

## REGULAR ARTICLE

# Half of all hospitalised children treated with antibiotics for pneumonia did not fulfil radiological, microbiological or laboratory criteria

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**Abstract**

**Aim:** Evaluating the management of paediatric pneumonia is important. We aimed to estimate the proportion of children receiving antibiotics for suspected community-acquired pneumonia (CAP) that were likely to have a bacterial infection. Furthermore, we described antibiotic use in relation to guidelines.

**Methods:** We conducted a prospective observational study from a paediatric department in Norway. During 2017, all admitted children aged 0–17 years receiving antibiotics for CAP were enrolled in the study. We collected relevant data and defined likely CAP as one or more of the following: radiologically confirmed pneumonia, c-reactive protein of at least 100 mg/L, positive bacterial culture from blood or pleura, detection of bacteria from the nasopharynx associated with atypical pneumonia.

**Results:** In total, 70 episodes of suspected CAP were included. Median age was 41.5 months, and 36 (51%) were girls. Of all treatments, 38 (54%) fulfilled our criteria for likely CAP. Median duration of treatment was 10 days. Of empirical treatments, 36 (57%) only involved penicillin. None of the children had neutropenia or complications, and only two needed intensive care.

**Conclusion:** Only half of children receiving antibiotics for suspected CAP were likely to have bacterial infection. Despite no obvious reason, antibiotic treatment was longer than currently recommended.

**KEYWORDS**

antibiotics, community-acquired pneumonia, c-reactive protein, paediatric pneumonia, radiologically confirmed pneumonia

**Abbreviations:** 95% CI, 95% confidence interval; CAP, community-acquired pneumonia; CRP, c-reactive protein; CXR, chest X-ray; IQR, interquartile range; PCR, polymerase chain reaction; RSV, respiratory syncytial virus.

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## 1 | INTRODUCTION

Despite the introduction of vaccines, pneumonia in children remains among the most frequently causes of morbidity and antibiotic use worldwide<sup>1,2</sup> and in Norway.<sup>3</sup> Hereafter, we use the expression community-acquired pneumonia (CAP) for bacterial infection.

Studies from high-income countries have reported that *Streptococcus pneumoniae* is the most common bacteria causing CAP also in the post-vaccination era.<sup>4,5</sup> Although a clinical diagnosis,<sup>6</sup> radiologically confirmed pneumonia on chest X-ray (CXR) has often been required for the diagnosis of CAP in clinical studies from hospitals<sup>4,7,8</sup>. Levels of c-reactive protein (CRP) of at least 100 increases the probability of bacterial aetiology and the risk for complications.<sup>9,10</sup> From a microbiological point of view, most cases of pneumonia are not supported by detected bacteria. Instead, a positive viral polymerase chain reaction (PCR) test from the nasopharynx is often observed, respiratory syncytial virus (RSV) being dominating.<sup>4,7</sup> Importantly, inappropriate use of antibiotics accelerates the global treat of antibiotic resistance.<sup>11</sup> Small children may catch undesirable long-term side effects of high antibiotic consumption.<sup>12</sup>

According to the Norwegian guideline, the diagnosis of CAP should be based on clinical symptoms, laboratory tests, microbiological results and CXR. The guideline emphasises that CAP is unlikely if no major infiltrates are present on CXR or if the CRP value stays below 100 mg/L. Penicillin for 7–10 days is generally recommended as empirical treatment. In cases of allergy or if atypical pneumonia is suspected, erythromycin is emphasised.<sup>13</sup> In international guidelines, an aminopenicillin for 3–7 days are often recommended as first-line treatment. Erythromycin, aminoglycosides and third-generation cephalosporins are mentioned as alternatives.<sup>6</sup> A study from our group indicated lower threshold for antibiotic therapy in a specific district hospital compared to a university hospital in Norway.<sup>14</sup> Thus, we wanted to explore the treatment of CAP in this district hospital with more detail.

The main aim of this study was to estimate the number of children treated with antibiotics for suspected CAP that were likely to have a bacterial infection. Furthermore, we aimed to describe choice, treatment length and doses of antibiotics in relation to national guidelines. The secondary aim was to investigate correlations between the CRP values, the CXR results, the microbiological results and the duration of treatment.

## 2 | METHODS

### 2.1 | Study setting and data collection

This was a prospective observational study from the paediatric department at Ålesund hospital in 2017. This is an 18 beds capacity district hospital situated at the western coast of Norway. During 2017, the department treated the majority of diseases in children, also at the intensive care unit when required. All children needing airway pressure support were admitted to the intensive care unit.

### Keynotes

- We described diagnostic and treatment characteristics in 70 hospitalised children that were prescribed antibiotics for community-acquired pneumonia.
- Radiologically confirmed pneumonia was present in 19% of the children, 47% had c-reactive protein levels of at least 100 mg/L and 11% had relevant bacterial findings.
- Duration of antibiotic treatment was at least 10 days in 60% of the children and 57% of all treatments only involved penicillin.

The uptake area of this paediatric department was mainly rural, and the number of children aged 0–17 years registered as inhabitants in 2017 was 50 274.

We collected data on children aged 0–17 years admitted to the hospital and receiving antibiotics for suspected CAP. Children with cystic fibrosis were not included, neither children with suspected sepsis. A standardised registration form was used for data collection, and study nurses performed the registration every day at 8am. A project participating medical doctor double-checked the registrations and added additional information based on the electronic journal. Our data collection was part of a large-scale registration of all children receiving antibiotics at the hospital.<sup>14</sup>

The diagnosis of CAP was based on the indication note for starting antibiotic therapy by the treating physician, but needed to fulfil at least two of the following three criteria: fever at admission or the same day, cough or tachypnoea. These were verification criteria and investigated by a study participant. To avoid cases where tachypnoea and fever were present at the same time, limits for defining tachypnoea were increased by 10 and five breath per minute per degree Celsius for children up to 5 years and more than 5 years, respectively.<sup>15</sup> Only cases where CAP was registered as the only indication for treatment were included. Registration included national identification number, age in months, weight, gender, comorbidity, name of antibiotic, dose, administration route, if penicillin allergy was present, in-hospital and total treatment length, intensive care unit admissions, maximum CRP value, results of CXR, PCR results from the nasopharynx and bacterial cultures from blood, pleura and the respiratory tract.

### 2.2 | Data processing

We divided the children in three age categories: infants less than one year, preschool children from 1–5 years and schoolchildren from 6 to 17 years. Comorbidities were specified on a separate list and were classified based on the paediatric complex chronic condition classification system.<sup>16</sup> Conditions with minor severity such as allergies and asthma without the need of daily medication were not regarded as comorbidities. CRP were analysed

using particle enhanced immune turbidimetry. The CRP value was categorised as high if it was at least 100 mg/L and low if it was less than 100 mg/L. Based on separate reports from the attending radiologist and a paediatrician, CXR results were sorted into one out of three categories based on guidelines from the World Health Organization.<sup>17</sup> These three categories were normal, un-specific or radiologically confirmed pneumonia, the latter requiring a focal opacity or a certain presentation of pleural fluid.<sup>17</sup> If abscess, empyema or effusion were present, this was noted specifically. Standard PCR panel from the nasopharynx included RSV, influenza-viruses and *Mycoplasma/Chlamydia pneumoniae* (atypical pneumonia).

We defined likely CAP as episodes including one or more of the following diagnostic findings: radiologically confirmed pneumonia, CRP of at least 100 mg/L, positive bacterial culture from blood or pleura, or detection of bacteria in the nasopharynx associated with atypical pneumonia. The total number of treatment days were categorised as minimum 10 days of treatment or less than 10 days of treatment. This was based on in-hospital treatment days and the prescription at discharge. Antibiotics used during hospitalisation were reported as the number of treatments involving one specific antibiotic and as the number of days one specific antibiotic was given.

### 2.3 | Analyses and statistics

We presented basic demographics and data on diagnostic and treatment outcomes for the entire group, and separately for those with and without comorbidities. Categorical variables were presented in absolute numbers and frequencies, continuous variables in medians and interquartile range (IQR). For categorical variables, comparison of variables between the groups was performed using a chi-square test or Fisher's exact test if any expected frequencies were less than five. For continuous variables, a Mann-Whitney *U* test was chosen for analyses.

Multivariate regression was used to analyse correlations between the CRP values, the CXR results, the virus-positive cases and the number of days with antibiotic treatment. We also used multivariate regression to analyse doses of penicillin in relation to the CRP values, the CXR results and the total treatment length. The results from the regression analyses were presented as odds ratio for categorical dependent variables and as the regression coefficient (beta) for continuous variables, both with corresponding 95% confidence interval (95% CI). A *p* value <0.05 was considered significant for all analyses. For statistics, we used Stata version 16.1 (StataCorp LLC).

### 2.4 | Ethics

The study was approved by the Regional Committee for Medical and Health Research Ethics (#2017/30/REK Midt).

## 3 | RESULTS

In total, 70 episodes of antibiotic treatments for suspected CAP were included in our study. The youngest child was four months at admission. These 70 episodes accounted for 4.8% of 1456 admissions at the department in 2017. Table 1 shows the basic demographics, the diagnostic findings and the treatment characteristics. In 13 (18.6%) of the episodes radiologically pneumonia was confirmed by CXR. Median CRP value for all episodes was 84 (IQR 38–186). Cough was present in 68 (97.1%) of the episodes, increased respiratory rate in 60 (85.7%) of the episodes and fever in 61 (87.1%) of the episodes. In total, 38 (54.3%) of the episodes fulfilled our criteria for likely CAP. No cases of empyema, abscess or effusion requiring surgery or drainage occurred in these children. Three cultures from the respiratory tract showed growth of bacteria whereof one was *Streptococcus pneumoniae*, susceptible to and treated with penicillin. The two others were *Hemophilus influenzae*, susceptible to and treated with amoxicillin. These cultures were collected in children who fulfilled our criteria for likely CAP based on CRP and, or, CXR.

Median duration of antibiotic treatment was 10 days (IQR 8–10). Among those not fulfilling our criteria for likely CAP, the median age was 34.5 months (IQR 14.5–76), the median CRP value was 38 (IQR 20–72) and the median treatment length was nine (IQR 7–10). Only two of these patients were treated less than five days. Comorbidity was observed in 27/70 (38.6%) of the episodes (Table 2). One child had a malignancy, but none had a neutrophilic granulocyte count of  $0.5 \times 10^9 / L$  or lower. None of the children had immune deficiencies. Empirical treatments only including penicillin were less frequently in children with comorbidities compared to previously healthy children (Table 1). None of the children was allergic to penicillin. All patients with atypical pneumonia were treated with erythromycin. Table 3 shows an overview of all antibiotics used in the treatment of CAP in-hospital.

Increasing CRP values were associated with increased number of total treatment days (Beta 14.1, 95% CI 4.9–23.3, *p* < 0.01) and with radiologically confirmed pneumonia (Beta 130.0, 95% CI 83.1–176.8, *p* < 0.001). However, radiologically confirmed pneumonia was not associated with change in the total number of treatment days (odds ratio 0.98, 95% CI 0.61–1.57, *p* = 0.927). The median CRP value for virus-positive cases was high, 151 mg/L, compared to non-positive cases, 76 mg/L (Figure 1). Appendix S1 shows the results of all regression analyses. Figure 2 shows the seasonal variation in the treatment of suspected CAP and that viral PCR was positive in 12/25 (48.0%) of the episodes in the first quarter.

Median penicillin dose was 98 mg/kg/day (IQR 77–120) for intravenous administrations and 60 mg/kg/day (52–74) for oral administrations. Increasing doses of intravenous penicillin were associated with increasing CRP values (Beta 0.2, 95% CI 0.1–0.3). See Appendix S2 for analyses of doses in relation to various parameters.

TABLE 1 Demographics, diagnostic findings and treatment characteristics of children treated for community-acquired pneumonia in a Norwegian district hospital, 2017

	All episodes (N = 70)	Episodes in previously healthy children (N = 43)	Episodes in children with comorbidities (N = 27)	p Value <sup>a</sup>
Basic demographics				
Children	62	43	19	—
Children ≥1 episode	6	0	6	—
Children readmitted ≤2 weeks	3	0	3	—
Age in months at onset	41.5 (22.0–81.0)	32.0 (18.0–72.0)	46.0 (22.0–95.0)	0.317
0–1 years	6 (8.6)	5 (11.6)	1 (3.7)	—
1–6 years	45 (64.3)	27 (62.8)	18 (66.7)	—
6–18 years	19 (27.1)	11 (25.6)	8 (29.6)	—
Weight in kg	14.0 (11.0–24.4)	13.2 (10.9–19.0)	16.5 (12.0–25.0)	0.437
Female sex	36 (51.4)	24 (55.8)	12 (44.4)	0.497
One month fatality	0 (0.0)	0 (0.0)	0 (0.0)	—
Nasopharynx PCR findings				
Test taken	63 (90)	37 (86.1)	26 (96.3)	—
Any virus	17 (24.3)	12 (27.9)	5 (18.5)	0.373
Respiratory syncytial virus	15 (21.4)	10 (23.3)	5 (18.5)	—
<i>Mycoplasma pneumoniae</i>	5 (7.1)	4 (9.3)	1 (3.7)	0.355
<i>Chlamydia pneumoniae</i>	1 (1.4)	1 (2.3)	0 (0.0)	—
Chest X-ray				
X-ray taken	64 (91.4)	39 (90.7)	25 (92.6)	0.575
Normal or unspecific	51 (72.9)	30 (69.8)	21 (77.8)	—
Radiological pneumonia <sup>b</sup>	13 (18.6)	9 (20.9)	4 (14.8)	0.522
CRP				
Mg/L	84 (38–186)	122 (38–226)	79 (38–169)	0.527
CRP <100	37 (52.9)	21 (48.8)	16 (59.3)	—
CRP ≥100	33 (47.1)	22 (51.2)	11 (40.7)	0.395
Other diagnostic tests				
Blood culture taken	28 (40.0)	16 (37.2)	12 (44.4)	0.552
Positive cultures	0 (0.0)	0 (0.0)	0 (0.0)	—
Pleura culture taken	0 (0.0)	0 (0.0)	0 (0.0)	—
Respiratory tract culture taken				
Positive cultures	17 (24.3)	8 (18.6)	9 (33.3)	—
Positive cultures	3	2	1	—
Treatment characteristics				
Antibiotic treatments in-hospital	81	49	32	—
Daily doses of antibiotics in-hospital	198	113	85	—
In-hospital treatment length	2 (1–3)	2 (1–3)	2 (1–5)	0.659
≤2 days	44 (62.9)	27 (62.8)	17 (63.0)	—
Total treatment length	10 (8–10)	10 (9–10)	10 (7–10)	0.380
≥10 days	42 (60.0)	27 (62.8)	15 (55.6)	—
Intravenous administrations	26 (37.1)	20 (46.5)	6 (22.2)	—
Only oral administrations	44 (62.9)	23 (53.5)	21 (77.8)	0.041
Switch of antibiotic type	4 (5.7)	3 (7.0)	1 (3.7)	0.498
Admissions to intensive care unit	2 (2.9)	0 (0.0)	2 (7.4)	—
Treatments only with penicillin <sup>c</sup>	36 (57.1)	27 (71.1)	9 (36.0)	0.006

(Continues)

TABLE 1 (Continued)

	All episodes (N = 70)	Episodes in previously healthy children (N = 43)	Episodes in children with comorbidities (N = 27)	p Value <sup>a</sup>
Fulfilling criteria for likely CAP <sup>d</sup>	38 (54.3)	25 (58.1)	13 (48.1)	0.417

Note: Categorical variables are presented in numbers and percentages, and continuous variables are presented in medians and interquartile range. All percentages were calculated based on all episodes.

Abbreviations: CRP, c-reactive protein; PCR, polymerase chain reaction.

a A chi-square test was used for proportions and a Mann-Whitney *U* test was used for continuous variables.

b Focal opacity or certain presentation of pleural effusion.<sup>16</sup>

c Cases that were PCR positive for *Mycoplasma/Chlamydia pneumoniae* or included cultures not susceptible to penicillin were extracted

d One or more of the following: radiologically confirmed pneumonia, CRP  $\geq 100$ , bacteria in blood/pleura, atypical pneumonia confirmed by PCR.

TABLE 2 Overview of comorbidities in children treated for community-acquired pneumonia in a Norwegian district hospital, 2017

Comorbidity	Episodes, n (%)
All	27 (100)
Neurologic or neuromuscular	13 (48.1)
Respiratory	9 (33.3)
Hematologic	2 (7.4)
Gastrointestinal	2 (7.4)
Malignancy (no neutropenia)	1 (3.7)

## 4 | DISCUSSION

In this study, we described the management of children treated with antibiotics for suspected CAP in a Norwegian district hospital. We observed that only one out of five episodes of CAP was radiologically confirmed by CXR and that roughly half of the episodes fulfilled our criteria for likely CAP.

Other studies targeting CAP in children have used radiologically confirmed pneumonia as selection criteria.<sup>4,7,8</sup> Our study is original because we based our observation on children receiving antibiotics for suspected CAP initiated by the treating physician. Thus, we were able to study real practice concerning inclusion for antimicrobial therapy. For the same purpose, we also decided to include children with all types of comorbidities, except cystic fibrosis.

The proportion of episodes with radiologically confirmed pneumonia is comparable with a study from the United States that targeted the results of paediatric CXR in the emergency department.<sup>18</sup> Another study concluded that the majority of children with respiratory tract symptoms and a negative CXR could be managed without antibiotics. However, the latter study included mainly outpatients.<sup>19</sup> A meta-analysis revealed a sensitivity in the range from 75% to 95%, and 10/11 studies observed a specificity of more than 90%.<sup>20</sup> The sensitivity of CXR in our study was very low when using antibiotic treatments as the reference for CAP (17/64, 27%), but also when using our criteria for likely CAP (17/38, 45%). Differences between studies could be explained by different definitions of CAP or by

different radiological assessment. For the future, ultrasound could be a promising alternative to CXR, also avoiding ionisation.<sup>20</sup> We can speculate that the use of ultrasound could have increased the proportion of radiologically confirmed CAP in our study.

Other studies have shown that high CRP values increased the specificity for CAP<sup>9</sup> and also increased the risk for prolonged hospitalisation.<sup>10</sup> We observed that the total number of treatment days increased in relation to higher CRP values, but we did not reveal the same connection for in-hospital treatment days. The high rate of virus positivity from the nasopharynx is mirrored in previous studies.<sup>4,7</sup> The high median CRP value that we observed in these episodes could explain the reason for starting antimicrobial therapy. This is also supported by a study that observed low CRP values in confirmed RSV cases without evidence of bacterial infection.<sup>9</sup>

Half of the episodes in this study did not meet our criteria for likely CAP. These children were mostly preschool children, they had low CRP values, and 90% received antibiotics for at least seven days. Clinical symptoms of CAP may justify antibiotic treatment regardless of other test results. Thus, our criteria do not allow us to conclude that these children should have been managed without antibiotics. Moreover, roughly half of these children had comorbidities, and we can neither rule out that some were treated based on previously positive bacterial cultures. However, by not fulfilling our criteria, the probability for bacterial infection is substantially lower. Clinical symptoms were not supported by neither CRP, CXR or microbiology. Thus, we can speculate that a notable proportion were exposed to antibiotics for too many days. Practice of reevaluating the antibiotic therapy before discharge could probably be improved at this hospital.

To minimise antibiotic resistance, one should aim for the shortest effective duration of treatment.<sup>21</sup> A systematic review including guidelines from the World Health Organization suggested three days of antibiotics for mild CAP and seven days or less for moderate and severe CAP.<sup>21</sup> Also, it is essential to reevaluate indication for antibiotic therapy continuously.<sup>22</sup> In our study, none of the children was treated for suspected sepsis and none had empyema, abscess or pleural effusion. Thus, we speculate that many of the children that met our criteria for likely CAP also received antibiotics for unnecessary many days. Most importantly, Norwegian guidelines,

**TABLE 3** Overview of antibiotic use in children treated for community-acquired pneumonia in a Norwegian district hospital, 2017. Data are presented in numbers and percentages.

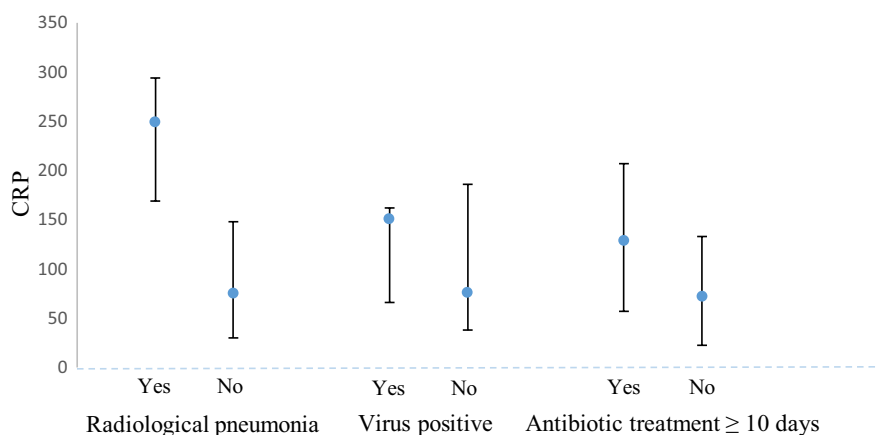
Antibiotic	All Episodes		Previously healthy children		Children with comorbidities	
	Treatments	Number of days	Treatments	Number of days	Treatments	Number of days
All	81	198	49	113	32	85
Penicillin <sup>a</sup>	41 (51)	107 (54)	30 (61)	74 (65)	11 (34)	33 (39)
Intravenous	21 (26)	43 (22)	18 (37)	38 (34)	3 (9)	5 (6)
Oral	29 (36)	64 (32)	19 (39)	35 (31)	10 (31)	29 (34)
Erythromycin <sup>b</sup>	15 (19)	44 (22)	11 (22)	23 (21)	4 (13)	21 (25)
Aminopenicillin	8 (10)	16 (8)	2 (4)	5 (4)	6 (19)	11 (13)
Co-trimoxazole	4 (5)	4 (2)	2 (4)	2 (2)	2 (6)	2 (2)
Cefotaxime	4 (5)	12 (6)	1 (2)	3 (3)	3 (9)	9 (11)
Gentamicin	3 (4)	7 (4)	2 (4)	5 (4)	1 (3)	2 (2)
Co-amoxiclav	1 (1)	2 (1)	–	–	1 (3)	2 (2)
Doxycycline	1 (1)	2 (1)	–	–	1 (3)	2 (2)
Metronidazole	1 (1)	1 (1)	–	–	1 (3)	1 (1)
Clindamycin	1 (1)	1 (1)	–	–	1 (3)	1 (1)
Meropenem	1 (1)	1 (1)	–	–	1 (3)	1 (1)
Cephalexin	1 (1)	1 (1)	1 (2)	1 (1)	–	–

Abbreviations: Co-amoxiclav, amoxicillin clavulanic acid; Co-trimoxazole, trimethoprim sulfamethoxazole.

a 9 treatments involved both intravenous and oral penicillin.

b 6 treatments were *Mycoplasma/Chlamydia pneumoniae* PCR positive.

**FIGURE 1** Association between levels of c-reactive protein (CRP) and other clinical measures in 70 episodes of paediatric community-acquired pneumonia in a Norwegian district hospital, 2017. All episodes were selected for antibiotic treatment. The blue circle shows the median CRP value, and the black line represents the 25th - 75th percentile. CRP, c-reactive protein

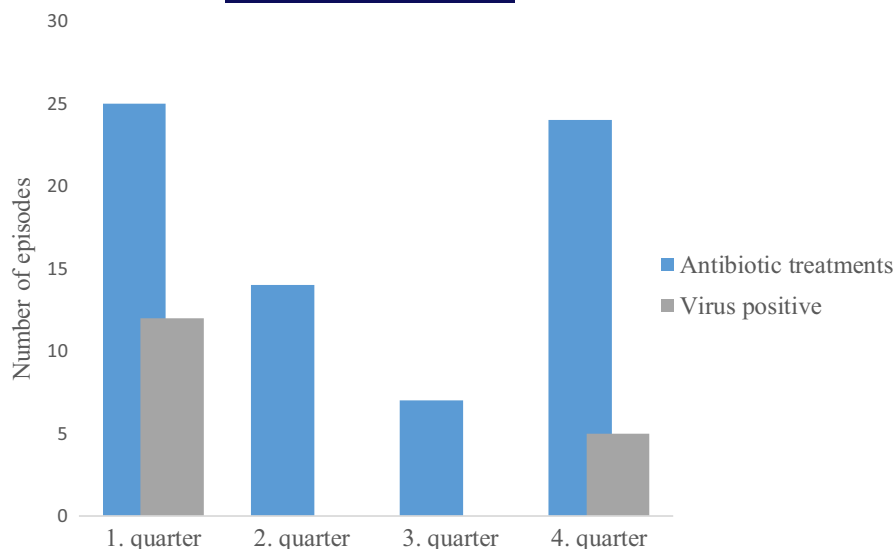


recommending 7-10 days of treatment, should consider modify recommended treatment length to cope with international guidelines.

In this study, children with bacterial findings were prescribed antibiotics according to these. In the remaining cases, only 57% were treated with penicillin as monotherapy. Penicillin use was also low compared to another hospital in Norway.<sup>8</sup> Aminopenicillins and erythromycin were commonly used. These are recommended as first- and second-line treatments, respectively, in most international guidelines.<sup>6</sup> Especially in children with comorbidities, it is hard to evaluate whether use of non-penicillin antibiotics was prudent. Some may have been treated according to previously bacterial cultures. Norwegian guidelines should probably present a more differentiated

list of recommendations and explain when non-penicillin antibiotics could be considered.

Doses of intravenous penicillin were in the lower range, IQR 77-120 mg/kg/day, compared to the recommendation in a respected paediatric formulary, 100-300 mg/kg/day.<sup>23</sup> However, doses were in line with the Norwegian pneumonia guidelines, recommending 100-120 mg/kg/day.<sup>13</sup> Recently published studies from Norway observed that a notable proportion of invasive *Streptococcus pneumoniae* isolates was susceptible to penicillin only with increased dose exposure.<sup>24,25</sup> The relatively low doses that we observed may indicate less severe disease, but intravenous treatments should generally be reserved for severe infections.<sup>6</sup>



**FIGURE 2** Episodes of community-acquired pneumonia in children 0–17 years involving antibiotic treatment in a Norwegian district hospital, 2017

Thus, the Norwegian guideline may consider to increase the dose recommendations.

In this study, we have included a wide range of variables related to the management of CAP. Due to our first-hand knowledge to the data collection, we had no missing variables. A limitation of the study is that we only included one hospital. However, this hospital was studied because previous results indicated high use of antibiotics for pneumonia.<sup>14</sup> Another limitation is the awareness of the study among the attending physicians at the hospital. This could have led to registration bias in terms of more strict use of antibiotics. Moreover, we did not have information on results from eventually previously taken cultures from the respiratory tract. This could potentially have explained antibiotic choices and treatment length. More detailed clinical information would make it easier to access the rationale for different treatment strategies.

## 5 | CONCLUSION

Only half of the children receiving antibiotic treatment for suspected CAP were likely to have a bacterial infection. Despite no obvious reason, antibiotic treatment was longer than currently recommended. Additionally, only half of the children were treated with penicillin as monotherapy. The current recommendations for treatment length and intravenous penicillin doses should be re-considered when updating the Norwegian guidelines.


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## CONFLICT OF INTEREST

None.

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## REFERENCES

- Hsia Y, Lee BR, Versporten A, et al. Use of the WHO Access, Watch, and Reserve classification to define patterns of hospital antibiotic use (AWaRe): an analysis of paediatric survey data from 56 countries. *Lancet Glob Health*. 2019;7:e861-e871.
- Walker CLF, Rudan I, Liu L, et al. Global burden of childhood pneumonia and diarrhoea. *Lancet*. 2013;381:1405-1416.
- Thaulow CM, Berild D, Eriksen BH, Myklebust TA, Blix HS. Po10tial for more rational use of antibiotics in hospitalized children in a Country With low resistance: data from eight point prevalence surveys. *Pediatr Infect Dis J*. 2019;38:384-389.
- Berg AS, Inchley CS, Aase A, et al. Etiology of pneumonia in a pediatric population with high pneumococcal vaccine coverage: a prospective study. *Pediatr Infect Dis J*. 2016;35:e69-e75.
- Elemraid MA, Sails AD, Eltringham GJ, et al. Aetiology of paediatric pneumonia after the introduction of pneumococcal conjugate vaccine. *Eur Respir J*. 2013;42:1595-1603.
- Mathur S, Fuchs A, Bielicki J, Van Den Anker J, Sharland M. Antibiotic use for community-acquired pneumonia in neonates and children: WHO evidence review. *Paediatr Int Child Health*. 2018;38(sup1):S66-S75.
- Jain S, Williams DJ, Arnold SR, et al. Community-acquired pneumonia requiring hospitalization among U.S. children. *N Engl J Med*. 2015;372:835-845.
- Senstad AC, Suren P, Brauteset L, Eriksson JR, Hoiby EA, Wathne KO. Community-acquired pneumonia (CAP) in children in Oslo, Norway. *Acta Paediatr*. 2009;98:332-336.
- Higdon MM, Le T, O'Brien KL, et al. Association of C-reactive protein with bacterial and respiratory syncytial virus-associated pneumonia among children aged <5 years in the PERCH study. *Clin Infect Dis*. 2017;64:378-386.
- Barak-Corren Y, Horovits Y, Erlichman M, Picard E. The prognostic value of c-reactive protein for children with pneumonia. *Acta Paediatr*. 2020. <https://doi.org/10.1111/apa.15580>. [epub ahead of print].

11. World Health Organization (WHO). Global action plan on antimicrobial resistance. 2015. Available from: <https://apps.who.int/iris/handle/10665/193736>
12. Korpela K, Salonen A, Virta LJ, et al. Intestinal microbiome is related to lifetime antibiotic use in Finnish pre-school children. *Nat Commun.* 2016;7:104-110.
13. Norwegian Pediatric Association. Akuttveileder i Pediatri (in Norwegian). 2013. Available at: <https://www.helsebiblioteket.no/pediatriveiledere>
14. Thaulow CM, Blix HS, Eriksen BH, Ask I, Myklebust TA, Berild D. Using a period incidence survey to compare antibiotic use in children between a university hospital and a district hospital in a country with low antimicrobial resistance: a prospective observational study. *BMJ Open.* 2019;9:e027836.
15. Davies P, Maconochie I. The relationship between body temperature, heart rate and respiratory rate in children. *Emerg Med J.* 2009;26(9):641-643.
16. Feudtner C, Feinstein JA, Zhong W, Hall M, Dai D. Pediatric complex chronic conditions classification system version 2: updated for ICD-10 and complex medical technology dependence and transplantation. *BMC Pediatr.* 2014;14:199.
17. World Health Organization (WHO). Standardization of interpretation chest radiographs for the diagnosis of pneumonia in children. Geneva 2001. Available from: <https://apps.who.int/iris/handle/10665/66956>
18. Zitek T, Lunn J, Ma A, Dadon N, Fisher J. Nondiagnostic pediatric chest X-rays are common: correlate clinically for pneumonia. *J Emerg Med Care.* 2018;1:101.
19. Lipsett SC, Monuteaux MC, Bachur RG, Finn N, Neuman MI. Negative chest radiography and risk of pneumonia. *Pediatrics.* 2018;142:e20180236.
20. Balk DS, Lee C, Schafer J, et al. Lung ultrasound compared to chest X-ray for diagnosis of pediatric pneumonia: a meta-analysis. *Pediatr Pulmonol.* 2018;53(8):1130-1139.
21. McMullan BJ, Andresen D, Blyth CC, et al. Antibiotic duration and timing of the switch from intravenous to oral route for bacterial infections in children: systematic review and guidelines. *Lancet Infect Dis.* 2016;16:139-152.
22. Lambert HP. Don't keep taking the tablets? *Lancet.* 1999;354:943-945.
23. British Medical Association. BNF for children 2016-2017, 1st edn. London, UK: BMJ Group, Pharmaceutical Press and RCPCH Publications Ltd; 2016.
24. Siira L, Vestrheim DF, Winje BA, Caugant DA, Steens A. Antimicrobial susceptibility and clonality of *Streptococcus pneumoniae* isolates recovered from invasive disease cases during a period with changes in pneumococcal childhood vaccination, Norway, 2004-2016. *Vaccine.* 2020;38:5454-5463.
25. Thaulow CM, Lindemann PC, Klingenberg C, et al. Epidemiology and antimicrobial susceptibility of invasive bacterial infections in children-a population-based study from Norway. *Pediatr Infect Dis J.* 2020. <https://doi.org/10.1097/INF.0000000000003013>. (published ahead of print).

### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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