STUDY PROTOCOL

REVISÉ Study Pre-protocol for “BronchStart - The Impact of the COVID-19 Pandemic on the Timing, Age and Severity of Respiratory Syncytial Virus (RSV) Emergency Presentations; a Multi-Centre Prospective Observational Cohort Study”

[version 2; peer review: 2 approved]

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Abstract

Background: Bronchiolitis (most frequently caused by respiratory syncytial virus; RSV) is a common winter disease predominantly affecting children under one year of age. It is a common reason for presentations to an emergency department (ED) and frequently results in hospital admission, contributing to paediatric units approaching or exceeding capacity each winter. During the SARS-CoV-2 pandemic, the circulation of RSV was dramatically reduced in the United Kingdom and Ireland. Evidence from the Southern Hemisphere and other European countries suggests that as social distancing restrictions for SARS-CoV-2 are relaxed, RSV infection returns, causing delayed or even summer epidemics, with different age distributions.

Open Peer Review

Approval Status

	1	2
version 2 (revision) 21 Jan 2022		
version 1 19 May 2021	view	view
1. Simon Drysdale , St George's University Hospitals NHS Foundation Trust, London, UK		

Study question: The ability to track, anticipate and respond to a surge in RSV cases is critical for planning acute care delivery. There is an urgent need to understand the onset of RSV spread at the earliest opportunity. This will influence service planning, to inform clinicians whether the population at risk is a wider age range than normal, and whether there are changes in disease severity. This information is also needed to inform decision on the timing of passive immunisation of children at higher risk of hospitalisation, intensive care admission or death with RSV infection, which is a public health priority.

Methods and likely impact: This multi-centre prospective observational cohort study will use a well-established research network (Paediatric Emergency Research in the UK and Ireland, PERUKI) to report in real time cases of RSV infection in children aged under two years, through the collection of essential, but non-identifying patient information. Forty-five centres will gather initial data on age, index of multiple deprivation quintile, clinical features on presentation, and co-morbidities. Each case will be followed up at seven days to identify treatment, viral diagnosis and outcome. Information be released on a weekly basis and used to support clinical decision making.

Keywords

COVID-19, Respiratory Syncytial Virus, Bronchiolitis, Infants, Children, Palivizumab

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Any reports and responses or comments on the article can be found at the end of the article.

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Competing interests: No competing interests were disclosed.

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The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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REVISED Amendments from Version 1

Author list: Robin Marlow assisted with the development of the data feed for the interactive dashboard, and the development of statistical analyses, and has accordingly been added to the author list.

Abstract: Forty-five PERUKI centres are currently participating in the study and have updated the manuscript to reflect this.

Methods: Due to rapid roll-out of the BranchSTART Study, it will be registered retrospectively rather than prospectively on ISRCTN.

Methods: The study has now received IRAS approval and the text has been updated to reflect this.

Methods: The study team, together with Microreact, has developed an interactive dashboard for study researchers and the general public, available at <https://beta.microreact.org/project/cTkH24NoshvmqK7THws13c-bronchstart-weekly>.

Extended data: These have been updated to reflect minor modifications to the baseline and follow up questionnaires, and an update to the PERUKI investigators who are coordinating local data entry.

Any further responses from the reviewers can be found at the end of the article

Introduction

Non-pharmaceutical interventions (NPIs) implemented to slow or eliminate the spread of SARS-CoV-2 have also had dramatic off-target consequences on transmission of other respiratory viruses, in particular respiratory syncytial virus (RSV) in children. RSV infection can cause a clinical syndrome termed bronchiolitis, most commonly in infants under one year of age, and lower respiratory infection associated with wheeze in older children, typically under two years of age. In a typical year in England, RSV bronchiolitis causes significant morbidity, leading to an estimated 36,028 annual admissions for RSV, mainly in infants under one year of age¹; every year 0.1% of all infants under one are admitted to paediatric intensive care units (PICUs) with a diagnosis of bronchiolitis². In the years preceding 2020/21, RSV infections in the United Kingdom and Ireland saw consistent seasonal peaks in infection and hospitalisation, with cases generally starting to rise in September, peaking in November/December, and falling to summer levels by April¹. As such, when lockdown measures were implemented during the early spring of 2020, the RSV season was already in recession in the Northern hemisphere and no clear impact was seen on RSV disease burden. However, in the corresponding Southern Hemisphere winter of 2020, the NPIs led to dramatically reduced cases and admissions of paediatric RSV and influenza in Australia³, New Zealand⁴, Chile and South Africa⁵. An associated reduced rate of admissions to PICUs across South America, mainly driven by a reduction in respiratory diagnoses, was also observed⁶.

Hierarchical variance of NPIs over time have interrupted transmission of some, but not all, respiratory viruses⁷. In the United Kingdom, test positivity for RSV in the Respiratory

DataMart system has remained at less than 1% throughout the winter of 2020/21 (last data 11 April 2021)⁸. Conversely, rhinovirus infections continued throughout the Southern and Northern Hemisphere winter seasons^{8,9}. A typical annual spike in rhinovirus infections in children was observed with the return to schools in England in September 2020⁸, and PICUs saw ongoing admissions for rhinovirus induced wheeze and bronchiolitis in the autumn/winter of 2020 despite lockdown measures (NHS Lothian data, unpublished).

Both observational and modelling studies suggest that RSV will arise out of season in the Northern hemisphere and may have a greater clinical impact¹⁰. Four Australian states, which after an initial lockdown imposed few physical distancing measures with re-opened schools, have now experienced delayed annual RSV epidemic peaks. The delayed peak in Western Australia, where infections rates surged during local Spring-Summer (September-December), was associated with even higher case rates than normally seen during winter, despite no change in testing practices¹¹. Some European countries such as France have already seen evidence of a delayed RSV season, with all French regions now having reported bronchiolitis case rates at epidemic levels¹².

From a clinical perspective, it is not possible to distinguish the viral aetiology of lower respiratory tract infection, with the exception of greater probability by season of infection. With the uncoupling of RSV and seasonality observed as an impact of NPIs, there is an urgent requirement to track RSV infection for season onset and to observe the impact on a larger unexposed at-risk population. It is likely that when RSV returns to the United Kingdom and Ireland in 2021 it will not follow its usual predictable seasonal pattern, particularly if lockdown measures are relaxed rapidly as SARS-CoV-2 immunisation coverage increases. Reasons why RSV might display unusual disease dynamics include a lack of circulation in the general population, leading to a reduction of transplacental antibodies and passive immunity for neonates, and the fact that children born after February 2020 will most likely not have been exposed to circulating RSV, thus reducing adaptive immune response to the virus when encountered. RSV infection is also associated with recurrent wheeze as a longer-term post infectious morbidity^{13,14}. A higher proportion of children affected by RSV may increase the subsequent healthcare burden of post infectious wheeze, giving a much longer-term burden on health services.

The objective of this study is to monitor RSV disease in children under two years of age attending emergency departments (EDs) across the UK and Ireland and examine the impact on timing, age and severity of clinical presentations as NPI restrictions are reduced throughout the UK and Ireland in 2021.

Study protocol

This protocol is structured in keeping with the principles of the [STROBE statement](#).

Sample selection

A national multi-centre prospective observational cohort study will be carried out through the Paediatric Emergency Research

in the UK and Ireland (PERUKI) Network¹⁵ with forty-five departments already participating in the study. All children meeting the inclusion criteria below will be eligible.

Inclusion criteria. Children under two years of age presenting to participating EDs with clinical features of bronchiolitis (cough, tachypnoea or chest recession, and wheeze or crackles on chest auscultation)¹⁶ or a first episode of acute viral wheeze.

Exclusion criteria. Children with previous episodes of wheeze responsive to bronchodilator, suggesting an underlying diagnosis of recurrent wheeze of early childhood.

Data collection

We will collect data at two time points: baseline (date of presentation to a participating ED) and seven days later.

Clinicians identifying a case for inclusion will keep a local log of participants that contain patient identifiable characteristics cross referenced to a study number. The study number alone is used in all communication/data entry with the study team. An email after seven days to the submitting clinician will prompt data entry at this point.

Anonymised data will be entered to a secure online database (REDCap data capture tool)^{17,18} (see below), by clinicians providing acute care within the ED.

Variables to be measured

At baseline, data including patient demographics, presenting characteristics, acuity, investigations and treatments will be obtained (see Supplementary File 2, *Extended data*)¹⁹, as will data on the number of siblings and travel. An external link will enable clinicians to enter a full postcode derived index of multiple deprivation score for database entry.

At seven days, data will include the child's ultimate outcome (discharged or admitted), highest acuity dependency (the ward they were placed on if admitted: normal, high dependency or intensive care), whether care is ongoing, patient was discharged or died and (if obtained) what viruses were identified by polymerase chain reaction (PCR) (see Supplementary File 3, *Extended data*)¹⁹.

RSV status will be identified by either nasopharyngeal aspirate (NPA) (a) point of care testing (rapid viral testing where available) at baseline presentation to ED, or (b) by laboratory PCR testing, if either is performed as part of standard care.

Sample size calculation

This is a convenience sample cohort study and as such a sample size is not calculated. However, the most recent bronchiolitis peak in France (epidemiological week 13, to 8 April 2021), involved 2,433 ED attendances and 953 hospital admissions in children under the age of two years, with a total of ~16,000 ED attendances and ~6,000 admissions since the start of 2021¹². The combined population of the United Kingdom and Ireland is 72 million, roughly equivalent to that of France (67 million). The PERUKI sites already enrolled

in this study are estimated to provide care for 25% of the total paediatric population, and if a similar trend is seen to France we would therefore expect to recruit 4,000 infants and children in the build-up to the peak of an RSV epidemic. By site this would be a mean of ~100 patients over three months, or approximately a patient a day per site. Previous PERUKI surveillance studies have recruited >1,000 patients in short time scales (1–2 months).

Study registration

The trial will be registered on [ISCRTN Registry](#).

Outcomes

Primary outcome. To report the timing, frequency and clinical severity of RSV infection in children under two years of age presenting to hospitals in the UK and Ireland.

Secondary outcomes

- i. To quantify clinical presentations at ED with respiratory disease by inclusion criteria by month of presentation and compare these figures to the published literature/health data sources.
- ii. To report the geographical timing and spread of RSV infection across the UK.
- iii. To identify differences in severity of illness and patient population affected by RSV in relation to typical seasonal ranges in the published literature.
- iv. To provide data to support and corroborate current RSV surveillance systems (i.e. [Respiratory Datamart](#)) and the [Emergency Department Syndromic Surveillance System \(EDSSS\)](#).
- v. To provide data to support decision making by government agencies (Joint Committee on Vaccination and Immunisation) in relation to the prescription of out of season Palivizumab for high risk children.
- vi. To provide data to support estimates of potential longer-term impact of changes in severity of illness and patient populations on health (long term recurrent wheeze) and associated healthcare resources.

Data analysis and statistical plan

- i. Demographics, regional frequencies, incidence estimates and logistic regression will be performed according to a statistical analysis plan (SAP) in place prior to full data analysis. This will include:
 - a. Weekly incidence (broken down nationally and regionally) calculated for population at risk for each ED.
 - b. Median age, co-morbidities, index of multiple deprivation, presenting features of recruited patients, compared to previous population studies to identify if similar age, spectrum of
- ii. *Descriptive statistics*

co-morbidities and presenting clinical features to previous epidemics.

- c. Proportion of RSV vs non-RSV of those tested.

iii. Identification of risk factors for severe disease

- a. A number of metrics will be examined as proxy measures for severity including:
 - i. Median saturations in air at presentation and frequency of attendance with SpO_2 <94% or <92% in room air.
 - ii. Median respiratory rate (with reference to age as per [Paediatric Early Warning Score](#)) at presentation.
 - iii. Blood gas composition (median H+ and pCO₂ measurements) at presentation.
 - iv. Proportion of children admitted to hospital and of those the proportion admitted to standard care / high dependency unit / PICU.
 - v. Proportion of children requiring respiratory support (supplementary oxygen, high flow oxygen, continuous positive airway pressure, bilevel positive airway pressure or invasive ventilation).
 - vi. Length of stay.
- b. Multivariable logistic regression analyses using random effects model (recruiting site, availability of on-site PICU facility) to examine risk factors for binary outcomes of hospitalisation, level of ventilatory support and PICU admission examined separately. Risk factors will be compared to predictors of severe disease published in population studies previously.

iv. Spatio-temporal dynamics of the 2021 epidemic

- a. Travel histories will be used to identify whether RSV is seeded into community in a number of separate introduction events, or spreads locally.

Ethical issues

This prospective observational surveillance study needs to be able to rapidly collate data that will enable other researchers and health services to make informed decisions about the extent of any RSV surge. For this reason, and the fact that the data being obtained is already obtained as part of the clinical record, we will not be asking for consent from families and carers. The clinician will only enter data regarding the outcomes of the child and no identifying information will be recorded. The patient's study number will be linked to the local hospital number to allow outcome data to be retrieved. This information will be held by the recruiting site only in secure research lockers in each ED and only available to appropriately trained staff or research nurses.

None of the data recorded centrally by the study team will mean the patient is identifiable, and there are no specific

details recorded that would make it possible to determine any individual child by proxy. This approach has been successfully adopted in other rapidly deployed studies the authors have been involved in [20,21](#). The security of the REDCap system we are using to collate data will add additional data protection safeguards.

The study has received Integrated Research Application System (IRAS) approval with University Hospitals of Leicester NHS Trust as the Study Sponsor, IRAS ID 297802. In view of the urgency needed to take this project forward, and the fact that no patient identifiable information will be collected, we believe it to be exempt from Research Ethics Committee (REC) Review. This is also in keeping with the Control of Patient Information Notice (Covid-19 – Notice under Regulation 3(4) of the Health Service Control of Patient Information Regulations 2002) last reviewed 3rd February 2021.

Data input, storage and management

Anonymised data will be entered using the validated online data entry software REDCap. (Research Electronic Data Capture tools) following the clinical report forms provided as *Extended data* (Supplementary Files 2 and 3)¹⁹. This software (REDCap) is hosted on the University Hospitals Bristol and Weston NHS Foundation Trust (UHBW) secure server, accessible on the Health and Social Care Network (HSCN) that is managed by NHS Digital. All research data reside within the hosting institution, and there will be a data transfer agreement made between University Hospitals of Leicester NHS Trust, Edinburgh University and University Hospitals Bristol and Weston NHS Foundation Trust in order to allow transfer of data on completion of data entry and cleaning. Processing of data will be undertaken on instruction of the Data Controller. The study sponsor organisation (University Hospitals of Leicester NHS Trust) will be the Data Controller throughout, and University Hospitals Bristol and Weston NHS Foundation Trust will have joint controllership for the duration of data entry and cleaning. REDCap uses a granular security model so that users can only review the data they have been explicitly authorised to access. REDCap also provides a comprehensive log/audit feature that records all individual changes with a date/time stamp and a change owner. Data that are captured and stored will only be available via the information technology systems linked to the Health and Social Care Network, which is the current validated system used by NHS Trusts to share and store patient information.

Limitations

As families are not contacted for follow-up, and follow-up information is collected by examination of the patient's local hospital record, it is possible that patients may attend a different hospital in the 7 day follow up period and that this information is lost to subsequent analyses.

Dissemination

Data will be presented in:

- i. Data submissions to the regulatory authorities and local study teams, including an interactive online dashboard created in conjunction with Microreact

(<https://beta.microreact.org/project/cTkH24Nosh-vmqK7THws13c-bronchstart-weekly>).

- ii. Conference presentations.
- iii. Peer reviewed scientific journals.
- iv. Collaboration with educational websites with international social media reach (www.dontforgetthebubbles.com).
- v. Engagement with the RSV patient network, part of the RESCEU Consortium.

Study status

Study sites have been enrolled, IRAS approval has been obtained and study recruitment commenced at the first sites June 2021.

Conclusions

There is an urgent need to better understand the effects of non-pharmaceutical interventions on the transmission and disease dynamics of RSV, a major cause of morbidity in infants in the United Kingdom. BronchStart is a multi-centre observational study embedded within the PERUKI network which will inform the immediate clinical response to a delayed RSV peak, improve our understanding of how RSV is seeded and spreads within the United Kingdom, and inform the implementation of future RSV immunisation campaigns.

Data availability

Underlying data

No underlying data are associated with this article.

Extended data

Edinburgh Research Archive: BronchStart Study Extended Data <http://dx.doi.org/10.7488/era/88519>.

This project contains the following extended data:

- BronchStart_supplementary_file1.pdf (PERUKI investigators who will be coordinating local data entry)
- BronchStart_supplementary_file2.pdf (Baseline questionnaire)
- BronchStart_supplementary_file3.pdf (Follow-up questionnaire)

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](https://creativecommons.org/licenses/by/4.0/) (CC-BY 4.0).

These supplementary files were updated 29-10-2021 to reflect minor modifications to the baseline and follow-up questionnaires and an update to the PERUKI investigators who are coordinating local data entry.

- BronchStart_supplementary_file1_v2.pdf (PERUKI investigators who will be coordinating local data entry)
- BronchStart_supplementary_file2_v2.pdf (Baseline questionnaire)
- BronchStart_supplementary_file3_v2.pdf (Follow-up questionnaire)

Acknowledgements

The authors would like to thank Mai Baquedano for technical support in the launch of the REDCap survey tool and ongoing data management. They would like to thank Darren Goble for information management and technology support, including maintenance of the server, and development of a data flow pipeline for the BronchStart outputs. They would also like to thank Anthony Underwood, Khalil Abu-Dahab and David Aanensen at Microreact for creating the live interactive dashboard.

References

1. Lewis KM, De Stavola B, Hardelid P: **Geospatial and seasonal variation of bronchiolitis in England: a cohort study using hospital episode statistics.** *Thorax*. 2020; **75**(3): 262–268. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
2. Green CA, Yeates D, Goldacre A, et al.: **Admission to hospital for bronchiolitis in England: Trends over five decades, geographical variation and association with perinatal characteristics and subsequent asthma.** *Arch Dis Child*. 2016; **101**(2): 140–6. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
3. Britton PN, Hu N, Saravanos G, et al.: **COVID-19 public health measures and respiratory syncytial virus.** *Lancet Child Adolesc Health*. 2020; **4**(11): e42–3. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
4. Huang QS, Wood T, Jelley L, et al.: **Impact of the COVID-19 nonpharmaceutical interventions on influenza and other respiratory viral infections in New Zealand.** *Nat Commun*. 2021; **12**(1): 1001. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
5. Olsen SJ, Azziz-Baumgartner E, Budd AP, et al.: **Decreased Influenza Activity During the COVID-19 Pandemic - United States, Australia, Chile, and South Africa, 2020.** *MMWR Morb Mortal Wkly Rep*. 2020; **69**(37): 1305–9. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
6. Vázquez-Hoyos P, Díaz-Rubio F, Monteverde-Fernandez N, et al.: **Reduced PICU respiratory admissions during COVID-19.** *Arch Dis Child*. 2020; archdischild-2020-32046. [PubMed Abstract](#) | [Publisher Full Text](#)
7. Williams TC, MacRae C, Swann OV, et al.: **Indirect effects of the COVID-19 pandemic on paediatric healthcare use and severe disease: a retrospective national cohort study.** *Arch Dis Child*. 2021; **106**(9): 911–917. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
8. Public Health England: **Weekly national Influenza and COVID-19 surveillance report.** 2021. [Reference Source](#)
9. Nicolaides Pathology S: **Respiratory Virus Report 2020.** 2020.
10. Baker RE, Park SW, Yang W, et al.: **The impact of COVID-19 nonpharmaceutical interventions on the future dynamics of endemic infections.** *Proc Natl Acad Sci*. 2020; **117**(48): 30547–53. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
11. Foley DA, Yeoh DK, Minney-Smith CA, et al.: **The Interseasonal Resurgence of Respiratory Syncytial Virus in Australian Children Following the Reduction of Coronavirus Disease 2019-Related Public Health Measures.** *Clin Infect Dis*. 2021; ciaa1906. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

12. Sante Publique France: **Bulletin épidémiologique bronchiolite, semaine 14. Saison 2020-2021.** 2021; (accessed April 16, 2021).
[Reference Source](#)
13. Hasegawa K, Mansbach JM, Camargo CA Jr: **Infectious pathogens and bronchiolitis outcomes.** *Expert Rev Anti Infect Ther.* 2014; **12**(7): 817–28.
[PubMed Abstract](#) | [Publisher Full Text](#)
14. Bacharier LB, Cohen R, Schweiger T, *et al.*: **Determinants of asthma after severe respiratory syncytial virus bronchiolitis.** *J Allergy Clin Immunol.* 2012; **130**(1): 91–100.e3.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
15. Lyttle MD, O'Sullivan R, Hartshorn S, *et al.*: **Pediatric Emergency Research in the UK and Ireland (PERUKI): Developing a collaborative for multicentre research.** *Arch Dis Child.* 2014; **99**(6): 602–3.
[PubMed Abstract](#) | [Publisher Full Text](#)
16. NICE. 1 Recommendations: **Bronchiolitis in children: diagnosis and management.** Guidance. NICE, (accessed April 2, 2021).
[Reference Source](#)
17. Harris PA, Taylor R, Minor BL, *et al.*: **The REDCap consortium: Building an international community of software platform partners.** *J Biomed Inform.* 2019; **95**: 103208.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
18. Harris PA, Taylor R, Thielke R, *et al.*: **Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support.** *J Biomed Inform.* 2009; **42**(2): 377–81.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
19. Williams T: **BronchStart Study Extended Data.** *Edinburgh Research Archive.* 2021.
<http://www.doi.org/10.7488/era/885>
20. Lai CC, Chen CH, Wang CY, *et al.*: **Clinical efficacy and safety of remdesivir in patients with COVID-19: a systematic review and network meta-analysis of randomized controlled trials.** *J Antimicrob Chemother.* 2021; dkab093.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
21. Waterfield T, Maney JA, Fairley D, *et al.*: **Validating clinical practice guidelines for the management of children with non-blanching rashes in the UK (PiC): a prospective, multicentre cohort study.** *Lancet Infect Dis.* 2021; **21**(4): 569–77.
[PubMed Abstract](#) | [Publisher Full Text](#)

Open Peer Review

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Reviewer Report 19 August 2021

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Patrick K. Munywoki

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With a primary objective to assess the impact of COVID-19 on RSV transmission and disease severity, this surveillance study in the UK is topical and important. The protocol is well designed and the methods are fully described. I have just minor comments.

1. Introduction: Reference(s) for statements on long-term effects RSV is missing. Kindly add.

2. Data analysis: Please confirm if you will use multivariate analysis or if it will be multivariable logistic regression with binary outcomes of hospitalization, level of ventilatory support and PICU admission examined separately. Currently it is not clear.

Is the rationale for, and objectives of, the study clearly described?

Yes

Is the study design appropriate for the research question?

Yes

Are sufficient details of the methods provided to allow replication by others?

Yes

Are the datasets clearly presented in a useable and accessible format?

Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: RSV; Infectious disease epidemiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 23 June 2021

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This is a protocol for a timely study in the UK. The study is well planned and pragmatic for busy EDs. I have minor comments only:

- Collection of data on participants' attendance at childcare / nursery etc would be useful.
- For the 7 day follow up, I assume families are not being contacted again but researchers are just looking at their local hospital record. Will you know if they attend at a different hospital (or GP) in the follow up period? This may need to be noted as a limitation.
- For the stratification of severity did you consider also using a scoring system (e.g. the ReSViNet score - I think you are collecting all the required data anyway?).
- It is unclear to me how "excess morbidity" will be defined / measured.
- On the supp file 2: units for H+ (pH) listed as mmHg, is this correct? (not nmol/L or nM)?

Is the rationale for, and objectives of, the study clearly described?

Yes

Is the study design appropriate for the research question?

Yes

Are sufficient details of the methods provided to allow replication by others?

Yes

Are the datasets clearly presented in a useable and accessible format?

Not applicable

Competing Interests: I have sat on RSV advisory boards for Merck and have been an investigator on clinical trials of RSV therapeutics for various pharmaceutical companies. I work with various EFPIA partners as part of the RESCEU consortium. I confirm that this potential conflict of interest did not affect my ability to write an objective and unbiased review of the article.

Reviewer Expertise: RSV, respiratory viruses, paediatrics

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.