



## INTRODUCTION

- Gonorrhoea is the second most commonly diagnosed STI in the United Kingdom.
  - In 2012, 25,525 new cases were diagnosed in England, a 21.4% increase relative to 2011 (1).
- Effective control and treatment of gonorrhoea has repeatedly been threatened by resistance developing in *Neisseria gonorrhoeae* (2-4).
  - Between 2007 to 2010, there was an increase in the proportion of isolates exhibiting DS and reports of treatment failure to cefixime in England and Wales (2, 5).
    - Hence changes to first-line treatment were recommended in 2011 from orally administered cefixime to injectable ceftriaxone (500mg) administered in combination with 1g of oral azithromycin.
- We investigated recent patterns and risk factors associated with gonococcal isolates exhibiting DS to currently recommended first and second line therapies.
  - We also explored associated risk factors at a reduced cut-off for ceftriaxone.

## METHODS

- GRASP (Gonococcal Resistance to Antimicrobials Surveillance Programme) is a national sentinel surveillance system set up to monitor antimicrobial resistant *Neisseria gonorrhoeae* in England & Wales.
  - Between July-September, 2012 gonococcal isolates from consecutive patients diagnosed with gonorrhoea attending 25 STD clinics were submitted for antimicrobial susceptibility testing to determine the Minimum Inhibitory Concentrations (MICs).
    - MIC cut-off at  $\geq 0.125$ mg/L and Lower cut-off at  $\geq 0.015$ mg/L<sup>2</sup> for ceftriaxone (first line therapy).
    - MIC cut-off at  $\geq 0.125$ mg/L<sup>1</sup> for cefixime (second line therapy).
- Antimicrobial results were linked to patient's clinical data extracted from the national STD surveillance database (Genitourinary Medicine Activity Dataset version 2).
- Pearson's chi-square test and univariate logistic regression was used to determine risk factors associated with isolates exhibiting DS to cefixime and ceftriaxone.
- Only isolates with MIC and linked patients' clinical data were included in the analysis.
  - Standard GRASP MIC cut-off.
  - Lower MIC cut-off to explore emerging less susceptible isolates.

## RESULTS

- 1670 gonococcal isolates were received during the sampling period of which 1535 (91.9%) had MIC data, representing ~5.9% of gonorrhoea diagnoses in England and Wales in 2012.
- Three isolates (0.2%) exhibited DS to ceftriaxone at MIC  $\geq 0.125$ mg/L and 263 (17.1%) isolates were less susceptible at MIC  $\geq 0.015$ mg/L.
- MIC distributions varied by sexual orientation with a bi-modal distribution of ceftriaxone MICs among isolates from men who have sex with men (MSM) (Figure 1).
- 5.6% of isolates exhibited DS to cefixime at MIC  $\geq 0.125$ mg/L in 2012, a significant decline ( $p < 0.001$ ) from 10.8% reported in 2011 (Figure 2).

- Isolates less susceptible to ceftriaxone at MIC  $\geq 0.015$ mg/L were associated with increasing age ( $p < 0.05$ ), being an MSM (OR 2.06, 95% CI 1.44-2.95); 6 or more sexual partners (OR 1.86, 95% CI 1.20-2.87); sex abroad (OR 1.89, 95% CI 1.30-2.75); a history of gonorrhoea (OR 1.58, 95% CI 1.15-2.19); and being HIV positive (OR 1.94, 95% CI 1.30-2.88) (Table).
- Isolates exhibiting DS to cefixime (MIC  $\geq 0.125$ mg/L) were more likely to be from older patients ( $p = 0.005$ ); and those reporting sex abroad (OR 2.05, 95% CI 1.15-3.66) but less like to be from females (OR 0.28, 95% CI 0.09-0.84) (Table).

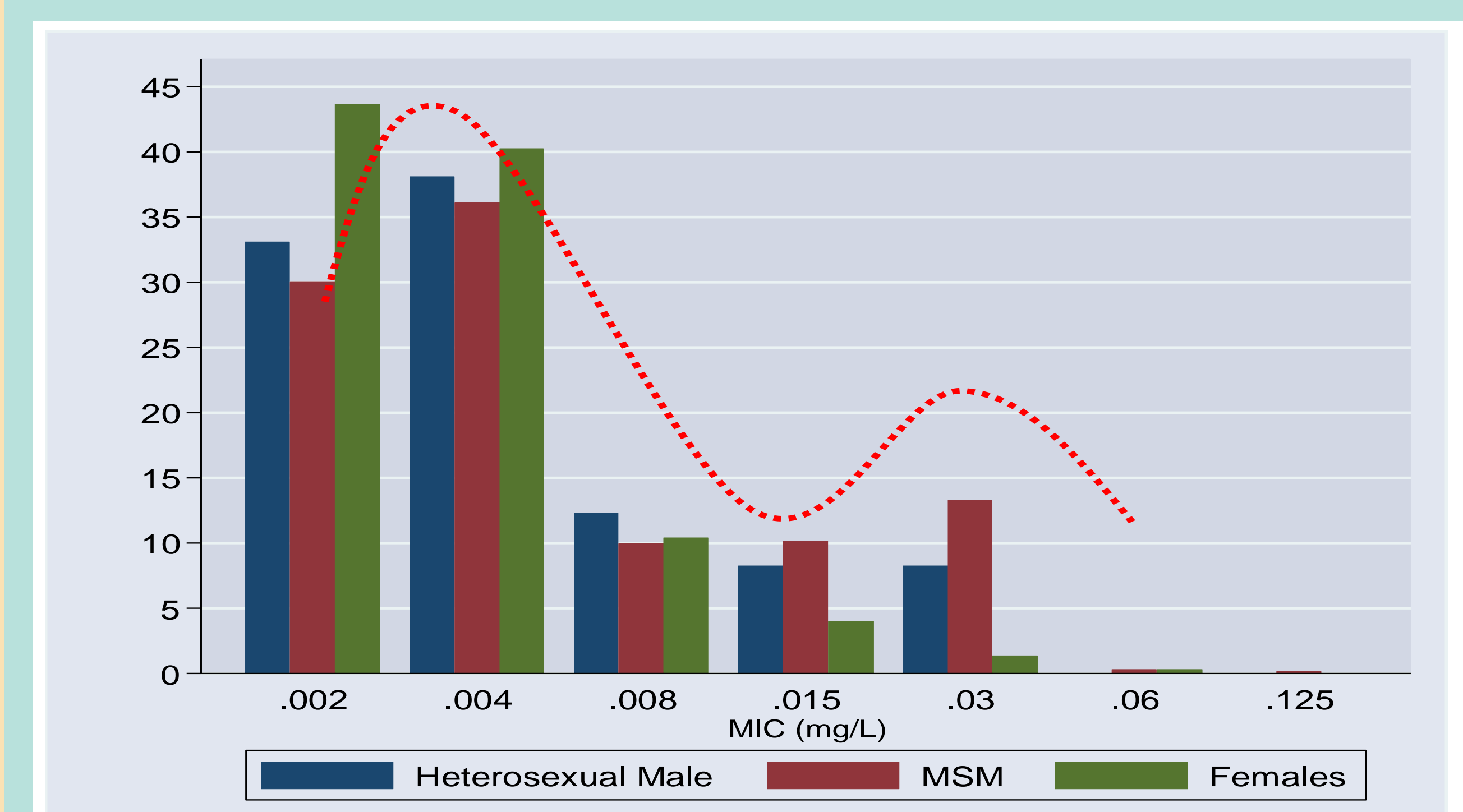


Figure 1. Ceftriaxone MIC (mg/L) by gender and sexual orientation, 2012.

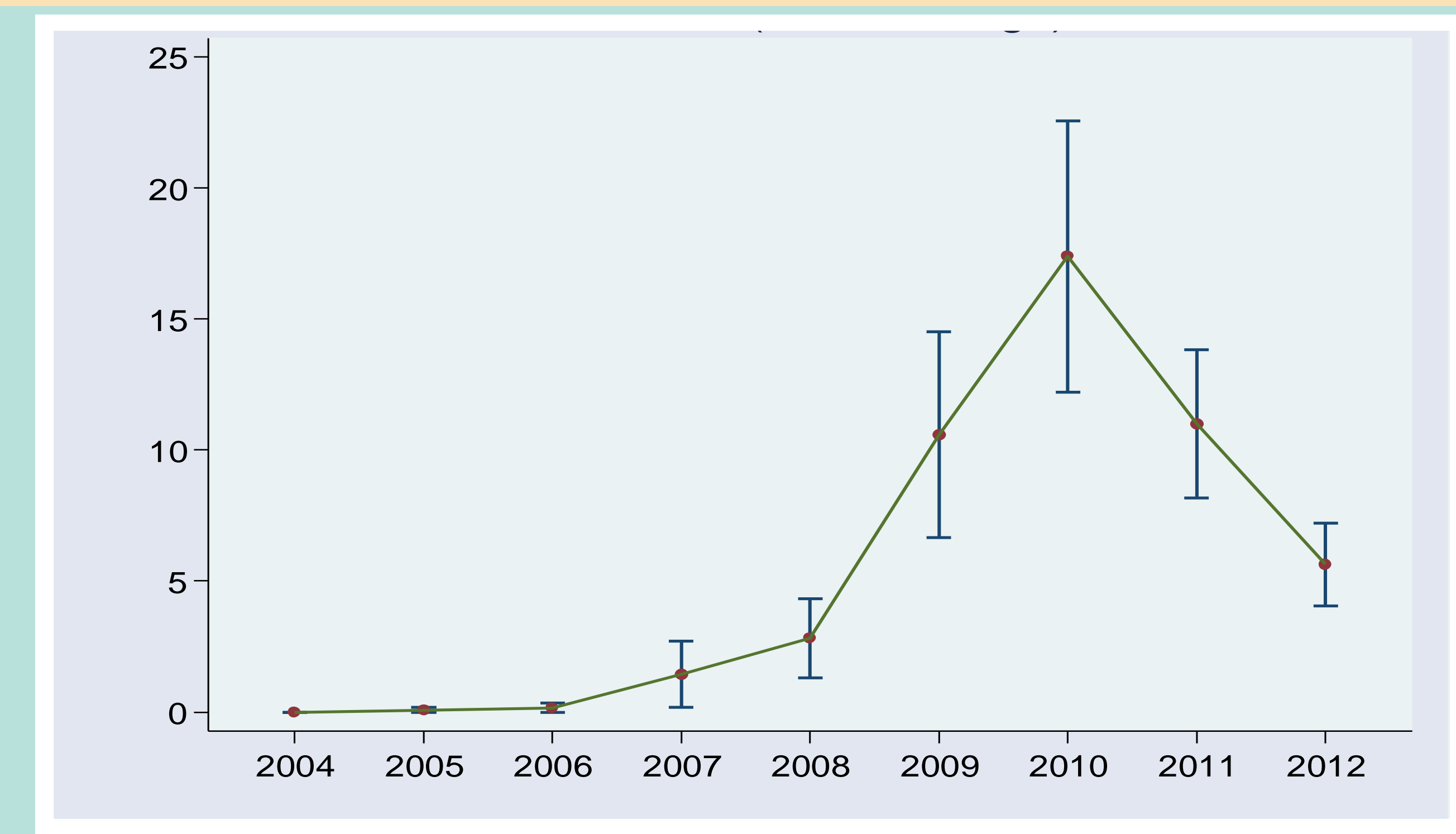


Figure 2. Proportion of isolates (with 95% confidence interval) exhibiting decreased susceptibility to cefixime (MIC  $\geq 0.125$ mg/L), 2004 – 2012.

	N	Ceftriaxone (MIC $\geq 0.015$ mg/L)		Cefixime (MIC $\geq 0.125$ mg/L)	
	1535	263 (17.1)		86 (5.6)	
		% (col)	Univariate analysis crude OR (95% CI)	% (col)	Univariate analysis crude OR (95% CI)
<b>Age Group</b>					
13-19	146	7.5	1	2.7	1
20-24	346	14.5	2.07 (1.05-4.11)*	4.0	1.50 (0.48-4.63)
25-34	536	18.8	2.84 (1.49-5.47)*	5.4	2.03 (0.70-5.87)
35-44	236	23.3	3.72 (1.88-7.40)*	10.2	4.01 (1.36-11.83)*
$\geq 45$	128	21.9	3.43 (1.63-7.23)*	6.3	2.37 (0.69-8.05)
<b>Sexual Orientation</b>					
Heterosexual Men	344	12.8	1	5.5	1
MSM	788	23.2	2.06 (1.44-2.95)*	6.9	1.25 (0.73 - 2.16)
Women	247	6.5	0.47 (0.26-0.8)*	1.6	0.28 (0.09-0.84)*
<b>Ethnicity</b>					
White	950	19.9	1	6.0	1
Black Caribbean	121	7.4	0.32 (0.16-0.65)*	2.5	0.40 (0.12-1.29)
Black African	45	11.1	0.50 (0.20-1.29)	4.4	0.73 (0.17-3.09)
Black Other	46	4.3	0.18 (0.04-0.76)*	4.3	0.71 (0.17-3.02)
Asian (including Chinese)	62	27.4	1.52 (0.85 - 2.72)	9.7	1.68 (0.69-4.07)
Other Ethnic group	40	17.5	0.85 (0.37 - 1.96)	10.0	1.74 (0.60-5.07)
Mixed Ethnic group	104	12.5	0.58 (0.31-1.05)	2.9	0.47 (0.14-1.51)
<b>Total Partners (past 3 months)</b>					
0-1	494	15.0	1	5.3	1
2-5	669	17.9	1.24 (0.90-1.70)	5.4	1.02 (0.61-1.72)
6+	162	24.7	1.86 (1.20-2.87)*	6.8	1.31 (0.63-2.72)
<b>Sex Abroad</b>					
No	1158	16.3	1	4.9	1
Yes	167	26.9	1.89 (1.30-2.75)*	9.6	2.05 (1.15-3.66)*
<b>Symptoms</b>					
No	321	19.6	1	7.2	1
Yes	953	17.1	0.84 (0.61-1.17)	5.6	0.76 (0.46-1.27)
<b>Previously diagnosed with gonorrhoea</b>					
No	1112	16.0	1	5.0	1
Yes	276	23.2	1.58 (1.15-2.19)*	7.6	1.55 (0.92-2.61)
<b>Concurrent STI</b>					
No	454	18.7	1	5.3	1
Yes	391	13.6	0.68 (0.47-1.00)*	3.8	0.71 (0.37-1.38)
<b>HIV Status</b>					
Negative	554	15.5	1	4.5	1
Positive	194	26.3	1.94 (1.30-2.88)*	6.7	1.52 (0.76-3.03)

Table. Univariate analyses of association among isolates less susceptible to ceftriaxone (MIC  $\geq 0.015$ mg/L) and cefixime (MIC  $\geq 0.125$ mg/L) and patient characteristics.

## LIMITATIONS

- There is a degree of sampling bias as GRASP over-represents MSM, symptomatic patients and those living in London.

## ACKNOWLEDGEMENTS

- We would like to thank all the GRASP collaborating genitourinary medicine (GUM) clinics involved in clinical data collection.
- The collaborating laboratories for sending isolates to the reference laboratory at Public Health England (PHE).
- Colleagues at the HIV/STI department and STBRU at PHE for their immense support.

## DISCUSSION/CONCLUSIONS

- This analysis shows a continuing downward trend in the prevalence of DS to cefixime in England and Wales, which may in part reflect changes to treatment guidelines.
- Isolates exhibiting DS to cefixime (MIC  $\geq 0.125$ mg/L) were more likely to be from older patients, men and those reporting sexual contact abroad.
- There is evidence of isolates exhibiting DS to ceftriaxone (MIC  $\geq 0.125$ mg/L) for the first time since it was last reported in 2009.
- Isolates less susceptible to ceftriaxone (MIC  $\geq 0.015$ mg/L) were more likely to be from older HIV positive MSM, with high rates of sexual partner change.
- Monitoring MIC drifts is crucial for detecting drift towards emerging resistance.
- To maintain the usefulness of the currently recommended cephalosporins, adherence to treatment guidelines remains paramount to ensure gonorrhoea remains a treatable bacterial infection.

## REFERENCES

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