoses***

Comparison of nationwide emergency medical paediatric admissions showed a reduction in these during the lockdown period (Figure 2C), with an odds ratio (OR) of 0.56 for an admission occurring in in epidemiological weeks 13-32, compared to equivalent weeks in 2018-19 (95% CI 0.55-0.57,  $p < 0.001$ ). There was no equivalent reduction in paediatric surgical admissions in the post-lockdown period overall, with an OR for admission of 1.03 (95% CI 0.95-1.12,  $p = 0.46$ ) (Figure 2D).

### ***Proportion of Emergency Department attendances to hospital admission during lockdown***

As a marker for seriousness of symptoms on presentation to the Emergency Department, the proportion of the number of children admitted as an emergency to the number who attended the emergency department was calculated (for data from 2018-20) (Figure 2E). In the early weeks of lockdown, there was a rise in the proportion of children admitted to hospital relative to emergency department attendances, with a peak in the first week of lockdown (epidemiological week 13; March 23- 29, 2020). In this week there was a 1.74-fold increase in the odds of an emergency admission as a proportion of ED attendances, compared to 2018-19 (95% CI 1.57-1.92,  $p < 0.001$ ). Comparing ED activity and the proportion of hospital admissions to ED attendances, by epidemiological week 22 the activity for ED attendances was still at a lower rate than the 2016-19 mean (Figure 2B); however, the proportion of admissions to attendances returned to baseline levels for years 2016-19(Figure 2E).

### ***Reduction in emergency admissions to PICU for children requiring invasive mechanical ventilation but no increase on severity scores on presentation***

Comparison of the number of events in epidemiological weeks 13-26 (March 23 to June 30, 2020; Figure 3A) with equivalent periods in 2016-19 showed that the OR of an emergency admission requiring invasive mechanical ventilation during the lockdown study period was 0.52 (95% CI 0.37-0.70,  $p < 0.001$ ). The most marked decrease (by 77%) was seen in admissions for disorders of the respiratory system (ICD-11 Chapter 12) ( $p < 0.001$ ) (Figure 3B, Table 1). There was also a decrease in admissions for disorders of the neurological system (ICD-11 Chapter 8),  $p = 0.01$ , Table 2). No change was seen when compared to previous years in admissions for injury, poisoning or certain other consequences of external causes (ICD-11 Chapter 22, Table 3). The PIM2R score for PICU emergency admissions requiring invasive mechanical ventilation during the lockdown study period did not differ from the equivalent epidemiological weeks in 2016-19 ( $p$ -value = 0.23, Kolmogorov-Smirnov test) (Figure 3C). During the lockdown study period there were no emergency admissions requiring invasive mechanical ventilation for bronchiolitis, lower respiratory tract infection or respiratory failure (Table 1).

### ***Childhood mortality***

Childhood mortality in epidemiological weeks 13-30 in 2020 did not differ significantly from mean in equivalent weeks in 2016-19, for overall deaths, deaths in ages 0-4 years, and deaths in ages 5-14 years (Figure 4A). Of note, the cause of death for a proportion of cases in years 2019 (10/70) and 2020 (14/78, Supplementary Table 1) had not yet been finalised and therefore could not be included (Figure 4B, grey bars).

### **Discussion**

Overall emergency paediatric healthcare utilisation by children in Scotland reduced significantly during the lockdown period, in with no immediate, measurable severe adverse

effects on physical child health at a population level observed. Specifically, a reduction in unscheduled primary care and ED attendances, and unplanned hospital admissions did not result in increased presentations or increased disease severity on presentation to PICU, or mortality rates. The number of admissions to PICU with respiratory disease in those requiring invasive mechanical ventilation during the lockdown study period was significantly reduced. This finding supports evidence from recent reports,<sup>9</sup> which are consistent with the hypothesis that widespread introduction of NPIs are associated with an overall reduction in non-COVID-19 related respiratory infections. During the same period, no increase was seen in children admitted to PICU within the category of injury, poisoning, or other external causes”, which may have been expected if lockdown was associated with reduced surveillance by health, education and social care workers. Our findings support those of an English study which other work examined paediatric emergency department presentation which reported a very small number of presentations with concerns relating to safeguarding<sup>22</sup>. However, both studies, a low incidence of attendances/admissions for this category of conditions limits our ability to make inferences about the consequences of reduced surveillance by health care professionals. In our study, no significant changes were seen in paediatric mortality for this period across any age group examined.

The causes for the observed reduction in rates of paediatric emergency healthcare utilisation during the lockdown study period are likely to be multifactorial. Changes in patterns of interaction between children, shielding measures for at risk groups, and restricted domestic and international travel during the lockdown study period are likely to have reduced the transmission rates of infectious pathogens, and may have reduced exposure to some of the triggers for respiratory diseases (e.g, air pollution in asthma).<sup>8</sup> Increased parental supervision may have improved adherence with medical therapies and thus reduced exacerbation frequency

by improved compliance with prescribed medications, such as anticonvulsants. Reduction in attendance rates to health care services might also be associated with caregiver reluctance to attend healthcare settings in the context of a viral pandemic. Reduced attendance rates without notable impact on severity of presentation might suggest that caregivers were able to utilise a higher threshold for seeking medical attention, therefore decreasing the burden on health systems for children without increasing harms. However, the observed changes in health care utilisation outlined in this study appear mainly related to medical issues since surgical presentations remain relatively unchanged (Figure 2C/D). This discrepancy suggests that the interruption of pathogen transmission by NPIs was probably the most significant factor in reducing medical presentations, rather than an alteration in caregiver care seeking behaviour.

Our study uses high quality, standardised population data from a variety of sources which address the study question from a number of different viewpoints. The use of complete national datasets allowed us to examine the entire paediatric population of Scotland during the lockdown study period and compare this with data collected in previous years. The results from all analyses are concordant with each other and similar analyses,<sup>23</sup> highlighting a picture of reduced healthcare seeking without short-term increase in severe paediatric disease or mortality.

Although further subcategorisation of age groups would provide information on how presentation rates differed by age, unfortunately more granular data on age groupings were not available within the datasets used. Minor differences in the coding of PICU admission (ICD-11) and causes of mortality (ICD-10) may make these groups harder to compare. Similarly, mortality data was incomplete for 2019-20, with some deaths still to be attributed a cause. It is possible that these missing deaths (Supplementary Table 1), once coded, could influence our findings. Another limitation of this study is the inability to examine non-severe disease: there

is growing body of evidence that the lockdown period may have had a detrimental effect, both in the short- and long- term,<sup>24</sup> particularly on the mental health of children.<sup>25,26</sup>

## **Conclusion**

Our analysis shows a reduction in paediatric emergency care-seeking utilisation that occurred as a consequence of the widespread adoption of NPIs and societal lockdown measures. This reduction is likely to be due to a combination of changes in health care seeking behaviour, and a fall in overall burden of infectious causes of childhood disease. These measures do not appear to have been associated with evidence of severe harm to children in Scotland during the lockdown period.

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**ICMJE Statement:** RJL and TCW conceived the study. CM, OS, SC, PD, NG, ST, DU and BG made substantial contributions to the design of the work. CL, RL, CM, JM, IP, AT and MVD contributed towards acquisition of data for the work. TCW, CM and HH performed the analysis and interpretation of the data. RJL, TCW, CM and OS drafted the manuscript; SC, PD, NG, ST, DU, BG, CL, RL, CM, JM, IP, AT and MVD revised it critically for important intellectual content. All authors gave final approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or

integrity of any part of the work are appropriately investigated and resolved.

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**Data sharing statement:** The source code for all the analyses, alongside the anonymized datasets used in these, has been published on GitLab ([https://git.ecdf.ed.ac.uk/twillia2/indirect\\_effects\\_covid-19\\_open\\_data](https://git.ecdf.ed.ac.uk/twillia2/indirect_effects_covid-19_open_data))



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**Table 1. Emergency admissions requiring invasive mechanical ventilation falling within ICD-11 Chapter 12 (Disorders of the respiratory system). PICU admissions from March 23 to June 30, 2020, compared to the same date range in previous years (2016-2019).**

<b>Diagnosis</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
Bronchiolitis	10	8	12	9	0
LRTI - cause unspecified	6	9	9	8	0
Respiratory Failure - cause unspecified	4	3	0	0	0
Asthma	0	2	2	0	0
Pleural Effusion	1	0	0	0	2
Pneumonia	1	5	0	4	1
Pneumothorax	0	0	0	0	1
Pulmonary Oedema	0	1	0	1	1
Tracheitis	0	0	0	0	1
Other	5	9	5	11	1

**Table 2. Emergency paediatric intensive care unit (PICU) admissions requiring invasive mechanical ventilation, diagnoses within ICD-11 Chapter 18 (disorders of the neurological system). PICU admissions from March 23 to June 30 2020, compared to the same date range in previous years (2016-2019).**

<b>Diagnosis</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
Seizure disorder	22	14	15	12	8
Autoimmune	1	0	0	0	0
Infection	0	1	0	0	0
Inflammatory	1	0	0	0	0
Intracranial Haemorrhage / Ischaemia	0	0	1	1	0
Headache	0	0	1	0	0
Hydrocephalus	1	0	0	0	0
Neuropathy	0	0	0	1	0
Motor Neurone Disease	0	0	1	0	0
Intracranial Haemorrhage / Toxic	0	1	0	0	0
Other	1	1	1	1	0

**Table 3. Emergency paediatric intensive care unit (PICU) admissions requiring invasive mechanical ventilation, diagnoses within ICD-11 Chapter 22 (injury, poisoning or certain other consequences of external causes). PICU admissions from March 23 to June 30, 2020, compared to the same date range in previous years (2016-2019).**

<b>Diagnosis</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
Trauma - Head	4	4	3	3	4
Trauma - Intra-abdominal	0	1	1	0	1
Trauma - Multiple Injuries	2	0	3	1	0
Trauma - Thoracic	2	0	0	0	0
Toxic	0	1	0	1	1
Other	2	0	1	2	2





## Figure legends

**Figure 1. Annotated SARS-CoV-2 epidemic curve for Scotland (A) and key events during the lockdown period (B).** (A) New positive SARS-CoV-2RT-PCR cases by day, annotated with key dates and events of relevance for this study. Data from Scottish Government.<sup>27</sup> (B) Date ranges for key social distancing measures in Scotland during the lockdown period.<sup>3</sup>

**Figure 2. Unscheduled primary care and emergency department (ED) attendances fell after lockdown.** (A) Out of hours (OOH) unscheduled primary care consultations. Number of unscheduled primary care consultations by epidemiological week compared to mean number of consultations, with 95% CIs, for 2016-19. Data shown from total of 273,455 consultations (including telephone consultations). (B) ED attendances. Data shown as for (A), for total of 462,437 attendances. (C) Emergency medical paediatric admissions. Number of emergency medical paediatric admissions in 2020, compared to admissions in 2018 and 2019. Data shown for total of 51,596 admissions. (D) Emergency surgical paediatric admissions. Data presented as in (C), for total of 2,480 admissions. All data in A-D normalized by population at risk per year. (E) Proportion of hospital admissions to ED attendances.

**Figure 3. PICU admissions.** (A) The overall number of emergency admissions to PICU requiring invasive mechanical ventilation in March-June 2020 fell when compared to the mean for previous years. Geometric mean and 95% CIs shown for 2016-19, expressed as number of admissions per 100,000 children at risk. Data shown for total of 413 admissions during the study period. (B) The reduction in admissions was most marked for diseases of the respiratory system. Geometric mean and 95% CIs shown for five most common ICD-11 chapters. There was a reduction in overall admissions for respiratory causes (77% reduction), and no change

in admissions for injury, poisoning or other external causes. P-values calculated from z-scores for 2020 compared to means and standard deviation for 2016-19. (C) A reduction in admissions was not associated with an increase in severity scores on arrival in the PICU. Median and interquartile ranges shown for  $\log_{10}$  PIM2R scores on admission for admissions between March 23 and June 30, 2020 compared with the equivalent period in 2016-19. Distributions compared using a Kolmogorov-Smirnov test,  $p = 0.23$ .

**Figure 4. Childhood mortality during lockdown study period.** (A) There was no significant change in child mortality in the lockdown study period compared to the equivalent period in previous years. Number of deaths per 100,000 children in Scotland in epidemiological weeks 13-30 for 2020, compared to the 2016-19. Horizontal lines show means with 95% CIs for years 2016-19. P-values calculated from z-scores for 2020 compared to means and standard deviation for 2016-20. (B) Childhood deaths by cause in 2020 compared to previous years. Deaths per 100,000 children classified by ICD-10 chapter. A number of deaths for 2019 and 2020 have not yet been classified by ICD-10 code and fall into the “Not yet classified” group.