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Brief Report

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# Impact of Selective Reporting of Antibiotic Susceptibility Test Results on Antibiotic Use in Patients with Bloodstream Infection with *Streptococcus pneumoniae*

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**Keywords**
Pneumococcal infection · Bloodstream infection · Antibiotic stewardship

**Abstract**
***Introduction:*** Invasive pneumococcal disease is a major cause of morbidity and mortality in infectious diseases. Selective reporting of antibiotic susceptibility test results might lead to a tailored antibiotic therapy and could therefore be an important antibiotic stewardship program intervention. The aim of this study was to analyse whether a switch to selective reporting of antibiotic test results leads to a more focused antibiotic therapy in patients with a bloodstream infection with *Streptococcus pneumoniae*. ***Methods:*** This study was performed as a retrospective cohort study at the University Hospital Regensburg, Germany. All blood cultures positive for *Streptococcus pneumoniae* between 2006 and 2021 were analysed. In 2014, a switch to selective reporting of antibiotic susceptibility test results omitting sensitivity results for agents not recommended was introduced. ***Results:*** Twenty-four hours after final antibiotic susceptibility test results were available, 20.9% before (BI) versus 15.4% after implementation (AI) of selective reporting of antibiotic test results received a narrow-spectrum penicillin, while only 2.3% BI versus 5.8% AI received a narrow-spectrum penicillin from the beginning. ***Conclusion:*** Selective reporting of antibiotic susceptibility test results without further antimicrobial stewardship interventions did not lead to a higher use of a narrow-spectrum penicillin in this study.



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## Introduction

Invasive pneumococcal disease is defined by the isolation of *Streptococcus pneumoniae* from blood or other sterile body sites. *Streptococcus pneumoniae* is the leading cause of lower respiratory infection mortality and morbidity globally [1]. Four different vaccines are available for the prevention of pneumococcal disease, but adherence is low [2, 3].

Antimicrobial stewardship (AMS) aims at a rational use of antibiotics. Antibiotics should be chosen under the aspect of perfectly targeting a pathogen, preventing resistance, and minimizing the negative impact on the microbiome [4–6]. Clinical microbiology therefore is an essential part of antibiotic stewardship. Selective reporting of antibiotic susceptibility test results might facilitate pathogen-directed antibiotic therapy and thus be an important antibiotic stewardship intervention [7–9], which was also highlighted in the previously revised German guideline on the rational use of antibiotics in medicine [10]. The aim of this study was to analyse whether selective antibiotic susceptibility reporting resulted in more focused antibiotic therapy in patients with *Streptococcus pneumoniae* bloodstream infection (BSI).

## Methods

*Study Population, Study Design, and Data Collection*

This study was performed as a retrospective cohort study at the University Hospital Regensburg, Germany. All blood cultures positive for *Streptococcus pneumoniae* between 1 January 2006 and 31 December 2021 were identified from the microbiological database. Papers and electronic files of patients were analysed. Selective reporting of antibiotic susceptibility test results was introduced in January 2014. The number of antibiotics included in the selective antibiogram changed several times during the implementation of selective reporting of test results (Table 2). We analysed antibiotic therapies initially and 24 h after final microbiological results were available. Clinicians at our hospital were able to request infectious disease consultation in all included years (via our electronic patient management system; an infectious disease specialist would then see the patient and give a recommendation within the same working day). Additionally, weekly AMS ward rounds were implemented in the ICU in 2013. A change to EUCAST reporting was performed in April 2018. The need for informed consent was waived by the Ethics Committee of the University of Regensburg (No. 21-2406-104).

*Statistics*

Statistics of continuous variables are presented as mean ± standard deviation. $\chi^2$ test and Fisher's exact test were used for categorical variables. All significance tests were two tailed. A $p$ value <0.05 was considered as the threshold for statistical significance. Analyses were performed using Microsoft Excel (version 2016, Redmond, WA, USA) and IBM SPSS (version 26.0, IBM, Armonk, NY, USA).

## Results

*Baseline Characteristics*

A total of 122 patients with positive blood cultures for *Streptococcus pneumoniae* were identified. Patients who did not receive therapy according to available medical records, patients with polymicrobial BSIs (except for concurrent detection of typical contaminants like coagulase-negative staphylococci), and patients with known penicillin or cephalosporin allergy according to available medical records were excluded (Fig. 1). Ninety-five patients were included in the analysis.

The average age before implementation of selective antibiogram (BI) was 58 years versus 53 years after implementation of selective antibiogram (AI). Most patients had relevant comorbidities. Charlson comorbidity score was 4.2 points BI versus 4.5 points AI. The Sequential Organ Failure Assessment score (SOFA score) was significantly higher AI compared to BI (6.0 vs. 4.0 points, $p = 0.021$). Mortality was also significantly higher with 23.1% AI than BI (2.0%). Detailed baseline characteristics of patients are shown in Table 1.

*Antibiotic Use*

Twenty-four hours after the collection of blood cultures (Fig. 2), all patients received beta-lactam antibiotics and 76.7% of patients BI and 71.2% of patients AI were treated with combination therapy (more than one antibiotic substance). The most common initial therapy was piperacillin/tazobactam (55.8% BI vs. 67.3% AI), followed by macrolides (32.6% BI vs. 36.5% AI). Only a few patients received a narrow-spectrum penicillin (i.e., penicillin G, ampicillin, and amoxicillin; 2.3% BI vs. 5.8% AI, Fig. 2).

Twenty-four hours after final antibiotic susceptibility (Fig. 2) test results were available, most patients (93.0% BI vs. 98.1% AI) continued to receive beta-lactams (Fig. 2). A total of 51.2% of patients BI and 51.9% of patients AI were still on combination therapy. The rate of patients who received a narrow-spectrum penicillin was 20.9% BI versus 15.4% AI (n.s.).

## Discussion

So far, selective reporting of antibiotic susceptibility test results is a well-known but not widely implemented AMS tool. Its effects are examined for urinary tract

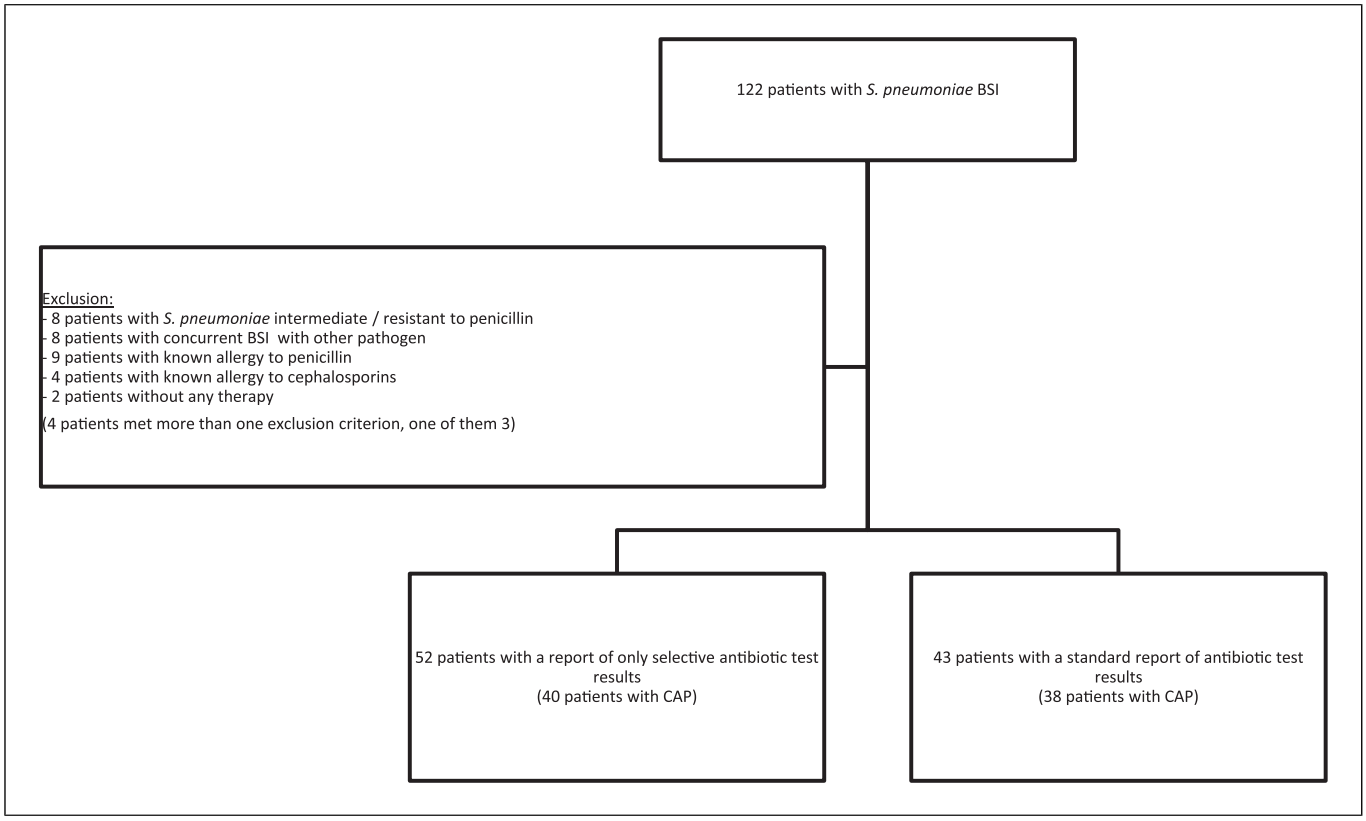


**Fig. 1.** Distribution of patients in the cohort.

**Table 1.** Baseline characteristics ($n$ = 95)

| | Standard reporting | Selective reporting | $p$ value |
|---|---|---|---|
| Total number of patients | 43 | 52 | – |
| Age (median) | 58±15.7 (median 62) | 53±23.6 (median 60) | n.s. |
| Female, $n$ (%) | 16 (37.2) | 20 (38.5) | n.s. |
| Charlson comorbidity score | 4.2±3.2 (median 4) | 4.5±2.9 (median 5) | n.s. |
| BSI extracted in ED, % | 76.7 | 76.9 | n.s. |
| Community-acquired pneumonia, % | 88.4 | 76.9 | n.s. |
| ECMO therapy, % | 4.7 | 1.9 | n.s. |
| Haemodialysis, % | 4.7 | 13.5 | n.s. |
| Plasma exchange, $n$ (%) | 0 (0.0) | 4 (7.7) | n.s. |
| On ICU, $n$ (%) | 13 (30.2) | 24 (46,2) | n.s. |
| Days on ICU | 9.5 (median 3.0), $n$ = 13 | 9.7 (median 3.5), $n$ = 24 | n.s. |
| Days on respirator | 10.7 (median 5.0), $n$ = 3 | 12.1 (median 7.0), $n$ = 10 | n.s. |
| ID consultation, $n$ (%) | 2 (4.7) | 8 (15.4) | n.s. |
| Active smokers, $n$ (%) | 5 (25.0) | 2 (7.7) | n.s. |
| HIV, $n$ (%) | 2 (4.7) | 1 (1.9) | n.s. |
| Immunosuppressive medication, $n$ (%) | 9 (20.9) | 14 (26.9) | n.s. |
| Mortality, $n$ (%) | 1 (2.3) | 12 (23.1) | **0.003** |
| SOFA score | 4.02±3.3 (median 3) | 6.04±4.7 (median 5) | **0.021** |

BSI, bloodstream infection; ED, emergency department; ICU, intensive care unit; ID, infectious disease; n.s., not significant (all metric values are shown as mean and standard deviation and categorial values as number and percentage).

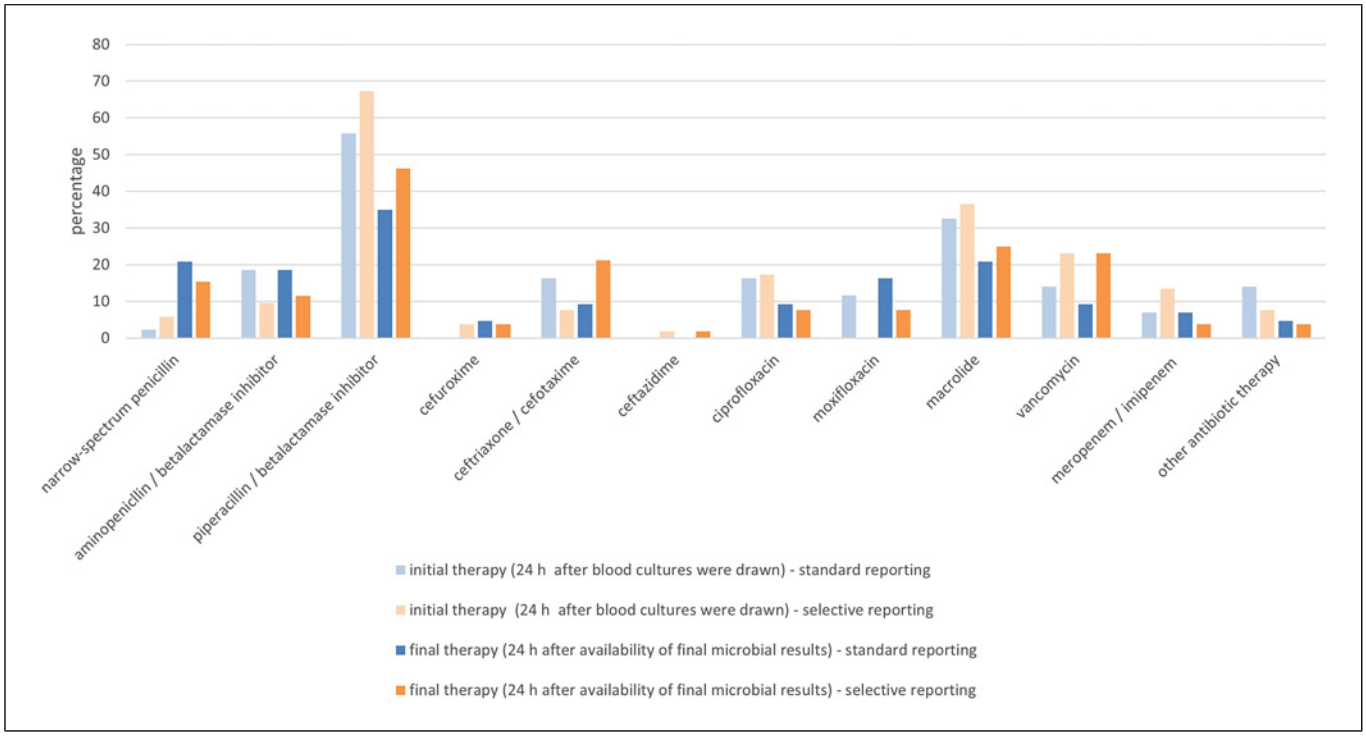


**Fig. 2.** Antibiotic therapy.

infections [11, 12]. Studies analysing the effect on BSIs are mainly related to gram-negative BSIs [13–16]. The impact of selective reporting of test results on antibiotic use in these studies is inconsistent.

To our knowledge, this is the first study that analyses the impact of selective reporting of antibiotic susceptibility test results on antibiotic use in patients with a BSI with *Streptococcus pneumoniae*. In summary, we could not demonstrate that selective reporting of antibiotic susceptibility test results alone led to a higher use of narrow-spectrum penicillin.

Reasons therefore might be diverse: although reporting of antibiotic susceptibility test results was shortened in the years 2014–2019 (Table 2), still several different antibiotics besides penicillin G were inconsistently reported. Another reason might be that the two groups before and after the implementation of selective reporting differed concerning the severity of the disease and intensivists often have concerns about de-escalating to an antibiotic therapy with a narrow spectrum [17]. In addition, our study was finally limited to 95 cases, although we evaluated all cases at a quaternary care university hospital over a total of 16 years.

We recently performed a similar study examining the impact of selective reporting of antibiotic susceptibility test results on the use of ampicillin in BSIs with *Enterococcus faecalis* [16]. In this study, these two points were not present and selective reporting of antibiotic susceptibility test results led to a significantly higher use of ampicillin. Likewise, Lestin-Bernstein et al. [9] reported a significantly higher use of narrow-spectrum penicillin after the implementation of selective reporting in BSI with *Staphylococcus aureus*. In this study, a comment on the microbiological report was also included, directing clinicians to the preferred choice of therapy; this possibly might have also contributed to the success of the intervention. In contrast, our in-hospital guidelines for antibiotic therapy did not clearly recommend which therapy to choose for BSI with *Streptococcus pneumoniae* during the whole study period. The comment on the report for *Streptococcus pneumoniae* also made a recommendation for a beta-lactam antibiotic, but not a narrow-spectrum antibiotic. Therefore, no further effect was to be expected in this regard.

Although we could not demonstrate that selective reporting of antibiotic susceptibility test results led to a

**Table 2.** Versions of susceptibility testing used in the years indicated

| 2006 | 2011 | 2014–2019 | 2014–2019 |
|---|---|---|---|
| Penicillin G | Penicillin G | Penicillin G | Penicillin G |
| Oxacillin/methicillin | – | – | – |
| Erythromycin | – | – | – |
| Clindamycin | – | – | – |
| Vancomycin | Vancomycin | – | – |
| Teicoplanin | – | – | – |
| Rifampicin | – | – | – |
| Fusidic acid | – | – | – |
| Linezolid | – | – | – |
| Ampicillin | – | – | – |
| Mezlocillin | – | – | – |
| Piperacillin | – | – | – |
| Amoxicillin/clavulanic acid | – | – | – |
| Ticarcillin/clavulanic acid | – | – | – |
| Piperacillin/tazobactam | – | – | – |
| Piperacillin/sulbactam | – | – | – |
| Imipenem | – | – | – |
| Meropenem | Meropenem | – | – |
| Cefazolin | – | – | – |
| Cefuroxime | – | – | – |
| Cefotaxime | – | – | – |
| Ceftriaxone | – | Ceftriaxone | |
| Ceftazidime | – | – | – |
| Cefepime | – | – | – |
| Aztreonam | – | – | – |
| Levofloxacin | – | – | – |
| Ciprofloxacin | – | – | – |
| – | Moxifloxacin | Moxifloxacin | – |
| Tetracycline | Tetracycline | – | – |
| Gentamicin | – | – | – |
| Tobramycin | – | – | – |
| Netilmicin | – | – | – |
| Amikacin | – | – | – |
| Polymyxin B | – | – | – |
| – | Trimethoprim/sulfamethoxazole | – | – |
| – | Telithromycin | – | – |
| – | – | Macrolides | – |

As of 2014, the following note was appended to the susceptibility reports: "Pneumococcus: Drug of choice: Penicillin G or other beta-lactam antibiotics. If the patient is allergic to beta-lactams, vancomycin or moxifloxacin can be used as an alternative (inferior effectiveness)."

higher use of narrow-spectrum penicillin, SR should not be rated to be not successful at all in promoting a more pathogen-targeted therapy in patients with BSI with *Streptococcus pneumoniae*. A different result might have been obtained without the presence of the above-mentioned limitations. Further, one single intervention meant to reduce unnecessary antibiotic prescribing might not be enough. Besides SR, further AMS implementations, e.g., in-hospital guidelines for antibiotic therapy and advanced postgraduate training in the interpretation of antibiotic test results, are crucial, as are regular AMS rounds in intensive care wards.

## Conclusion

In this study, selective reporting of antibiotic susceptibility test results did not lead to a higher use of a narrow-spectrum penicillin in patients with a BSI with *Streptococcus pneumoniae*.

## Limitations

The study is subject to certain limitations. It was a single-centre study and retrospective, and second, the cohort contained only a limited number of patients. Furthermore, the two study groups we examined differed significantly in the severity of the disease.

## Statement of Ethics

The study was approved by the Ethics Committee of the University of Regensburg (No. 21-2406-104). The need for informed consent was waived by the Ethics Committee of the University of Regensburg (No. 21-2406-104).

## Conflict of Interest Statement

Arno Mohr received travel grants from Gilead. Bernd Salzberger received a consulting honorarium from Roche AG. All other authors declare they have no financial interests.


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## Author Contributions

Florian Geismann, Florian Hitzenbichler, Kathleen Brueckner, and Arno Mohr wrote the main manuscript text. Kathleen Brueckner and Tamara Ruegamer collected the data. Florian Geismann and Arno Mohr analysed the data. Michael Pfeifer, Bernd Salzberger, Stilla Bauernfeind, Michaela Simon, Aila Caplunik-Pratsch, Wulf Schneider-Brachert, Clemens Wiest, Thilo Hinterberger, and Tamara Ruegamer reviewed the manuscript.

## Data Availability Statement

Data are not publicly available due to ethical reasons. Further enquiries can be directed to the corresponding author.

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