Potential impact of Covid-19 response measures on invasive pneumococcal disease in England and Wales

Yoon Hong Choi* and Elizabeth Miller

1. Statistics and Modelling Economics Department, Public Health England, London, England
2. Department of Infectious Disease Epidemiology, Faculty of Epidemiology & Population Health, London School of Hygiene & Tropical Medicine, London, England

* Corresponding author. Yoon.choi@phe.gov.uk

Key words: COVID-19, Social distancing, Pneumococcal transmission model, Invasive pneumococcal disease, Pneumococcal Conjugate Vaccine

Abstract

Objectives

In January 2020, the United Kingdom (UK) removed one of the two infant doses of the 13-valent pneumococcal conjugate vaccine (PCV13), leaving a single priming dose at 3 months and a 12 month booster. We modelled the potential impact on invasive pneumococcal disease (IPD) of a drop in PCV13 coverage associated with the restrictions on non-essential health care visits introduced to combat COVID-19 in the UK on 23 March 2020.

Design

Using a previously published model of pneumococcal transmission in England and Wales we simulated the impact of reducing PCV13 coverage by 50% for 3 months from 23 March without subsequent catch-up vaccination. To implement social distancing, we reduced mixing between and within age-groups by either 10% or 50%. In a sensitivity analysis we explored the effect of complete cessation of PCV13 vaccination during the “lockdown” and of extending its duration to 6 months.

Main outcome measures

Annual numbers of IPD cases predicted by the model under different vaccination and “lockdown” scenarios with uncertainty intervals (UI) generated from the minimum and maximum values of the model predictions using 500 parameter sets with values within a pre-specified range of the maximum likelihood set.
Results

The model predicted that any increase in IPD cases from a reduction in PCV13 coverage would be more than offset by a reduction in pneumococcal transmission due to social distancing, with a net reduction in cumulative IPD cases (UI -1,479, -1,061, all ages) over the next five years. Similar results were obtained in the sensitivity analysis, though with a greater reduction with a 6 month “lockdown”.

Conclusion

COVID-19 social distancing measures are predicted to have had a profound effect on pneumococcal transmission resulting in a reduction in pneumococcal carriage prevalence and IPD incidence over the first two years after the “lockdown”. Carriage studies will be informative in confirming the predicted impact of the social distancing measures after they have been lifted.

Introduction

Following the first identification of local transmission of SARS-CoV-2 in England on February 28 [1] the UK government instituted a series of control measures to reduce spread of the virus. On March 18 schools along with restaurants and places of entertainment and leisure were closed, and on March 23rd all non-essential travel was banned with members of the population only permitted to leave their home for exercise once a day, or in order to obtain food or medication [2]. The public was advised to only use the National Health Service when essential [3] and many general practices replaced face-to-face consultations with an online service [4].

In the UK, paediatric vaccinations are given in general practice and there is concern that the measures taken to limit spread of SARS-CoV-2 may result in many children’s vaccinations being postponed with a resulting increase in vaccine-preventable infections [5]. Indeed early coverage data for measles/mumps/rubella vaccine for the first 3 weeks of the “lockdown” in London suggest a drop of over 40% compared with the same period in 2019 [6]. Of particular concern is the impact of a drop in coverage of the 13 valent pneumococcal conjugate vaccine (PCV13) for which the national 2+1 schedule (2, 4, and 12 months) was changed on 1 January 2020 to a 1+1 schedule at 3 and 12 months [7]. The rationale for the schedule change was that after a decade of high coverage with PCV13 much of the protection of young children against vaccine-type invasive pneumococcal disease (IPD) is through herd immunity generated by the 12 month booster dose and that dropping a priming dose would have little effect on this. The supporting evidence for the schedule change came from an immunogenicity study showing similar post-booster antibody responses to PCV13 serotypes with a 2+1 and 1+1 schedule [8] and a modelling study which predicted little impact on IPD cases in
children or adults if protection against vaccine-type carriage was similar post-booster with the two schedules [9].

Using our previously described pneumococcal transmission model [9] we investigated the impact on IPD if PCV13 coverage was substantially reduced during the “lockdown” period in the UK. We also took account in the model of the likely impact on pneumococcal transmission of the social mixing restrictions put in place to limit the spread of the SARS-CoV-2 virus.

Model and assumptions.

The same compartmental deterministic model and estimated parameter values as described by Choi et al. [9] were used in this study. Briefly, the model simulates the transmission dynamics of carried pneumococci between and within different age groups and predicts carriage changes by serotype grouping, either vaccine type (VT) or non-vaccine type (NVT), under different vaccination scenarios. Carriage changes are then translated into IPD cases using case-carrier ratios (CCRs) that describe the invasive potential of different carried serotypes. The model has 26 parameters which describe the propensity for vaccine-induced replacement of VTs with NVTs in carriage, and the CCRs, in different age groups. The maximum likelihood values of these parameters and their uncertainty ranges are estimated by fitting the model to IPD data up to the end of the epidemiological year July 2015 to June 2016 [9]. In implementing the effect of the 1+1 schedule, the model described by Choi et al. [9] assumed that one priming dose at 3 months of age provides half the protection against VT carriage as two doses or, under a more conservative assumption, that a single priming dose provides no protection against VT carriage. The latter assumption was not included in the current analysis; in addition the change to the 1+1 PCV13 schedule reflected the actual start date of January 2020, not the assumed date of September 2018 as in the original model.

We assumed as a base case a 3 month “lockdown” period starting from March 23 during which there was a 50% reduction in coverage for children who would otherwise have received a priming or booster dose of PCV13 during this period and that there would be no subsequent catch up vaccination for these children. To implement the impact of reduced social mixing we used the same mixing matrix as before [9] based on the POLYMOD study [10] but reduced the number of contacts between and within each age group by either 10% or 50%. In a sensitivity analysis we explored an extreme scenario of cessation of all PCV13 vaccination for the duration of the 3 month “lockdown”, and of extending the duration of the “lockdown” for 6 months with 50% reduction in coverage.

Results are shown as the median of the model outputs under the different scenarios. The uncertainty interval (UI) for each scenario represents the minimum and maximum values generated.
with 500 parameters sets in which each of the 26 model parameters had values within a pre-specified range (± 0.3) of the maximum likelihood set [9]. The impact on IPD of the temporary changes in PCV13 coverage and social mixing is presented by VT, which includes PCV13 serotypes minus serotypes 1 and 3, and NVT; serotype 3 is included with the NVT group in the model on the grounds that it has shown an increase post-PCV13 similar to that seen for NVTs [9].

Results

Fig 1 shows the predicted number of IPD cases in England and Wales by epidemiological year out to 2030/31 in under 5 year olds and in 65+ year olds by VT and NVT group assuming a 50% reduction in PCV13 coverage and a 10% or 50% reduction in contact rates for 3 months. Even with only a 10% reduction in contact rates, the predicted impact of reduced mixing outweighed any increase in IPD due to reduction in PCV13 coverage. The longer term increase in NVT IPD cases in those aged 65 years and over is the consequence of the increasing mean age of this population and the steep increase in IPD incidence with age in this group. Under the extreme assumption that none of the children eligible for PCV13 during the 3 month “lockdown” was ever vaccinated, the results still showed an overall reduction in IPD cases in under 5 year olds and 65+ year olds (Fig S1, Appendix). The predicted beneficial effect of the lockdown on IPD cases was even more marked with a 6 month “lockdown” period (Fig S2, Appendix).
Figure 1. Annual number of IPD cases by VT and NVT and epidemiological year (July to June) from 2018/19 to 2030/31 with a 50% reduction in PCV13 coverage for 3 months starting 23 March 2020 obtained from the long-term simulation model: A. Under 5 year olds with 10% reduction in contact rates; B. Under 5 year olds with 50% reduction in contact rates. C. 65+ year olds with 10% reduction in contact rates; D. 65+ year olds with 50% reduction in contact rates (Width of lines indicates uncertainty intervals). (IPD, Invasive pneumococcal disease; VT, Vaccine types; NVT, Non-vaccine types)

The cumulative number of additional IPD cases predicted in England and Wales over the first five epidemiological years starting from July 2019 is shown in Table 1 by age group and serotype grouping for a 3 month “lockdown” period and a 10% reduction in contact rates. Across all ages the model predicted a net saving of 1,239 IPD cases (UI -1,479, -1,061) over this period compared with the predicted number of IPD cases without the “lockdown”. Without any reduction in contact rates, under the worst case of no PCV13 vaccination for 6 months and no catch up, the model predicted an additional 274 (UI 136, 450) VT IPD cases, of which 27 (UI 14, 44) were in children under 2 years of age.
age. The overall predicted increase in IPD cases was smaller (208 (UI 102, 338)) due to a concomitant reduction in NVT IPD cases.

Table 1. Cumulative difference in cases of invasive pneumococcal disease over 5 epidemiological years (July to June) starting from 2019/2020 by age group and serotype grouping with a 50% reduction in PCV13 coverage, 10% reduction in contact rates and 3 month “lockdown” period starting 23 March 2020. Results show median and minimum and maximum of the range of model outputs generated by 500 best fitting parameter sets [9]

|      | 0-1Y | 2-4Y | 5-14Y | 15-44Y | 45-65Y | 65Y+ | Overall |
|------|------|------|-------|--------|--------|------|---------|
| VT   | 0    | 0    | -2    | -18    | -22    | -38  | -80     |
|      | (-1,1)| (0,0)| (-3,-1)| (-31,-8)| (-39,-11)| (-66,-18)| (-140,-36) |
| NVT  | -36  | -13  | -23   | -172   | -295   | -621 | -1,160  |
|      | (-46,-26)| (-16,-9)| (-30,-21)| (-195,-157)| (-365,-252)| (-735,-522)| (-1388,-987) |
| Overall | -36 | -13 | -25   | -190   | -317   | -658 | -1,239  |
|      | (-46,-26)| (-17,-9)| (-32,-23)| (-216,-174)| (-390,-273)| (-776,-557)| (-1476,-1061) |

Discussion

In line with many other countries, the UK adopted a “lockdown” strategy to minimise social contacts and thereby reduce the spread of the SARS-CoV-2 virus. The restriction on non-essential travel and GP visits raised concerns that vaccine coverage in children might be substantially reduced [5], echoing similar concerns raised at the global level [11]. With the recent change to a 1+1 PCV13 schedule in the UK, which is reliant on the booster dose to maintain herd immunity [8,9], a substantial reduction in PCV13 coverage could compromise control of IPD. Our modelling study suggests that any potential impact of the social distancing policy on PCV13 coverage and herd immunity will be more than offset by a reduction in pneumococcal transmission such that a net reduction in IPD cases should occur. This reduction in IPD would be the result of an overall reduction in pneumococcal carriage prevalence over the first two years after the lockdown, unlike the IPD reduction achieved with PCV. Carriage studies in England before and after the introduction of PCVs have shown little impact on overall carriage prevalence with the reduction in carriage of vaccine serotypes offset by an increase in non-vaccine serotypes [12]. The overall reduction in IPD cases achieved by PCVs is the consequence of the generally lower CCR of the NVTs that replaced VTs in carriage.
Invasive pneumococcal disease is a consequence, albeit rare, of carriage of *Streptococcus pneumoniae* in the nasopharynx. Acquisition of the pneumococcus is by person-to-person transmission and occurs via respiratory droplets with transmission enhanced in settings with close mixing such as day care centres and military camps [13]. Visits to the GP for mild upper respiratory tract disease have also been shown to be a risk factor for pneumococcal acquisition [14]. It is therefore to be expected that the measures taken to reduce spread of SARS-CoV-2 would also reduce pneumococcal transmission. A study of the social contacts of 1356 UK adults conducted between 24 and 27 March suggested a 74% reduction [15] compared with the historical rates documented in the POLYMOD study [10]. However, this study could not assess the impact on contacts made by children, particularly those of pre-school age who are the main drivers of pneumococcal transmission [9]. Hence, we adopted a more conservative range for the reduction in social contacts across all ages in our model. Nevertheless, even with only a 10% reduction in mixing a substantial net reduction in IPD cases over the next 5 years was predicted.

Whether a reduction in coverage caused by the “lockdown” would have a similar effect on other vaccine-preventable infections cannot be assessed with our model as it is specific to pneumococcal infection. However, the average number of weekly notifications of whooping cough and meningococcal septicaemia in England in the eight weeks from 23 March 2020 showed a 76% and 87% reduction respectively compared with the weekly average for the previous 45 weeks [15]. As with IPD, nasopharyngeal colonisation is a pre-requisite for whooping cough and meningococcal disease. While the completeness of notifications by doctors may have suffered somewhat as a result of the COVID-19 epidemic, the magnitude of the decline in these two other infections is consistent with a substantial reduction in new colonisation episodes following the “lockdown” and suggests that, at least in the short term, this has outweighed any potential increase due to a reduction in coverage of pertussis or meningococcal vaccines. For measles, which is highly infectious, small reductions in coverage can have more of an impact as shown by the loss of the UK’s former measles elimination status in 2019 following relatively small declines in vaccine coverage that allowed the re-establishment of endemic measles transmission [16]. While measles notifications have shown an 84% decline since the start of the “lockdown” many such notifications turn out not be measles when laboratory confirmation is sought [15]. As with IPD, published data on confirmed measles cases during the “lockdown” are not yet available and may be difficult to interpret due to interruption of the normal processes that lead to laboratory confirmation of suspected cases during the COVID-19 epidemic.
In conclusion, our pneumococcal model predicts that the effect of the COVID-19 “lockdown” on pneumococcal carriage rates will result in a reduction in IPD cases over the next two years, thus obscuring the predicted small increase in VT IPD due to the adoption of a 1+1 PCV13 schedule [9]. Pneumococcal carriage studies conducted over the next few years could help elucidate the impact of the social distancing measures and of the adoption of the 1+1 PCV13 schedule on the future incidence of VT and NVT IPD.

References

1. Coronavirus: First Covid-19 transmission within the UK confirmed | inews. https://inews.co.uk/news/uk/coronavirus-first-covid-19-transmission-uk-confirmed-2004500 (accessed 27 May 2020).

2. COVID-19: guidance on social distancing and for vulnerable people - GOV.UK. https://www.gov.uk/government/publications/covid-19-guidance-on-social-distancing-and-for-vulnerable-people (accessed 27 May 2020).

3. NHS. Staying at home and away from others (social distancing) - GOV.UK. https://www.gov.uk/government/publications/full-guidance-on-staying-at-home-and-away-from-others/full-guidance-on-staying-at-home-and-away-from-others (accessed 27 May 2020).

4. How to get medical help from home - Coronavirus (COVID-19) - NHS. https://www.nhs.uk/conditions/coronavirus-covid-19/staying-at-home-to-avoid-getting-coronavirus/how-to-get-medical-help-from-home/ (accessed 27 May 2020).

5. Missed vaccinations could lead to other fatal outbreaks, doctors warn | Society | The Guardian. https://www.theguardian.com/society/2020/apr/26/missed-vaccinations-could-lead-to-other-fatal-outbreaks-doctors-warn (accessed 27 May 2020).

6. McDonald HI, Tessier E, White JM, et al. Early impact of the coronavirus disease (COVID-19) pandemic and physical distancing measures on routine childhood vaccinations in England, January to April 2020. *Eurosurveillance* 2020;25:2000848. doi:10.2807/1560-7917.ES.2020.25.19.2000848

7. Changes to the infant pneumococcal conjugate vaccine schedule. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_d
Goldblatt D, Southern J, Andrews NJ, et al. Pneumococcal conjugate vaccine 13 delivered as one primary and one booster dose (1 + 1) compared with two primary doses and a booster (2 + 1) in UK infants: a multicentre, parallel group randomised controlled trial. *Lancet Infect Dis* 2018;18:171–9. doi:10.1016/S1473-3099(17)30654-0

Choi YH, Andrews N, Miller E. Estimated impact of revising the 13-valent pneumococcal conjugate vaccine schedule from 2+1 to 1+1 in England and Wales: A modelling study. *PLOS Med* 2019;16:e1002845. doi:10.1371/journal.pmed.1002845

Mossong JJ, Hens N, Jit M, et al. Social contacts and mixing patterns relevant to the spread of infectious diseases. *PloS Med* 2008;5:e74.

Hirabayashi K. The impact of COVID-19 on routine vaccinations: Reflections during World Immunization Week 2020. https://www.unicef.org/eap/stories/impact-covid-19-routine-vaccinations (accessed 27 May 2020).

Southern J, Andrews N, Sandu P, et al. Pneumococcal carriage in children and their household contacts six years after introduction of the 13-valent pneumococcal conjugate vaccine in England. *PLoS One* 2018;13:e0195799.

Sleeman KL, Daniels L, Gardiner M, et al. Acquisition of Streptococcus pneumoniae and Nonspecific Morbidity in Infants and Their Families. *Pediatr Infect Dis J* 2005;24:121–7. doi:10.1097/01.inf.0000151030.10159.b1

Jarvis CI, Van Zandvoort K, Gimma A, et al. Quantifying the impact of physical distance measures on the transmission of COVID-19 in the UK. *BMC Med* 2020;18:124. doi:10.1186/s12916-020-01597-8

Public Health England. Notifiable diseases: last 52 weeks - GOV.UK. https://www.gov.uk/government/publications/notifiable-diseases-last-52-weeks (accessed 27 May 2020).

Public Health England. Measles in England - Public health matters. https://publichealthmatters.blog.gov.uk/2019/08/19/measles-in-england/ (accessed 27 May 2020).