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Does the rise in seasonal respiratory viruses foreshadow the return of invasive pneumococcal disease this winter?

Early in the COVID-19 pandemic, there were concerns that the introduction of the novel respiratory virus, SARS-CoV-2, would lead to a rise in secondary bacterial infections, especially pneumococcal disease, which has been associated with high fatality rates in previous influenza pandemics. In particular, early reports of hospitalised patients in China found that 50% of COVID-19 non-survivors had bacterial co-infection compared with 15% of survivors.¹ Fortunately, the first pandemic peak saw huge declines in, or in some cases, complete suppression of infections caused by many pathogens, including *Streptococcus pneumoniae*.² In England, cases of invasive pneumococcal disease declined by 30%, from 5666 in the 2018–19 epidemiological year (ie, July–June) to 3964 in 2019–20.³ Additionally, co-infections (n=40) or secondary COVID-19 after invasive pneumococcal disease (n=27) were rare but associated with a high fatality.³

It was posited that these declines were probably due to the interruption of person-to-person transmission of *S pneumoniae* because of government stay-at-home orders, physical distancing, and increased infection control measures to reduce the spread of SARS-CoV-2.^{2,3} Contemporaneous reductions in respiratory viral infections will have also reduced the risk of secondary pneumococcal infections.⁴ Interestingly, nasopharyngeal pneumococcal carriage rates in children reduced only slightly during the pandemic in Israel, while serotype distribution remained similar to pre-pandemic years.⁴

As the winter season approaches, we compared cases of invasive

pneumococcal disease in England from 2020–21 to the 3 previous epidemiological years. In England, the first SARS-CoV-2 cases were detected in January, 2020, and increased rapidly from March, 2020, leading to a national lockdown that included school closures. Lockdown was eased during the summer but was re-implemented in November, 2020, and January, 2021, with gradual easing from March, 2021, and removal of all mitigations from July 19, 2021. Invasive pneumococcal disease surveillance in England has been described previously.³ Briefly, National Health Service hospitals electronically report all infections and routinely

submit invasive pneumococcal isolates for serotyping to Public Health England (now known as the UK Health Security Agency). In the UK, the 23-valent pneumococcal polysaccharide vaccine (PPV23) is offered to all individuals aged 65 years or older and children with comorbidities aged 2 years or older, while the 13-valent pneumococcal conjugate vaccine (PCV13) has been offered to infants at a 2+1 schedule (ie, at 8 weeks, 16 weeks, and 1 year) since 2010 and replaced with a 1+1 schedule at 12 weeks and 1 year since Jan 1, 2020.⁵

Cases of invasive pneumococcal disease declined from March, 2020,



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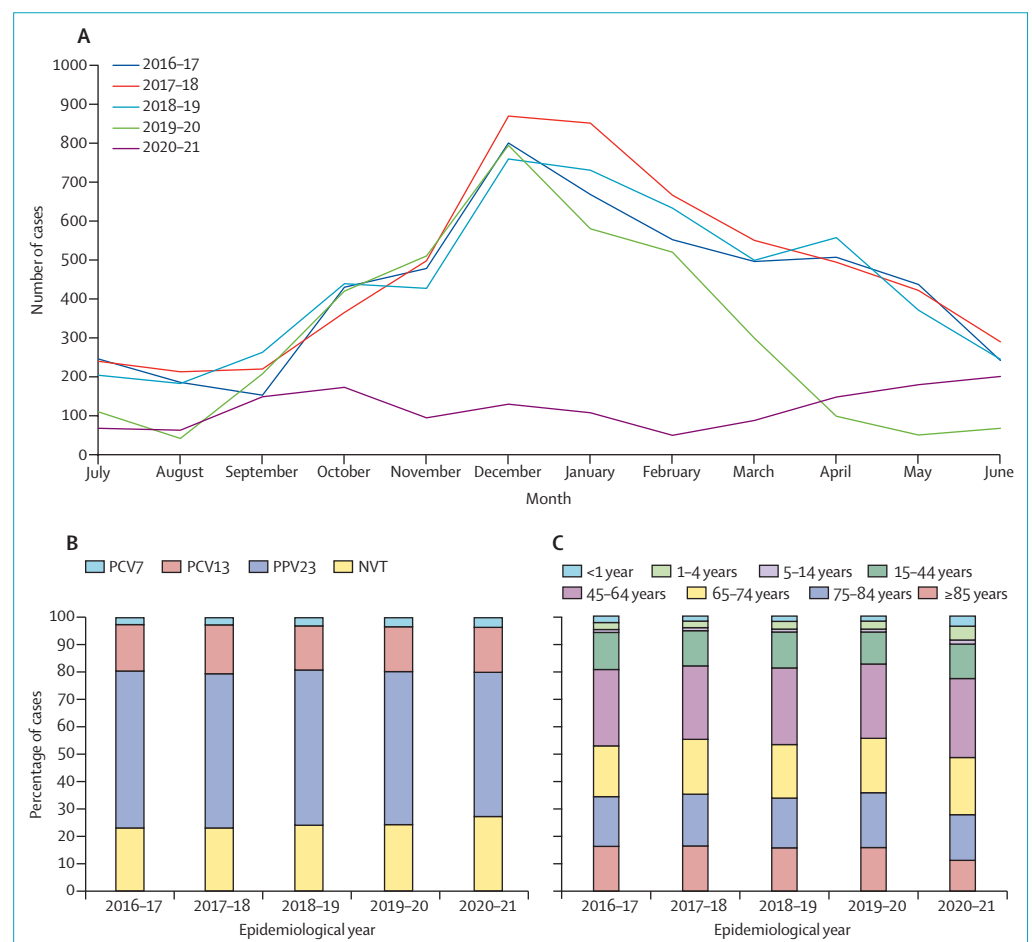


Figure: Cases of invasive pneumococcal disease in England from 2016–17 to 2020–21

(A) Number of cases by month for each epidemiological year. (B) Percentage of cases by serotype group for each epidemiological year.

(C) Percentage of cases by age group for each epidemiological year. PCV7 serotypes include 4, 6B, 9V, 14, 18C, 19F, and 23F. PCV13 serotypes include additional serotypes not included in PCV7 (ie, 1, 3, 5, 7F, 6A, and 19A). PPV23 serotypes include additional serotypes (except 6A) not included in PCV13 (ie, 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, and 33F). NVT includes additional serotypes not included in any vaccine. NVT=non-vaccine type. PCV7=7-valent pneumococcal conjugate vaccine. PCV13=13-valent pneumococcal conjugate vaccine. PPV23=23-valent pneumococcal polysaccharide vaccine.

reaching a nadir in February, 2021, when they accounted for 8% of the pre-pandemic 3-year average for February. Since then, cases have increased gradually, such that, by June, 2021, they were only 25% lower than the pre-pandemic 3-year average for June (figure 1A). The annual incidence of invasive pneumococcal disease in 2020–21 was 3 per 100 000 compared with the pre-pandemic 3-year average of 11 per 100 000. Serotype distribution was similar to pre-pandemic years (figure 1B), with a non-significant decline of 5.7% in PPV23-type invasive pneumococcal disease—largely due to reductions in serotype 12F—but the proportion of cases was significantly higher in children older than 5 years (8.7% [95% CI 7.3–10.2] vs 4.6% ([4.3–4.9]) and lower in those aged 85 years or older (11.2% [9.6–13.0] vs 16.1% [15.6–16.7]) compared with pre-pandemic years (figure 1C). This difference might be due to various factors, including continued educational and social mixing among children, whereas older adults remained largely shielded. Among children older than 1 year who were eligible for the 1+1 PCV13 schedule, there were 35 cases of invasive pneumococcal disease from April, 2020, to March, 2021, including six (17%) due to PCV13-serotypes (three with serotype 19A, two with serotype 3, and one with serotype 19F).

In England, the gradual increase in cases of invasive pneumococcal disease following resumption of normal social activities has been associated with increased reporting of viral infections outside their typical seasonality, including respiratory syncytial virus, which started increasing in May, 2021, and peaked in August, 2021, instead of the typical annual peaks every December.⁶ There are also concerns about potentially higher-than-average surges in respiratory viral infections (especially influenza) this coming winter, because of the population immunity debt following 18 months of lockdown and social isolation.⁷

For this reason, the UK extended recommendations for influenza vaccination to include all children aged 2–15 years on Aug 31, 2021, and every effort is being made to maximise vaccine uptake, including PPV23 for those aged 65 years or older and those with comorbidities.^{8,9} High pneumococcal and influenza vaccine uptake is important: a person is 8 times more likely to die within 30 days if they are co-infected with invasive pneumococcal disease and SARS-CoV-2 than if they are infected with invasive pneumococcal disease alone; they are 6 times more likely to die if they are co-infected with influenza and SARS-CoV-2 compared with having neither of these infections.^{3,10} In conclusion, after the first winter season and three COVID-19 waves in England, cases of invasive pneumococcal disease remained reassuringly low across all age groups, confirming a low risk of invasive pneumococcal disease with or after SARS-CoV-2 infection. Ongoing surveillance will be crucial now that all mitigations are removed in England.

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