

Acinetobacter baumannii Susceptibility: Global and Regional Analysis from SMART 2002-present

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Revised Abstract

Background: Therapy of *A. baumannii* (Ab) is challenging due to frequent multidrug resistance. Increasing resistance in other organisms such as ESBL+ *E. coli* and *K. pneumoniae* has led to use of carbapenems in infections previously treatable with other drugs. In many of these infections, imipenem is often used as a drug of “last resort”. The SMART program has tracked the susceptibility of pathogens from intra-abdominal infections (IAI) globally since 2002. This report shows susceptibility trends of Ab to imipenem and other drugs from global and regional perspectives.

Methods: 1,154 isolates of Ab from IAI were collected in hospitals in 43 countries from 2002-2009 (563 from Asia). Susceptibility (%S) was determined using custom MicroScan broth microdilution panels, and interpreted using CLSI M100-S21 guidelines. The Cochran-Armitage test was used to determine significance of changes.

Results: Five drugs (shown in the table below) showed significant changes in %S from 2002-2009. All other drugs (amikacin, ceftazidime, ceftriaxone, and ciprofloxacin) did not change significantly either globally or in Asia.

Drug	Region	2002	2003	2004	2005	2006	2007	2008	2009	p ^a
Cefepime	Global	31.9	26.2	29.6	22.2	25.8	18.4	17.0	22.4	0.014
	Asia	31.0	15.4	35.9	12.2	21.3	19.2	15.4	20.3	0.157
Cefotaxime	Global				12.2	18.6	10.6	13.5	20.5	0.046
	Asia				8.2	16.4	9.6	11.0	20.3	0.051
Imipenem	Global	76.4	64.3	67.9	56.7	51.6	44.0	44.8	44.3	<.0001
	Asia	92.9	53.9	76.9	59.2	52.5	47.9	36.3	28.4	<.0001
Levofloxacin	Global		33.3	38.3	26.7	40.2	22.0	20.2	27.6	0.013
	Asia		30.8	46.2	20.4	42.6	20.2	22.0	27.7	0.089
Pip-Tazo	Global	38.9	32.1	38.3	35.6	36.1	24.1	18.8	24.3	<.0001
	Asia	45.2	33.3	48.7	30.6	37.7	26.6	19.8	21.6	<.0001

^aSignificant values (p<.05) are shaded and boldfaced.

Conclusions: Globally and in Asia, %S for all drugs except imipenem fluctuated between 10-50% from 2002-2009. Although imipenem started in 2002 at 76% globally, it declined steadily to ~44% globally in 2007 and remained at that level into 2009. Imipenem showed even greater decline in Asia, dropping from 93% in 2002 to 28% in 2009; however, despite this decline, it remained the most active study drug in 2009. Resistance in Ab continues to be problematic with none of the drugs evaluated in SMART inhibiting >44% (30% in Asia) of isolates.

Introduction

Acinetobacter baumannii has long been recognized as one of the most difficult-to-treat bacterial pathogens in hospitals due to multidrug resistance frequently associated with this species, especially in intensive care units (ICUs). Carbapenems are usually considered to be primary agents of choice for such infections; however, increasing resistance in other organisms such as extended-spectrum beta-lactamase-producing (ESBL+) *Escherichia coli* and *Klebsiella pneumoniae* has led to use of carbapenems in infections previously treatable with other drugs, such as cephalosporins or fluoroquinolones. In many of these infections, a carbapenem is often used as a drug of “last resort”. The SMART program has tracked the global susceptibility of pathogens from intra-abdominal infections (IAI) since 2002, and, starting late 2009, from urinary tract infections (UTI). This report shows susceptibility trends of *A. baumannii* to imipenem and other drugs from global and Asia/Pacific data, and compares trends from ICU vs. non-ICU infections as well as community-associated vs. hospital-associated infections.

Materials & Methods

- ❖ 1,126 (549 from Asia/Pacific) isolates of *A. baumannii* from IAI were collected in hospitals in 43 countries from 2002-2009, and 28 isolates (14 from Asia) were collected from UTI (2009 only).
- ❖ Isolates were considered “community-associated” if they were recovered from specimens collected within 48 hours of admission to hospital, and “hospital-associated” if recovered ≥48 hours of admission to hospital.
- ❖ Susceptibility testing was done at each collecting site until 2008, from which time all isolates were sent to a central laboratory in the USA (IHMA, Inc., Schaumburg, Illinois) for confirmation of identification and susceptibility testing.
- ❖ Susceptibility (%S) was determined in all years using custom dried MicroScan broth microdilution panels, following the manufacturer’s and Clinical and Laboratory Standards Institute (CLSI) guidelines [1] Minimal inhibitory concentrations were re-interpreted using CLSI M100-S21 guidelines [2] for this analysis.
- ❖ CLSI-recommended quality control (QC) organisms were tested concurrently each day that clinical isolates were tested, and results were only included in the database if all QC results were within prescribed ranges published by the CLSI, using the most current version each year.
- ❖ The Cochran-Armitage test was used to determine statistical significance of linear trends.

References

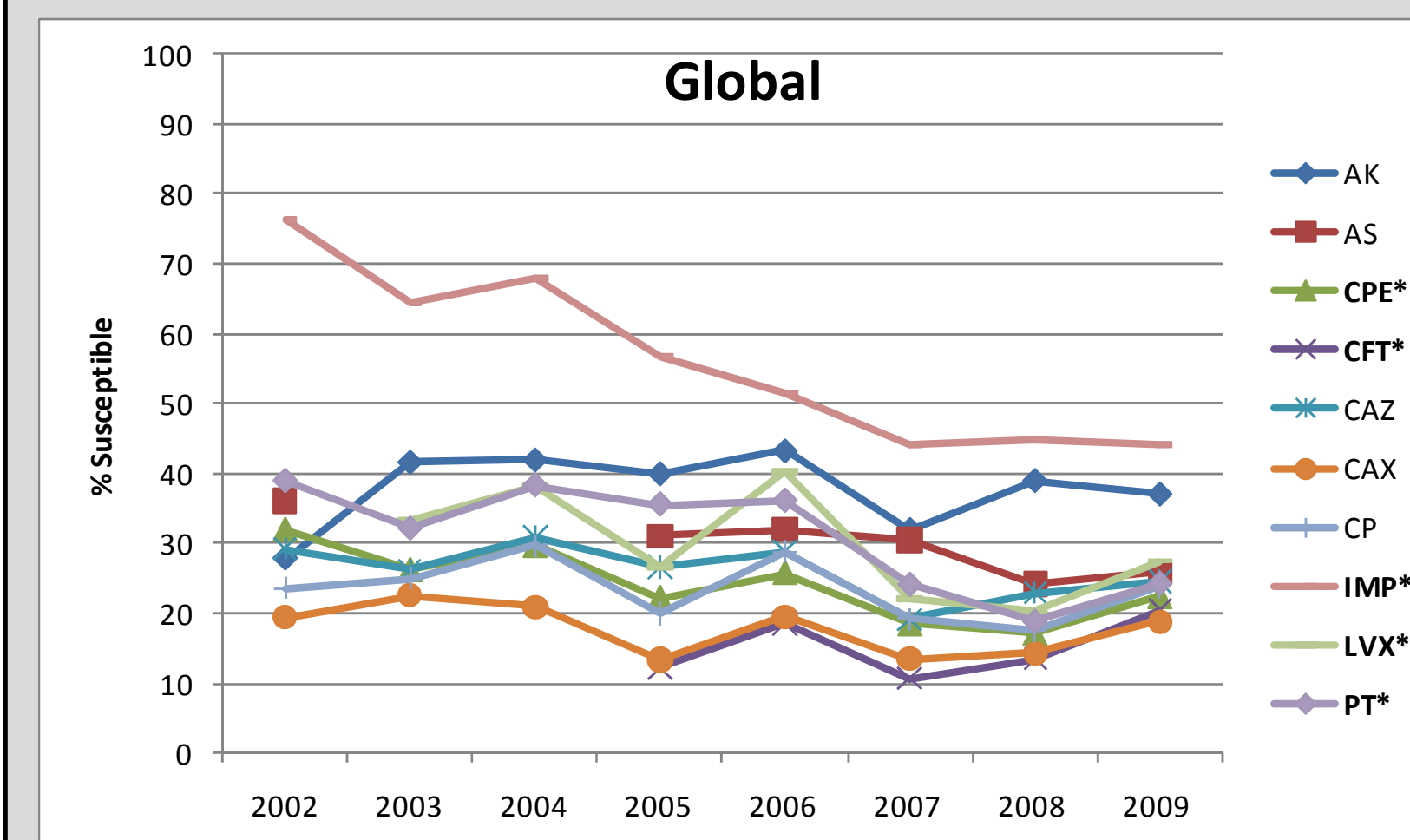
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2. Clinical and Laboratory Standards Institute. 2011. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-First Informational Supplement. CLSI Document M100-S21. Wayne, PA.

Acknowledgements

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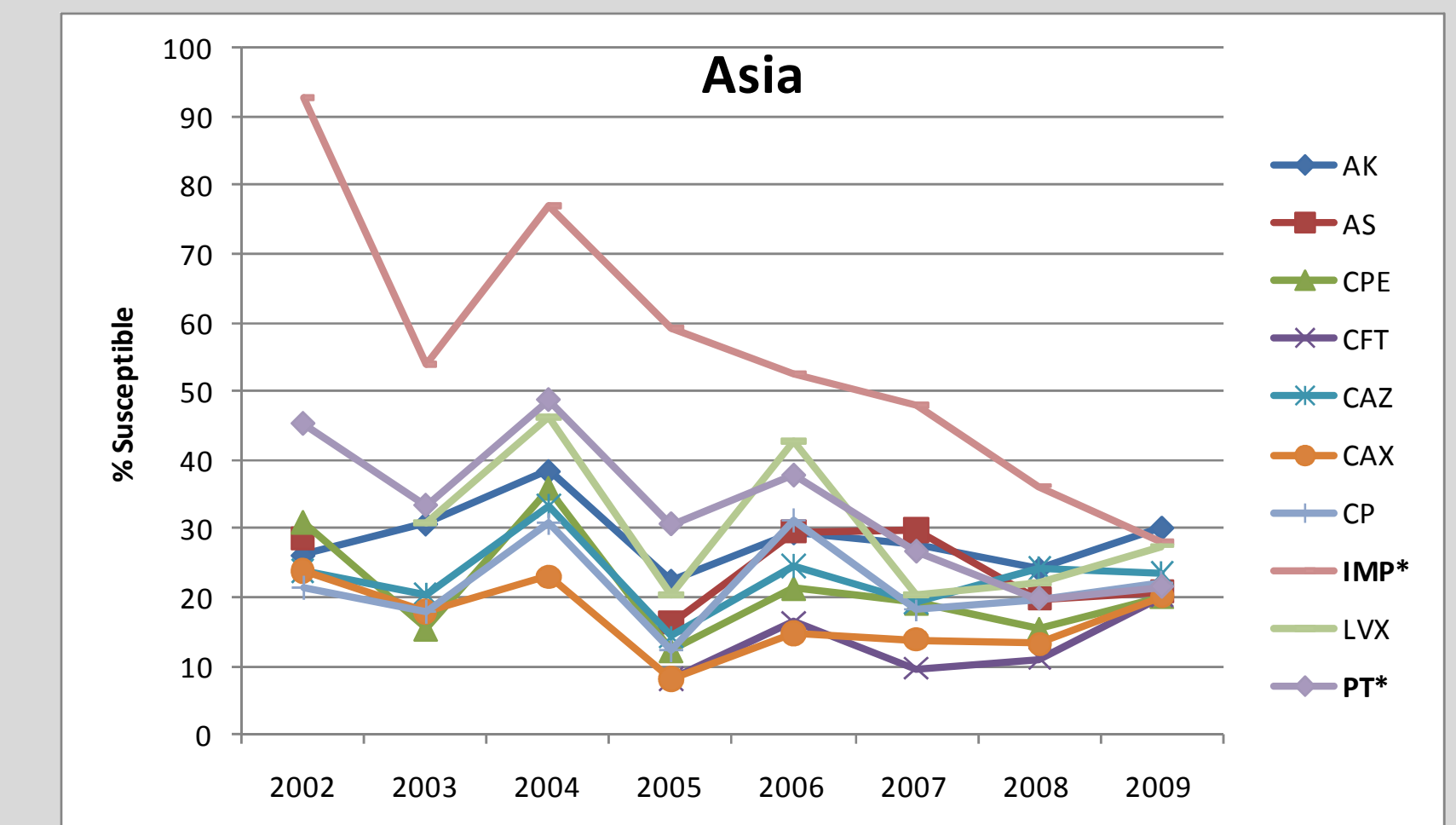
Results

Figure 1. Global susceptibility trends of *A. baumannii* from 2002-2009.



Ak=amikacin; AS=ampicillin-sulbactam; CPE=cefepime; CFT=cefotaxime; CAZ=ceftazidime; CAX=ceftriaxone; CP=ciprofloxacin; IMP=imipenem; LVX=levofloxacin; PT=piperacillin-tazobactam.
*Asterisks and boldfaced text signify drugs for which statistically significant (p<0.05) trends in declining susceptibility were observed.

Figure 2. Asian susceptibility trends of *A. baumannii* from 2002-2009.



Ak=amikacin; AS=ampicillin-sulbactam; CPE=cefepime; CFT=cefotaxime; CAZ=ceftazidime; CAX=ceftriaxone; CP=ciprofloxacin; IMP=imipenem; LVX=levofloxacin; PT=piperacillin-tazobactam.
*Asterisks and boldfaced text signify drugs for which statistically significant (p<0.05) trends in declining susceptibility were observed.

Figure 3. Imipenem susceptibility trends of *A. baumannii* from ICU vs. non-ICU: global data 2002-2009.

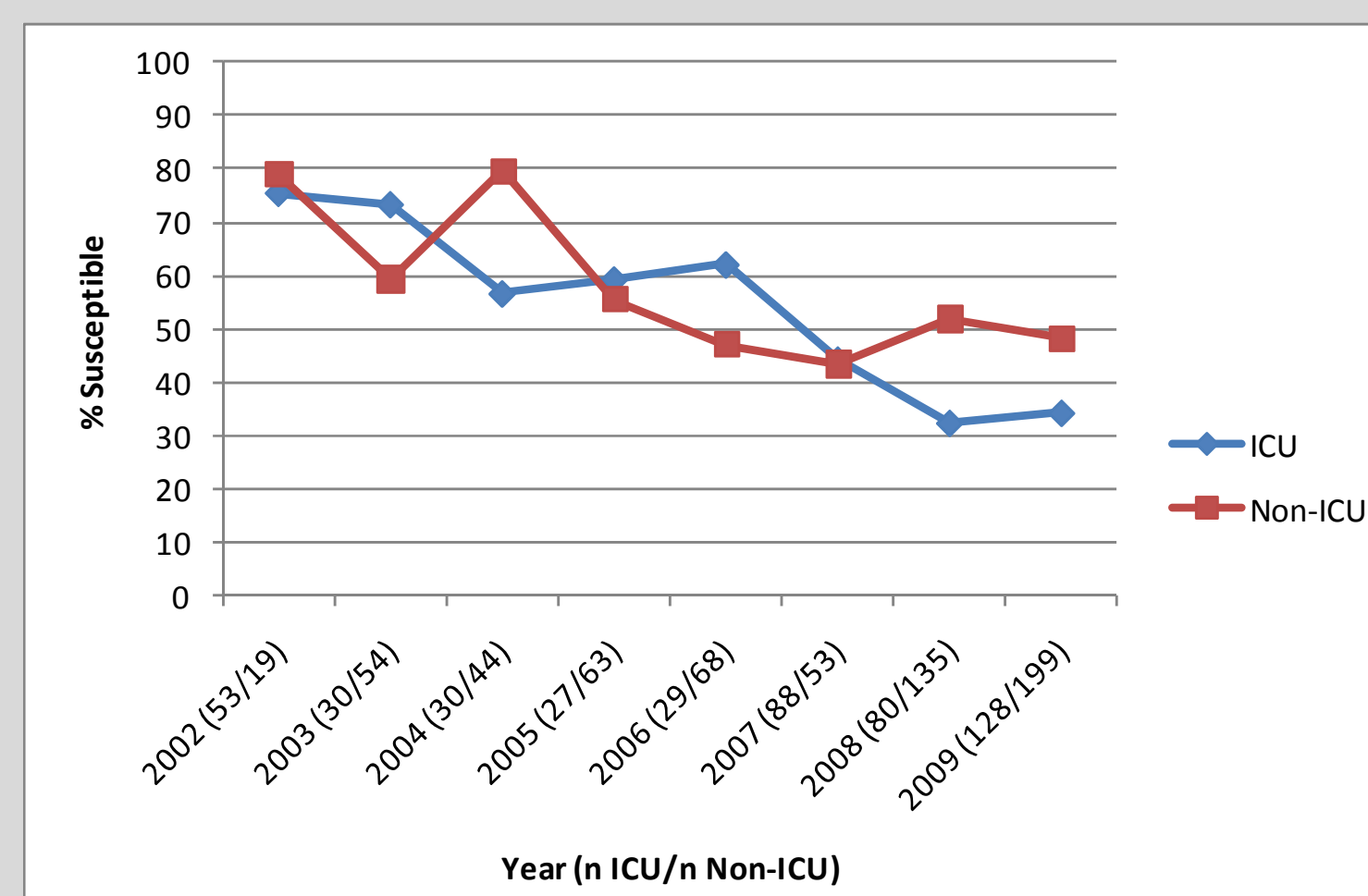
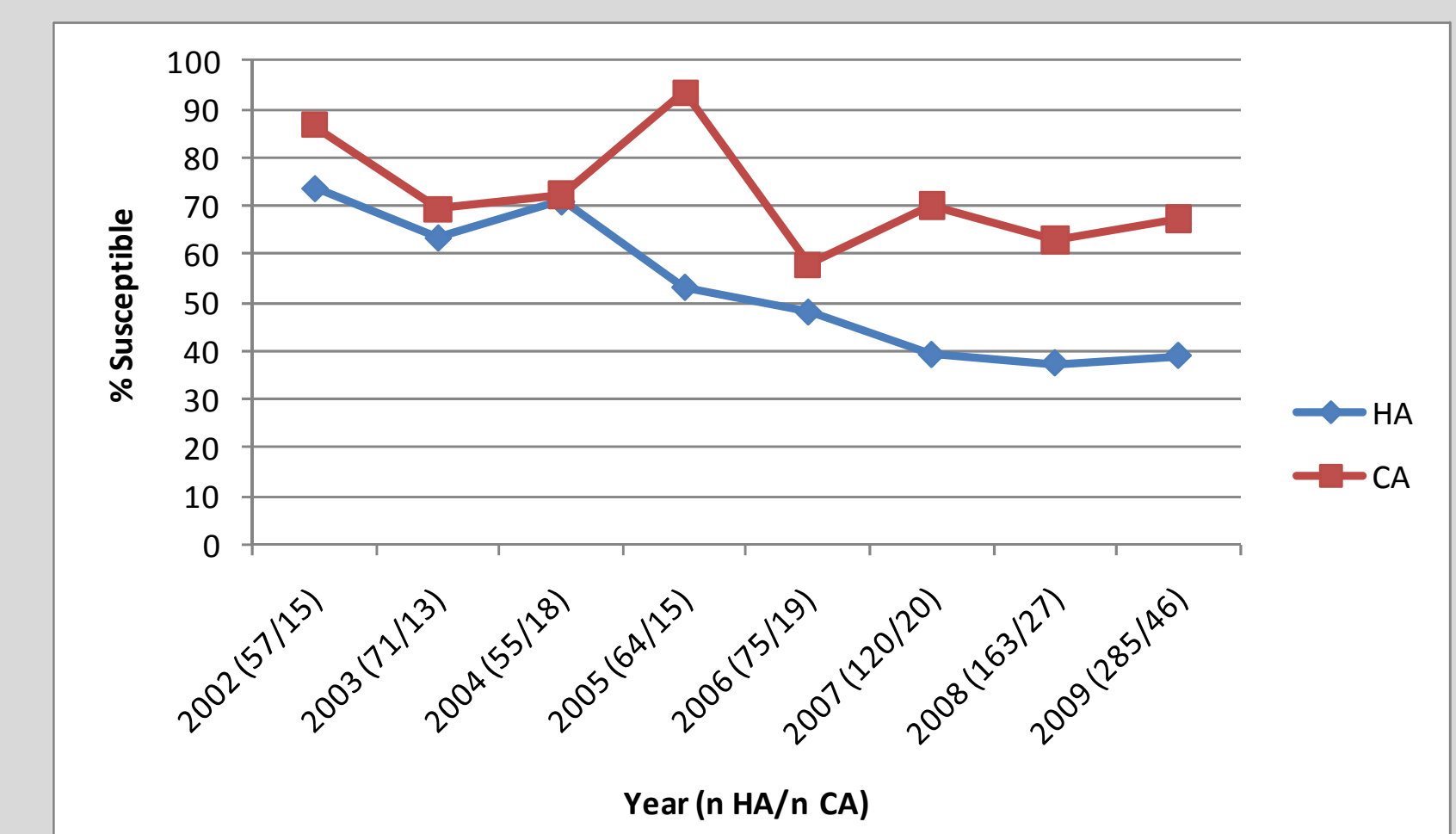


Figure 4. Imipenem susceptibility trends of *A. baumannii* from hospital-associated (HA) vs. community-associated (CA) infections: global data 2002-2009.



Conclusions

- ❖ Globally and in Asia, %S for all drugs except imipenem fluctuated between 10-50% from 2002-2009. Although imipenem started in 2002 at 76% globally, it declined steadily to ~44% in 2007 and remained at that level into 2009.
- ❖ Susceptibility of *A. baumannii* to imipenem showed even greater decline in Asia, dropping from 92.9% in 2002 to 28.4% in 2009; nevertheless, it remained the most active study drug *in vitro*, just above levofloxacin (27.7% susceptible).
- ❖ There was little difference in imipenem susceptibility between ICU and non-ICU isolates of *A. baumannii*, suggesting that resistance is not just a concern for ICU patients.
- ❖ Differences were much more striking between community- and hospital-associated infections, with isolates from the former remaining more susceptible (at 60-70%) than the latter (at 40%). Although imipenem susceptibility of isolates from both hospital- and community-associated infections declined over the eight years of the study, that of hospital-associated infection isolates did so at an even faster rate.
- ❖ Resistance in *A. baumannii* continues to worsen, with only imipenem (44%) and amikacin (37%) among drugs tested in SMART inhibiting more than 27% of isolates globally in 2009, while all study drugs inhibited <30% in Asia.