seem much less stark.[4] This might be predicted to lead to proportionately more replacement disease after PCV in that age group, the extent of which might further vary by patient population characteristics. At least worthy of further investigation.

I declare no competing interests.

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Authors' reply

We are grateful to William P Hausdorff for his interesting letter[1] regarding our Personal View[2] on the perplexing variation in the extent of pneumococcal serotype replacement, especially among adults aged 65 years and older, suggesting a role for systematic differences in surveillance and the severity of the underlying invasive pneumococcal disease (IPD). It is true that differences in blood culturing practices can influence estimates of IPD incidence, and the serotype distribution associated with IPD. A systematic difference in the reduction in IPD incidence following pneumococcal conjugate vaccine (PCV) implementation might be explained by differences in the nature of the disease measured in each place, coupled with differences in the way PCVs affected the serotypes associated with those disease manifestations.

The correlation plotted by Hausdorff would suggest that surveillance systems capturing a broader spectrum of clinical illness (such as that in the USA) might report larger reductions in cases because of the prevention of milder illness, with severe cases persisting. However, a pronounced drop in IPD among older adults followed PCV7 implementation in both the USA and the UK.[3,4] It is only following PCV13 that these patterns have diverged, with incidence appearing to stabilise in the USA but increasing, to the time of writing, in the UK.[2]

Puzzlingly, these observations cannot be reconciled with the logic of severity alone. If the reduction in the USA is due to the removal of less severe disease, then why was the initial effect of PCV7 similar in the UK, which according to this hypothesis underestimates the incidence of milder infections? And then if, following PCV13, there has been an increase in severe disease in the UK, why has there been no similar increase in the USA, where surveillance should be more than capable of detecting it alongside milder infections?

In short, the mystery remains. As Hausdorff argues, how pneumococcal serotypes vary in the nature and severity of disease in the older population has been hitherto neglected.[5] Why carried serotypes would cause disease among older adults in the UK, but curiously not the USA, is an issue that we agree wholeheartedly should be addressed. Studies of colonisation, transmission, and disease progression among older adults are warranted to identify epidemiological dynamics at play. The continuing discussion and ongoing observation of replacement illustrates the importance of this work to basic science and public health.

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Identification of *Streptococcus pyogenes* $M1_{UK}$ clone in Canada

Nicola Lynskey and colleagues[1] reported on the rapid emergence of a new group A streptococcus (GAS) *emm*1 lineage in the UK ($M1_{UK}$), which was characterised by increased production of the SpeA toxin. Isolates were associated with scarlet fever cases and invasive *emm*1 cases, providing a possible explanation for the increased incidence of invasive GAS disease in the UK. Despite numerous large-scale genomic studies examining the association between genetic variation and virulence, the exact reasons for the recurrent epidemics of invasive GAS disease remain unresolved.[2,3]

The $M1_{UK}$ strain was found to differ from pandemic *emm*1 ($M1_{global}$) by 27 key single-nucleotide polymorphisms (SNPs). Of all the GAS genomes available in the published global genomic databases, only single $M1_{UK}$ clones were identified, in Denmark and the USA.[1]

From 2010 to 2017, the incidence of invasive GAS cases increased in Canada by 63%, from 4·1 cases per 100 000 population to 6·7 cases per 100 000 population.[4] Laboratory-based surveillance for invasive GAS *emm* types and antimicrobial resistance has been

done at the Public Health Agency of Canada since 2010. In 2017, information about *emm* types and antimicrobial resistance was available for 2417 (97%) of 2486 invasive GAS cases reported to the Canadian Notifiable Diseases Surveillance System.[4] *Emm*1 has been the most prevalent *emm* type in Canada since 2010, representing 449 (18%) of 2473 isolates tested in 2017.

In 2017, the Public Health Agency of Canada began an invasive GAS genomics initiative to support surveillance and outbreak investigations, and this collection now includes a wide distribution of *emm*, antimicrobial-resistance, and multilocus-sequence types. The collection is comprised of approximately 3000 genomes from cultures isolated since 2010 from all regions of Canada. We did a core SNP phylogenetic analysis at the Public Health Agency of Canada on 178 Canadian invasive GAS *emm*1 genomes and representative $M1_{UK}$ (n=16), $M1_{intermediate}$ (n=5), and $M1_{global}$ (n=17) genomes described by Lynskey and colleagues.[1] 17 (10%) Canadian isolates clustered with the representative $M1_{UK}$ genomes (appendix). The 17 Canadian genome sequences had the same 27 key SNPs, including the transcriptional regulator RofA mutations Met197Ile, Phe198Val, and Asp370Asn, as were found in the $M1_{UK}$ genomes. The Canadian $M1_{UK}$ isolates were collected between February, 2016, and June, 2019, and were broadly distributed across Canada.

Further investigations, including sequencing of additional historical *emm*1 isolates, proteomic studies, and a review of epidemiological data on clinical manifestations, disease severity, and risk assessments, are planned. The successful international dissemination of the $M1_{UK}$ clone with enhanced invasive potential supports the call for improved surveillance activities, both nationally and globally, to monitor the spread of such clones and provide a rapid response and support for public health interventions.

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Against the trend: a decrease in scarlet fever in New Zealand

We read with interest the study by Nicola Lynskey and colleagues[1] that the seasonal rise in scarlet fever in England in 2016, and the concomitant rise in invasive *Streptococcus pyogenes* (group A streptococcus) disease, was associated with an *emm*1 strain ($M1_{UK}$) with invasive potential. Scarlet fever notifications have risen in England since 2014, and the incidence has increased throughout Asia (China, Hong Kong, and Singapore) since 2009.[2] Apart from the 2016 emergence of $M1_{UK}$, contemporary scarlet fever outbreaks have been polyclonal and associated with multiple *emm*-types. Earlier this year, Walker and colleagues[3] reported the isolation of an epidemic *emm*12 GAS strain from scarlet fever patients in Australia.

Scarlet fever is not notifiable in New Zealand and hence population surveillance data are not routinely available. We extracted data on International Classification of Diseases for scarlet fever (code A38) from the national hospitalisation database between 2009 and 2018 for children aged 15 years and younger. We included all admissions with the specified code in any diagnosis column, and found 98% of cases coded as scarlet fever in the primary diagnosis column on discharge. By contrast with other settings, scarlet fever admissions decreased in 2012 and remained low for 4 years, before returning to baseline admission levels in 2016 (figure).

The observed decrease in scarlet fever hospital admissions coincides with a reduction in first-episode acute rheumatic fever incidence

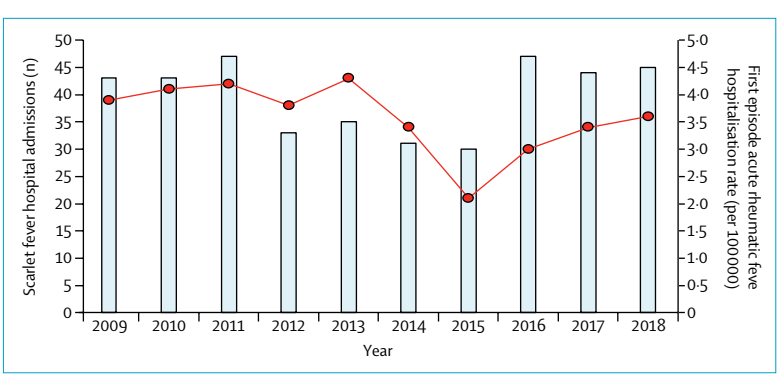

Figure: **Annual number of hospital admissions for scarlet fever in children aged 15 years and younger and hospitalisation rate for acute rheumatic fever in New Zealand, 2009–18**

See **Online** for appendix