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Addition of point-of-care test reduces antibiotic prescription in hospitalised children with suspected respiratory tract infection: A pre-test–post-test study

Lotte Høeg Hansen | Katrine Dueholm Nissen | Andreas Pedersen | Christian Backer Mogensen | Helene Skjøt-Arkil

Abstract

Aim: Prompt and accurate aetiological diagnostics are needed if physicians are to improve and target antibiotic treatment. We aimed to investigate whether antibiotic-prescribing decisions are improved with availability of point-of-care polymerase chain reaction (POC-PCR) diagnostic testing of children with suspected respiratory tract infection, and if it had an impact on referral for additional medical procedures.

Methods: This was a single-centre one-group pre-test–post-test study. Children visiting our paediatric department with respiratory tract infection symptoms were included if the treating paediatrician was considering an antibiotic prescription. Throat swabs were analysed for pathogens using POC-PCR. The paediatrician registered treatment decisions, referrals for additional procedures and decisions about hospitalisation into a questionnaire before and after receiving the POC-PCR results.

Results: We included 95 children. The availability of results from POC-PCR analysis significantly changed the prescribed antibiotic treatment to non-antibiotic treatment in 46% (36%–56%) of the children and the reverse in 2% (1%–8%). Paediatricians referred significantly fewer patients to additional medical procedures with availability of POC-PCR.

Conclusion: POC-PCR significantly reduced the odds of antibiotic prescription and referral for additional medical procedures. Thus, POC-PCR presents an opportunity to improve antibiotic-prescribing practices if it is combined with standard clinical evaluation.

Keywords
antibiotics, hospitalised children, paediatrics, respiratory tract infection

Abbreviations: CI, Confidence interval; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; OR, odds ratio; PCR, polymerase chain reaction; PD, paediatric emergency department; POC, point-of-care; TREND, Transparent Reporting and Evaluations with Non-randomised Designs; USA, United States of America.
1 | BACKGROUND

Increasing antibiotic resistance poses a worldwide threat to public health.1,2 As a result, hospitals are focusing on reducing the prescription of antibiotics.3

Respiratory tract infections are a common cause of referral to the paediatric emergency departments.4 In Denmark, approximately 9000 children (<15 years) are referred annually to the paediatric emergency departments with suspected acute respiratory tract infections.5 Studies report that 66% of respiratory tract infections are viral,6 and only approximately 15% of hospital referrals require antibiotic treatment due to bacterial infection.4,6 Differentiating between viral and bacterial infections is crucial in reducing antibiotic consumption. A prerequisite for appropriate use of antibiotics is timely access to accurate diagnostic tests ensuring initiation of targeted treatment as soon as possible.

Differentiating between viral and bacterial respiratory tract infections is challenging, since symptoms and inflammatory biomarkers overlap. In addition, there are uncertain microbiological diagnostic methods such as sampling from the upper airway for a bacterial culture rather than collecting a specimen of the actual pathogen from the lower airways.7-9 Finally, some microbiological diagnostic methods take a long time to process results, sometimes up to 3 days.10,11 POC-PCR has been reported as reliable in detecting relevant pathogens in children with lower respiratory tract infections12 and reducing antibiotic prescription and additional medical procedures.4 Systems are available today based on polymerase chain reaction (PCR) methods, with results available within 1 h for various viral and bacterial agents.13 Often these diagnostic tools are installed in microbiology departments rather than being placed in clinical departments to ensure direct access for treating physicians.

Prompt and accurate aetiological diagnostics are needed if physicians are to improve and target antibiotic treatment. Therefore, studies are required to determine whether direct access to point-of-care diagnostic tools for treating physicians alters and ultimately improves treatment decisions for children with respiratory tract infection symptoms.

We hypothesised that introducing POC-PCR analysed swab samples for all children with suspected respiratory tract infections would ensure a more targeted antibiotic treatment and reduce referrals to additional procedures without increasing the number of admissions.

1.1 | Aim

This study aimed to investigate whether treatment decisions by hospital paediatricians were affected by direct availability of POC-PCR diagnostic testing for children with suspected respiratory tract infection. The objectives were (1) to analyse how antibiotic-prescribing decisions of hospital physicians altered after results from POC-PCR testing were made available and (2) to analyse the impact of POC-PCR testing on the number of referrals for additional medical procedures.

2 | METHOD

2.1 | Study design

This quasi-experiment was a single-centre one-group pre-test–post-test study. The treating paediatricians completed a questionnaire on treatment decisions after usual patient care (pre-test). The POC-PCR test was then performed and the paediatrician completed a new questionnaire after results from the intervention were made available (post-test). The post-test results were then compared with the pre-test results for the individual patients. The study was reported according to the TREND (Transparent Reporting and Evaluations with Non-randomised Designs) guidelines.14

2.2 | Setting

The study took place in a Danish Paediatric Emergency Department (PD) at the Hospital Sønderjylland, Aabenraa, Denmark, from December 2019 to June 2020. Our PD examines approximately 3000 acute ill children per year; however, the COVID-19 pandemic lockdown and restrictions in Denmark from March 2020 reduced the numbers of children admitted to the hospital in the study period. Most of the children visiting the department were referred by a general practitioner for a same-day examination. A minority of children were admitted by ambulance without prior medical evaluation. Patients younger than 1 month were examined at a neonatal ward, and patients aged 18 years or older were referred to the adult emergency department and therefore not included in the study population. During the study period, the paediatricians in the PD consisted of nine specialists and 12 residents. Two of the paediatricians were the study assistants responsible for informing and training colleagues.

Key Notes

- We investigated whether antibiotic prescribing was improved with the availability of point-of-care polymerase chain reaction diagnostic testing of children with suspected respiratory tract infection.
- Antibiotic prescription was reduced from 73% to 32% of the children.
- Point-of-care polymerase chain reaction at the paediatric department presents an opportunity to improve antibiotic-prescribing practices if it is combined with standard clinical evaluation.
2.3 | Participants and recruitment

Patients with symptoms of respiratory tract infections were invited to participate in the study if the paediatrician was considering treatment with antibiotics. Patients were excluded if:

- The paediatrician, after initial clinical evaluation, assumed the infection was viral.
- The same child had been enrolled in the study within the previous week.
- Throat sampling or tracheal suction was not possible (e.g. anatomical complications).
- The paediatrician assessed study participation would delay lifesaving treatment.

Written and verbal information about the study was distributed to the child and parents. Then, if the family chose to participate, written consent from parents was obtained (the project’s timeline is outlined in Appendix A).

2.4 | Pre-test—Usual care

Immediately after inclusion, the treating paediatrician was instructed to register treatment decisions after usual care. These decisions included antibiotic treatment, referral to other medical procedures including chest x-ray, or additional blood samples (the first blood sample was taken at admission), and ward admission. These decisions were registered in a written questionnaire (see Appendix B).

2.5 | Intervention—POC-PCR

All participants had an oropharyngeal swab (E-swab, Copan, SSI Diagnostica, Hillerød, Denmark) performed by the treating paediatrician. However, if the paediatrician had decided in pre-test that bacterial culturing was required, tracheal suction rather than the oropharyngeal swab, was used to collect the sample.

When performing tracheal suction the tip of a suitable catheter is lubricated with sterile saline and inserted into the nares and gently advanced without applying suction. When the clinician estimated the tip of the catheter to be in trachea, the suction catheter port was covered, and suctioning was performed before withdrawing the catheter. Suction was set at 200–400 mmHg negative pressure. Finally, sterile saline is sucked in to get the specimen transferred to the sterile container.

The collected sample was analysed by POC-PCR (QIAstat-Dx Respiratory panel V2) located in the PD. The treating paediatrician performed the POC-PCR analysis of the sample at the PD. All analyses took approximately 1 h, and paediatricians followed the procedure described by QIAstat, saving the results electronically.15

The POC-PCR Respiratory panel V2 detects 18 viruses and three bacteria: Adenovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus OC43, Coronavirus NL63, Human Metapneumoviruses, Human Rhinovirus/Enterovirus, Influenza A, Influenza A/H1, Influenza A/H1N1, Influenza A/H3, Influenza B, Parainfluenza 1, Parainfluenza 2, Parainfluenza 3, Parainfluenza 4, Respiratory Syncytial Virus and Bocavirus. Bordetella pertussis, Mycoplasma pneumoniae and Legionella pneumophila.15 Unfortunately, this POC-PCR kit was unable to detect severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), so after breakout of COVID-19 the patients had two oropharyngeal swabs performed in the same procedure, one for the project and one for COVID-19 analysis.

2.6 | Post-test

After the results of the POC-PCR analysis were available, the treating paediatrician was asked again to register the decision about the ultimate treatment at the given time. These treatment decisions were recorded on the same written questionnaire completed before the POC-PCR analysis was available. These completed questionnaires were collected using a study mailbox at the department.

2.7 | Data collection

The results from the questionnaires by the treating paediatricians and results from POC-PCR were collected by project assistants and entered into a project database using an electronic survey tool (SurveyExact, Rambøl). Questionnaires completed by the child’s parents about symptoms were also recorded (see Appendix C). In addition, the project assistants recorded symptoms, signs and clinical variables from the child’s medical record. These variables included C-reactive protein (CRP), leucocyte count, neutrophilocyte count, respiratory frequency, saturation and chronic respiratory illness measured at arrival to the PD. In addition, final antibiotic treatments prescribed at follow-up on Day five after arrival at the PD were collected from medical records.

2.8 | Outcome

The primary outcome was the number of antibiotic prescriptions. The secondary outcomes were the number of (1) prescribed chest x-rays, (2) prescribed additional blood samples, (3) ward admissions and (4) the number of antibiotic prescriptions at the 5-day follow-up.

2.9 | Statistical analysis

A power calculation was conducted to assess the number of study participants required using Monte Carlo simulation for a chi-square test. We aimed to describe a clinical meaningful reduction in antibiotic prescription from 98% of the patients under normal circumstances (pre-test) to 75% after the POC-PCR (post-test).
Therefore a total of 82 patients needed to be included to achieve a power of 80% and a significance level of 0.05.

We used descriptive statistics to assess the distribution of potential confounders between those who had antibiotics prescribed at follow-up and those who had not for the characteristic variables. We used chi-square or Fischer’s exact test for categorical variables, dependent if Cochrane’s rule was fulfilled. For non-categorical variables, we used the student t-test or Wilcoxon rank-sum test, depending on data distribution. The normality of the variables was assessed using quantile-quantile plots.

Change in the treatment decision for each child was calculated, and confidence intervals on the proportions were made with multinomial logistic regressions.

A multivariate mixed-effect logistic model and generalised estimating equation were used due to repeated measurements for the prescription of antibiotics, use of chest x-ray, additional blood samples and admittance to a ward. The mixed-effect logistic model was used in order to get the subjective specific odds ratio (OR SS), that is the effect of the exposure for a given patient. The generalised estimating equation model was used to estimate the population average odds ratio (OR PA), which is the effect of the exposure average over all the patients. The models were adjusted for the variables from the descriptive analysis, which could be possible confounders.

The model control for the mixed-effect logistic model was to assess the normality of the deviance residuals before and after the POC-PCR and use follow-up by way of quantile-quantile plots. A model control for the generalised estimating equation was not conducted because of robust estimation of the population-averaged odds ratio and use of bootstrapped confidence intervals.

As a sensitivity analysis, a comparison by way of mixed-effect logistic model was made between the odds for an antibiotic prescription before the availability of results from POC-PCR and the odds for an antibiotic prescription either right after the availability of POC-PCR results or later at follow-up. In addition, a univariate analysis was conducted to assess confounding. No correction for multiple testing was utilised.

All statistical analyses were performed in Stata IC version 15.

2.10  |  Ethical considerations

The study was considered a quality improvement study by the Regional Committees on Health Research Ethics for Southern Denmark (Nr: 20192000-150). Verbal and written consent for participation from parents was collected before inclusion in the study. The study was registered by the Danish Data Protection Agency (no 19/50462).

3  |  RESULTS

During the study period, 1387 children arrived at the department. The paediatricians invited 103 children to participate, of which the parents of seven children did not give informed consent. The POC-PCR analysis failed for one participant and was not repeated, and the results were therefore excluded. Thus, 95 participants were included in the study.

Table 1 shows the characteristics of patients at follow-up. Chronic respiratory disease was most often reported as asthma or bronchitis. In 82 children, at least one pathogen was detected (total of 104 positive findings). There were no identified pathogens in 13 children.

Change in the treatment decision for each child is showed in Table 2. Antibiotic prescription was reversed to a non-antibiotic prescription in 46% (95% confidence interval [CI] 36%–56%) the prescription in the post-test measure, and non-antibiotic prescription was reversed to antibiotic prescription in 2% (1%–8%).

Of the children 72 (76%) would have been prescribed antibiotics as usual care (Table 3). Availability of POC-PCR results reduced the number of prescriptions of antibiotics to 30 (32%), which is a significant reduction in relation to both multivariate analysis models (OR SS of 0.03 (95% CI 0.01–0.1), OR PA of 0.13 (95% CI 0.07–0.24)) after adjusting for strong predictors such as type of bacterial infection. Although the number of antibiotic prescriptions increased at the 5-day follow-up; however, there is still a significant reduction compared with the pre-test antibiotic prescription decisions (OR PA of 0.17 (95%CI: 0.07–0.43)). Our sensitivity analysis supports these results (OR of 0.28 (95% CI: 0.12–0.60, p = 0.001)). The ORs for the treatments chest x-ray, additional blood samples and admission to ward were also significantly reduced with the availability of POC-PCR results to the prescribing paediatrician both in relation to OR SS and OR PA (see Table 3).

A medical record audit of all 95 children did not reveal any subsequent admissions or adverse effects due to a lack of antibiotic prescriptions.

4  |  DISCUSSION

Direct availability of POC-PCR in the PD significantly reduced the number of antibiotic prescriptions both short and long terms. In addition, it significantly reduced the number of requested treatments planned prior to the availability of POC-PCR.

Approximately half of the children had no changes made in their treatment after POC-PCR. This increased after follow-up, mostly due to continued symptoms or worsening of clinical status, which was interpreted to be a bacterial coinfection. Almost half of children had their treatment changed from antibiotic prescription to non-antibiotic prescription; however, this was reduced after follow-up. Few children had their treatment changed from a non-antibiotic treatment to an antibiotic treatment, primarily because of detection of Mycoplasma pneumonia. However, the changed increased at follow-up mostly because of worsening of the clinical status during admission.

This paediatric population is similar to previous studies where CRP, leucocytes, neutrophilocytes are significantly elevated in children with suspected bacterial infection. However, as in other studies,
these biomarkers cannot be confidently used to differentiate between viral and bacterial infection.\textsuperscript{10,11} Furthermore, we found no significant differences between the two groups in the prevalence of rhinorrhoea and fever, despite these symptoms previously being reported to be significant when differentiating between viral and bacterial respiratory infections.\textsuperscript{11}

Our findings seem to corroborate results from similar studies, albeit in different contexts. For example, an Argentinian study\textsuperscript{4} reported that 23% of children had a reduction in antibiotic prescription with the availability of POC-PCR results. In comparison, Busson et al.\textsuperscript{16} examined patients from Brussels during an influenza epidemic. These patients were expected to be admitted or had a

\textbf{TABLE 1} Characteristics at arrival of participants according to prescription of antibiotic treatment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Children with no antibiotics prescribed at follow-up</th>
<th>Children with antibiotics prescribed at follow-up</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total, n (%)</td>
<td>44 (46)</td>
<td>51 (53)</td>
<td></td>
</tr>
<tr>
<td>Sex—number of females (%)</td>
<td>20 (45)</td>
<td>27 (53)</td>
<td>0.47*</td>
</tr>
<tr>
<td>Age—median in months (IQR)</td>
<td>18.5 (11.19)</td>
<td>18.0 (10, 54)</td>
<td>0.50†</td>
</tr>
<tr>
<td>Parent-reported cough, n (%)</td>
<td></td>
<td></td>
<td>0.58</td>
</tr>
<tr>
<td>Yes</td>
<td>41 (93)</td>
<td>44 (86)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2 (5)</td>
<td>5 (10)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (2)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Parent-reported rhinorhoea, n (%)</td>
<td></td>
<td></td>
<td>0.70</td>
</tr>
<tr>
<td>Yes</td>
<td>40 (91)</td>
<td>43 (84)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3 (7)</td>
<td>6 (12)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (2)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Chronic respiratory disease, n (%)</td>
<td></td>
<td></td>
<td>0.36*</td>
</tr>
<tr>
<td>Yes</td>
<td>15 (34)</td>
<td>13 (25)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>29 (66)</td>
<td>38 (75)</td>
<td></td>
</tr>
<tr>
<td>Temperature in mean °C (SD)</td>
<td>38.0 (1.1)</td>
<td>38.4 (1.0)</td>
<td>0.13*</td>
</tr>
<tr>
<td>CRP in median mg/L (IQR)</td>
<td>20 (9, 30)</td>
<td>47 (16, 103)</td>
<td>&lt;0.01†</td>
</tr>
<tr>
<td>Leucocyte count in median 10\textsuperscript{9}/L (IQR)</td>
<td>10.2 (4.8, 13.1)</td>
<td>13.4 (9.6, 20.0)</td>
<td>0.02†</td>
</tr>
<tr>
<td>Neutrophilocytes in median 10\textsuperscript{9}/L (IQR)</td>
<td>4.7 (1.7, 8.5)</td>
<td>8.8 (4.7, 14.0)</td>
<td>0.01†</td>
</tr>
<tr>
<td>Respiration frequency in mean breath/min (SD)</td>
<td>41 (13)</td>
<td>40 (14)</td>
<td>0.69*</td>
</tr>
<tr>
<td>Saturation in median % (IQR)</td>
<td>98 (95, 100)</td>
<td>96 (94, 100)</td>
<td>0.26†</td>
</tr>
<tr>
<td>Detected pathogens by POC-PCR, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total positive findings</td>
<td>52 (50)</td>
<td>52 (50)</td>
<td>0.78*</td>
</tr>
<tr>
<td>Respiratory Syncytial virus</td>
<td>15 (34)</td>
<td>16 (31)</td>
<td>0.52*</td>
</tr>
<tr>
<td>Rhinovirus/Enterovirus</td>
<td>12 (27)</td>
<td>11 (22)</td>
<td></td>
</tr>
<tr>
<td>Adenovirus</td>
<td>3 (7)</td>
<td>8 (16)</td>
<td>0.21</td>
</tr>
<tr>
<td>Human Metapneumovirus</td>
<td>7 (16)</td>
<td>3 (6)</td>
<td>0.18</td>
</tr>
<tr>
<td>Bocavirus</td>
<td>5 (11)</td>
<td>2 (4)</td>
<td>0.24</td>
</tr>
<tr>
<td>Coronavirususes</td>
<td>6 (14)</td>
<td>1 (2)</td>
<td>0.05</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>0 (0)</td>
<td>6 (12)</td>
<td>0.03</td>
</tr>
<tr>
<td>Influenza A</td>
<td>3 (7)</td>
<td>3 (6)</td>
<td>1.00</td>
</tr>
<tr>
<td>Parainfluenza viruses</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>1.00</td>
</tr>
<tr>
<td>Bordetella pertussis</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>1.00</td>
</tr>
<tr>
<td>No findings</td>
<td>3 (7)</td>
<td>10 (20)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Note: Wilcoxon rank-sum test: †. t-test: +. X\textsuperscript{2}-test: *. Fischer’s exact test: unmarked.

\textbf{TABLE 2} Changes in treatment decisions for each child after POC-PCR results

<table>
<thead>
<tr>
<th>Prescribed treatment</th>
<th>Proportions (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre to post</td>
</tr>
<tr>
<td>Unchanged</td>
<td>52% (41%–62%)</td>
</tr>
<tr>
<td>Changed from AB to non-AB</td>
<td>46% (36%–56%)</td>
</tr>
<tr>
<td>Changed from non-AB to AB</td>
<td>2% (1%–8%)</td>
</tr>
</tbody>
</table>

Abbreviation: AB, antibiotics.
The addition of POC-PCR impacted the treatment of children acutely admitted with a suspected respiratory tract infection. It significantly reduced the odds of antibiotic prescription, chest x-rays, chronic disease. In this study, prescription rates of children with POC-PCR results and admission rates were not lower. The only factor that impacted admittance rates was influenza B.

In most cases, a POC-PCR analysis will add extra information for the paediatrician to evaluate and assist in the decision as to whether or not the child should receive antibiotics. In this study, there were only 13 out of 95 children whose POC-PCR analysis of throat swabs did not detect a pathogen. This correlates with reports from previous studies.12,17 Therefore, in combination with normal clinical evaluation, this information enables better differentiation between bacterial and viral infections and thereby better antibiotic stewardship.

In some cases, the paediatrician’s first decision based on the POC-PCR changed within the following 5 days, resulting in a later antibiotic prescription. However, a medical record audit of the 95 children did not identify any inappropriate delays. It is essential that POC-PCR analysis is used in combination with normal clinical evaluation by the treating paediatrician. The POC-PCR may not always reveal a bacterial coinfection. One previous study from the USA reported 7% co-infections in a similar population.6 However, in our study, only mycoplasma pneumoniae and coronaviruses had significantly different distributions between the children receiving antibiotics and those who did not. Regarding mycoplasma pneumoniae, our results indicate perhaps more children received relevant treatment earlier, since the children with mycoplasma pneumonia all received relevant antibiotics. We have not made calculations on how many in this group would not have received antibiotics without POC-PCR. All in all these results indicate that in most cases, the decision was not exclusively based on the POC-PCR results but was a result of the combination of clinical evaluation and POC-PCR result.

In addition, POC-PCR significantly reduced the odds ratio of children being exposed to an x-ray, additional blood samples and being admitted to a ward and therefore diminishes anxiety, pain and waiting time. It reduced the odds of being admitted to hospital and thus reduced costs to the health system.17,18 Thus, POC-PCR presents an opportunity for a more efficient and patient friendly visit in the paediatric emergency department. Future research should involve an economic evaluation of POC-PCR availability.

### Table 3: Prescribed treatment before and after availability of POC-PCR results

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Time of measure</th>
<th>Number of children (%)</th>
<th>Odds ratio (95% CI) SS</th>
<th>Odds ratio (95% CI) PA</th>
<th>p-value SS</th>
<th>p-value PA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics</td>
<td>Pre-test</td>
<td>72 (76%)</td>
<td>0.03 (0.01-0.1)</td>
<td>0.13 (0.07-0.24)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Post-test</td>
<td>30 (32%)</td>
<td>0.17 (0.07-0.43)</td>
<td>0.35 (0.21-0.59)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Follow-up day five</td>
<td>51 (54%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>Pre-test</td>
<td>57 (60%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post-test</td>
<td>27 (28%)</td>
<td>0.21 (0.09-0.46)</td>
<td>0.31 (0.17-0.57)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Additional blood samples</td>
<td>Pre-test</td>
<td>74 (78%)</td>
<td>0.13 (0.05-0.36)</td>
<td>0.28 (0.17-0.46)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Post-test</td>
<td>47 (49%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission to ward</td>
<td>Pre-test</td>
<td>67 (71%)</td>
<td>0.07 (0.01-0.78)</td>
<td>0.71 (0.52-0.97)</td>
<td>0.032</td>
<td>0.031</td>
</tr>
<tr>
<td></td>
<td>Post-test</td>
<td>60 (63%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: PA, population averaged; SS, subject specific.

### 4.1 Strength and limitations

POC-PCR had a high and significant clinical impact on all of the outcomes. Therefore, a strength of this study was the low risk of false positives (type I errors).

Another strength of this study is that our paediatric department uses a national Danish guideline to treat this patient group as all other paediatric departments in Denmark, and this guideline is also similar to British and American guidelines.19 Therefore, findings from this population can be transferred to PDs in other high-income countries.

The proposed sample size was calculated from an incorrect analysis, thus increasing the risk of type II errors. Nevertheless, the confidence intervals lie far away from one for the majority of our outcomes in Table 3, therefore we conclude the risk of type II error is negligible.

The COVID-19 pandemic challenged recruitment to the study. Fewer children were admitted due to general behavioural changes in the public. This resulted in fewer referrals and fewer sick children. Nevertheless, as our results show no signs of false negatives (type II errors), we concluded that 95 participants were adequate.

The decision to use a questionnaire to evaluate the impact of POC-PCR on a paediatrician’s prescribing practice is both a strength and a limitation. The strength of this method is that the paediatrician evaluates and reports their own decisions, making them their own control. However, this may have introduced an information bias as it was well known that the participating paediatricians were keen to introduce the POC-PCR tool. Therefore, paediatricians may have overreported the amount of pre-test antibiotic prescriptions compared to usual care to increase the effect of POC-PCR. In future research, it should be considered to make a randomised control trial, splitting and blinding the pre-test decision and post-test decision in order to avoid these biases.

### 5 Conclusion

The addition of POC-PCR impacted the treatment of children acutely admitted with a suspected respiratory tract infection. It significantly reduced the odds of antibiotic prescription, chest x-rays,
additional blood tests and admission to a ward. Thus, the more direct availability of POC-PCR in a department could assist in more rational use of antibiotics and reduce the number of additional procedures requested for children with suspected respiratory tract infections. In addition, POC-PCR may contribute to a reduction in antibiotic resistance and optimise patient care. Future research should focus on safety and cost–benefit analyses if POC-PCR is part of everyday life in the paediatric ward.

**AUTHOR CONTRIBUTIONS**

Lotte Høeg Hansen, Christian Backer Mogensen and Helene Skjøt-Arkil conceptualised and all authors designed the study. Lotte Høeg Hansen and Katrine Dueholm Nissen informed and trained paediatricians and collected data. Andreas Pedersen made the statistical analysis, and Lotte Høeg Hansen, Katrine Dueholm Nissen and Helene Skjøt-Arkil contributed to manuscript development. All authors participated in the critical scrutiny and revision of the manuscript and approved the final version.

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**FUNDING INFORMATION**

The POC-PCR analysis kits were funded by the University Hospital of Southern Denmark, Aabenraa Denmark. QIAstat had no role in study design, data collection or analysis. Statistical validity: All statistics was made by a certified statistician (author A.P.).

**CONFLICT OF INTEREST**

Statistics was made by a certified statistician (author A.P.).

**DATA AVAILABILITY STATEMENT**

Due to Danish laws on personal data, data cannot be shared publicly. To request these data, please contact the corresponding author for more information.

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**REFERENCES**


APPENDIX A

TIMELINE OF ENROLMENT, INTERVENTIONS AND ASSESSMENTS

<table>
<thead>
<tr>
<th>Study period</th>
<th>Recruitment</th>
<th>Allocation</th>
<th>Post-allocation</th>
<th>Close-out</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timepoint (h = hours, d = days)</td>
<td>-½ h</td>
<td>0 h</td>
<td>&lt;½ h</td>
<td>&lt;1 h</td>
</tr>
</tbody>
</table>

Study period

Eligibility screen | x
Informed consent | x
Allocation | x
Interventions
Oropharyngeal swab | x
Assessments
Characteristics (look up in medical record) | x
Parents written questionnaire | x
Doctors written questionnaire including prescribed treatments | x | x
Final antibiotic prescription (look up in medical record) | x

APPENDIX B

QUESTIONNAIRE TO THE DOCTORS—MUST BE COMPLETED BEFORE AND AFTER POC-PCR

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Chest x-ray</th>
<th>Additional blood samples</th>
<th>Admission to ward</th>
</tr>
</thead>
<tbody>
<tr>
<td>Would you normally (without presence of POC-PCR) have ordered/considered</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>What is your decision now that you have the POC-PCR result?</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

APPENDIX C

QUESTIONNAIRE TO THE PARENTS—MUST BE COMPLETED AFTER STUDY INCLUSION

<table>
<thead>
<tr>
<th>Has your child had the following symptoms within the last 24 h?</th>
<th>Yes</th>
<th>No</th>
<th>Do not know</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>