Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Quantifying the RSV immunity debt following COVID-19: a public health matter

Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infection in children younger than 5 years. In 2019, a meta-analysis estimated that RSV was associated with 33 million acute lower respiratory infection episodes and 3·6 million hospitalisations for acute lower respiratory infection annually.[1] In England alone, an average of 33 561 annual RSV-associated hospitalisations were observed between 2007 and 2012.[2] Before the COVID-19 pandemic, RSV was highly seasonal in temperate countries like England.[3] RSV activity dropped shortly after the implementation of non-pharmaceutical interventions to slow the spread of SARS-CoV-2 (eg, physical distancing and school closures) in March, 2020.[4] Subsequently, multiple countries reported out-of-season RSV resurgences after a silent winter season.[5] As the drivers or RSV seasonality and the mechanisms by which RSV is re-seeded annually are not fully understood,[6,7] estimating the impact of non-pharmaceutical interventions on RSV is an important tool for public health decision makers to plan surveillance activities and hospital preparedness.

In *The Lancet Infectious Diseases*, Megan Bardsley and colleagues[8] investigated the effect of non-pharmaceutical interventions on RSV-attributable disease among children younger than 5 years in England since March, 2020. The authors conducted interrupted time-series analyses and compared predicted RSV-attributable disease activity based on pre-pandemic seasons (2015–16 onwards) with RSV activity in winter 2020–21, summer 2021, and winter 2021–22, across a range of RSV activity indicators based on laboratory, clinical, and syndromic surveillance data. In pre-pandemic seasons, an annual peak of RSV activity was observed in December, as shown by the numbers and positivity rates of laboratory-confirmed RSV cases and the number of RSV-attributable admissions, as well as syndromic surveillance data in primary care, out-of-hours services, and emergency care. In winter 2020–21, non-pharmaceutical interventions slowed the spread of respiratory viruses, with reductions across various indicators compared with their predicted values, ranging from a 73·7% decrease (95% prediction interval –73·7 to –73·7) in the number of cough-related calls to the remote health advice telephone line managed by the National Health Service (NHS 111 calls) to a 99·5% decrease (–100·0 to –99·1) in the number of laboratory-confirmed cases of RSV infection. In summer 2021, after the relaxation of non-pharmaceutical interventions, an out-of-season RSV epidemic occurred. The summer peak lasted until autumn and was followed by a mild winter 2021–22 season compared with pre-pandemic seasons, with a 26·9% decrease (–27·0 to –26·8) in number of RSV cases and a 48·2% decrease (–48·2 to –48·1) in number of general practitioner (GP) in-hours consultations for respiratory tract infections.

By including multiple surveillance systems to capture changes in RSV-related outcomes, the authors provide a comprehensive overview of the impact of non-pharmaceutical interventions on RSV activity at different severity levels in England. Although taken independently each indicator is subject to the limitations inherent to surveillance data, the common trends of different indicators reinforce the validity of the results as different surveillance systems would not have been affected the same by the pandemic. Recommendations to limit unnecessary contacts with primary care providers in 2020 might have decreased primary care attendance in GP syndromic surveillance but not hospitalisations for severe acute lower respiratory infection. Similarly, syndromic indicators have low specificity but would not be affected by changes in testing practices. Multiple indicators also allow comparisons with countries with less extensive RSV surveillance, which will be important to understand the distinct patterns of RSV resurgences.

Out-of-season RSV resurgences are explained by decreased population immunity following a prolonged period of minimal RSV exposure, also referred to as RSV immunity debt.[5,9] It is important to quantify these effects of prolonged periods of low exposure over time. Out-of-season RSV resurgences pose major challenges to health-care systems already strained by two and a half years of pandemic.[10] RSV should be monitored all year round for as long as out-of-season RSV resurgences are among plausible scenarios. With no specific treatment against RSV currently licensed,

Flickr/Willie Stark

Lancet Infect Dis 2022

Published Online
September 2, 2022
https://doi.org/10.1016/S1473-3099(22)00544-8

See Online/Articles
https://doi.org/10.1016/S1473-3099(22)00525-4

hospitals must ensure sufficient bed capacity to provide supportive care, notably respiratory support, during epidemics. Long-lasting uncertainties about the timing of epidemics could force hospitals to maintain a high level of readiness for extended periods each year. In addition to the current work by Bardsley and colleagues,[8] immunological surveillance could be used to further close the gap in knowledge regarding the consequences of prolonged use of non-pharmaceutical interventions on seasonal respiratory viruses. Monitoring population immunity levels should, therefore, be part of the public health toolbox.

Overall, Bardsley and colleagues reported substantial changes in RSV-attributable disease during the COVID-19 pandemic in England.[8] Their observations confirm the concept of immunity debt as an unintended consequence of non-pharmaceutical interventions. Estimating the magnitude of these changes is essential for public health decision makers.

LJB has regular interaction with pharmaceutical and other industrial partners; he has not received personal fees or other personal benefits. LJB is the founding chairman of the ReSViNET Foundation. The authors' institution, University Medical Center Utrecht, has received major funding (>€100 000 per industrial partner) for investigator-initiated studies from AbbVie, MedImmune, AstraZeneca, Sanofi, Janssen, Pfizer, MSD, and MeMed Diagnostics; major funding for the RSV GOLD study from the Bill and Melinda Gates Foundation; major funding as part of the public–private partnership IMI-funded RESCEU and PROMISE projects with partners GlaxoSmithKline, Novavax, Janssen, AstraZeneca, Pfizer, and Sanofi; major funding by Julius Clinical for participating in clinical studies sponsored by MedImmune and Pfizer; minor funding (€1000–25 000 per industrial partner) for consultation and invited lectures by AbbVie, MedImmune, Ablynx, Bavaria Nordic, MabXience, GlaxoSmithKline, Novavax, Pfizer, Moderna, Astrazeneca, MSD, Sanofi, Genzyme, and Janssen. MB declares no competing interests.

*Marie-Noëlle Billard, *Louis J Bont*
l.bont@umcutrecht.nl

Department of Pediatrics, University Medical Center Utrecht, Utrecht, 3584 EA, Netherlands

1 Li Y, Wang X, Blau DM, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis. *Lancet* 2022; **399:** 2047–64.

2 Reeves RM, Hardelid P, Gilbert R, Warburton F, Ellis J, Pebody RG. Estimating the burden of respiratory syncytial virus (RSV) on respiratory hospital admissions in children less than five years of age in England, 2007–2012. *Influenza Other Respir Viruses* 2017; **11:** 122–29.

3 Li Y, Reeves RM, Wang X, et al. Global patterns in monthly activity of influenza virus, respiratory syncytial virus, parainfluenza virus, and metapneumovirus: a systematic analysis. *Lancet Glob Health* 2019; **7:** e1031–45.

4 Sullivan SG, Carlson S, Cheng AC, et al. Where has all the influenza gone? The impact of COVID-19 on the circulation of influenza and other respiratory viruses, Australia, March to September 2020. *Euro Surveill* 2020; **25:** 2001847.

5 Li Y, Wang X, Cong B, Deng S, Feikin DR, Nair H. Understanding the potential drivers for respiratory syncytial virus rebound during the coronavirus disease 2019 pandemic. *J Infect Dis* 2022; **225:** 957–64.

6 Zheng Z, Pitzer VE, Warren JL, Weinberger DM. Community factors associated with local epidemic timing of respiratory syncytial virus: a spatiotemporal modeling study. *Sci Adv* 2021; **7:** eabd6421.

7 Baker RE, Mahmud AS, Wagner CE, et al. Epidemic dynamics of respiratory syncytial virus in current and future climates. *Nat Commun* 2019; **10:** 5512.

8 Bardsley M, Morbey RA, Hughes HE, et al. Epidemiology of respiratory syncytial virus in children younger than 5 years in England during the COVID-19 pandemic, measured by laboratory, clinical, and syndromic surveillance: a retrospective observational study. *Lancet Infect Dis* 2022; published online Sept 2. https://doi.org/10.1016/S1473-3099(22)00525-4.

9 Cohen R, Ashman M, Taha M-K, et al. Pediatric Infectious Disease Group (GPIP) position paper on the immune debt of the COVID-19 pandemic in childhood, how can we fill the immunity gap? *Infect Dis Now* 2021; **51:** 418–23.

10 Williams TC, Sinha I, Barr IG, Zambon M. Transmission of paediatric respiratory syncytial virus and influenza in the wake of the COVID-19 pandemic. *Euro Surveill* 2021; **26:** 2100186.