

# Evolving susceptibility patterns in invasive *Salmonella* enterica serotype Typhi isolates in South Africa from 2003-2014

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# Introduction

- » A recognised, but under-reported public health problem in sub-Saharan Africa
- » Endemic disease remains a problem in South Africa
- » Outbreaks reported in 2005 and 2010
- » Recommended treatment in South Africa is ciprofloxacin - alternatively ceftriaxone or azithromycin
- » MDR typhoid strains was first described in South Africa in 1992 (Coovadia *et al* 1992)
- » During 2003-2007, 27 *Salmonella* Typhi isolates from South Africa, showed reduced susceptibility to ciprofloxacin: MICs from 0.125-0,5 µg/ml (Smith *et al* 2010)
- » Patient in contact with a traveller to Bangladesh, acquired fluoroquinolone resistant typhoid fever (Keddy *et al* 2010)

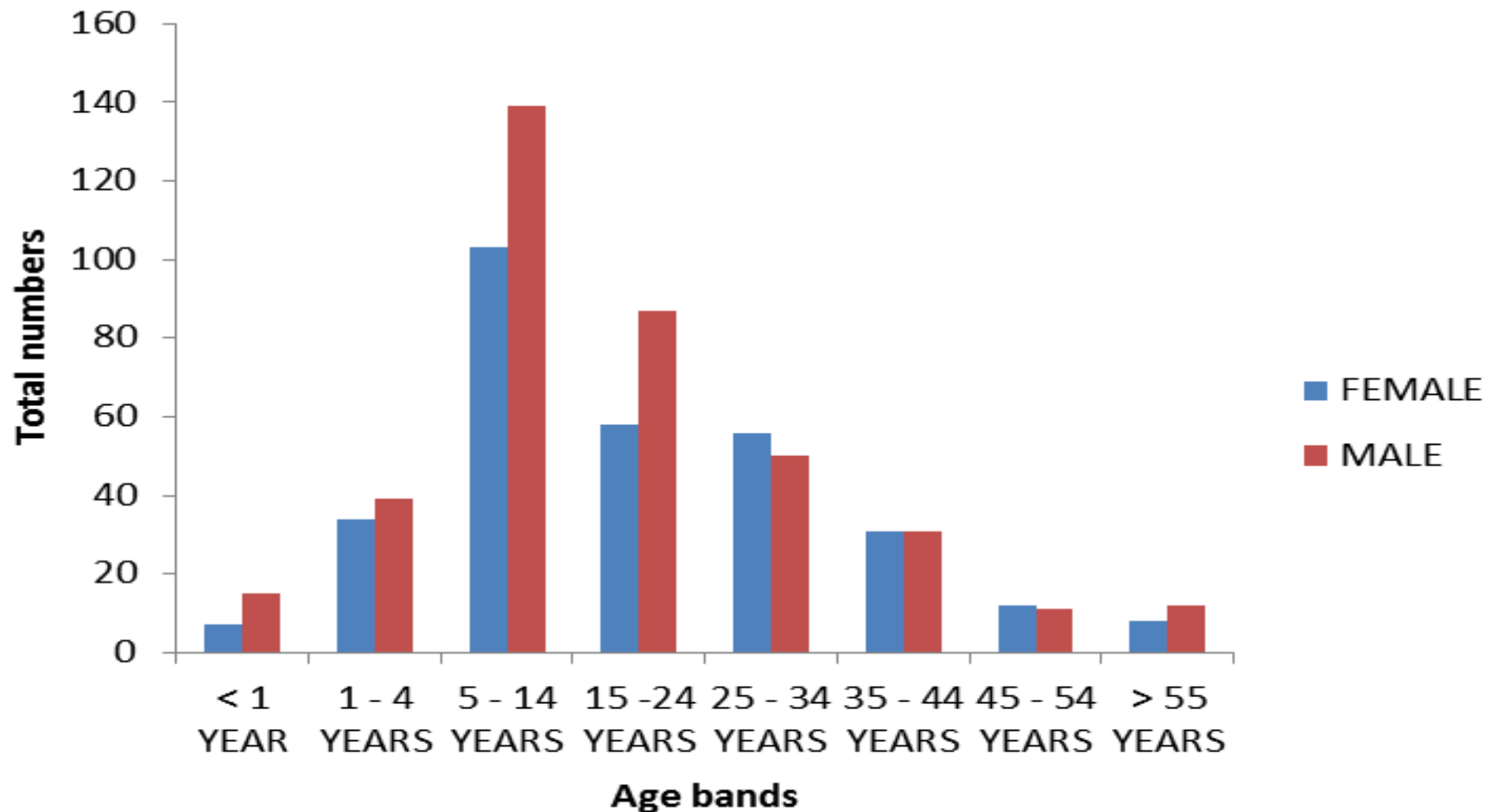
# Objectives

To evaluate the resistance patterns of antimicrobials in the treatment of typhoid fever in South Africa.

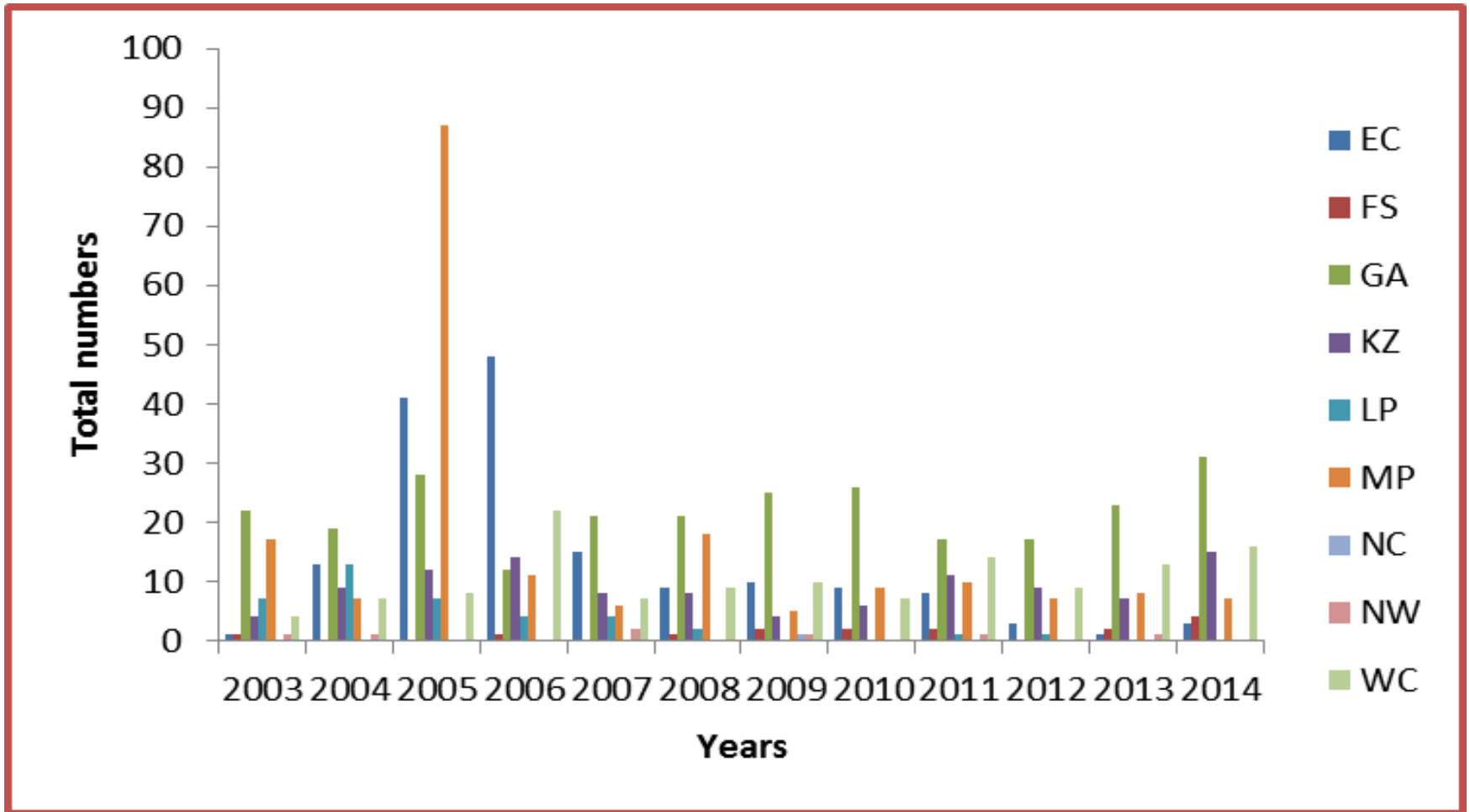
# Method: laboratory procedures

- » 2003-2014: 819 *Salmonella* Typhi isolated by clinical laboratories in South Africa from sterile sites submitted to CED
- » ETEST® strips and the VITEK® used to establish antimicrobial resistance
- » 2003-current: Isolates screened for ampicillin, chloramphenicol and ciprofloxacin resistance
- » 2011: Azithromycin susceptibility testing introduced
- » Antimicrobial breakpoints based on CLSI guidelines
- » Patients age and gender status noted
- » Molecular typing of strains: Pulse Field Gel Electrophoresis according to PulseNet protocol

# Results: Age and gender

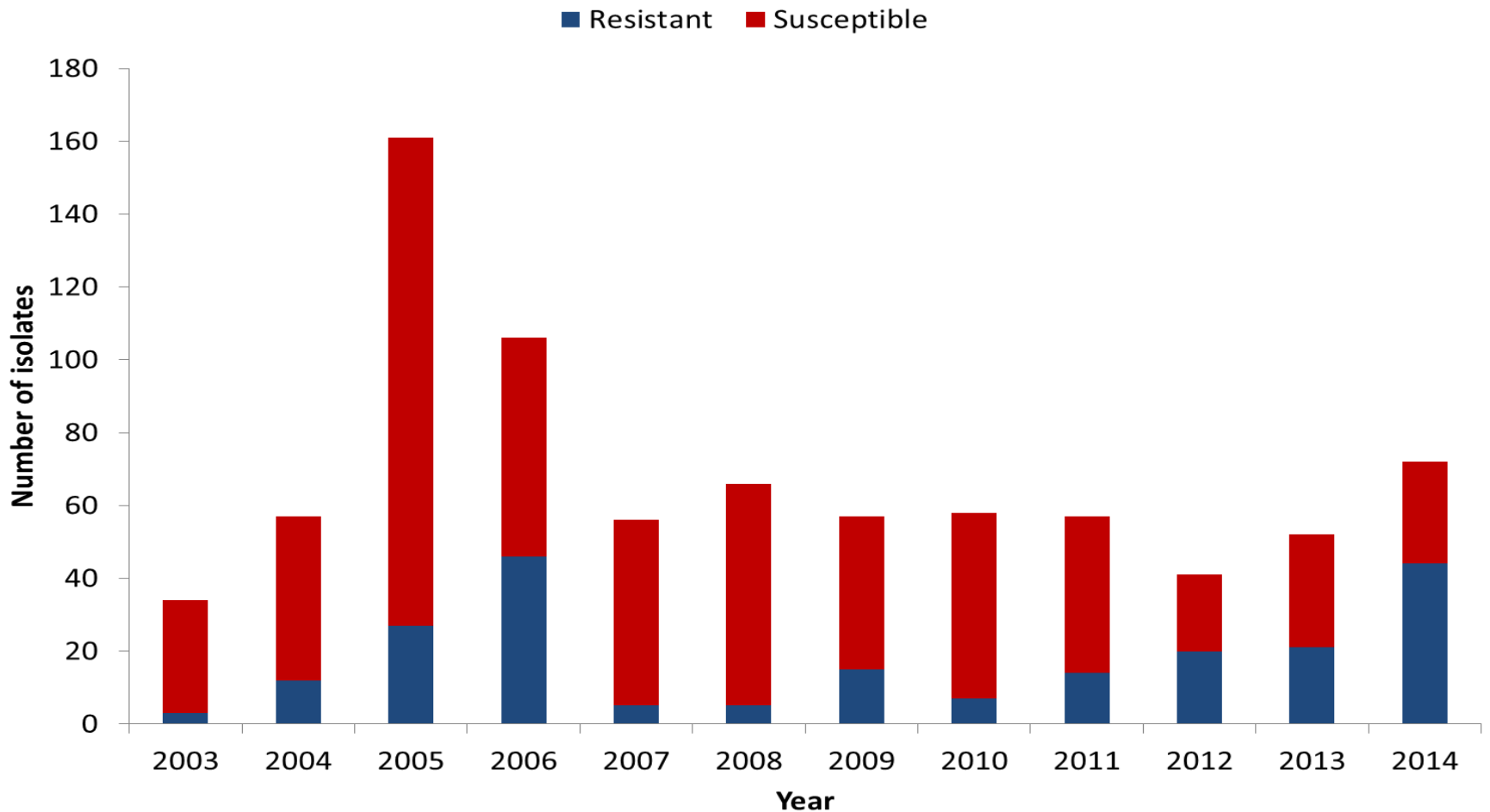


# Numbers per province

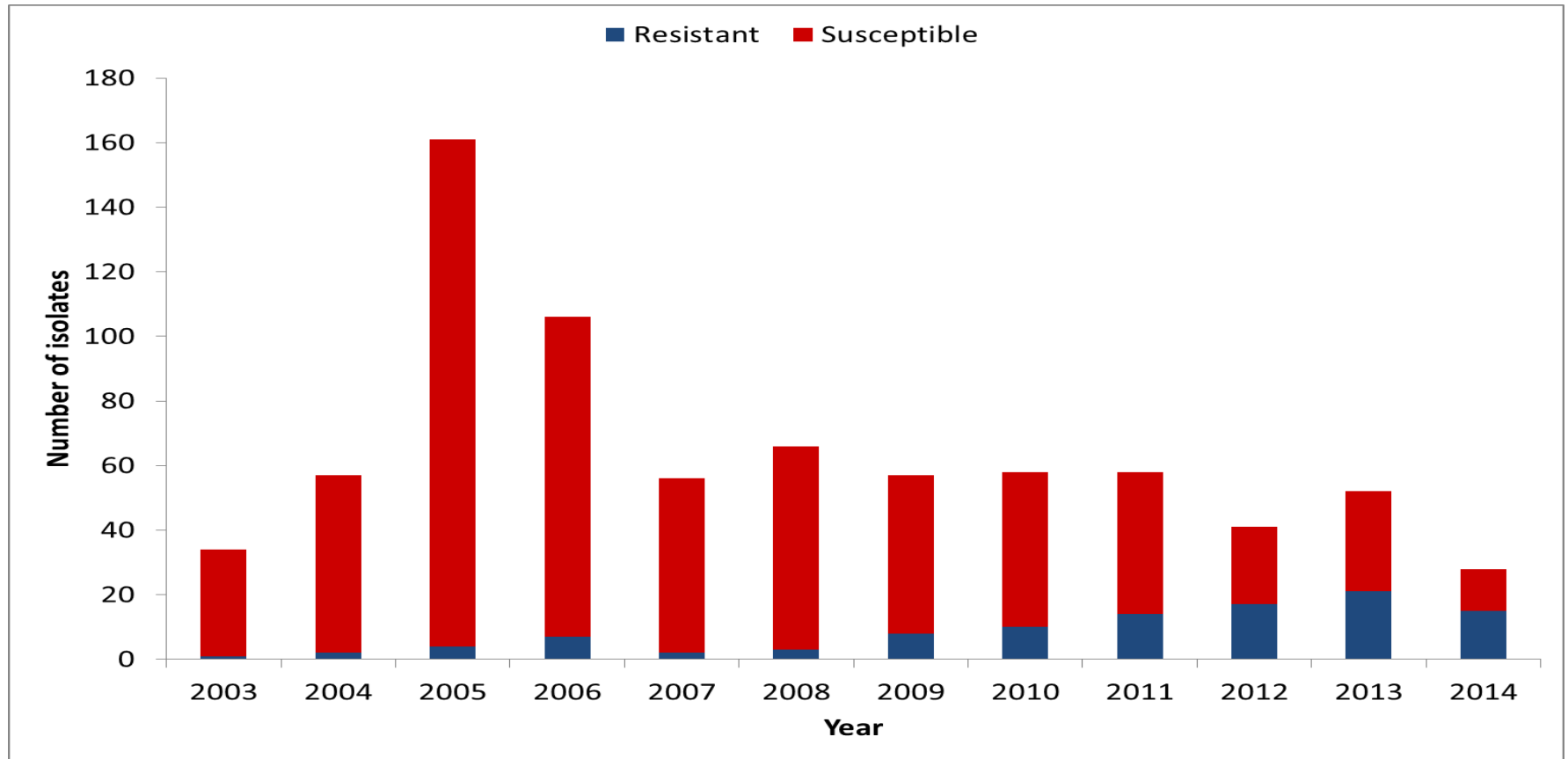


# Ampicillin susceptibility results (N=817)

209 (25.5%) isolates showed resistance to ampicillin (MIC $\geq$ 32 $\mu$ g/ml)  
(OR 16.2 CI 0.7-10.6 P= $<$ 0.001)



# Chloramphenicol susceptibility (N=774)

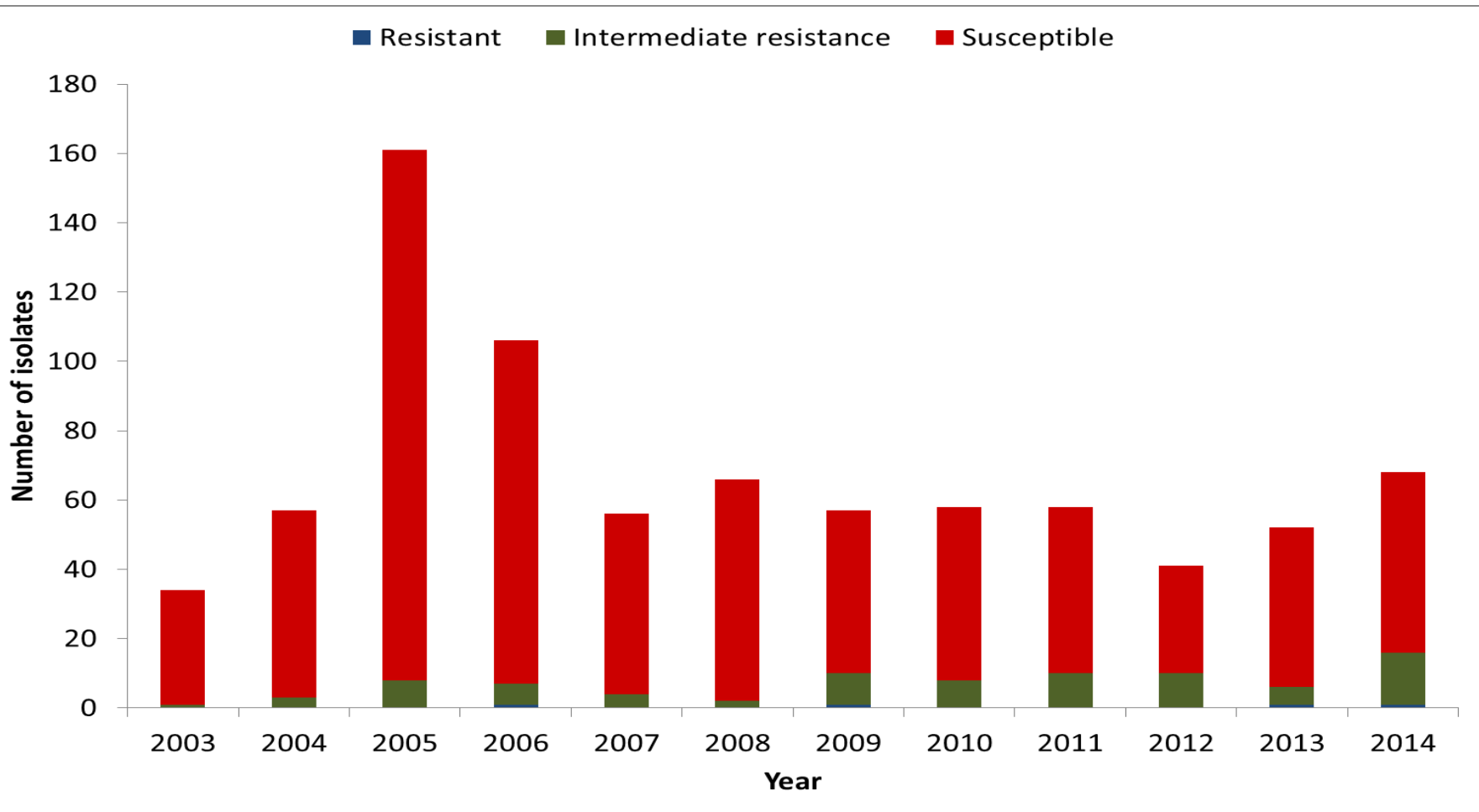


102 (13.5%) isolates showed resistance to chloramphenicol ( $MIC \geq 32 \mu g/ml$ ) (OR 38.1 CI 4.6-318.4  $P < 0.001$ )

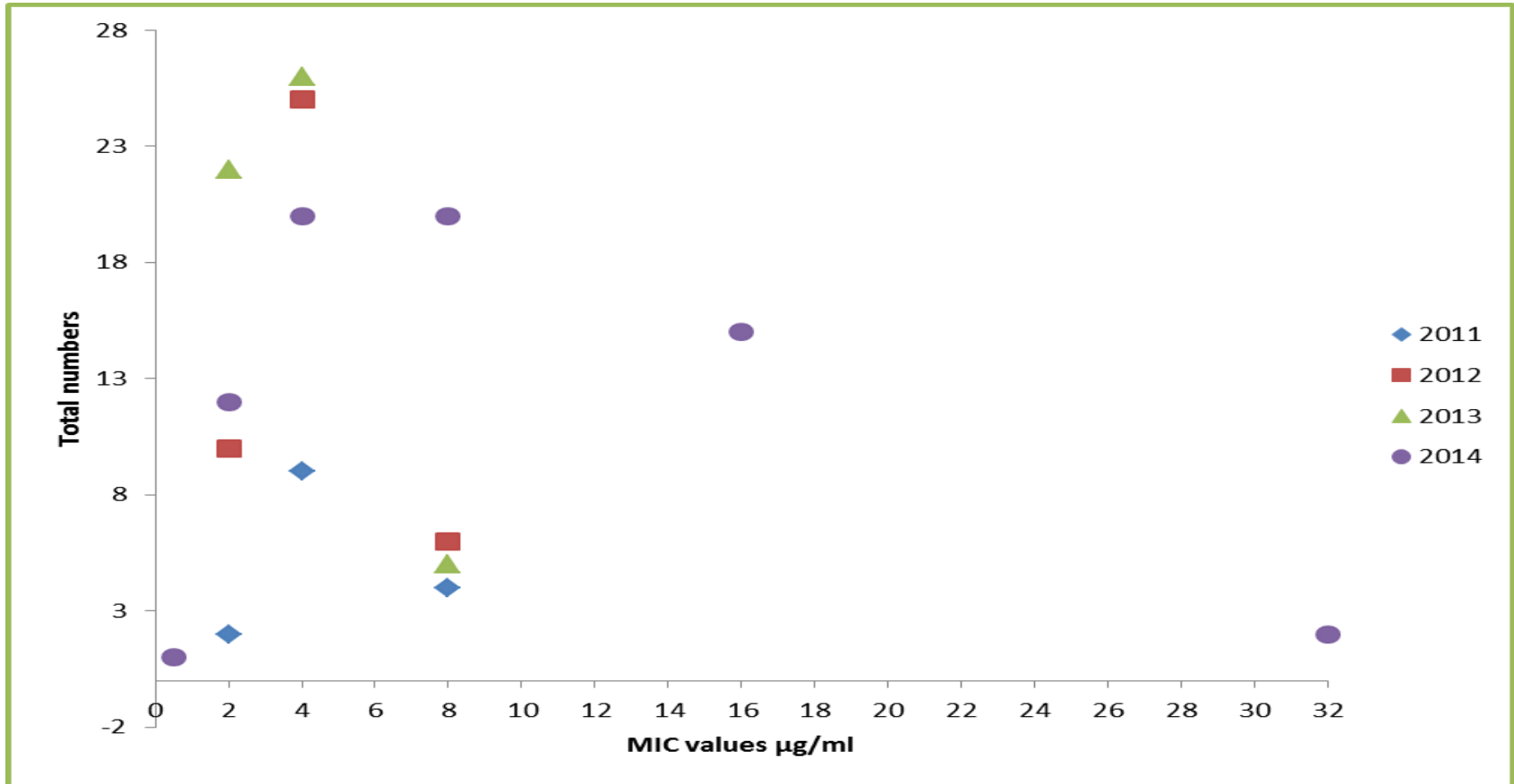


# Ciprofloxacin susceptibility results (N=814)

4 isolates (0.5%) fully resistant to ciprofloxacin ( $\text{MIC} \geq 1 \mu\text{g/ml}$ ) (OR 10.2 CI 1.3-80.2 P=0.02)  
106 isolates (10.3%) showed intermediate resistance ciprofloxacin ( $\text{MIC} \geq 0.125 \mu\text{g/ml}$ ).



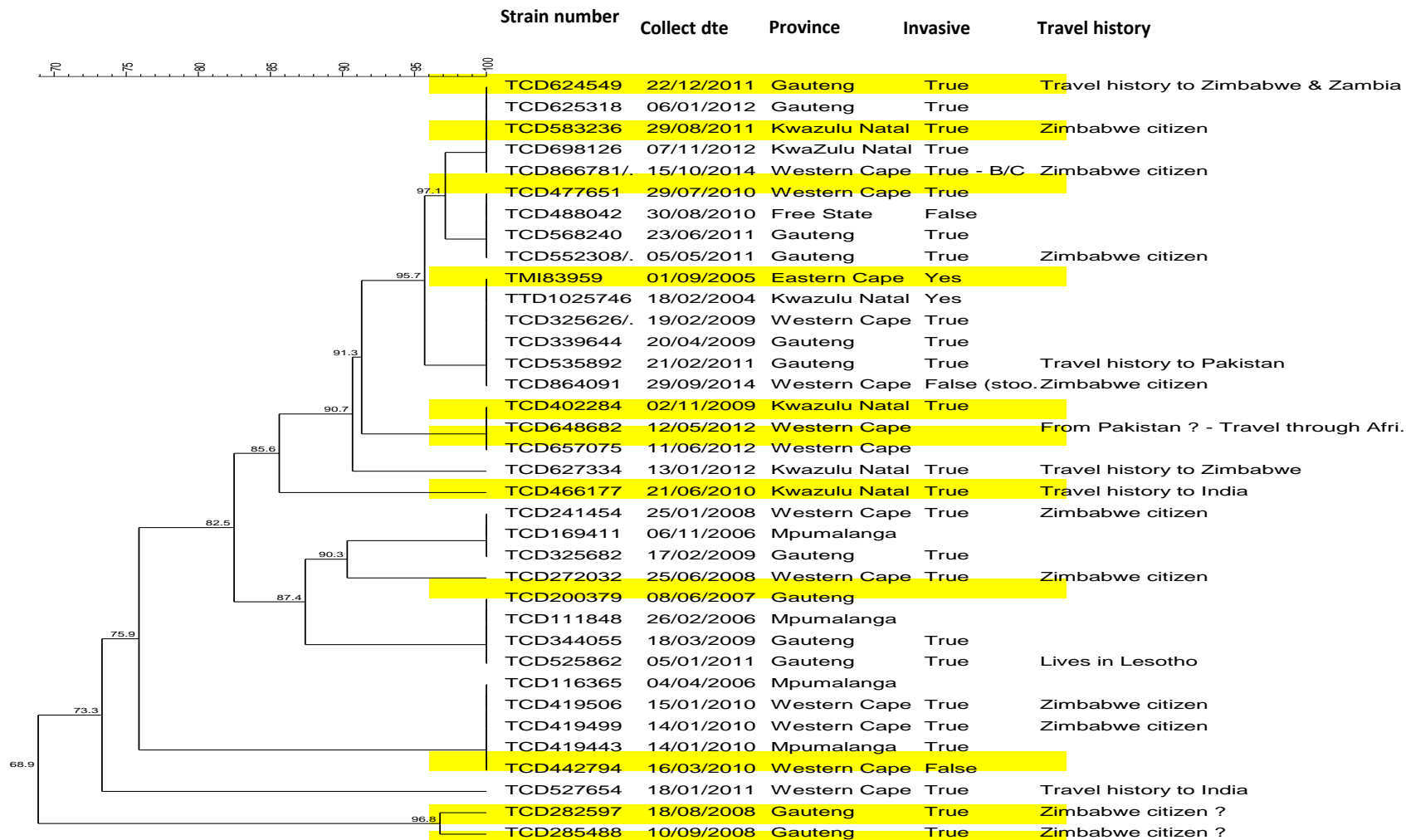
# Azithromycin susceptibility results (N=224)



MIC testing of azithromycin showed a distinct right shift from 2011 to 2014

# Pulse field gel electrophoresis pattern

PFGE-S.Braen-Xba1



Isolates from patients with travel history to other endemic areas (Zimbabwe, Zambia, Pakistan, India), had indistinguishable PFGE patterns to South African strains

# Azithromycin resistant isolate

Azithromycin resistant isolate clustered with other susceptible South African isolates

PFGE-S.Braen-Xba1

Strain number	Country	Collect dte	Province	Town	Invasive
TCD0769556	South Africa	2/7/2013	Western Cape	Cape Town	True
TCD0777454	South Africa	7/08/2013	Western Cape	MILNERTON	False
TCD0844293	South Africa	23/06/2014	Free State	Mangaung	True
TCD0843519	South Africa	16/06/2014	Kwazulu Natal	Pietermaritzburg	True
TCD857364	South Africa	29/08/2014	Western Cape	Nomzamo	True
TCD863531	South Africa	01/10/2014	Gauteng	Johannesburg	True
TCD863546	South Africa	28/09/2014	Gauteng	Pretoria	True
TCD863917	South Africa	15/09/2014	Mpumalanga	Nelspruit	True
TCD866403	South Africa	21/10/2014	Free State	Kroonstad	True

# Limitations of study:

- » This is not a true reflection of the total number typhoid cases in South Africa from 2003-2014
- » Isolates not received, and serologically positive typhoid cases were excluded
- » The results was based isolates received
- » Insufficient patient travel history

# Conclusion

- Ampicillin and chloramphenicol resistance continues to rise
- Ciprofloxacin remains the drug of choice for treatment of typhoid fever, concern about increasing resistance
- The use of ceftriaxone a third generation cephalosporin but reports of ESBL-production
- Increasing MICs values for azithromycin threaten this alternative treatment
- National surveillance is vital to monitor emerging resistance and guide treatment.

# History of antibiotics and antimicrobials..

- 2000 years ago: eat this plant
- 300 years ago: drink this potion
- 1941: that potion is poison – take this penicillin
- 1947: Oops! The germs are penicillin-resistant – take this streptomycin
- 1948: Oops! The germ is now streptomycin-resistant – take this new drug
- 67 years and 40+ oops later: eat this plant? (Matt Mikoleit 2011)

# Thank you



# Acknowledgements

- Dr Karen Keddy
- CED team
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