

## Supplementary file

### —“Use of piperacillin/tazobactam and meropenem in patients in a Danish ICU”

Table 1. Demographic and Clinical Characteristics of Patients, all results.

Characteristic's	Overall (N=184)	Meropenem (N=76)	Piperacillin/tazobactam (N=80)	Meropenem and piperacillin/tazobactam (N=28)
<b>Age, median (IQR), years</b>	63.3 (48.0 to 71.3)	59.9 (46.6 to 67.3)	63.0 (48.3 to 74.2)	68.2 (58.8 to 74.7)
<b>Adult</b>	170 (92.4%)	71 (93.4%)	73 (91.3%)	26 (92.9%)
<b>&lt;18 years</b>	14 (7.6%)	5 (6.6%)	7 (8.8%)	2 (7.1%)
<b>Male sex, No. (%)</b>	112 (60.9%)	47 (61.8%)	51 (63.8%)	14 (50.0%)
<b>Height<sup>a</sup>, median (IQR), cm</b>	172.0 (165.0 to 180.0)	173.5 (168.0 to 180.5)	171.0 (163.0 to 180.0)	168.0 (163.8 to 175.3)
<b>Weight, median (IQR), kg</b>	79.10 (65.0 to 90.0)	81.7 (70.0 to 96.0)	74.8 (63.1 to 90.0)	70.0 (61.5 to 81.2)
<b>Antibiotic allergy<sup>b</sup></b>				
• beta-lactams	8 (4.3%)	8 (10.5%)	0 (0%)	0 (0%)
• cephalosporins	0 (0%)	0 (0%)	0 (0%)	0 (0%)
• aminoglycosides	3 (1.6%)	2 (2.6%)	1 (1.3%)	0 (0%)
• glycopeptides				
• quinolones	0 (0%)	0 (0%)	0 (0%)	0 (0%)
• macrolides	1 (0.5%)	0 (0%)	1 (1.3%)	0 (0%)
• tetracyclines	0 (0%)	0 (0%)	0 (0%)	0 (0%)
• sulfonamides	1 (0.5%)	0 (0%)	1 (1.3%)	0 (0%)
• oxazolides	1 (0.5%)	0 (0%)	1 (1.3%)	0 (0%)
	0 (0%)	0 (0%)	0 (0%)	0 (0%)
<b>Coexisting conditions, No. (%)</b>				
<b>Diabetes<sup>c</sup></b>	36 (19.6%)	18 (23.7%)	14 (17.5%)	4 (14.3%)
<b>Haematologic cancer</b>	17 (9.2%)	11 (14.5%)	4 (5.0%)	2 (7.1%)
<b>Use of corticosteroids within 3 months prior to admission<sup>d</sup></b>	14 (7.6%)	9 (11.8%)	3 (3.8%)	2 (7.1%)
<b>Metastatic cancer<sup>e</sup></b>	14 (7.6%)	5 (6.6%)	8 (10.0%)	1 (3.6%)
<b>Solid organ transplant<sup>f</sup></b>	15 (8.2%)	3 (3.9%)	10 (12.5%)	2 (7.1%)
<b>Chronic Kidney Disease<sup>g</sup></b>	8 (4.3%)	6 (7.9%)	1 (1.3%)	1 (3.6%)
<b>Acute Kidney Injury<sup>h</sup></b>	53 (28.8%)	19 (25.0%)	24 (30.0%)	10 (35.7%)
<b>Length of hospital stay prior to ICU admission</b>	<b>Overall (N=184)</b>	<b>Meropenem (N=76)</b>	<b>Piperacillin/tazobactam (N=80)</b>	<b>Meropenem and piperacillin/tazobactam (N=28)</b>
<b>Days, median (IQR)</b>	1.5 (0.5-5.5)	1.5 (0.5-6)	2 (0.5-4.5)	3 (1.5-8)
<b>Source of ICU admission, No. (%)</b>				
<b>Emergency department or trauma centre</b>	35 (19.0%)	16 (21%)	13 (16.3%)	6 (21.5%)
<b>Hospital ward</b>	47 (25.5%)	21 (27.6%)	21 (26.3%)	5 (17.9%)
• Medical	34 (18.5%)	18 (23.7%)	13 (16.3%)	3 (10.7%)
• Surgical	13 (7.1%)	3 (3.9%)	8 (10.0%)	2 (7.1%)
<b>Another ICU</b>	43 (23.4%)	18 (23.7%)	16 (20.0%)	9 (32.1%)

<b>Operating or recovery room</b>	59 (32.1%)	21 (27.6%)	30 (37.5%)	8 (28.6%)
• Planned surgery	18 (9.8%)	5 (6.6%)	11 (13.8%)	2 (7.1%)
• Acute surgery	41 (22.3%)	16 (21.1%)	19 (23.8%)	6 (21.4%)
<b>Known colonisation<sup>l</sup> with a bacterium with acquired antibiotic resistance, No. (%)</b>				
• MRSA	1 (0.5%)	1 (1.3%)	0	0
• CPO	1 (0.5%)	1 (1.3%)	0	0
• ESBL	0	0	0	0
• VRE	6 (3.3%)	4 (5.3%)	2 (2.5%)	0
<b>Suspected infection at baseline No. (%)</b>				
<b>Yes</b>	155 (84.2%)	74 (97.4%)	55 (68.8%)	26 (92.9%)
<b>No<sup>j</sup></b>	29 (15.8%)	2 (2.6%)	25 (31.3%)	2 (7.1%)
<b>Source of infection No. (%)</b>	<b>Overall (N=155)<sup>k</sup></b>	<b>Meropenem (N=74)</b>	<b>Piperacillin/tazobactam (N=55)</b>	<b>Meropenem and piperacillin/tazobactam (N=26)</b>
<b>Community acquired infection<sup>l</sup></b>	81 (52.3%)	41 (55.4%)	27 (49.1%)	13 (50.0%)
<b>Nosocomial infection<sup>m</sup></b>	69 (44.5%)	29 (39.2%)	28 (50.9%)	12 (46.2%)
<b>Unknown</b>	5 (3.2%)	4 (5.4%)	0 (0%)	1 (3.8%)
<b>Focus of infection No. (%)</b>	<b>Overall (N=184)</b>	<b>Meropenem (N=76)</b>	<b>Piperacillin/tazobactam (N=80)</b>	<b>Meropenem and piperacillin/tazobactam (N=28)<sup>n</sup></b>
<b>Central nervous system</b>	8 (4.3%)	7 (9.2%)	0 (0%)	1 (3.6%)
<b>Pulmonary</b>	57 (31.0%)	20 (26.3%)	26 (32.5%)	11 (39.3%)
<b>Skin or soft tissue</b>	34 (18.5%)	29 (38.2%)	0 (0%)	5 (17.9%)
<b>Abdominal</b>	24 (13.0%)	6 (7.9%)	13 (16.3%)	5 (17.9%)
<b>Urinary tract</b>	5 (2.7%)	1 (1.3%)	2 (2.5%)	2 (7.1%)
<b>Catheter-related infection</b>	1 (0.5%)	1 (1.3%)	0 (0%)	0 (0%)
<b>Unknown focus</b>	24 (13.0%)	9 (11.8%)	13 (16.3%)	2 (7.1%)
<b>Other</b>	2 (1.1%)	1 (1.3%)	1 (1.3%)	0 (0%)
<b>Simplified Acute Physiology Score III (SAPS-3)</b>				
<b>SAPS-3<sup>o</sup>, median score (IQR)</b>	63.0 (52.5 to 73.5)	64.0 (57.0 to 71.5)	60.5 (49.8 to 75.5)	66.5 (55.8 to 76.0)
<b>Life support, first 24 hours in ICU, No. (%)</b>				
<b>Invasive mechanical ventilation<sup>p</sup></b>	119 (64.7%)	57 (75.0%)	42 (52.5%)	20 (71.4%)
<b>Vasopressors<sup>q</sup></b>	150 (81.5%)	66 (86.8%)	58 (72.5%)	26 (92.9%)
<b>Renal replacement therapy<sup>r</sup></b>	36 (19.6%)	19 (25.0%)	13 (16.3%)	4 (14.3%)
• CRRT	29 (15.8%)	15 (19.7%)	10 (12.5%)	4 (14.3%)
• HD	7 (3.8%)	4 (5.3%)	3 (3.8%)	0 (0%)
<b>No use of life support first 24 hours in ICU</b>	23 (12.5%)	6 (7.9%)	16 (20.0%)	1 (3.6%)
<b>Indication for antibiotic treatment at inclusion<sup>s</sup>, No. (%)</b>				
	184	83 (45.1%)	101 (54.9%)	-
• Prophylactic	34 (18.5%)	4 (4.8%)	30 (29.7%)	-
• Empirical	143 (77.7%)	73 (88.0%)	70 (69.3%)	-

• Definitive	6 (3.3%)	5 (6.0%)	1 (1.0%)	-
• Unknown	1 (0.5%)	1 (1.2%)	0 (0%)	-
<b>Antibiotic treatment prior to ICU admission</b>	<b>Overall (N=184)</b>	<b>Meropenem (N=76)</b>	<b>Piperacillin/tazobactam (N=80)</b>	<b>Meropenem and piperacillin/tazobactam (N=28)</b>
<b>Treated with piperacillin/tazobactam at ICU-admission<sup>†</sup></b>	69 (37.5%)	2 (2.6%)	51 (63.8%)	16 (57.1%)
<b>Treated with meropenem at ICU-admission</b>	60 (32.6%)	53 (69.7%)	1 (1.3%)	6 (21.4%)
• Had received piperacillin/tazobactam before meropenem was prescribed	24 (13.0%)	18 (23.7%)	1 (1.3%)	5 (17.9%)
<b>Treated with both agents at ICU-admission</b>	2 (1.1%)	2 (2.6%)	0 (0%)	0 (0%)
<b>No ongoing treatment with piperacillin/tazobactam or meropenem at ICU-admission</b>	53 (28.8%)	19 (25.0%)	28 (35.0%)	6 (21.4%)
• Had received piperacillin/tazobactam ≤24 hours before ICU-admission	8 (4.3%)	3 (3.9%)	5 (6.3%)	0 (0%)
• Had received meropenem ≤24 hours before ICU-admission	1 (0.5%)	0 (0%)	1 (1.3%)	0 (0%)
• Had neither received piperacillin/tazobactam or meropenem ≤24 hours before ICU-admission	44 (23.9%)	16 (21.1%)	22 (27.5%)	6 (21.4%)
<b>Antibiotic treatment during ICU-admission</b>				
<b>Change<sup>u</sup> from meropenem to piperacillin/tazobactam No. (%)</b>	4 (2.2%)	NA	1 (1.3%)	3 (10.7%)
<b>Reason for change</b>				
• Enhanced microbial coverage	3 (1.6%)	NA	1 (1.2%)	2 (7.1%)
• Other	1 (0.5%)	NA	0 (0%)	1 (3.6%)
<b>Change<sup>u</sup> from piperacillin/tazobactam to meropenem No. (%)</b>	21 (11.4%)	1 (1.3%)	NA	20 (71.4%)
<b>Reason for change</b>				
• Clinical deterioration	7 (3.8%)	0 (0%)	NA	7 (25.0%)
• Enhanced microbial coverage	14 (7.6%)	1 (1.3%)	NA	13 (46.4%)
• Resistance	1 (0.5%)	0 (0%)	NA	1 (3.6%)
• Other	3 (1.6%)	0 (0%)	NA	3 (10.7%)
• Unknown	1 (0.5%)	0 (0%)	NA	1 (3.6%)

Abbreviations: *No./N*: numbers; *IQR*: Interquartile range; *ICU*: Intensive Care Unit; *MRSA*: Methicillin-Resistant *Staphylococcus aureus*; *CPO*: Carbapenemase-Producing Organisms; *ESBL*: Extended Spectrum Beta-Lactamase; *VRE*: Vancomycin-Resistant *Enterococci*; *SAPS-3*: Simplified Acute Physiology Score III; *CRRT*: Continuous Renal Replacement Therapy; *HD*: haemodialysis.

- <sup>a</sup> Information on height was missing for 1 (0.5%) patient
- <sup>b</sup> Antibiotic allergy: Any antibiotic allergy registered in the patients' electronic medical record
- <sup>c</sup> Treatment at time of hospital admission with any anti-diabetic medications.
- <sup>d</sup> Adults: Daily use of prednisolone  $\geq 20$ mg or other steroid-equivalent dose for minimum 10 days in a row. Pediatric patients: Daily use of prednisolone 1mg/kg/body weight other steroid in equivalent dose for minimum 10 days in a row.
- <sup>e</sup> Proven non-haematological metastasis by surgery, CT-scan, or any other method.
- <sup>f</sup> Any transplant of liver, kidney, heart, pancreas, lung(s).
- <sup>g</sup> Need for chronic renal support including continuous or intermittent renal replacement therapy or S-creatinine  $> 300 \mu\text{mol/L}$  prior to hospital admission. OR "Chronic Kidney Disease"/"CKD" found written in text in medical record by physician.
- <sup>h</sup> Serum creatinine 3 times baseline OR Increase in serum creatinine to  $353.6 \text{ mmol/l}$  OR Initiation of renal replacement therapy OR "Acute Kidney Injury"/"AKI"/"Akut nyresvigt" found written in text in medical record by physician.
- <sup>i</sup> Antibiotic resistance confirmed by positive cultures registered in medical record prior to ICU admission OR positive screening test for bacterium with acquired antibiotic resistance  $\leq 12$  hours after ICU-admission.
- <sup>j</sup> No clinical or paraclinical signs of infection.
- <sup>k</sup> Only registered among those with suspected infection at inclusion, N=155.
- <sup>l</sup> Infection present on admission to hospital or developing within 48 h of admission.
- <sup>m</sup> Infection not present on admission to hospital however developed 48 h or more after admission or secondary to a medical/surgical intervention.
- <sup>n</sup> Patients who received both agents during ICU stay received these sequentially, i.e., they received one of the two agents at inclusion, which was hereafter changed to the other (typically piperacillin/tazobactam first). Baseline characteristics regarding status of infection represent data from the first antibiotic treatment registered.
- <sup>o</sup> Only registered on adult patients. Score missing for 65 (35.3%) patients; 21 (27.6%) of the patients who received meropenem, 32 (40%) of the patients receiving piperacillin/tazobactam and 12 (42.9%) among patients receiving both agents.
- <sup>p</sup> Invasive mechanical ventilation, invasive mechanical ventilation is defined as the use of positive pressure ventilation using a ventilator via a cuffed tube (oral, nasal or tracheostomy). CPAP is NOT invasive mechanical ventilation.
- <sup>q</sup> any continuous treatment with norepinephrine, epinephrine, phenylephrine, vasopressin analogues, dopamine, dobutamine, milrinone or levosimendan
- <sup>r</sup> any form of renal replacement therapy (e.g. dialysis, hemofiltration or hemodiafiltration).
- <sup>s</sup> No patients were in simultaneous therapy with piperacillin/tazobactam and meropenem during ICU stay, indication for treatment is presented for the antibiotics respectively and not after stratification model. Thus, patients treated with both antibiotics during ICU stay was already included when change to the other studied antibiotic agent was made. The table reflects that those patients receiving both agents during ICU stay typically started with piperacillin/tazobactam.
- <sup>t</sup> None of the patients treated with piperacillin/tazobactam upon ICU-admission had received meropenem within 24 hours before receiving piperacillin/tazobactam.
- <sup>u</sup>  $\leq 24$  hours between termination of piperacillin/tazobactam and initiating treatment with meropenem, or *vice versa*.
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Table 2. Primary and Secondary Outcomes. All results.

	<b>Overall (N=184)</b>	<b>Meropenem (N=76)</b>	<b>Piperacillin/ tazobactam (N=80)</b>	<b>Meropenem and piperacillin/tazoba ctam (N=28)</b>
<b>90-day mortality<sup>a</sup></b>	49	19	22	8
<b>No. (%) [95% CI]<sup>b</sup></b>	(26.9%) [20.6 to 34.0]	(25.7%) [16.2 to 37.2]	(27.5%) [18.1 to 38.6]	(28.6%) [13.2 to 48.7]
<b>Outcome ICU stay</b>				
<b>No. (%) [95% CI]<sup>b</sup></b>				
• Discharged to another ICU	27 (14.7%) [9.9 to 20.6]	10 (13.2%) [6.5 to 22.9]	12 (15.0%) [8.0 to 24.7]	5 (17.9%) [6.1 to 36.9]
• Discharged to ward	128 (69.6%) [62.4 to 76.1]	52 (68.4%) [56.7 to 78.6]	57 (71.3%) [60.0 to 80.8]	19 (67.9%) [47.6 to 84.1]
• Death	29 (15.8%) [10.8 to 21.8]	14 (18.4%) [10.5 to 29.0]	11 (13.8%) [7.1 to 23.3]	4 (14.3%) [4.0 to 32.7]
<b>ICU readmission<sup>c</sup></b>	13 (7.1%) [4.5 to 13.9]	4 (5.3%) [1.8 to 15.7]	6 (7.5%) [3.3 to 18.0]	3 (10.7%) [2.7 to 32.4]
<b>Length of ICU stay in days, median (IQR)</b>	3.5 (2.5 to 8.5)	5.5 (2.5 to 9.5)	2.5 (1.5 to 4.5)	9.5 (3.5 to 18)
<b>Procalcitonin during ICU-stay</b>				
<b>No. (%) [95% CI]<sup>b</sup></b>				
• Measured at day 1	105 (57.1%) [49.6 to 64.3]	43 (56.6%) [44.7 to 67.9]	46 (57.5%) [45.9 to 68.5]	16 (57.1%) [37.2 to 75.5]
• Measured daily ≥ 3 days	71 (38.6%) [31.5 to 46.0]	38 (50.0%) [38.3 to 61.7]	16 (20.0%) [11.9 to 30.4]	17 (60.7%) [40.6 to 78.5]
• Number of tests during admission, median (IQR)	2 (1 to 5)	3.5 (1 to 7)	1 (1 to 3)	4.5 (2 to 9)
<b>Renal replacement therapy in ICU</b>				
<b>No. (%) [95% CI]<sup>b</sup></b>				
• CRRT	23 (12.5%) [39.7 to 71.5]	11 (14.5%) [33.5 to 79.7]	10 (12.5%) [41.9 to 91.6]	2 (7.1%) [3.2 to 65.1]
• HD	5 (2.7%) [4.1 to 26.2]	2 (2.6%) [1.3 to 33.1]	3 (3.8%) [4.7 to 50.8]	0 (0%) [0.0 to 36.9]
• Both	13 (7.1%) [18.1 to 48.1]	6 (7.9%) [12.6 to 56.6]	1 (1.3%) [0.2 to 33.9]	6 (21.4%) [34.9 to 96.8]
<b>Antibiotic resistance</b>	<b>Overall (N=184)</b>	<b>Meropenem (N=76)</b>	<b>Piperacillin/taz obactam (N=80)</b>	<b>Meropenem and piperacillin/tazoba ctam (N=28)</b>

<b>New positive culture with a resistant bacteria in specimen in ICU<sup>d,e</sup></b>				
<b>No. (%) [95% CI]<sup>b</sup></b>				
• MRSA	0 (0%) [0.0 to 2.0]	0 (0%) [0.0 to 4.7]	0 (0%) [0.0 to 4.5]	0 (0%) [0.0 to 12.3]
• CPO	0 (0%) [0.0 to 2.0]	0 (0%) [0.0 to 4.7]	0 (0%) [0.0 to 4.5]	0 (0%) [0.0 to 12.3]
• ESBL	0 (0%) [0.0 to 4.7]	0 (0%) [0.0 to 4.7]	0 (0%) [0.0 to 4.5]	0 (0%) [0.0 to 12.3]
• VRE <sup>f</sup>	2 (1.1%)	0 (0%)	0 (0%)	2 (7.1%)
• Linezolid-resistant <i>enterococci</i>	1 (0.5%) [0.0 to 3.0]	0 (0%) [0.0 to 4.7]	0 (0%) [0.0 to 4.5]	1 (3.6%) [0.1 to 18.3]
<b>New positive culture with a resistant bacteria in specimen after ICU-discharge but during index hospital admission<sup>g</sup></b>				
<b>No. (%) [95% CI]<sup>b</sup></b>				
• MRSA	0 (0%) [0.0 to 2.0]	0 (0%) [0.0 to 4.7]	0 (0%) [0.0 to 4.5]	0 (0%) [0.0 to 12.3]
• CPO	1 (0.5%) [0.0 to 3.0]	0 (0%) [0.0 to 4.7]	0 (0%) [0.0 to 4.5]	1 (3.6%) [0.1 to 18.3]
• ESBL	0 (0%) [0.0 to 2.0]	0 (0%) [0.0 to 4.7]	0 (0%) [0.0 to 4.5]	0 (0%) [0.0 to 12.3]
• VRE <sup>g</sup>	7 (3.8%)	3 (3.9%)	4 (5.0%)	0 (0%)
• Linezolid-resistant <i>enterococci</i>	1 (0.5%) [0.0 to 3.0]	0 (0%) [0.0 to 4.7]	1 (1.3%) [0.0 to 6.8]	0 (0%) [0.0 to 12.3]
<b>New positive culture with a resistant bacteria in specimen, time for development unknown due to missing tests<sup>h</sup> No. (%)</b>				
• MRSA	0 (0%)	0 (0%)	0 (0%)	0 (0%)
• CPO	0 (0%)	0 (0%)	0 (0%)	0 (0%)
• ESBL	0 (0%)	0 (0%)	0 (0%)	0 (0%)
• VRE	7 (3.8%)	2 (2.6%)	3 (3.8%)	2 (7.1%)
• Linezolid-resistant <i>enterococci</i>	0 (0%)	0 (0%)	0 (0%)	0 (0%)
<b>Treatment duration (days), median (IQR)</b>	<b>Overall<sup>i</sup></b>	<b>Pre-ICU</b>	<b>ICU</b>	
<b>Meropenem</b>	12 (8 to 17.5)	2 (1 to 4)	5 (3 to 11)	
<b>Piperacillin/tazobactam</b>	6 (4 to 10)	2 (1 to 3)	3 (2 to 5)	
Abbreviations: <i>No./N</i> : numbers; <i>IQR</i> : Interquartile range; <i>CI</i> : Confidence interval; <i>ICU</i> : Intensive Care Unit; <i>CRRT</i> : Continuous Renal Replacement Therapy; <i>HD</i> : haemodialysis; <i>MRSA</i> : Methicillin-Resistant <i>Staphylococcus aureus</i> ; <i>CPO</i> : Carbapenemase-Producing Organisms; <i>ESBL</i> : Extended Spectrum Beta-Lactamase; <i>VRE</i> : Vancomycin-Resistant <i>Enterococci</i> .				
<sup>a</sup> Two (1.1%) patients were lost to analysis on primary outcome. Both patients were treated with meropenem, corresponding to 2.6% of patients in this group.				

<sup>b</sup> Only presented for frequencies

<sup>c</sup> patient discharged from ICU and returning after  $\geq 24$  hours

<sup>d</sup> Antibiotic resistance not present at baseline test. Antibiotic resistance confirmed by positive cultures collected during ICU admission but earliest  $\geq 12$  hours after admission.

<sup>e</sup> Information on this variable is missing for one patient (0.5%).

<sup>f</sup> In this analysis we have excluded 95% confidence interval due to insecurities in time for development for 7 (43.8%) new cases of VRE during hospital stay.

<sup>g</sup> Antibiotic resistance not present at baseline test or during ICU-stay. Antibiotic resistance confirmed by positive cultures collected after ICU discharge but within same hospital stay.

<sup>h</sup> This part of table represent new cases of antibiotic resistance where time for development is unknown, therefore 95% confidence interval is not presented.

<sup>i</sup> This includes treatment duration pre ICU, during ICU stay and after ICU discharge. Patients who received both antibiotics in ICU within 90 days has, for practical reasons, been excluded from the analysis. The corresponding treatment duration for patients receiving both antibiotics within 90 days is median 12 days (IQR; 7 to 19.2).

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List of Variables

Variable	Baseline	AB-Form	Follow-Up
<b>Demographics</b>			
Date, hospital admission	x		
Date, ICU admission	x		
Social security number	x		
Weight	x		
Height	x		
Antibiotic allergy	x		
<b>Clinical data</b>			
Source of ICU admission	x		
Site of infection	x		
Infection, type - Nosocomial - Community-acquired	x		
Coexisting conditions - Diabetes - Haematologic cancer - Use of corticosteroids within 3 months prior to admission - Metastatic cancer - Solid organ transplant - Chronic Kidney Disease - Acute Kidney Injury	x		
Life-support within the first 24 hours after ICU-admission - Invasive mechanical ventilation - Vasopressors - Renal replacement therapy	x		
SAPS-3 (Simplified Acute Physiology Score)	x		
Antibiotic resistance at baseline - Methicillin-Resistant <i>Staphylococcus aureus</i> (MRSA) - Carbapenemase-Producing Organisms (CPO) - Extended Spectrum Beta-Lactamase (ESBL) - Vancomycin-Resistant <i>Enterococci</i> (VRE) - Other	x		
<b>Antibiotic treatment (piperacillin/tazobactam or meropenem) before ICU-admission</b>			
Treatment duration and location for initiation of treatment	x		
<b>Antibiotic treatment, ICU</b>			
Days in ICU before piperacillin/tazobactam or meropenem were prescribed		x	



Indication - Prophylactic - Empirical - Definitive - Unknown		x	
Dose		x	
Change of - Dose - Frequency - Termination, date		x	
<b>Follow-up</b>			
Length of stay, ICU			x
Readmission			x
Outcome on ICU discharge			x
Procalcitonin (frequencies and number of tests)			x
eGFR, ml/min/1.73m <sup>2</sup> Lowest value during ICU admission, adults			x
Creatinin (umol/l), population ≤18 years of age Highest value during ICU admission			
Renal replacement therapy during ICU-admission			x
New antibiotic resistance during ICU admission - MRSA - CPO - ESBL - VRE - Other			x
Change from piperacillin/tazobactam to meropenem or vice versa during ICU admission			x
Collection of relevant specimen if "yes" to above y/n			x
Duration of antibiotic treatment after ICU-discharge			x
New antibiotic resistance after ICU discharge but within same hospital stay - MRSA - CPO - ESBL - VRE - Other			x
Mortality day 90			x

## Definitions

### Baseline characteristics

#### Elective surgery, (y/n).

- Surgery planned 24 hours or more in advance during the current hospitalization but prior to ICU admission.

#### Antibiotic allergy, (y/n).

- Any antibiotic allergy registered in the patients electronic medical record

### Comorbidities prior to ICU admission

#### Acute kidney Injury, (y/n).

- Serum creatinine 3.0 times baseline OR Increase in serum creatinine to 353.6 µmol/l  
OR
- Initiation of renal replacement therapy  
OR
- "Acute Kidney Injury"/"AKI"/"Akut nyresvigt" found written in text in medical record by physician

#### Chronic renal failure, (y/n).

- Need for chronic renal support including continuous or intermittent renal replacement therapy or S-creatinine > 300 µmol/L prior to hospital admission.  
OR
- "Chronic Kidney Disease"/"CKD"/ found written in text in medical record by physician

#### Metastatic cancer, (y/n).

- Proven non-haematological metastasis by surgery, CT-scan, or any other method.

#### Diabetes mellitus, (y/n).

- Treatment at time of hospital admission with any anti-diabetic medications.

#### Chronic use of systemic corticosteroids within the last 3-months, (y/n).

- Adults: Daily use of prednisolone  $\geq 20$ mg or other steroid in equivalent dose for minimum 10 days in a row.
- Pediatric patients: Daily use of prednisolone 1mg/kg/body weight other steroid in equivalent dose for minimum 10 days in a row.

#### Any haematological malignancy, (y/n).

#### Major organ transplant, (y/n)

- Solid organ i.e., liver, kidney, heart, pancreas, lung(s).

### Life support

#### Infusion of vasopressors, (y/n).

- Any continuous treatment with norepinephrine, epinephrine, phenylephrine, vasopressin analogues, dopamine, dobutamine, milrinone or levosimendan.

Invasive mechanical ventilation, (y/n).

- Invasive mechanical ventilation is defined as the use of positive pressure ventilation using a ventilator via a cuffed tube (oral, nasal or tracheostomy). CPAP is NOT invasive mechanical ventilation.

Renal replacement therapy, (y/n).

- Any form of renal replacement therapy (e.g. dialysis, hemofiltration or hemodiafiltration) at any rate.

### Infection

- Community-acquired. Infection present on admission to hospital or developing within 48 h of admission.
- Nosocomial. Infection not present on admission to hospital and developing 48 h or more after admission or secondary to a medical/surgical intervention.
- Suspected infection at baseline y/n: clinical or clinically relevant paraclinical signs of infection noticed by physician.

### Antibiotic resistance

- Antibiotic resistance confirmed by positive cultures registered in medical record prior to ICU admission OR positive screening test for antibiotic resistance  $\leq 12$  hours after ICU-admission.
- Antibiotic resistance not present at baseline test. Antibiotic resistance confirmed by positive cultures collected during ICU admission but earliest  $\geq 12$  hours after admission.
- Antibiotic resistance not present at baseline test or during ICU-stay. Antibiotic resistance confirmed by positive cultures collected after ICU discharge but within same hospital stay