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## Revised Abstract

**Objectives:** The Study for Monitoring Antimicrobial Resistance Trends (SMART) has tracked susceptibility levels and incidence of extended-spectrum beta-lactamase producing (ESBL+) *Escherichia coli* causing intra-abdominal infections (IAI) since 2002. In late 2009 pathogens from inpatient urinary tract infection (IAI) were added to the study. This report compares susceptibility and ESBL+ rates of *E. coli* from IAI and UTI in Europe in 2009-2010.

**Methods:** 39 hospitals in 12 European countries each collected up to 100 consecutive non-selected isolates from IAI and up to 50 from UTI. All isolates were sent to a central laboratory (IHMA, Inc., USA) for confirmation of identification, susceptibility testing, and ESBL determination; the latter two were done following CLSI guidelines. Percent susceptibility was determined using EUCAST breakpoints. Fisher's exact test was used to determine statistical significance of differences between IAI and UTI susceptibility levels.

**Results:** 3,578 isolates of *E. coli* were tested (IAI 2,692 UTI 886). ESBL+ rates were 10.7% in IAI and 18.2% in UTI. The following table summarizes % susceptible of *E. coli* overall and the ESBL+ subset from IAI and UTI:

Source	Organism	ETP	IMP	CPE	CFT	CAZ	CAX	AS	PT	AK	CP	LVX
UTI	<i>E. coli</i> (n=886)	99	100	81	80	82	80	43	87	91	66	68
IAI	<i>E. coli</i> (n=2692)	99	100	89	87	87	87	46	89	94	75	77
	p	0.2173	1	<.0001	<.0001	<.0001	<.0001	0.1391	0.0644	0.0086	<.0001	<.0001

Source	Organism	ETP	IMP	CPE	CFT	CAZ	CAX	AS	PT	AK	CP	LVX
UTI	<i>E. coli</i> ESBL+ (n=161)	96	100	5	1	9	1	5	65	65	21	24
IAI	<i>E. coli</i> ESBL+ (n=288)	98	100	7	2	10	3	6	69	67	22	25
	p	0.1537	1	0.5421	0.7171	0.8695	0.3415	1	0.3992	0.7548	0.8105	0.8196

Values ≥90% are shaded; boldfaced signifies p<0.05.

ETP=ertapenem, IMP=imipenem, CPE=cefepime, CFT=cefotaxime, CAZ=ceftazidime, CAX=ceftriaxone, AS=ampicillin-sulbactam, PT=piperacillin-tazobactam, AK=amikacin, CP=ciprofloxacin, LVX=levofloxacin.

**Conclusions:** Although differences in susceptibility percentages between IAI and UTI *E. coli* were generally small (all <10%), 7/11 drugs showed significantly lower susceptibility in UTI than in IAI (p<0.05). This is at least partially explained by the significantly higher (p<0.05) ESBL+ rate seen in UTI isolates (18.8%) than in IAI (11.1%). Imipenem, ertapenem, and amikacin were the only study drugs to inhibit >90% of *E. coli* from both IAI and UTI. ESBL+ isolates were ≥96% susceptible to both carbapenems, but <69% susceptible to all other study drugs. The relatively high rate of ESBL+ *E. coli* in UTI in Europe is concerning, as further increases could render many drugs commonly used to treat UTI inappropriate for empiric therapy.

## Introduction

The Study for Monitoring Antimicrobial Resistance Trends (SMART) has tracked and reported on the susceptibility trends of aerobic gram-negative pathogens of intra-abdominal infections (IAI) since 2002. In late 2009, the program's scope was expanded to include surveillance of aerobic gram-negative pathogens of in-patient urinary tract infections (UTI). Since ertapenem has approved indications for treatment of IAI and complicated UTI in several countries outside of Europe, the data collected can be useful in developing empiric treatment guidelines for both infection types. SMART has documented increasing rates of extended-spectrum beta-lactamase (ESBL) producing *Escherichia coli* and *Klebsiella pneumoniae* in IAI in most regions of the world, with concomitantly increasing rates of resistance to many of the antimicrobials studied in this program. Since *E. coli* is by far the predominant pathogen of both IAI and UTI, this report will summarize the recent (2009-2010) IAI and UTI data from SMART to determine if there are significant differences in ESBL+ rates and antimicrobial susceptibility levels of *E. coli* between them.

## Materials & Methods

- Participating sites each collected up to 100 consecutive, non-selected isolates of gram-negative aerobic bacilli from intra-abdominal infections, and up to 50 from urinary tract infections (UTI); 3,578 isolates of *E. coli* were collected in 2009 and 2010 at 39 hospitals in 12 European countries.
- Isolates were sent to a central laboratory (IHMA, Inc., Schaumburg, Illinois, USA) for confirmation of identification and susceptibility testing.
- Minimum inhibitory concentrations (MICs) and production of extended spectrum beta-lactamase (ESBL) were determined using custom MicroScan dehydrated broth microdilution panels (Siemens Medical Solutions Diagnostics, West Sacramento, CA), following manufacturer and CLSI guidelines [1,2]. MICs were analyzed using European Committee on Antimicrobial Susceptibility Testing (EUCAST) interpretive breakpoints [3].
- Quality control was done each day of testing following CLSI guidelines [2].
- Fisher's exact test was used to compare susceptibility levels and ESBL+ rates of *E. coli* from UTI vs. those from IAI.

## References

- Clinical and Laboratory Standards Institute. 2009. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard—Seventh Edition, in Document M7-A8. Wayne, PA.
- Clinical and Laboratory Standards Institute. 2011. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-first Informational Supplement. CLSI document M100-S21. Wayne, PA.
- The European Committee on Antimicrobial Susceptibility Testing – EUCAST Clinical Breakpoints 2010; [http://www.eucaast.org/clinical\\_breakpoints/](http://www.eucaast.org/clinical_breakpoints/).

## Acknowledgements

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## Results

Figure 1.

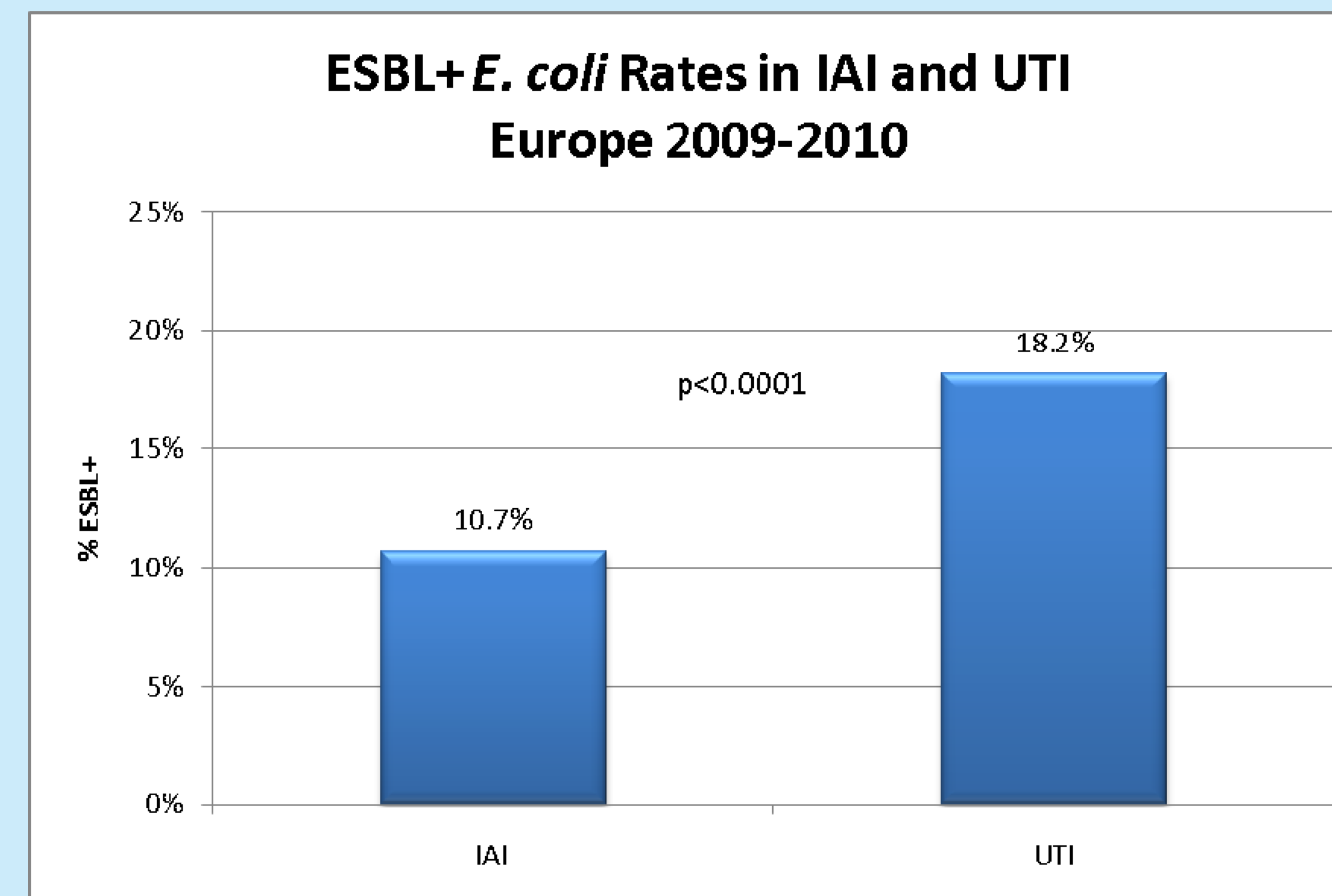
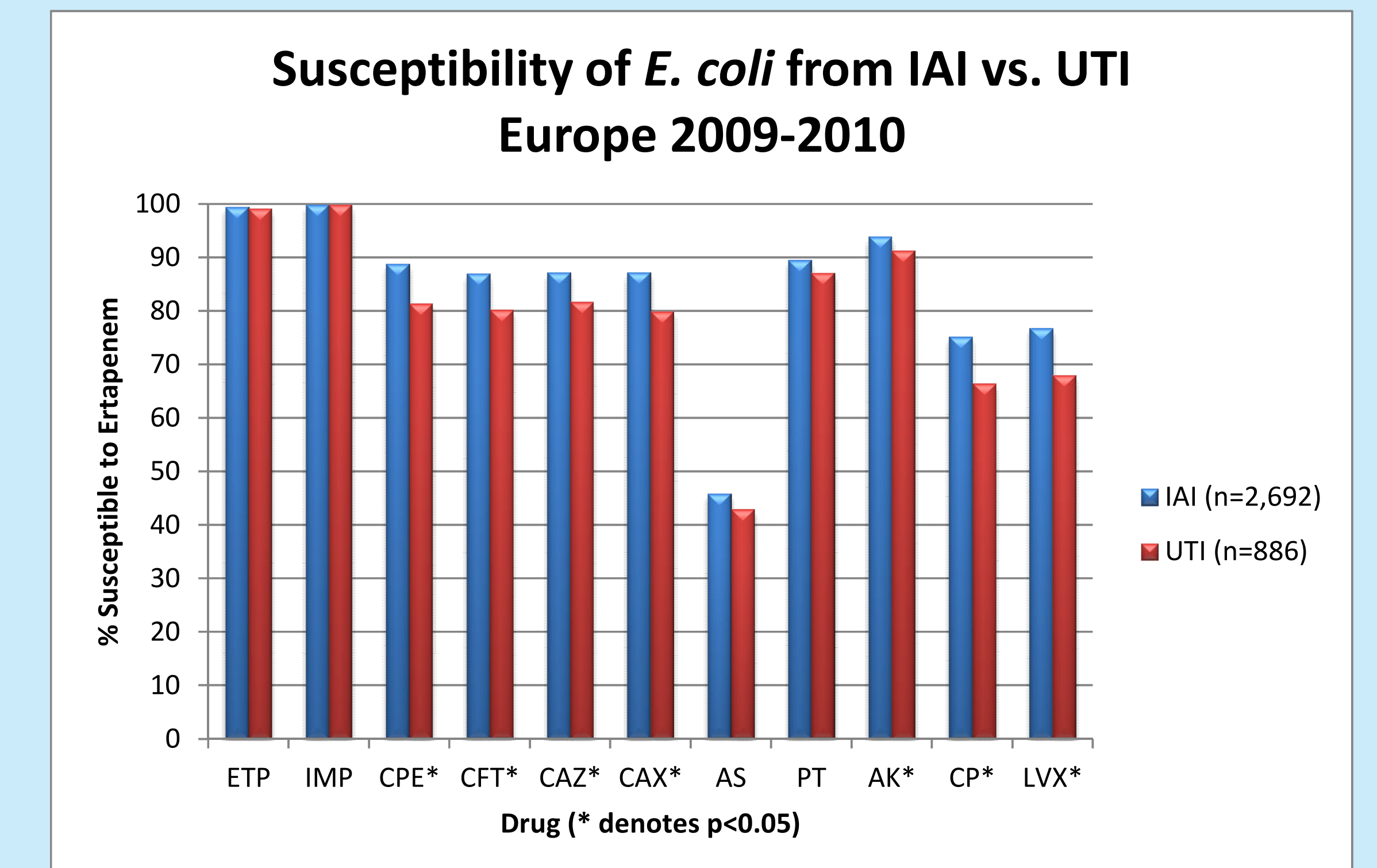
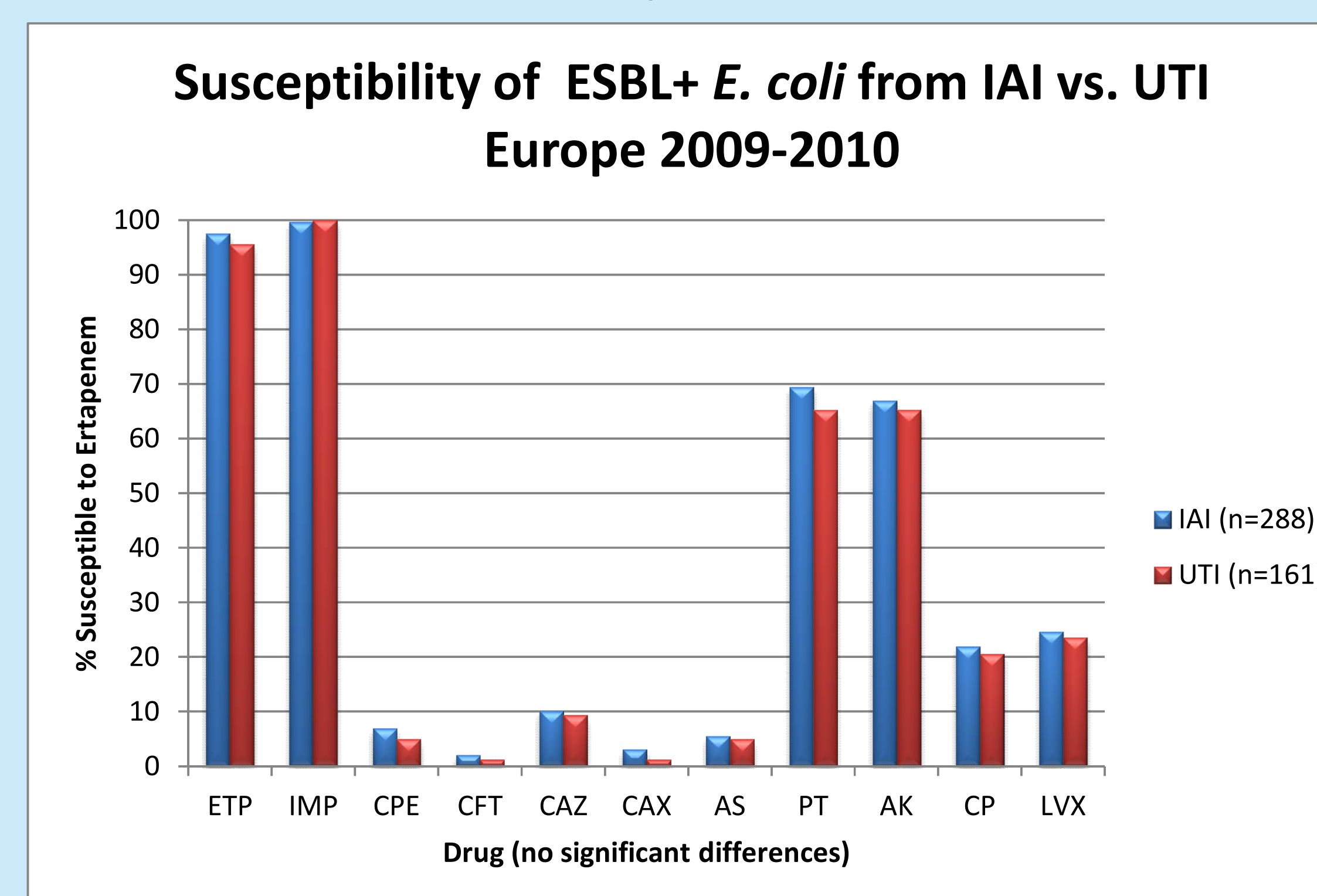


Figure 2.



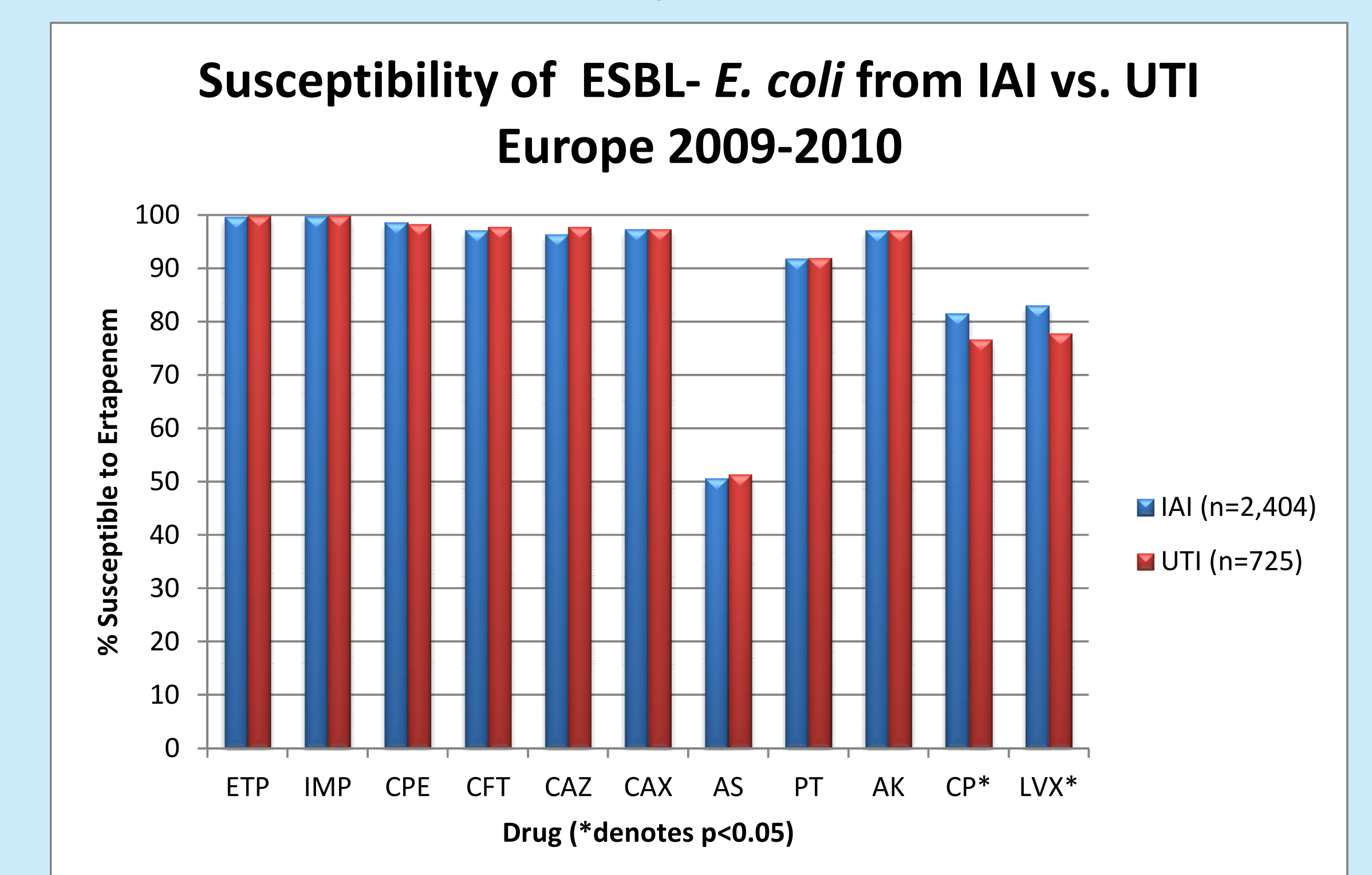
ETP=ertapenem, IMP=imipenem, CPE=cefepime, CFT=cefotaxime, CAZ=ceftazidime, CAX=ceftriaxone, AS=ampicillin-sulbactam, PT=piperacillin-tazobactam, AK=amikacin, CP=ciprofloxacin, LVX=levofloxacin.

Figure 3.



ETP=ertapenem, IMP=imipenem, CPE=cefepime, CFT=cefotaxime, CAZ=ceftazidime, CAX=ceftriaxone, AS=ampicillin-sulbactam, PT=piperacillin-tazobactam, AK=amikacin, CP=ciprofloxacin, LVX=levofloxacin.

Figure 4.



ETP=ertapenem, IMP=imipenem, CPE=cefepime, CFT=cefotaxime, CAZ=ceftazidime, CAX=ceftriaxone, AS=ampicillin-sulbactam, PT=piperacillin-tazobactam, AK=amikacin, CP=ciprofloxacin, LVX=levofloxacin.

## Conclusions

- ESBL-positive *E. coli* were significantly (p<0.05) more common in UTI (18.2%) than in IAI (10.7%) in Europe in 2009-2010.
- Although differences in susceptibility percentages between IAI and UTI *E. coli* were generally small (all <10%), 7/11 drugs showed significantly lower susceptibility in UTI than in IAI (p<0.05). This is at least partially explained by the higher ESBL-positive rate seen in UTI isolates than in IAI.
- Imipenem, ertapenem, and amikacin were the only study drugs to inhibit >90% of *E. coli* from both IAI and UTI. ESBL-positive isolates were ≥96% susceptible to both carbapenems, but <69% susceptible to all other study drugs, including amikacin and piperacillin-tazobactam.
- The diminished susceptibility to fluoroquinolones seen in ESBL-negative isolates in UTI may be due to extensive use of the agents to treat UTI over the years; no other drugs in SMART showed significant susceptibility differences between UTI and IAI for the ESBL-negative isolates.
- The relatively high rate of ESBL-positive *E. coli* in UTI in Europe (>18%) is concerning, as further increases could render many drugs commonly used to treat UTI—especially fluoroquinolones—inappropriate for empiric therapy of these infections.