Reduction in incidence of non-COVID-19 respiratory virus infection amongst haematology inpatients following UK social distancing measures

Since the SARS-CoV-2 pandemic began, countries across the globe have seen repeated periods of government-enforced social distancing to restrict transmission in response to rises in COVID-19 incidence.[1] Social distancing in the UK was first introduced in March 2020, and for six of the following 12 months the population was under strict national restrictions. This led to substantially reduced contact between different households,[2] with mass gatherings prohibited.

Prior to this pandemic, respiratory viral infections were a common cause of morbidity amongst haematology patients,[3] including those immunosuppressed or post haematopoietic stem cell transplantation (HSCT), with reported incidences of 3–30% per year.[4,5] Respiratory syncytial virus (RSV) is the virus most likely to progress from upper respiratory tract infection to pneumonia in patients who have undergone HSCT,[6–8] and the British Society of Haematology recommends ribavirin and intravenous immunoglobulin in this group.[9] Influenza, parainfluenza, and adenovirus can all cause severe disease in the immunocompromised, and SARS-CoV-2 has been shown to cause severe disease and excess mortality in those who have undergone HSCT and some haematological malignancies.[10,11]

Regional surveillance networks have noted a significant reduction in influenza transmission in both southern[12] and northern hemispheres[13] (https://www.cdc.gov/flu/weekly/index.html) during their respective winter seasons in 2020–21. This has been attributed to non-pharmacological interventions and social distancing introduced to reduce SARS-CoV-2 transmission.

Here, we describe the impact of UK social distancing measures on the incidence of non-SARS-CoV-2 respiratory viral infection in a cohort of haematology patients.

Methods

Data were obtained from Oxford University Hospitals (OUH), a large UK teaching hospital. BioFire FilmArray (bioMérieux, Basingstoke) multiplex polymerase chain reaction (PCR) was performed on respiratory samples to detect the presence of respiratory viruses (influenza A & B, parainfluenza 1–4, RSV, human enterovirus/rhinovirus, coronaviruses 229E, HKU1, NL63, OC43, adenovirus, as well as *Mycoplasma pneumoniae*) as part of routine care of haematology patients presenting with respiratory symptoms or fever. It is comparable in performance to several other similar platforms,[14] and has been updated to include SARS-CoV-2 detection.

All PCR results performed during haematology inpatient admissions (including encounters to the triage unit) were obtained from the Infections in Oxfordshire Research Database which has generic Research Ethics Committee, Health Research Authority and Confidentiality Advisory Group approvals (19/SC/0403, 19/CAG/0144). Data were also obtained on baseline characteristics including gender, age, ethnicity, haemato-oncological or benign haematology specialist care, and comorbidity indices (Charlson comorbidity index, CCI).

We used piecewise linear regression to model changes in admissions over time, and Poisson regression to model changes over time in incidence of testing per 100 admissions for respiratory viruses, allowing for a step change in incidence from March to April 2020, that is, around the introduction of the first UK national lockdown on 16 March 2020, and a linear trend before and after this. We do not adjust for seasonality and so trends presented represent averages across seasonal peaks and troughs.

Results

Between 1 January 2016 and 28 February 2021, across all haematological specialities at OUH, there were 22 536 inpatient encounters. Median age of patients was 59 (interquartile range, IQR, 18–71), 13 534 (60%) were male, 14 940/16 502 (91%) with recorded ethnicity were white and 21 817 (97%) were managed by a haemato-oncologist. Across this period, 3 380 BioFire PCR tests were performed in 2 719 haematology inpatients. Tested patients were older than untested patients, median (IQR) age 61 (49–70) vs 58 (16–71) years ($P < 0{\cdot}001$) and had more comorbidities, CCI median (IQR) 8 (0–8) vs 0 (0–0) ($P < 0{\cdot}001$; Table SI). There was no evidence of a difference by sex or ethnicity.

The number of encounters remained stable across 2016–2019 [estimated change per month in daily rate 0·00 (95% CI −0·02, 0·02; $P = 0{\cdot}88$)] but fell markedly at the start of the pandemic [change in daily rate −4·99 (−6·25, −3·74)], and there was a trend towards a rise following [0·17 (−0·02, 0·36; $P = 0{\cdot}08$); Fig 1A]. Between January 2016 and March 2020 there were 12·5 admissions per day, and 8·5 admission per day from April 2020 to Febuary 2021.

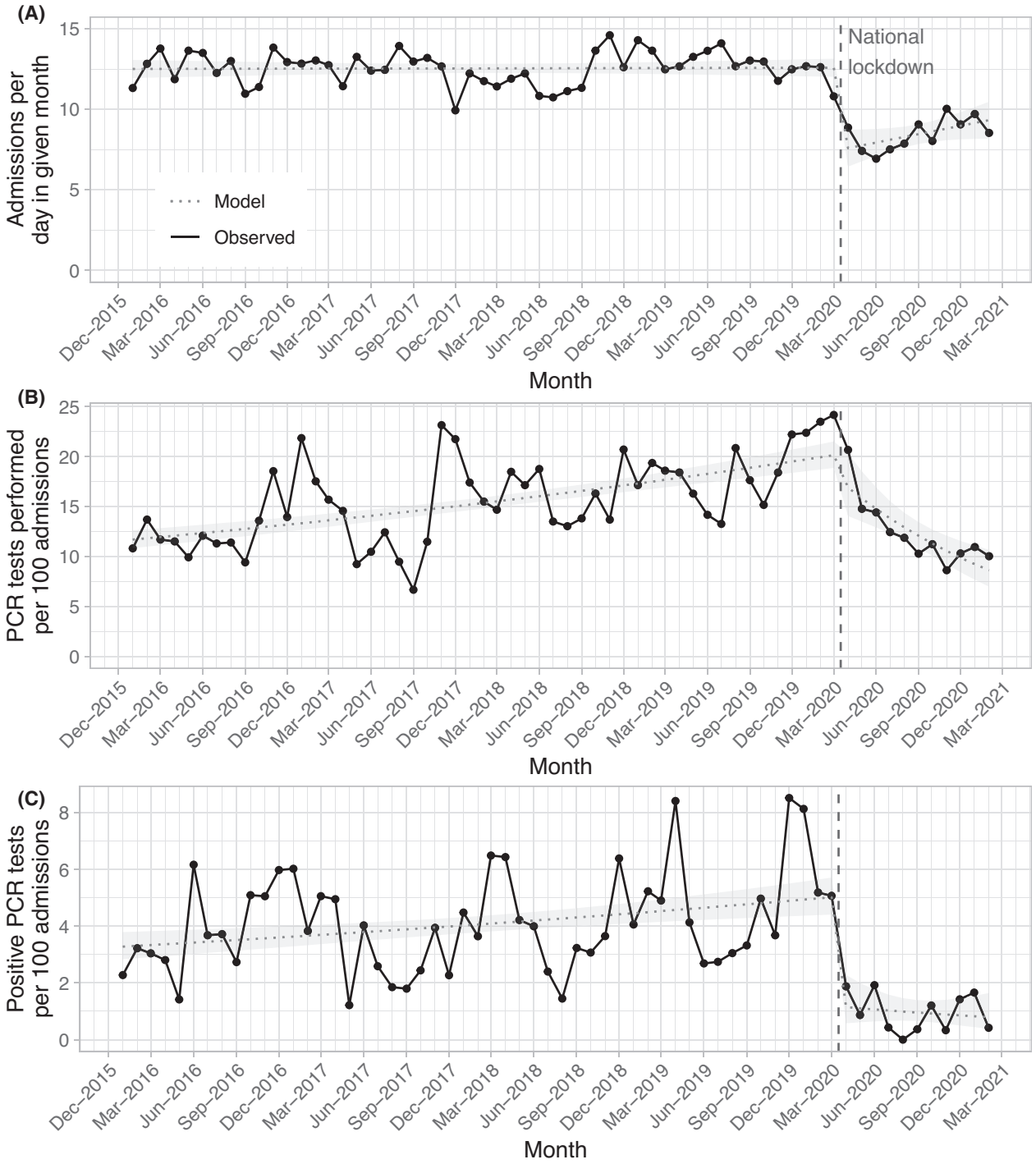

Fig 1. (A) Monthly haematology inpatient admissions. (B)Monthly respiratory virus polymerase chain reaction (PCR) testing rates. (C)Monthly respiratory virus detection rates. The black line indicates observed values and the blue dotted line the modelled incidence, with the ribbon indicating the 95% confidence interval. The start of UK national social distancing restrictions is shown as a dashed red vertical line.

Use of PCR testing was rising prior to the pandemic [monthly increase in tests per 100 admissions, 0·01 (95% CI 0·01, 0·01; $P < 0·001$] but fell during the pandemic [−0·08 (−0·11, −0·04; $P < 0·001$)], with marginal evidence for a step change at the start [−0·19 (−0·38, 0·01; $P = 0·06$); Fig 1B]. The number of positive PCR tests was rising similarly prior to the pandemic [monthly increase in positive tests per 100 admissions 0·01 (95% CI 0·00, 0·01; $P < 0·001$)] but fell by substantially more than could be explained by reduced testing alone at the start of the pandemic [−1·48 (−2·18, −0·78; $P < 0·001$)] and remained stably low following this [−0·05 (−0·16, 0·07; $P = 0·46$; Fig 1C].

Overall, there were 974 positive PCR tests, 943 during 19 465 admissions (4·8/100 admissions) between January 2016 and March 2020 and 31 during 2 951 admissions (1·1/100 admissions) between April 2020 and Febuary 2021. The most frequently detected pathogens were rhinovirus/enterovirus (detected using the same PCR target; 385, 40%), parainfluenza virus (139, 14%), non-SARS-CoV-2 coronaviruses (128, 13%) and RSV (102, 10%; Fig 2). Our data also show expected seasonal variation in common and clinically relevant viruses. Typical seasonal patterns are notable during 2016–2019 with winter peaks of RSV, rhinovirus/enterovirus and coronaviruses. A rapid and sustained fall in all viruses is seen from the second quarter of 2020 until last follow-up when UK social distancing measures remain in place.

Discussion

Our results show a clear, rapid decline in the incidence of pathogenic non-COVID-19 respiratory viruses in our cohort of haematology patients since the introduction of UK social distancing and other infection control measures. This mirrors a decline in detection rates of other respiratory viruses, including influenza, in the general population.[12,13] RSV, influenza and adenovirus can be particularly pathogenic in the immunosuppressed, including those who have undergone HSCT or other T-cell-depleting therapies, who form a significant proportion of our cohort. Although we have not directly studied mortality overall or in particular patient groups, based on historical data[6–8] it can reasonably be inferred that the reduction in incidence seen may have led to a concurrent reduction in viral-related mortality.

It is predicted that there may be a rebound in RSV incidence once social distancing measures are relaxed,[15] due to increased RSV susceptibility following reduced transmission during COVID-19-related restrictions. If this occurs, ongoing risk mitigation policies regarding personal social distancing and face mask use by subsets of haematology patients could be considered. However, immunosuppressed patients and their clinicians will need to weigh infection-related risks against the impact of social restrictions on patients' overall well-being, particularly given the restrictions already faced during the pandemic. We advocate for the ongoing surveillance of these pathogenic respiratory viral infections in the general population, to allow informed discussions with our patients, and counselling of the risks of complications of these infections considering current prevalence.

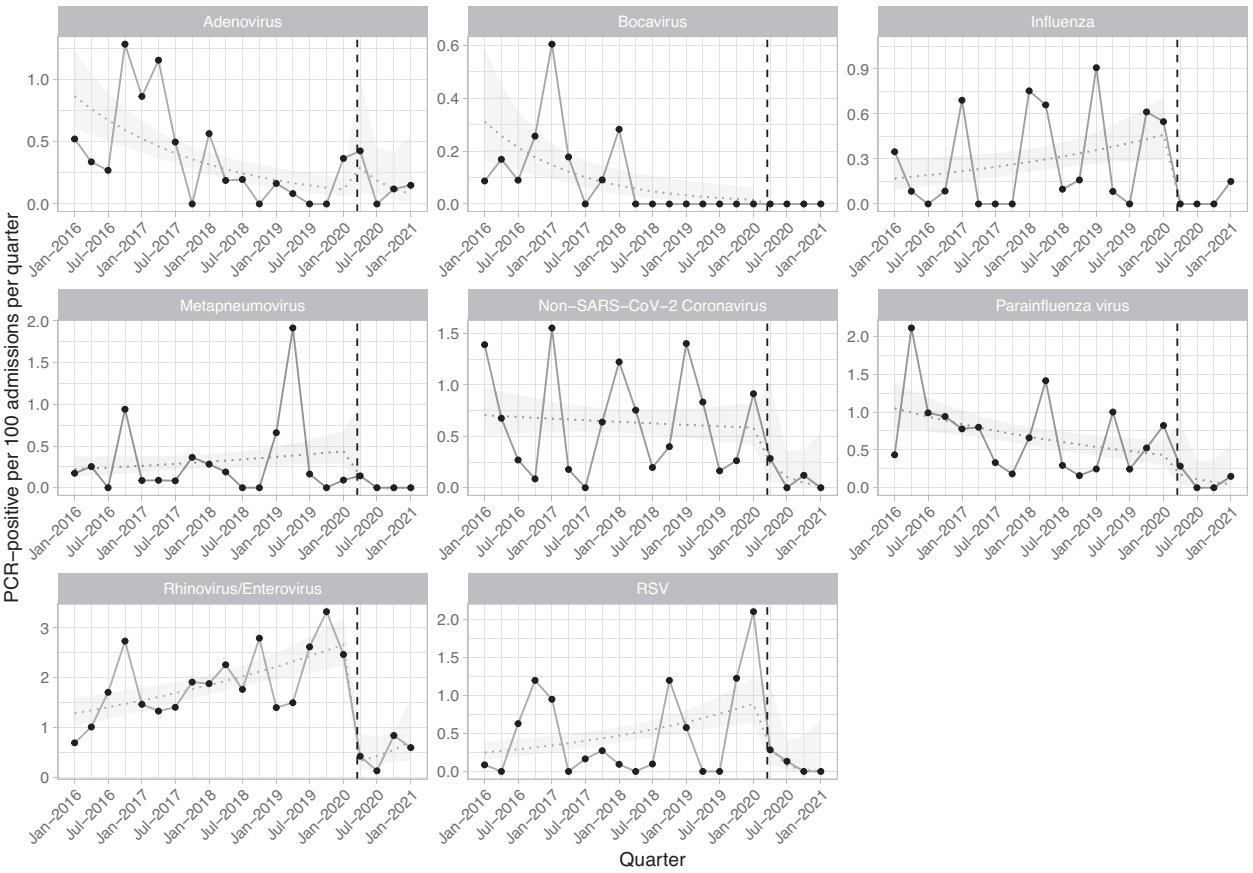

Fig 2. Quarterly incidence of respiratory virus infection in haematology inpatients. For each virus the dashed line indicates the modelled incidence, and the ribbon the 95% confidence interval, allowing for a linear trend before and after the onset of UK national social distancing restrictions, and a step change at this point (shown with a vertical dashed red line). PCR, polymerase chain reaction.

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Author contributions

TAE and DWE: study design, data collection, coordination, analysis, and interpretation, manuscript writing, editing. LP: analysis, and interpretation, manuscript writing. MIA and AP: interpretation, manuscript editing. DWE: statistical analysis.

Conflicts of interest

TAE declares personal advisory and/or lecture fees following Roche, KITE Gilead, Janssen, Abbvie, AstraZeneca, Loxo Oncology, Beigene and Incyte and research funding from Gilead, AstraZeneca and Beigene. DWE declares lecture fees from Gilead outside the submitted work. MIA declares research and consultant fees from Prenetics. No other authors have any relevant conflict of interest to declare.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table SI. Patient characteristics for haematology inpatients tested and not tested for respiratory viruses between January 2016 and February 2021.

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