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Centre for Health Protection

Antimicrobial Resistance (AMR) Surveillance on Urine 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 suggested to harmonise 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 urine specimens from 2016 to 2020

Methodology

WHO GLASS Recommendations (1)

- Based on *WHO GLASS Manual for Early Implementation (2015):*
  - WHO Priority Organisms captured from urine:
    - *Escherichia coli*
    - *Klebsiella pneumoniae*
  - Organisms other than the above were grouped as “Other spp.”
  - Location of onset
    - Community-onset - organisms isolated from urine specimens collected in non-inpatient settings or within 48 hours after hospital admission
    - Hospital-onset - organisms isolated from urine specimens 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

- For urine specimen:
  - Only midstream urine was included for analysis
  - Positive urine culture was defined as specimen with pure growth of organism reaching bacterial count ≥10^5 CFU/ml
- Taking local context into account, the following modification was 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

Scope of Data

- The following information were collected from patients who had urine 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 urine culture
  - Number of patients with urine culture by age distribution
  - Percentage of patients with positive urine culture
- Overview on WHO priority organisms isolated from urine
  - No. of patients with positive culture results by organisms and year
  - 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

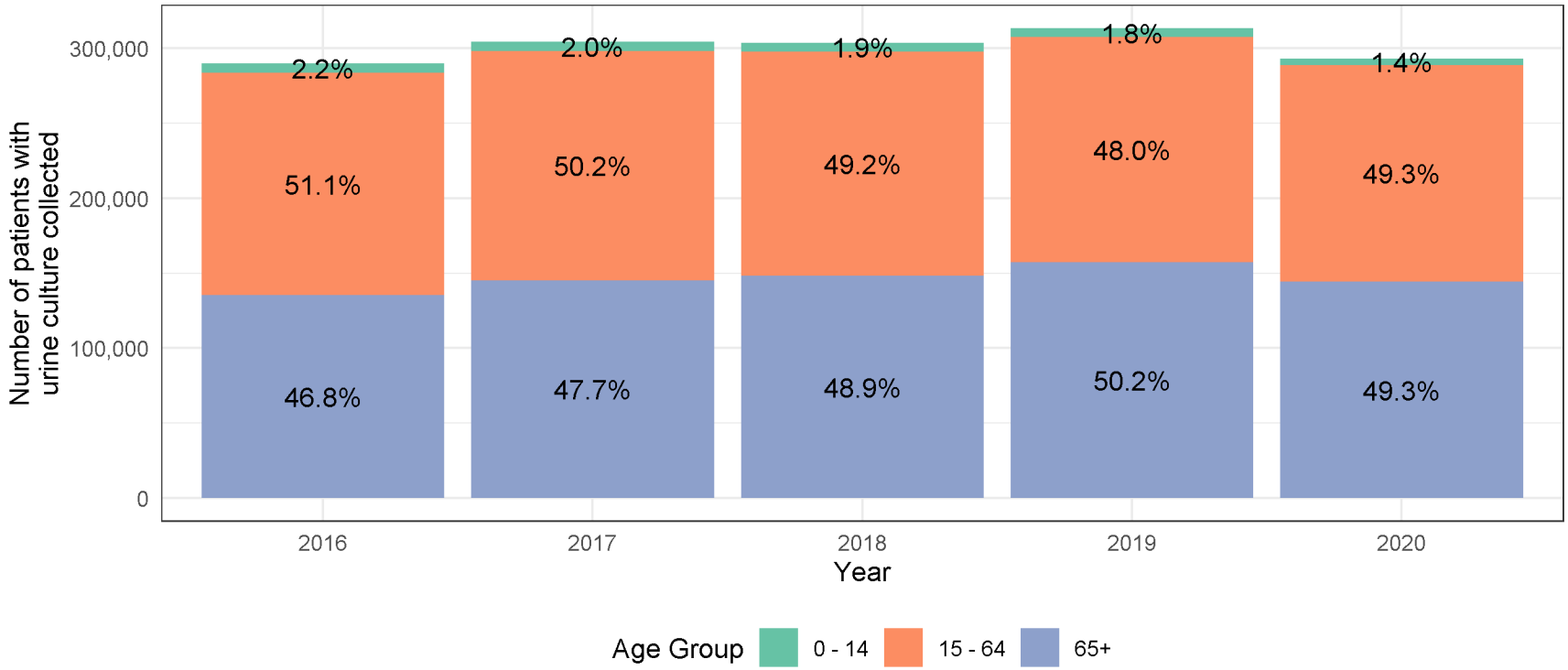
Statistical Analysis on AST Results

- % 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 urine culture

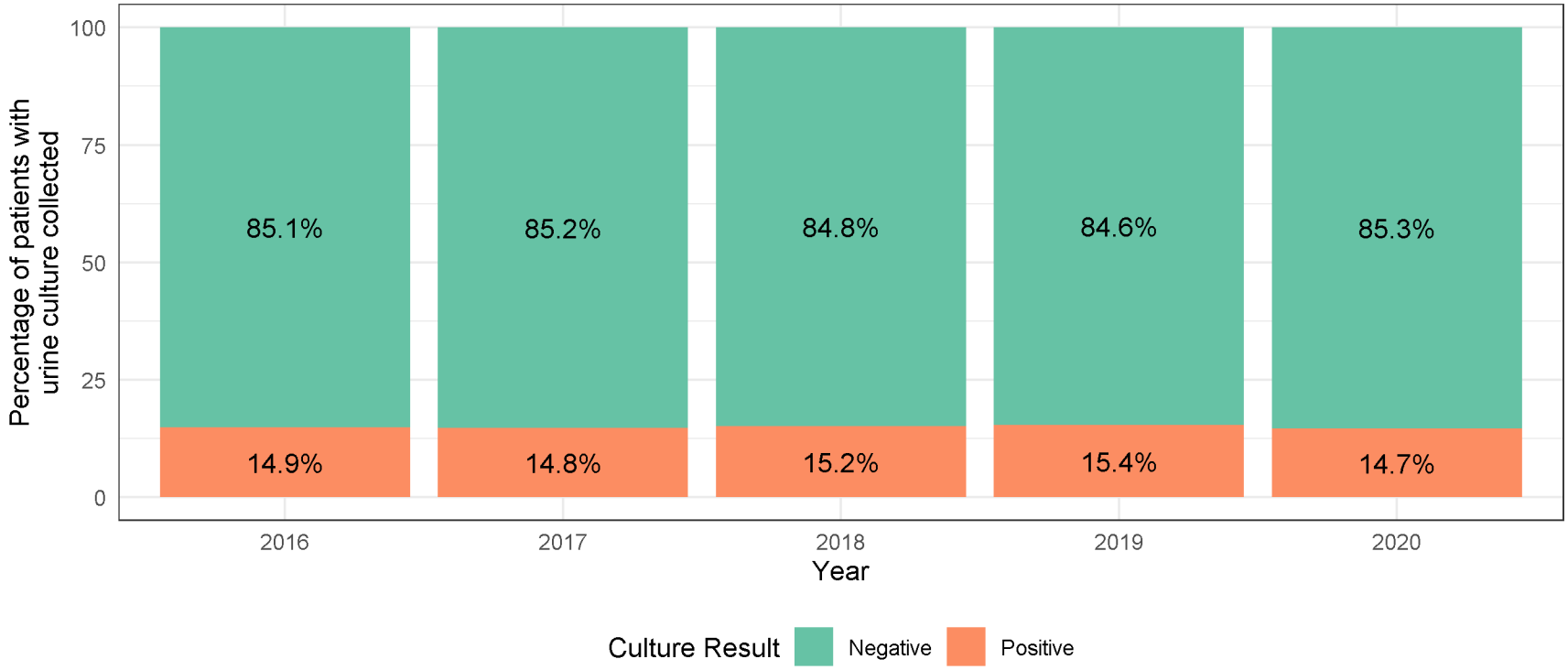
Age distribution of patients with urine culture



Due to rounding, sum of percentages may not equal to 100%

- ⇧ No. of patients with urine culture from 2016 to 2019 (~290,000 in 2016 to ~313,000 in 2019), and then decreased to 293,000 in 2020
- Proportion of patients with urine culture decreased gradually for those aged 15-64 (51.1% in 2016 to 49.3% in 2020) and increased gradually for those aged 65+ (46.8% in 2016 to 49.3% in 2020)

Percentage of Patients with Positive Urine Culture



- % patients with positive urine culture remained stable over the past years at around 15%

Results

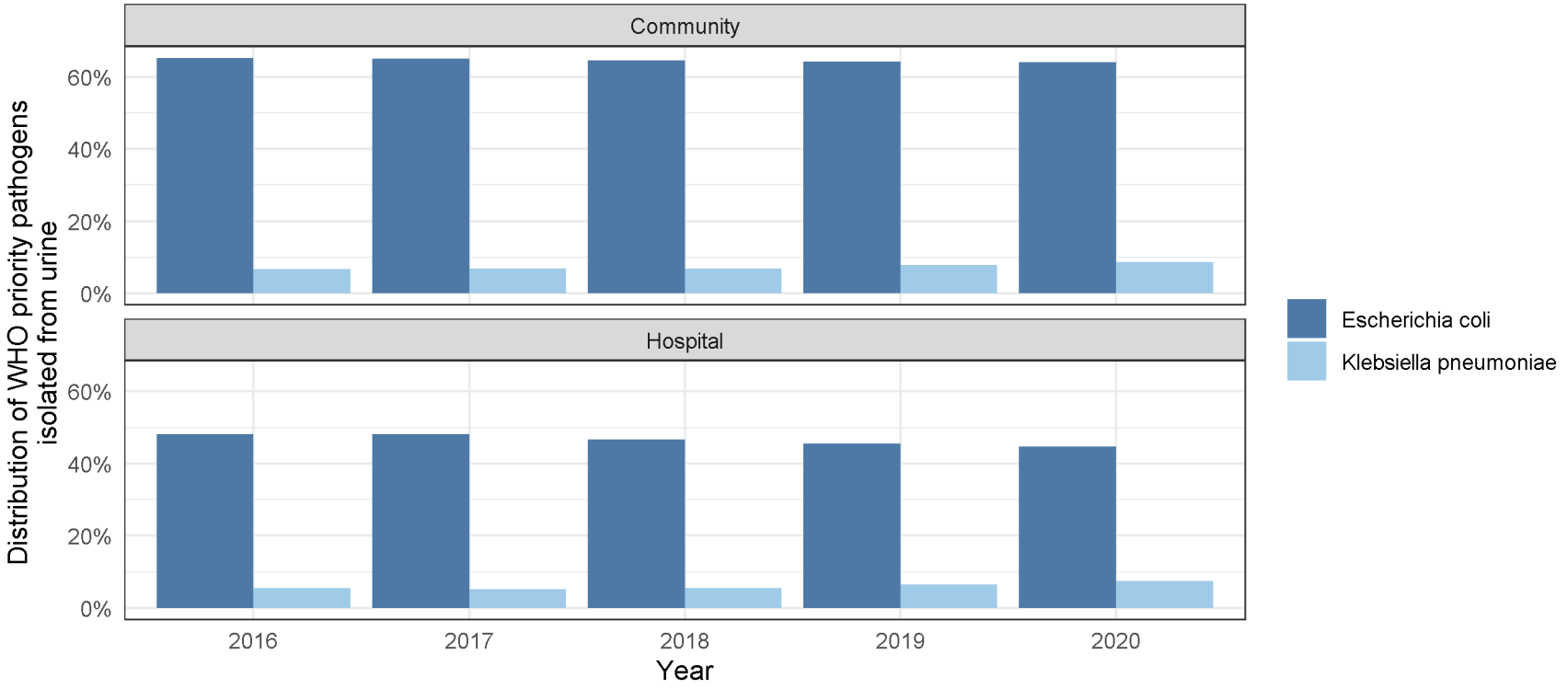
2. Overview on WHO priority organisms isolated from urine

Distribution of Organisms by Year

Organism	No. of patients with positive urine culture by organisms and year (%)				
	2016	2017	2018	2019	2020
Escherichia coli	27,010 (62.7%)	28,050 (62.5%)	28,440 (61.8%)	29,600 (61.4%)	26,320 (61.2%)
Klebsiella pneumoniae	2,900 (6.7%)	2,990 (6.7%)	3,120 (6.8%)	3,730 (7.7%)	3,680 (8.6%)
Other spp.	17,460 (40.5%)	18,320 (40.8%)	19,050 (41.4%)	19,840 (41.2%)	17,310 (40.3%)
Total no. of patients	43,100	44,880	46,020	48,220	43,010

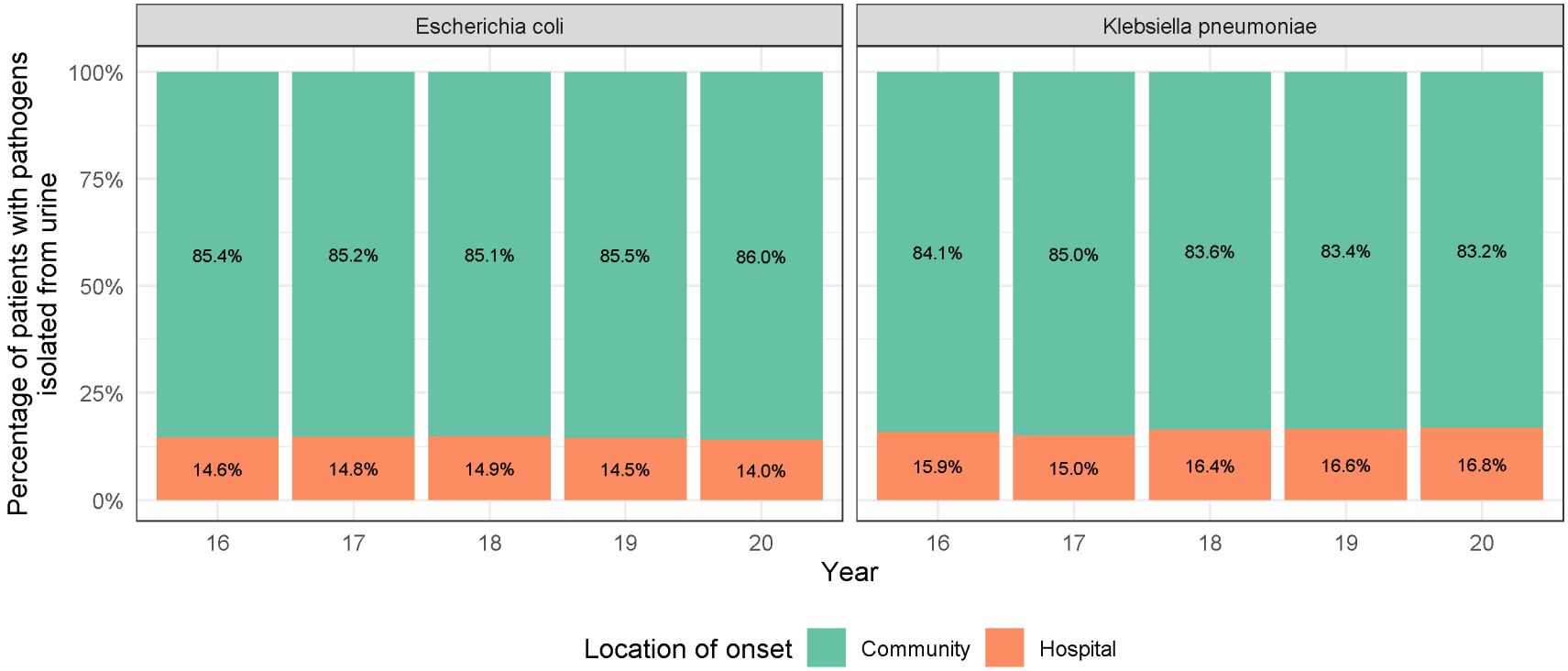
Note:
- Patient headcounts were rounded to nearest ten, percentages were rounded to one decimal place
- A patient might have urine culture(s) with growth of multiple organisms

Distribution of Organisms by Location of Onset (1)



- By location of onset (following WHO's definition):
  - Distributions of the 2 priority organisms of hospital- and community-onset were similar over the years
  - For community-onset specimens in 2020, 64.1% of patients with positive urine culture had *Escherichia coli* isolated, followed by *Klebsiella pneumoniae*. (8.6%)
  - For hospital-onset specimens in 2020, 44.7% of patients with positive urine culture had *Escherichia coli* isolated, followed by *Klebsiella pneumoniae* (7.42%)

Distribution of Organisms by Location of Onset (2)



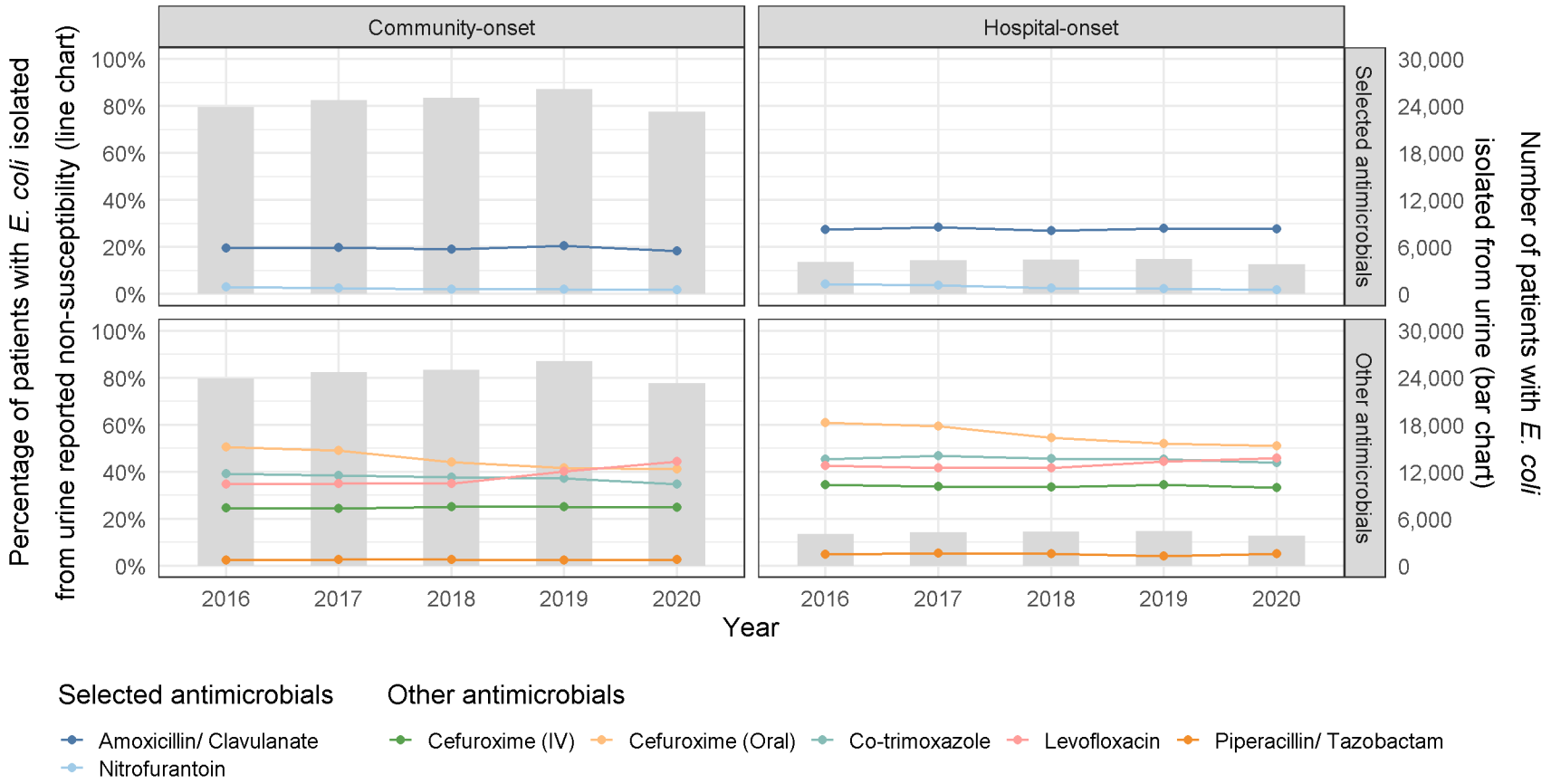
In Year 2020:

- *Escherichia coli* (86.0%) and *Klebsiella pneumoniae* (83.2%) were predominantly community-onset

Results

3.1 AST results for *Escherichia coli*

AST results for *Escherichia coli* - Overview



- % NS to amoxicillin/clavulanate and nitrofurantoin among *Escherichia coli* isolates remained >18% and >1% respectively during 2016 to 2020

AST results for *Escherichia coli* - 2019 vs 2020

Antimicrobial group	Antimicrobial	Community Onset % NS 2019	Community Onset % NS 2020	Community Onset p-value† (19 vs 20)	Hospital Onset % NS 2019	Hospital Onset % NS 2020	Hospital Onset p-value† (19 vs 20)
Combinations of penicillins, incl. beta-lactamase inhibitors	Amoxicillin/clavulanate	20.7%	18.3%	<0.05	27.8%	27.8%	-
	Piperacillin/tazobactam	2.5%	2.6%	-	4.2%	5.1%	-
Second-generation cephalosporins	Cefuroxime (IV)	25.2%	24.8%	-	34.5%	33.2%	-
	Cefuroxime (Oral)	41.6%	41.1%	-	52.1%	50.9%	-
Combinations of sulfonamides and trimethoprim, incl. derivatives	Co-trimoxazole	37.1%	34.8%	<0.05	45.4%	43.9%	-
Fluoroquinolones	Levofloxacin	40.3%	44.4%	<0.05	44.2%	45.8%	-
Nitrofuran derivatives	Nitrofurantoin	2.1%	1.8%	<0.05	2.2%	1.7%	-

Broad spectrum antimicrobials (Big Guns) highlighted in yellow

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

- For community-onset isolate:
  - ⇩ % NS towards amoxicillin/clavulanate, co-trimoxazole and nitrofurantoin
  - ⇧ % NS towards levofloxacin

AST results for *E. coli*
Trend 2016-2020 (Community Onset)

		Community Onset					
		% NS					p-value†
Antimicrobial group	**Antimicrobial**	**2016**	**2017**	**2018**	**2019**	**2020**	**16 - 20**
Combinations of penicillins, incl. beta-lactamase inhibitors	Amoxicillin/clavulanate	19.6%	19.7%	19.0%	20.7%	18.3%	↘ p <0.05
	Piperacillin/tazobactam	2.4%	2.6%	2.7%	2.5%	2.6%	-
Second-generation cephalosporins	Cefuroxime (IV)	24.7%	24.5%	25.1%	25.2%	24.8%	-
	Cefuroxime (Oral)	50.7%	49.0%	44.2%	41.6%	41.1%	↘ p <0.01
Combinations of sulfonamides and trimethoprim, incl. derivatives	Co-trimoxazole	39.2%	38.5%	37.7%	37.1%	34.8%	↘ p <0.01
Fluoroquinolones	Levofloxacin‡	34.8%	34.9%	35.0%	40.3%	44.4%	↗ p <0.01
Nitrofuran derivatives	Nitrofurantoin	2.9%	2.6%	2.1%	2.1%	1.8%	↘ p <0.01

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

‡Revised levofloxacin interpretive criteria for Enterobacteriaceae (except *Salmonella* spp.) was released by CLSI in 2019. The increase since 2019 may be contributed by a change in CLSI criteria.

- Statistically significant ⇧ trends of % NS towards levofloxacin were observed from 2016 to 2020
- Statistically significant ⇩ trend of % NS towards amoxicillin/clavulanate, cefuroxime (oral), co-trimoxazole and nitrofurantoin was observed from 2016 to 2020

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AST results for *E. coli*
Trend 2016-2020 (Hospital Onset)

		Hospital Onset					
		% NS					p-value†
Antimicrobial group	**Antimicrobial**	**2016**	**2017**	**2018**	**2019**	**2020**	**16 - 20**
Combinations of penicillins, incl. beta-lactamase inhibitors	Amoxicillin/clavulanate	27.5%	28.6%	26.9%	27.8%	27.8%	-
	Piperacillin/tazobactam	5.0%	5.4%	5.1%	4.2%	5.1%	-
Second-generation cephalosporins	Cefuroxime (IV)	34.5%	33.7%	33.6%	34.5%	33.2%	-
	Cefuroxime (Oral)	61.0%	59.4%	54.6%	52.1%	50.9%	↘ p <0.01
Combinations of sulfonamides and trimethoprim, incl. derivatives	Co-trimoxazole	45.4%	46.7%	45.6%	45.4%	43.9%	↘ p <0.05
Fluoroquinolones	Levofloxacin‡	42.6%	41.7%	41.8%	44.2%	45.8%	↗ p <0.01
Nitrofuran derivatives	Nitrofurantoin	4.3%	3.7%	2.4%	2.2%	1.7%	↘ p <0.01

Legend: ↗ Increasing trend; ↘ Decreasing trend Broad spectrum antimicrobials (Big Guns) highlighted in yellow

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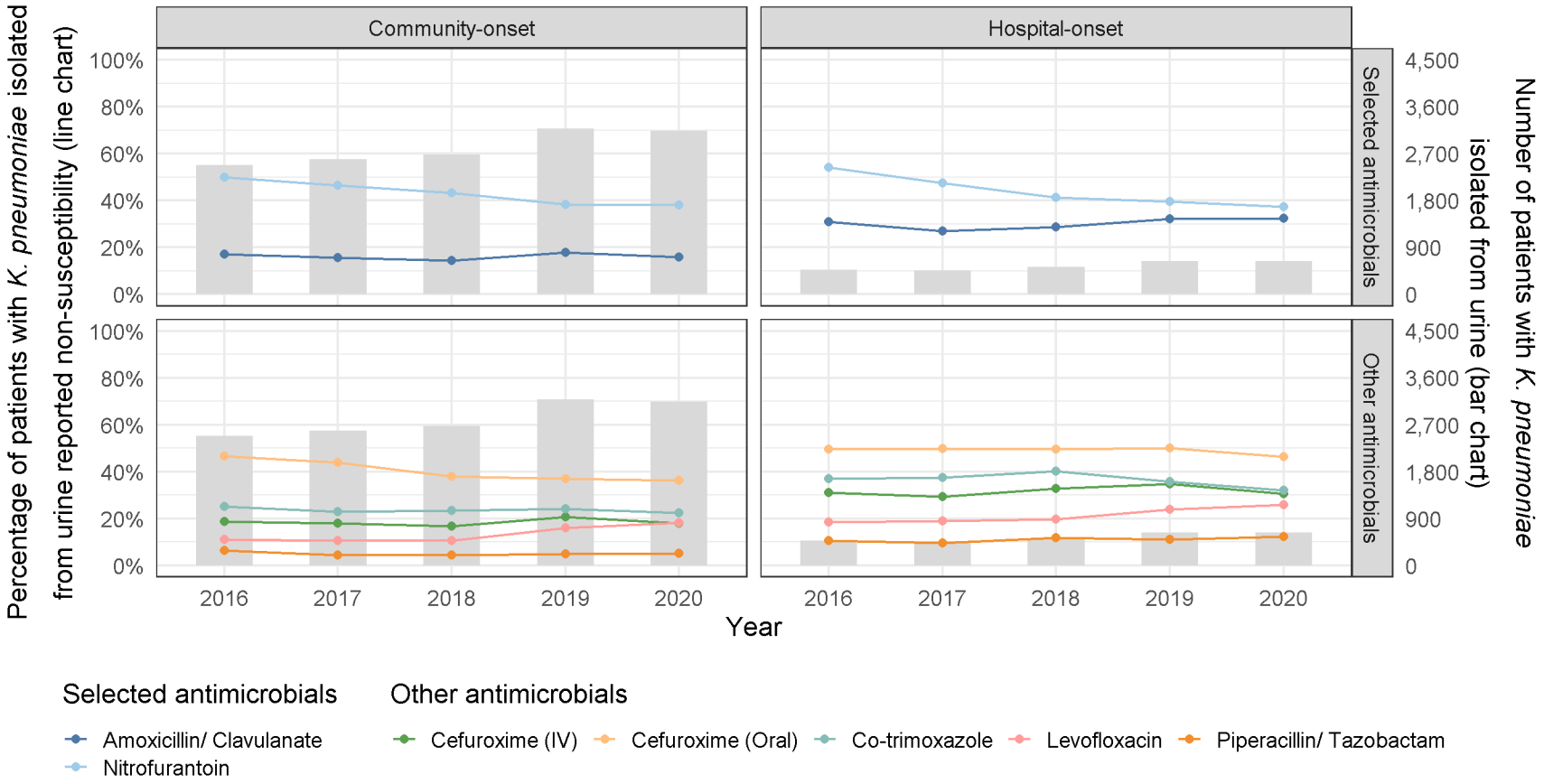
‡Revised levofloxacin interpretive criteria for Enterobacteriaceae (except *Salmonella* spp.) was released by CLSI in 2019. The increase since 2019 may be contributed by a change in CLSI criteria.

- Statistically significant ⇧ trends of % NS towards levofloxacin were observed from 2016 to 2020
- Statistically significant ⇩ trend of % NS towards cefuroxime (oral), co-trimoxazole and nitrofurantoin was observed from 2016 to 2020

Results

3.2 AST results for *Klebsiella pneumoniae*

AST results for *Klebsiella pneumoniae* - Overview



- % NS to amoxicillin/clavulanate and nitrofurantoin among *Klebsiella pneumoniae* isolates remained >14% and >37% respectively during 2016 to 2020
- In general, % NS to selected antimicrobials were lower among *K. pneumoniae* isolates of community-onset than those of hospital-onset

AST results for *Klebsiella pneumoniae* - 2019 vs 2020

Antimicrobial group	Antimicrobial	Community Onset % NS 2019	Community Onset % NS 2020	Community Onset p-value† (19 vs 20)	Hospital Onset % NS 2019	Hospital Onset % NS 2020	Hospital Onset p-value† (19 vs 20)
Combinations of penicillins, incl. beta-lactamase inhibitors	Amoxicillin/clavulanate	17.9%	15.9%	<0.05	32.2%	32.3%	-
	Piperacillin/tazobactam	4.9%	5.2%	-	11.1%	12.2%	-
Second-generation cephalosporins	Cefuroxime (IV)	20.7%	18.0%	<0.05	34.7%	30.5%	-
	Cefuroxime (Oral)	37.1%	36.1%	-	49.9%	46.3%	-
Third-generation cephalosporins	Ceftazidime	-‡	-‡	-	26.0%	23.0%	-
Carbapenems	Meropenem	-‡	-‡	-	1.3%	1.2%	-
Combinations of sulfonamides and trimethoprim, incl. derivatives	Co-trimoxazole	24.1%	22.5%	-	35.7%	32.1%	-
Fluoroquinolones	Levofloxacin	16.0%	18.1%	<0.05	23.8%	25.8%	-
Nitrofuran derivatives	Nitrofurantoin	38.4%	38.1%	-	39.7%	37.4%	-

Broad spectrum antimicrobials (Big Guns) highlighted in yellow

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

‡Since the susceptibility test was performed for less than 70% of isolates, test results were not reported

- For community-onset isolate:
  - ⇩ % NS towards amoxicillin/clavulanate and cefuroxime (IV)
  - ⇧ % NS towards levofloxacin

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AST results for *K. pneumoniae*
Trend 2016-2020 (Community Onset)

		Community Onset					
		% NS					p-value†
Antimicrobial group	**Antimicrobial**	**2016**	**2017**	**2018**	**2019**	**2020**	**16 - 20**
Combinations of penicillins, incl. beta-lactamase inhibitors	Amoxicillin/clavulanate	17.1%	15.6%	14.4%	17.9%	15.9%	-
	Piperacillin/tazobactam	6.2%	4.5%	4.5%	4.9%	5.2%	-
Second-generation cephalosporins	Cefuroxime (IV)	18.7%	18.0%	16.7%	20.7%	18.0%	-
	Cefuroxime (Oral)	46.6%	43.8%	38.0%	37.1%	36.1%	↘ p <0.01
Combinations of sulfonamides and trimethoprim, incl. derivatives	Co-trimoxazole	25.1%	22.9%	23.4%	24.1%	22.5%	-
Fluoroquinolones	Levofloxacin‡	11.1%	10.6%	10.5%	16.0%	18.1%	↗ p <0.01
Nitrofuran derivatives	Nitrofurantoin	49.9%	46.4%	43.3%	38.4%	38.1%	↘ p <0.01

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

‡Revised levofloxacin interpretive criteria for Enterobacteriaceae (except *Salmonella* spp.) was released by CLSI in 2019. The increase since 2019 may be contributed by a change in CLSI criteria.

- Statistically significant ⇧ trend of % NS towards levofloxacin was observed from 2016 to 2020
- Statistically significant ⇩ trend of % NS towards nitrofurantoin was observed from 2016 to 2020

AST results for *K. pneumoniae*
Trend 2016-2020 (Hospital Onset)

		Hospital Onset					
		% NS					p-value†
Antimicrobial group	**Antimicrobial**	**2016**	**2017**	**2018**	**2019**	**2020**	**16 - 20**
Combinations of penicillins, incl. beta-lactamase inhibitors	Amoxicillin/ Clavulanate	30.9%	26.9%	28.7%	32.2%	32.3%	-
	Piperacillin/ Tazobactam	10.5%	9.6%	11.7%	11.1%	12.2%	-
Second-generation cephalosporins	Cefuroxime (IV)	30.9%	29.3%	32.7%	34.7%	30.5%	-
	Cefuroxime (Oral)	49.6%	49.8%	49.4%	49.9%	46.3%	-
Third-generation cephalosporins	Ceftazidime	20.9%*	16.2%*	18.9%	26.0%	23.0%	↗ p <0.05
Carbapenems	Meropenem	0.5%*	0.4%*	1.3%*	1.3%	1.2%	-
Combinations of sulfonamides and trimethoprim, incl. derivatives	Co-trimoxazole	37.0%	37.5%	40.0%	35.7%	32.1%	↘ p <0.05
Fluoroquinolones	Levofloxacin‡	18.4%	19.0%	19.8%	23.8%	25.8%	↗ p <0.01
Nitrofuran derivatives	Nitrofurantoin	54.2%	47.4%	41.4%	39.7%	37.4%	↘ 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 levofloxacin interpretive criteria for Enterobacteriaceae (except *Salmonella* spp.) was released by CLSI in 2019. The increase since 2019 may be contributed by a change in CLSI criteria.

- Statistically significant ⇧ trends of % NS towards ceftazidime and levofloxacin were observed from 2016 to 2020
- Statistically significant ⇩ trend of % NS towards co-trimoxazole and nitrofurantoin was observed from 2016 to 2020

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Remarks on Interpretation of Results

- Differentiation of location of onset of patients with urine infections for surveillance purposes depends on the operational definition (hospital-onset for organism isolated from urine specimen collected > 48 hours after hospital admission):
  - Factors affecting differentiation of location of onset:
    - Timing of urine specimen taken
    - Rate of disease progression
- CLSI guidelines for sensitivity testing involving fluoroquinolones (including ciprofloxacin and levofloxacin) interpretive criteria for *Enterobacteriaceae* (except *Salmonella* spp.) has been updated in 2019. For laboratories that chose to apply the new criteria for reporting in 2019, some *Escherichia coli* and *Klebsiella pneumoniae* isolates previously categorised as susceptible to ciprofloxacin would be categorised as non-susceptible using the updated 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.

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Summary Table on Key Findings

WHO priority organism	Proportion of isolates being non-susceptible to antimicrobials, 2016 vs 2020	
	Community-onset	Hospital-onset
E. coli	⇩ Amoxicillin/clavulanate (19.6% → 18.3%) ⇩ Cefuroxime (Oral) (50.7% → 41.1%) ⇩ Co-trimoxazole (39.2% → 34.8%) ⇩ Nitrofurantoin (2.9% → 1.8%)	⇩ Ceufroxime (Oral) (61.0% → 50.9%) ⇩ Co-trimoxazole (45.4% → 43.9%) ⇩ Nitrofurantoin (4.3% → 1.7%)
	⇧ Levofloxacin (34.8% → 44.4%)	⇧ Levofloxacin (42.6% → 45.8%)
K. pneumoniae	⇩ Cefuroxime (oral) (46.6% → 36.1%) ⇩ Nitrofurantoin (49.9% → 38.1%)	⇩ Co-trimoxazole (37.0% → 32.1%) ⇩ Nitrofurantoin (54.2% → 37.4%)
	⇧ Levofloxacin (11.1% → 18.1%)	⇧ **Ceftazidime (20.9% → 23.0%)** ⇧ Levofloxacin (18.4% → 25.8%)

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

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Summary

- A statistically significant increasing trend of %NS from 2016 to 2020 for *Escherichia coli* and *Klebsiella pneumoniae* towards levofloxacin was observed (for both community- and hospital-onset)
- A statistically significant increasing trend of %NS from 2016 to 2020 for hospital-onset *Klebsiella pneumoniae* towards ceftazidime was observed
- A statistically significant decreasing trend of %NS from 2016 to 2020 for *Escherichia coli* towards cefuroxime (oral), co-trimoxazole and nitrofurantoin (for both community- and hospital-onset), and amoxicillin/clavulanate (for community-onset) was observed
- A statistically significant decreasing trend of %NS from 2016 to 2020 for *Klebsiella pneumoniae* towards, co-trimoxazole (for hospital-onset), cefuroxime (oral) (for community-onset), and nitrofurantoin (for both community- and hospital-onset) was observed

Recommendations

- In view of increasing trend of non-susceptibility of the following antimicrobial – organism combinations, further monitoring of the phenomenon may be warranted:
  - Levofloxacin for *Escherichia coli* and *Klebsiella pneumoniae*
  - Ceftazidime for *Klebsiella pneumoniae*
- To alert working partners of HA about increasing trend of non-susceptibility of the aforesaid antimicrobial – organism combinations for their further investigation and management as appropriate
- Further exploration with subgroup analysis as a separate exercise in future could be conducted to identify age, gender and specialty of patient population which are more likely to carry the non-susceptible organisms

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THE END

Thank you

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