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Features of the transposed seasonality of the 2021 RSV epidemic in the UK and Ireland: analysis of the first 10,000 patients

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Complete List of Authors:	Roland, Damian; Leicester Royal Infirmary; University of Leicester, Health Sciences Williams, Thomas; University of Edinburgh Division of Clinical and Surgical Sciences Lyttle, Mark; Bristol Royal Hospital for Children, Emergency Department; University of the West of England, Academic Department of Emergency Care Marlow, Robin; Bristol Royal Hospital for Children, Emergency Department Hardelid, Pia; UCL, Centre for Paediatric Epidemiology and Biostatistics Sinha, Ian; Alder Hey Children's NHS Foundation Trust; University of Liverpool Division of Child Health Swann, Olivia; University of Edinburgh Division of Medical and Radiological Sciences Maxwell-Hodkinson, Abigail; University of Liverpool Cunningham, Steve; Royal Hospital for Sick Children, Department of Paediatric Respiratory and Sleep Medicine; The University of Edinburgh Centre for Inflammation Research,
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Features of the transposed seasonality of the 2021 RSV epidemic in the UK and Ireland: analysis of the first 10,000 patients

Authors: Roland D^{1,2}, Williams T³, Lyttle D. M^{4,5}, Marlow R⁵, Hardelid P⁶, Sinha I^{7,8}, Swann O^{3,9}, Maxwell-Hodkinson A⁷, Cunningham S^{10,11} on behalf of the REspiratory Syncytial virus Consortium in EUrope (RESCEU) investigators and the Paediatric Emergency Research United Kingdom and Ireland (PERUKI) network.

1. Paediatric Emergency Medicine Leicester Academic (PEMLA) Group, Leicester Royal Infirmary
2. Sapphire Group, Health Sciences, Leicester University, University of Leicester, UK
3. Child Life and Health, University of Edinburgh, UK
4. Faculty of Health and Applied Sciences, University of the West of England
5. Emergency Department, Bristol Royal Hospital for Children, Bristol, UK
6. Great Ormond Street Institute of Child Health, University College London, UK
7. University of Liverpool, Liverpool, UK
8. Alder Hey Children's Hospital, Liverpool, UK
9. Department of Paediatric Infectious Diseases and Immunology, Royal Hospital for Children, Glasgow, UK
10. Centre for Inflammation Research, University of Edinburgh
11. Department of Paediatric Respiratory and Sleep Medicine, Royal Hospital for Children and Young People, Edinburgh, UK

Corresponding Author:

Damian Roland

SAPPHIRE Group, Health Sciences, Leicester University, Leicester, UK

Paediatric Emergency Medicine Leicester Academic (PEMLA) Group, Children's Emergency Department, Leicester Royal Infirmary, Leicester, UK

dr98@leicester.ac.uk

Contributions

Thomas C. Williams: Conceptualization, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing

Mark D. Lyttle: Conceptualization, Methodology, Project Administration, Software, Writing – Original Draft Preparation, Writing – Review & Editing

Steve Cunningham: Conceptualization, Methodology, Project Administration, Writing – Original Draft Preparation, Writing – Review & Editing

Ian Sinha: Conceptualization, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing

Olivia V. Swann: Conceptualization, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing

Abigail Maxwell-Hodkinson: Conceptualization, Methodology, Writing – Review & Editing

1
2
3 Pia Hardelid: Methodology, Writing – Review and Editing

4 Robin Marlow: Methodology, Data Management

5 Damian Roland: Conceptualization, Methodology, Project Administration, Writing – Original Draft
6 Preparation, Writing – Review & Editing
7

8 9 **Collaborators**

10
11 A list of collaborators can be found in table one.
12

13 14 **Competing Interests**

15 No competing interests were disclosed.
16

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19
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27 publication.
28
29

30 31 **Acknowledgements**

32
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35 thank Mai Baquedano for technical support in the launch of the REDCap survey tool and
36 ongoing data management, and Darren Goble for information management and
37 technology support, including maintenance of the server and development of a data flow
38 pipeline for the BronchStart outputs. We thank Elizabeth Whittaker for input at the
39 project planning stage. We thank the RESCEU investigators for their support.
40
41
42

43 44 **Data availability**

45 Data from the BronchStart Study has been made openly available on a dashboard created
46 by Microreact (<https://tinyurl.com/Bronch-Start>).
47
48

49 50 **Ethics**

51 This study has been registered with the NIHR (Research Ethics Committee number
52 21/HRA/1844) and clinicaltrials.gov (Identifier NCT04959734).
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55 **Word Count:** 509
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Main text

Non-pharmaceutical interventions (NPIs) introduced globally to limit the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) led to disruption of the typical RSV seasonality[1]. Studies examining the resurgence of RSV have been limited by sample size, and lack of information on secondary care episodes and clinical features. The BronchStart study is a prospective multi-centre cohort study. Paediatric emergency departments (PED) within PERUKI (Paediatric Emergency Research in the UK and Ireland) submitted data on all children under 2 years of age who visit a PED with symptoms of an acute lower respiratory tract infection (diagnosed as bronchiolitis, lower respiratory tract infection, or first episode of acute wheeze). Follow-up information is submitted 7 days later, and study data is made available on a live online dashboard hosted by Microreact [2].

We present initial data for 10,347 infants and children from 44 study sites for the period 1st June to 5th December 2021. The 2021 RSV epidemic in the UK has finished with infections having peaked in August (Figure 1A). Comparing the age distribution of hospitalised infants <12 months to previous years at two large paediatric centres participating in BronchStart (Leicester Children's Hospital and Bristol Royal Hospital for Children), we observed a similar age distribution (Figure 1B). This suggests either reduced community exposure to RSV during the 15 months preceding the start of the season did not result in a clinically significant lack of protective maternal antibody transfer to those <3 months of age, or the NPIs introduced didn't prevent low level transmission.

Unlike New Zealand, the overall hospital burden of bronchiolitis admissions in the UK and

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3 Ireland in 2021 was lower than previous seasons [3]. Disease severe enough to require
4
5 intensive care was 2.5% in our cohort (infants 6 weeks to one year), comparable to 4.2%
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7 reported in the BIDS trial [4] (odds ratio using Fisher's exact test 0.59, 95% confidence interval
8
9 0.31-1.18, $p = 0.09$). We noted a low probability of a SARS-CoV-2-positive RT-PCR test
10
11 (83/4,328 children tested, 1.9%; of which 39 were co-infections with another virus) in children
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13 presenting with acute lower respiratory tract infection.
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20 We observed a frequent number of PED visits and admissions for RSV-positive 12-23 month
21
22 old children in BronchStart: 362 out of 1,468 (24.7%) admissions. This age group, when infants,
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24 would have had lack of RSV exposure as a result of the delayed seasonal epidemic. Maternal
25
26 RSV vaccination may have a similar effect in future and this observation, if corroborated,
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28 would support the future long-term follow-up of those children born to mothers who receive a
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30 future RSV vaccination.
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37 Our initial findings indicate that the 2021 summer infection peak in the UK and Ireland
38
39 predominantly affected younger age groups as in previous years. The trend for a lower burden
40
41 of disease in 2021 (as demonstrated by ICU admissions) suggests incomplete infection by RSV
42
43 of its usual susceptible population, potentially the result from some ongoing NPIs (such as
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45 mask wearing and hand washing) over the study period. Incomplete penetrance raises the
46
47 possibility of a further wave of infection in the coming months; this has not yet occurred.
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Table 1 List of Contributors

Site	Country	City	Site lead	Co-lead
Alder Hey Children's Hospital NHS Foundation Trust	England	Liverpool	Meriel Tolhurst-Cleaver	
Birmingham Children's Hospital	England	Birmingham	Stuart Hartshorn	
Bolton NHS Foundation Trust	England	Bolton	Jessica Watson	
Bristol Royal Hospital for Children	England	Bristol	Roisin Begley	
Chelsea and Westminster NHS Foundation Trust	England	London	Sakura Hingley	Manali Dutta, Gemma Ramsden
Children's Health Ireland at Crumlin	Ireland	Dublin	Eleanor Ryan	
Children's Health Ireland at Tallaght	Ireland	Dublin	Sheena Durnin	Stanley Koe
Countess of Chester NHS Foundation Trust	England	Chester	Steve Brearey	
Croydon University Hospital	England	Croydon	Darren Ranasinghe	
East Cheshire NHS Trust	England	Macclesfield	Mudiyur Gopi	
Frimley Park Hospital	England	London	Patrick Aldridge	Vicky Owens
Hull Royal Infirmary	England	Hull	Simon Richardson	
Ipswich Hospital	England	Ipswich	David Hartin	
John Radcliffe Hospital	England	Oxford	Jiske Steensma	Sahana Rao
Leicester Royal Infirmary	England	Leicester	Damian Roland	
Leighton Hospital	England	Crewe	Jo Tillett	Simon Dowson
Medway Hospital NHS Foundation Trust	England	Gillingham	Adebayo Da Costa	Alfred Sime
Newham University Hospital	England	Newham	Claire Kirby	
North Middlesex Hospital	England	London	Adam Lawton	
Nottingham University Hospitals NHS Trust	England	Nottingham	Ruth Wear	Christopher Gough
Ormskirk & District General Hospital	England	Ormskirk	Sharryn Gardner	Craig Rimmer
Poole Hospital	England	Poole	Heather Deall	
Queen Elizabeth Hospital, Woolwich	England	London	Sharon Hall	
Royal Aberdeen Children's Hospital	Scotland	Aberdeen	Catriona Middleton	
Royal Alexandra Children's Hospital	England	Brighton	Emily Walton	Friyana Dastur Mackenzie
Royal Berkshire NHS Foundation Trust	England	Reading	Manish Thakker	
Royal Derby Hospital	England	Derby	Gisela Robinson	Graham Johnson

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2					
3	Royal Hospital for Children, Glasgow	Scotland	Glasgow	Steve Foster	
4	Royal Hospital for Children & Young People, Edinburgh	Scotland	Edinburgh	Jen Browning	Lynsey Rooney
5	Royal Wolverhampton NHS Trust	England	Wolverhampton	Lorna Bagshaw	
6	Salisbury NHS Foundation Trust	England	Salisbury	Seb Gray	
7	Sheffield Children's NHS Foundation Trust	England	Sheffield	Sally Gibbs	
8	South Tyneside & Sunderland NHS Foundation Trust	England	Sunderland	Niall Mullen	
9					
10	Southampton Children's Hospital	England	Southampton	Jane Bayreuther	
11	St George's Hospital, London	England	London	Heather Jarman	
12	St Helens & Knowsley NHS Trust	England	Rainhill	Clare O'Leary	
13	The Royal London	England	London	Raine Astin-Chamberlain	
14					
15	University Hospital Crosshouse	Scotland	Kilmarnock	Lawrence Armstrong	Joanne Mulligan
16	University Hospital Lewisham	England	London	Sophie Keers	
17	Watford General Hospital (West Herts NHS Trust)	England	Watford	Richard Burridge	
18	Wexham Park Hospital	England	Slough	Sarah Wilson	
19	Whipps Cross Hospital	England	London	Amutha Anpananthar	
20	Wirral University NHSFT	England	Birkenhead	David Lacy	
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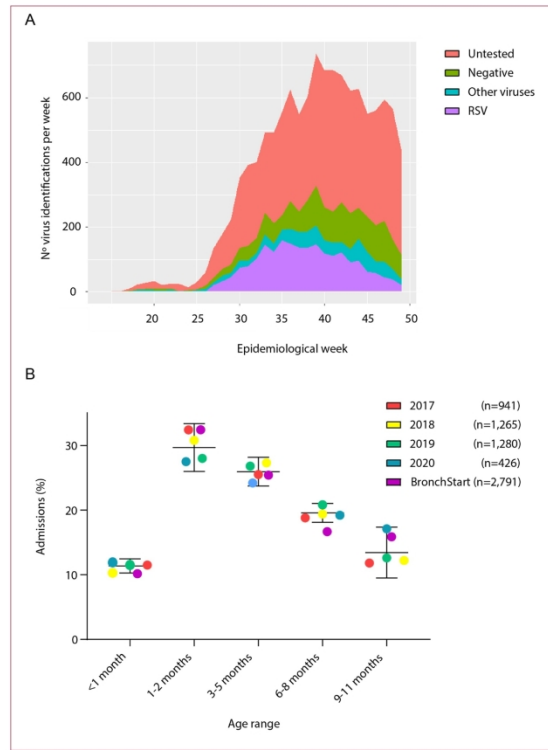


Figure 1

Figure 1 - Virus Identifications over time

190x338mm (300 x 300 DPI)

Response to Reviewers

Reviewer: 1

Very curious to know your thoughts, when you publish the full study, did the Summer seasonality have a negative effect on the peak of RSV and can we expect the seasonality now to change? Although there may have been a reduced burden of disease, were the overall numbers greater as the season was spread over a longer period? What percentage of children admitted had prophylaxis as the palivizumab season was started early as well? Figure 1A suggests many of the children were untested or didn't have a virus. National data suggests much of the later bronchiolitis was due to human metapneumovirus; will this be picked up in the study?

Many thanks for these questions. Early evidence from both Bronchstart and other national data suggests a flattened curve, which had a smaller peak but broader width i.e. as you say an overall greater spread over a longer period. Unfortunately we did not collect specific information on Palivizumab administration. In the full extraction of data we will be able to report on other viruses association with a clinical diagnosis of bronchiolitis.

Reviewer: 2

Comments to the Author

Thank you for submitting this manuscript. First, it is fantastic that paediatric emergency departments are collaborating to produce surveillance work on this sort of scale and this is a vital piece of work in helping us to understand what the post-pandemic landscape is for acute paediatric services, as relates to RSV.

Thank you.

My first comment is a pedantic one but relates to the use of "aseasonal" in the title and in the text. Aseasonal would imply the absence of seasonality, whereas what we are talking about is a shift of season, but still very much the existence of an "RSV season". There may not be an easy single word to substitute but I think more accurately you are describing an atypical RSV season (shifted seasonality) or indeed an out-of-season RSV surge, but there has still been a clear seasonality to the RSV surge, it just peaked in August instead of November/December/January. If the authors do not feel there is a better phrase that captures the meaning, I can accept that too, but I just don't think it quite means what is being said.

Many thanks – we have adjusted the title to 'transposed' seasonality and removed the term aseasonal from the document.

Otherwise, on page 4 line 57, consider rewording or splitting the long sentence. Where it says "...or that NPIs introduced were not strong enough to prevent...", I'm not sure which way you mean this, as in whether it does or doesn't suggest this, as there is also a double negative in the first clause of the sentence. It isn't totally clear whether the second part continues on from "reduced community exposure...did not result..." or whether it is a new clause entirely.

The structure of this sentence has been altered to clarify the meaning and remove the double negative.

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2
3 *"This suggests either reduced community exposure to RSV during the 15 months preceding the start*
4 *of the season did not result in a clinically significant lack of protective maternal antibody transfer to*
5 *those <3 months of age, or that the NPIs introduced didn't prevent low level transmission"*
6
7

8 Page 5 line 25: "this observation...should support future long-term follow up of children..."
9 Could you elaborate on this? It's not really clear what you mean. Do you mean follow up of the
10 children or (I'm assuming) following up epidemiologically whether RSV vaccination reduces the
11 burden for this group? I think this point needs to be explained a little more specifically.
12

13
14 *The paragraph has been altered for clarity. Commencing 'We also observed a frequent...'*
15

16 Page 5 line 40: "The overall lower burden of disease in 2021 suggests incomplete infection..."
17 This refers back to the opening paragraph of the page where you reference the overall hospital
18 burden, but the only statistical comparison you have given is of ICU admissions which was reduced,
19 but not in a statistically significant way. It might be worth elaborating (briefly) on the data showing
20 overall hospital use was down.
21

22
23 *Thank you, we have altered the emphasis here to be clearly about the absence of significance. We*
24 *may need to refer to the editor as we could add in another diagram using national (publically*
25 *available) data to demonstrate that overall hospital burden probably was less (contained in reference*
26 *3) but this obviously adds to word count and the number of figures? We have clarified that the*
27 *overall burden of 'admissions' was reduced and given a reference [3] for this.*
28

29 In addition, the assertion that this was "probably due to the effect of ongoing NPIs over the study
30 period" - the study period was June to December 2021, during which time the only period with
31 population wide NPIs ended on July 19th. I'm not sure we can say very confidently that those 6
32 weeks of NPIs amongst 6 months of data could have that effect, unless there is more to support that
33 assertion specifically (or, whether there is anything to suggest continued use of NPIs in hospitals
34 could have contributed to a reduction on that scale?).
35

36
37 *This is an important point and we have just added that we meant later NPIs like mask wearing and*
38 *hand washing which will have had an increased uptake.*
39

40 Overall, this is an excellent manuscript and a project of truly brilliant scale for our specialty and I
41 want to commend everyone for the fantastic work. I think it is important that this is published.
42 Grateful for the consideration of the minor revisions I have suggested.
43

44
45 *Many thanks again.*
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