

Antimicrobial Resistance (AMR) Surveillance on Blood Culture Specimen in Public Hospitals and Clinics - Hospital Authority AMR Data (2020)

January 2022



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Background



Background

- The Hong Kong Strategy and Action Plan 2017-2022 was issued in July 2017
- Activity 1.2.1 suggests harmonising AMR surveillance reporting criteria with reference to the Global Antimicrobial Resistance Surveillance System (GLASS), developed by the World Health Organization (WHO)
- This presentation briefly accounts the surveillance findings of blood specimens from 2016 to 2020



Methodology



WHO GLASS Recommendations (1)

- Based on *WHO GLASS Manual for Early Implementation (2015)*:
 - WHO Priority Organisms captured:
 - *Escherichia coli*
 - *Klebsiella pneumoniae*
 - *Staphylococcus aureus*
 - *Salmonella* spp.
 - *Acinetobacter* spp.
 - *Streptococcus pneumoniae*
 - Organisms other than the above were grouped as “Other spp.”
 - Location of onset
 - Community-onset organisms isolated from blood specimen collected in non-inpatient settings or within 48 hours after hospital admission
 - Hospital-onset organisms isolated from blood specimen collected more than 48 hours after hospital admission
 - Using 48 hours instead of 2 calendar days of WHO as agreed by HA



WHO GLASS Recommendations (2)

- Based on *WHO GLASS Manual for Early Implementation (2015)*:
 - Removal of duplicate results (deduplication)
 - For each surveillance period (one calendar year), only the first result would be reported for each patient per specimen type per organism for the same location of onset
 - Antimicrobial susceptibility test (AST) result being “Intermediate” or “Resistant” was considered as “non-susceptible”
 - AST results derived from < 10 isolates per calendar year were excluded from analysis



Local Adaptation

- Taking local context into account, the following modifications were also agreed in consultation with HA experts in the Working Group:
 - To avoid misleading or interference by selection bias, percentages of non-susceptibility derived from less than 70% of total isolates were not reported, or remarked to remind readers to interpret with caution
 - Location of onset for *Salmonella* spp. and *Streptococcus pneumoniae*
 - Information on location of onset was not considered when analysing AST results, as they rarely cause hospital-associated infections
 - AST results were interpreted as “community (undifferentiated)-onset” as a whole
 - WHO’s definition of community- / hospital-onset still applies when presenting the organisms by location of onset
 - “Day-14” rule
 - Positive cultures for the same organism within a 14-day period from the same patient would be regarded as a single episode

Graphical Illustration
of “Day-14” rule



Scope of Data

- The following information was collected from patients who had blood culture:
 - Demographic data
 - Microbiology data
 - Organisms cultured
 - AST results
 - Susceptible (sensitive)
 - Non-susceptible (intermediate or resistant)



Broad-spectrum Antimicrobials (Big Guns)

- Where appropriate, AST results of the following broad-spectrum antimicrobials identified by experts in HA were examined because of their importance on treating resistant infections
 - Piperacillin/tazobactam
 - Ceftazidime
 - Cefoperazone/sulbactam
 - Cefepime
 - Ceftaroline fosamil
 - Ceftolozane/tazobactam
 - Ceftazidime/avibactam
 - Meropenem
 - Ertapenem
 - Imipenem/cilastatin
 - Vancomycin
 - Linezolid
 - Daptomycin
 - Colistin
 - Teicoplanin



Scope of Reporting

- Overview on patients with blood culture
 - Number of patients from whom a blood culture was taken
- Overview on WHO priority organisms isolated from blood
 - Number of patients with positive and negative culture results
 - Distribution of organisms by location of onset
- AST results on WHO priority organisms
 - Number and % of patients with non-susceptibility results
 - Trend of antimicrobial non-susceptibility
 - 2019 vs 2020
 - 2016 - 2020 trend



Statistical Analysis on AST Results

- % non-susceptibility (% NS) in 2019 vs 2020
 - Fisher's exact test or chi-squared test for comparison
 - $P < 0.05$ was considered statistically significant
- 2016 – 2020 trend analysis
 - Year 2016 was chosen as the baseline for comparison as the Hong Kong Strategy and Action Plan on AMR was issued in 2017 and such decision was endorsed by the High Level Steering Committee
 - One-way Cochran-Armitage test was used to look for trend
 - $P < 0.05$ was considered statistically significant
 - $P < 0.01$ was considered statistically highly significant
 - For ease of presentation of trends with $p < 0.05$
 - Increasing trend of % NS – Red in colour
 - Decreasing trend of % NS – Green in colour

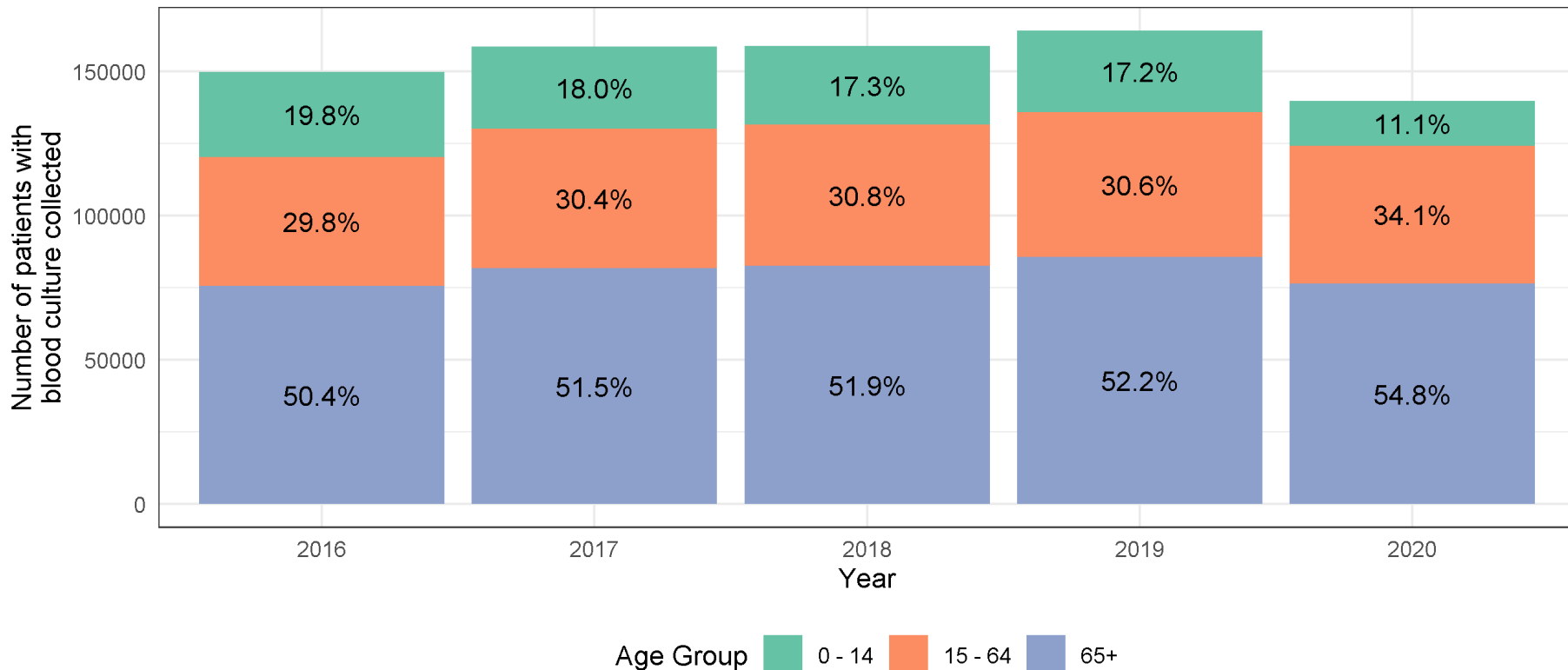


Results

1. Overview on patients with blood culture



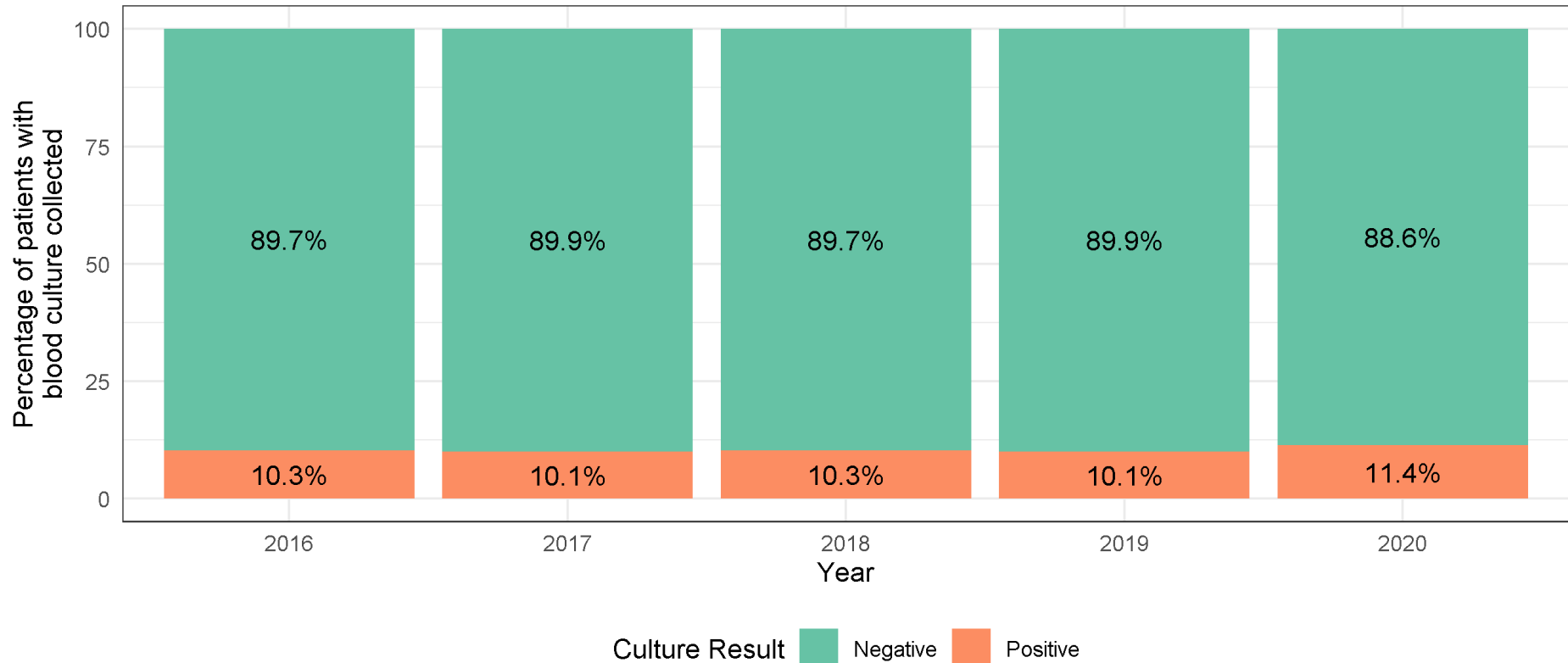
Age distribution of patients with blood culture



- ↑ No. of patients with blood culture from 2016 to 2019 (~150,000 in 2016 to ~164,000 in 2019)
- ↓ No. of patients with blood culture in 2020 (~140,000) which was contributed mostly by the age group of 0 - 14 (44.9% drop from 28,000 in 2019 to 16,000 in 2020)
- > 50% patients aged 65 years or above each year



Percentage of Patients with Positive Blood Culture



- % patients with positive blood culture remained stable over the past years at around 10 – 11%

Results

2. Overview on WHO priority organisms isolated from blood



Distribution of Organisms by Year

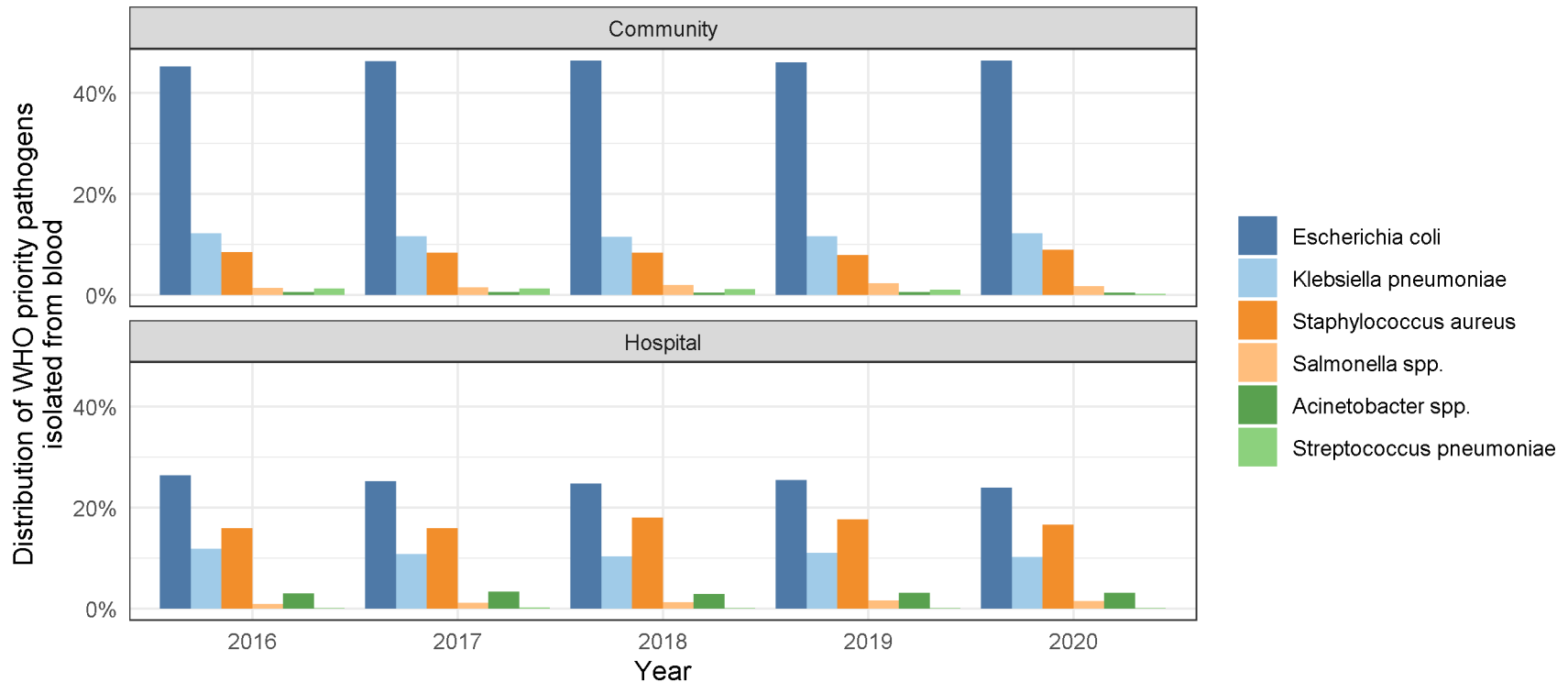
Organism	Number of patients with positive blood culture by organisms and year (%)				
	2016	2017	2018	2019	2020
<i>Escherichia coli</i>	6,330 (40.9%)	6,590 (41.2%)	6,750 (41.2%)	6,830 (41.2%)	6,560 (41.3%)
<i>Klebsiella pneumoniae</i>	1,910 (12.3%)	1,860 (11.7%)	1,880 (11.4%)	1,930 (11.7%)	1,890 (11.9%)
<i>Staphylococcus aureus</i>	1,660 (10.7%)	1,700 (10.6%)	1,830 (11.2%)	1,780 (10.8%)	1,780 (11.2%)
<i>Salmonella</i> spp.	210 (1.3%)	240 (1.5%)	300 (1.8%)	360 (2.2%)	280 (1.7%)
<i>Acinetobacter</i> spp.	200 (1.3%)	230 (1.4%)	200 (1.2%)	220 (1.3%)	190 (1.2%)
<i>Streptococcus pneumoniae</i>	150 (1.0%)	160 (1.0%)	150 (0.9%)	130 (0.8%)	30 (0.2%)
Other spp.	6,970 (45.0%)	7,200 (45.0%)	7,290 (44.5%)	7,440 (44.9%)	7,180 (45.1%)
Total no. of patients	15,500	16,000	16,410	16,550	15,890

Note:

- Patient headcounts were rounded to nearest ten, percentages were rounded to one decimal place
- A patient might have blood culture(s) with growth of multiple organisms
- Significant drop in number of patients with *Streptococcus pneumoniae* isolated from blood in year 2020 was observed.



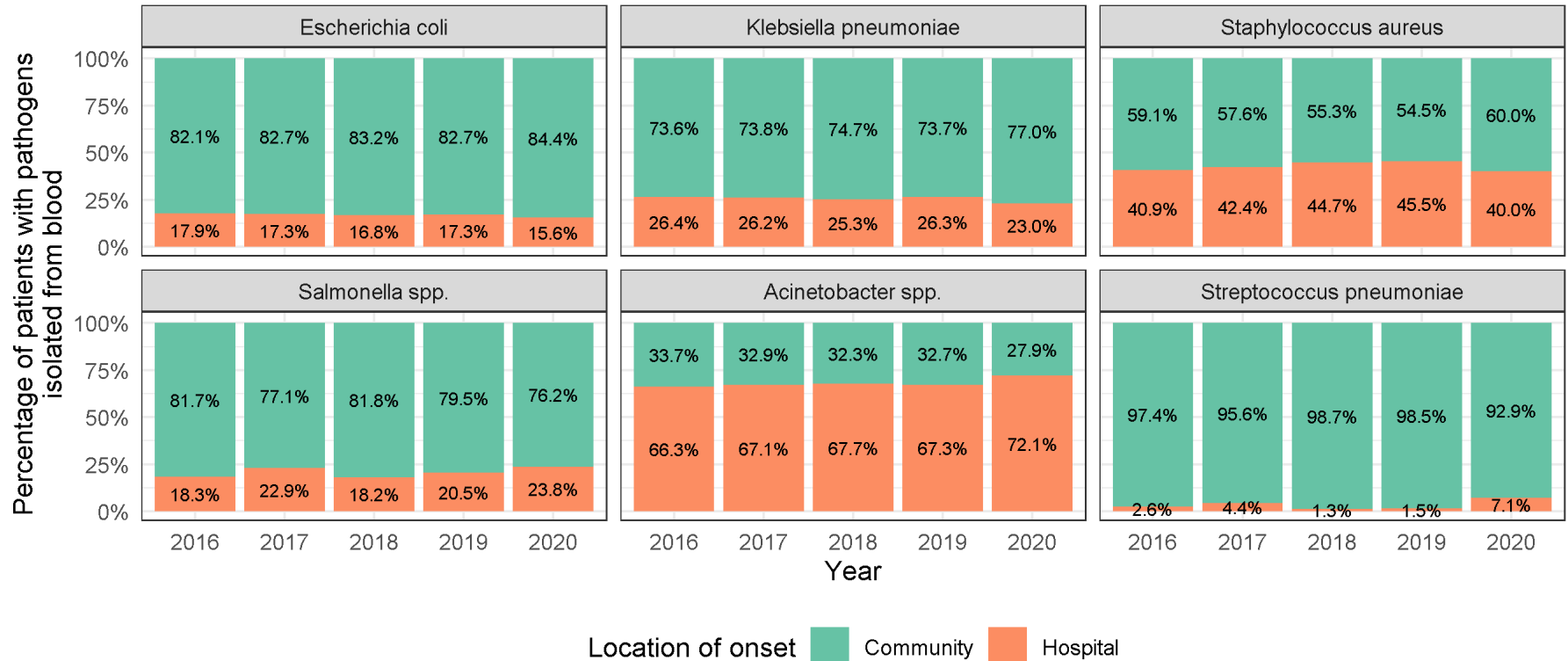
Distribution of Organisms by Location of Onset (1)



- By location of onset (following WHO's definition):
 - Distributions of the 6 priority organisms of hospital- and community-onset were similar over the years
 - For community-onset specimens in 2020, 46.4% of patients with positive blood culture had *Escherichia coli* isolated, followed by *Klebsiella pneumoniae* (12.2%) and *Staphylococcus aureus* (8.9%)
 - For hospital-onset specimens in 2020, 24.0% of patients with positive blood culture had *Escherichia coli* isolated, followed by *Staphylococcus aureus* (16.6%) and *Klebsiella pneumoniae* (10.1%)



Distribution of Organisms by Location of Onset (2)



In Year 2020:

- *Escherichia coli* (84.4%), *Klebsiella pneumoniae* (77.0%), *Salmonella* spp. (76.2%) and *Streptococcus pneumoniae* (92.9%) were predominantly community-onset
- *Acinetobacter* spp. (72.1%) was predominantly hospital-onset

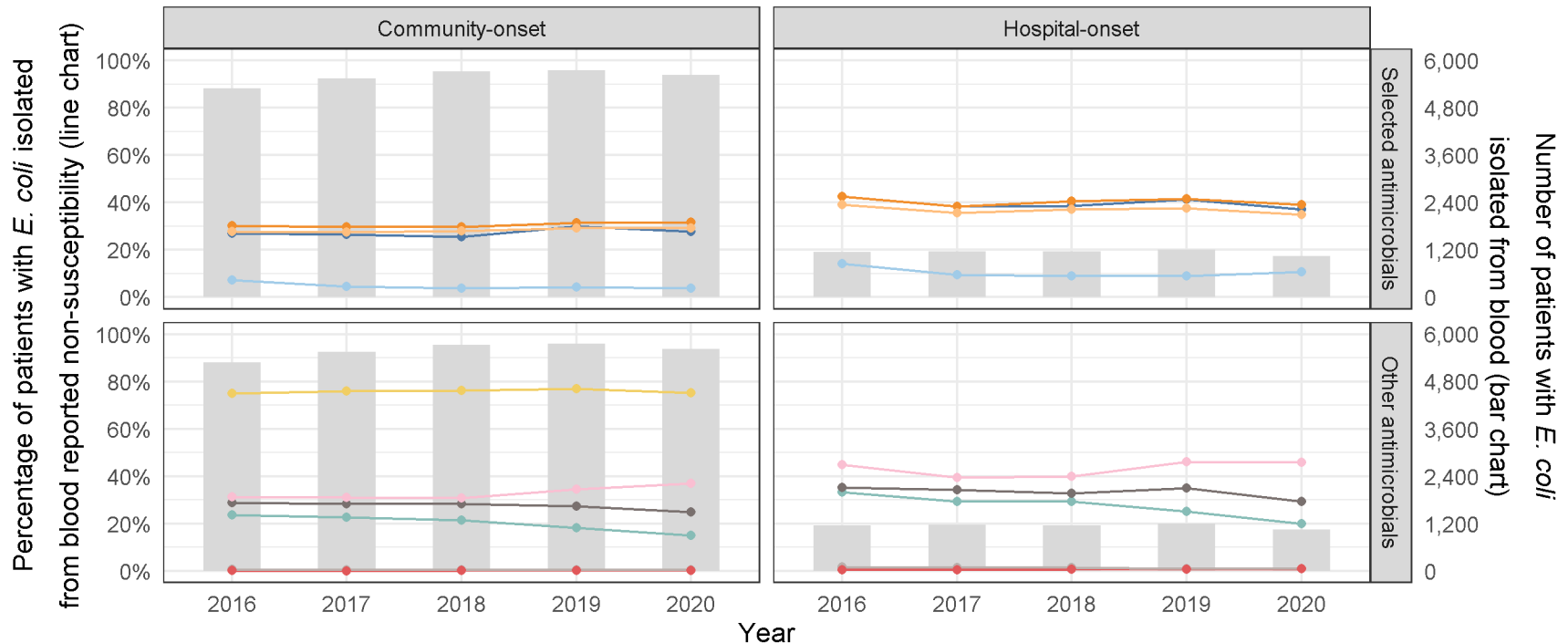


Results

3.1 AST results for *Escherichia coli*



AST results for *E. coli* - Overview



Selected antimicrobials

- Amoxicillin/ Clavulanate
- Piperacillin/ Tazobactam
- Cefuroxime
- Cefotaxime

Other antimicrobials

- Amikacin
- Ampicillin
- Cefepime
- Ertapenem
- Gentamicin
- Levofloxacin

- % NS to selected antimicrobials (i.e. more commonly used antimicrobials) were lower among *E. coli* isolates of community-onset than those of hospital-onset



AST results for *E. coli* - 2019 vs 2020

Antimicrobial group	Antimicrobial (Big guns in yellow)	Community-onset			Hospital-onset		
		% NS		p-value [†]	% NS		p-value [†]
		2019	2020	19 vs 20	2019	2020	19 vs 20
Penicillins with extended spectrum	Ampicillin	76.9%	75.3%	-	-	-	-
Combinations of penicillins, incl. beta-lactamase inhibitors	Amoxicillin/clavulanate	29.8%	27.8%	<0.05	41.2%	37.0%	<0.05
	Piperacillin/tazobactam	4.4%	3.8%	-	9.0%	10.7%	-
Second-generation cephalosporins	Cefuroxime	31.3%	31.6%	-	41.5%	39.0%	-
Third-generation cephalosporins	Cefotaxime	29.2%	29.1%	-	37.7%	35.0%	-
	Ceftazidime	14.7%	14.0%	-	21.1%	17.4%	-
Fourth-generation cephalosporins	Cefepime	18.2%	15.1%	<0.05	25.2%	19.9%	<0.05
	Meropenem	-	-	-	0.8%*	1.2%	-
Carbapenems	Ertapenem	0.06%	0.2%	-	0.6%	1.0%	-
	Imipenem	0.02%	0.1%*	-	0.3%	0.5%*	-
	Gentamicin	27.2%	24.9%	<0.05	35.0%	29.4%	<0.05
Other aminoglycosides	Amikacin	0.4%	0.5%	-	0.8%	0.9%	-
	Levofloxacin	34.6%	37.1%	<0.05	46.1%	45.9%	-

* Non-susceptibility percentage should be interpreted with caution as the figure is derived from less than 70% of total isolates for surveillance. The figure may be affected by selection bias.

[†]P-value was calculated using chi-squared test or Fisher's exact test, whether appropriate

Broad spectrum antimicrobials (Big Guns) highlighted in yellow

- Statistically significant results related to broad-spectrum antimicrobials
 - Both community- and hospital-onset isolates showed ↓ % NS towards cefepime



AST results for *E. coli*

Trend 2016-2020 (Community-onset)

Antimicrobial group	Antimicrobial (Big guns in yellow)	Community-onset					p-value [†] 2016 - 2020
		% NS					
		2016	2017	2018	2019	2020	
Penicillins with extended spectrum	Ampicillin	74.9%	75.9%	76.1%	76.9%	75.3%	-
Combinations of penicillins, incl. beta-lactamase inhibitors	Amoxicillin/clavulanate	27.1%	26.4%	25.4%	29.8%	27.8%	↗ p <0.01
	Piperacillin/tazobactam	7.2%	4.5%	3.7%	4.4%	3.8%	↘ p <0.01
Second-generation cephalosporins	Cefuroxime	30.1%	29.7%	29.6%	31.3%	31.6%	↗ p <0.01
Third-generation cephalosporins	Cefotaxime	27.8%	27.4%	28.0%	29.2%	29.1%	↗ p <0.05
	Ceftazidime	15.0%	13.9%*	13.3%	14.7%	14.0%	-
Fourth-generation cephalosporins	Cefepime	23.6%	22.6%	21.5%	18.2%	15.1%	↘ p <0.01
Carbapenems	Ertapenem	0.1%	0.04%	0.1%	0.06%	0.2%	-
	Imipenem	0.04%	0%	0.05%	0.02%	0.1%*	↗ p <0.05
Other aminoglycosides	Gentamicin	28.9%	28.3%	28.2%	27.2%	24.9%	↘ p <0.01
	Amikacin	0.7%	0.4%	0.4%	0.4%	0.5%	-
Fluoroquinolones	Levofloxacin [‡]	31.2%	31.0%	30.8%	34.6%	37.1%	↗ p <0.01

Legend: ↗ Increasing trend; ↘ Decreasing trend

Broad spectrum antimicrobials (Big Guns) highlighted in yellow

* Non-susceptibility percentage should be interpreted with caution as the figure is derived from less than 70% of total isolates for surveillance. The figure may be affected by selection bias.

[†]P-value reports the statistical significance of trend observed during the captioned time period, it was calculated using Cochran-Armitage test, only trends with statistical significance (i.e. p<0.05) and high statistical significance (p<0.01) were reported

[‡]Revised fluoroquinolones interpretive criteria for Enterobacteriaceae (except *Salmonella* spp.) was released by CLSI in 2019. The increase in 2019 and thereafter compared with 2018 and before may be contributed by a change in CLSI criteria.

- Statistically significant results related to broad-spectrum antimicrobials
 - ↘ trends towards piperacillin/tazobactam and cefepime
 - ↗ trends towards imipenem but not with ertapenem; %NS were <1%. The 2020 result of imipenem was derived from less than 70% of the total isolates and therefore should be interpreted with caution



AST results for *E. coli*

Trend 2016-2020 (Hospital-onset)

Antimicrobial group	Antimicrobial (Big guns in yellow)	Hospital-onset					p-value [†]
		% NS					
		2016	2017	2018	2019	2020	
Penicillins with extended spectrum	Ampicillin	85.3%	85.5%	85.8%*	84.9%*	85.6%*	-
Combinations of penicillins, incl. beta-lactamase inhibitors	Amoxicillin/clavulanate	42.6%	38.3%	38.6%	41.2%	37.0%	↘ p <0.05
	Piperacillin/tazobactam	14.1%	9.5%	9.0%	9.0%	10.7%	↘ p <0.01
Second-generation cephalosporins	Cefuroxime	42.5%	38.4%	40.6%	41.5%	39.0%	-
Third-generation cephalosporins	Cefotaxime	39.1%	35.6%	37.2%	37.7%	35.0%	-
	Ceftazidime	23.2%	20.5%*	18.3%*	21.1%	17.4%	↘ p <0.01
Fourth-generation cephalosporins	Cefepime	33.1%	29.4%	29.4%	25.2%	19.9%	↘ p <0.01
	Meropenem	0.7%*	0.8%*	1.3%*	0.8%*	1.2%	-
Carbapenems	Ertapenem	0.5%	0.5%	0.6%	0.6%	1.0%	-
	Imipenem	0.2%	0.4%	0.5%	0.3%	0.5%*	-
Other aminoglycosides	Gentamicin	35.3%	34.2%	32.7%	35.0%	29.4%	↘ p <0.01
	Amikacin	1.6%	1.3%	1.4%	0.8%	0.9%	↘ p <0.05
Fluoroquinolones	Levofloxacin [‡]	44.8%	39.5%	40.0%	46.1%	45.9%	↗ p <0.05

Legend: ↗ Increasing trend; ↘ Decreasing trend

Broad spectrum antimicrobials (Big Guns) highlighted in yellow

* Non-susceptibility percentage should be interpreted with caution as the figure is derived from less than 70% of total isolates for surveillance. The figure may be affected by selection bias.

[†]P-value reports the statistical significance of trend observed during the captioned time period, it was calculated using Cochran-Armitage test, only trends with statistical significance (i.e. p<0.05) and high statistical significance (p<0.01) were reported

[‡]Revised fluoroquinolones interpretive criteria for Enterobacteriaceae (except *Salmonella* spp.) was released by CLSI in 2019. The increase in 2019 and thereafter compared with 2018 and before may be contributed by a change in CLSI criteria.

- Statistically significant results related to broad-spectrum antimicrobials
 - ↘ trends towards piperacillin/tazobactam, ceftazidime and cefepime

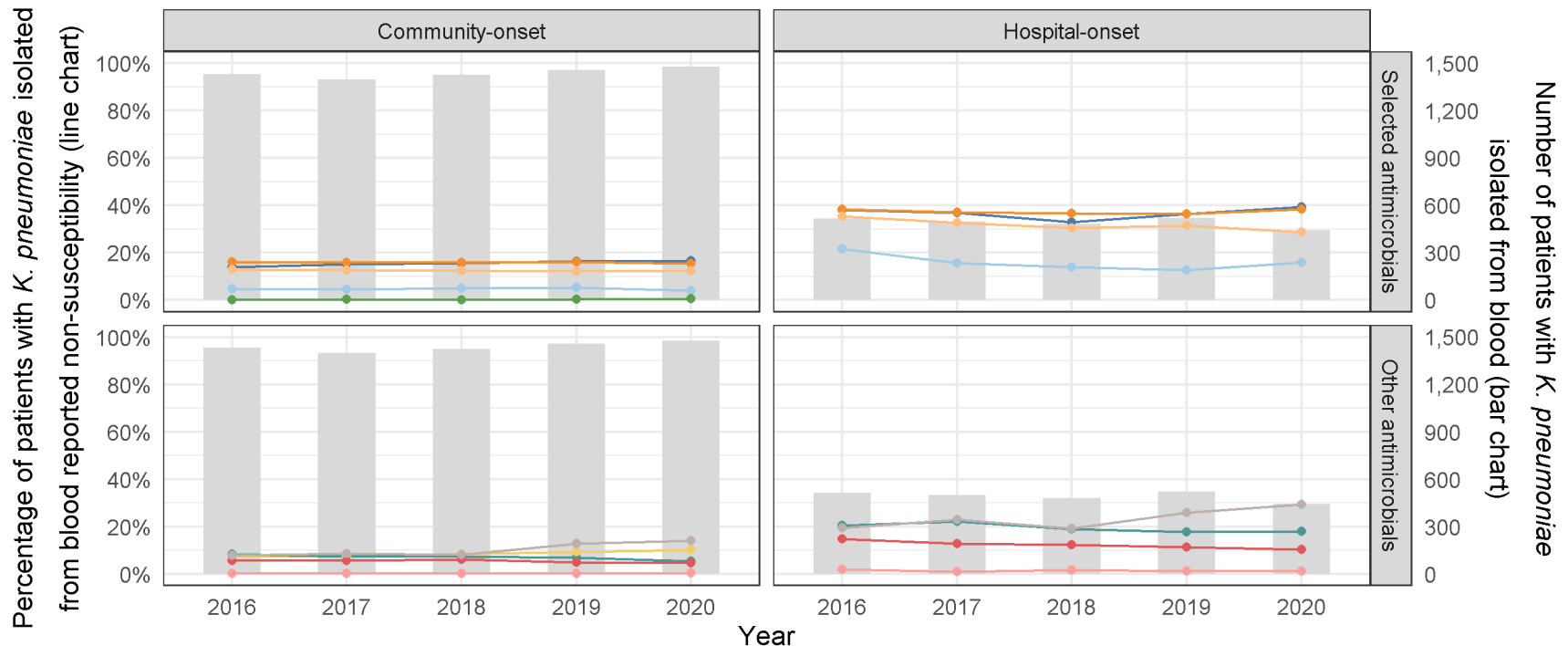


Results

3.2 AST results for *Klebsiella pneumoniae*



AST results for *K. pneumoniae* - Overview



Selected antimicrobials

- Amoxicillin/ Clavulanate
- Piperacillin/ Tazobactam
- Cefuroxime
- Cefotaxime
- Imipenem

Other antimicrobials

- Amikacin
- Cefepime
- Ceftazidime
- Gentamicin
- Levofloxacin

- % NS to antimicrobials were lower among *K. pneumoniae* isolates of community-onset than those of hospital-onset



AST results for *K. pneumoniae* - 2019 vs 2020

Antimicrobial group	Antimicrobial (Big guns in yellow)	Community-onset			Hospital-onset		
		% NS		p-value [†]	% NS		p-value [†]
		2019	2020	19 vs 20	2019	2020	19 vs 20
Combinations of penicillins, incl. beta-lactamase inhibitors	Amoxicillin/clavulanate	16.3%	16.5%	-	36.5%	39.4%	-
	Piperacillin/tazobactam	5.2%	4.0%	-	12.6%	15.7%	-
Second-generation cephalosporins	Cefuroxime	16.2%	15.4%	-	36.3%	38.2%	-
Third-generation cephalosporins	Cefotaxime	12.2%	12.4%	-	31.4%	28.7%	-
	Ceftazidime	9.4%	9.9%	-	24.0%	24.6%	-
Fourth-generation cephalosporins	Cefepime	6.8%	5.5%	-	17.8%	18.0%	-
	Meropenem	0.6%	0.2%	-	2.7%	4.6%	-
	Ertapenem	0.8%	0.3%	-	2.9%	4.0%	-
Carbapenems	Imipenem	0.2%	0.5%	-	-	-	-
	Co-trimoxazole	-	-	-	38.9%	40.4%*	-
Other aminoglycosides	Gentamicin	4.9%	4.6%	-	11.3%	10.4%	-
	Amikacin	0.2%	0.3%	-	1.2%	1.2%	-
Fluoroquinolones	Levofloxacin	12.7%	14.0%	-	25.9%	29.4%	-

* Non-susceptibility percentage should be interpreted with caution as the figure is derived from less than 70% of total isolates for surveillance. The figure may be affected by selection bias.

[†]P-value was calculated using chi-squared test or Fisher's exact test, whether appropriate

Broad spectrum antimicrobials (Big Guns) highlighted in yellow

- No statistically significant results related to broad-spectrum antimicrobials



AST results for *K. pneumoniae*

Trend 2016-2020 (Community-onset)

Antimicrobial group	Antimicrobial (Big guns in yellow)	Community-onset					p-value [†]
		% NS					
		2016	2017	2018	2019	2020	2016 - 2020
Combinations of penicillins, incl. beta-lactamase inhibitors	Amoxicillin/clavulanate	13.9%	15.1%	15.6%	16.3%	16.5%	↗ p <0.05
	Piperacillin/tazobactam	4.9%	4.6%	5.1%	5.2%	4.0%	-
Second-generation cephalosporins	Cefuroxime	16.1%	16.0%	15.8%	16.2%	15.4%	-
	Cefotaxime	12.9%	12.6%	12.5%	12.2%	12.4%	-
Third-generation cephalosporins	Ceftazidime	7.3%	7.4%	8.4%	9.4%	9.9%	↗ p <0.01
	Cefepime	8.4%	7.3%	7.3%	6.8%	5.5%	↘ p <0.01
Carbapenems	Meropenem	0.4%*	0.3%*	0.1%*	0.6%	0.2%	-
	Imipenem	0.2%	0.3%	0%	0.2%	0.5%	-
Other aminoglycosides	Gentamicin	5.5%	5.5%	6.0%	4.9%	4.6%	-
	Amikacin	0.3%	0.2%	0.1%	0.2%	0.3%	-
Fluoroquinolones	Levofloxacin [‡]	7.9%	8.5%	8.0%	12.7%	14.0%	↗ p <0.01

Legend: ↗ Increasing trend; ↘ Decreasing trend

Broad spectrum antimicrobials (Big Guns) highlighted in yellow

* Non-susceptibility percentage should be interpreted with caution as the figure is derived from less than 70% of total isolates for surveillance. The figure may be affected by selection bias.

[†]P-value reports the statistical significance of trend observed during the captioned time period, it was calculated using Cochran-Armitage test, only trends with statistical significance (i.e. p<0.05) and high statistical significance (p<0.01) were reported

[‡]Revised fluoroquinolones interpretive criteria for Enterobacteriaceae (except *Salmonella* spp.) was released by CLSI in 2019. The increase in 2019 and thereafter compared with 2018 and before may be contributed by a change in CLSI criteria.

- Statistically significant results related to broad-spectrum antimicrobials
 - ↓ trends towards cefepime
 - ↑ trend towards ceftazidime



AST results for *K. pneumoniae*

Trend 2016-2020 (Hospital-onset)

Antimicrobial group	Antimicrobial (Big guns in yellow)	Hospital-onset					p-value [†]
		% NS					
		2016	2017	2018	2019	2020	
Combinations of penicillins, incl. beta-lactamase inhibitors	Amoxicillin/clavulanate	38.1%	36.8%	33.0%	36.5%	39.4%	-
	Piperacillin/tazobactam	21.5%	15.6%	13.8%	12.6%	15.7%	↘ p <0.01
Second-generation cephalosporins	Cefuroxime	38.4%	37.0%	36.6%	36.3%	38.2%	-
Third-generation cephalosporins	Cefotaxime	35.4%	32.6%	30.5%	31.4%	28.7%	↘ p <0.05
	Ceftazidime	22.8%	25.4%*	23.6%	24.0%	24.6%	-
Fourth-generation cephalosporins	Cefepime	20.3%	22.2%	18.8%	17.8%	18.0%	-
Carbapenems	Meropenem	1.2%*	0.4%*	3.9%	2.7%	4.6%	↗ p <0.01
	Imipenem	1.3%	0.5%	3.2%*	2.3%*	4.0%*	↗ p <0.01
Combinations of sulfonamides and trimethoprim, incl. derivatives	Co-trimoxazole	48.3%*	42.6%*	36.9%*	38.9%	40.4%*	↘ p <0.05
Other aminoglycosides	Gentamicin	14.6%	12.9%	12.4%	11.3%	10.4%	↘ p <0.05
	Amikacin	2.0%	1.0%	1.7%	1.2%	1.2%	-
Fluoroquinolones	Levofloxacin [‡]	19.5%	22.8%	19.2%	25.9%	29.4%	↗ p <0.01

Legend: ↗ Increasing trend; ↘ Decreasing trend

Broad spectrum antimicrobials (Big Guns) highlighted in yellow

* Non-susceptibility percentage should be interpreted with caution as the figure is derived from less than 70% of total isolates for surveillance. The figure may be affected by selection bias.

[†]P-value reports the statistical significance of trend observed during the captioned time period, it was calculated using Cochran-Armitage test, only trends with statistical significance (i.e. p<0.05) and high statistical significance (p<0.01) were reported

[‡]Revised fluoroquinolones interpretive criteria for Enterobacteriaceae (except *Salmonella* spp.) was released by CLSI in 2019. The increase in 2019 and thereafter compared with 2018 and before may be contributed by a change in CLSI criteria.

- Statistically significant results related to broad-spectrum antimicrobials
 - ↗ trend towards meropenem and imipenem (For imipenem, the 2018-2020 results were derived from <70% of the total isolates and therefore should be interpreted with caution)
 - ↘ trend towards piperacillin/tazobactam

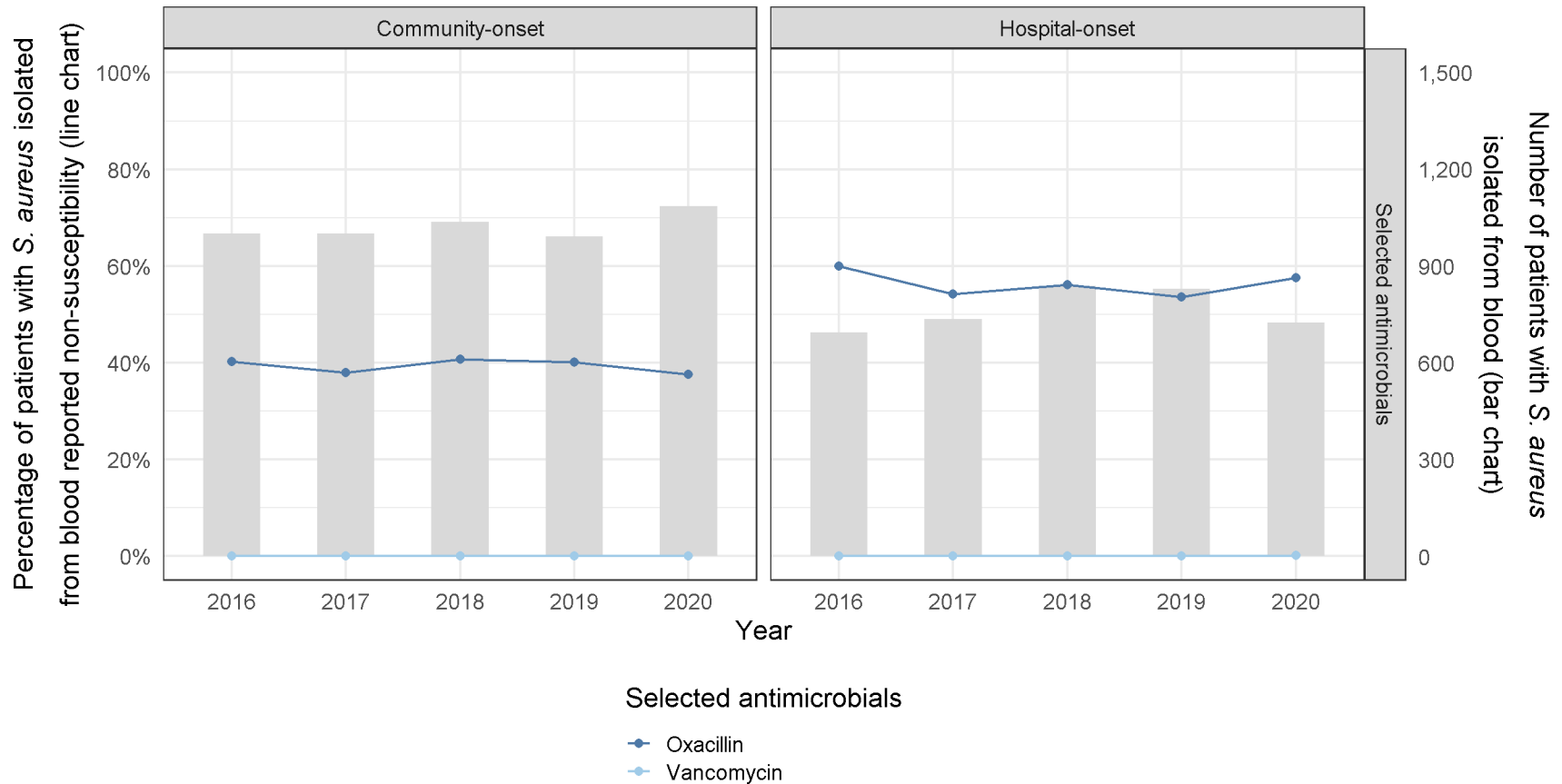


Results

3.3 AST results for *Staphylococcus aureus*



AST results for *S. aureus* - Overview



- % NS to oxacillin* for *S. aureus* isolates of hospital-onset higher than those of community-onset

*Sensitivity testing results of penicillinase stable penicillins (oxacillin, cloxacillin and methicillin) and ceftiofur towards *Staphylococcus aureus* were collectively grouped as "oxacillin" following the recommendation of CLSI.



AST results for *S. aureus* - 2019 vs 2020

Antimicrobial group	Antimicrobial (Big guns in yellow)	Community-onset			Hospital-onset		
		% NS		p-value [†]	% NS		p-value [†]
		2019	2020	19 vs 20	2019	2020	19 vs 20
Beta-lactamase resistant penicillins	Oxacillin*	40.1%	37.6%	-	53.6%	57.6%	-
Glycopeptide antibacterials	Vancomycin	0%	0%	-	0%	0.1%	-

[†]P-value was calculated using chi-squared test or Fisher's exact test, whether appropriate

*Sensitivity testing results of penicillinase stable penicillins (oxacillin, cloxacillin and methicillin) and ceftazidime towards *Staphylococcus aureus* were collectively grouped as "oxacillin" following the recommendation of CLSI. Broad spectrum antimicrobials (Big Guns) highlighted in yellow

- In 2020, 0.1% (1 out of 678 isolates) of the *S. aureus* isolates of hospital-onset were found non-susceptible towards vancomycin



AST results for *S. aureus*

Trend 2016-2020 (Community-onset)

Antimicrobial group	Antimicrobial (Big guns in yellow)	Community-onset					p-value [†]
		2016	2017	2018	2019	2020	
Beta-lactamase resistant penicillins	Oxacillin*	40.3%	37.9%	40.7%	40.1%	37.6%	-
Glycopeptide antibacterials	Vancomycin	0%	0%	0%	0%	0%	-

Legend: ↗ Increasing trend; ↘ Decreasing trend

Broad spectrum antimicrobials (Big Guns) highlighted in yellow

[†]P-value reports the statistical significance of trend observed during the captioned time period, it was calculated using Cochran-Armitage test, only trends with statistical significance (i.e. $p < 0.05$) and high statistical significance ($p < 0.01$) were reported

*Sensitivity testing results of penicillinase stable penicillins (oxacillin, cloxacillin and methicillin) and ceftioxin towards *Staphylococcus aureus* were collectively grouped as "oxacillin" following the recommendation of CLSI.

- None of the *S. aureus* isolates of community-onset were found non-susceptible towards vancomycin



AST results for *S. aureus*

Trend 2016-2020 (Hospital-onset)

Antimicrobial group	Antimicrobial (Big guns in yellow)	Hospital-onset					p-value [†]
		% NS					
		2016	2017	2018	2019	2020	
Beta-lactamase resistant penicillins	Oxacillin*	60.0%	54.2%	56.1%	53.6%	57.6%	-
Glycopeptide antibacterials	Vancomycin	0%	0%	0%	0%	0.1%	-

Legend: ↗ Increasing trend; ↘ Decreasing trend

Broad spectrum antimicrobials (Big Guns) highlighted in yellow

[†]P-value reports the statistical significance of trend observed during the captioned time period, it was calculated using Cochran-Armitage test, only trends with statistical significance (i.e. $p < 0.05$) and high statistical significance ($p < 0.01$) were reported

*Sensitivity testing results of penicillinase stable penicillins (oxacillin, cloxacillin and methicillin) and ceftioxin towards *Staphylococcus aureus* were collectively grouped as "oxacillin" following the recommendation of CLSI.

- 0.1% *S. aureus* isolates of hospital-onset were found non-susceptible towards vancomycin



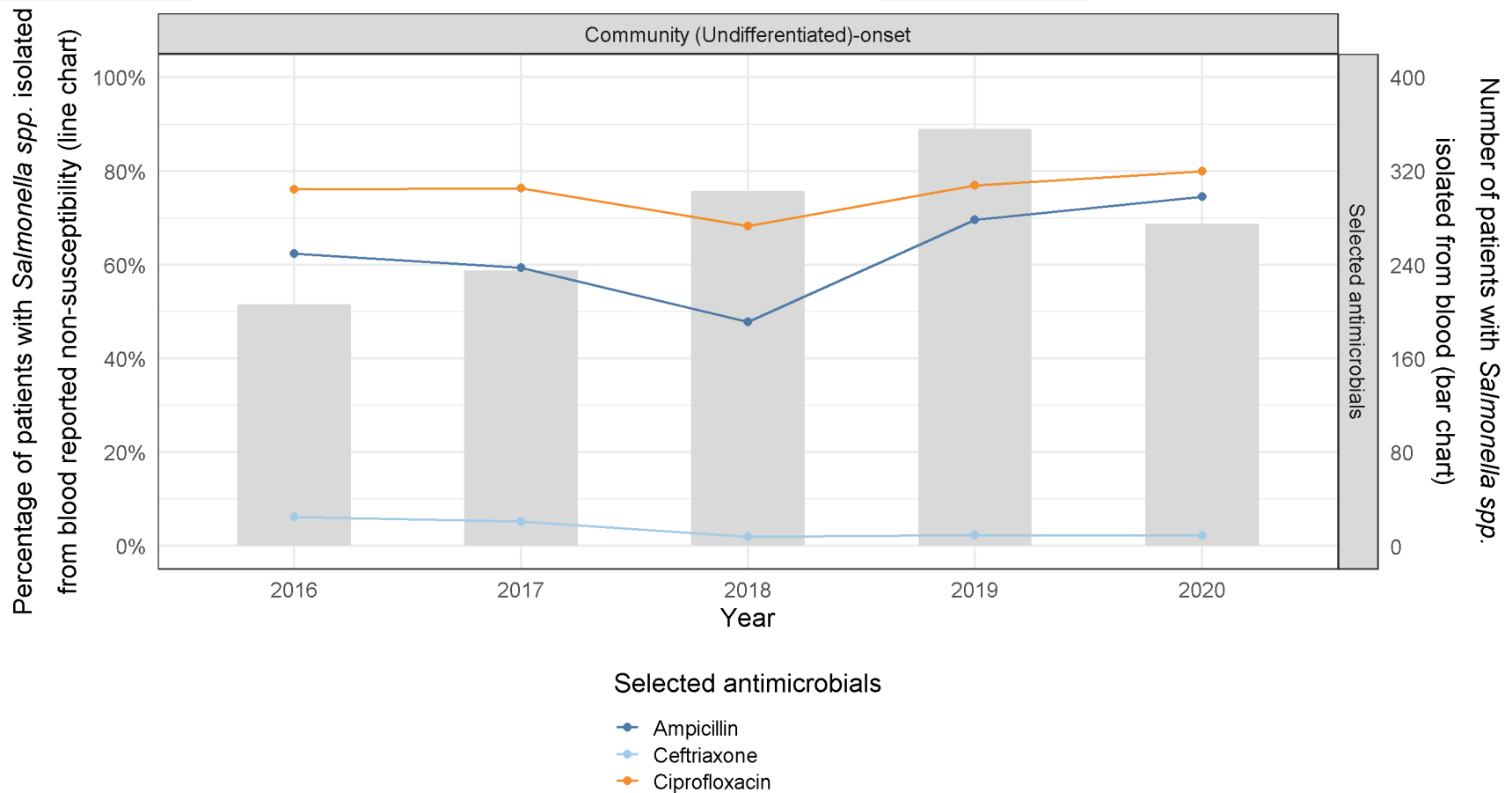
Results

3.4 AST results for *Salmonella* spp.

Remarks: Only community (undifferentiated)-onset is reported for Salmonella spp.



AST results for *Salmonella* spp. - Overview



AST results for *Salmonella* spp. - 2019 vs 2020

Antimicrobial group	Antimicrobial	Community (Undifferentiated)-onset		
		% NS		p-value [†]
		2019	2020	19 vs 20
Penicillins with extended spectrum	Ampicillin	69.7%	74.5%	-
Third-generation cephalosporins	Ceftriaxone	2.3%	2.2%	-
Fluoroquinolones	Ciprofloxacin	76.9%	79.9%	-

[†]P-value was calculated using chi-squared test or Fisher's exact test, whether appropriate



AST results for *Salmonella* spp. Trend 2016-2020 (Community (Undifferentiated)-onset)

Antimicrobial group	Antimicrobial	Community (Undifferentiated)-onset					p-value [†]
		% NS					
		2016	2017	2018	2019	2020	
Penicillins with extended spectrum	Ampicillin	62.4%	59.4%	47.9%	69.7%	74.5%	↗ p <0.01
Third-generation cephalosporins	Ceftriaxone	6.2%	5.2%	2.0%	2.3%	2.2%	↘ p <0.01
Fluoroquinolones	Ciprofloxacin	76.1%	76.4%	68.3%	76.9%	79.9%	-

Legend: ↗ Increasing trend; ↘ Decreasing trend

[†]P-value was calculated using Cochran-Armitage test, only trends with statistical significance (p<0.05) and high statistical significance (p<0.01) were reported

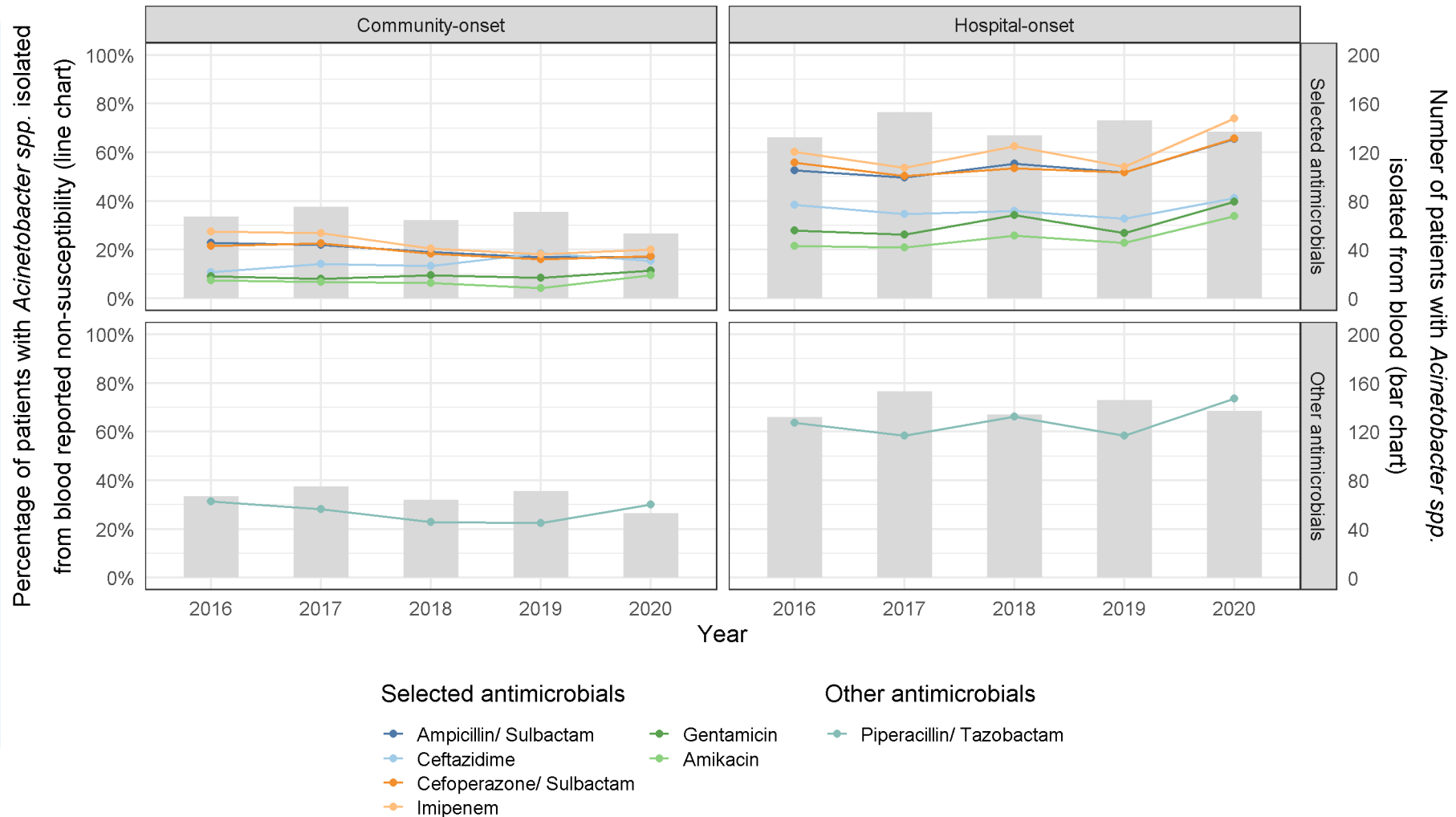


Results

3.5 AST results for *Acinetobacter* spp.



AST results for *Acinetobacter* spp. - Overview



- % NS were lower among *Acinetobacter* spp. isolates of community-onset than those of hospital-onset in general

AST results for *Acinetobacter* spp. - 2019 vs 2020

Antimicrobial group	Antimicrobial (Big guns in yellow)	Community-onset			Hospital-onset		
		% NS		p-value [†]	% NS		p-value [†]
		2019	2020	19 vs 20	2019	2020	19 vs 20
Combinations of penicillins, incl. beta-lactamase inhibitors	Ampicillin/sulbactam	16.9%	17.0%	-	51.7%	65.4%	<0.05
	Piperacillin/tazobactam	22.5%	30.0%	-	58.3%	73.5%	<0.05
Third-generation cephalosporins	Ceftazidime	18.6%	15.4%	-	32.6%	41.2%	-
	Cefoperazone/sulbactam	15.9%	17.3%	-	51.8%	65.7%	<0.05
Fourth-generation cephalosporins	Cefepime	24.6%	23.7%	-	58.6%	73.9%	<0.05
Carbapenems	Meropenem	22.0%	31.3%*	-	66.3%*	80.2%	<0.05
	Imipenem	18.2%	20.0%	-	54.1%	74.0%	<0.05
Other aminoglycosides	Gentamicin	8.5%	11.3%	-	26.9%	39.7%	<0.05
	Amikacin	4.2%	9.4%	-	22.8%	33.8%	-
Fluoroquinolones	Ciprofloxacin	25.0%	19.4%*	-	-	-	-
	Levofloxacin	18.3%	26.1%	-	57.4%	70.3%	-

* Non-susceptibility percentage should be interpreted with caution as the figure is derived from less than 70% of total isolates for surveillance. The figure may be affected by selection bias.

[†]P-value was calculated using chi-squared test or Fisher's exact test, whether appropriate

Broad spectrum antimicrobials (Big Guns) highlighted in yellow

- Statistically significant results related to broad-spectrum antimicrobials
 - Hospital-onset isolates showed ↑ % NS towards piperacillin/tazobactam, cefoperazone/sulbactam, cefepime, meropenem and imipenem in 2020



AST results for *Acinetobacter* spp. Trend 2016-2020 (Community-Onset)

Antimicrobial group	Antimicrobial (Big guns in yellow)	Community-onset					p-value [†]
		% NS					
		2016	2017	2018	2019	2020	
Combinations of penicillins, incl. beta-lactamase inhibitors	Ampicillin/sulbactam	22.8%	21.9%	19.0%	16.9%	17.0%	-
	Piperacillin/tazobactam	31.3%	28.2%	23.0%	22.5%	30.0%	-
Third-generation cephalosporins	Ceftazidime	10.8%	14.1%	13.3%	18.6%	15.4%	-
	Cefoperazone/sulbactam	21.5%	22.5%	18.3%	15.9%	17.3%	-
Fourth-generation cephalosporins	Cefepime	25.8%*	28.6%*	25.6%*	24.6%	23.7%	-
Carbapenems	Meropenem	33.3%*	28.9%*	26.3%*	22.0%	31.3%*	-
	Imipenem	27.4%	26.9%	20.4%	18.2%	20.0%	-
Other aminoglycosides	Gentamicin	9.0%	8.0%	9.4%	8.5%	11.3%	-
	Amikacin	7.5%	6.7%	6.3%	4.2%	9.4%	-
Fluoroquinolones	Ciprofloxacin	27.1%	32.1%	24.3%*	25.0%	19.4%*	-
	Levofloxacin	23.3%*	25.5%*	28.6%	18.3%	26.1%	-

Legend: ↗ Increasing trend; ↘ Decreasing trend

Broad spectrum antimicrobials (Big Guns) highlighted in yellow

* Non-susceptibility percentage should be interpreted with caution as the figure is derived from less than 70% of total isolates for surveillance. The figure may be affected by selection bias.

[†]P-value reports the statistical significance of trend observed during the captioned time period, it was calculated using Cochran-Armitage test, only trends with statistical significance (i.e. $p < 0.05$) and high statistical significance ($p < 0.01$) were reported

- No statistically significant results related to broad-spectrum antimicrobials



AST results for *Acinetobacter* spp. Trend 2016-2020 (Hospital-onset)

Antimicrobial group	Antimicrobial (Big guns in yellow)	Hospital-onset					p-value [†]
		% NS					
		2016	2017	2018	2019	2020	
Combinations of penicillins, incl. beta-lactamase inhibitors	Ampicillin/sulbactam	52.5%	49.7%	55.4%	51.7%	65.4%	↗ p <0.05
	Piperacillin/tazobactam	63.6%	58.3%	66.2%	58.3%	73.5%	-
Third-generation cephalosporins	Ceftazidime	38.4%	34.7%	35.9%	32.6%	41.2%	-
	Cefoperazone/sulbactam	55.6%	50.3%	53.4%	51.8%	65.7%	-
Fourth-generation cephalosporins	Cefepime	67.2%*	71.8%*	62.2%*	58.6%	73.9%	-
Carbapenems	Meropenem	59.0%*	59.1%*	62.5%*	66.3%*	80.2%	↗ p <0.01
	Imipenem	60.2%	53.6%	62.5%	54.1%	74.0%	↗ p <0.05
Other aminoglycosides	Gentamicin	27.9%	26.2%	34.1%	26.9%	39.7%	↗ p <0.05
	Amikacin	21.5%	20.8%	25.8%	22.8%	33.8%	↗ p <0.05
Fluoroquinolones	Levofloxacin	55.7%*	55.2%*	57.7%	57.4%	70.3%	↗ p <0.05

Legend: ↗ Increasing trend; ↘ Decreasing trend

Broad spectrum antimicrobials (Big Guns) highlighted in yellow

* Non-susceptibility percentage should be interpreted with caution as the figure is derived from less than 70% of total isolates for surveillance. The figure may be affected by selection bias.

[†]P-value reports the statistical significance of trend observed during the captioned time period, it was calculated using Cochran-Armitage test, only trends with statistical significance (i.e. p<0.05) and high statistical significance (p<0.01) were reported

- Statistically significant results related to broad-spectrum antimicrobials
 - ↗ trend towards meropenem and imipenem



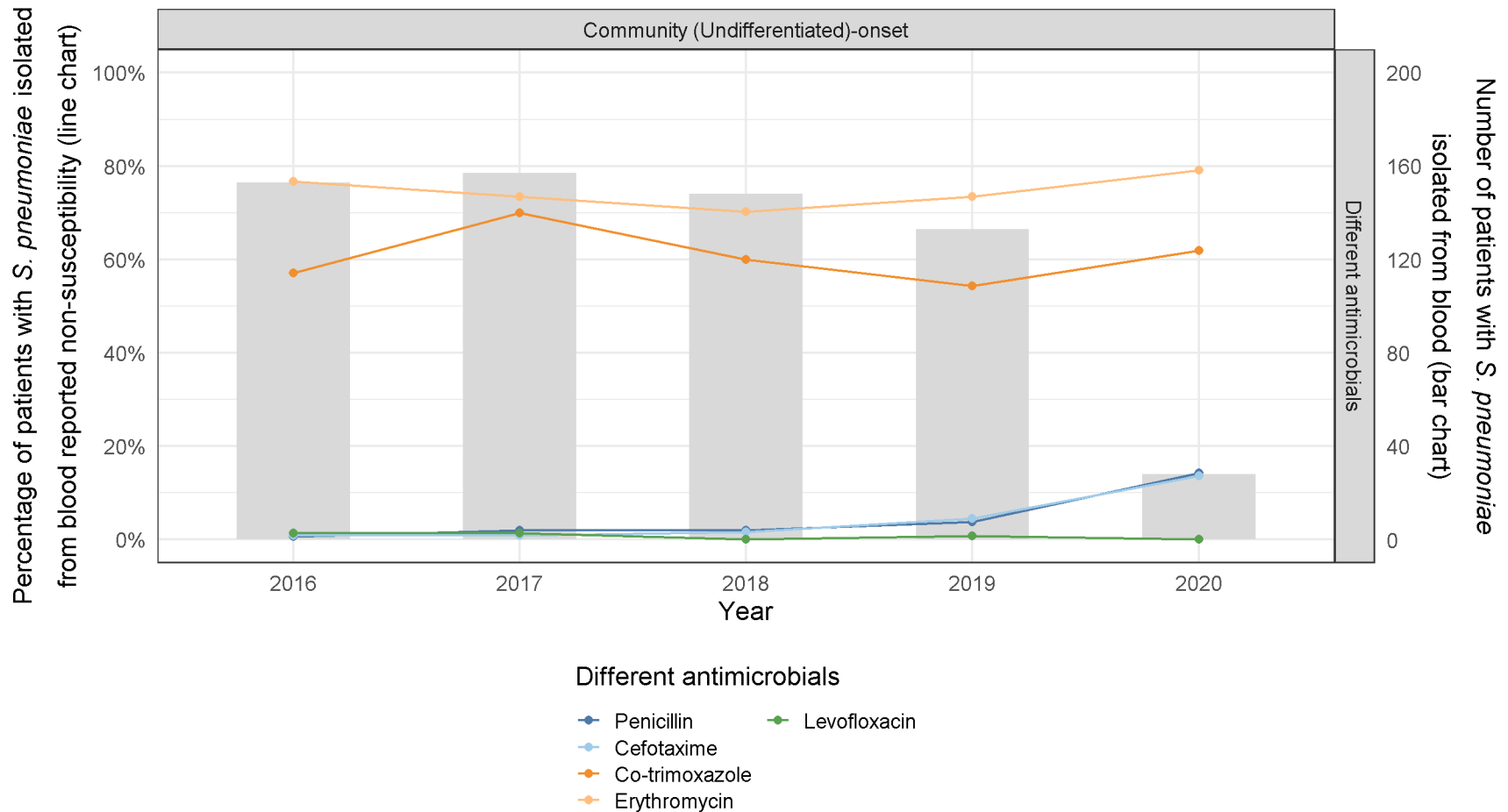
Results

3.6 AST results for *Streptococcus pneumoniae*

*Remarks: Only community (undifferentiated)-onset is reported for *Streptococcus pneumoniae**



AST results for *S. pneumoniae* - Overview



AST results for *S. pneumoniae* - 2019 vs 2020

Antimicrobial group	Antimicrobial	Community (Undifferentiated)-onset		
		% NS		p-value [†]
		2019	2020	19 vs 20
Beta-lactam antibacterials, penicillins	Penicillin	3.8%	14.3%	-
Third-generation cephalosporins	Cefotaxime	4.5%	13.6%	-
Combinations of sulfonamides and trimethoprim, incl. derivatives	Co-trimoxazole	54.3%	61.9%	-
Macrolides	Erythromycin	73.5%	79.2%	-
Fluoroquinolones	Levofloxacin	0.8%	0%	-

[†]P-value was calculated using chi-squared test or Fisher's exact test, whether appropriate

- No statistically significant results observed



AST results for *S. pneumoniae*

Trend 2016-2020 (Community (Undifferentiated)-onset)

Antimicrobial group	Antimicrobial	Community (Undifferentiated)-onset					p-value [†]
		% NS					
		2016	2017	2018	2019	2020	
Beta-lactam antibacterials, penicillins	Penicillin	0.7%	2.0%	2.0%	3.8%	14.3%	↗ p < 0.01
Third-generation cephalosporins	Cefotaxime	0.9%	0.9%	1.6%	4.5%	13.6%	↗ p < 0.01
Combinations of sulfonamides and trimethoprim, incl. derivatives	Co-trimoxazole	57.0%	70.0%	60.0%	54.3%	61.9%	-
Macrolides	Erythromycin	76.8%	73.4%	70.2%	73.5%	79.2%	-
Fluoroquinolones	Levofloxacin	1.3%	1.3%	0%	0.8%	0%	-

Legend: ↗ Increasing trend; ↘ Decreasing trend

[†]P-value was calculated using Cochran-Armitage test, only trends with statistical significance ($p < 0.05$) and high statistical significance ($p < 0.01$) were reported

- % NS of *Streptococcus pneumoniae* isolates towards penicillin and cefotaxime showed an increasing trend with statistical significance



Remarks on Interpretation of Results

- Differentiation of location of onset of patients with bloodstream infections for surveillance purposes depends on the operational definition (hospital-onset for organism isolated from blood specimen collected > 48 hours after hospital admission):
 - Factors affecting differentiation of location of onset:
 - Timing of blood specimen taken
 - Rate of disease progression
- CLSI guidelines for sensitivity testing involving levofloxacin interpretive criteria for Enterobacteriaceae (except *Salmonella* spp.) has been updated in 2019. In case laboratories in HA chose to apply the criteria for reporting in 2019, some *E. coli* and *K. pneumoniae* isolates previously categorised as sensitive to levofloxacin / ciprofloxacin using the old criteria would become non-susceptible following a change in zone size requirement under the 2019 criteria.
- Laboratories of different hospitals might use different panels for AST. This could result in bias of results toward those laboratories performing a major proportion of a particular AST especially if number of isolates tested is small.
 - In the report, the issue of small number of isolates is partially addressed, in accordance of recommendation by WHO GLASS, that non-susceptibility results derived from <10 isolates were not included for analysis.



Summary Table on Key Findings

WHO priority organism	Proportion of isolates being non-susceptible to antimicrobials, 2016 vs 2020	
	Community-onset	Hospital-onset
<i>E. coli</i>	↓ Piperacillin/tazobactam (7.2% → 3.8%) ↓ Cefepime (23.6% → 15.1%) ↓ Gentamicin (28.9% → 24.9%)	↓ Amoxicillin/clavulanate (42.6% → 37.0%) ↓ Piperacillin/tazobactam (14.1% → 10.7%) ↓ Ceftazidime (23.2% → 17.4%) ↓ Cefepime (33.1% → 19.9%) ↓ Gentamicin (35.3% → 29.4%) ↓ Amikacin (1.6% → 0.9%)
	↑ Amoxicillin/clavulanate (27.1% → 27.8%) ↑ Cefuroxime (30.1% → 31.6%) ↑ Cefotaxime (27.8% → 29.1%) ↑ Imipenem (0.04% → 0.1%) ↑ Levofloxacin (31.2% → 37.1%)	↑ Levofloxacin (44.8% → 45.9%)
<i>K. pneumoniae</i>	↓ Cefepime (8.4% → 5.5%)	↓ Piperacillin/tazobactam (21.5% → 15.7%) ↓ Cefotaxime (35.4% → 28.7%) ↓ Co-trimoxazole (48.3% → 40.4%) ↓ Gentamicin (14.6% → 10.4%)
	↑ Amoxicillin/clavulanate (13.9% → 16.5%) ↑ Ceftazidime (7.3% → 9.9%) ↑ Levofloxacin (7.9% → 14.0%)	↑ Meropenem (1.2% → 4.6%) ↑ Imipenem (1.3% → 4.0%) ↑ Levofloxacin (19.5% → 29.4%)
<i>S. aureus</i>	None observed	None observed
<i>Acinetobacter</i> spp.	None observed	↑ Ampicillin/sulbactam (52.5% → 65.4%) ↑ Meropenem (59.0% → 80.2%) ↑ Imipenem (60.2% → 74.0%) ↑ Gentamicin (27.9% → 39.7%) ↑ Amikacin (21.5% → 33.8%) ↑ Levofloxacin (55.7% → 70.3%)

Remark: Broad spectrum antimicrobials (Big Guns) highlighted in bold

Figures reported here are with statistical significance

Summary Table on Key Findings

WHO priority organism	Proportion of isolates being non-susceptible to antimicrobials, 2016 vs 2020
	Community (Undifferentiated)-onset
<i>Salmonella</i> spp.	↓ Ceftriaxone (6.2% → 2.2%)
	↑ Ampicillin (62.4% → 74.5%)
<i>S. pneumoniae</i>	↑ Penicillin (0.7% → 14.3%)
	↑ Cefotaxime (0.9% → 13.6%)

Figures reported here are with statistical significance



Summary

- Among the broad-spectrum antimicrobials being tested against WHO priority organisms isolated from blood specimens from year 2016 to 2020:
 - *Escherichia coli*
 - **Imipenem** showed increasing trend in non-susceptibility (community-onset)
 - **Piperacillin/tazobactam** and **cefepime** showed decreasing trends in non-susceptibility (both community- and hospital-onset)
 - **Ceftazidime** showed decreasing trends in non-susceptibility (hospital-onset)
 - *Klebsiella pneumoniae*
 - **Ceftazidime** showed increasing trend in non-susceptibility (community-onset)
 - **Meropenem** and **imipenem** showed increasing trend in non-susceptibility (hospital-onset)
 - **Piperacillin/tazobactam** showed decreasing trends in non-susceptibility (hospital-onset)
 - **Cefepime** showed decreasing trends in non-susceptibility (community-onset)
 - *Staphylococcus aureus*
 - No trend were observed for vancomycin (both community- and hospital-onset)
 - *Salmonella* spp.
 - No trend were observed among commonly used antimicrobials
 - *Acinetobacter* spp.
 - **Meropenem, imipenem** showed increasing trend in non-susceptibility (hospital-onset)
 - *Streptococcus pneumoniae*
 - Among commonly used antimicrobials, **penicillin** and **cefotaxime** showed increasing trend



Recommendations

- In view of increasing trend of non-susceptibility of the following broad-spectrum antimicrobial-organism combinations, further monitoring of the phenomenon would be warranted, especially for meropenem which was found to have an increased dispensing* in 2020 for about 14% (in compound annual growth rate) for inpatient service compared with 2016:
 - Meropenem & imipenem for *Klebsiella pneumoniae* (hospital-onset)
 - Meropenem & imipenem for *Acinetobacter* spp. (hospital-onset)
- To alert working partners of HA about increasing trend of non-susceptibility of the aforesaid broad-spectrum antimicrobial – organism combinations for their further investigation and management as appropriate.

*In terms of DDD per 1000 patient-days





THE END

Thank you

