

Trends in Susceptibility of Gram-negative Pathogens Isolated from Intra-abdominal Infections in North America from 2003 to 2007 – The SMART Study

#P 1036

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Revised Abstract

Objectives: The Study for Monitoring Antimicrobial Resistance Trends (SMART) program has been monitoring the activity of ertapenem, amikacin, cefepime, ceftazidime, ceftazidime, ceftriaxone, ciprofloxacin, imipenem, levofloxacin, and piperacillin/tazobactam against gram-negative bacteria isolated from intra-abdominal infections (IAI) since 2003. This report compares susceptibility levels in 2003 vs. 2007 for key IAI pathogens in North America (U.S.).

Methods: 10-14 labs in the U.S. collected up to 100 consecutive gram-negative isolates from IAI each year. MICs were determined by broth microdilution following CLSI guidelines, and % susceptible (%S) rates in 2003 and 2007 were compared for species with ≥ 30 strains per year. 2003/2007 n's of *E. coli*, *K. pneumoniae*, *E. cloacae*, and *P. aeruginosa* were 427/252, 147/81, 80/33, and 161/73, respectively. **Results:** 30/38 drug/bug combinations analyzed showed decreased %S from 2003 to 2007, but only 8/36 (*E. coli* vs. ceftriaxone, cefepime, amikacin, ciprofloxacin and levofloxacin; *P. aeruginosa* vs. ceftazidime, pip-tazo, and imipenem) were statistically significant ($p < 0.05$). Average change and range of changes in %S for all drugs for *E. coli*, *K. pneumoniae*, *E. cloacae*, and *P. aeruginosa* were -2.5% (+1% to -7%), -5.5% (-1% to -8%), -0.4% (+6% to -12%), and -9% (0% to -18%), respectively.

Conclusions: *E. coli*, *K. pneumoniae*, and *P. aeruginosa* showed decreasing susceptibility to most drugs, but only ceftriaxone, cefepime, amikacin, ciprofloxacin and levofloxacin vs. *E. coli*, and ceftazidime, pip-tazo, and imipenem vs. *P. aeruginosa* were significantly lower in 2007 than in 2003 ($p < 0.05$).

E. cloacae showed little very little change from 2003-2007 except for a 12% drop in susceptibility to pip-tazo; however, this was not statistically significant ($p > 0.05$).

In vitro activity of ertapenem has not changed significantly against gram-negative IAI pathogens in North America from 2003 to 2007.

Introduction

Bacterial resistance to antimicrobials continues to evolve, and levels of such resistance and cross-resistance can vary dramatically geographically. Consequently, it is increasingly important to monitor susceptibility trends in different worldwide regions over time to detect, define, track, and communicate those trends so that effective therapeutic measures can be determined and customized to meet local needs.

The Study for Monitoring Antimicrobial Resistance Trends (SMART) monitors the activity of ertapenem, imipenem, amikacin, cefepime, ceftazidime, ceftazidime, ceftriaxone, ciprofloxacin, levofloxacin, ampicillin/sulbactam, and piperacillin/tazobactam against gram-negative aerobic bacteria from intra-abdominal infections (IAI). This program has been ongoing in the U.S. since 2003, with 14 laboratories in 13 states participating in 2003, and 10 laboratories in 8 states participating as of 2007. One of the main goals of the study is to ensure that current susceptibility patterns of IAI pathogens are well-understood and widely disseminated, leading ultimately to the most effective choice of therapy for IAI while helping prevent further spread of resistance through inappropriate use of antimicrobics. This report evaluates the extent of susceptibility changes between 2003 and 2007 for the most frequently isolated aerobic bacteria from IAI in the U.S.

Materials & Methods

All isolates were non-repeat isolates derived from IAIs. Only one isolate per species per patient was accepted into the study. Each participating laboratory collected up to 100 consecutive non-selected gram-negative pathogens each year of the study. Isolates were identified to the species level and tested at each site.

Minimum inhibitory concentrations (MICs) were determined using MicroScan dehydrated broth microdilution panels manufactured by Siemens Medical Solutions Diagnostics (West Sacramento, California, USA), following Clinical and Laboratory Standards Institute (CLSI) guidelines [1]. All antimicrobial agents were supplied by the panel manufacturer. The following antimicrobial agents were included on the panels with their dilution ranges (expressed in mcg/ml): ertapenem 0.03-4, imipenem 0.06-8, cefepime 0.5-32, ceftazidime 0.5-128, ceftazidime/clavulanic acid 0.12-16, ceftazidime 2-16, ciprofloxacin 0.25-2, amikacin 4-32, levofloxacin 0.5-4, cefotaxime 0.5-128, cefotaxime/clavulanic acid 0.12-16, piperacillin/tazobactam 2/4-64/4, ampicillin/sulbactam 2/2-16/2, and ceftriaxone 1-32.

MIC interpretive criteria followed published guidelines established by CLSI [2].

E. coli, *K. pneumoniae* and *K. oxytoca* strains were classified as extended spectrum beta-lactamase (ESBL) producers if there was at least an eight-fold reduction of MIC for ceftazidime or ceftazidime tested in combination with clavulanic acid versus their MICs when tested alone [2]. In 2003, however, ESBL confirmation testing was done using cefepime with and without clavulanic acid, which has subsequently been suggested to underestimate true ESBL rates [3].

Quality control testing (QC) was done by each testing site on each day of testing using the CLSI-recommended QC strains: *E. coli* ATCC 25922, *K. pneumoniae* ATCC 700603 (positive ESBL control), and *Pseudomonas aeruginosa* ATCC 27853. Results were included in the analysis only when corresponding QC isolates tested within the acceptable range according to CLSI guidelines [2].

Development of a centralized database of study results was managed by International Health Management Associates, Inc. located in Schaumburg, IL, USA.

Only species which had ≥ 20 isolates in both 2003 and 2007 were included in the statistical analysis; tests for statistical significance were done using Fisher's exact test (two-tailed).

References

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Acknowledgements

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Results

Table 1 summarizes 2003 vs. 2007 susceptibility levels of the four species with ≥ 30 isolates in each of those years. Figures 1-4 present the same data graphically by species. Table 2 shows percentage of ESBL+ *E. coli* and *K. pneumoniae* among isolates in this study.

Table 1. % susceptible of gram-negative IAI pathogens with $n \geq 30$ in 2003 and 2007. 2007 values lower or higher than 2003 are red- or green-highlighted, respectively; p values < 0.05 are yellow-highlighted.

	n	P/T ¹	Caz	Cax	Cpe	Cfx	Imp	Etp	Cp	Lvx	Ak
<i>E. coli</i>											
2003	427	96.5	97.2	98.6	99.3	92.7	100	100	88.8	89.2	100
2007	252	94.8	96.4	95.6	97.2	93.7	98.8	98.8	81.8	82.4	98.4
$p < .05$		no	no	yes	yes	no	no	no	yes	yes	yes
<i>K. pneumoniae</i>											
2003	147	91.2	95.2	93.9	96.6	85.7	99.3	98.0	88.4	93.2	98.6
2007	81	84.0	87.7	88.9	90.1	80.3	96.3	92.6	81.5	86.4	97.5
$p < .05$		no	no	no	no	no	no	no	no	no	no
<i>E. cloacae</i>											
2003	80	72.5	56.3	55	87.5	7.5	100	96.3	81.3	86.3	97.5
2007	33	60.6	60.6	60.6	84.9	6.1	100	93.9	81.9	87.9	100
$p < .05$		no	no	no	no	no	no	no	no	no	no
<i>P. aeruginosa</i>											
2003	161	88.2	84.5	23.0	83.9	na ²	88.2	na	77.0	77.0	96.9
2007	73	78.1	71.2	23.3	72.6	na	69.9	na	68.5	69.9	93.2
$p < .05$		yes	yes	no	no	no	yes	no	no	no	no

¹P/T=piperacillin/tazobactam; Caz=ceftazidime; Cax=ceftriaxone; Cpe=cefepime; Cfx=cefoxitin; Imp=imipenem; Etp=ertapenem; Cp=ciprofloxacin; Lvx=levofloxacin; Ak=amikacin.

²na=not applicable.

Table 2. North American ESBL+ rates for *E. coli* and *K. pneumoniae* in 2003 and 2007

	% ESBL-Positive (n)		
	2003	2007	P
<i>E. coli</i>	3.3% (14/427)	5.6% (14/252)	0.1646
<i>K. pneumoniae</i>	6.1% (9/147)	16.0% (13/81)	0.0194

Figure 1.

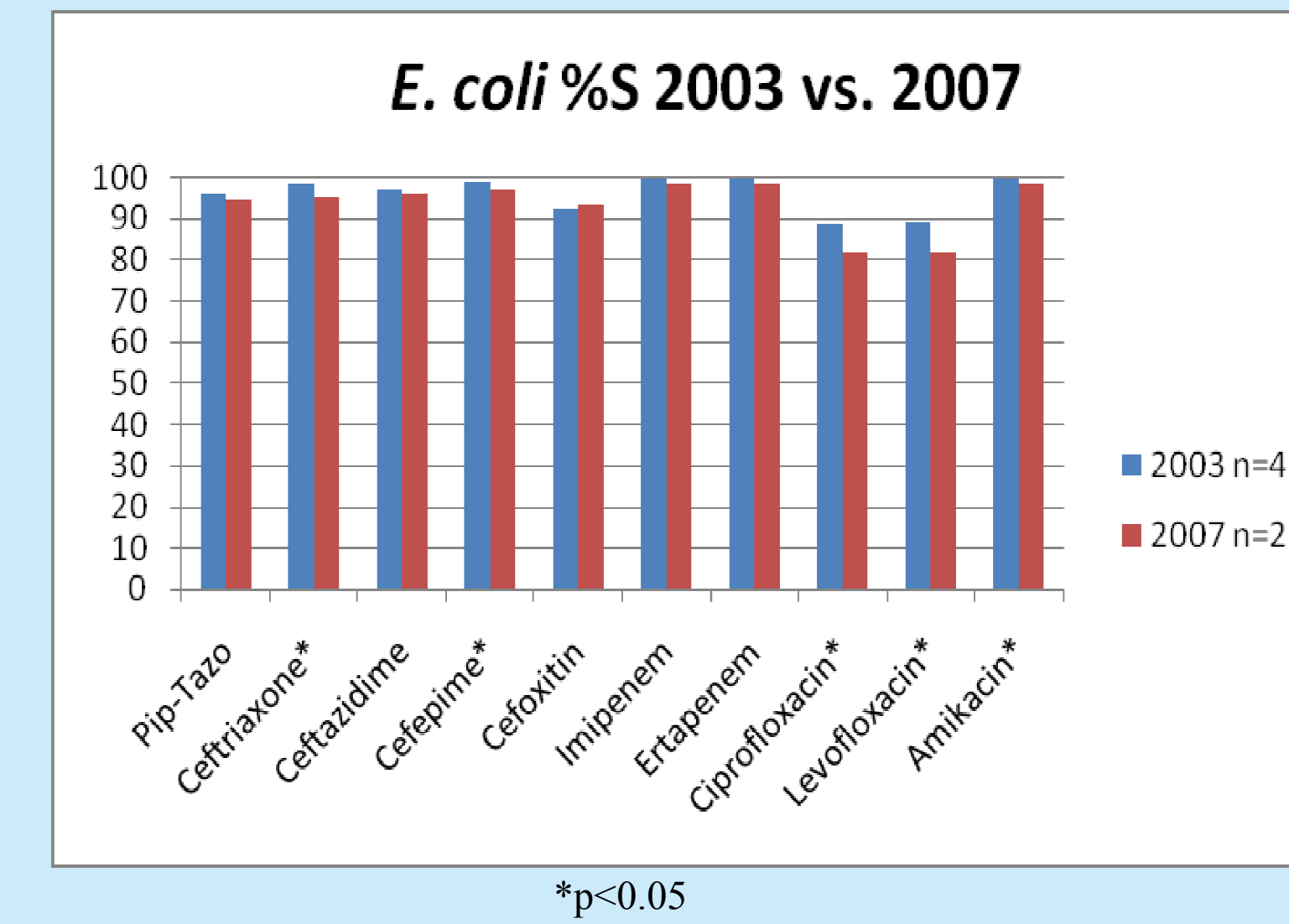


Figure 2.

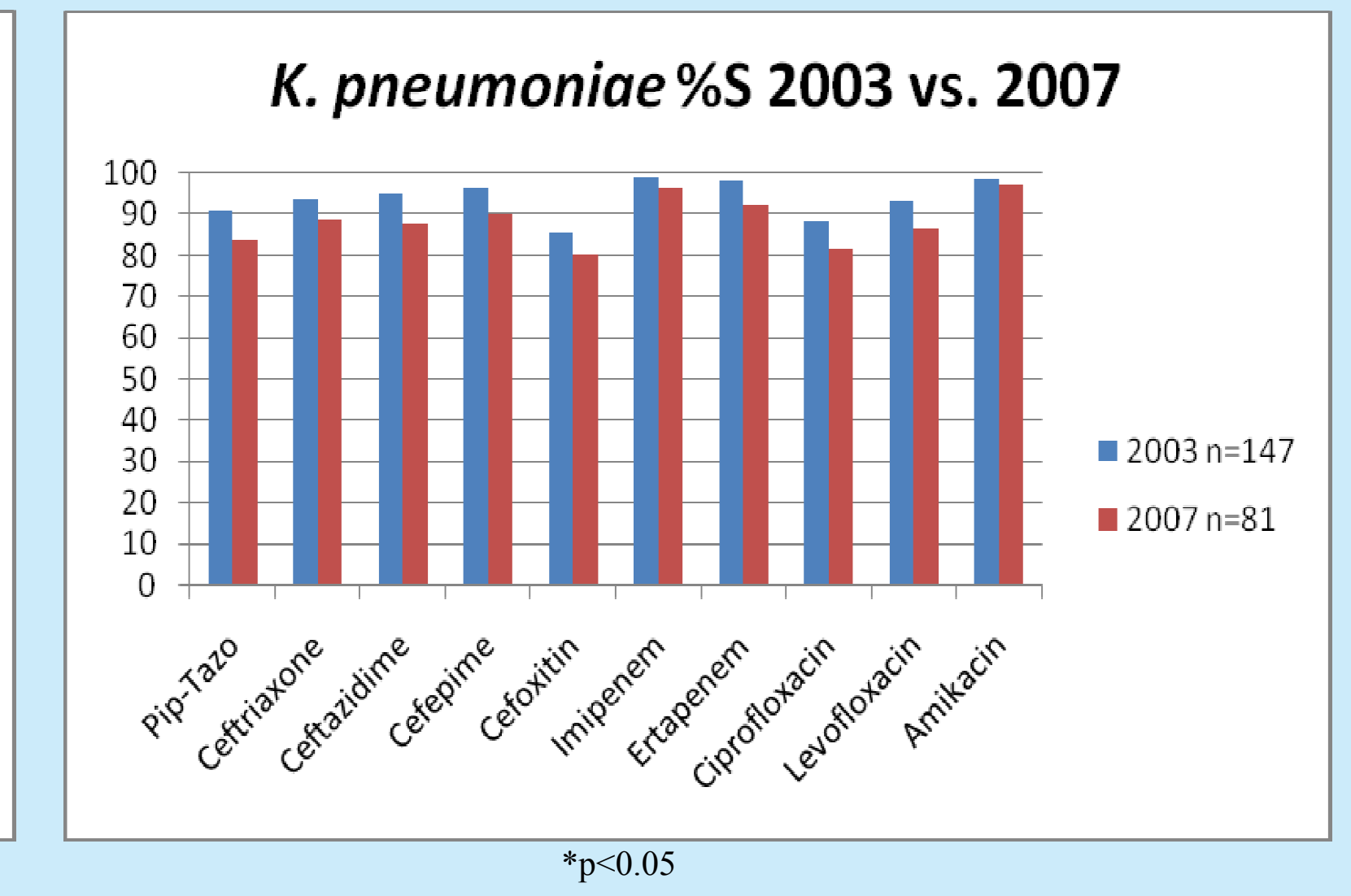


Figure 3.

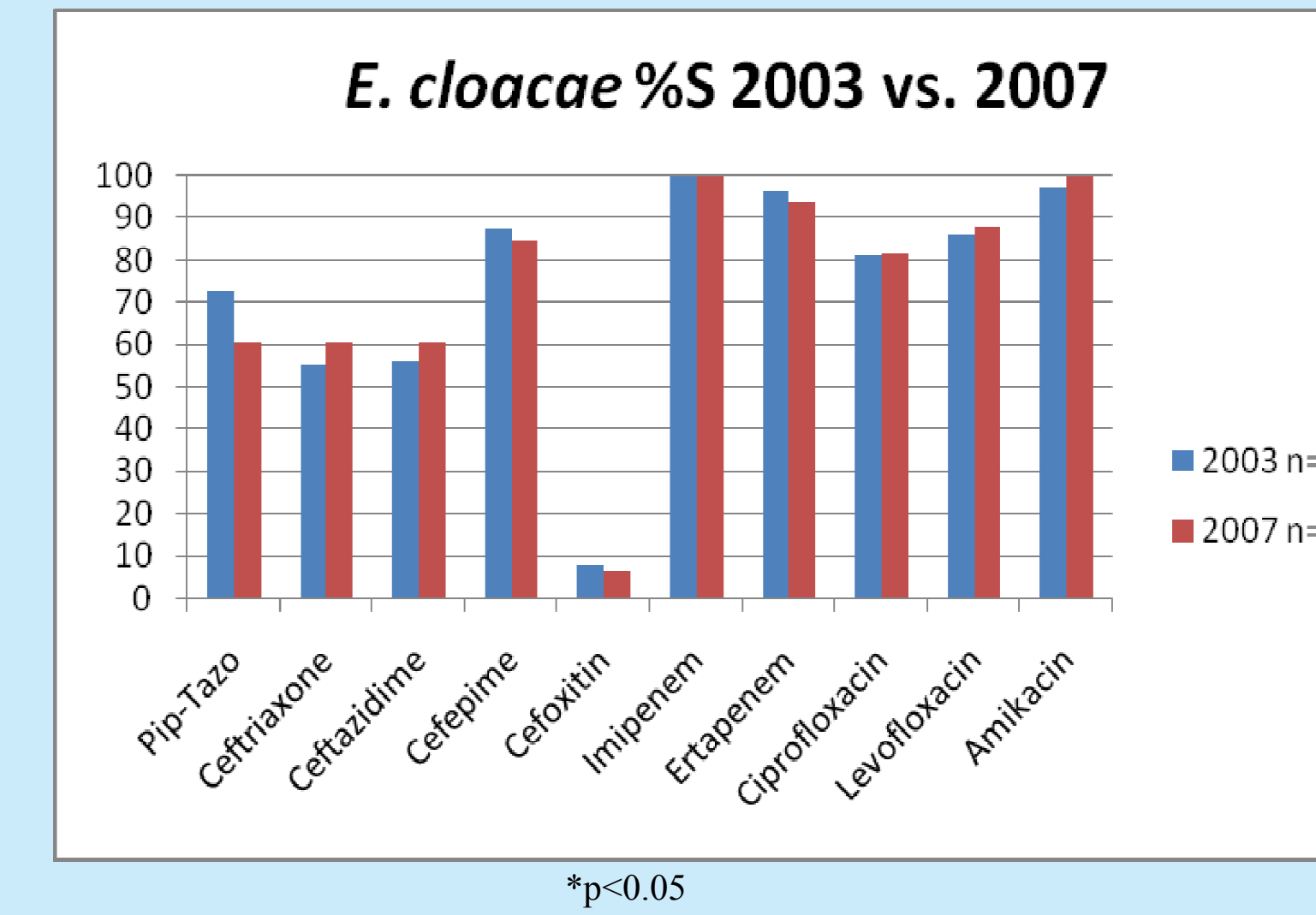
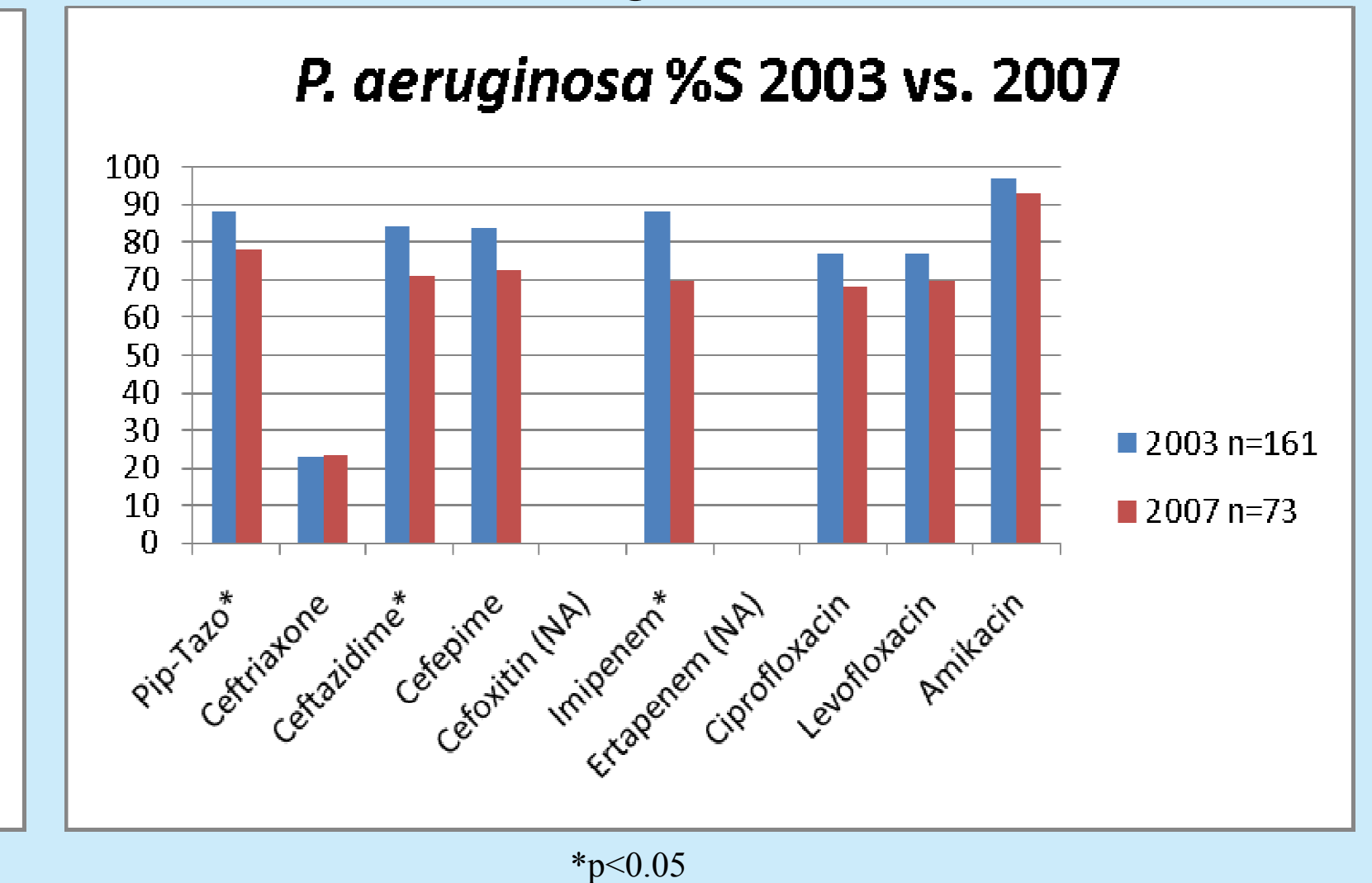


Figure 4.



Conclusions

- E. coli*, *K. pneumoniae*, and *P. aeruginosa* showed diminished susceptibility to most drugs, but only ceftriaxone, cefepime, amikacin, ciprofloxacin and levofloxacin vs. *E. coli*, and ceftazidime, pip-tazo, and imipenem vs. *P. aeruginosa* were significantly lower in 2007 than in 2003 ($p < 0.05$).
- E. cloacae* showed little very little change from 2003-2007 except for a 12% drop in susceptibility to pip-tazo (72.5-60.6%); however, even that difference was not statistically significant ($p > 0.05$).
- In vitro activity of ertapenem has not changed significantly against gram-negative IAI pathogens in North America from 2003 to 2007.