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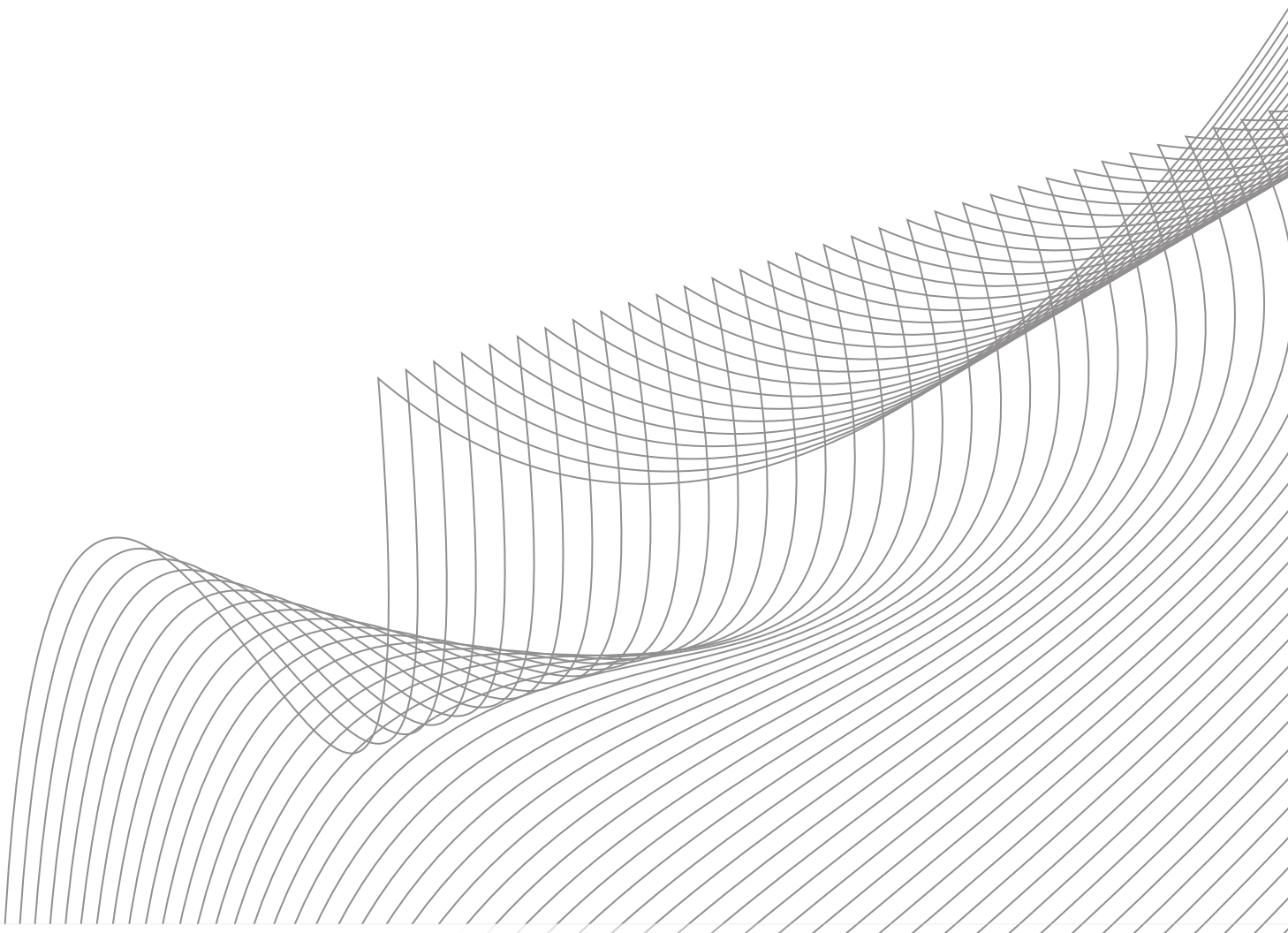

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Original article

Public health response to an outbreak of meningococcal B disease in a secondary school in Far North Queensland

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Abstract

This article describes the public health response to an outbreak of meningococcal B disease, linked to a secondary school in Far North Queensland. Tropical Public Health Services in Cairns were notified of three cases of meningococcal disease in the same week in May 2022. The cases occurred in individuals who all attended, or worked in, the same secondary school. All cases were serogroup B and shared the same molecular genotype. The public health response included prompt provision of information, distribution of clearance antibiotics and two doses of MenB-4C vaccine to the entire staff and student population. Antibiotic coverage and vaccination coverage were achieved in 99% and 85% of the student population respectively. Following the intervention, no further cases were detected in the region during the subsequent nine months.

Keywords: disease outbreak; meningococcal B; *Neisseria meningitidis*; MenB-4C vaccine

Introduction

Invasive meningococcal disease (IMD) is a notifiable condition in Australia.[1] It is a rare disease which predominantly affects young children and adolescents, but can result in significant morbidity and mortality. Most cases are sporadic; however, clusters of infection require an outbreak response.[2]

Neisseria meningitidis can be classified into one of twelve serogroups based on its capsular polysaccharide. Serogroups A, B, C, W, X and Y are the primary causes of IMD worldwide.[3] Vaccination protects against IMD.[3] There are three types of meningococcal vaccine available in Australia (monovalent MenC, conjugate quadrivalent MenACWY, and Men B) that cover the different serogroups, A, B, C, W, and Y. As the MenACWY vaccines are conjugate vaccines, they can impact carriage and transmission, providing benefits to the whole population.[4] The vaccines targeting Meningococcus B are protein-based and are therefore considered less effective against carriage and transmission. Vaccination is strongly recommended in people at increased risk of exposure or at increased risk of severe disease, a group that includes travellers, young children, and adolescents.

State and national programs will fund vaccination for high-risk populations or to control transmission, according to local disease epidemiology.[5] Currently the National Immunisation Program funds meningococcal B vaccination for populations at higher risk of invasive disease (Table 1).

The standard public health response to notifications of single cases of IMD includes case restrictions and treatment; clearance antibiotics for higher risk contacts (defined by significant degree and duration of exposure, typically household members); and the provision of information to both higher- and lower-risk contacts.[1] Vaccination may also be advised for higher-risk contacts, depending on the serogroup.[3]

Table 1: National Immunisation Program schedule for meningococcal B vaccine[a]

Category	Eligible population
Meningococcal B vaccine funded	Aboriginal and Torres Strait Islander children aged two months, four months and 12 months (also six months for certain medical conditions)
	People with asplenia / hyposplenia, complement deficient or receiving eculizumab
Meningococcal B vaccine strongly recommended (not funded)	Infants and children aged < two years
	People aged 15 to 24 years old living in close quarters eg residential accommodation/ military recruits or current smokers
	People aged greater than 15 years old with occupational risk eg laboratory personnel
	Adolescents aged 15 to 19 years old
	People with specific medical conditions

a Source: reference 4.

Table 2: Communicable Diseases Network Authority (CDNA) national guidelines: outbreak definition[a]

Outbreak category	Definition
Organisation-based	Two or more probable or confirmed (where the available microbiological characterisation of the organisms is the same) cases with onset in a four-week interval, among people who have a common organisation-based affiliation (such as attending the same high school, extended families and/or social groups) but no close contact with each other, in a grouping which makes epidemiological sense.
Community	Three or more probable or confirmed cases where there is no direct epidemiological link, with onset in a three-month interval among persons residing in the same area and the primary attack rate is at least 10 per 100,000 persons.

a Source: reference 1.

Outbreaks of IMD are infrequently declared in Australia.[6] The national guidelines define outbreaks as either 'organisation-based' or 'community' (see Table 2).

Despite the clear definition of an organisation-based outbreak, responses can still require nuanced decision making, even in school settings,[7] because of the limited information on the effectiveness of countermeasures.[8] Here we describe the decision-making process and implementation of the response following a cluster of cases, which may inform similar responses in the future.

Methods

Epidemiological investigation

This is a descriptive analysis of the decision-making process and implementation of a public health response to a school-based meningococcal disease outbreak. The investigation and response were conducted under the *Queensland Public Health Act 2005*. The reporting of the response did not require the approval of an ethics committee.

CDNA guidelines[1] were followed in the implementation of the outbreak response. Higher-risk contacts were initially classified as household members for the first case, and subsequently as all secondary students and staff who had been regularly attending the school during the exposure period. The exposure period was taken as the seven days prior to the earliest known date for onset of symptoms until the last date of attendance at the school prior to hospitalisation of the third case. Case histories were obtained through interview using standard contact tracing and report forms for Queensland Health.

Molecular finetyping

Finetyping was performed by sequencing the variable regions of the *porA* and *fetA* genes using the methods and scheme hosted at the PubMLST website.[i]

Statistical analysis

Descriptive data, taken from Excel spreadsheets utilised in the response, are presented. No statistical analysis was performed.

Results

Across six days in May 2022, Tropical Public Health Services (TPHS) in Cairns were notified of three cases of invasive meningococcal disease linked to a local secondary school. The three confirmed cases were identified as two primary cases and one secondary case, constituting an organisation-based outbreak per the National Guidelines.[1]

Case 1: Following the first notification of suspected meningitis by the hospital treating team, a public health response was initiated with case interview, contact tracing, clearance antibiotics to household members (defined as higher-risk contacts), and communication with the school. Two days later, *Neisseria meningitidis* was confirmed by polymerase chain reaction (PCR) on cerebrospinal fluid (CSF) and isolation and PCR on blood cultures. A letter was distributed to the entire school community with information regarding symptoms of meningococcal disease.[1] Subsequent serotyping identified serogroup B and the higher-risk contacts were informed that a vaccine was available at their own expense, for protection against the disease.

Six days after the initial notification was received, a further two cases were notified within hours of each other.

Case 2: Symptom onset for Case 2 was three days prior to onset of symptoms in Case 1. Initially, Case 2 was managed as sepsis of unknown origin, with a lumbar puncture performed later during the admission. The patient's CSF was subsequently confirmed to be PCR positive for *N. meningitidis*, at which time TPHS was notified. There were no identified epidemiological links to Cases 1 or 3, other than presence at the same school prior to the onset of symptoms.

Case 3: Onset of symptoms for Case 3 was five days after the onset of Case 1's symptoms. This case was a known contact of the index case and is considered a secondary case. Case 3 was not classified as a 'higher-risk' contact of Case 1,[1] and so had not been recommended to receive antibiotic clearance treatment. They had received the information sheet for lower-risk contacts which facilitated presentation to health care at the onset of symptoms. This case was also diagnosed with PCR positive *N. meningitidis* on CSF with the result received on the same day as that for Case 2.

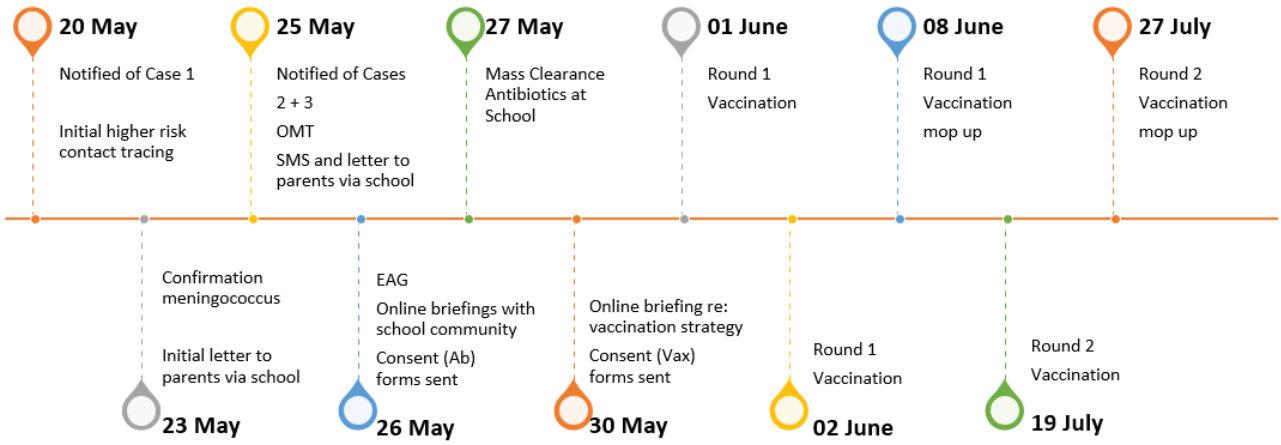
On the day when Cases 2 and 3 were both identified through laboratory results and notified to the public health unit (PHU), an organisation-based outbreak was declared, and an outbreak management team (OMT) was established.[1] The immediate response, established with the school leadership, was to provide further written communication to the school community about the situation and to offer mass antibiotic clearance to the staff and students using ciprofloxacin.

Face-to-face and online meetings with the public health team, for the school community, were organised by the school on the advice of TPHS and took place the following day to provide information and to address any concerns. The same day, a state-wide expert advisory group (EAG) met to discuss further interventions, particularly vaccination. Serotyping for Cases 2 and 3 was still pending, and it was decided that if Case 2 (with no direct epidemiological link) was also serogroup B, provision of vaccination to the entire school would be appropriate.

The following day, a TPHS clinical team, supported by the school staff, implemented mass

i Source: https://pubmlst.org/organisms/neisseria-spp.

Figure 1: Timeline of Public Health response to outbreak



distribution of clearance antibiotics to the entire student body and staff. Pharmaceutical support for supply, packaging, and advice on weight-based dosage was provided by the Cairns Hospital pharmacy department. The school facilitated consent through existing electronic processes and the students were brought through in their year groups. Medical advice was available onsite for discussion of risk or contraindications. Students were provided with ciprofloxacin. An area for any students who needed support to take tablets was established and a route for a 'pick up' option was also available. There was one outreach visit to a school sports team the same day.

The following week, after confirmation that Cases 2 and 3 were also serogroup B, the vaccination program was implemented. Further information sessions were provided about the planned vaccination campaign. Vaccination took place in two rounds, separated by seven weeks. Any students or staff who had received their first dose through their general practitioner (GP) received the second dose through the school program.

The school administration team obtained consent electronically and produced lists of consented students for vaccination to TPHS. At the time of vaccination, the school administration team confirmed consent had been received when entering the hall. Vaccination was performed by year level, with the majority receiving their vaccine on the first day. Mop-up vaccination was provided the following week for any staff or students unable to attend initially. All vaccine doses given were entered directly into the Australian Immunisation Register (AIR).

Outcome

The three cases of meningococcal infection all recovered. Whilst the public health response commenced on confirmation that all cases were of the same serogroup, subsequent testing confirmed that all three cases were a clonal match for the same molecular genotype of *PorA*:*FetA* P1.18-1,30-8,F4:FetA4-1. No cases matching this group have been identified on typing in Queensland from 2004 to November 2022.

Coverage

Antibiotics: From a student population of 1,003, a total of 950 (95%) received clearance antibiotics. An additional 122/171 teachers (71%) were also covered.

Vaccination: Outcomes of the vaccination for the 1,003 school students are presented in Table 3.

Six students left the school between round 1 and round 2 of vaccination. The overall second dose coverage was 845/997 (85%).

In addition, 121/171 staff (71%) received dose 1 and 96 (56%) received dose 2 of the vaccine. Vaccination was also provided opportunistically to four household contacts who presented to the school.

Utilisation

Antibiotics: Of 1,120 tablets of ciprofloxacin that were provided, 1,072 doses were utilised and six doses were wasted, with 42 tablets returned to pharmacy following the intervention.

Vaccination: Vaccine utilisation in each round is described in Table 4. Overall, 1,980 doses were procured with 1,958 (98.8%) used and 14 discarded (wastage of 0.7%); eight doses were returned to pharmacy following implementation.

Safety

Antibiotics: Anecdotal reporting of reactions included some episodes of nausea and vomiting, but there were no significant adverse events identified, and none of the reactions required hospitalisation.

Vaccine: Two vaccine administration errors occurred, with students receiving doses at the school as well as externally via GP. Two adverse events following immunisation (AEFI) were reported (0.1% of vaccinations). Both developed local cellulitis—a recognised risk—shortly after administration. One of the cases required hospitalisation for inpatient antibiotic therapy.

The direct costs incurred during the school vaccination are described in Table 5. Additional costs, such as use of consumable materials, the use of the full time TPHS staff for planning and implementation, entering data and reporting

Table 3: Student vaccination coverage during response

Vaccination outcome	Dose 1	Dose 2
Consented for campaign	890	870
Vaccinated at school	885	843
Vaccinated at GP	9	2
Late consent (dose 1 vaccine received in round 2)	5	—
Total	**899**	**845**
Overall coverage	**89.6%**	**84.7%**

Table 4: Vaccine utilisation

Category	Round 1	Round 2
Day 1	906	780
Day 2	49	168
Day 3	53	—
Vaccine administration error	0	2
Wastage	9	5
Total	**1,017**	**955**

Table 5: Direct costs incurred

Resource required	Cost (AUD)
Additional human resources	$5348.22
Antibiotics: 1,120 × ciprofloxacin 500 mg	$135.20
Vaccines: 1,980 × Bexsero 0.5 ml	$183,150.02
Total	**$188,633.44**

back to stakeholders, and the time of pharmacy staff are not included here. Similarly, the costs incurred by the school in terms of staff utilisation have not been calculated.

Discussion

Responding to meningococcal outbreaks can be complex. IMD can cause death and permanent disability, but an outbreak's course is unpredictable.[7] As a result, the effectiveness of a response is difficult to measure.[6] The three key decision points in responding to an outbreak are declaring an outbreak; providing antibiotic clearance; and offering vaccination.

Declaration of an outbreak

On this occasion the criteria for an 'organisation-based outbreak' were met, with three cases of the same serogroup linked to the school in a six-day period. Community-based outbreaks are more difficult to define, particularly with regards to the definition of a population that constitutes a 'community'. Even in an organisation-based outbreak, defining a target population can still be difficult, as described in a Brisbane boarding school.[5] However, a virulent strain of bacteria spreading in an unimmunised adolescent population requires an urgent public health response. On this occasion, the outbreak was serogroup B, for which vaccination of this age group is not included in the Queensland vaccination schedule. The three cases in this outbreak included two students from the same year level, but also a staff member with no identified interaction with the students during the infectious period. Consideration was given to whether only selected year levels should receive response measures; however, students from different year levels interacted with each other and the staff member also interacted with all year levels. The PHU and EAG therefore determined that a precautionary approach involving the entire school community was warranted. An associated primary school population was assessed as lower risk and information was provided to this effect.

Antibiotic clearance

Carriage of *N. meningitidis* is common; it is estimated that 3–25% of the general population are asymptomatic carriers at any point in time.[1] Use of antibiotics to clear meningococcal carriage for contacts of sporadic cases is confined to those at higher risk of ongoing transmission.[1,9] The benefit of clearance must be balanced against the risk of antibiotic harm including side effects, elimination of protective flora and development of resistance.[1] Clearance of nasopharyngeal carriage is likely to be temporary, as the bacteria can be subsequently reintroduced from a wider network.[10]

In the event of an organisation-based outbreak, the National Guidelines advise that clearance antibiotics and vaccination can be considered for the wider group.[1] Antibiotics can protect the individual through clearance of carriage, as well as through reducing the overall transmission risk. An analysis by McNamara et al,[9] examining the role of mass clearance antibiotics in outbreaks, proposes prevention of continuing transmission is best if the correct population is identified, high coverage (> 90%) is reached, and distribution occurs as soon as possible after a cluster of cases is identified. They also highlight that clearance antibiotics will allow time for vaccination provision and induction of immunity to be achieved when a combination strategy is used. As 4CMenB vaccines

are directed at bacterial antigens, they may not impact carriage and may take longer to achieve protective immunity than the vaccine against serogroups A,C,W, and Y (MenACWY). Thus a combined strategy, including clearance antibiotics to allow time for vaccination to be effective, may be particularly beneficial in the response to meningococcal B outbreaks.

Vaccination

Protection against meningococcal B infection in immunocompetent school-age children and adults requires two doses of vaccine and takes time to develop.[11] The effectiveness of current meningococcal B vaccines is dependent on whether the proteins included in the vaccine are present in the bacteria.[12] In New Zealand, for example, a vaccine targeting a single epidemic strain was implemented temporarily as a control measure. Similarly in Quebec, Canada an increased incidence of disease linked to a single clone was controlled through widespread vaccination.[13] In South Australia, it has been estimated that 4CMenB would be effective against 90% of the strains causing invasive disease. The South Australian Government currently provide MenB vaccination in the state schedule for populations identified as having high local rates of disease.[14] An Australian study in 2007–2011 predicted vaccine effectiveness against 76% of strains detected.[15]

The CDNA National Guidelines for IMD advise that vaccine provision should be considered if the outbreak is due to a vaccine-preventable serogroup. There are no published reports of vaccination in the event of an outbreak of meningococcal B infection in Australia.[16] Previous responses to school outbreaks caused by meningococcal C infections have included mass vaccination programs; however, since this serogroup is part of the regular vaccination schedule, outbreaks in unimmunised populations are not described.[17] In the United States of America, use of meningitis B vaccination to control outbreaks at two universities was described in 2014.[18]

Whilst the Australian Technical Advisory Group on Immunisation (ATAGI) recommends a standard interval between 4CMenB vaccine doses of eight weeks,[4] the decision was made to provide the second dose within a shorter time frame. This was supported by the EAG and based on Therapeutic Goods Administration product information and United Kingdom (UK) guidelines,[19] weighing the possibility of reduced effectiveness against the potential benefit of controlling an outbreak. Whilst the initial intent in this outbreak was to give the second round of vaccine after four weeks, the final implementation was delayed until week seven (due to school holidays) to facilitate maximum uptake.

Overall, there was good vaccine coverage during the response. This was facilitated significantly by support from the school community. Utilisation of the staff and facilities contributed greatly to an orderly, measured, and calm response. Concerns about a potential backlash against vaccination—coming so soon after the first significant waves of coronavirus disease 2019 (COVID-19)—failed to eventuate. Clear, consistent, and open communication throughout the process also assisted the response. Two written communications, and some livestreamed and recorded video conferences coordinated by the school, were very effective for communicating with staff, students and families, and allowed opportunities for concerns to be addressed. The school reported few additional questions received outside of these sessions.

Cost of disease vs cost of vaccination

Several studies have considered the direct cost of case management of IMD,[20] and the costs to public health from outbreak response.[21] Whilst we have included the additional costs incurred in responding to this outbreak, there are background costs through use of permanent staff and stored materials that are not included. Analyses of the cost of case management identify that it may not incorporate the cost to societal wellbeing from a serious and potentially fatal disease which disproportionately impacts children and

adolescents. Significant disruption to family life and educational facilities can also occur as a result.[22]

The effectiveness of a response is difficult to measure due to the uncertainty of whether subsequent cases are likely to occur. The UK has previously estimated that most subsequent cases in an outbreak will occur within the first three weeks; however, there are also reports of outbreaks with ongoing cases for months.[7] Whilst the cost of response to this outbreak was considerable, the risk of continuing transmission in a vulnerable population needed to be addressed. As this was an organisation–based outbreak, it was possible to implement a relatively small containment approach. There are greater costs incurred if larger facilities are affected or if community-based outbreaks occur.

Conclusions

We describe a rare occurrence of an organisation-based outbreak of meningococcal B infection in an Australian secondary school. The public health response included a combination of clearance antibiotics and vaccination which was informed by current evidence. National guidelines allow for local decision-making discretion, which can be complex when faced with an outbreak of serogroup B in a non-immune population. On this occasion, a combined response to the entire school community using antibiotics and vaccination was felt to be appropriate. Our experience of responding to an outbreak in a non-immune, high-risk population with both antibiotics and vaccination was successful, with no further cases following these measures. However, it is not possible to assess whether less comprehensive approaches – only one measure, or in a more targeted population – would have achieved the same outcome. The successful response was only feasible due to significant resourcing and effective coordination and communication by the Public Health team and the school community. It is hoped that the detailed description of the components of the apparently successful strategy might inform the management of similar outbreaks in the future.

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The urgent public health response to this situation was facilitated significantly by the support of the patients and their families, the school administration and wider school community.

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