

# Trends in Antimicrobial Resistance of *Citrobacter* Isolates Over a 14-Year Time Period

## BACKGROUND

Antimicrobial resistance is a global health concern. *Citrobacter* spp. are nosocomial gram-negative bacterial pathogens with the potential for multidrug resistance. Unfortunately, because *Citrobacter* spp. have been classified as low priority pathogens, they have received little attention in the published literature.

## OBJECTIVE

To evaluate changes in antimicrobial resistance patterns of *Citrobacter* clinical isolates collected from inpatients at Sunnybrook Health Sciences Centre (SHSC), Toronto, Ontario over a 14-year time period.

## METHODS

Patient-level data for clinical isolates of *Citrobacter* spp. were retrospectively extracted from the SHSC Microbiology database from October 2002 to September 2016. Annual trends in ciprofloxacin, ceftazidime, ceftriaxone, co-trimoxazole, ertapenem, gentamicin, meropenem, and piperacillin/tazobactam resistance were assessed using linear regression at a significance level of 0.05.

## RESULTS

Of 1256 *Citrobacter* clinical isolates identified, 70% were from urine, 9% from blood, 8% from respiratory sources, and 13% from other human specimens. Isolates were obtained from patients on the wards (52%), in the emergency department (29%), and in intensive care units (19%). Fifty-five percent of isolates were collected after 48 hours of hospital admission, an 45% were collected within 48 hours of admission.

The most prevalent species were *Citrobacter freundii* (49%) and *Citrobacter koseri* (32%). Other species included *Citrobacter braakii* (6%), *Citrobacter amalonaticus* (4%), *Citrobacter farmeri* (2%), and undifferentiated *Citrobacter* species (5%).

*Citrobacter* spp. remained 100% susceptible to ertapenem and meropenem across the 14-year study period. Significant increases in co-trimoxazole (+1.0% sensitive/year;  $p=0.006$ ) and gentamicin (+0.7% sensitive/year;  $p=0.006$ ) susceptibility were detected. Susceptibility to ciprofloxacin, ceftazidime, ceftriaxone, and piperacillin/tazobactam remained stable over time.

## STRENGTHS & LIMITATIONS

Study is the first in Canada to evaluate changes in antimicrobial resistance of *Citrobacter* isolates to specific antibiotic agents over an extended timeframe. However, as a single center study, the resistance patterns observed among SHSC isolates may not be representative of isolates at other healthcare institutions.

Study reports changes in the percentage of resistant isolates to individual antibiotic agents over time, but changes in the absolute number (or prevalence) of resistant isolates and patterns of multi-drug resistance were not assessed.

Simple linear regression was used to characterize changes in susceptibility over time. However, yearly data points are not independent, and the statistical significance of findings may change once autocorrelation is incorporated into mathematical models.

## CONCLUSION

This study represents the first in Canada to evaluate changes in antimicrobial resistance of *Citrobacter* to specific antibiotic agents over an extended timeframe. This is valuable information for antimicrobial stewardship practitioners and compliments the growing body of literature on gram-negative bacterial resistance.

## RESULTS

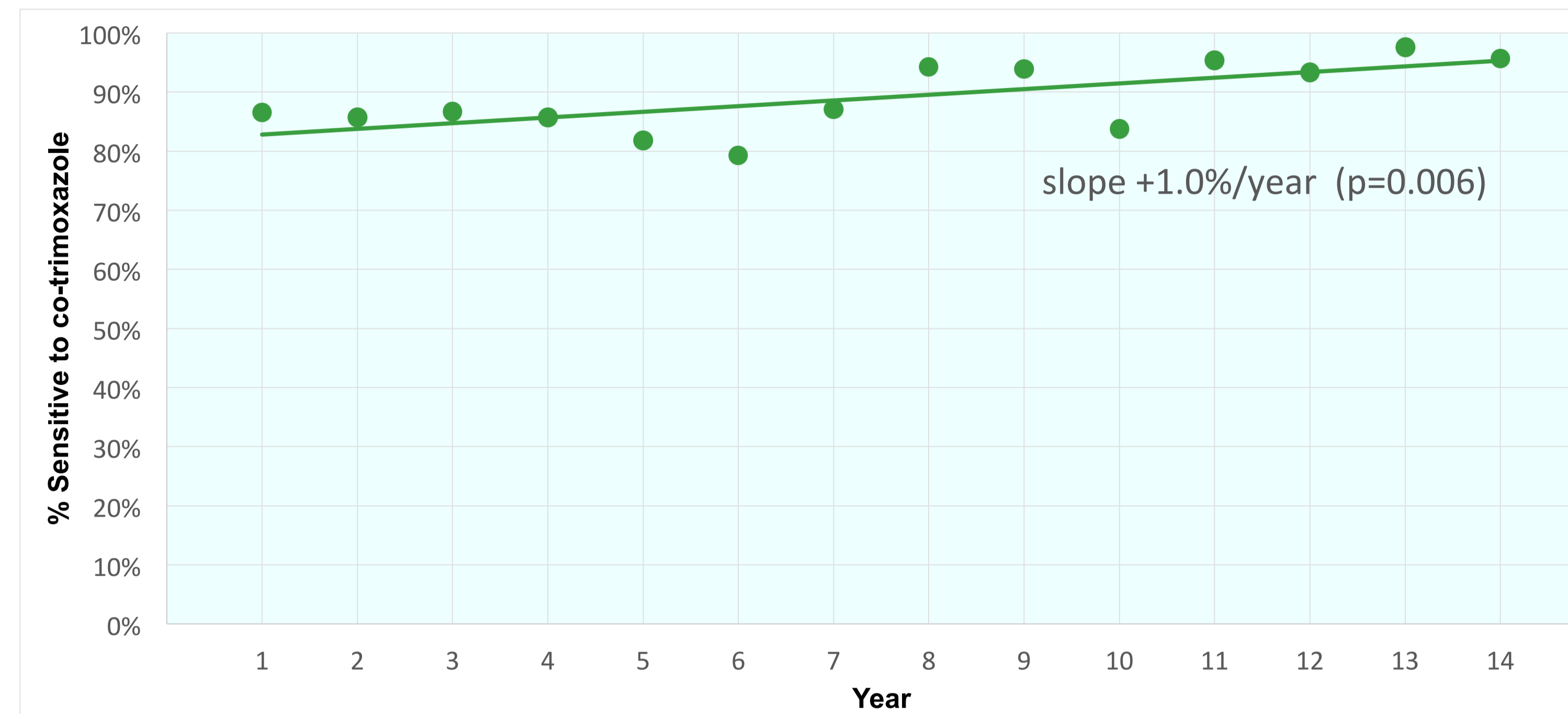


Figure 1: Percentage of *Citrobacter* isolates sensitive to co-trimoxazole each year between October 2002 to September 2016.

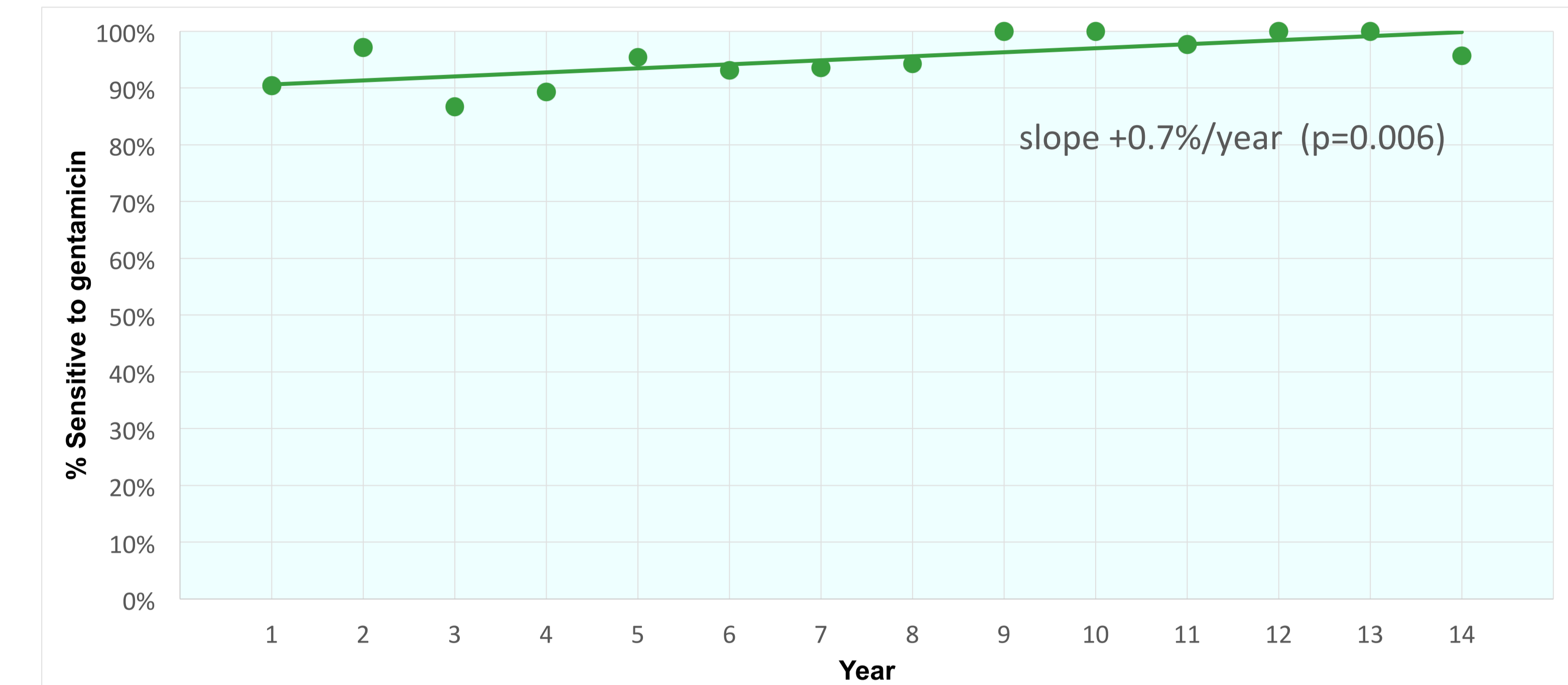


Figure 2: Percentage of *Citrobacter* isolates sensitive to gentamicin each year between October 2002 to September 2016.

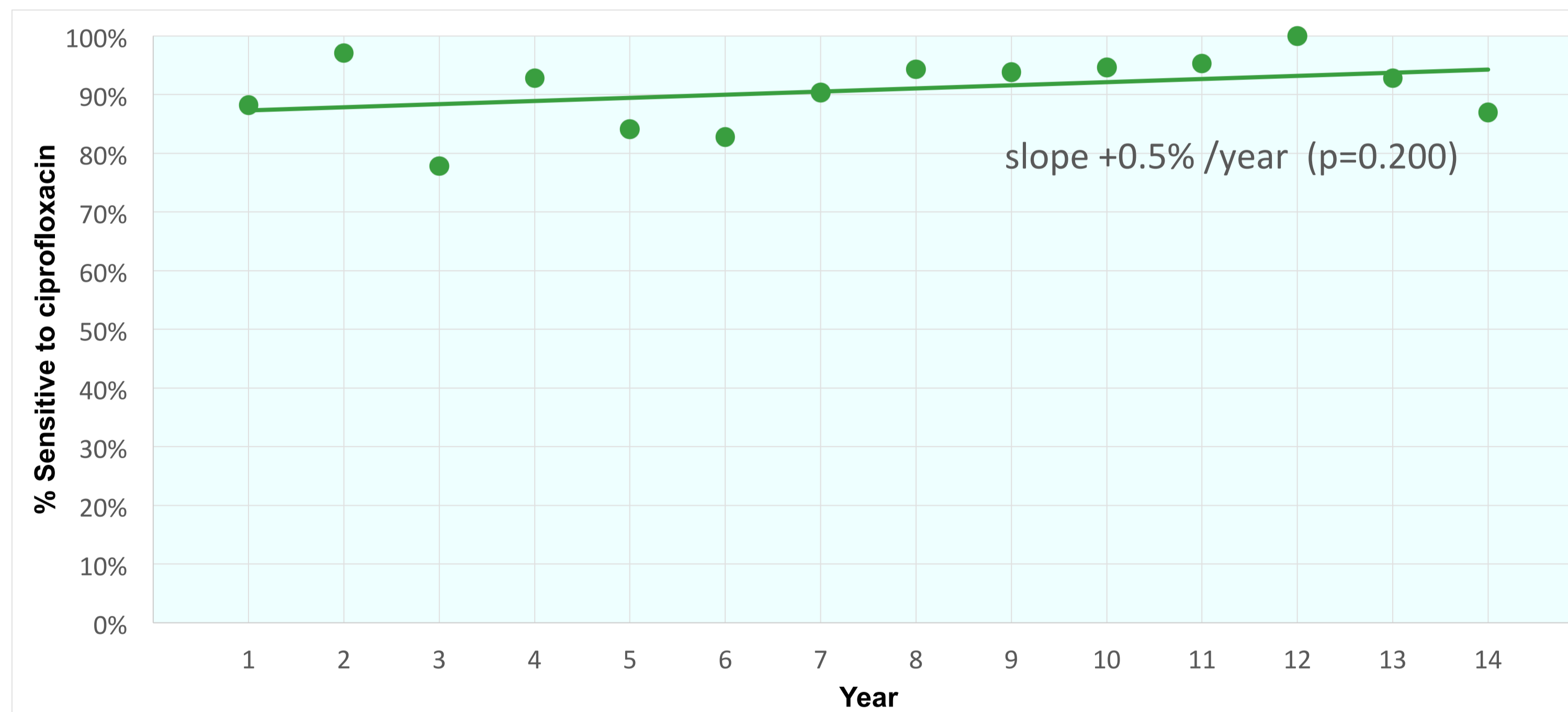


Figure 3: Percentage of *Citrobacter* isolates sensitive to ciprofloxacin each year between October 2002 to September 2016.

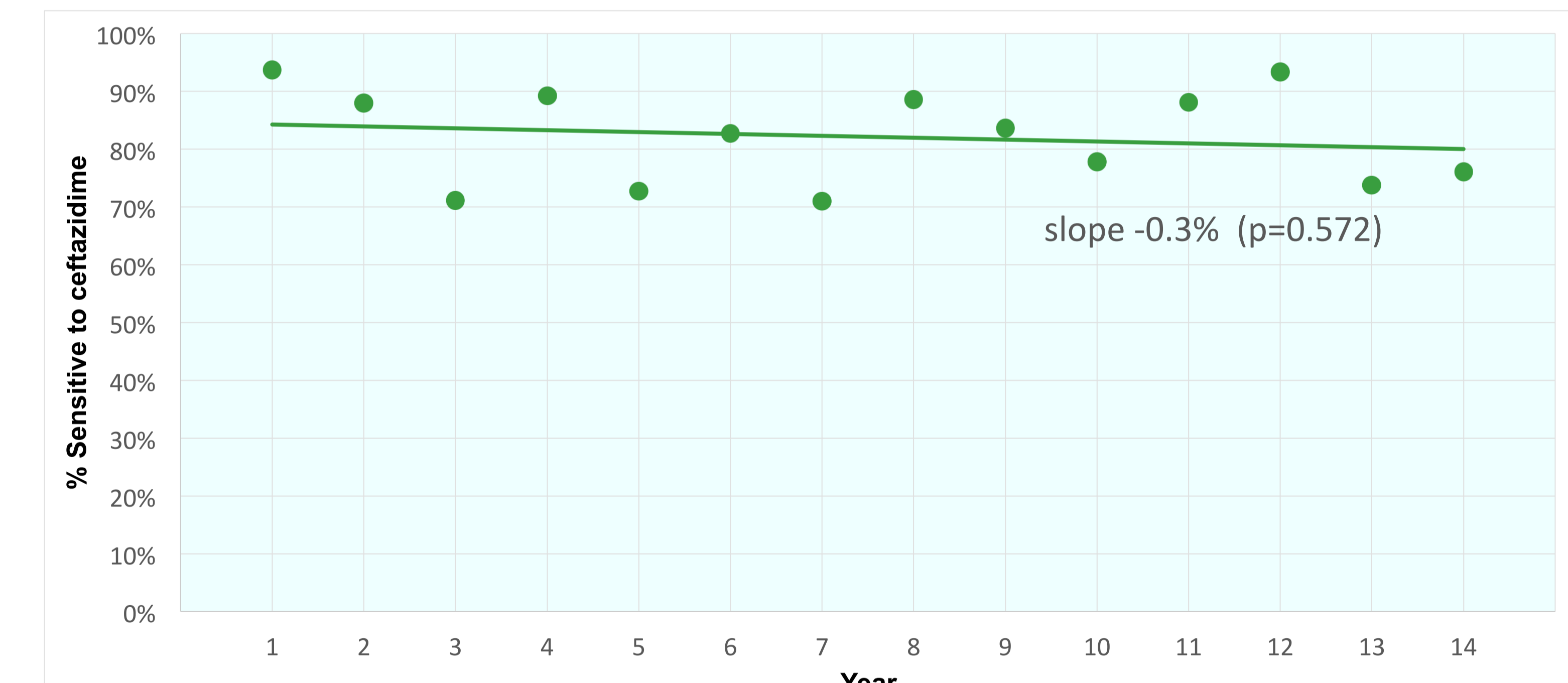


Figure 4: Percentage of *Citrobacter* isolates sensitive to ceftazidime each year between October 2002 to September 2016.

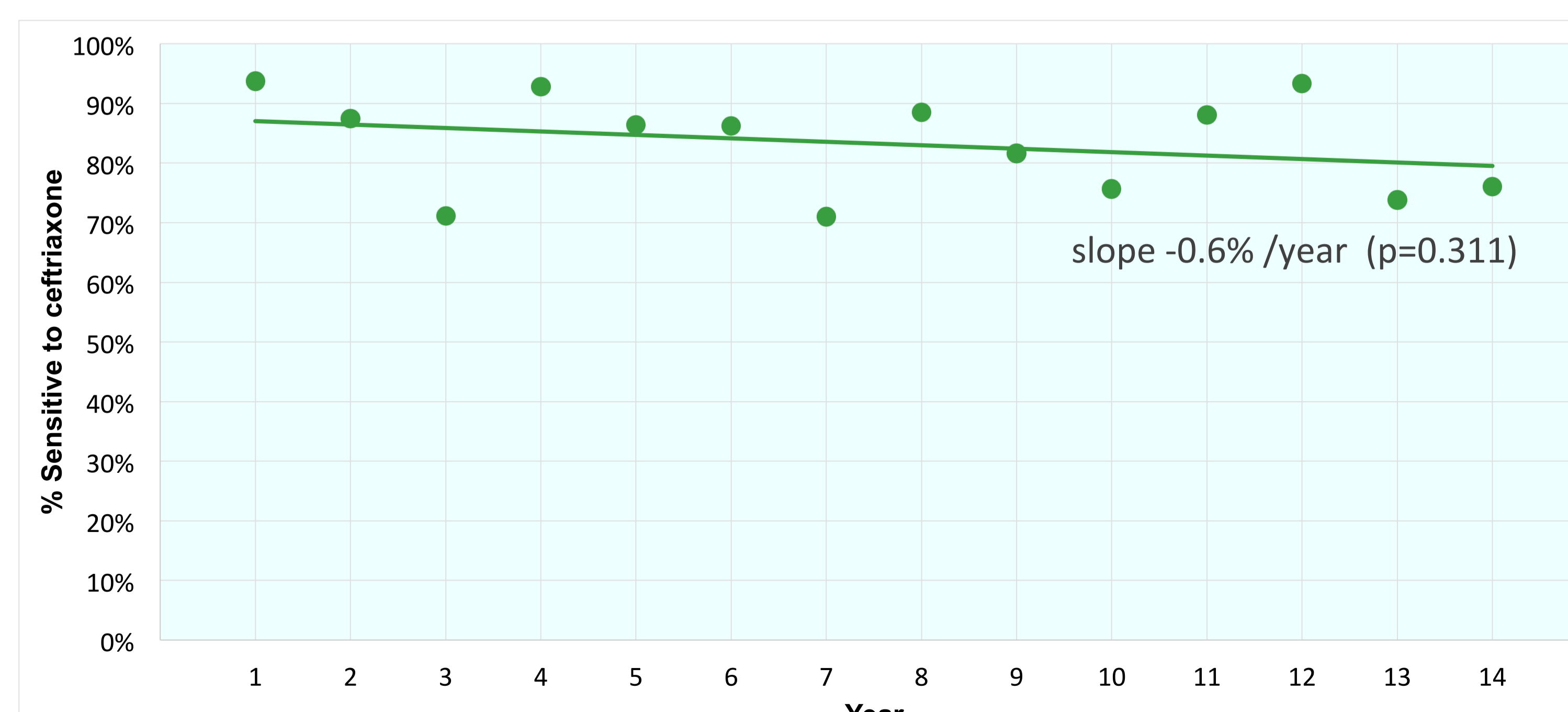


Figure 5: Percentage of *Citrobacter* isolates sensitive to ceftriaxone each year between October 2002 to September 2016.

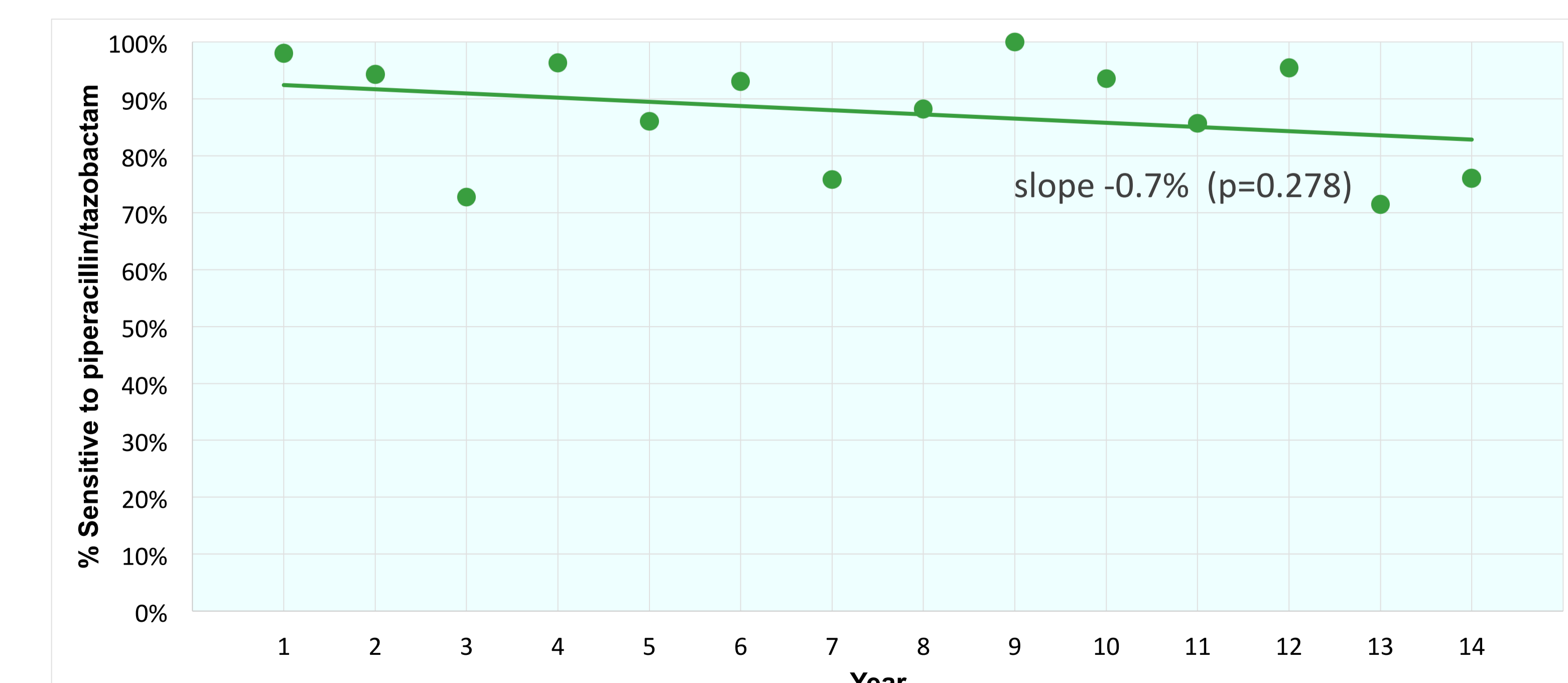


Figure 6: Percentage of *Citrobacter* isolates sensitive to piperacillin/tazobactam each year between October 2002 to September 2016.

## ACKNOWLEDGEMENTS

Leslie Dan Faculty of Pharmacy  
Shaping Student Life and Learning  
Academic Conference Grant

## DISCLOSURES

No author has any  
conflict of interest  
related to this study



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