Public Health England

Protecting and improving the nation's health

Guidelines for the public health management of clusters of severe pneumococcal disease in closed settings

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Executive summary

These guidelines, produced by Public Health England (PHE), outline the investigation and public health management of clusters of severe pneumococcal disease (severe pneumococcal pneumonia requiring hospitalisation and/or intravenous antibiotics, or invasive pneumococcal disease) in closed settings. All suspected clusters identified by or notified to PHE Health Protection Teams (HPTs) should be assessed and investigated. Following confirmation of a cluster of severe pneumococcal disease in a closed setting with high-risk individuals (including the frail elderly and those at high risk of pneumococcal disease), the recommended interventions include: implementation of infection control measures, warning and informing, antiviral treatment in clusters involving influenza co-infection, antimicrobial chemoprophylaxis and pneumococcal vaccination. For clusters that do not involve high-risk individuals, antimicrobial chemoprophylaxis and pneumococcal vaccination are not indicated unless there are special circumstances, such as a particularly virulent strain or disease caused by a vaccine-preventable strain in an unimmunised group, but other control measures may still be necessary. Public health action is not required for individual cases or for non-invasive/non-severe pneumococcal disease. These guidelines update the 2008 interim UK guidelines for the public health management of clusters of serious pneumococcal disease in closed settings following the introduction of the pneumococcal conjugate vaccine into the national immunisation programme[1].

1 Introduction

Pneumococcal disease is a major cause of morbidity and mortality worldwide. The causative agent, *Streptococcus pneumoniae*, commonly known as the pneumococcus, is an encapsulated Gram-positive diplococcus, of which there are almost 100 recognised serotypes.[2-4] It is transmitted from person-to-person through droplets. Asymptomatic carriage of the pneumococci in the nasopharynx is common, occurring in up to half of all children under 5 years and decreases in adulthood to about 8%.[5] The mean duration of carriage is approximately 50 days in children and 20 days in adults.[7] In children, higher rates of carriage are associated with several risk factors including day-care attendance, number of siblings and smoking.[6,7] Nasopharyngeal acquisition is a precursor to disease, which usually presents as mild upper respiratory tract illnesses such as otitis media and sinusitis. The incubation period varies but can be as short as one to 3 days. Occasionally, the pneumococcus can also cause severe disease including pneumococcal pneumonia and invasive pneumococcal disease (IPD), typically presenting as meningitis and septicaemia, but rare cases of septic arthritis, peritonitis, endocarditis and infections at other sites have been reported. Though rarer since the introduction of antibiotics, pneumococcus can from time to time cause clusters of severe disease including septicaemia, pneumonia and meningitis in closed settings.

Reports in the literature of clusters of severe pneumococcal disease in different closed settings, both in the UK and elsewhere, have included hospitals, long-term care facilities, children's day-care centres, schools, military barracks and as well as a shipyard (see literature review).[8] A variety of public health interventions have been implemented in an attempt to control these outbreaks.[9, 10] In 2008, PHE (then the Health Protection Agency) published a document providing evidence-based guidance for the management of these clusters.[1]

1.1 Revised guidelines 2020

These revised guidelines have been updated with more recent data on disease epidemiology, changes to the national immunisation programme and schedules, and more specific guidance on the public health management of clusters of pneumococcal disease in the UK. The review is based on available published evidence, with the levels of evidence graded according to established guidelines (Scottish Intercollegiate Guidelines Network, SIGN). Where insufficient evidence was available, agreement was reached through consensus expert opinion. The current guidance has been reviewed by the PHE Vaccine Preventable Invasive Bacterial Infections (VaPIBI) Group and agreed by the PHE Vaccine Science and Surveillance Group (VSSG).

1.2 Objectives of guidelines

The guidance is intended for those in PHE, National Health Service (NHS) (including microbiology laboratories), local authorities and equivalent organisations in Scotland, Wales and Northern Ireland who will be involved in the clinical, microbiological and public health management of pneumococcal clusters.

1.3 Summary of main recommendations

The health protection team (HPT) should ensure epidemiological, laboratory and clinical information on suspected clusters are gathered and captured on HPZone (or an alternative system).

Infection control measures should be implemented and reinforced including isolation/cohort nursing, hand and respiratory hygiene and respiratory protective equipment, as appropriate.

An Outbreak Control Team (OCT) should be convened and all relevant teams including national public health teams, reference laboratories, national surveillance team, microbiology, infection control teams, local authorities, clinical commissioning groups (CCG), NHS local acute trust and communications teams should be invited, as appropriate.

In clusters with healthy individuals, assessment, infection control measures, warning and informing, and antiviral treatment for any influenza co-infection should be considered.

In clusters involving high-risk individuals, antimicrobial chemoprophylaxis and pneumococcal vaccination should be considered in addition to the above. Antimicrobial prophylaxis should provide immediate protection. PPV23 is the preferred vaccine unless eligible contacts are under 2 years of age, PPV23 is unavailable or the infecting serotype is 6A/6C, under which circumstances PCV13 should be considered.

If unimmunised or partially immunised children or adults are identified in an outbreak, where possible, HPTs should ensure that all are appropriately immunised according to the national immunisation schedule.

In special circumstances, such as when there is a particularly virulent strain or disease caused by a vaccine-preventable strain in an unimmunised group, chemoprophylaxis and/or pneumococcal vaccination may be appropriate for healthy individuals in closed settings.

Public health action is not required after a single case of severe, invasive or non-severe/non-invasive pneumococcal disease even when the case occurs in a closed setting.

2 Background

2.1 Pneumococcal polysaccharide vaccines

A 23-valent pneumococcal polysaccharide vaccine, PPV23 (Pneumovax23®, Merck), was licensed in Europe more than 3 decades ago. In the UK, a single dose of PPV23 has been recommended for individuals at increased risk of pneumococcal disease since the early 1990s and included as part of routine immunisation for older adults aged ≥65 years by phased introduction from 2003, starting with those ≥80 years, then ≥75 years and finally ≥65 year-olds in April 2005.[10] In Scotland, there was no phasing to the introduction. The vaccine is currently offered to all adults aged ≥65 years and to individuals aged ≥2 years who are at increased risk of pneumococcal disease, as defined in the Green Book (Immunisation against disease).[10] In addition to age (being very young or elderly), the major risk factors for pneumococcal disease include solid organ (eg lung, heart, liver and kidney) dysfunction and immunosuppression, including splenic dysfunction and malignancy.[11] Prior to the introduction of the pneumococcal conjugate vaccine (PCV) into the UK immunisation programme, the serotypes covered by PPV23 were responsible for more than 96% of cases of invasive pneumococcal disease (IPD).[12] PPV23 is used widely worldwide, although the literature on effectiveness remains inconclusive with limited vaccine effectiveness and short-term protection. A recent meta-analysis of randomised controlled trials estimated 73% efficacy against invasive pneumococcal disease and 64% against pneumococcal pneumonia.[13] The duration of protection is uncertain but pooled estimates from cohort and case-control studies 5 years after vaccination reported vaccine effectiveness of 45% and 59% against IPD, respectively, and 48% and 53% against pneumococcal pneumonia, respectively.[13]

National data from England and Wales suggests although PPV23 is effective, there is waning of protection over time with vaccine effectiveness reducing from 48% at <2 years after vaccination to 15% over 5 years after vaccination among individuals aged over 65, irrespective of risk group. There is a lack of evidence of the impact of PPV23 use on IPD incidence however individual protection, particularly among healthy individuals aged between 65-74 years of age, is indicated to be higher and maintained for longer in this group as compared with those older or with clinical risk factors.[14]

2.2 Pneumococcal conjugate vaccines

Polysaccharide conjugate vaccines are composed of a polysaccharide antigen covalently bound (conjugated) to a carrier protein, such as tetanus toxoid or the non-toxic diphtheria toxoid mutant protein, cross-reacting material 197 (CRM_{197}). Conjugate vaccines have a number of advantages over polysaccharide vaccines in that they:

- are immunogenic in all age groups including infants from birth, while polysaccharide vaccines are ineffective in <2 year olds and poorly effective in 2-5 year olds[15]
- generate IgM and IgG antibodies
- induce immunological memory through a T-cell and B-cell mediated immune response, with boosting of vaccine-induced antibodies and improved antibody avidity with each dose of vaccine[16]
- reduce acquisition of pneumococcal carriage in vaccinated individuals resulting in reduced transmission to unvaccinated children and adults, resulting in indirect (herd or population) protection[17]

Conjugating the polysaccharide to a protein carrier alters the polysaccharide from T-cell-independent to a T-cell-dependent antigen, thereby eliciting a longer-lasting immune response, particularly in children under 2 years of age for whom PPV23 is ineffective.[15, 18, 19] Carriage studies undertaken before and after PCV7 introduction demonstrated a reduction in vaccine-type (VT) carriage in vaccinated children under 5 years and their contacts combined with an increase in non-vaccine-type (NVT) carriage resulting in no significant change in carriage prevalence overall.[20]

A 7-valent pneumococcal conjugate vaccine (Prevenar7®, Pfizer) was licensed in 2000.

PCV7 protects against 7 of the then most common pneumococcal serotypes causing invasive disease (4, 6B, 9V, 14, 18C, 19F, and 23F), which are individually conjugated to CRM_{197}. In the UK, PCV7 was initially recommended for at-risk children aged <5 years in 2002, and subsequently included in the routine childhood immunisation programme from 04 September 2006. Although PCV7 was licensed at a 3-dose priming schedule followed by a booster (3+1 schedule), infants in the UK were offered the vaccine at 8 and 16 weeks of age, followed by a booster at 12-13 months, alongside their routine immunisations, after clinical trials demonstrated similar immunogenicity between these 2 schedules.[21] A limited 12-month catch-up was also undertaken, offering the vaccine to all children up to their second birthday.[22] On 1 April 2010, PCV7 was replaced in the UK immunisation programme with a 13-valent vaccine (PCV13, Prevenar13®, Pfizer) at the same schedule, which covered 6 additional serotypes (1, 3, 5, 6A, 7F, and 19A).[23] A recent randomised control trial (RCT), comparing a 1+1 PCV13 schedule (given at 12 weeks with a booster at 12 months) to the current UK 2+1 schedule demonstrated a significantly higher immunogenicity after the booster dose for serotypes 1, 4, 14 and 19F, lower immunogenicity for serotypes 6A, 6B, 18C and 23F, and non-significant differences for the remaining 5 serotypes, including serotypes 3 and 19A.[24]

Another conjugate vaccine not used in the routine UK schedule, the 10-valent PCV (PCV10, Synflorix, GSK) is also licensed – some of the serotypes are conjugated to a non-typeable *Haemophilus influenzae* protein – which does not contain *S. pneumoniae*

serotypes 3, 6A and 19A, but there is some evidence of cross-protection against serotype 19A in children immunised with PCV10 because of cross-reacting antibodies induced by serotype 19F in the vaccine.[25]

2.3 Vaccine impact

In the UK, the introduction of PCV7 in 2006 and its replacement with PCV13 in 2010 has led to rapid and sustained declines in vaccine-type and overall incidence of invasive pneumococcal disease. These conjugate vaccines are not only effective at preventing vaccine-type invasive and non-invasive pneumococcal disease in vaccinated children but, by reducing carriage in young children – who are the main carriers of the pneumococcus in the nasopharynx – have also halted transmission to older unvaccinated children and adults, leading to large reductions in vaccine-type IPD across all age-groups through a combination of direct and indirect (herd) protection. A small increase in pneumococcal disease due to non-PCV serotypes was observed after the introduction of both PCV7 and PCV13, but overall IPD incidence remains substantially below the pre-vaccine period. New vaccines are also currently in development; using proteins from the surface of pneumococci is one approach being explored and could potentially extend the protection offered by PCVs.[26]

2.4 Current epidemiology

Between 1 July 2016 and 30 June 2017, the overall annual incidence of IPD in England and Wales was 9.87 per 100,000. Although the incidence has increased from the record low in 2013/14 of 7.12 cases per 100,000, it is still 37% and 7% lower than pre-PCV7 and pre-PCV13 periods, respectively. This recent increase is largely due to a considerable rise in IPD due to non-PCV13 serotypes, especially in adults aged 45 years and older. As IPD disproportionately affects young children and the elderly, incidence in these age groups is much higher compared to the overall rate, with 13.9 cases per 100,000 in children under 2 years and 28.9 cases per 100,00 in adults over 65 years of age.[27] Seasonal variations in IPD have been reported, with the highest incidence reported in winter.[28] Climactic factors and increased indoor air pollution during the winter months have been implicated; however, this is not fully understood.[29]

3 Literature review

As part of the 2008 guidelines, a critical systematic review of the literature was undertaken to for the period covering 1980 to 2006. A total of 42 outbreaks or clusters of severe pneumococcal disease were described in 39 papers. The majority were reported from hospitals,[30-42] and long-term care facilities.[43-45] A handful of reports were of outbreaks in households,[46-48] military barracks,[49, 50] day care centres, [51-53], homeless shelters,[54, 55] and prisons.[56] Sixteen articles reported interventions to prevent secondary cases and gave details of their impact.[30-33, 43-45 30-33, 43-45, 49-53, 57-60] Of these uncontrolled observational studies, thirteen reported an intervention including use of antibiotic chemoprophylaxis,[30, 31, 33, 43, 44, 49-52, 57, 58, 61] in 7, the intervention included pneumococcal polysaccharide vaccination,[43-45, 57-59, 61] and one infection control only.[32] No interventions with pneumococcal conjugate vaccine were reported. A subsequent systematic review including literature from 1950 to 2010 also reviewed the effectiveness of interventions used to prevent the spread of infection and the use of antibiotic prophylaxis on reduction of pneumococcal carriage.[9]

To inform the 2018 guidelines, an updated systematic review was undertaken including reports of clusters of severe pneumococcal disease from 1 January 2010 to 6 September 2018 using a combination of MeSH terms and key words for pneumococcal disease and outbreaks.[62] In total, 11 instances of a cluster or outbreak of severe pneumococcal disease were described. The settings included hospital wards,[63-67] military training units,[68, 69] care home,[70] prison,[71] and at an oil rig.[72] Clusters occurred in 6 different countries, occurring between 2005 and 2015. Of the 11 clusters, 8 specified use of antibiotic chemoprophylaxis for the prevention of secondary cases, with amoxicillin and azithromycin being the most commonly reported antibiotic. The remaining 3 clusters reported that infection control measures alone had been adequate in preventing further cases. PPV23 remains the main vaccine offered with 5 clusters reporting its usage, while PCV13 was only offered in 2 clusters – in one of which, it was offered in conjunction with PPV23. In 4 of the remaining clusters where vaccine administration was not reported, occurred in a hospital setting where the clusters were controlled through infection control practices including isolation and antibiotic treatment. Of the infecting serotypes, 7 were serotypes included in both PPV23 and PCV13, 2 were in either PCV13 (6A) or PPV (ST8), with a further PCV13-related serotype (6C) and non-vaccine serotypes (11E/15A). Further information on the systematic review is presented in the body of the guidelines (boxes 1-6). All evidence was evaluated according to the Scottish Intercollegiate Guidelines Network (SIGN) described in Table 1.

Table 1: SIGN guidelines

Levels of evidence

1++ High quality meta analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias.

1+ Well conducted meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.

1- Meta analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.

2++ High quality systematic reviews of case-control or cohort studies. High quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal.

2+ Well conducted case control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal.

2- Case control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal.

3 Non-analytic studies, eg case reports, case series.

4 Expert opinion.

Grades of recommendation

A At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or a systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results.

B. A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+.

C. A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++.

D. Evidence level 3 or 4; or; Extrapolated evidence from studies rated as 2+.

www.sign.ac.uk/assets/sign50_2015.pdf

4 Laboratory investigation

To guide the appropriate public health response, it is important that pneumococcal disease is rapidly confirmed, and that serotype information is quickly available. Hence, it is important that early liaison should occur between clinicians, local microbiologists and the respective national reference laboratories to ensure that appropriate clinical samples are taken in a timely manner and submitted for confirmation and serotyping (see section 8 for Contact Information).

Most clusters of severe pneumococcal disease will come to light following the isolation of *Streptococcus pneumoniae*, or detection of pneumococcal antigen or DNA, from a normally sterile site from one or more patients in the suspected cluster. Investigations to confirm pneumococcal disease will be dictated in large part by their clinical presentation; the following investigations should be performed wherever possible.

4.1 Culture

Culture of *Streptococcus pneumoniae* from blood, CSF or any other normally sterile site represents the optimal confirmation method for severe pneumococcal disease. In addition to local antimicrobial susceptibility testing, all isolates should be sent to the respective national reference laboratory for confirmation and serotyping as soon as possible. From 1 October 2017, the pneumococcal national (England) reference laboratory, PHE Colindale replaced some phenotypic services for *S. pneumoniae* identification confirmation and capsular typing with whole genome sequencing (WGS). It is possible to accurately predict pneumococcal capsular type from WGS in the majority of cases. If required, capsular typing can still be performed using phenotypic methods for the few serotypes which cannot be differentiated by WGS or to expedite results.[73, 74]

Blood culture

Blood for culture should be obtained from all cases sufficiently unwell to be admitted to hospital. A number of factors influence the sensitivity of blood culture including recent antibiotic treatment, volume of blood collected, and the bacterial load. It is important to note that only 20-25% of lobar pneumonia cases will yield a positive blood culture.[75]

CSF culture-positive/culture-negative specimens

Where possible, CSF should be obtained for culturing in cases of clinically suspected pneumococcal meningitis. Culture negative samples with a high index of suspicion of pneumococcal disease (eg as suggested from microscopy) may be tested locally for

pneumococcal antigen, with an immunochromatographic test (ICT), for example Alere BinaxNOW® *S. pneumoniae* Antigen Card, Uni-Gold™ *S. pneumoniae* (Trinity Gold), ImmuView® *S. pneumoniae* Antigen Test (SSI Diagnostica) or similar and/or by *S. pneumoniae* specific PCR and/or referred to the respective reference laboratory for additional tests, including pneumococcal PCR, *S. pneumoniae* serotyping PCRs and/or serotype-specific antigen detection using a multiplex immunoassay. If in doubt, discuss with the national reference laboratory (see section 8) about the appropriate samples for referral, expediting the laboratory testing and reporting to the PHE HPT. It should be noted that whilst reported specificity and sensitivities for these commercial ICT assays are generally good, cross-reactions with non-*S. pneumoniae* streptococcal species may occur.

Aspirate from other normally sterile sites (eg joint or pleural fluid)

Culture of pneumococci from these sites confirms invasive infection. Culture-negative samples with a high index of suspicion of pneumococcal disease (eg as suggested from microscopy) should be discussed with the respective reference laboratory for pneumococcal PCR, serotyping PCR and/or serotype specific antigen detection using a multiplex immunoassay. If in doubt, discuss with the reference laboratory about the appropriate samples for referral, expediting the laboratory testing and reporting to the PHE HPT.

Sputum

A positive culture of sputum for *S. pneumoniae* is **not** on its own adequate for a diagnosis of pneumococcal pneumonia; it should be interpreted in the context of clinical and radiological findings.

Nasopharyngeal swabs

Nasopharyngeal swabs of cases can provide supportive evidence of pneumococcal infection. However, positive cultures are **not** confirmatory of pneumococcal disease, since carriage occurs and is particularly common in young children (up to 50% in the age group 1 to 4 years). Swabs should be taken and transported (usually to the local hospital microbiology laboratory) using standard methods. Nasopharyngeal swabs collected from healthy contacts of cases within the cluster is not part of the routine public health management of these clusters, but on occasion may help guide further management (see section 7).

Antimicrobial susceptibility testing

All pneumococcal isolates obtained from patients known or suspected to be involved in the cluster should be subjected to antimicrobial susceptibility testing including the agents suggested for antimicrobial prophylaxis within these guidelines.

4.2 Non-culture diagnostic tests

Urinary antigen detection

Immunochromatographic rapid urinary antigen tests including those described above have been shown to be rapid and have good sensitivity and specificity for the diagnosis of pneumococcal pneumonia and IPD in adults and older children.[76-80]

However, the clinical utility of these tests is reduced in younger children as the positive predictive value is lower. A positive antigen test in this group may merely reflect pneumococcal carriage.[81-84]

In cases where the local urinary antigen test is positive by ICT and there are no positive cultures available for serotyping, subsequent serotype specific antigen detection should be undertaken on the urine as soon as possible after discussing with the relevant reference laboratory. This may allow serotyping for culture-negative cases.

PCR

PCR-based assays for the detection of specific DNA sequences of *S. pneumoniae* are available at the reference and some hospital laboratories. These can be used on CSF, blood and fluids from other normally sterile sites. In PCR-positive culture-negative cases, capsular serotyping by PCR may be an option to discern serotype (www.cdc.gov/streplab/pneumococcus/resources.html).[85] As noted above, positive results on blood samples from younger children (<2 years) must be interpreted with caution and in the context of clinical observations and other investigations due to high pneumococcal carriage within this age group.

4.3 Serotyping of *Streptococcus pneumoniae*

Rapid ascertainment of serotype is an important tool to confirm or exclude a suspected cluster, to assess the relatedness of cases within a cluster and to inform public health management.

Serotyping of invasive pneumococcal isolates and other clinical samples can be undertaken at reference laboratories in the UK. If a cluster is being considered, the

respective national reference laboratory should be contacted early in the course of investigation so that serotyping can be expedited in suspected clusters.

At least one bacterial and/or antigen positive sample from each case should be sent to a reference laboratory for serotyping. Such laboratories will be able to undertake further genomic/serotype characterisation as necessary. Test requests and appropriate specimens should be discussed with senior staff at the reference laboratory (see Section 8 for Contact Information) prior to despatch of outbreak/incident-related specimens to ensure prioritisation on arrival.

Pneumococcal isolates sent to PHE Colindale for confirmation of identification and capsular typing will undergo routine whole genome sequencing. Identification and capsular type will be derived from this, which will be reported as previously. If required, capsular typing can be performed using phenotypic methods in order to expedite results and/or for the few serotypes which cannot be differentiated by WGS.[74, 86] To assist in the investigation of clusters and outbreaks, multi-locus sequence typing data derived from WGS analysis can be provided and further analysis using single nucleotide polymorphism (SNP) analysis can be performed, if required, but this should not delay any public health actions.

5 Risk of transmission in a closed setting

Recommendations for public health action have been considered based on the risk of transmission to individuals and their risk of developing severe illness in a closed setting.

An interval of 2 weeks between cases corresponds to the period of maximally elevated risk after the initial case (Box 1). Outbreaks with longer intervals between cases have been described and, if there is any uncertainty regarding public health action, then the respective national public health team should be contacted for advice.

BOX 1: Risk of transmission - Evidence grade D

1 Of the 42 clusters of severe pneumococcal disease (involving at least 2 clinical cases) in closed settings found on reviewing the literature, 26 had sufficient data to elucidate an epidemic curve. Of these 26 clusters, 25 involved the same serotype. In these 25 outbreaks, the median outbreak size was 4 with a range of 2 to 46. 81% of all cases occurred within 14 days of onset of the index case, and 91% within the first 28 days. Serotypes/groups most commonly associated with clusters were 14 (7 clusters), 4 (5 clusters), 9, 1, and 9V, all causing 4 clusters each. Reported attack rates ranged from 0.18% – 66% (median 8.9%). No secondary transmission leading to severe pneumococcal disease in staff was reported in any of the outbreaks.

Table: Distribution of number of cases per cluster and length of outbreak

No. of cases in cluster	No. of clusters	Illness onset in contacts *(median and range in days after illness onset in index case)*
2-4	13	4 (1 – 95)
5-9	4	16 (10 – 58)
10-14	4	12.5 (5 – 20)
≥15	4	20 (8 – 30)

In the updated review publications between 2010 and 2018, 11 additional clusters were identified. Of the 13 responsible serotypes, the most common was serotype 3 which was responsible for 3 clusters. All but 3 serotypes were vaccine-type and the majority (8 serotypes) were included in both PCV13 and PPV. Serotype 3 is one of most prevalent serotypes in the UK. IPD caused by this serotype has fluctuated in incidence but has been increasing since 2013/14. Serotype 14 was one of the most common PCV7-serotype in older adults.[27] Both serotypes 3 and 14 have high invasiveness potential.[87]

6 Definitions

6.1 Severe pneumococcal disease

6.1.1 Confirmed case of severe pneumococcal disease

(i) **IPD** (pneumococcus isolated from normally sterile site; eg blood, CSF, joint, peritoneum or other, but not sites such as the eye)

or

(ii) **Severe pneumococcal pneumonia** (requiring hospitalisation and/or intravenous antibiotic treatment) – clinical pneumonia AND at least one of the following:

- pneumococcus identified (culture/PCR/antigen) in pleural fluid
- pneumococcal DNA or antigen detected in fluid from a normally sterile site (except for blood in children under 2 years of age in whom pneumococcal carriage alone may result in blood PCR positivity)
- pneumococcal antigen detected in urine (except in children under 2 years of age in whom pneumococcal carriage alone may result in urine antigen positivity)

6.1.2 Probable case of severe pneumococcal disease

6.1.3 Confirmed case of severe pneumococcal disease

(iii) **IPD** (pneumococcus isolated from normally sterile site; eg blood, CSF, joint, peritoneum or other, but not sites such as the eye)

or

(iv) **Severe pneumococcal pneumonia** (requiring hospitalisation and/or intravenous antibiotic treatment) – clinical pneumonia AND at least one of the following:

- pneumococcus identified (culture/PCR/antigen) in pleural fluid
- pneumococcal DNA or antigen detected in fluid from a normally sterile site (except for blood in children under 2 years of age in whom pneumococcal carriage alone may result in blood PCR positivity)
- pneumococcal antigen detected in urine (except in children under 2 years of age in whom pneumococcal carriage alone may result in urine antigen positivity)

6.1.4 Probable case of severe pneumococcal disease

- clinical diagnosis of severe pneumococcal disease where the responsible clinician or microbiologist in consultation with a senior member of the HPT considers that *S. pneumoniae* is the most likely pathogen responsible, based on available clinical, microbiological and epidemiological evidence (eg lobar pneumonia or empyema, or an epidemiological link to a confirmed case)
- probable cases should have appropriate microbiological investigations to rapidly confirm or exclude the diagnosis (see section 4)

6.2 High-risk individuals

High-risk individuals include the frail elderly (defined as individuals over 65 years of age who are dependent on others for activities of daily living, and often in institutional care)[88], and those belonging to a clinical risk group as defined below (Table 2) in the Green Book (Immunisation against disease).[10]

Table 2: Clinical risk groups for pneumococcal disease

Clinical risk group	Examples (decision based on clinical judgement)
Asplenia or splenic dysfunction	This also includes conditions such as homozygous sickle cell disease and coeliac syndrome that may lead to splenic dysfunction.
Chronic respiratory disease (chronic respiratory disease refers to chronic lower respiratory tract disease)	This includes chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema; and such conditions as bronchiectasis, cystic fibrosis, interstitial lung fibrosis, pneumoconiosis and bronchopulmonary dysplasia (BPD). Children with respiratory conditions caused by aspiration, or a neurological disease (eg cerebral palsy) with a risk of aspiration. Asthma is not an indication, unless so severe as to require continuous or frequently repeated use of systemic steroids (as defined in Immunosuppression below).
Chronic heart disease	This includes those requiring regular medication and/or follow-up for ischaemic heart disease, congenital heart disease, hypertension with cardiac complications, and chronic heart failure.
Chronic kidney disease	Nephrotic syndrome, chronic kidney disease at stages 4 and 5 and those on kidney dialysis or with kidney transplantation.
Chronic liver disease	This includes cirrhosis, biliary atresia and chronic hepatitis.
Diabetes	Diabetes mellitus requiring insulin or oral hypoglycaemic drugs. This does not include diabetes that is diet controlled.
Immunosuppression	Due to disease or treatment, including patients undergoing chemotherapy leading to immunosuppression, bone marrow transplant, asplenia or splenic dysfunction, HIV infection at all stages, multiple myeloma or genetic disorders affecting the immune system (eg IRAK-4, NEMO, complement deficiency) Individuals on or likely to be on systemic steroids for >1 month

	at a dose equivalent to prednisolone at ≥20mg/day (any age), or for children under 20kg, a dose of ≥1mg/kg per day.
Individuals with cochlear implants	It is important that immunisation does not delay the cochlear implantation.
Individuals with cerebrospinal fluid leaks	CSF leak following trauma or major skull surgery.
Occupational risk	There is an association between exposure to metal fume and pneumonia and infectious pneumonia, particularly lobar pneumonia and between welding and IPD.

6.3 Clusters and outbreaks

6.3.1 Clusters

Two or more cases (at least one confirmed) of severe pneumococcal disease (due to undetermined serotype)* occurring in a closed setting within a 14 day period.

6.3.2 Outbreak

An outbreak is defined as cluster with a common infecting serotype.

* if the cases are identified to be due to different pneumococcal serotypes, then they should be considered unrelated and do not require additional public health action

6.4 Closed settings

6.4.1 Closed settings with high-risk individuals

Closed settings with high-risk individuals may include the frail elderly residing in a care home, premature infants in a neonatal unit or immunocompromised individuals in an oncology ward as examples.

6.4.2 Closed settings with healthy and high-risk individuals

Some clusters in closed settings may involve both healthy and high-risk individuals (eg a cluster in a nursery with a small number of immunosuppressed children). Such clusters will need to be assessed on a case-by-case basis. In most situations, it may be sufficient to ensure that the high-risk individuals are appropriately immunised according to national recommendations. Public health interventions such as antibiotic prophylaxis and additional pneumococcal vaccination may be considered for the high-risk

individuals in such settings, depending on risk of exposure, vulnerability of the individual(s) at risk, infecting pneumococcal serotype and severity of infection among other factors.

6.4.3 Closed settings with healthy individuals

Clusters involving individuals that do not belong to the high-risk group will still need to be assessed by local HPTs. Pneumococcal clusters involving healthy adults in a closed setting (eg prison) are rare because of low pneumococcal carriage rates in adults and reduced transmission risk. In clusters involving healthy children in closed settings (eg day-care centres or schools) where the vast majority of UK children will have been immunised with PCV13, the majority of cases will be due to non-PCV13 serotypes.[89] Public health action such as antibiotic chemoprophylaxis will only temporarily reduce pneumococcal carriage in this setting, but the high carriage rate in children is likely to return once the chemoprophylaxis is completed. In these settings, therefore, antimicrobial chemoprophylaxis and pneumococcal vaccination are unlikely to be beneficial, unless there are special circumstances such as a particularly virulent strain or disease caused by a vaccine-preventable strain in an unimmunised group.

7 Public health management

7.1 Role of public health

HPTs have an important role in investigating and managing pneumococcal clusters and outbreaks. HPTs are not expected to conduct active surveillance or monitoring for pneumococcal clusters or outbreaks. However, HPTs may be informed of a possible cluster by parties outside the respective public health team, such as the local microbiology laboratory, local education authority, local GPs, A&E doctors, paediatricians, clinicians, care home managers or prison services. It is important that such parties are aware of the public health importance of pneumococcal clusters and the need to liaise with the respective PHE HPTs to ensure appropriate assessment, investigation and interventions are undertaken.

Invasive *Streptococcus pneumoniae* infection is statutorily notifiable by registered medical practitioners under the health protection legislation (2010) (www.legislation.gov.uk/uksi/2010/659/schedule/2/made), and under Scottish (2008) legislation (www.legislation.gov.uk/asp/2008/5/schedule/1). The responsible person for leading the management of a cluster will vary depending upon the setting and location. For a cluster in a hospital, it is likely that the hospital infection control team will take the lead with involvement from the Director of Infection Prevention and Control; for a community cluster, it is likely to be the local HPT. Reference should be made to the

local outbreak control plans. Clinicians, microbiologists and Infection Control Teams should inform the Proper Officer as soon as a cluster of severe pneumococcal disease is suspected so that appropriate public health assessment and actions can be undertaken.

Recommendation 1: Role of public health

An experienced member of the HPT should ensure that comprehensive information on the cases and the setting is gathered to help facilitate local public health management and surveillance. The information should include epidemiological, laboratory and clinical information, which should be recorded on HPZone or an alternative system.

Evidence grade D

7.2 Initiating an Outbreak Control Team (OCT)

An early teleconference involving the HPT, local microbiologists and epidemiologists and national experts from both public health, and microbiology and Infection Control Teams should take place to ensure optimal cluster management and good communication. Early engagement with NHS (or HSC), Clinical Commissioning Groups (CCGs) and the local authority is essential to enable operational arrangements for the delivery of antibiotics and vaccine. The regional Communications Manager should also be informed.

In England, HPTs should enter all the details of reported events on HPZone, a web-based software for public health management of infectious diseases including any public health actions taken.

Depending upon local arrangements and the setting, the team leading the outbreak control response should make a careful and rapid assessment of the suspected cluster. The following information should be gathered for the cases and the setting and also reported to the national team (see Appendix 1 for the reporting form). When gathering this information, hospital laboratories should be reminded of the need to liaise with and send samples/isolates urgently to the reference laboratory.

Case and setting details

Cases

- basic demographics – age, sex, address, occupation/school/nursery
- risk factors for pneumococcal disease – eg splenic dysfunction, immunosuppression, solid organ (heart, lung, liver, kidney) dysfunction.
- clinical features, particularly
  - dates of onset of illness
  - signs and symptoms of bacteraemia, acute pneumonia or meningitis
  - outcome – hospitalised, dead
  - supportive diagnostic information

    eg radiological information (for example lobar pneumonia - highly predictive of pneumococcal infection)

- microbiological data, particularly
  - culture and/or detection of DNA antigen from blood, CSF, urine, sputum, pleural fluid, joint aspirates, etc.
  - antimicrobial susceptibility
  - serotype information
- date of initial referral to the HPT/Hospital Infection Control Team
- vaccination status
  - type of vaccine (23-valent polysaccharide, 13-valent conjugate)
  - number of doses and when administered

Setting and population at risk

- type of setting
- number of persons in the setting with basic epidemiological description (age, sex, employment, vaccination status, duration in setting)
- identification of any highly exposed sub-group eg bay in ward

7.3 Confirmation of cases

Where one or more cases in a suspected cluster remain unconfirmed, additional investigations may be required before considering any public health action. Investigations should be undertaken in discussion with the clinicians, infectious disease specialists and/or microbiologists (as appropriate) and include pneumococcal specific tests (as listed in section 0) and testing for other infections should be undertaken as indicated by the clinical picture.

For cases of severe pneumococcal pneumonia (ie requiring hospitalisation and/or intravenous antibiotics), testing for respiratory viruses, especially influenza for which antivirals are available, should be undertaken since such viral infections often precede pneumococcal pneumonia, especially in closed settings.

For cases presenting with meningitis or septicaemia, testing for meningococcal and other bacterial infections as appropriate to the clinical picture, along with additional laboratory findings should be considered.

7.4 Confirmation of a cluster

An evaluation should be undertaken to ascertain whether the cases fulfil the definition of a cluster, whether the cluster occurred in a closed setting, whether the cluster involves high-risk individuals and whether the cluster constitutes an outbreak.

In a cluster occurring in a closed setting involving high-risk individuals with one confirmed and at least one probable case, serotyping of the probable case(s) should be expedited to confirm/exclude an outbreak. This can be done by contacting the respective national reference laboratory. Public health actions should not be delayed while awaiting the results of serotyping for the second case.

7.5 Public health actions

After initial assessment, public health actions in a suspected cluster of severe pneumococcal disease in a closed setting will include:

- implementation of infection control practices (Section 0)
- communication (“warn and inform”) (Section 0)
- if influenza transmission is identified, then antivirals should be considered (refer to PHE guidance on use of antiviral agents for the treatment and prophylaxis of seasonal influenza)[90]

If the cluster is confirmed and includes high-risk individuals, then:

- antibiotic chemoprophylaxis should be considered (Section 0)

If a vaccine serotype is responsible (this should already have been reported for the first case in the cluster), or if the serotype is not known for any of the cases (or the information is unlikely to be available quickly, say, within 48 hours), then:

- pneumococcal vaccination should be considered (Section 7.7)

7.5.1 Infection control measures

BOX 2: Infection control

In published outbreaks, infection control measures have been instituted including isolation of patients, cohorting and reinforcement of hand washing.[30-32, 43-45, 57, 59] In only one outbreak, these interventions were used in isolation; the outbreak terminated 7 days after infection-control measures were commenced, with a further 5 cases occurring in the intervening period.[32]

In the updated review, reinforcement of hand and respiratory hygiene was the most commonly reported measure used in 4/8 clusters. In some cases, isolation (n=3), use of respiratory protective equipment (n=2) and cohorting (n=1) were also described. Infection control measures were not described for 3 clusters.

Evidence grade D

For non-residential settings such as nurseries or schools, there are no grounds to close classes or exclude contacts. For residential settings or hospitals, the team managing the incident will need to consider closure to new admissions until control measures are in place. Infection control measures should include:

Recommendation 2: Infection control measures

Isolation/cohorting

In care home settings, many residents will be cared for in single rooms. If possible, patients should be kept in single rooms for the first 24 hours after antibiotic treatment has commenced. In settings where single rooms for cases are not available, cohorting should be implemented. This may include settings such as acute hospitals and prisons.

Evidence grade D

Cohort nursing

Wherever possible staff should either be allocated to the ill or the well.

Hand and respiratory hygiene practice

Good hand and respiratory hygiene should be encouraged, including for staff, relatives and visitors.

Evidence grade D

Respiratory protection

Fluid Repellent Surgical Facemasks are not necessary for routine care but should be worn if splashing or spraying of blood, body fluids, secretions or excretions onto the respiratory mucosa (nose and mouth) is anticipated/likely. Non-sharing of respiratory devices such as spacers and nebulisers should be reinforced.[91, 92]

Evidence grade D

7.5.2 Risk of pneumococcal disease in staff members

The recent systematic review identified one confirmed IPD and 3 probable cases of severe pneumococcal disease in staff members, unlike the previous review which did not report any cases of secondary transmission to staff.

Of the 6 studies that reported on staff members,[63, 65, 68, 93, 94] one occurred at a paediatric psychiatric unit where one of 3 confirmed IPD cases and 2 of 8 probable cases occurred in staff members.[63] Another occurred at an assisted-living facility with one probable case in a staff member who had underlying asthma.[94] Two studies reported that none of the staff who were symptomatic developed pneumococcal disease,[65, 70] including one that reported no carriage among staff members.[65] On the other hand, none of the staff members in a military training unit were symptomatic but 17% of staff members and 44% of military recruits were identified as pneumococcal nasopharyngeal carriers.[68] One outbreak occurred at a mental health facility where 10 staff members were diagnosed with influenza B infection, none of whom went on to develop pneumococcal disease.[93]

The attack rate for pneumococcal disease in one of the reports was <3% for staff compared to 25% among patients,[63] suggesting that the risk to staff members, especially those with no underlying comorbidities, is likely to be very low.

7.5.3 Communication ("warn and inform")

Individuals that are part of the cluster, their carers and close contacts should be warned and informed of the symptoms and signs of severe pneumococcal disease as soon as a cluster is suspected (see Appendix 2 for an information sheet).

It is important to provide information to all concerned. There may be different information needs for high-risk individuals requiring antibiotics and vaccine and those who do not. Explain what the situation is, and that close contacts are at a possibly increased risk of infection. Explain that they need to be aware that if they develop particular symptoms suggestive of pneumococcal infection they should contact or attend relevant health care services. Information should explain that antibiotics with or without vaccine reduce the risk of disease, but do not guarantee 100% protection.

Recommendation 3: Disseminating information

With the formation of an Outbreak Control Team (OCT) with a clear lead person, the OCT should follow the standard current guidelines for pneumococcal outbreak response.

In subsequent communication, it will be important to consider relevant parties including NHS, Clinical Commissioning Groups, the local authority, local education authority, Care Quality Commission, local GPs, A&E, paediatricians or clinicians etc, as required.

The respective national public health team and reference laboratory should be involved in the management of pneumococcal clusters and outbreaks as soon as possible, to provide specialist advice and to record and monitor the outbreaks nationally in order to inform the relevant authorities if needed and to inform the future development of these guidelines.

7.5.4 Antibiotic prophylaxis

The aim of antimicrobial prophylaxis is to significantly reduce the risk of pneumococcal disease in high-risk individuals by providing individual protection for those who may be in the incubation phase. Since pneumococcal carriage is relatively common, a short course of antibiotics is unlikely to eliminate carriage beyond a few weeks. Antibiotic

chemoprophylaxis will provide initial protection until infection control measures and, where indicated, protection through pneumococcal vaccination take effect.

If the cluster takes place in a population where influenza is confirmed in at least one case, antiviral prophylaxis should be strongly considered at the same time as antibiotic prophylaxis. Refer to PHE guidance on use of antiviral agents for the treatment and prophylaxis of seasonal influenza.[90]

BOX 3: Antimicrobial prophylaxis in cluster reports

In 13 published clusters and outbreaks, an antibiotic intervention was used where the impact is detailed.[30-33, 43, 44, 49-52, 58, 61, 95] In all reports there were no control subjects and the timing of antibiotics varied from within 6 days of the first case to 2 months after the last case.

Prophylaxis of contacts with rifampicin-containing regimes,[31, 33, 43, 51-53] azithromycin,[50, 95] penicillin,[49, 58, 61] and erythromycin,[30, 44] have been used. Additional agents included quinolones,[31, 43] clindamycin,[51] and mupirocin,[31, 33] for antibiotic-resistant organisms.

In terms of preventing further cases, where rifampicin,[52, 53] or penicillin,[49, 58, 61] alone was given, no further cases after administration were detected. Further cases occurred in both outbreaks where azithromycin prophylaxis was employed,[50, 95] and one of 2 where erythromycin was used.[44]

In the updated review, use of antibiotic chemoprophylaxis was reported in 8/11 clusters. In the remaining 3 clusters[64, 66, 96] which occurred in psychiatric (n=2) or respiratory (n=1) units, outbreak control measures were deemed adequate to prevent further cases, although in one of the settings, patients hospitalised in the same unit had nasopharyngeal carriage of the infecting outbreak serotype.[64] Azithromycin was the most common antibiotic, used in 3 clusters, followed by penicillin, used in 2 clusters.

Evidence grade D

Recommendation 4: Indications for chemoprophylaxis

Prophylaxis indicated

Chemoprophylaxis should be offered to individuals in the following categories:

- high-risk individuals in the closed setting. In some settings, prophylaxis may need to be offered to all individuals within the closed setting (see *Prophylaxis Uncertain* below)
- members of staff and health care workers within the closed setting who are at increased risk of pneumococcal disease (as defined in the Green Book on Immunisation against disease) should also be offered chemoprophylaxis and ensure that they are up to date with their vaccinations

Prophylaxis for the case is not required

Cases should complete standard recommended antibiotic therapy to treat their disease, which will clear pneumococcal carriage in the case; additional antimicrobial prophylaxis will, therefore, not be required.

Evidence grade C

Prophylaxis for high-risk individuals who have already received antibiotics

High-risk individuals who have completed a course of antibiotics within the previous 7 days do not required any additional antibiotics.

Evidence grade C

Prophylaxis for healthy staff is not required

Healthy staff working in closed settings (eg care homes) do not require public health action apart from communication (“warn and inform”) because their risk of developing severe pneumococcal disease is very low. However, staff members may develop influenza infection and should be reminded to have annual influenza vaccination, especially if working closely with at-risk patients.

Evidence grade C

Timing of antibiotic chemoprophylaxis

If indicated, antimicrobial prophylaxis should be offered as soon as possible (ideally within 24 hours of identifying a cluster) to the individuals within the closed setting, regardless of vaccination status.

Evidence grade C

Antibiotic prophylaxis may be offered up to 14 days after the onset of illness in the last case in the cluster.

Evidence grade C

Prophylaxis uncertain

The division between those who do and do not receive prophylaxis can be arbitrary as the evidence on risk and benefit is limited. The outbreak control team will need to use their judgement to decide whether or not to advise prophylaxis for those who do not clearly fall into the high-risk group or if they fall into the excluded categories in Box 2.

7.6 Choice of agent for chemoprophylaxis

The choice of antimicrobial prophylaxis must always be guided by the *in vitro* susceptibility of the bacteria isolated and the target population (age, pregnancy, etc.). Most laboratories will not test for amoxicillin susceptibility in pneumococci, but this can be inferred readily from the penicillin result. Azithromycin susceptibility can be inferred from the results of erythromycin susceptibility testing. Rifampicin susceptibility can be requested if needed.

BOX 4: Antimicrobials in pneumococcal carriage studies

There are 15 published studies with data on the impact of antibiotics on nasopharyngeal pneumococcal carriage mainly in the context of acute otitis media.[17, 97-110] In 6 studies, azithromycin was used,[17, 100, 103, 104, 107, 108] in 3 ceftriaxone,[101, 105, 106] and in 7 amoxicillin or co-amoxiclav.[97-99, 101-104] Follow-up was 10 days to 3 weeks.

In a systematic review examining the effectiveness antibiotics on reduction of pneumococcal serotypes in carriage, a median carriage reduction of 90%

(IQR 73-100%) was observed in 17 regimens sampled 10-14 days after the initiation of antibiotics amoxicillin (with or without clavulanic acid) and/or penicillin.[9] The duration of treatment ranged from 3 to 12 days (median, 10 days), with dosage varying from 40mg/kg to 90mg/kg given commonly either twice or thrice daily (n=18). Usage of macrolides azithromycin (n=6) and telithrocmycin (n=1) sampled within the same range offered carriage reductions of 73% (range 69-83%) and 70% (range 69-83%), respectively. The duration of treatment ranged from 1 to 5 days (median – 4 days). In 5 carriage studies where ceftriaxone was used daily at 50mg/kg, median carriage was 68% (range 22-92%) when sampled 4-5 days after initiating antibiotics but lowered to 25% (range 4-77%) at 10-14 days.

Smaller reductions were usually observed when using oral cephalosporins including cefuroxime (86%, 95% CI 41-97%), cefpodoxime (64%, 95% CI 27-82%), cefaclor (17%, 95% CI –33-48%) and cefprozil (57%, 95% CI –10-83%) compared to amoxicillin and azithromycin. A dose of 20mg/kg of rifampicin given alone once daily for 2 days led to a 70% (–6 to 92%) carriage reduction.

Evidence grade C

No antimicrobials are licensed for this purpose. Recommendations have been made based on a review of the literature of the use of antibiotics in the management of clusters (Box 3) and in clearance of carriage (Box 4). Providing the organism is penicillin sensitive, amoxicillin is recommended as first-line choice therapy. Azithromycin (assuming macrolide sensitivity is confirmed) and rifampicin are second-line alternatives. Given the high-risk populations likely to receive antibiotic prophylaxis, where possible, the prescribing clinician should be aware of any individual risks, such as history of *C. difficile* or unexplained diarrhoea when prescribing penicillin, or potential drug interactions when prescribing any antibiotic.

Information should be provided about what management is recommended and its rationale. This should include explaining that antibiotic prophylaxis is not fully protective.

Recommendation 5: Prophylaxis regimens for contacts

Amoxicillin

Adults and >12 years	500mg BD orally for 7 days
Children 5-12 years	250 mg BD orally for 7 days
Children up to 5 years	125 mg BD orally for 7 days

A twice daily regime rather than thrice-daily is recommended as the former has both demonstrated effectiveness and is operationally more practical. In those individuals with penicillin allergy or a resistant strain, alternatives should be guided by *in vitro* susceptibility testing and include azithromycin or rifampicin.

Azithromycin

Adult	500mg OD orally for 3 days
Child >6 m	10mg/kg OD (max 500mg) orally for 3 days

Since macrolide resistance amongst invasive pneumococcal isolates does occur in the UK, it is important to ascertain the antimicrobial sensitivity profile of the responsible serotype before offering azithromycin.

Rifampicin

Adults and children over 12 years of age	600mg OD orally for 4 days
Children 1-12 years	20 mg/kg OD orally for 4 days
Infants under 12 months of age	10mg/kg OD orally for 4 days

Rifampicin is recommended in the case of penicillin and macrolide resistance and/or penicillin allergy. It can be used in all age groups. Rifampicin is contraindicated in the presence of jaundice or known hypersensitivity. Interactions with other drugs, such as anticoagulants, phenytoin, and hormonal contraceptives should be considered. Side effects should be explained including staining of body fluids and contact lenses.

In clusters caused by multiple resistant *S. pneumoniae*, combination prophylaxis should be considered in consultation with the local microbiologist.

7.6.1 Pregnancy

All 3 options (amoxicillin, azithromycin and rifampicin) can be used in pregnancy. As always, any drug should be used with caution in pregnancy, as there is a limited evidence base for safety. Rifampicin should be avoided in the later stages of pregnancy. For azithromycin, there is no evidence of harm in the foetus in animals; however, it should only be used in pregnancy when no adequate alternative is available.

7.7 Choice of Vaccination

Two types of pneumococcal vaccine are used in the UK, which include a variable number of capsular serotypes: the 23-valent-pneumococcal polysaccharide vaccine (PPV) and the 13-valent pneumococcal conjugate vaccine (PCV13). PCV13 is currently offered to all infants at 6 and 12 weeks of age, followed by a booster on their first birthday. This vaccine has been highly effective in reducing the risk of PCV13-type IPD across all age groups through direct and indirect (herd) protection.[27] PCV13 is also offered to severely immunocompromised children and adults who are at increased risk of IPD. PPV23 is routinely offered to older adults at 65 years of age, as well as at-risk individuals aged 2 years or older.

Several meta-analyses of both RCTs and observational studies have demonstrated the effectiveness of PPV23 against IPD. Although PPV23 offers modest protection against IPD caused by PPV23 serotypes, the level of protection does wane over time with vaccine effectiveness reducing to less than 21% 2 years after vaccination among individuals aged over 65, irrespective of risk group.[111]

Both PCV13 and PPV23 offer protection against the following serotypes:

4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F, 3, 19A

Only PPV23 offers protection against the following serotypes;

2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F

Only PCV13 offers protection against the following serotypes:

6A

7.7.1 23-valent pneumococcal polysaccharide vaccine (PPV23)

BOX 5: Pneumococcal polysaccharide vaccine and clusters

There are 7 published clusters in which 23-valent PPV23 was given.[11, 43-45, 57, 58, 61] In 5 of these, antibiotics were also administered.[43, 44, 57, 58, 61] Of these 5, in 3 there were further cases within one and 14 days of the intervention.[44, 57, 61] In one cluster,[61] PPV23 was given alone initially; within 3 days of PPV, 4 further cases occurred and chemoprophylaxis was then undertaken. In another cluster,[44] those receiving only PPV23 were 4 times more likely to develop pneumonia within 2 weeks than those who additionally received antibiotics.

In the updated review, PPV23 was used in a further 6 clusters which was concomitant with antibiotic chemoprophylaxis in 5 clusters.

Evidence grade D

7.7.2 13-valent pneumococcal conjugate vaccine (PCV13)

BOX 6: Pneumococcal conjugate vaccine and clusters

There have been only 2 reports of PCV13 being used, one cluster of serotype 3 IPD in an assisted-living facility, another in a cluster of serotype 9V in an adult respiratory ward where it was offered alongside PPV23 in conjunction with chemoprophylaxis to contacts within 14 days of exposure. There were no further cases of 9V; however, it is not possible to quantify the impact of PCV13 as the studies did not specify the number of contacts receiving PCV13 compared to PPV.

Evidence grade D

Recommendation 6: Vaccination

In the management of a cluster, PPV23 or PCV13 will not provide protection in the first 10-14 days following vaccination. Simultaneous antimicrobial prophylaxis is thus required for this intervening period.

In a cluster of severe pneumococcal disease in a closed setting with high-risk individuals, pneumococcal vaccination should be considered in addition to antibiotic chemoprophylaxis to provide longer-term individual protection. Vaccination can be offered up to 14 days after the onset of illness in the last case in the cluster.

PPV23 is the vaccine of choice if the infecting serotype is included in the vaccine or if the infecting serotype is not known. The rationale for this recommendation is that nearly all IPD episodes are currently due to serotypes that are covered by PPV23 and not PCV13. PPV23 provides adequate short-term protection which is sufficient in an outbreak setting and the vaccine is substantially cheaper than PCV13.

PPV23 should be offered to all high-risk individuals as well as staff and healthcare workers who are at increased risk of pneumococcal disease (as defined in the Green Book on Immunisation against disease) unless they have received PPV23 in the previous 12 months.

PCV13 should be used (i) in outbreaks involving young children (especially in <2 year-olds), (ii) if the outbreak is due to serotype 6A/6C or (iii) if the responsible strain is a PCV13 serotype and PPV23 is not available. PCV13 is not required for those who received PCV13 or PPV23 in the previous 12 months. In clusters involving infants and children, HPTs should ensure that all unimmunised and partially immunised children are appropriately immunised according to the national immunisation schedule.

7.8 Swabbing of contacts

Where deemed acceptable, nasopharyngeal swabbing of contacts pre- and post-intervention may be considered to:

- identify any individuals who remain culture-positive and may require repeat antimicrobial prophylaxis
- inform the evidence-base regarding the effectiveness of these interventions

However, prophylaxis should not be delayed while awaiting swabbing results. Information from swabbing of close contacts may also inform possible repeat antimicrobial prophylaxis in individuals who are still culture-positive.

8 Contact information

	National Public Health Team	**National Reference Laboratory**
England	Public Health England, Immunisation and Countermeasures Division, Colindale, London	Respiratory and Vaccine Preventable Bacteria Reference Unit (RVPBRU), Colindale, London
Wales	Public Health Wales, Health Protection Division, Cardiff	
Scotland	Health Protection Scotland, NHS National Services Scotland, Glasgow, NSS.HPSImmunisation@nhs.net	Scottish Haemophilus, Legionella, Meningococcus and Pneumococcus Reference Laboratory, Glasgow gg-uhb.glasgowsmrl@nhs.net
Northern Ireland	Public Health Agency, Belfast	

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Appendix 1: Reporting form for a cluster in a closed setting

Section 1: Cluster details

Location/name of premises: _____

Total number and clinical features of cases:

	Total no.	Meningitis	Pneumonia	Bacteraemia	Other
Confirmed cases					
Probable cases					

Date of onset (dd/mm/yy): _____

First case: _____ Last case: _____

Have any of the confirmed cases been serotyped? Yes ☐ No ☐

If yes, what serotype(s)? _____

Section 2: Type of setting (tick as appropriate)

Care home ☐ Hospital ☐

Prison ☐ Military establishment ☐

Other closed setting (please describe): _____

Section 2: Other respiratory infections

Location/name of premises: _____

Section 3: Population at risk and action taken (tick as appropriate)

Number of high-risk individuals in the closed setting: _____

Antibiotics: _____

PPV: _____

PCV: _____

How many pneumococcal cases occurred after the intervention? _____

Section 4: Nasopharyngeal swabbing of contacts (tick as appropriate)

Undertaken before ☐ If yes, date _____ How many swabbed? _____

If yes, how many were positive for *Streptococcus pneumoniae*? _____

Undertaken after ☐ If yes, date _____ How many swabbed? _____

If yes, how many were positive for *Streptococcus pneumoniae*? _____

How many were positive for the cluster serotype? _____

Section 5: Additional comments

Form completed by: _____ Position: _____

Date: _____

Please email the form to: ipdsurveillance@phe.gov.uk

Appendix 2: Communication with high-risk individuals, carers and staff following a cluster of severe pneumococcal disease in a closed setting

IMPORTANT: PNEUMOCOCCAL DISEASE INFORMATION FOR CARERS and STAFF

What is pneumococcal disease?

Pneumococcal disease is a term used to describe the range of infections which can be caused by a bacterium called *Streptococcus pneumoniae* (the pneumococcus)

How do you catch it?

The pneumococcus can be spread by close contact with someone who is carrying the bacteria when that person coughs or sneezes. They can also be spread by direct contact with respiratory secretions from an infected person, such as used paper tissues.

Many people carry the bacteria in the backs of their noses and throats without ever becoming ill while others can go on to develop a pneumococcal infection. It is not known why it only affects some people, but it is known that some groups of people are more at risk than others. These groups include:

- the very young or the very old
- people with a chronic illness such as disease of heart, lung, kidneys or liver
- people without a spleen or with a damaged spleen
- people whose immune system is not working properly

What kind of infections do the bacteria cause?

The bacteria can cause a variety of infections ranging from sinusitis and ear infections to more serious illnesses such as pneumonia, meningitis and septicaemia (blood-poisoning).

Can you catch a pneumococcal infection from close contact with someone at home or school who has it?

The vast majority of people who come into contact with someone with a pneumococcal infection remain well and symptom-free. It is extremely rare for healthy people to catch the infection from a relative or a member of their household.

Why are close contacts being offered antibiotics?

When 2 or more cases of severe pneumococcal infection are identified in people in the same setting (such as a care home or a hospital ward) within 14 days, then other people in that setting may be at a slightly increased risk of developing the infection. As a precaution, they are offered information about the infection, a course of antibiotics and sometimes immunisation.

Can people be immunised against pneumococcal disease?

All children born after September 2004 have routinely been offered a vaccine that helps protect against certain strains of the pneumococcus. In addition, anyone aged 65 years or older and those who have a higher risk of getting pneumococcal disease are also offered a different vaccine to protect against certain strains of the pneumococcus. Depending on the strain that is responsible, pneumococcal vaccination may be offered in addition to the antibiotics.

What are the symptoms of pneumococcal disease?

Developing a serious pneumococcal infection after coming into contact with an infected person is very rare. Antibiotics and vaccination may help reduce the risk of pneumococcal risk further but is not 100% effective. If you or someone you know develops any of the following symptoms in the next 2 weeks you should seek medical attention and show the letter and this leaflet to the doctor or nurse advising you.

The symptoms to watch out for are:

- a severe cough
- shortness of breath
- chest pains
- confusion or drowsiness
- a severe prolonged headache
- stiff neck, aversion to light
- fever
- seizures

If you need further support or advice, please contact *insert contact details*