

Trends in antimicrobial susceptibility of *Neisseria gonorrhoea* in a STD clinic in central Israel, 2009 to 2014

Presentation
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BACKGROUND

- Gonorrhoea is the second most common STD after Chlamydia infections
- There is a continuing gradual world wide increase in the prevalence of the disease
- In women, *N. gonorrhoea* is a major cause of
 - PID
 - Ectopic pregnancy
 - Infertility
- Treatment has become more challenging because *N. gonorrhoea* has successively developed resistance to each antibiotic recommended for treatment
 - Penicillinase-producing *N. gonorrhoea*
 - Fluoroquinolone resistance
- Recently
 - Ceftriaxone resistance
 - Macrolide resistance
- Resistance first becomes apparent in men having sex with men before emerging among heterosexuals

A continuing change in treatment recommendations

- Currently the CDC recommends
 - Combination of 250 mg of ceftriaxone as a single IM dose and a single 1 gr oral dose of azithromycin
- Azithromycin is not recommended for monotherapy because of the ease with which *N. gonorrhoeae* can acquire macrolide resistance
- Two mechanisms have been commonly implicated in gonococcal reduced azithromycin susceptibility:
 - Overexpression of an efflux pump due to *mtrR*-coding region mutations
 - Decreased antimicrobial affinity due to mutations in genes encoding the 23S ribosomal subunit

Gonorrhoea susceptibility in Israel

- A study performed in Central Israel during 2002-2007
- 406 gonococcal strains obtained in a STI clinic (Levinski)
 - 27.1% of isolates were resistant to ciprofloxacin
 - Resistance increased over the years
 - All isolates remain susceptible to ceftriaxone and spectinomycin

Dan et al. *Ssexually Transmitted Diseases* 2010;37:451.

EUCAST clinical breakpoints for *N. gonorrhoea*

	MIC breakpoint mg/L	
	S ≤	R >
Penicillin	0.06	1
Ceftriaxone	0.125	0.125
Tetracycline	0.5	1
Ciprofloxacin	0.03	0.06
Azythromycin	0.25	0.5
Spectinomycin	64	64
Gentamicin	8 mg/L?	NA

METHODS

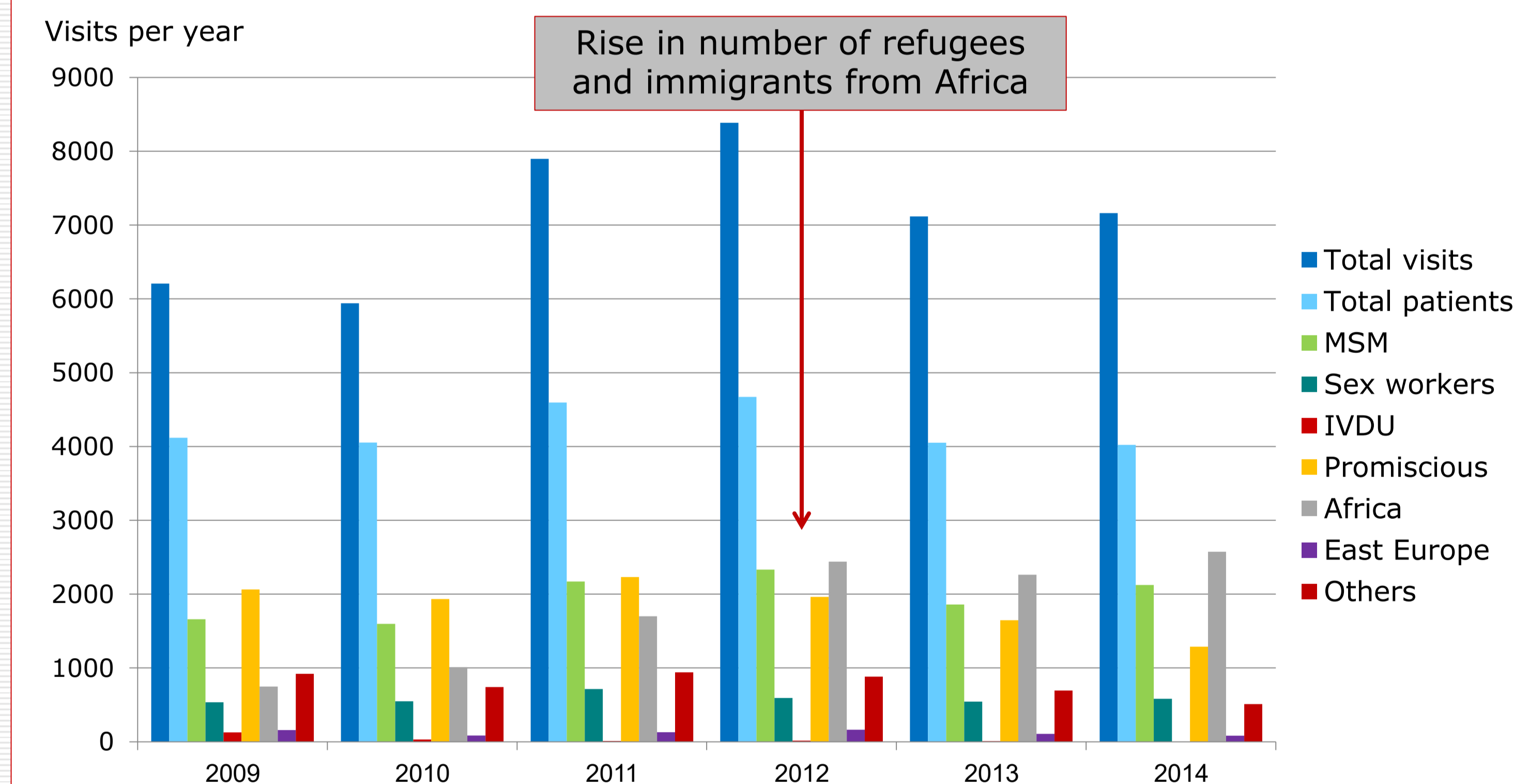
- Time period - 1.1.2009 to 30.7.2014
- N. gonorrhoea* strains were isolated from clinical specimens
- Samples were plated immediately on New-York plates
- Isolates were identified by microscopy, phenotypic tests, and VITEK system
- Susceptibility to antibiotics was performed using Etests:
 - Penicillin; Ceftriaxone; Tetracycline; Ciprofloxacin; Azithromycin; Spectinomycin
 - Gentamicin susceptibility by Etest was introduced during 2011 and thus was performed to only 44% of the isolates
- Susceptibility and resistance were determined according to EUCAST criteria
- Mean MICs were calculated by geometrical means

Samples

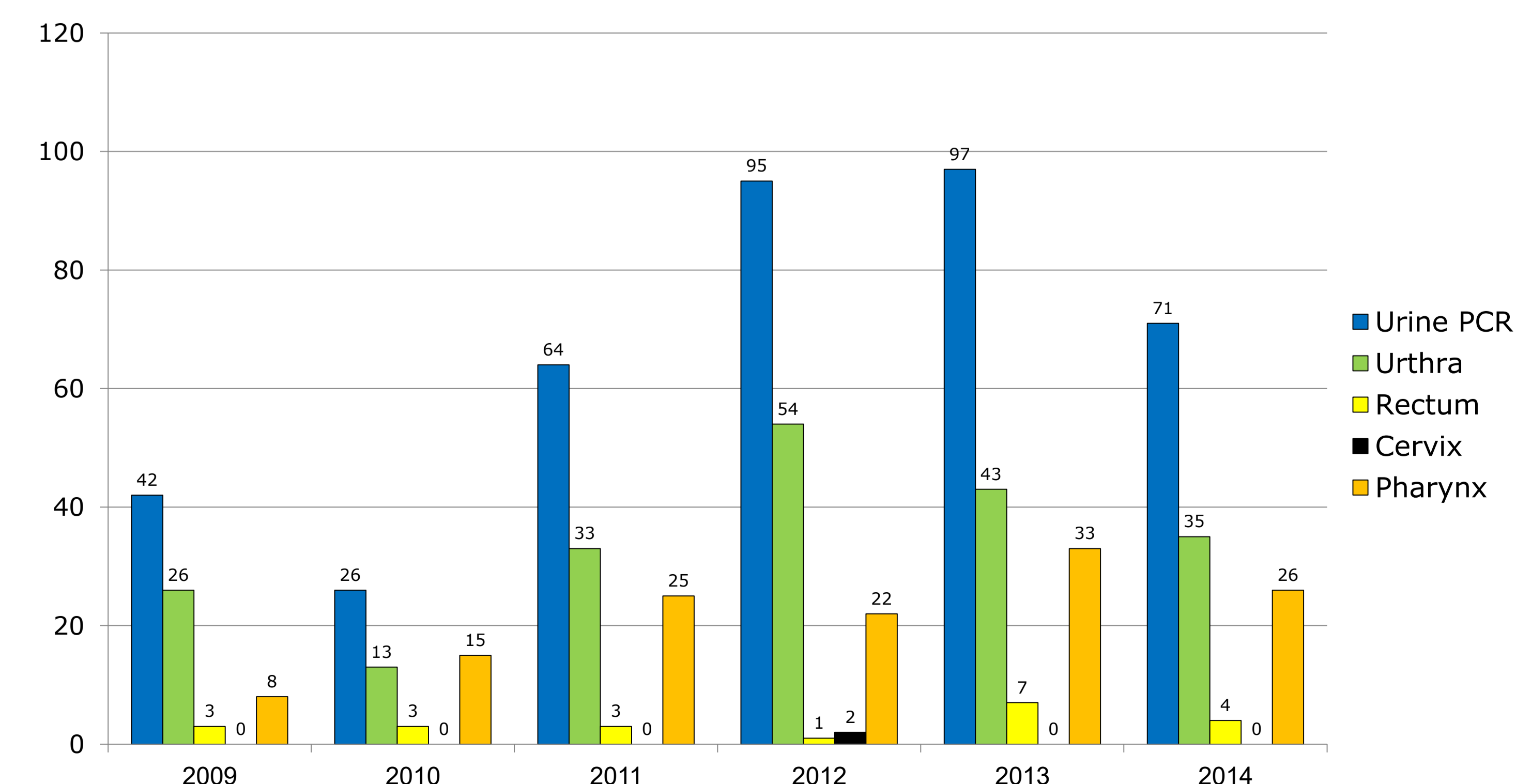
- 338 isolates were tested
- Mean age was 34 (SD 9.1) years
- Site of culture
 - Urethra - 190 (56.2%)
 - Pharynx - 130 (38.5%)
 - Rectum - 18 (5.3%)

RESULTS

Number of visits to Levinsky clinic during 2009-2014



Positive PCR and cultures for *N. gonorrhoea*

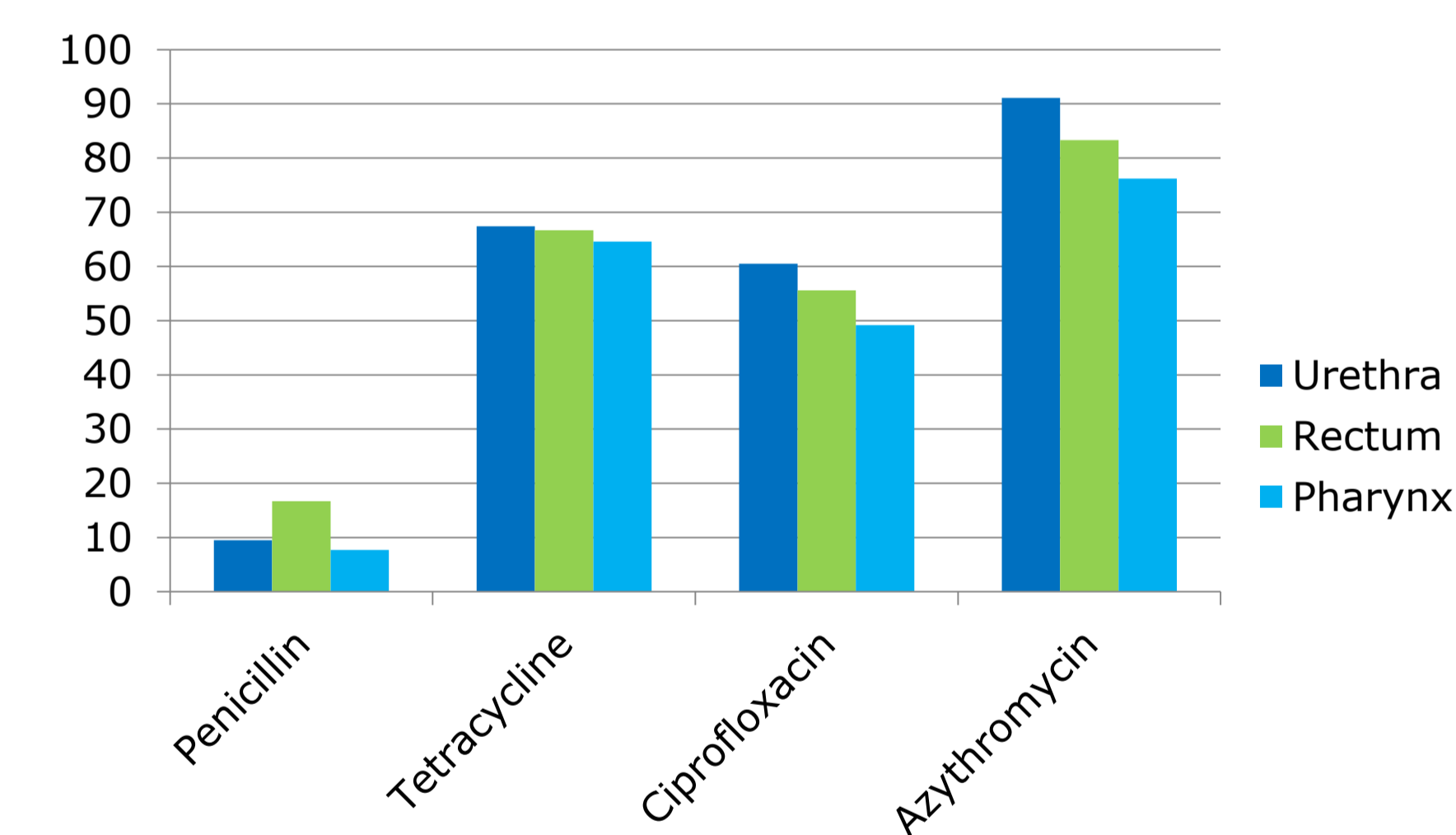


Antibiotic susceptibility

	Penicillin N=338	Ceftriaxone N=338	Tetracycline* N=338	Ciprofloxacin N=338	Azithromycin* N=337	Spectinomycin* N=338	Gentamicin* N=115
2009	0.358 4.2/14.6	0.008 100/0	0.817 60.4/25.0	0.140 50.0/50.0	0.233 81.2/10.4	8.813 100/0	-
2010	0.417 13.3/16.7	0.006 100/0	0.880 66.7/20.0	0.163 46.7/53.3	0.183 93.3/0	7.972 100/0	-
2011	0.244 14.3/14.3	0.005 100/0	0.806 83.9/3.6	0.020 75.0/25.0	0.224 98.2/0	8.540 100/0	3.984 -
2012	0.266 15.8/13.2	0.005 100/0	0.570 81.6/15.8	0.068 61.8/38.2	0.180 94.7/0	7.942 100/0	3.932 -
2013	0.470 2.3/18.6	0.005 100/0	1.483 59.3/36.0	0.125 54.7/45.3	0.265 72.1/5.8	10.567 100/0	5.499 -
2014	0.479 7.1/14.3	0.006 100/0	4.356 35.7/54.8	0.570 35.7/64.3	0.240 73.8/0	12.325 100/0	6.397 -

MIC geometric means, % sensitive/resistant. *P<0.05

% susceptible by sites



DISCUSSION

- The rate of susceptible isolates to tetracycline, ciprofloxacin and azithromycin has decreased significantly particularly as of 2013
- MICs are also increasing within the susceptible range for
 - Ceftriaxone
 - Spectinomycin
 - Gentamicin
- Clinical failures were not common but follow-up and test of cure is not performed in most cases
- Macrolide resistance is also emerging for additional pathogens such as *Mycoplasma genitalium* not assessed in this study

This study demonstrates

- Importance of surveillance to assess resistant trends
- Importance of cultures as resistance to beta lactams is not performed by molecular methods
- Importance of test of cure
- Importance of genetic determination of resistance when possible
- Importance of surveillance to define appropriate treatment algorithms locally and globally