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Title: Surveillance of Pediatric Parapneumonic Effusion/Empyema in New Zealand

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Abstract

Aim:

The incidence of childhood empyema has been increasing in some developed countries despite the introduction of pneumococcal vaccination. This study aimed to document the incidence, bacterial pathogens, and morbidity/mortality of parapneumonic effusion/empyema in New Zealand.

Methods:

A prospective study of 102 children <15 years of age requiring hospitalization with parapneumonic effusion/empyema between 1-May-2014 and 31-May-2016 notified via the New Zealand Paediatric Surveillance Unit. Parapneumonic effusion/empyema was defined as pneumonia and pleural effusion persisting ≥7 days, and/or any pneumonia, and pleural effusion necessitating drainage. Notifying pediatricians completed standardized questionnaires.

Results:

Annual pediatric parapneumonic effusion/empyema incidence was 5.6/100,000 (95%CI 4.7–6.9). Most children (80%) required surgical intervention and 31% required intensive care. A causative organism was identified in 71/102 (70%) cases. Although *Staphylococcus aureus* (25%) and *Streptococcus pneumoniae* (25%) infection rates were similar, prolonged hospitalization, and intensive care admission was more common in children with *S. aureus*. Māori and Pasifika children were over-represented at 2.2 and 3.5 times, their representation in the NZ pediatric population. Pneumococcal vaccination was incomplete, with only 61% fully immunized and 30% unimmunized. *Haemophilus influenzae* type b vaccine uptake was near complete at 89/94 (95%), with influenza immunization only 3/78 (4%).

Conclusions:

New Zealand has a high incidence of pediatric complicated parapneumonic effusion/empyema with significant morbidity. *S. aureus* was a significant cause of severe empyema in New Zealand, particularly for Māori and Pasifika children. Improvements in vaccine coverage are needed along with strategies to reduce *S. aureus* disease morbidity.

Introduction

Pleural empyema is an uncommon but serious complication of childhood community-acquired pneumonia,[1] resulting in prolonged hospitalization, extended antibiotic therapy, and often requiring invasive intervention.[2]

The most common causative organism reported internationally in pediatric empyema is *Streptococcus pneumoniae*, accounting for 41-79% of cases[2-5] with *Streptococcus pyogenes* and *Staphylococcus aureus* less frequently recorded.[2-5] However, New Zealand (NZ) children have a high burden of *S. aureus*-related disease overall,[6,7] with previous studies identifying *S. aureus* as a significant cause of complicated pneumonia/parapneumonic effusion and empyema.[8-10]

An increase in childhood empyema incidence has recently been reported in developed nations including Australia, the United States (US), the United Kingdom (UK), and other European countries.[11-15] Similarly, in a retrospective regional NZ study, parapneumonic effusion/empyema (PPE/E) incidence in a South Auckland hospital increased ten-fold from 1/100,000 in 1998 to 10/100,000 in 2012.[9] Several factors could be behind this increase: antibiotic resistance, particularly methicillin-resistant *S. aureus* (MRSA); changes in antibiotic prescribing at primary healthcare level; delayed presentation to hospital; and pre-hospital use of non-steroidal anti-inflammatory drugs (NSAIDs).[2,16,17] This increase has occurred despite the introduction of pneumococcal conjugate vaccines (PCVs), which have resulted in a reduction of community-acquired pneumonia. However, empyema has continued to increase with emergence of *S. pneumoniae* serotypes not included in PCVs.[11,12] Since 2008, the NZ national immunization schedule included PCV for all infants. In 2008 the 7-valent pneumococcal vaccine (PCV7; Prevenar-7®) was introduced into the NZ Immunization Schedule, four doses delivered at six-weeks and three-months, five-months and 15-months of age.[18] It was replaced by PCV10 (Synflorix®) in 2011 and PCV13 (Prevenar-13®) in 2014. PCV10 was reintroduced in 2017.

Secondary bacterial infections, particularly with *S. pneumoniae, S. aureus* and *Haemophilus influenzae,* can lead to increased morbidity and mortality during influenza pandemics.[19] There is also evidence that invasive pneumococcal disease (bacteremia, PPE/E) follows regular seasonal influenza.[20] During the 2009 Influenza A (H1N1) pandemic increased PPE/E hospitalizations were reported in some but not all studies.[9,21,22]

International and local guidelines recommend empiric antibiotic treatment of empyema to ensure cover for *S. pneumoniae*, *S. aureus*, and MRSA, or other organisms as clinically indicated.[23-25] Interventions include thoracostomy (chest drain) insertion, either alone or with fibrinolytics; video-assisted thorascopic surgery (VATS); or open thoracotomy.[26] Meta-analysis revealed that, while VATS is more invasive and often more expensive than thoracotomy, it may reduce the length of hospital stay by a mean of two days.[26] The value of fibrinolytics in treatment has been difficult to assess.[26]

The aim of this study was prospective national surveillance of PPE/E over a two-year period in NZ. We evaluated the demographics, infectious etiology, underlying conditions, management, complications, and immediate outcomes of children hospitalized with parapneumonic effusion or empyema. We hypothesized that we would find a significant burden of parapneumonic effusion/empyema associated with *S. aureus* disease.

Methods

Study design and setting

A prospective surveillance study utilizing the New Zealand Paediatric Surveillance Unit (NZPSU, https://www.otago.ac.nz/nzpsu) from 1st May 2014 to 31st May 2016, including two influenza seasons. Through the study period, 235-245 clinicians participated in in the surveillance with an average response rate to monthly report emails of >90% (https://www.otago.ac.nz/nzpsu).

The National Health and Disability Ethics Committee (HDEC) granted ethical approval for NZPSU surveillance with approval for this study obtained by amendment OTA/95/10/113/AM04.

Participants

Children (<15 years) admitted to hospital with PPE/E within the timeframe. Parapneumonic effusion and empyema were defined as (i) pneumonia and pleural effusion lasting ≥7 days; OR (ii) any pneumonia and pleural effusion with radiologic features of empyema, such as echogenic material or loculated pleural fluid; OR (iii) pneumonia and pleural effusion necessitating drainage.[27,28]

Parapneumonic effusion/empyema surveillance

Participating pediatricians submitted monthly electronic report cards notifying of any infant or child PPE/E aged less than or up to 15 years to NZPSU. The reporting pediatrician then completed the study questionnaire[29] reporting the child's demographic information; clinical history and investigations; immunization status (validated by National Immunisation Register if available);

underlying medical conditions; clinical management and antibiotics; disease severity and outcome. Due to changes in NZ Immunization schedule over time participants in our study received PCV7, PCV10, PCV13, or a combination. We defined pneumococcal immunization status as full (3-4 doses received); partial (1-2 doses received); unknown number of doses of PCV7, PCV10, or PCV13 received; or unimmunized. Ethnicity was collected from health records and prioritized according to Ministry of Health protocols, with priority given to Māori, Pasifika, non-European, and European ethnicities, respectively.[30] To enhance case notification, pediatric surgeons and microbiologists at NZ's four major pediatric surgical centers were informed about the study and asked to complete notifications.

Pathogen Identification

Pathogen identification was from sterile sites, including blood, pleural fluid, cerebrospinal fluid, and pericardial fluid. Laboratory identification of bacterial organisms included routine bacterial culture, serology, and *S. pneumoniae* antigen detection (immunochromatography), or *S. pneumoniae* polymerase chain reaction (PCR) on pleural fluid. In addition, if pleural fluid was collected and was culture negative pediatricians were requested to refer these to the Institute of Environmental Science and Research (ESR) for further molecular diagnosis using 16s ribosomal RNA (rRNA) sequencing.

Statistical analyses

Data were analyzed using JMP v13.0 (SAS Inc.), StatsDirect v3 (StatsDirect Ltd.) and SAS v9.4 (Cary, NC, USA). Annual incidence was calculated based on NZ

government national population estimates for children aged <15 years old during the years 2014-2016 with a 25 month denominator.[31] Incidence confidence interval calculation used the Poisson method.

Results

Parapneumonic effusion/empyema in children <15 years of age

During the study period there were 127 notifications of PPE/E with 108 eligible cases and follow up questionnaire data available for 102 cases (94% response rate) (Figure 1). There was no report of multiple PPE/E events. This gave a nationwide incidence of pediatric PPE/E of 5.6 (95% confidence interval (CI) 4.7-6.9) per 100,000 children aged <15 years per year. The cases came from 18 of the 20 District Health Boards (DHBs) in NZ, with 46% coming from the 3 DHBs in the Auckland region, where 35% of all New Zealand children aged 0-20 years live.[31]

The affected children had a median age of 3.7 years (range 0.3-14.9 years) and 55/102 (54%) were male (Table 1). PPE/E occurred more commonly in children under five years of age (65/102, 64%) (Figure 2). Māori and Pasifika children were over-represented with 33/101 (33%) Māori and 25/101 (25%) Pasifika notifications despite being 15% and 7%, respectively, of the pediatric population in the 2013 census (Table 1).[31] Ethnicity was not reported for one child. PPE/E incidence was higher in Māori (7.8/100,000, 95%CI 5.6-11.0), Pasifika (11.4/100,000, 95%CI 7.7-16.8), and Asian (8.4/100,000, 95%CI 5.2-13.5) compared to European (1.9/100,000, 95%CI 1.3-2.9) children. There were 26/102 (25%) children with comorbid medical conditions, which included eczema,

asthma, neurological and developmental disorders, diabetes, and other conditions (Table 1).

Immunization status

Of those children who had the required immunization documentation, almost all had received *Haemophilus influenzae* type b (Hib) vaccine 89/94 (95%) (Table 1). For pneumococcal vaccine, 57/93 (61%) were fully immunized, 4/93 (4%) partially immunized, and 28/93 (30%) unimmunized with a combination of PCV7, PCV10, and PCV13 vaccines. There were no significant differences in PCV vaccination with respect to ethnicity, with 47% of European, 70% of Māori, 74% of Pasifika and 62% of Asian children fully vaccinated with PCV. Of those who had not received any PCV doses, the majority were born prior to introduction of universal PCV immunization (25/28, 89%). The remaining children were born overseas or were too young to receive the pneumococcal vaccine. Influenza immunization was uncommon and data were incomplete, with only 3/78 (4%) reporting influenza vaccination.

Pathogen identification

A causative organism was identified in 71/102 (70%) cases (Table 2). The most common pathogens were *S. aureus* 25/102 (25%), *S. pneumoniae* 26/102 (25%), and *S. pyogenes* 10/102 (10%). In 20/70 (29%) pleural samples no causative organism was detected. Isolation of *S. aureus* was more common in children of Māori or Pasifika ethnicity (19/25, 76%) compared to children of European/Asian/Other ethnicity (6/25, 24%) (P=0.030). *S. pneumoniae* was the

more common pathogen in younger children (one to four years old), while *S. aureus* dominated in older children (10 to 14 years old) (Figure 2).

Methicillin-resistant *S. aureus (*MRSA) represented 4/25 (16%) of *S. aureus* isolates. Seven *S. pneumoniae* isolates had antibiotic susceptibility data, four were penicillin susceptible (minimum inhibitory concentration (MIC) <0.06mg/L), two had intermediate susceptibility (MIC 0.125mg/L and 0.19mg/L) and one was resistant (MIC 2mg/L). All pneumococcal cases were successfully treated with either high dose penicillin G/amoxicillin or other Beta-lactam antibiotics. All *S. pyogenes* isolates were fully susceptible to penicillin.

Only three *S. pneumoniae* cases had serotype data. Two had serotype 19A (blood culture), one had received three doses of PCV10, and the other had received three doses of PCV10 and one dose of PCV13. One had serotype 3 (pleural fluid) and received three doses of PCV7, a formulation that does not cover this serotype.

Parapneumonic effusion/empyema management

Pre-Hospital

Median symptom duration prior to hospital admission was 7 days (range 0-35) (Table 3). Just over one-quarter of children received antibiotics prior to hospital admission (27/102, 27%) with median treatment duration 3.5 days (range 1-12). Amoxicillin was most frequently prescribed followed by co-amoxiclavulinate, cotrimoxazole and cefaclor.

Hospital

Almost all 101/102 (99%) of the children with PPE/E received intravenous antibiotics during hospitalization (Table 3). The majority required surgical management (82/102, 80%) and 19/102 (19%) were treated conservatively with intravenous (IV) antibiotics alone. The most common surgical procedures were VATS (37/82, 45%), chest drain plus a fibrinolytic agent (13/82, 16%) and chest drain alone (8/82, 10%). Twenty-two children (27%) required more than one surgical intervention. There was no significant difference in type or frequency of surgical procedures between pathogens, including *S. aureus*.

Length of Stay and Immediate Outcomes

The children were hospitalized for a median of 18 days (range 6-56) (Table 3). Almost one-third of children (32/102, 31%) required admission to an intensive care unit (ICU) for a median of 5 days (range 1-36). Of those admitted to ICU, almost half had *S. aureus* PPE/E (14/32, 44%; $P<0.001$) (Table 2). All four children with MRSA PPE/E required ICU admission. In contrast, only 6/32 (19%) children were admitted to ICU with *S. pneumoniae* PPE/E. Children with *S. aureus* PPE/E spent longer in ICU than those with other causative organisms, with 8/29 (28%) compared to 5/29 (17%), respectively, spending >5 days in ICU ($P=0.027$). No children with PPE/E died during this study.

Discussion

This is the first prospective surveillance study of pediatric PPE/E in NZ and demonstrates national incidence of 5.6 per 100,000 per year. Māori and Pasifika children were overrepresented in notified cases of PPE/E. The main causative

organisms identified were *S. aureus* (25%) and *S. pneumoniae* (25%). A 2009-2014 NZ study demonstrated an empyema incidence of 5.8/100,000 in 0-18 year aged children from Auckland [8] but a lower rate (2.2/100,000) in Christchurch.[8] A 1998-2012 study at KidzFirst Hospital (South Auckland NZ) reported a higher incidence of empyema 10.2/100,000 and PPE incidence of 5.7/100,000 in 2012.[9] In both these studies Māori and Pasifika children were overrepresented. In North Queensland, Australia, empyema incidence was (8.5/100,000) in a population with 52% Australian Indigenous children.[15] Within this population, Indigenous children had an empyema incidence of 19.8/100,000.[15] A Sydney children's hospital reported increasing PPE/E admissions from 2011 to 2018, 1.7 to 7.1/1,000 admissions.[32] In the last decade, rates in North America and Europe range from 2.0 to 6.0/100,000.[12,13,33-36].

The overrepresentation of Māori and Pasifika children in this and previous studies[8,9] is similar to that found in other indigenous populations. Indigenous Australian children have empyema incidence rates 2.3 times that of all Australian children.[15] Alaskan Native children under ten years of age are hospitalized for empyema at 1.7 times the rate of all US children.[37]

Māori and Pasifika children experience greater exposure to adverse social determinants of health, reduced access to healthcare, and reduced quality of healthcare.[38] At the time of our study, Māori children were 1.4 times and Pasifika children were 1.3 times more likely to have unmet primary healthcare needs than non-Māori and non-Pasifika children.[39] These inequities contribute to the increased risk Māori and Pasifika children have of hospitalization with any infectious disease, particularly respiratory infections.[40] Māori and Pasifika

children have a relative risk of respiratory infection hospitalization 2.7 and 3.4 times that of European children, respectively.[40]

PPE/E is predominantly a disease of young children with 64% of children in our study less than five years of age, consistent with previous NZ and international data, where children under five account for 53-74% of pediatric cases.[8,12,15]

We found equal pediatric empyema cases attributable to *S. aureus* and *S. pneumoniae* rather than *S. pneumoniae* dominance seen elsewhere.[2-5] This could be due to the documented high rate of *S. aureus* colonisation[41] and invasive *S. aureus* disease[6] in young children in NZ, with overrepresentation of Māori and Pasifika children.[6] Isolation of *S. aureus* was more common in children of Māori or Pasifika ethnicity in our study. Alternatively, given that one-third of our cases had unknown etiology and we only had three cases with PCR-confirmed *S. pneumoniae*, we may have underestimated PPE/E due to *S. pneumoniae*, a limitation of our study. However, an Australian study reported a similar pathogen profile, with 32% (*S. aureus*) and 33% (*S. pneumoniae*) of PPE/E caused by these organisms, with Indigenous children overrepresented.[15] Despite these differences in PPE/E pathogen profile, empiric antibiotic treatment according to Thoracic Society of Australia and New Zealand guidelines remained appropriate for areas without high rates of methicillin resistant *S. aureus*.[25]

One-third of PPE/E cases required ICU admission and hospital stays were long, at a median of 18 days. ICU admission was more likely and longer in children with *S. aureus* PPE/E, reflecting the severity of *S. aureus* PPE/E when compared with PPE/E caused by *S. pneumoniae*. A recent Auckland study of invasive *S. aureus* disease burden found that 45% of those with respiratory disease were admitted to

ICU and all of the deaths (2% overall) occurred in children with respiratory disease.[6] Similarly, an Australian study reported 26% of children with empyema required ICU admission, although this severity was not linked to a specific pathogen.[32]

All children with MRSA required ICU admission. However, the overall proportion of disease caused by MRSA remained low (4%), in keeping with previous findings in NZ children (6%).[42] MRSA represented 16% of all invasive *S. aureus*, similar to an Australian/NZ study of *S. aureus* bacteremia in children (13.2%)[43] and a European study (18.5%).[44] Gautam et al. (2018) report a high overall rate of MRSA infection (23%), with Australian Indigenous children even more susceptible (34%).[15] Thus, although *S. aureus* is an important cause of PPE/E in NZ children, MRSA remains uncommon. Nevertheless, MRSA is associated with longer hospital stays and ICU admission, as has been reported previously.[43]

Four out of five children required surgery and IV antibiotics for PPE/E, while the remainder received IV antibiotics alone. One in five (22%) required more than one surgical intervention, reflecting the complexity of empyema management. A similar repeat intervention rate (28%) was reported in an Australian empyema management study.[32] Total surgical intervention rates were also similar to those reported elsewhere.[28] Regional variations in intervention type most likely reflect local experience and are unlikely to affect clinical outcome.[8,28,45]

With such high morbidity and significant cost, the main strategy of immunization to prevent PPE/E needs to be reviewed and prioritized. Currently most developed and developing countries have universal infant pneumococcal conjugate and

Haemophilus influenzae type b (Hib) vaccination schedules. Children in this study received PCV7, PCV10, or PCV13 pneumococcal vaccines, or a combination due to the staggered introduction and accessibility of PCV for high risk groups.[18] Whilst catch-up immunization programs were provided, not all children were eligible and this is reflected in the only moderate pneumococcal immunization coverage in our cohort.

Influenza may precede *S. pneumoniae* or *S. aureus* related respiratory complications.[19] National influenza surveillance has demonstrated high influenza-related hospitalization rates for children aged <5 years in NZ and led to targeted influenza vaccine funding from 2014 for children <5 years of age only if a history of significant respiratory illness or presence of a medical condition increasing risk of influenza.[18] The very low influenza vaccine uptake seen in our cohort reflects the limited funded vaccine available.

There are limitations to this study. Reliance on physician surveillance for case notification and data collection may have led to an underestimation of the incidence of PPE/E even with enhanced laboratory and surgical center involvement. Clinicians submitted notifications monthly, creating a delay in the request/receipt of pleural specimens for further molecular analyses. Additionally, molecular serotyping for pneumococcus is not available in NZ, only cultured *S. pneumoniae* isolates were able to be serotyped. Laboratory services are regional in NZ, processes and techniques vary, and molecular diagnostics are not available in all centers. We relied on the transfer of samples to the national reference laboratory (ESR) for PCR serotyping. Unfortunately, this limited our ability to confirm and serotype *S. pneumoniae* using molecular techniques. Regardless, we

established an etiologic pathogen in 70% of PPE/E cases, which is higher than prior reports.[3] Domicile codes were unavailable for the majority of participants, limiting our ability to examine the relationship between household deprivation and burden of PPE/E disease. There is now evidence, published during the time of our study, that use of NSAIDs during acute viral infections and community-acquired pneumonia increases the risk of PPE/E.[16,17] We had not planned to collect this data and so could not confirm this association.

In summary, children in New Zealand have a high burden of PPE/E, particularly *S. aureus* related infection and amongst Māori and Pasifika children. Prolonged hospitalization, ICU admission, parenteral antibiotic therapy, and multiple surgical interventions reflect the complex nature and management of this disease. Although *S. aureus* and *S. pneumoniae* are equally likely to be causative of PPE/E, children with *S. aureus* are more likely to require ICU admission and a longer duration of admission. Future surveillance of pediatric PPE/E in NZ should consider collecting data on pre-hospital use of ibuprofen, uniform management of sterile site specimens including molecular diagnostics, and ensuring serotype data available for cases caused by *S. pneumoniae.* Given our observation of more frequent and longer ICU admissions in children with *S. aureus* PPE/E, the relationship between *S. aureus* and PPE/E morbidity should be the focus of future studies.

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Figure Legends

Figure 1. Flowchart of parapneumonic effusion/empyema notification to the New Zealand Paediatric Surveillance Unit (NZPSU) and study inclusion**.**

Figure 2. Child's age at presentation to hospital with parapneumonic effusion/empyema and organism identified (n=102).

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Table 1. Demographic and health characteristics of children admitted to hospital with parapneumonic effusion or empyema (n=102).

Child demographic and health characteristics	**n=102**	
Age (years), median (range) (n=102)	3.7 (0.3-14.9)	
Sex, n (%) (n=102)		
Female	47	(46)
Male	55	(54)
Ethnicity, n (%) (n=101)[a]		
NZ European	23	(23)
Māori	33	(33)

Pasifika	25	(25)
Asian	17	(17)
Other	3	(3)
Comorbid medical conditions, n (%) (n=26)		
Eczema	5	(19)
Asthma[b]	6	(23)
Neurodevelopmental disorders[c]	7	(27)
Type 1 Diabetes Mellitus[b]	2	(8)
Other conditions[d]	7	(27)
Immunisation Status		
***Haemophilus influenzae* type b (Hib)**, n (%) (n=94)		
Yes	89	(95)
No	5	(5)
Pneumococcal (PCV7, PCV10, PCV13)[e], n (%) (n=93)		
Full (3-4 doses)	57	(61)
Partial (1-2 doses)	4	(4)
Dose number unspecified	4	(4)
None	28	(30)
Influenza, n (%) (n=78)		
Yes	3	(4)
No	75	(96)

[a] Ethnicity not reported for one child.
[b] Both conditions found in one individual.
[c] Includes cerebral palsy, autism spectrum disorder, Down syndrome, anti-N-methyl-D-aspartic acid receptor encephalitis and global developmental delay.
[d] Includes polyarticular juvenile idiopathic arthritis (receiving etanercept), stage IV neuroblastoma, repaired congenital diaphragmatic hernia, prematurity, gastro-oesophageal reflux disease with oesophageal stricture, anaemia, and inhaled foreign body left main bronchus.
[e] Participants received PCV7, PCV10, PCV13, or a combination of these as part of the immunization schedule.

Table 2. Organisms detected in sterile sites from children hospitalised with parapneumonic effusion or empyema admitted to intensive care unit (n=102).

Pathogen	Total (n=102) n (column %)	Site of infection					Intensive Care Unit Admission[b] (n=32) n (column %)
		Blood (n=16) n (row %)	Pleural fluid (n=65) n (row %)	Blood + second site[a] (n=8) n (row %)	Pericardial fluid (n=1) n (row %)	No intervention (n=11) n (row %)	
S. pneumoniae[c]	26 (25)	6 (2	17 (6	3 (1	0 (	0 (0	6 (1
S. aureus[d]	25 (25)	4 (1	17 (6	4 (1	0 (	0 (0	14 (4
S. pyogenes	10 (10)	4 (4	4 (4	1 (1	1 (1	0 (0	5 (1
Other[e]	9 (9)	2 (2	7 (7	0 (	0 (	0 (0	5 (1
None[f]	32 (31)	0 (	20 (6	0 (	0 (	11 (34	2 (

[a] Second sites were pleural fluid (n=5), left tibia aspirate (n=1), shoulder aspirate (n=1) and cerebrospinal fluid (n=1).
[b] $P<0.001$ (Chi-square test).
[c] Culture positive (n=8); immunocytochemistry/polymerase chain reaction positive (n=16); identification method not reported (n=2)
[d] 4/25 (16%) were methicillin-resistant *S. aureus (*MRSA). All children with MRSA-positive empyema required intensive care unit admission.
[e] Other includes oral *Streptococcus* isolates: *S. constellatus* (n=3), *S. oralis* (n=1) and *S. intermedius* (n=1), non-typeable *Haemophilus influenzae* (n=2), Group B *Streptococcus* (n=1) and *Fusobacterium nucleatum* (n=1).
[f] Includes *Mycoplasma pneumoniae* (n=1) detected via serology.

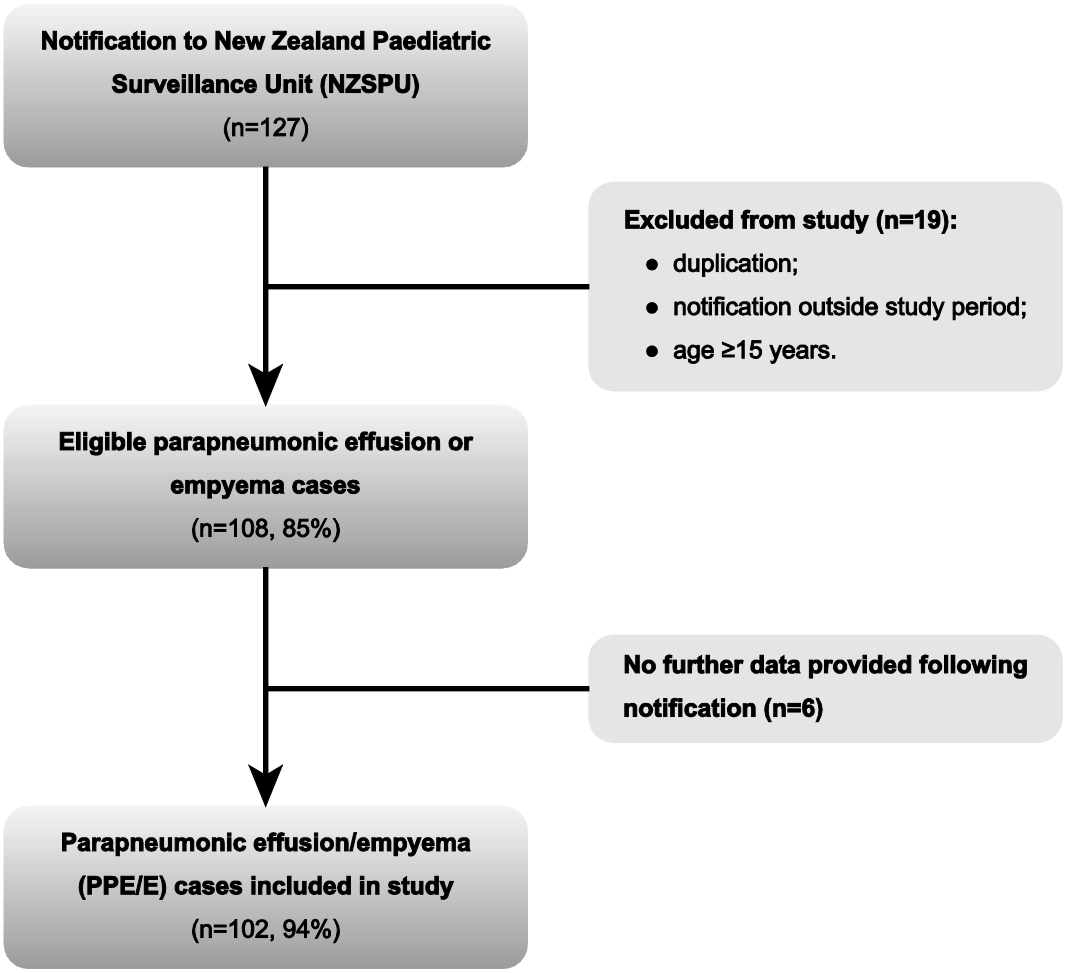
Table 3. Clinical characteristics and management of parapneumonic effusion/empyema prior to and during hospitalisation (n=102).

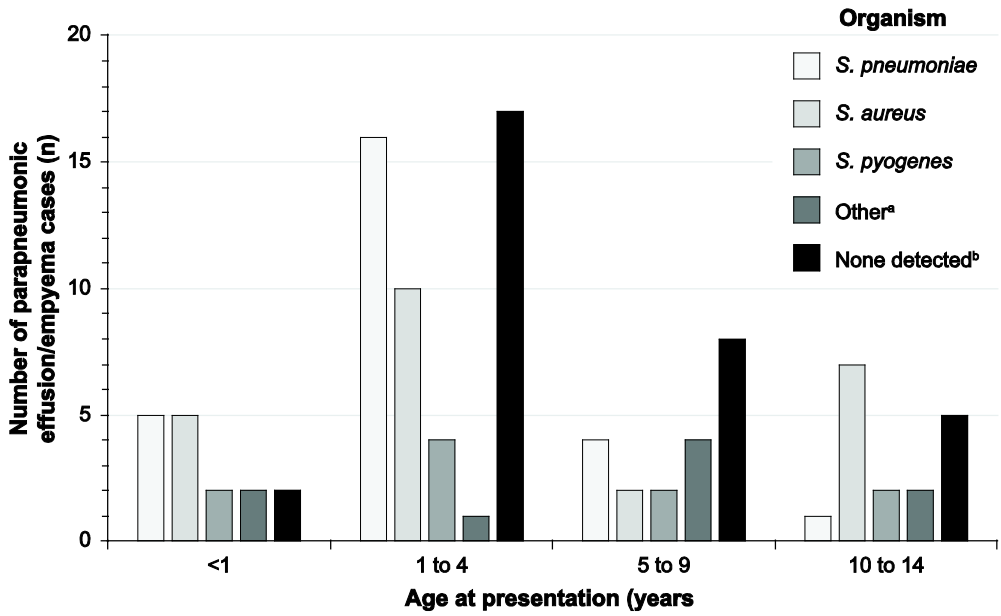
Empyema characteristics and management	n=102
Pre-hospitalisation	
Disease duration prior to hospital admission (days), median (range), (n=102)	7 (0-35)
Antibiotic treatment, n (%) (n=100)	27 (27)
Duration of antibiotic treatment (days), median (range) (n=24)	3.5 (1-12)
During hospitalisation	
Antibiotics, n (%) (n=101)	
Intravenous antibiotics alone	19 (19)

Intravenous antibiotics + surgery	82	(80)
Intervention, n (%) (n=83)		
Pleural aspirate	1	(1)
Thoracostomy	8	(10)
Thoracostomy + fibrinolytic	13	(16)
Video-Assisted Thoracoscopic Surgery (VATS)	37	(45)
Open thoracotomy	1	(1)
Two interventions[a]	19	(23)
Three interventions[b]	3	(4)
Surgical intervention unknown procedure	1	(1)
Length of hospital stay (days), median (range)	18 (6-56)	
Intensive care unit (ICU) admission, n (%) (n=102)	32	(31)
Length of ICU admission (days), median (range) (n=29)	5 (1-36)	

[a] Pleural aspirate / VATS (n=1); Pleural aspirate / Thoracostomy + fibrinolytic (n=2); VATS / Thoracostomy (n=4); VATS / Thoracostomy + fibrinolytic (n=7); Thoracostomy / Thoracostomy + fibrinolytic (n=2); Thoracostomy / Open thoracotomy (n=3).

[b] VATS / Thoracostomy / Thoracostomy + fibrinolytic (n=1); VATS / Thoracostomy / Open thoracotomy (n=1); VATS / Thoracostomy + fibrinolytic / Open thoracotomy (n=1).





[a] Other includes oral *Streptococcus* isolates: *S. constellatus* (n=3), *S. oralis* (n=1), and *S. intermedius* (n=1); non-typeable *Haemophilus influenzae* (n=2); Group B *Streptococcus* (n=1); and *Fusobacterium nucleatum* (n=1).

[b] Includes *Mycoplasma pneumoniae* (n=1) detected via serology.