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# **ORIGINAL ARTICLE**

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# Adherence to Antibiotic Guidelines in Acute Patients With Suspected Severe

Pneumonia: A Cohort Study

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#### **Abstract**

### Introduction

Community-acquired pneumonia (CAP) accounts for a substantial part of antibiotic prescriptions in emergency departments (EDs). Guidelines for empiric antibiotic treatment support rational use of antibiotics and should sharpen the indication and prevent overuse of antibiotics.

#### **Aim**

This study aimed to investigate whether ED patients who were prescribed antibiotics for suspected severe pneumonia fulfilled the criteria for the treatment.

#### **Methods**

This was a retrospective cohort study. The population consisted of adults hospitalized in two Danish EDs in the Central Denmark Region between July 1, 2022, and June 30, 2023, who were prescribed antibiotic treatment using the Standard Prescription Package: "Start package of severe pneumonia" (SPP-SP), containing piperacillin/tazobactam (Pip/Taz) plus clarithromycin. Review of electronic medical records (EMRs) was performed to decide whether the patients met the criteria for the SPP-SP.

270 patients were included. In total, 103/270 (38%) patients fulfilled the criteria for treatment with the SPP-SP, whereas 167/270 (62%) patients did not.

#### Conclusion

The criteria for prescribing antibiotics based on the severe pneumonia prescription package were fulfilled in only 38% of patients, reflecting a deviation in guideline adherence. This study provides useful and practical knowledge for implementation of new guidelines and focus areas in line with Antibiotic Stewardship.

Keywords: Pneumonia; Antibiotics; Antimicrobial Stewardship; Guideline Adherence; Community-Acquired Pneumonia



# Introduction

ommunity-acquired pneumonia (CAP) accounts for a substantial part of diagnoses in patients admitted to emergency departments (EDs) (1). The estimated number of hospital admissions for patients with upper respiratory infections and pneumonia was 29,000 in 2022 (2). Appropriate antibiotic treatment for patients with CAP is crucial. Antimicrobial resistance (AMR) is a health concern for both individual patients and public health in general (3). The use of broad-spectrum antibiotics is a driving factor behind the development of AMR (4). Piperacillin/tazobactam (Pip/Taz) is a broad-spectrum antibiotic, but resistance to Pip/Taz has increased in Denmark concomitantly with its increased usage (5). Pneumonia guidelines in Central Denmark Region emphasize that empirical Pip/Taz should only be used for CAP patients with severe pneumonia (6).

Adherence to antibiotic guidelines has been shown to be low in Danish settings (7-9), and the Antimicrobial Stewardship Program emphasizes the importance of identifying opportunities for improving antibiotic use (10). Thus, it is important to investigate if patients with CAP in the EDs meet the criteria for the administration of Pip/Taz in accordance with guidelines.

The primary aim was to investigate whether patients treated with the regional Standard Prescription Package (SPP) for severe pneumonia (SPP-SP) met the criteria for administration of the SPP.

# Methods

# STUDY DESIGN

This was a retrospective cohort study with a review of electronic medical records (EMRs), reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (11). The study was conceived as a quality improvement project; thus, there was no need for informed consent according to Danish regulations. Permission to perform the data retrieval was granted by the two EDs and the hospital managements.

#### **HVAD VED VI?**

Antibiotikabehandling af patienter med samfundserhvervet pneumoni udgør en betydelig andel af de patienter, der behandles med antibiotika på akutmodtagelser. Anvendelsen af bredspektrede antibiotika, såsom piperacillin/tazobactam, er høj. Det er af største interesse at identificere patientgrupper, hvor antibiotikabehandlingen kan reduceres til mindre bredspektrede antibiotika, hvilket er en af de centrale målsætninger inden for Antibiotic Stewardship.

Fact box (in Danish)

# **SETTING AND COHORT SELECTION**

We included adult patients aged ≥ 18 years with a Danish civil registration number who were admitted to the ED of Aarhus University Hospital (AUH) or Regional Hospital Randers (RRA) between July 1, 2022, and June 30, 2023, and who were prescribed the SPP-SP and were administered either one or both antibiotics from this SPP-SP: Pip/Taz and/or clarithromycin. The SPP recommends giving both antibiotics; however, the clinician can choose to select only one of the antibiotics, e.g., if the patient was prescribed either Pip/Taz or clarithromycin, or the clinician deemed it relevant or appropriate to deselect one of them.

We excluded patients who had previously enrolled in the study. AUH is an 858-bed university hospital serving an area with 353,640 inhabitants, while RRA is a 200-bed regional hospital serving 226,253 inhabitants. Patients were identified through the Business Intelligence (BI) Data Warehouse of the Central Denmark Region, enabling extraction based on the inclusion criteria. The BI Data Warehouse stores routinely collected data from all patient journals (12).

#### SPP

In the Central Denmark Region, SPPs function as tools to simplify the prescription process for physicians as well as to nudge clinicians to prescribe the recommended antibiotics. More specifically, SPPs consist of standard prescriptions for specific diagnoses, conditions, microbes, etc. The clinician suspects a patient to have, i.e., pneumonia, and must select the relevant SPPs based on the severity of pneumonia (defined by the CURB-65 score): mild, moderate, or severe. Choosing the relevant SPP elicits specific antibiotics, doses, and durations. SPPs are based on regional antibiotic guidelines (6). In this study, the cohort consists of patients treated with the SPP for severe pneumonia, abbreviated as SPP-SP. The criteria for prescribing the SPP-SP used in the present study are shown in Table 1 (6). Patients with hospital-acquired pneumonia and aspiration pneumonia were not included in this study, since there are separate SPPs for those indications. Further details on SPPs are presented in Supplementary Material, Text S1.

Definition of pneumonia	1. Temperature above 38 °C	Cand									
	2. New infiltrate on chest x-ray and 3. Leukocytosis or leukocytopenia with neutrophilia or a rise in CRP and 4. Minimum one of the symptoms below										
						Symptoms:  • Cough					
	Severity of CAP	Criteria	Antibiotic treatment	Antibiotic treatment							
			(type and dosage)	(duration)							
	Mild pneumonia	CURB-65: 0-2	Standard Prescription Package								
			(SPP); "Start package for <i>mild</i> pneu-								
			monia:	5 days							
		Benzylpenicillin 0.6 g IV every 6 h									
Moderate-severe pneumo-	CURB-65: 3-5	SPP: "Start package for <i>moderate-se-</i>									
nia	Respiratory stable, nasal oxygen	vere pneumonia: Benzylpenicillin									
	cannula needed only, and in-	1.2 g IV every 6 h									
	volvement of one lung lobe.	+ 7 days									
		Clarithromycin 500 mg IV/oral									
		every 12 h									
Severe pneumonia (*)	CURB65: 3-5 and involvement of	SPP: "Start package for <i>severe</i> pneu-									
•	multiple lung lobes on chest x-ray	monia:									
	or severe hypoxia with O2-satura-	Piperacillin/tazobactam 4 g/0.5 g									
	tion < 92% or PO2 < 8.0 kPa or	IV every 6 h									
	criteria of sepsis fulfilled.	+	7 days								
		Clarithromycin 500 mg IV/oral									
		every 12 h									

(\*) COPD and pneumonia: Frail patients with severe COPD e.g., FEV1 < 50 % and/or home oxygen therapy, chronic hypercapnia, or repeated exacerbations must be treated as severe pneumonia no matter the CURB-65 score (confusion, urea, respiratory rate, blood pressure, and age  $\geq$ 65). For the definition of the CURB-65 score, see Table S3.

# **DATA VARIABLES**

Data were obtained through EMRs. The main variable categories were: demographics; comorbidities; vital signs; laboratory values; microbiology findings; imaging results; sequential organ failure assessment (SOFA) score (Table S2); CURB-65 score: confusion, uremia, respiratory rate, blood pressure, and age  $\geq$  65 years (Table S3); and antibiotic treatment (type of antibiotic, administration route and duration). Sepsis was defined as a SOFA score  $\geq$  2. SOFA score and CURB-65 score were calculated and determined by the first author (SS). Vital signs at triage and blood sample values from the emergency department were used to calculate the scores.

Imaging was described by a radiologist, who categorized infiltrates on X-ray or computed tomography (CT) scan as either new or chronic (i.e., previously detected during hospitalization). Each description was reviewed, and multilobar involvement was identified if infiltrates were reported in more than one lobe.

It was assumed that all patients had pneumonia, or at least suspected pneumonia. Patients were classified as "criteria fulfilled" if they had a CURB-65 score of 3-5 *and* 

severe hypoxia, sepsis, and/or involvement of multiple lung lobes on chest X-ray. If patients were considered to have severe chronic obstructive pulmonary disease (COPD), they were classified as "criteria fulfilled" regardless of CURB-65 score, in line with the pneumonia guidelines (Table 1). In this study, severe COPD was defined as FEV1 < 50 %, home oxygen treatment, and/or combined inhalation medicine compatible with severe COPD.

All data were collected and managed by the first author (SS) using REDCap, hosted by the Central Denmark Region.

# **DATA ANALYSIS**

Descriptive statistics are presented using the median (interquartile range [IQR]) and mean (standard deviation), as appropriate. Normal distribution was assessed using QQ plots. Binary variables are presented as the number (n) and percentage (%). Analyses were performed using Stata 18.0 (StataCorp, Texas, USA).

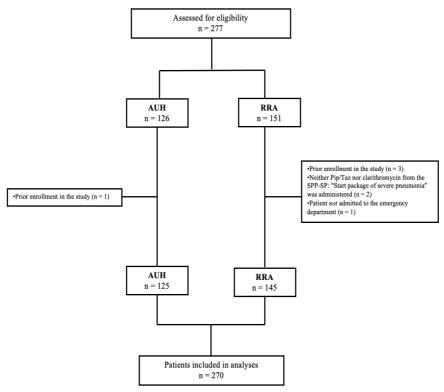


Figure 1. Flowchart of patient enrollment

# Results

# PATIENT CHARACTERISTICS

During the study period, 277 patients were admitted to the EDs of AUH and RRA and prescribed the SPP-SP. However, 7 patients were excluded (Figure 1), leaving a total of 270 patients for the analyses; 125 patients from AUH and 145 patients from RRA. Median age was 76 years (IQR: 65–83), and 156/270 (58%) were male. Table 2 presents the patients' characteristics. The most frequent comorbidities were chronic heart disease, followed by COPD. The median SOFA score was 2 (IQR: 1–3), and the mean CURB-65 score was 2 (SD: 1).

Table 2. Patient characteristics

Variable	All patients treated with SPP-SP (n = 270)	Criteria for SPP-SP fulfilled (n = 103)	Criteria for SPP-SP not fulfilled (n = 167)
Age (years), median [IQR]	76 [65–83]	78 [68–85]	74 [61–83]
Gender, male, n (%)	156 (58)	61 (59)	95 (57)
COMORBIDITIES a, n (%)			
Diabetes <sup>b</sup>	61 (23)	26 (25)	35 (21)
COPD <sup>c</sup>	77 (29)	57 (55)	20 (12)
Severe COPD d	49 (18)	49 (48)	0 (0)
Asthma <sup>c</sup>	55 (20)	28 (27)	27 (16)
Chronic heart disease e	109 (40)	52 (50)	57 (34)
Chronic liver disease <sup>f</sup>	16 (6)	6 (6)	10 (6)
Chronic kidney disease g	28 (10)	15 (15)	13 (8)
None mentioned above	65 (24)	14 (14)	51 (31)
No patient journal available <sup>h</sup>	< 5 (< 2)	< 5 (< 5)	< 5 (< 3)
VITAL SIGNS AT TRIAGE	• •	· ·	· ·
Oxygen treatment, n (%)	162 (60)	72 (70)	90 (54)
Nasal cannula	138 (85)	54 (75)	84 (93)
High Nasal Flow	0 (0)	0 (0)	0 (0)
NIV	< 5 (<2)	< 5 (<7)	0 (0)
Intubated	< 5 (<2)	< 5 (<7)	0 (0)
Other <sup>i</sup>	19 (12)	13 (18)	6 (7)
Oxygen flow (L/min), median [IQR]	2 [0–4]	2 [0–5]	1 [0-4]
Oxygen saturation (%), median [IQR]	93 [91–96]	92 [90–94]	94 [92–96]
Respiratory rate (breaths/min), median [IQR]	24 [20–28]	24 [20–31]	24 [20–28]
Severe hypoxia *, n (%)	171 (63)	74 (72)	97 (58)
Systolic blood pressure (mmHg), mean (SD)	134 (28)	128 (29)	137 (27)
Diastolic blood pressure (mmHg), median [IQR]	72 [61–83]	65 [57–82]	74 [67–84]
Mean arterial pressure (mmHg), mean (SD), median [IQR]	94 (21)	87 [75–105]	97 (18)
Heart rate (beats/min), mean (SD)	101 (22)	100 (25)	102 (19)
Temperature (°C), mean (SD)	38.0 (1.1)	38.0 (1.1)	38.1 (1.1)
GCS score, median [IQR]	15 [15–15]	15 [14–15]	15 [15–15]
	(full range: 3-15)	(full range: 3-15)	(full range: 9-15)
LABORATORY VALUES <sup>j</sup> , median [IQR]		<u> </u>	
Bilirubin (μmol/L)	11 [7–16]	9 [6–16]	11 [8–16]
Creatinine (µmol/L)	83 [61–114]	102 [73–137]	78 [58–101]
Urea (mmol/L)	7.3 [5–10.5]	9.2 [7.2–13.5]	5.9 [4.7–8.6]
C-reactive protein (mg/L)	141 [58–261]	111 [46–232]	155 [73–283]
Leucocytes (x10 <sup>9</sup> /L)	12.5 [9.7–17.3]	13 [10.7–18.1]	12 [9.3–16.9]

Platelet count (x10 <sup>9</sup> /L)	255 [191–323]	260 [195–331]	253 [186–315]
Arterial blood gas performed <sup>j</sup> , n (%)	196 (73)	83 (81)	113 (68)
Arterial blood gas PaO2 (kPa), median [IQR]	8.7 [7.6–9.8]	8.7 [7.4–9.9]	8.7 [7.7–9.8]
SCORING SYSTEMS			
Total SOFA score k, median [IQR]	2 [1–3]	2 [2–4]	2 [1–2]
Sepsis **, n (%)	186 (69)	83 (81)	103 (62)
Total CURB65 score k mean (SD), median [IQR]	2(1)	3 [2–3]	2 [1–2]
Confusion (C), n (%)	57 (21)	37 (36)	20 (12)
Urea > 7 mmol/L (U), n (%)	137 (51)	80 (78)	57 (34)
Respiration $\geq$ 30/min (R), n (%)	57 (21)	34 (33)	23 (14)
Blood pressure (B), n (%)	62 (23)	44 (43)	18 (11)
Systolic < 90 mmHg and/or diastolic ≤ 60 mmHg	` '		
Age ≥ 65 (65), n (%)	203 (75)	87 (84)	116 (69)
CURB65 score 3-5, n (%)	82 (30)	75 (73)	7 (4)
TREATMENT, n (%)			
Treatment with only Pip/Taz (SPP-SP)	98 (36)	33 (32)	65 (39)
Treatment with <i>only</i> clarithromycin (SPP-SP)	24 (9)	7 (7)	17 (10)
Treatment with both Pip/Taz and clarithromycin (SPP-SP)	148 (55)	63 (61)	85 (51)
Clarithromycin iv administration <sup>1</sup>	170/172 (99)	70/70 (100)	100/102 (98)
n (iv) /n (clarithromycin) (%)			
Treatment duration m (days) Pip/Taz, median [IQR]	4 [2-6]	4 [2–6]	4 [3–6]
Treatment duration m (days) clarithromycin, median [IQR]	2 [0-3]	2 [0–3]	2 [0-3]
HOSPITALIZATION, median [IQR]			
Time from hospitalization to SPP-SP prescription, hours	2.8 [1.6-4.4]	2.5 [1.1–4.2]	2.9 [1.9-4.6]
Length of stay (LOS), days	5 [3–8]	5 [3–9]	5 [3–8]
MORTALITY, n (%)			
In-hospital	36 (13)	20 (19)	16 (10)
30-days	53 (20)	31 (30)	22 (13)
90-days	68 (25)	34 (33)	34 (20)

Abbreviations: COPD, chronic obstructive pulmonary disease; GCS, Glasgow Coma Scale; iv, intravenous; SPP-SP, Standard Prescription Package for severe pnemonia; NIV, non-invasive ventilation; SPP-time, Physician prescription time of the SPP.

#### Table 2 (continued).

<sup>\*)</sup> Severe hypoxia is defined as oxygen saturation < 92 % and/or PaO<sub>2</sub> < 8, kPa without supply of oxygen or oxygen saturation < 95 % with oxygen supply  $\geq$  2 L/min and/or PaO<sub>2</sub>/FiO<sub>2</sub> < 300

<sup>\*\*)</sup> Suspected infection and SOFA score  $\geq 2$ 

<sup>&</sup>lt;sup>a</sup> Comorbidities are based on medical history, ICD-10 codes, and medical treatment overview.

<sup>&</sup>lt;sup>b</sup> Diabetes type 1 or 2, medical treatment (oral or injection).

<sup>&</sup>lt;sup>c</sup> COPD and/or asthma requiring daily medicine.

 $<sup>^{\</sup>mathrm{d}}$  Severe COPD is defined as FEV1 < 50 %, home oxygen treatment, and/or combined inhalation medicine compatible with severe COPD.

<sup>&</sup>lt;sup>e</sup>Chronic heart disease, including ischemic heart disease, cardiac arrest (earlier), chronic heart failure with/without preserved ejection fraction, atrial fibrillation/atrial flutter (paroxysmal, persistent, chronic), earlier myocardial infarction (ST or non-ST), unstable angina pectoris.

 $<sup>{}^{\</sup>rm f}{\rm Chronic}$  liver disease, including hepatitis, cirrhosis, steatosis, and steatohepatitis.

 $<sup>{\</sup>ensuremath{\tt g}}$  Chronic kidney disease stage 3A or worse (GFR < 60 mL/min/1.73  $m^2$  ) or kidney transplant.

<sup>&</sup>lt;sup>h</sup> Patients from other regions, e.g., the Capital Region of Denmark, where the patient journal is not available.

<sup>&</sup>lt;sup>1</sup>Hudson mask, venturi mask, mask unspecified.

i Laboratory values in the emergency department where the patient was admitted. If several blood tests (or arterial blood gas) were performed, the test closest to SPP-time was chosen.

 $<sup>^</sup>k$ Based on vital signs at triage. SOFA score; see Supplementary Table S2. CURB-65 score (C = Confusion, Urea > 7 mmol/L, Respiratory rate ≥ 30/min, Blood pressure (Diastolic ≤ 60 mmHg or systolic < 90 mmHg, age ≥ 65 years).

 $<sup>^{\</sup>rm l}$  Based on the first administration. The remaining was oral administration.

<sup>&</sup>lt;sup>m</sup> Treatment duration refers to the number of days during which the patient receives Pip/Taz or clarithromycin during hospitalization, independent of the indication. Outpatient therapy with continuous infusion using elastomeric pumps was included in the treatment duration

# **PRIMARY OUTCOME**

#### Guideline adherence and use of the SPP-SP

Overall, 103/270 (38%) patients met the criteria for prescription of the SPP-SP (Table 3), while 167/270 (62%) patients did not fulfill the criteria. Patient characteristics for subgroups with criteria fulfilled and not fulfilled are shown in Table 2.

The strict definition of severe pneumonia combines a CURB-65 score of 3–5 and at least one complicating criterion (i.e., >1 infected lobe, oxygen saturation < 92%, or sepsis) or a suspected pulmonary infection *and* severe COPD.

#### Antibiotic administration

Patients were included if Pip/Taz and/or clarithromycin from the prescribed SPP-SP were administered. Most commonly, both Pip/Taz and clarithromycin from the SPP-SP were administered (148/270, 55%), whereas 98/270 (36%) patients received only Pip/Taz and 24/270 (9%) patients received only clarithromycin (Table 2). In total, 172/270 patients were administered clarithromycin, with the first dose being administered intravenously in 170/172 (99%) patients.

Imaging and microbiology

A chest X-ray was performed in 235/270 (87%) patients, whereas 35/270 (13%) patients had a CT scan of the thorax performed (Table S5A). No new infiltrates were detectable in 63/235 (27%) patients, whereas new infiltrate/infiltrates were identified in the remaining 172/235 (73%).

Polymerase chain reaction for *Legionella pneu-mophila* and *Mycoplasma pneumoniae* was performed in 99 patients, with positive results in fewer than 5 patients. The imaging and microbiology results are shown in Tables S5A–5B.

A urine culture was performed in 110/270 (41%). In total 34/110 (31%) cultures were positive, with *Escherichia coli* being the most frequent bacteria (Tables S5B and S6A). Blood and sputum cultures were performed in 257/270 (95%) and 130/270 (48%) patients, respectively (Table S5B). The culture results are presented in Tables S6A–6C.

Table 3. Primary outcome

	All patients treated with SPP-SP (n = 270)	Criteria fulfilled (n = 103)	Criteria not fulfilled (n = 167)
PRIMARY OUTCOME			
Criteria fulfilled <sup>a</sup> , n (%)	103 (38)	103 (100)	-
CURB-65 3-5 and multiple lobes involved, n (%)*	=	41 (40)	-
CURB-65 3-5 and severe hypoxia <sup>b</sup> , n (%)*	=	53 (51)	-
CURB-65 3-5 and sepsis c, n (%)*	=	63 (61)	-
Suspected pulmonary infection and severe COPD $^{\rm d},$ n (%)*	-	49 (48)	-

Abbreviations: COPD, chronic obstructive pulmonary disease; Pip/Taz, piperacillin/tazobactam.

<sup>\*)</sup> Some patients fulfilled the criteria for several of the indications, why the numbers exceed n=103.

<sup>&</sup>lt;sup>a</sup> Based on vital signs at triage.

<sup>&</sup>lt;sup>b</sup> Severe hypoxia is defined as oxygen saturation < 92 % and/or PaO<sub>2</sub> < 8, kPa without supply of oxygen or oxygen saturation < 95 % with oxygen supply ≥ 2 L/min and/or PaO<sub>2</sub>/FiO<sub>2</sub> < 300.

 $<sup>^{</sup>c}$ Suspected infection and SOFA score ≥ 2.

 $<sup>^{</sup>m d}$  Severe COPD defined as FEV1 < 50 %, home oxygen treatment and/or combined inhalation medicine compatible with severe COPD.

# Discussion

Approximately one-third of patients treated according to the SPP-SP actually met the criteria for prescription of this SPP.

International and national studies found low antibiotic guideline adherence in patients with pneumonia (8, 13). According to a study from the United States, 37.2% of the most common antibiotic prescribing scenarios had potential for improvement (14). A study from another Danish region found guideline adherence of only 31% in patients with suspected CAP (8). In our study, the cohort included patients with suspected severe pneumonia, which might explain the slightly higher adherence. Several studies have shown a significant impact of antibiotic stewardship programs on antibiotic use and clinical outcomes in CAP patients (15, 16). In a Norwegian setting with low antimicrobial resistance, audit and feedback interventions led to a significant improvement in appropriate empirical antibiotic prescribing, increasing from 61.7% to 83.8% (P < 0.001) (17).

The absence of documentation of the CURB-65 score in the EMRs may explain the low guideline adherence observed in our study. In pneumonia guidelines for the Central Denmark Region, version 18 (Table 1), severe pneumonia was strictly defined as a CURB-65 score ≥ 3 plus involvement of multiple lobes and/or severe hypoxia and/or sepsis (6). Our study highlights that it can be difficult to translate biological and individual clinical presentations into scoring systems. The definition of sepsis is a suspected or documented infection with organ dysfunction (Table S2) (18, 19). If a patient fulfills sepsis criteria and has a CURB-65 score of 1 or 2, does this patient have severe pneumonia or "Sepsis of unknown origin"? It may be obvious at the bedside, but not necessarily obvious in the scoring systems. Even the most thorough clinical guidelines cannot cover all individual clinical presentations, leaving room for interpretation and potentially under- or overdiagnosis, resulting in overuse of broad-spectrum antibiotics. The overlap between sepsis and severe pneumonia criteria is notable. A prospective study of hospitalized CAP patients showed that the prognostic performance of qSOFA for in-hospital mortality and ICU admission was similar to CURB-65 (20).

# **HVAD TILFØJER STUDIET?**

Vores studie fandt, at kun godt en tredjedel af patienterne opfyldte kriterierne for ordination af standardordinationspakken (SOP): "Startpakke svær pneumoni", hvilket afslører en patientgruppe med mulighed for at reducere brugen af bredspektrede antibiotika. Læger bør informeres om denne bekymrende afvigelse fra guidelines for at fremme en mere rationel anvendelse af antibiotika og minimere antibiotikaresistens.

Fact box (in Danish)

As expected, patients meeting the SPP-SP criteria had a high CURB-65 score and had more comorbidities, increasing their mortality. These findings support using CURB-65 to stratify patients by mortality risk. The majority of patients in this study had a CURB-65 score < 3; thus, they should have been prescribed a more narrowspectrum antibiotic in line with the applied guidelines. In the present retrospective study, we followed the definitions in the guidelines strictly; however, in a clinical setting, the treatment of patients is not always as simple as the guidelines imply. Since the data collection for this study, new guidelines have been published simplifying the definition of severe pneumonia and changing recommended antibiotics (21). Whether these measures translate into changes in prescription behaviors for severe pneumonia remains to be revealed.

In this study, several confounding factors are relevant. Relevant confounding factors were previous infections with *Pseudomonas aeruginosa*, pneumonia caused by SARS-CoV-2, penicillin allergy, and diverse clinical interpretations of COPD severity. These factors were not possible to further investigate.

# STRENGTHS AND LIMITATIONS

The retrospective study design avoided dropout and minimized the risk of selection bias. By not involving ongoing trial attention to topics like antibiotics, we reduced the risk of falsely favorable outcomes (i.e., the Hawthorne effect) (22).

Surprisingly, there were only 277 patients who had the SPP-SP prescribed at the two hospitals over a one-year period (Figure 1). A possible explanation might be that some of the patients with a pulmonary focus were treated with another SPP, such as that for "Sepsis/Septic shock of unknown origin". Our cohort did not cover any other SPPs, which is why this possible explanation cannot be further qualified.

We obtained a description of imaging performed by a radiologist. In the ED, physicians must interpret the images themselves and then rapidly decide upon the most appropriate treatment; the X-ray is described later. Assessing multilobar infiltrates can be challenging. While most patients had chest X-rays, fewer had CT-thorax. Chest Xrays, particularly in the supine position, may lack the detail needed to accurately identify multilobar infiltrates. Due to the high patient turnover and diagnostic uncertainty in EDs, physicians may be inclined to prescribe broad-spectrum antibiotics. A Dutch interview-based study found that physicians' concern about patient outcomes when prescribing narrow-spectrum antibiotics was a key barrier to guideline-adherent therapy (23). This may also apply in Denmark, but further research is needed.

Broad-spectrum antibiotics appear to be overused in Danish EDs, at least in part due to the overdiagnosis of severe pneumonia, as substantiated by the findings of this study. However, based on the data in this study, we are not able to answer whether the results are caused by poor prescription practice or poor guideline interpretation. The overuse of Pip/Taz has detrimental effects, such as increasing AMR, which renders it essential to focus on and monitor Pip/Taz use to avoid overuse.

# Conclusion

We found that only 38% of patients treated empirically according to the SPP-SP fulfilled the criteria for that SPP. The applied version of guidelines may leave room for different interpretations among clinicians, with a possible under- or overdiagnosis of severe pneumonia.

# Conflict of Interest

The authors declare that they have no conflicts of interest.

# Funding

None.

# **PERSPEKTIVERING**

Fokus på indikation for valg af antibiotika på baggrund af den mistænkte diagnose og retningslinjerne herfor er essentielt for, at bredspektret antibiotika forbeholdes de rigtige patienter, med det formål at mindske den bekymrende udvikling af antibiotikaresistens. Studiets resultater kan endvidere være gavnlige i forbindelse med implementering af nye retningslinjer.

Fact box (in Danish)

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