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MAJOR ARTICLE

Pneumococcal carriage and disease in adults in England 2011-2019: the importance of adults as a reservoir for pneumococcus in communities

El Safadi D[1], Hitchins L[1], Howard A[1], Aley P[2,3], Bowman J[2], Bertran M[4], Collins A[1], Colin-Jones R[2], Elterish F[2], Fry NK[4], Gordon SB[1], Gould K[5,6], Hinds J[5,6], Horn E[1], Hyder-Wright A[1], Kandasamy R[2], Ladhani S[4], Litt D[4], Mitsi E[1,2], Murphy A[1], Pollard AJ[2], Plested E[2,3,7], Pojar S[1], Ratcliffe H[2], Robertson MC[1], Robinson H[2,3,7], Snape MD[2,3], Solórzano C[1,2], Voysey M[2], Begier E[8], Catusse J[8], Lahuerta M[8], Theilacker C[8], Gessner BD[8], Tiley KS[2*], Ferreira DM[1,2*]

[1] Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, United Kingdom; [2] Oxford Vaccine Group, Department of Paediatrics, University of Oxford, Oxford, United Kingdom; [3] National Institute for Health Research, Oxford Biomedical Research Centre, Oxford, United Kingdom; [4] Immunisations and Vaccine Preventable Diseases, UK Health Security Agency (UKHSA), London, United Kingdom; [5] Institute for Infection and Immunity, St George's University, London, United Kingdom; [6] BUGS Bioscience, London Bioscience Innovation Centre, London, United Kingdom; [7] National Institute for Health Research Clinical Research Network, Thames Valley and South Midlands, Oxford, United Kingdom; [8] Pfizer Vaccines, Pfizer Inc, Collegeville, Pennsylvania, USA

*joint senior authors
Corresponding author: Karen S. Tiley, Oxford Vaccine Group, Centre for Clinical Vaccinology and Tropical Medicine (CCVTM), Churchill Hospital, Old Road, Headington, Oxford, OX3 7LE, United Kingdom, Email: karen.tiley@paediatrics.ox.ac.uk
NB please change in final manuscript to: Daniela M. Ferreira, Oxford Vaccine Group, Centre for Clinical Vaccinology and Tropical Medicine (CCVTM), Churchill Hospital, Old Road, Headington, Oxford, OX3 7LE, United Kingdom, E-mail: daniela.ferreira@paediatrics.ox.ac.uk

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Background Pneumococcal carriage in children has been extensively studied, but carriage in healthy adults and its relationship to invasive pneumococcal disease (IPD) is less understood.

Methods Nasal wash samples from adults without close contact with young children (Liverpool, UK), 2011-2019, were cultured, and culture-negative samples tested by PCR. Pneumococcal carriage in adults 18-44 years was compared with carriage among PCV-vaccinated children 13-48 months (nasopharyngeal swabs, Thames Valley, UK) and IPD data for England for the same ages for 2014-2019. Age-group specific serotype invasiveness was calculated and used with national IPD data to estimate carriage serotype distributions for adults aged 65+ years.

Results In total 98 isolates (97 carriers) were identified from 1,631 adults aged 18+ years (age and sex standardized carriage prevalence 6.4%), with only three identified solely by PCR. Despite different carriage and IPD serotype distributions between adults and children, serotype invasiveness was highly correlated (R=0.9). Serotypes 3, 37 and 8 represented a higher proportion of adult carriage than expected from direct low-level transmission from children to adults. The predicted carriage serotype distributions for 65+ years aligned more closely with the carriage serotype distribution for young adults than young children.

Conclusions The nasal wash technique is highly sensitive; additional benefit of PCR is limited. Comparison of carriage serotype distributions suggests some serotypes may be circulating preferentially within these specific young adults. Our data suggest that for some serotypes carried by adults 65+ years, other adults may be an important reservoir for transmission. Age groups such as older children should also be considered.

Key words: pneumococcal, carriage, transmission, invasive pneumococcal disease, adults, children

INTRODUCTION

Invasive pneumococcal disease (IPD) is caused by infection with *Streptococcus pneumoniae* (pneumococcus) and includes pneumonia, septicemia, and meningitis. Over 100 serotypes of *S. pneumoniae* (characterized by polysaccharide capsule differences) have been identified [1].

Vaccine-type IPD declined in the UK following the introduction of pneumococcal conjugate vaccines (PCVs) into the national childhood immunization program. PCV7, targeting seven serotypes (4, 6B, 9V, 14, 18C, 19F, 23F), was introduced in 2006 and by 2009/2010 had reduced vaccine-type IPD in England and Wales by 98% in children <2 years and by 81% in adults 65+ years [2]. However, several non-vaccine serotypes increased in frequency ('serotype replacement') [2]. In 2010, PCV13, which targets an additional six serotypes (1, 3, 5, 6A, 7F, 19A), replaced PCV7 [3]. PCV13 led to a significant reduction in vaccine-type IPD amongst all ages and by 2016/2017, despite the increases in non-vaccine-type IPD, total IPD across all ages was 37% lower than the pre-PCV7 period [4].

Reductions in IPD have occurred via direct protection of vaccinated children and indirect protection of all age groups through the ability of PCVs to reduce vaccine-type carriage and hence transmission. However, reductions in PCV13 vaccine-type IPD have plateaued in adults since 2013/2014 [4] and PCV13 vaccine-type pneumonia remains common [5–7] despite vaccination of adults 65+ years (~70% coverage) with a pneumococcal polysaccharide vaccine (PPV23) since 2005 [8].

PCV15 (containing PCV13 serotypes and serotypes 22F and 33F) and PCV20 (containing PCV15 serotypes and serotypes 8, 10A, 11A, 12F and 15B) have been licensed for use in the UK and in June 2023 the Joint Committee for Vaccination and Immunisation advised that either PCV20 or PPV23 could be used for the adult pneumococcal program in the future [9–12].

The prevalent paradigm is that carriage occurs most commonly in young children and that transmission is almost entirely driven from this age cohort to other age cohorts [13]. How carriage in children relates to carriage in adults, and adult IPD is less understood. We aimed to compare carriage and IPD serotype distributions for children and adults in England and relate these to IPD and estimated carriage serotype distributions in older adults, to better understand adult carriage, and potential benefits of higher valency PCV introduction to adults.

METHODS

Sampling and laboratory methods

Carriage in adults

Healthy volunteers aged 18+ years were enrolled, with informed consent, in the experimental human pneumococcal carriage (EHPC) research program in the Liverpool School of Tropical Medicine, UK, 2011-2019. All 17 studies were approved by the local National Health Service Research Ethics Committee. Methods, and inclusion/exclusion criteria have been previously reported [14]. All participants had no close contact with at-risk individuals during the study, including children aged <5 years, healthcare workers, patients with respiratory or immunosuppressive comorbidities or those receiving steroid therapy (Supplementary methods). Vaccination status was not ascertained but participants were not eligible for PCV (all born prior to 2002), though adults 65+ years may have received PPV23.

All volunteers underwent nasal wash (NW) screening for pneumococcal colonization at their first visit; all baseline results were included in this analysis. Methods for collection and the processing of NWs for bacteriological detection have been previously described [14,15]. Pneumococcal isolates were serotyped by latex agglutination test and confirmed, when required, by the Senti-SP v1.6 molecular serotyping microarray (BUGS Bioscience, UK).

For negative-culture samples, bacterial genomic DNA was extracted from both raw and culture-enriched NW samples (Supplementary methods).

Carriage in children

Carriage data for children aged 13-48 months were combined from two cross-sectional studies in the Thames Valley, UK carried out between February 2014 and August 2015 (988 children, 473 carriers (47.9%), 572 isolates), and between June 2017 and August 2019 (795 children, 413 carriers (51.8%), 492 isolates) [16,17]. Serotype-specific carriage was stable between these two time periods, apart from an increase in 7C [16].

All children included in these studies had received three doses of PCV13 according to the UK immunization schedule [18].

Nasopharyngeal swabs were collected and processed according to World Health Organization (WHO) guidelines [19][16].

IPD in adults and children

IPD is characterized by detection of pneumococcus in a normally sterile site by culture or through PCR in cerebrospinal or pleural fluid. Numbers of IPD cases in England aged 13-48 months, 18-44 years and 65+ years, for each serotype, were extracted from the national database for England maintained by the UK Health Security Agency (UKHSA) for 2014-2019. Serotyping of IPD isolates was performed by UKHSA [4].

Statistical methods

Adult pneumococcal carriage prevalence in England and 95% confidence intervals were calculated using a binomial exact method for age groups 18-29 years, 30-44 years, and 45+ years, and for males and females. An age and sex standardized estimate for England was calculated using 2015 (mid-point 2011-2019) Office for National Statistics population estimates [20].

Carriage geometric mean density measurements (colony forming units per ml) for adults were compared for PCV13 and non-PCV13 serotypes.

Carriage data for a subset of adults aged 18-44 years were compared with data for children aged 13-48 months and presented as the percent of each serotype out of total isolates. 'Excess' serotypes in adults and child serotype distributions were calculated by subtracting the percentage of each serotype found in child carriage from the percentage of each serotype found in adult carriage and vice versa. The age group 18-44 years was chosen to align with published data for IPD in England, and because the majority of our participants were young adults (Supplementary figure 1).

Serotype-specific comparisons of carriage between children and adults were performed using Fisher's exact test, reported as odds ratios (ORs, ratio of carriers/non-carriers for children/adults)

with 99% confidence intervals. P-values <0.01 were considered significant to allow for multiple comparisons.

IPD numbers were adjusted to account for the proportion of cases within each year that were not serotyped, assuming these cases had the same serotype distribution as those serotyped.

To enable comparisons of different numbers of isolates/cases for each age cohort, child and adult carriage and IPD serotype distributions were presented as the percent of each serotype out of total isolates or IPD cases.

Serotype-specific case-carrier ratios for children and adults were calculated by dividing the average annual number of serotype-specific IPD cases in England 2014-2019 by the estimated annual number of carriers of that serotype in England. The latter was calculated by multiplying study carriage prevalence of the serotype for 2014-2019 by the age-specific population of England in 2017 (mid-point). A measure of certainty in the estimates for each serotype was calculated by summing the numerators for carriage and IPD across children and adults (larger total numerators = greater certainty). A weighted (based on certainty) linear regression line was fitted and correlation coefficient determined from R^2.

To calculate the predicted number of each serotype in carriage for adults aged 65+ years, the number of IPD cases in adults 65+ years for each serotype was divided by the case-carrier ratio calculated for children or young adults. Where case-carrier ratios were not available the child case--carrier ratio could sometimes be estimated from the adult ratio (and vice versa) by using the fitted regression line relationship so that 33 serotypes were included in total. 'Other' serotypes comprised 5% for children and 12.5% for adults so a mid-point 9% was used for 65+ years.

Predicted serotype distributions in carriage for adults aged 65+ years were compared with actual 18-44 years and child carriage serotype distributions and the percentage agreement calculated by subtracting the percentage in carriage in young adults or children for each serotype from the predicted percentage in carriage for 65+ years. Positive differences were then summed and subtracted from 100.

Analyses were performed in R version 4.3.1.

RESULTS

Adult carriage population

Carriage prevalence

Results were available for 1,631 participants between 2011 and 2019 (Supplementary tables 1 and 2), of whom 967 (59.3%) were female. Median age was 21 years (range 18-80 years) reflecting a predominantly student population (Supplementary figure 1).

S. pneumoniae was detected in 97/1,631 (5.9%) participants. England age and sex standardized prevalence was 6.4% (Table 1). Carriers ranged from 18 to 58 years old. More than a single serotype was detected in only one participant, carrying serotypes 3 and 8.

Serotype distribution

In 2011-2019, 23/1,631 adults aged 18+ years (1.4%, 95% CI, 0.9%–2.1%) were carrying a PCV13 serotype, most commonly serotypes 3 (12/1,631, 0.7%, 95% CI 0.4%–1.3%) and 19F (4/1,631, 0.2%, 95% CI 0.1%–0.6%) (Figure 1). Of the two additional PCV15 serotypes (22F and 33F), only serotype 33F was detected (in 4 adults, 0.2%). A further 19 adults (1.2%) were carrying serotypes 8, 11A, 15B/C, 10A, and 12F contained in PCV20. The five most frequently isolated serotypes in our cohort were 3, 35F, 23B, 37, and 8 (Figure 1). Serotypes not contained in PCV20 were carried by 52/1,631 adults (3.2%, 95% CI 2.4%-4.2%).

In total, 94 (95 isolates) carriers were identified by culture, and three additional carriers (three isolates; one 7C, and two NT) were identified by molecular methods on culture-negative samples (Figure 1).

Colony density

Density measurements were available for 74/98 (76%) isolates during 2011-2019 (Supplementary figure 2), of which 72/74 were from 2014-2019. There was no significant difference in geometric mean density overall between PCV13 serotypes (175 CFU/ml, n=17) and non-PCV13 serotypes (53 CFU/ml, n=57) (p=0.26). Geometric mean density across all serotypes was 70 CFU/ml (median 44 CFU/ml).

Comparison with carriage in children (2014-2019)

Serotype distribution

In a subset of adults aged 18-44 years (N=1,289), 72 carriers (all single isolates) were identified (Supplementary table 2). The adult (18-44 years) serotype distribution contained a higher proportion of PCV13 serotypes (16/72, 22.2%) compared with children (46/1,064, 4.3%) (Figure 2). The most frequently isolated serotypes in adults were 3 (8 isolates, 11.1%), 37 (6 isolates, 8.3%), 8 and 35F (5 isolates each, 6.9%), 11A and 23B (4 isolates each, 5.6%). In children the most frequent serotypes were 15B/C (145 isolates, 13.6%), 23B (115 isolates, 10.8%), 11A (96 isolates, 9.0%), 21 (86 isolates, 8.1%) and 10A (75 isolates, 7.0%). Serotypes 3, 37 and 8 contributed 21 (2.0%), 1 (0.1%) and 6 (0.6%) isolates respectively in children.

Serotypes with the greatest 'excess' isolates in adult carriage were 3, 37 and 8 (Figure 3C). Serotypes found in higher proportions in child compared with adult carriage were 15B/C, 21, 10A and 23B (Figure 3D).

For serotypes detected in adults and children, the odds of carriage was not significantly different (p>0.01) between adults and children for serotypes 37, 8, 19F, 3, 31, 12F, 6C, 9N (remaining serotypes all greater odds of carriage in children) (Supplementary figure 3, Supplementary table 3).

Invasive pneumococcal disease

In total 4,237 IPD cases in adults aged 18-44 years (average annual incidence 3.6 cases per 100,000) and 776 IPD cases in children aged 13-48 months (average annual incidence 6.3 cases per 100,000) were reported in England between 2014 and 2019 inclusive, of which 3,898 (92%) and 684 (88%) respectively were serotyped.

The top five serotypes causing IPD in adults aged 18-44 years 2014-2019 were 8 (1,258 cases, 32.3% of those serotyped), 12F (642 cases, 16.5%), 9N (229 cases, 5.9%), 3 (227 cases, 5.8%) and 22F (189 cases, 4.8%); the top five serotypes causing IPD in children aged 13-48 months were 12F (100 cases, 14.6% of those serotyped), 15B/C (81 cases, 11.8%), 10A (68 cases, 9.9%), 23B (56 cases, 8.2%) and 24F (49 cases, 7.2%).

Despite differences in carriage and IPD serotype distributions between children and adults (Figure 4), case-carrier ratios for children and adults were highly correlated (R=0.9) (Figure 5).

In general, serotypes with highest case-carrier ratios caused most disease (Supplementary figures 4a-c). The majority of case-carrier ratios (14/20) were not significantly different between adults and children (Supplementary figure 4a). The remainder were higher in adults and there was a general pattern of higher case-carrier ratios in adults compared with children (Supplementary figure 4a, Figure 5).

The predicted 65+ years carriage serotype distribution based on the case-carrier ratios for adults aged 18-44 years (Figure 6A) showed 78.5% agreement with the young adult carriage serotype distribution and 59.4% agreement with the children's carriage serotype distribution (Supplementary figure 5). The predicted 65+ years carriage serotype distribution based on child case-carrier ratios (Figure 6B) showed 61.9% agreement with the young adult carriage serotype distribution and 58.8% agreement with the children's carriage serotype distribution (Supplementary figure 6). The IPD serotype distribution in adults 65+ years is provided for reference (Supplementary figure 7).

DISCUSSION

Key findings

We found a higher proportion of PCV13 serotypes (22.2%) in our young adult population compared with children (4.3%). The different serotype distribution in young adults compared with children, and particular abundance of serotypes 3, 37 and 8 suggests these serotypes may be

circulating within this adult population, or amongst older children in whom the carriage serotype distribution is currently unknown.

Invasiveness was generally higher in young adults compared with children and ratios were correlated. The close alignment of the predicted 65+ years carriage serotype distributions with the young adult carriage serotype distribution suggests adult-to-adult transmission could be important, but does not rule out transmission occurring from younger and older children to adults, and between older adults themselves.

Our study demonstrates that molecular techniques only minimally improve the sensitivity of *S. pneumoniae* detection when using NW to assess carriage. This contrasts with the substantial improvement in detection by molecular technique relative to classical microbiology using naso- or oropharyngeal swabs, the current WHO gold standard technique for carriage detection in adults [19,21].

Comparison to other studies

Previous studies of carriage in England post-PCV13 introduction have taken nasopharyngeal swabs within young-family households and found adult carriage prevalence 2.8-9% [22–24]. The similar carriage prevalence in our adult population, despite using the more sensitive NW technique, may reflect lack of contact with children. Previous studies in England have found proportions of vaccine-serotypes 0-44% within adult populations though limited by small numbers [22–24]. These estimates are point prevalences and longitudinal prevalence estimates in adults are rare [25]; any particular carriage study only samples a fraction of the upper airway, with variation depending on methodology; it is likely that even in sampled areas it is difficult to obtain pneumococci contained in biofilms, residing below the mucosal surface, or occurring at low density. Consequently, true carriage prevalences over time may be much higher than reported in the literature.

Serotype distributions for UK children aged 6-12 months and 12-48 months have previously been found similar [16]. However, different serotype carriage serotype distributions have been observed between younger (<24 months) and older (24-59 months) children in Israel, and the patterns in older children correlated better with patterns of IPD in adults (adult carriage data unavailable), supporting the idea of carriage serotype distributions changing between early childhood and adults [26]. Correlation between case-carrier ratios for adults and children, as well as higher ratios in adults compared with children, has previously been observed for Navajo Nation adults and children in the US [27]. Serotype-specific invasiveness in children has previously been shown to be stable across different time periods and geographies [28]. Our invasiveness estimates correlate with recently published estimates by Løchen *et al.* (Supplementary figures 8a-b) [29]. Carriage prevalence in adults 65+ years is estimated at ~2%, but even if 6%, as seen in young adults, we would expect case-carrier ratios for this age group to be higher than for young adults given the higher numbers of IPD cases in adults aged 65+ years [22,30].

Carriage data for UK adults 65+ years are not available in sufficient numbers to compare with our predicted profile [22] and comparisons with other countries are limited by differences in vaccination schedules and/or family/population structures. Alignment of the 65+ years predicted serotype distributions with the young adult serotype distributions and suggestion of adult-to-adult transmission is supported by similar odds of carriage for children and adults for particular serotypes, and mixing matrices for the 65+ years age group indicating higher contact rates with younger adults compared with children [31,32]. Our young adult population did not have contact with young children, further suggesting acquisition of pneumococci from other age groups.

The observed abundance of serotype 3 and other PCV13 serotypes in adults indicates that these serotypes circulate within the unvaccinated adult population despite years of PCV13 use in children. Although serotype 37 was prominent in adult carriage, it was not reported in adult (or child) IPD for the same period suggesting low invasiveness for this serotype currently. In contrast, serotype 8 is one of the main causes of IPD in adults in England. Recent modelling suggests that elimination of serotype 33F (included in both PCV15 and PCV20) could result in serotype switching to serotypes 11A and 8 (both included in PCV20 but not PCV15) [33], which could potentially increase the circulation of the latter if a vaccine is used that contains 33F but not 8 and 11A. Presence and possible transmission of serotype 8 among adults suggests introduction of PCV20 only in children may have less impact than might otherwise be expected and more substantial reductions may require direct immunization of adults.

In a cross-sectional study in 2010/2011, serotype 22F was the most frequently detected serotype in 3/9 colonized UK parents, followed by serotypes 3 and 19A (2 isolates each) [22]. Serotype 22F was not detected in our adult cohort, but it was detected in children, In a 2014/2015 UK carriage study the most frequently isolated serotypes from parents were 21, 23B and 38 (each found in 3/21 colonized parents), of which only serotype 23B was detected in our young adult study population (all three serotypes were isolated from our child comparison population [17]). These serotypes could mainly be transmitted from children to adults.

Our adult study population was predominantly students, a population group with many social contacts in crowded settings providing multiple opportunities for transmission. Young adults are a reservoir of infection for *Neisseria meningitidis*[34,35]; and increasing carriage prevalence as attendance at university/college progresses [36]. We did not have sufficient numbers to explore this, but it is plausible that this population group could be a reservoir for the serotypes found at particular abundance within young adult carriage. A longitudinal study of adults aged 25-50 years in Portugal found that approximately 20% of the adults were intermittent carriers and 10% were persistent carriers (>4 months), and suggested some adults may act as reservoirs of pneumococci[37].

Similar colony density in adults for PCV13 and non-vaccine serotypes contrasts with the finding in PCV13-vaccinated children [16]. Density measurements cannot be directly compared between

children and adults because of different methodology but lower orders of magnitude for adult measurements suggest lower colony density in adults.

Strengths and limitations

The IPD data relate to the national population and for adults will likely have tended towards older individuals within the 18-44 years age band, and those with underlying co-morbidities, unlike our young, healthy adult study population. Crucially also our study population was not exposed to children. However, although the study population met specific exclusion criteria, they may have mixed with others who did not meet those criteria, or had contact with risk groups prior to enrolment meaning serotypes with long durations of carriage would have been unaffected.

Different methods were used to sample adults and children, and the serotype identification methodology differed, though there was some overlap.

The adult and child populations were from different geographical areas of England, we therefore cannot exclude regional differences in circulating serotypes, however, vaccination coverage of the PCV booster dose at age two years was similar across both study regions [38,39].

The 65+ years predicted carriage serotype distributions are approximate and limited to the 33 serotypes with available case-carrier ratios. The case-carrier ratios have different sized confidence intervals; this uncertainty was not incorporated into the predicted serotype distributions. The assumption that 'other' serotypes comprise around 9% of 65+ years carriage was chosen to try to minimize bias towards either the adult or child serotype distribution, but this value is unknown. Serotype 37 was prominent in the young adult serotype distribution but could not be incorporated into the older adult serotype distribution because its case-carrier ratio could not be calculated (zero IPD cases).

We did not calculate predicted serotype distributions in carriage for older children because these would be based on relatively low IPD case numbers [40].

CONCLUSIONS

Our finding of a distinct adult pneumococcal carriage serotype distribution gives an important insight into overall and serotype-specific carriage and disease dynamics. The identification of particular serotypes that may be circulating in adults, and the similarity of the predicted serotype distributions for older adults to the serotype distribution in young adults suggests that this group of adults could be a reservoir for pneumococcus in the community. With advancements in molecular methods for detection, future studies should investigate carriage and serotype distributions in adults 65+ years. Further studies are needed to better understand the role of adults and older children as transmitters of pneumococcus, particularly associated with increased nasal colonisation density driven by upper respiratory tract virus co-infections [27,41,42]. This has

implications for the optimal use of vaccines against pneumococcus and respiratory viruses (e.g. RSV, influenza) to provide increased protection for adults at risk including the elderly.

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Author contributions:

Study concept and design: DES, DMF, KST

Recruiting and consent of participants: AC, RC-J, RK, EP, HRa, HRo, AHW

Data collection and management: PA, MB, RC-J, DES, LH, RK, EP, HRa, HRo

Sample processing: JB, DES, NKF, KG, AH, EH, FE, JH, LH, DL, EM, SP, MCR, CS, AM

Statistical planning and analysis: KST, MV

Data analysis and interpretation: EB, MB, DES, DMF, NKF, BDG, DL, EM, AH, LH, AJP, SP, CS, CT, KST, MV

All authors read and approved the manuscript.

Data availability

Adult and child pneumococcal carriage data are available in supplementary material.

UKHSA collects data as part of national surveillance – requests for invasive pneumococcal disease data can be made to UKHSA directly.

Presentation of research

These study findings were presented at the 13th Meeting of the International Society of Pneumonia & Pneumococcal Diseases (ISPPD), 17-20 March 2024, Cape Town, South Africa (Home ISPPD2024 | ISPPD 2024 - 13th Meeting of ISPPD (kenes.com))

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The UKHSA has legal permission to process confidential information for national surveillance of communicable diseases without individual patient consent (Regulation 3 of Health Service Regulations 2002) and, as such, ethics committee approval was not required for the collection of Invasive Pneumococcal Disease (IPD) data.

Conflict of interest statements:

MDS has been an investigator on behalf of the University of Oxford for studies funded or otherwise supported by vaccine manufacturers including Glaxosmithkline, Janssen, Pfizer, Novavax and MCM vaccines. Since 2022 MDS has been employed by Moderna Biotech Distributors UK and holds equity in Moderna Inc.

NKF and DL's laboratory has received grant funding from vaccine manufacturers for investigator-led research on pneumococcal carriage and disease.

JH has received project grants (all payments to institution) from Pfizer.

AJP is Chair of the UK DHSC Joint Committee on Vaccination & Immunisation (JCVI)

BG, JC, CT, EB and ML are employees of Pfizer and may hold stock and/or stock options.

All other authors no conflict of interest

These may not be relevant as they are to do with separate studies:

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AstraZeneca - Oxford University has entered into a partnership with AZ for development of COVI19 vaccines.

Serotypes such as 3, 37 and 8 are found at higher frequency in young adult carriage than would be expected from direct low-level transmission from children suggesting young adults could be a possible reservoir of infection for some serotypes.

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Table 1. Adult pneumococcal carriage prevalence by age group and sex, Liverpool, England, 2011-2019, and age and sex standardised to England 2015 population

Age group (years)	Sex	Number of participants	Number of pneumococcal carriers	Carriage prevalence (95% confidence intervals)
18-29		1391	79	5.7 (4.5, 7.0)
	M	557	35	6.3 (4.4, 8.6)
	F	834	44	5.3 (3.9, 7.0)
30-44		137	13	9.5 (5.1, 15.7)
	M	62	8	12.9 (5.7, 23.9)
	F	75	5	6.7 (2.2, 14.9)
45+		103	5	4.9 (1.6, 11.0)
	M	45	4	8.9 (2.5, 21.2)
	F	58	1	1.7 (0.0, 9.2)
Overall (18+)		1631	97	5.9 (4.8, 7.2)
	M	664	47	7.1 (5.2, 9.3)
	F	967	50	5.2 (3.9, 6.8)
Age and sex standardised England estimate				6.4 (2.5, 14.6)
Age-standardised England estimate males				9.4 (3.7, 19.3)
Age-standardised England estimate females				3.6 (1.3, 10.2)

Figure 1. Serotypes detected in carriage in adults aged 18+ years 2011-2019, Liverpool, England (98 isolates from 97 adults) PCV=pneumococcal conjugate vaccine (number indicates valency), NT=non-typable

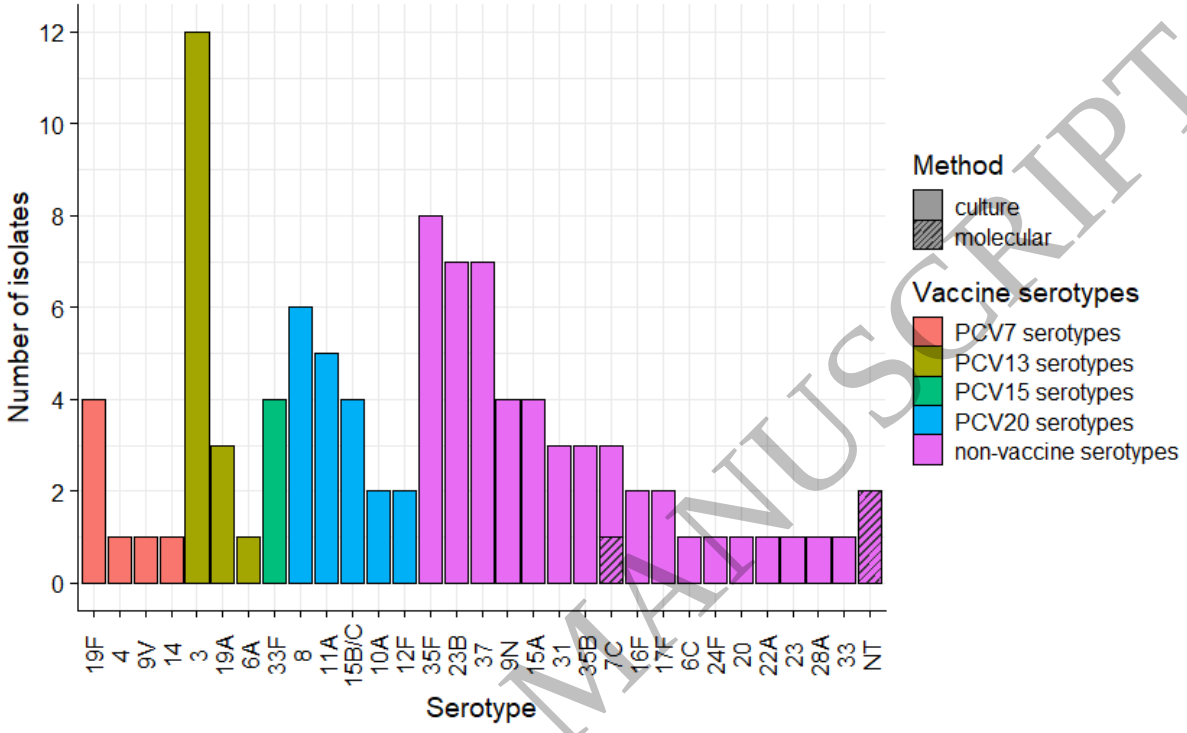

Figure 2. Comparison of adult (2014-2019) and children's (2014/15 and 2017/19) pneumococcal carriage serotype distributions PCV=pneumococcal conjugate vaccine (number indicates valency), NT=non-typable

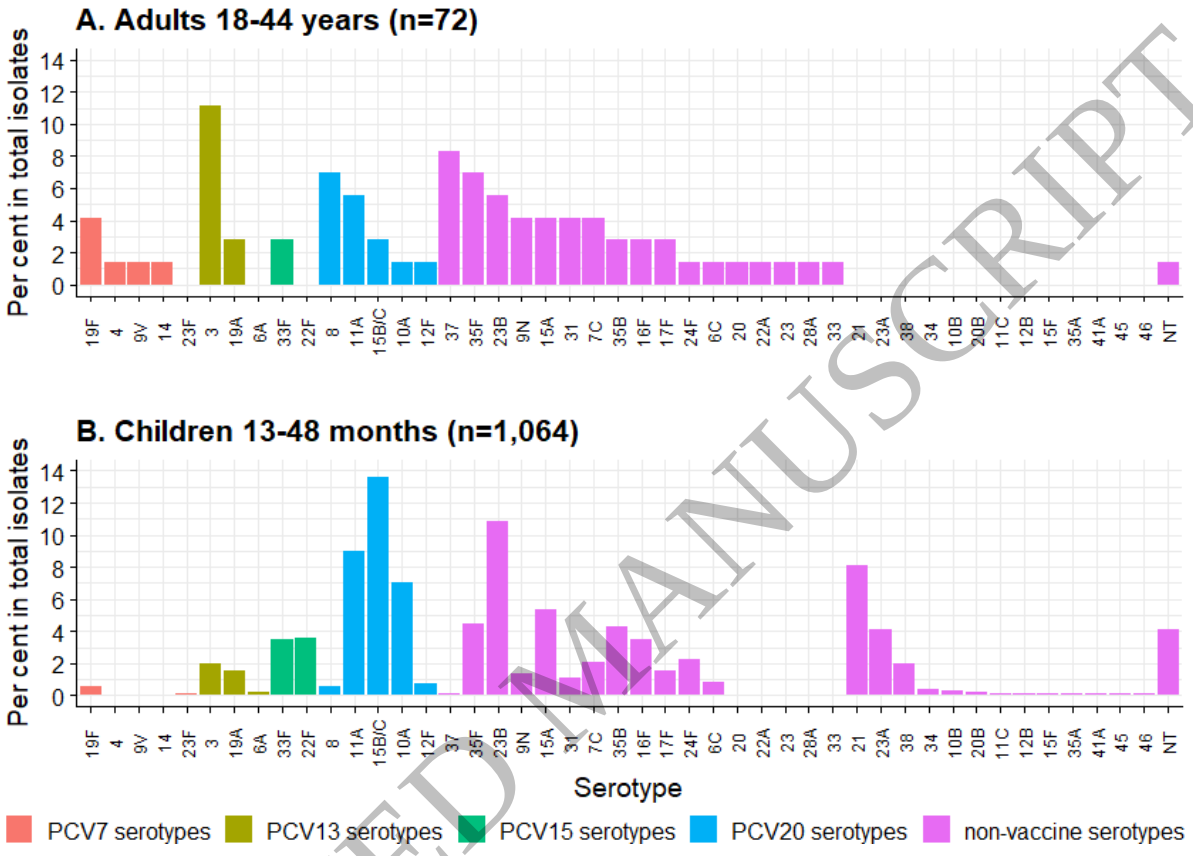

Figure 3. Adult (2014-2019) and children's (2014/15 and 2017/19) pneumococcal carriage serotype distributions overlaid (grey) and subtracted from one another to show excess isolates in each distribution PCV=pneumococcal conjugate vaccine (number indicates valency), NT=non-typable.

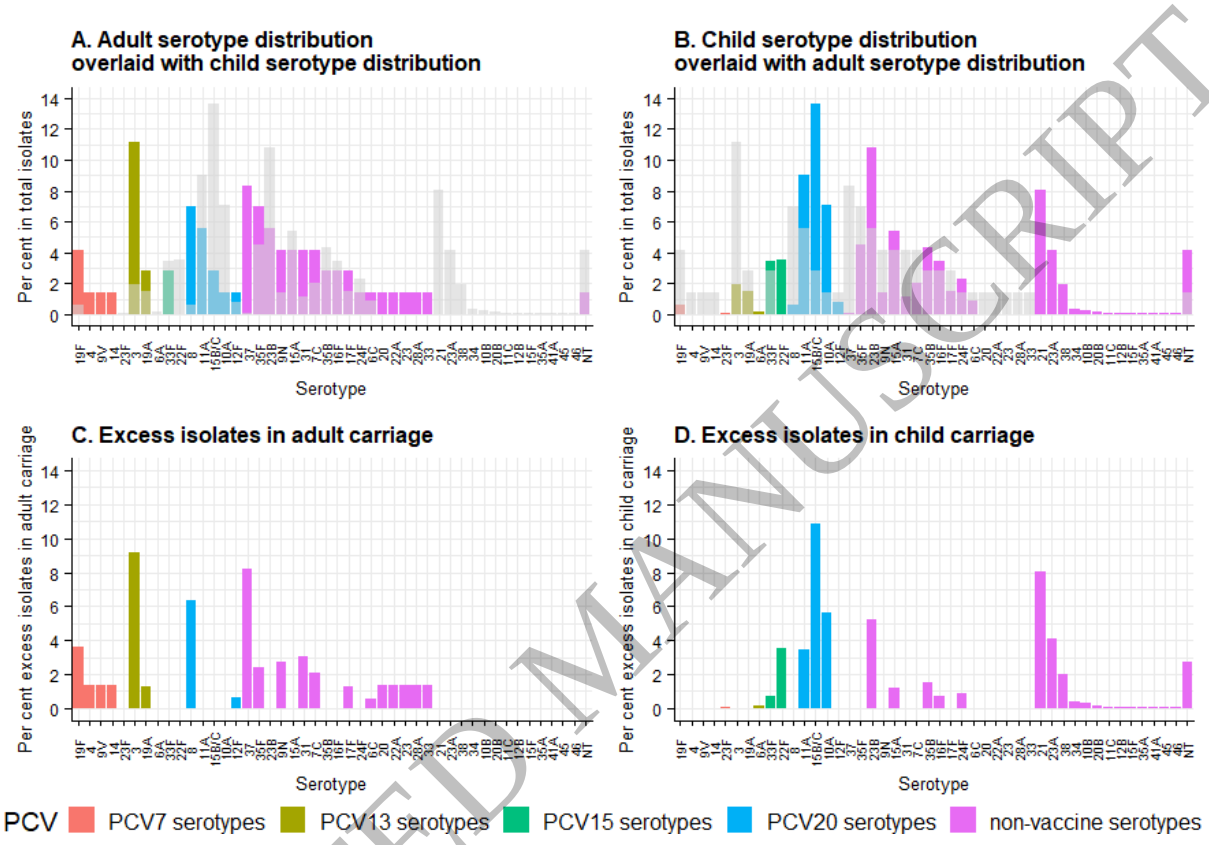

Figure 4. Comparison of child (13-48 months) and adult (18-44 years) carriage (A) and IPD (B) isolates 2014-2019. NT=non-typable

Note to assist comparison of serotype distributions, this is for serotypes included >=1% in carriage and/or disease for children and/or adults only. Serotypes in numerical order within vaccine group.

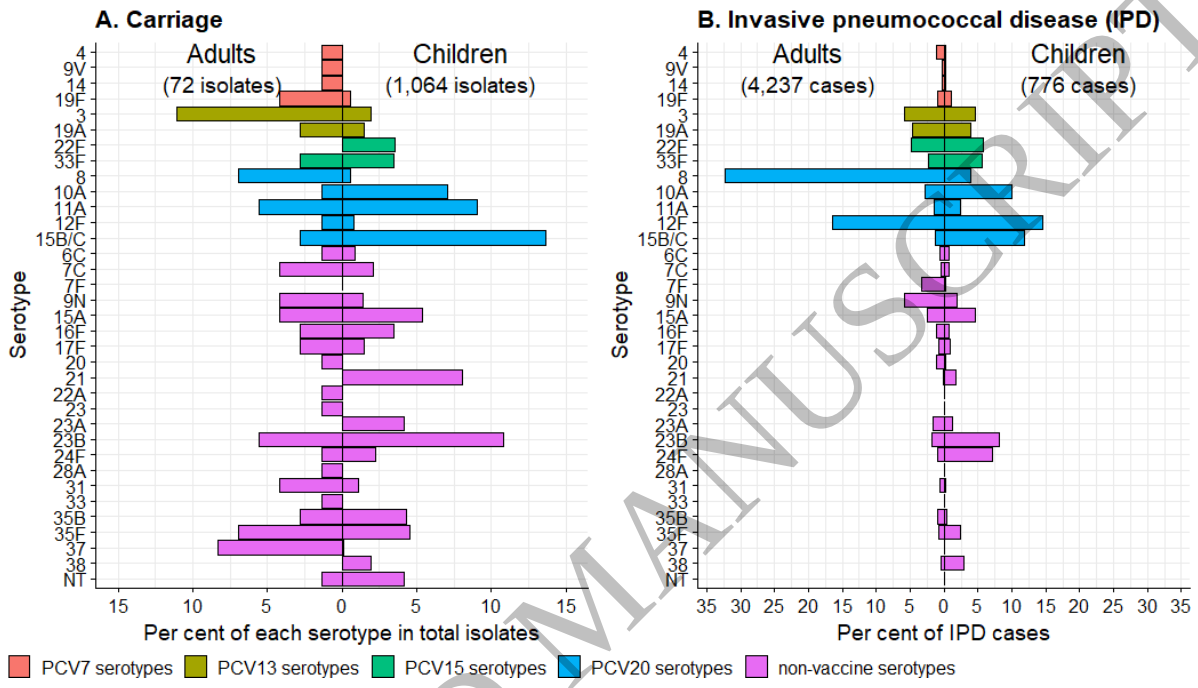

Figure 5. Case-carrier ratios per 100,000 population, children 13-48 months 2014-2019 vs adults 18-44 years 2014-2019, for serotypes with at least 1 case and carrier detected across both cohorts. Larger circles indicate more confidence. Blue line is weighted linear regression line: log10(y)= 0.7181 + 0.8820*log10(x), R^2=0.8

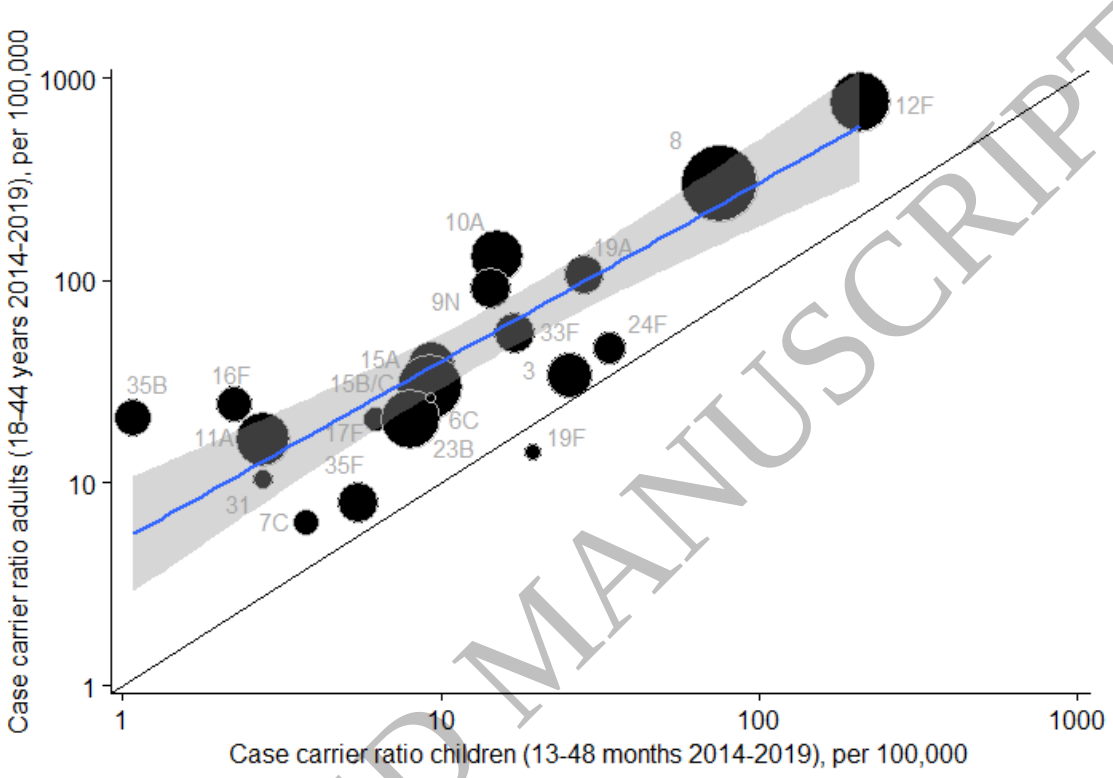

Figure 6. 65+ years predicted carriage serotype distributions based on 65+ years national invasive pneumococcal disease data, calculated with A. young adult (18-44 years) case-carrier ratios and B. child (13-48 months) case-carrier ratios