Public Health England

Protecting and improving the nation's health

Surveillance of antimicrobial resistance in *Neisseria gonorrhoeae*

Key findings from the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP)

Data up to October 2016

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1. Key Points

- gonorrhoea is caused by the bacterium *Neisseria gonorrhoeae* and is the second most common bacterial sexually transmitted infection in England

- current first-line treatment for gonorrhoea involves dual therapy with ceftriaxone (500 mg IM) and azithromycin (1 g oral), but treatment effectiveness is threatened by antimicrobial resistance

- in 2015, the world's first documented case of treatment failure to dual ceftriaxone and azithromycin therapy was reported in England; the isolate was confirmed by PHE to be resistant to ceftriaxone (minimum inhibitory concentration (MIC) 0.25 mg/L) and azithromycin (MIC 1.0 mg/L)

- apart from the treatment failure, no further cases of ceftriaxone resistance were confirmed by the PHE reference laboratory

- azithromycin resistance is of concern:

    - sentinel surveillance indicates the prevalence of azithromycin resistance (MICs >0.5 mg/L) was approximately 10% in 2015, although MICs for the great majority (91%) of these resistant isolates were 1 mg/L, only just above the breakpoint for resistance

    - the outbreak of high-level azithromycin-resistant *N. gonorrhoeae* (MICs ≥256 mg/L), first identified in Leeds in 2015, persists and in 2016 spread to other parts of England

Box 1: Key recommendations to reduce the spread of antimicrobial-resistant *N. gonorrhoeae*

- all primary diagnostic laboratories should test gonococcal isolates for susceptibility to first-line antimicrobials and refer suspected azithromycin- and/or ceftriaxone-resistant isolates to the PHE reference laboratory for confirmation and follow-up
- practitioners should ensure all patients with gonorrhoea are treated and managed according to national guidelines and be alert to changes in antimicrobials recommended for front-line use
- sexual health services should report possible cases of treatment failure to PHE via the online HIV and STI web-portal
- anyone having sex with new or casual sexual partners should be advised to use condoms consistently and correctly and test regularly for sexually transmitted infections

2. Introduction

Gonorrhoea is caused by the bacterium *Neisseria gonorrhoeae* and is the second most common bacterial sexually transmitted infection (STI) diagnosed in England. In recent years, the number of new cases of gonorrhoea has increased in England, with a total of 41,193 cases reported in 2015 (data from 460 specialist and non-specialist services), a 53% increase from 2012 (26,880 to 41,193).[1] Men who have sex with men (MSM) and black Caribbean populations are at highest risk. Untreated infection may cause pelvic inflammatory disease and lead to tubal infertility, highlighting the need to maintain effective management.[2]

It has long been recognised that antimicrobial resistance (AMR) in *N. gonorrhoeae* threatens effective treatment and infection control. Strategies to address this threat are outlined in national, regional and global action plans, [3-5] all of which emphasise the importance of high quality surveillance of AMR, prompt recognition and effective management of potential treatment failures, and good communication of emerging problems to allow timely review of empirical treatment guidelines and public health policies. The World Health Organization (WHO) recommends that treatment guidelines are changed whenever resistance to the first-line therapy reaches a prevalence of 5%.[5]

The Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) includes a suite of initiatives to detect and monitor AMR in *N. gonorrhoeae* and potential treatment failures. The cornerstone of the programme is a national sentinel surveillance system, which collects *N. gonorrhoeae* isolates from consecutive patients attending a network of genitourinary medicine (GUM) clinics across England and Wales between July and September annually. These isolates undergo centralised antimicrobial susceptibility testing by Public Health England's (PHE) National Infection Service (NIS), and the susceptibility data are linked to demographic, clinical and behavioural data, which are collected by PHE from GUM clinics. These data are supplemented by data from the Second Generation Surveillance System (SGSS), which includes unconfirmed gonococcal antimicrobial susceptibility data from testing undertaken in primary diagnostic laboratories. Data are reported on a voluntary basis to SGSS by primary diagnostic laboratories and comes from a range of healthcare providers, including GUM clinics, general practitioners (GP) and hospitals across England. In addition, PHE's national reference laboratory receives gonococcal isolates for susceptibility testing and confirmation from primary diagnostic laboratories. Information on suspected treatment failures is reported to PHE through a bespoke web tool on the HIV/STI web portal.

This report presents findings on emerging trends on gonococcal susceptibility to current and previous antimicrobials used for treatment and explores the recent epidemiology of clinically-relevant AMR.

3. Patient Characteristics

3.1 Sentinel surveillance system

Sampling frame

In 2015, 39,696 gonorrhoea diagnoses were reported by 232 GUM clinics in England. During the sentinel surveillance collection period (July to September 2015), 5,140 gonorrhoea diagnoses were reported by the 23 participating English GUM clinics. A total of 3,170 isolates of *N. gonorrhoeae* were sent to PHE, including diagnoses from the two Welsh clinics that also take part in the sentinel surveillance system, a marked increase on previous years. Figure 1 illustrates the rate of gonorrhoea diagnosis by PHE Centre area and location of participating clinics. To enable timely completion of testing, only isolates with a specimen date between 1 July 2015 to 7 September 2015 were included. Following deduplication and data cleaning, 2,302 isolates were available for testing. From these, 1,699 unique patient isolates were successfully retrieved, tested for antimicrobial susceptibility and matched to clinical data. [Footnote1]

Characteristics of cases

Of the 1,699 patients with isolates included in the sample, nearly two-thirds were resident in London (62%) (Appendix 7.4 Table 4). The majority of patients in the sample were men (87%), and 72% (1,226/1,699) were men who had sex with men (MSM). Most patients were white (73%) and the modal age group was 25-34 years (44%). The characteristics of patients with specimens included in the sentinel system were similar to those of all patients diagnosed with gonorrhoea in the same clinics. Compared with all gonorrhoea diagnoses in GUM clinics in England [Footnote2], the sentinel surveillance sample over-represented MSM and London residents.

Footnote 1 The difference between the number of samples sent to PHE and the number included in the analysis was due to the removal of isolates that were (i) duplicate isolates/collected outside the collection period (868); (ii) not matched to clinical data/from a clinic in the sentinel surveillance system (230) (Appendix 7.1); (iii) irretrievable or contaminated isolates (336); and (iv) did not grow on Diagnostic Sensitivity Test (DST) agar with lysed blood (37) (Appendix 7.3).

Footnote 2 PHE does not collect routine surveillance data on gonorrhoea diagnoses from Wales therefore comparison of the sentinel surveillance data can only be made to diagnoses made in England.

3.2 Second Generation Surveillance System (SGSS)

Reporting sites

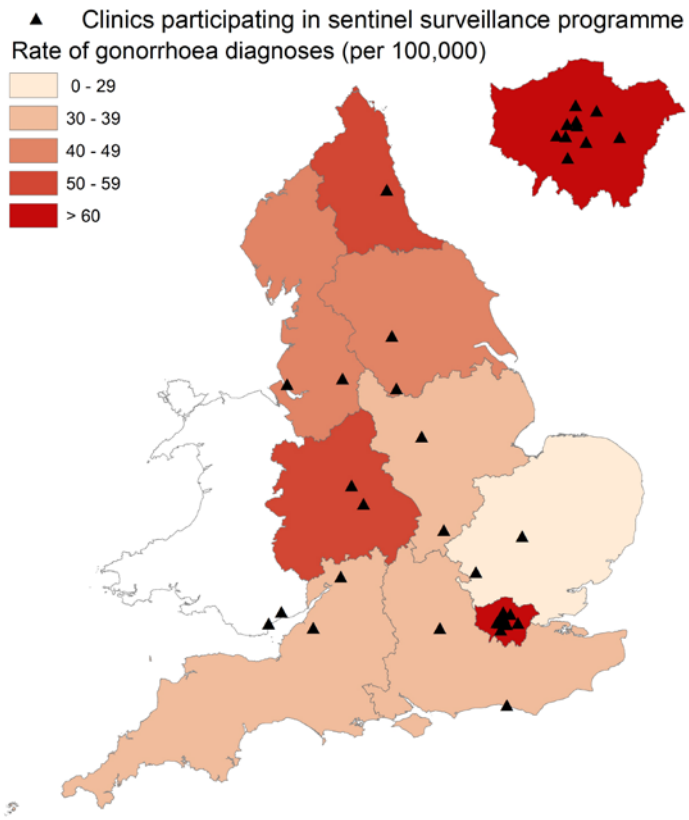
In 2015, there were 117 primary diagnostic laboratories across England reporting antimicrobial susceptibility results for *N. gonorrhoeae* to SGSS, from which 19,372 episodes of gonorrhoea with relevant antibiotic susceptibility results were analysed.

Characteristics of cases

Of all episodes with antibiotic susceptibility results, 80% were from men. The modal age group was 25-34 years old (38%). Almost half of the isolates (47%) were reported from London laboratories. Sexual orientation is not recorded in SGSS.

Figure 1: Rate of gonorrhoea diagnoses by PHE centre areas* (excluding Wales) and locations of GUM clinics collaborating in the sentinel surveillance system: 2015

* PHE Centre areas: East Midlands, East of England, London, North East, North West, South East, South West, West Midlands, Yorkshire and the Humber



4. Antimicrobial susceptibility

Antimicrobial surveillance data are presented in three parts for each antimicrobial: data from the sentinel surveillance system (resistance by patient characteristic in Appendix 7.6 Table 6); data from SGSS voluntary laboratory reports; and notable reports arising from submissions to the national reference service.

Box 1 outlines the definitions of antimicrobial resistance used in the sentinel surveillance system. Primary diagnostic laboratories reporting to SGSS predominantly use disc diffusion methods to ascertain antimicrobial susceptibility. In SGSS, susceptibility results to individual antimicrobials were reported as 'R' for resistance, 'S' for susceptible, 'I' for intermediate resistance, and 'NULL' where no result was reported. All reports in SGSS are unconfirmed by PHE's national reference laboratory. Further information on the methodology of the sentinel surveillance system and SGSS is provided in Appendix 7.1 and 7.2.

Box 1: Definitions of antimicrobial resistance in the sentinel surveillance system

Resistance Classification	Definition
Resistance to ceftriaxone*	Ceftriaxone MIC ≥ 0.125 mg/L
Resistance to azithromycin	Azithromycin MIC > 0.5 mg/L
High-level resistance to azithromycin	Azithromycin MIC ≥256 mg/L
Resistance to cefixime*	Cefixime ≥ 0.125 mg/L
Resistance to ciprofloxacin*	Ciprofloxacin MIC ≥ 1.0 mg/L
Resistance to penicillin*	Penicillin MIC≥ 1.0 mg/L or β-lactamase positive
Penicillinase-producing *N. gonorrhoeae* (PPNG)	β-lactamase positive
Resistance to tetracycline	Tetracycline MIC ≥ 2.0 mg/L
Resistance to spectinomycin	Spectinomycin MIC ≥ 128 mg/L

*Please note these are different to EUCAST breakpoints

EUCAST breakpoints:

- Resistance to ceftriaxone (MIC >0.125 mg/L)
- Resistance to cefixime (MIC >0.125 mg/L)
- Resistance to ciprofloxacin (MIC >0.06 mg/L))
- Resistance to penicillin (MIC > 1.0mg/L)

Impact of change in testing media in 2015

For the sentinel surveillance system in 2015, the supplier of the Diagnostic Sensitivity Test (DST) agar used for antimicrobial susceptibility testing was changed due to the inability of some *N. gonorrhoeae* isolates to grow on the DST agar used in previous years (Appendix 7.3). MICs for a selection of *N. gonorrhoeae* isolates from 2012, 2014 and 2015 were compared on both the new and old DST media. MICs determined on the new medium were higher for ceftriaxone, azithromycin, cefixime, penicillin and ciprofloxacin. The modal MICs of the control strains (n=10) with the new DST were generally in concordance with the old DST and the expected MICs for penicillin and ciprofloxacin. The 'expected' MICs are used for internal quality assurance purposes and were previously established by calculating the model MIC of each control strain from longitudinal GRASP data and from published data. [6] For ceftriaxone and cefixime, the modal MICs of the control strains with the new DST were either the same as the old DST and the expected values (four strains with ceftriaxone and five with cefixime), or were one dilution higher.

For azithromycin, MICs on the new medium were higher. The azithromycin modal MICs of the control strains with the new DST generally were as expected albeit with an increase of one doubling dilution for two out of ten control strains. However, with the old DST the modal MICs of the control strains were either one dilution lower or the same as the control strain modal MICs on the new DST and the expected MICs. For tetracycline, MICs on the new medium were lower. The tetracycline modal MICs of seven control strains on the new DST were one doubling dilution lower compared to using the old DST and the expected MICs. Given this substantial change in the sentinel surveillance system 2015 testing protocol, trends in resistance prevalence and MIC drift analyses should be interpreted with caution, especially for azithromycin. This is highlighted throughout the report.

4.1 Summary

Susceptibility to first-line antimicrobials, ceftriaxone and azithromycin:

- in 2015, the world's first documented treatment failure to dual ceftriaxone and azithromycin therapy was reported in England; the isolate was referred to PHE and confirmed as resistant to ceftriaxone (MIC 0.25 mg/L) and azithromycin (MIC 1.0 mg/L)
- no other cases of ceftriaxone resistance (MIC ≥0.125 mg/L) were confirmed in 2015
- resistance to azithromycin (MICs >0.5 mg/L) was 10% in the sentinel surveillance system in 2015, although MICs for the great majority (91%) of these resistant isolates were 1 mg/L, only just above the breakpoint for resistance; 2% of *N. gonorrhoeae* tested in primary diagnostic laboratories were reported resistant to azithromycin
- an outbreak of high-level azithromycin-resistant *N. gonorrhoeae* (MICs ≥256 mg/L) is under investigation in England; between November 2014 and August 2016 there have been a total of 56 confirmed cases; all cases have been susceptible to ceftriaxone

Other antimicrobial susceptibility data in 2015:

- resistance to cefixime remained low (resistance prevalence: sentinel surveillance system 1%, SGSS 1%)
- 39% of isolates in the sentinel surveillance system and 29% of isolates reported in SGSS were resistant to ciprofloxacin
- 24% of isolates in the sentinel surveillance system and 29% of isolates in SGSS were resistant to penicillin
- 39% of isolates in the sentinel surveillance system and 53% of isolates in SGSS were resistant to tetracycline
- no isolates in the sentinel surveillance system and 0.2% of isolates reported in SGSS were resistant to spectinomycin

Table 1: Percentage of gonococcal isolates in the sentinel surveillance system that were resistant to selected antimicrobials: 2011-2015

**Note: due to changes in the DST medium used to test antimicrobial susceptibility of sentinel surveillance system 2015 isolates, resistance prevalence trends should be interpreted with caution, particularly for azithromycin and tetracycline*

Antimicrobials	Percentage resistant (number resistant)				
	2011 N=1,289	2012 N=1,535	2013 N=1,750	2014 N=1,568	2015* N=1,699
Ceftriaxone (MIC ≥ 0.125mg/L)	**0.0** (0)	**0.2** (3)	**0.2** (3)	**0.0** (0)	**0.0** (0)
Ceftriaxone (MIC ≥ 0.25mg/L)	**0.0** (0)	**0.0** (0)	**0.0** (0)	**0.0** (0)	**0.0** (0)
Azithromycin	**0.5** (7)	**0.7** (11)	**1.6** (28)	**1.0** (16)	**9.8** (166)
Cefixime (MIC ≥ 0.125mg/L)	**10.9** (140)	**5.6** (86)	**5.2** (91)	**1.4** (22)	**1.1** (18)
Cefixime (MIC ≥ 0.25mg/L)	**1.3** (17)	**2.1** (32)	**1.3** (23)	**0.1** (2)	**0.4** (6)
Ciprofloxacin	**34.1** (440)	**25.0** (384)	**29.3** (513)	**37.3** (585)	**39.1** (665)
Penicillin	**11.5** (148)	**14.6** (224)	**18.4** (322)	**22.6** (354)	**24.1** (410)
Tetracycline	**69.9** (901)	**76.3** (1,171)	**72.9** (1,276)	**82.8** (1,298)	**39.4** (670)
Spectinomycin	**0.0** (0)	**0.0** (0)	**0.0** (0)	**0.0** (0)	**0.0** (0)

Table 2: Percentage of gonococcal isolates tested for selected antimicrobials in primary diagnostic laboratories, SGSS: 2014 and 2015

Antimicrobial	Percentage of isolates susceptibility tested (range across PHE centre areas)	
	2014 (N=18,536)	2015 (N=19,372)
Ceftriaxone	**87.2** (68.2-98.6)	**91.1** (79.1-98.6)
Azithromycin	**80.1** (20.5-97.3)	**88.1** (35.7-98.9)
Cefixime	**66.4** (27.1-92.5)	**62.7** (41.6-88.5)
Ciprofloxacin	**88.8** (70.3-99.5)	**91.0** (80.4-99.7)
Penicillin	**59.2** (32.0-99.6)	**59.7** (29.9-95.6)
Tetracycline	**49.8** (33.5-84.8)	**53.2** (37.3-85.9)
Spectinomycin	**68.4** (3.4-91.2)	**67.6** (2.4-92.2)

Table 3: Number of isolates susceptibility tested and percentage of gonococcal isolates in primary diagnostic laboratories reported resistant to selected antimicrobials, SGSS: 2014 and 2015

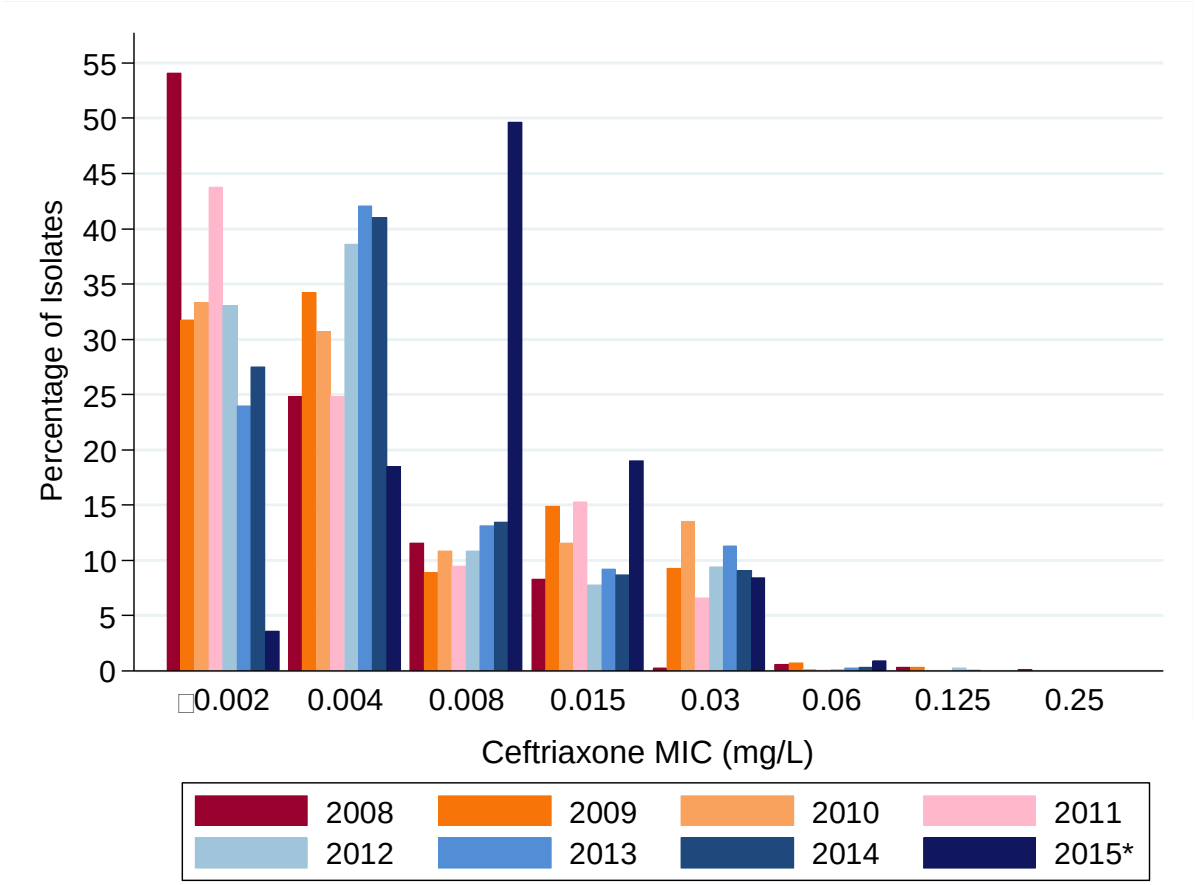
Antimicrobial	Percentage of episodes resistant (range across PHE centre)		Number of isolates susceptibility tested (n)	
	2014	2015	2014	2015
Ceftriaxone	**0.3** (0.0-0.8)	**0.5** (0.0-2.4)	16,155	17,650
Azithromycin	**1.3** (0.6-3.8)	**1.6** (0.7-5.2)	14,845	17,057
Cefixime	**0.3** (0.0-1.3)	**0.6** (0.3-2.7)	14,286	15,589
Ciprofloxacin	**30.0** (14.7-37.3)	**29.0** (15.7-35.5)	16,465	17,619
Penicillin	**25.1** (11.0-40.8)	**29.3** (17.0-42.3)	10,960	11,583
Tetracycline	**19.9** (8.3-24.9)	**20.9** (15.9-26.7)	9,234	10,329
Spectinomycin	**0.4** (0.0-3.7)	**0.2** (0.0-0.9)	12,685	13,088

4.2 Ceftriaxone

Sentinel surveillance system (July-September 2015)

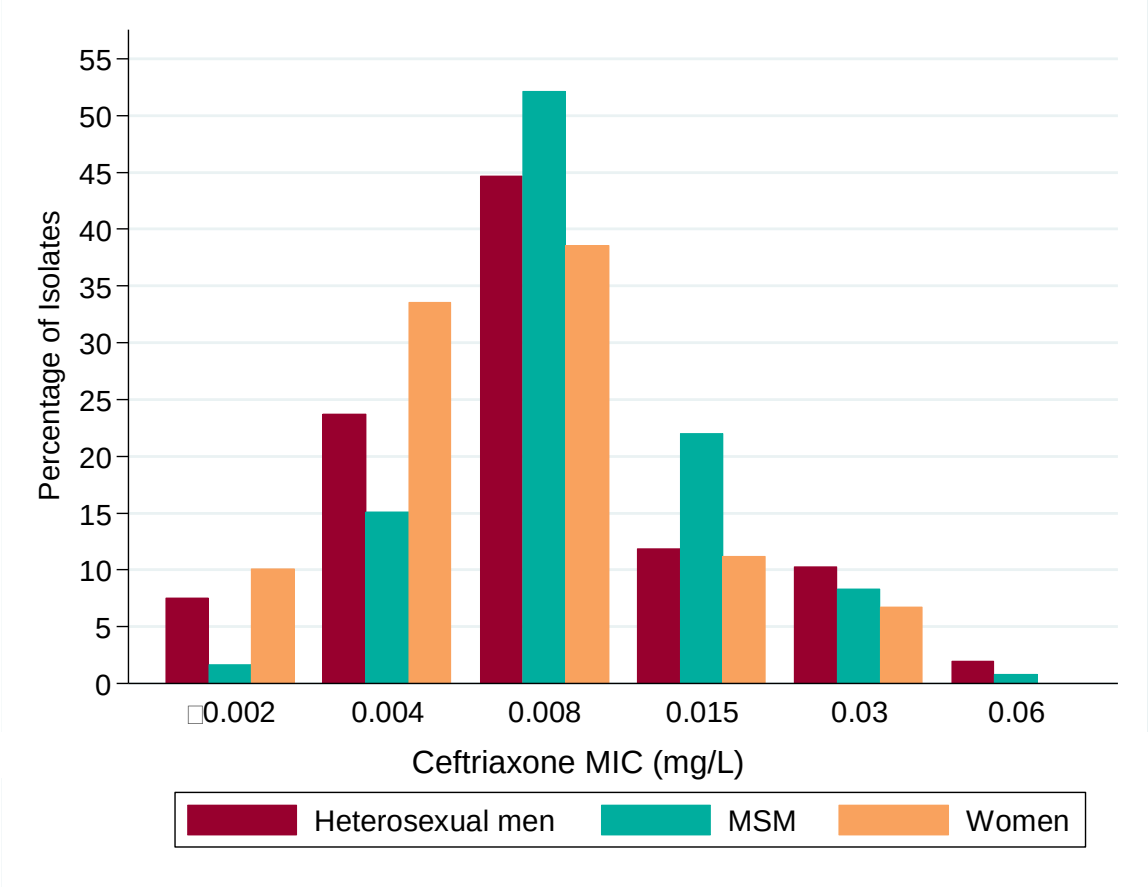
No isolates were identified with resistance to ceftriaxone in the 2015 sentinel surveillance system. However, the modal MIC has increased by one dilution to 0.008 mg/L compared with previous years (this is partly due to the DST media change) (Figure 2). Isolates from MSM were less susceptible to ceftriaxone than isolates from heterosexual men or women (Figure 3).

Figure 2: Distribution of ceftriaxone MICs (mg/L) for gonococcal isolates within the sentinel surveillance system: 2008-2015



**Note: due to changes in the DST medium used to test antimicrobial susceptibility of sentinel surveillance system 2015 isolates, resistance prevalence trends should be interpreted with caution, particularly for azithromycin and tetracycline*

Figure 3: Distribution of ceftriaxone MICs (mg/L) for gonococcal isolates by gender and sexual orientation within the sentinel surveillance system: 2015



SGSS voluntary laboratory reports (January-December 2015)

Susceptibility testing coverage

In 2015, 91% (17,650/19,372) of gonococci reported to SGSS had a ceftriaxone susceptibility result (Table 2) [Footnote 3]. Testing of ceftriaxone susceptibility varied by PHE centre, ranging between 79% and 99%, but has increased overall for England from 87% to 96% from 2014 to the first two quarters of 2016 (Figure 4).

Susceptibility results

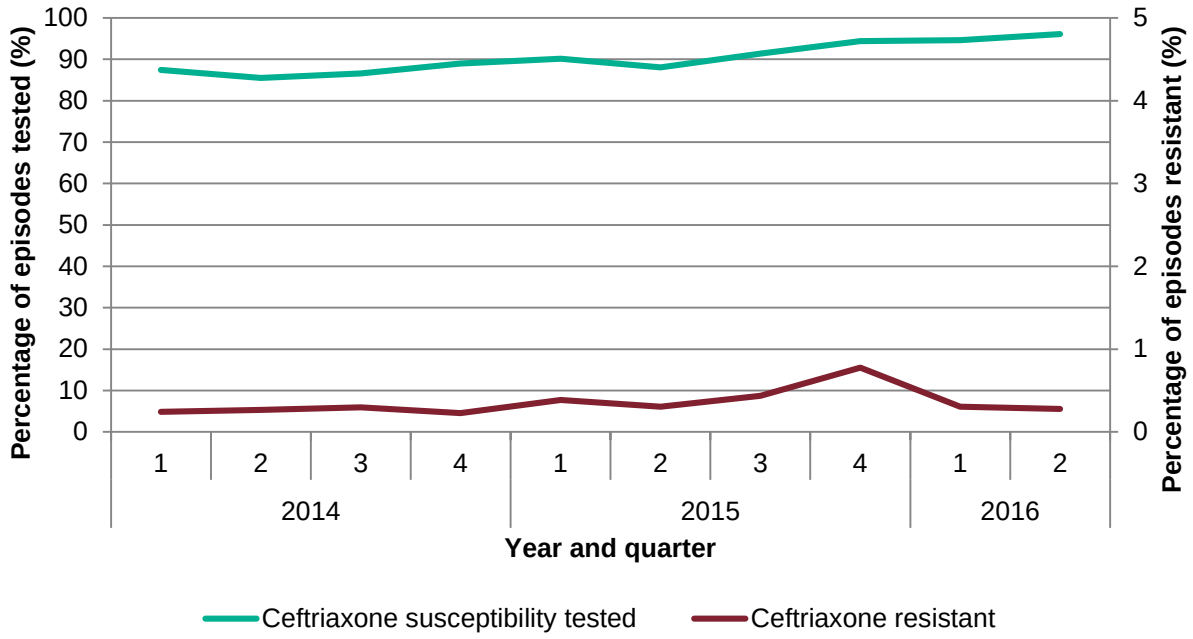
Of those tested, 0.5% (86/17,650) were reported to have resistance to ceftriaxone (Table 3). This has remained relatively unchanged since 2014. The percentage of gonococci reported resistant in 2015 varied by PHE centre areas, ranging between 0% and 2%.

Footnote 3 In primary diagnostic labs, ceftriaxone susceptibility is often inferred by testing cefuroxime as a proxy cephalosporin. Please refer to Appendix 7.2 for further information.

National reference service

In 2015 one isolate sent to PHE's national reference service was confirmed to have resistance to ceftriaxone (MIC 0.25 mg/L). This isolate also showed low-level resistance to azithromycin (MIC 1.0 mg/L) and was later reported as the world's first documented case of treatment failure to dual ceftriaxone and azithromycin therapy[7]. This was an imported isolate from Japan and, to date, no treatment failures of gonorrhoea acquired within the UK have been identified.

Figure 4: Percentage of gonococcal isolates tested for ceftriaxone susceptibility and reported as resistant by primary diagnostic labs in England: January 2014 - June 2016 by year and quarter



4.3 Azithromycin

Sentinel surveillance system (July-September 2015)

In the 2015 sentinel surveillance sample, the prevalence of azithromycin resistance was 10% (Figure 5). Although MICs for the majority (91%) of these resistant isolates were 1 mg/L, only just above the breakpoint of resistance (Figure 6). Isolates from MSM were less susceptible to azithromycin than isolates from heterosexual men or women (Figure 7). Due to changes in the DST medium used to test antimicrobial susceptibility of 2015 isolates, azithromycin resistance prevalence in 2015 cannot be compared with resistance prevalence in previous years.

Two isolates exhibiting high-level azithromycin resistance (MIC ≥256 mg/L) were identified. Both isolates were from young, heterosexual women attending GUM clinics in Northern England, and both isolates were also resistant to tetracycline but susceptible to all other antibiotics tested, including ceftriaxone.

Figure 5: Percentage of azithromycin-resistant gonococcal isolates (MIC >0.5 mg/L) by gender and sexual orientation within the sentinel surveillance system: 2005 - 2015
**Note: due to changes in the DST medium used to test antimicrobial susceptibility in the sentinel surveillance system 2015 isolates, azithromycin resistance prevalence in 2015 cannot be compared with resistance prevalence in previous years*

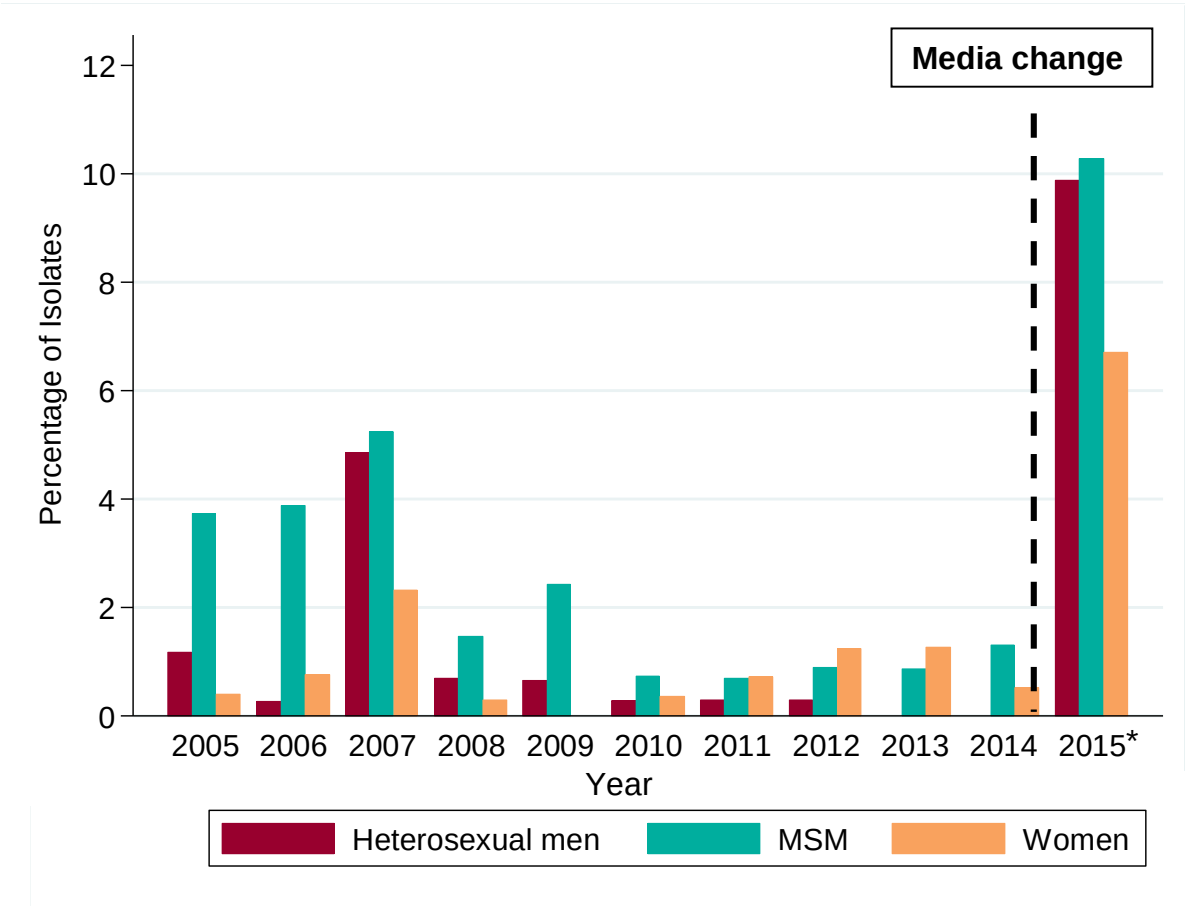


Figure 6 Distribution of azithromycin MICs (mg/L) for gonococcal isolates within the sentinel surveillance system: 2008 - 2015

**Note: due to changes in the DST medium used to test antimicrobial susceptibility in the sentinel surveillance system 2015 isolates, azithromycin resistance prevalence in 2015 cannot be compared with resistance prevalence in previous years*

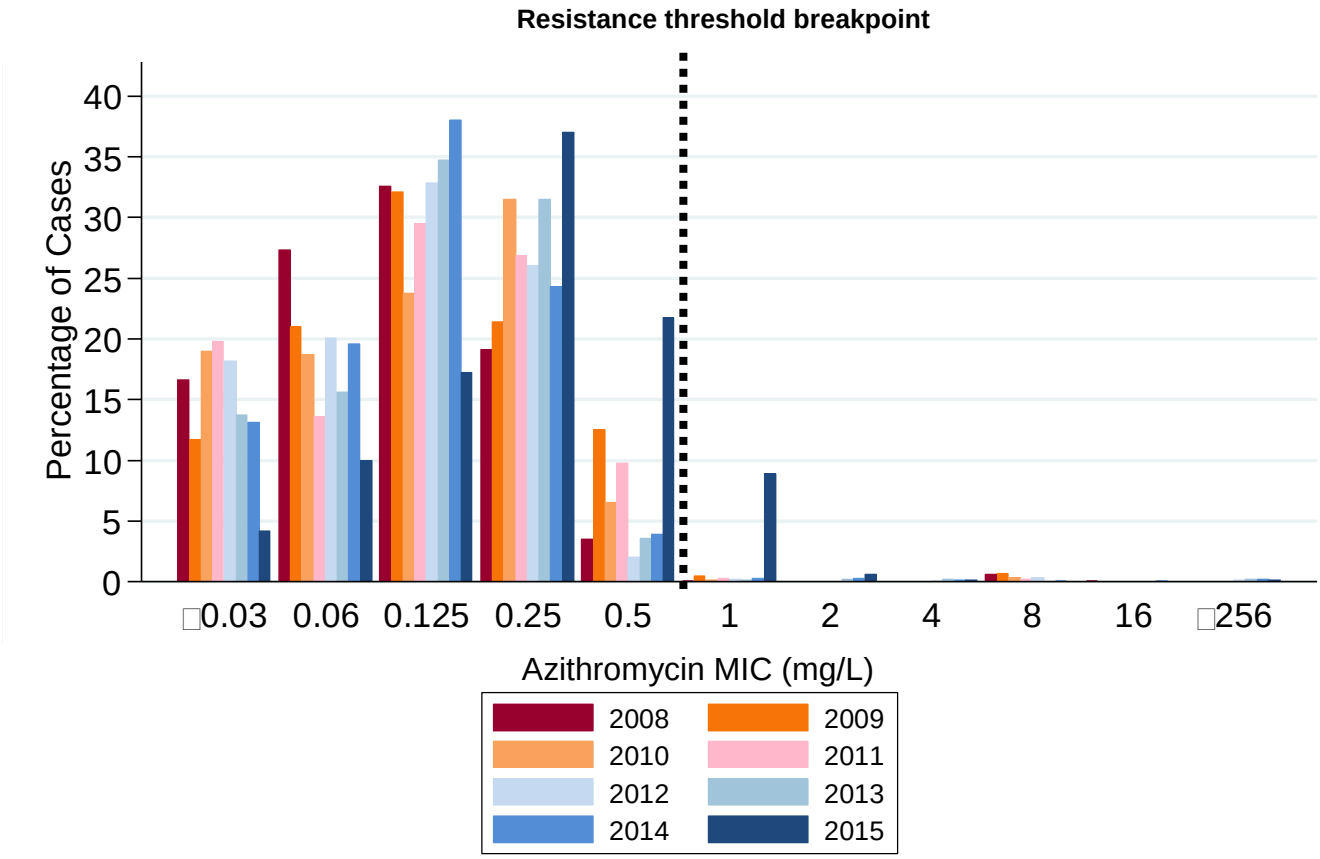
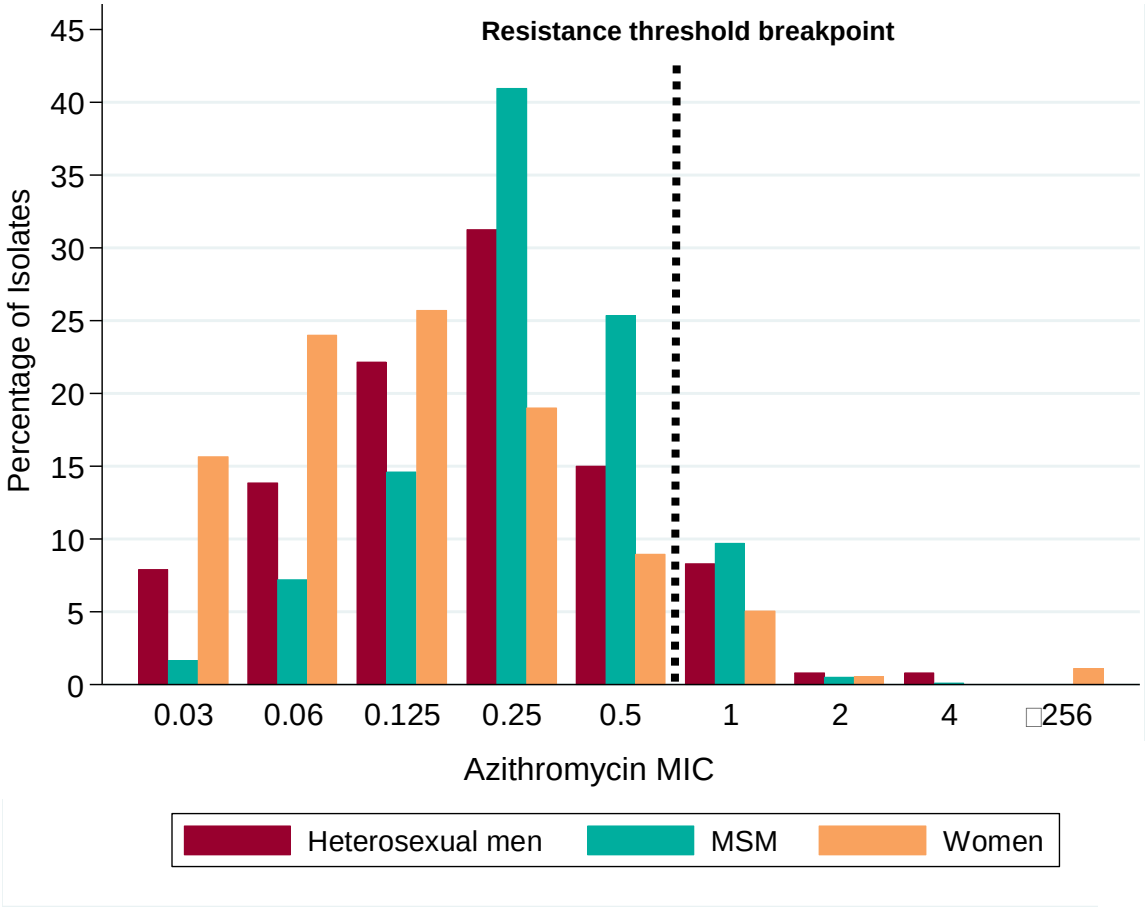


Figure 7: Distribution of azithromycin MICs (mg/L) for gonococcal isolates by gender/sexual orientation within the sentinel surveillance system: 2015



SGSS voluntary laboratory reports (January-December 2015)

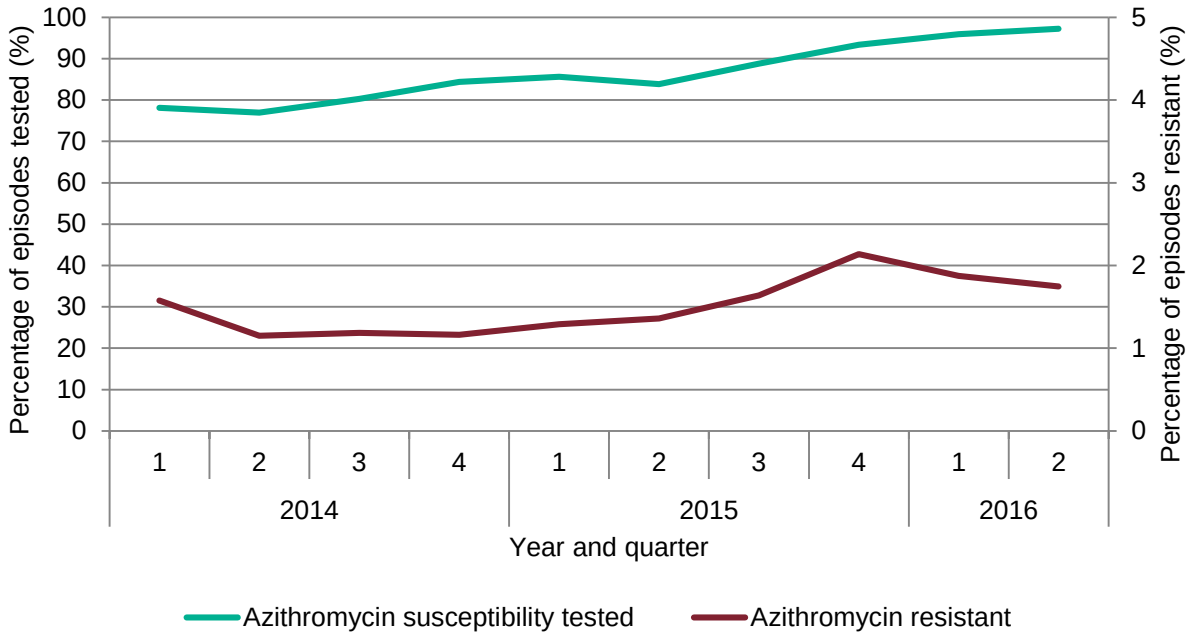
Susceptibility testing coverage

In 2015, 88% (17,057/19,372) of gonococci reported to SGSS had an azithromycin susceptibility result (Table 2). This is an improvement from 2014 where only 80% of isolates were tested. Furthermore, in 2016 testing increased to over 97% in the first two quarters (Figure 8). Nevertheless, testing of azithromycin susceptibility varied by PHE centre areas ranging between 36% to 99%.

Susceptibility results

Among the isolates tested, 2% (279/17,102) were reported to be resistant to azithromycin (Table 3), which is a slight increase from 2014 (1%; 187/14,845). The percentage of reported resistance varied by PHE centre areas, ranging between 1% and 5%. Isolates reported as azithromycin-resistant by primary diagnostic laboratories were not all confirmed by PHE's national reference services.

Figure 8: Percentage of gonococcal isolates tested for azithromycin susceptibility and reported as resistant by primary diagnostic labs in England: January 2014 - Jun 2016 by quarter



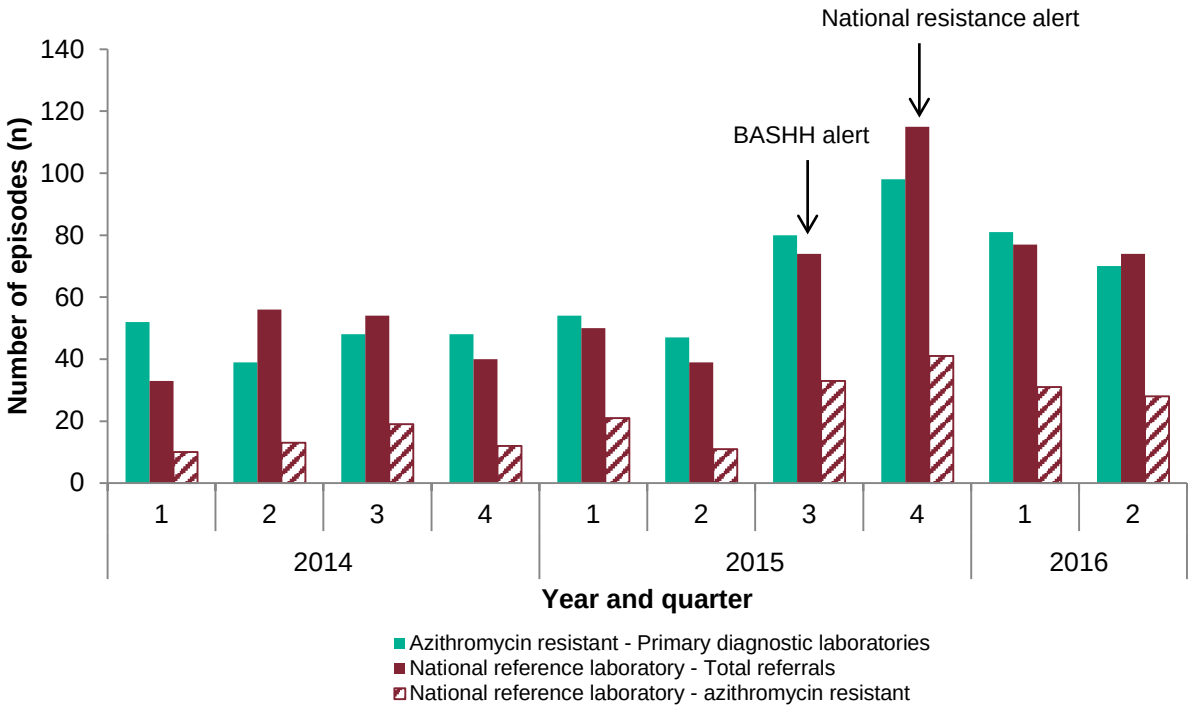
National reference service

Gonococcal isolates identified as azithromycin-resistant by primary diagnostic laboratories should refer them to PHE's national reference service for confirmation. Figure 9 shows the number of azithromycin-resistant isolates reported by primary diagnostic laboratories compared with the total number of referrals received by the reference laboratory by year and quarter. The number of episodes confirmed as azithromycin resistant is also shown. To note, isolates may be referred for reasons other than for confirmation of azithromycin resistance.

In 2015, the PHE reference service detected an outbreak of high-level azithromycin-resistant N. gonorrhoeae (MICs ≥256 mg/L) in heterosexual patients. This emerged in northern England. In September 2015, a British Association of Sexual Health and HIV (BASHH) alert was sent to advise clinicians to ensure HL-AziR are followed up and receive a test-of-cure (TOC). In October 2015 a National Resistance Alert was issued to all microbiologists to remind them to carry out susceptibility testing to first-line antimicrobials, and refer resistant isolates to the national reference lab at PHE Colindale.

This outbreak has since spread to other parts of the country, particularly in London and the South East. The outbreak is no longer confined to heterosexuals, after the identification of cases among MSM. As of October 2016, a total of 56 confirmed cases have been identified. PHE has convened a Level 2 Incident Control Team to monitor and respond to the HL-AziR gonorrhoea outbreak. To date, these isolates have been susceptible to ceftriaxone. More information related to the outbreak can be found here: https://www.gov.uk/government/publications/high-level-azithromycin-resistant-gonorrhoea-in-england

Figure 9: Number of azithromycin-resistant gonococcal isolates reported by primary diagnostic labs compared with total number of referrals received and azithromycin-resistant gonococci confirmed by the national reference laboratory in England: January 2014 – June 2016 by quarter



4.4 Cefixime

Sentinel surveillance system (July-September 2015)

The percentage of isolates resistant to cefixime (MIC ≥0.125 mg/L) was ≤2% in all patient sexual orientation sub-groups (Figure 10). The modal MIC was 0.015mg/L (Figure 11). All cefixime-resistant isolates exhibited higher ceftriaxone MICs (≥0.015mg/L) and half were also resistant to azithromycin. Isolates exhibiting higher ceftriaxone MICs were also resistant to cefixime (Figure 12).

SGSS voluntary laboratory reports (January-December 2015)

Susceptibility testing coverage
In 2015, 80% (15,589/19,372) of gonococci reported to SGSS had a cefixime susceptibility result (Table 2).[4] Testing of cefixime susceptibility varied by PHE centre areas, ranging between 49% to 94%.

Susceptibility results
Of those tested, 0.6% (99/15,589) were reported to have resistance to cefixime (Table 3). Isolates reported as cefixime-resistant by primary diagnostic laboratories were not all confirmed by PHE's national reference laboratory.

Footnote [4] In primary diagnostic labs, cefixime susceptibility is often inferred by testing cefuroxime as a proxy cephalosporing. Please refer to Appendix 7.2 for further information.

Figure 10: Percentage of cefixime-resistant gonococcal isolates (MIC ≥0.125 mg/L) by gender and sexual orientation within the sentinel surveillance system: 2005 - 2015

**Note: due to changes in the DST medium used to test antimicrobial susceptibility in the sentinel surveillance system 2015 isolates, cefixime resistance prevalence in 2015 cannot be compared with resistance prevalence in previous years*

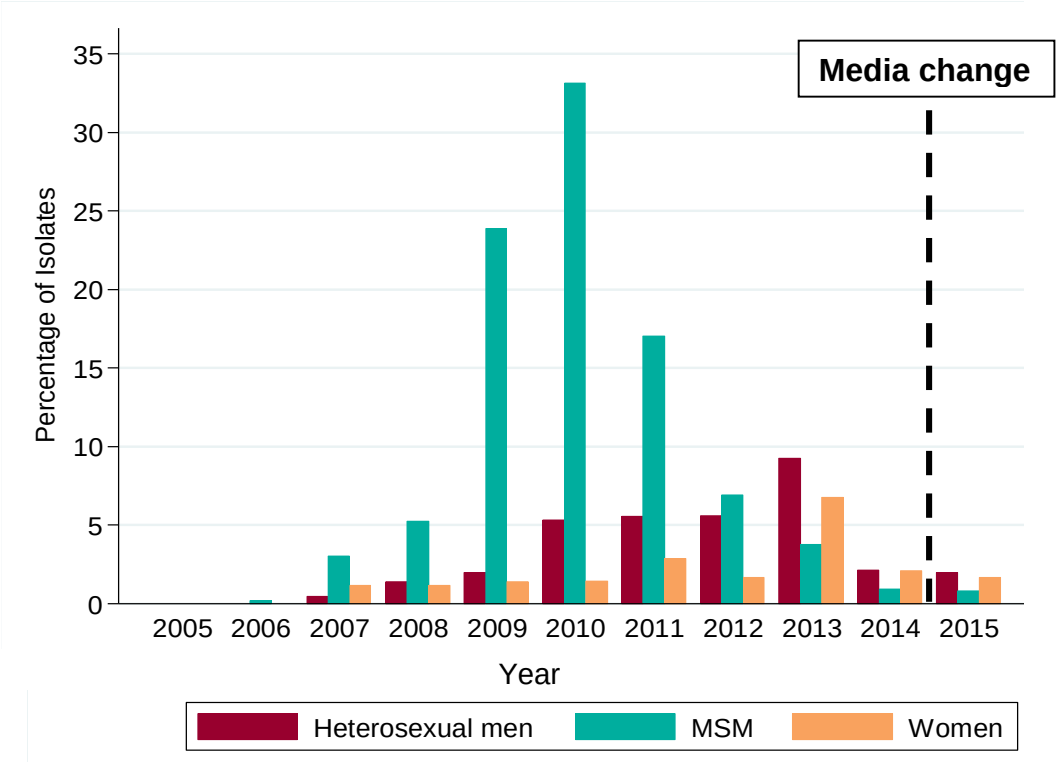


Figure 11: Distribution of cefixime MICs (mg/L) for gonococcal isolates within the sentinel surveillance system: 2008 - 2015

**Note: due to changes in the DST medium used to test antimicrobial susceptibility in the sentinel surveillance system 2015 isolates, cefixime resistance prevalence in 2015 cannot be compared with resistance prevalence in previous years*

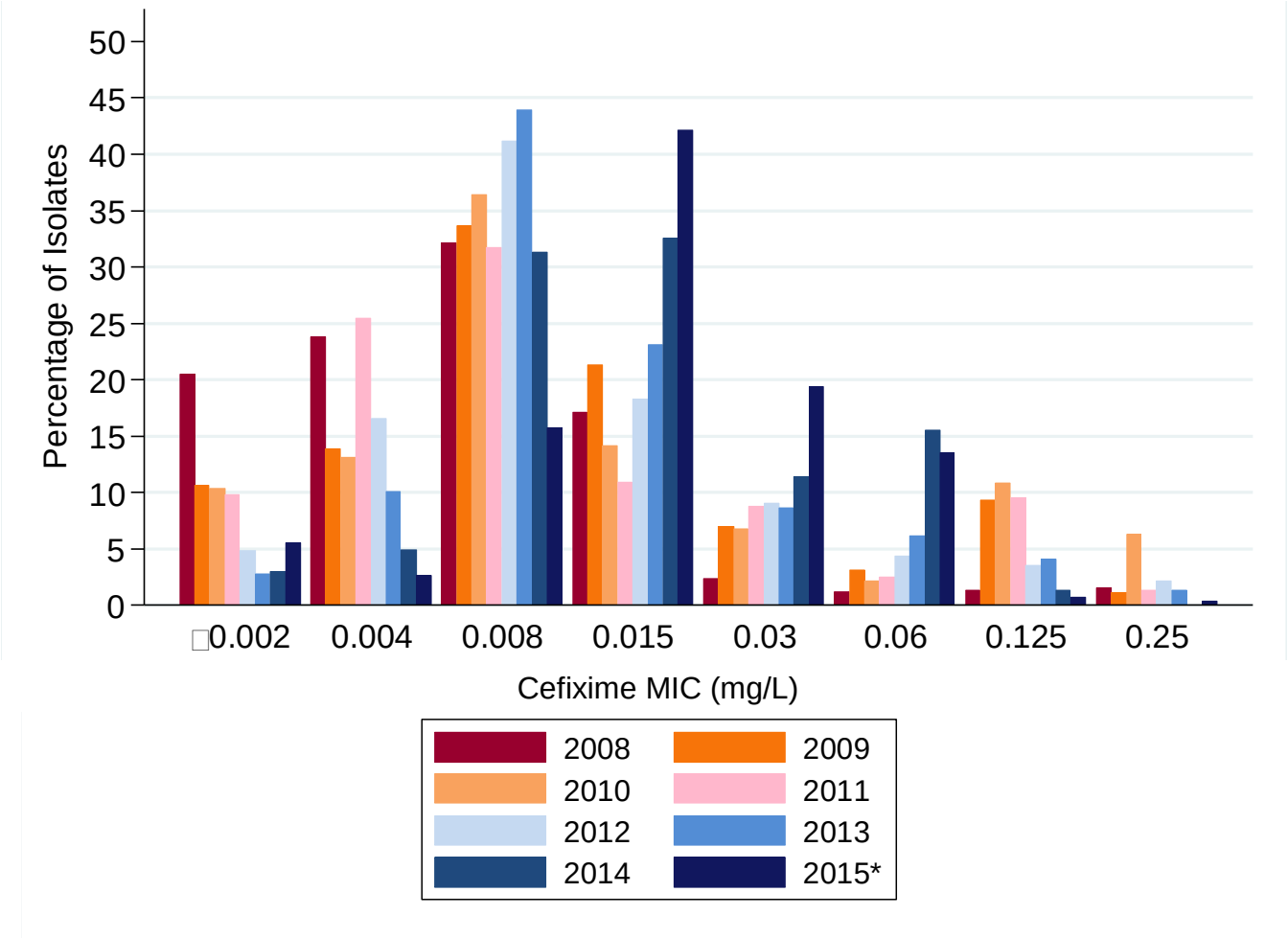
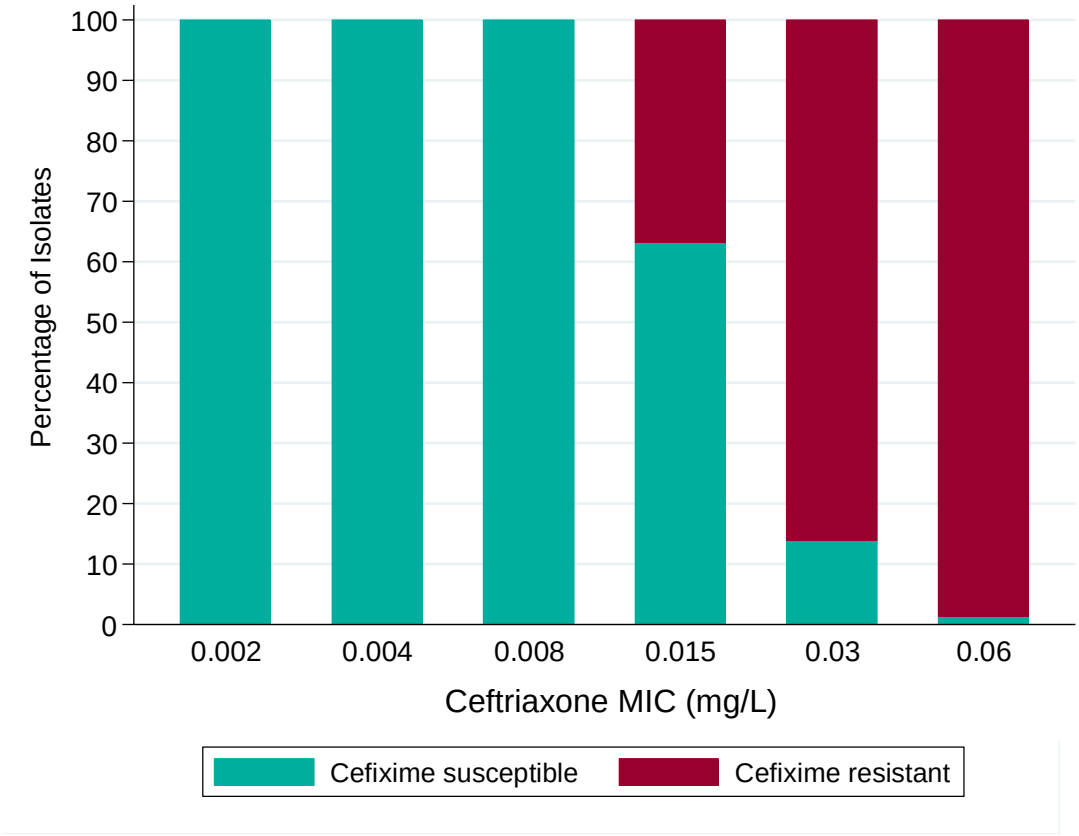


Figure 12: Percentage of gonococcal isolates showing resistance to cefixime (MIC ≥0.125 mg/L) by ceftriaxone MICs (mg/L) within the sentinel surveillance system: 2015



4.5 Ciprofloxacin

Sentinel surveillance system (July-September 2015)

In 2015, 39% of isolates were resistant to ciprofloxacin (MICs ≥1 mg/L). Resistance was more frequent in isolates from MSM and heterosexual men (Figure 13).

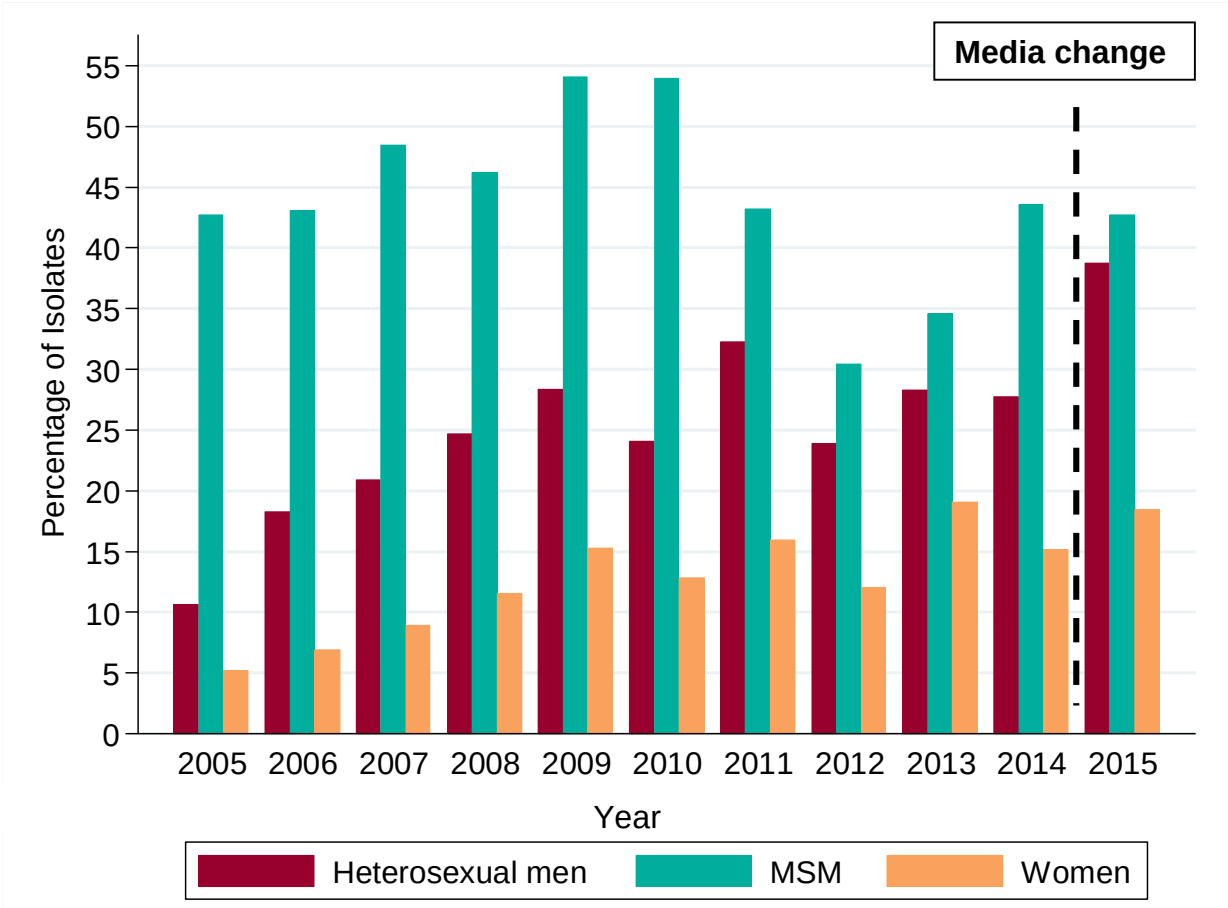
SGSS voluntary laboratory reports (January-December 2015)

Susceptibility testing coverage
In 2015, 91% (17,619/19,372) of gonococci reported to SGSS had a ciprofloxacin susceptibility result (Table 2). Testing of ciprofloxacin susceptibility varied by PHE centre areas, ranging between 80% and 100%.

Susceptibility results
Of those tested, 29% (5,123/17,619) were reported to have resistance to ciprofloxacin (Table 3), which is unchanged from 2014. Isolates reported as ciprofloxacin-resistant by primary diagnostic laboratories were not all confirmed by PHE's national reference laboratory.

Figure 13: Percentage of gonococcal isolates resistant to ciprofloxacin by gender and male sexual orientation within the sentinel surveillance system: 2005 - 2015

**Note: due to changes in the DST medium used to test antimicrobial susceptibility in the sentinel surveillance system 2015 isolates, ciprofloxacin resistance prevalence in 2015 cannot be compared with resistance prevalence in previous years*



4.6 Penicillin

Sentinel surveillance system (July-September 2015)

In 2015, 24% of isolates were resistant to penicillin (MICs ≥1 mg/L). Resistance was more frequent in isolates from MSM and heterosexual men (Figure 14). The majority (16%) of penicillin-resistant isolates were penicillinase-producing N. gonorrhoeae (PPNG), which have plasmid-mediated resistance, as opposed to chromosomally-mediated resistance in non-PPNG (Figure 15).

SGSS voluntary laboratory reports (January-December 2015)

Susceptibility testing coverage
In 2015, 60% (11,583/19,372) of gonococci reported to SGSS had a penicillin susceptibility result (Table 2). Testing of penicillin susceptibility varied by PHE centre areas, ranging between 30% and 100%.

Susceptibility results
Of those tested, 29% (3,396/11,583) were reported to have resistance to penicillin (Table 3). Isolates reported as penicillin-resistant by primary diagnostic laboratories were not all confirmed by PHE's national reference laboratory.

Figure 14: Percentage of gonococcal isolates resistant to penicillin (≥1 mg/L or β-lactamase +) by gender and sexual orientation within the sentinel surveillance system: 2005 - 2015

**Note: due to changes in the DST medium used to test antimicrobial susceptibility in the sentinel surveillance system 2015 isolates, penicillin resistance prevalence in 2015 cannot be compared with resistance prevalence in previous years*

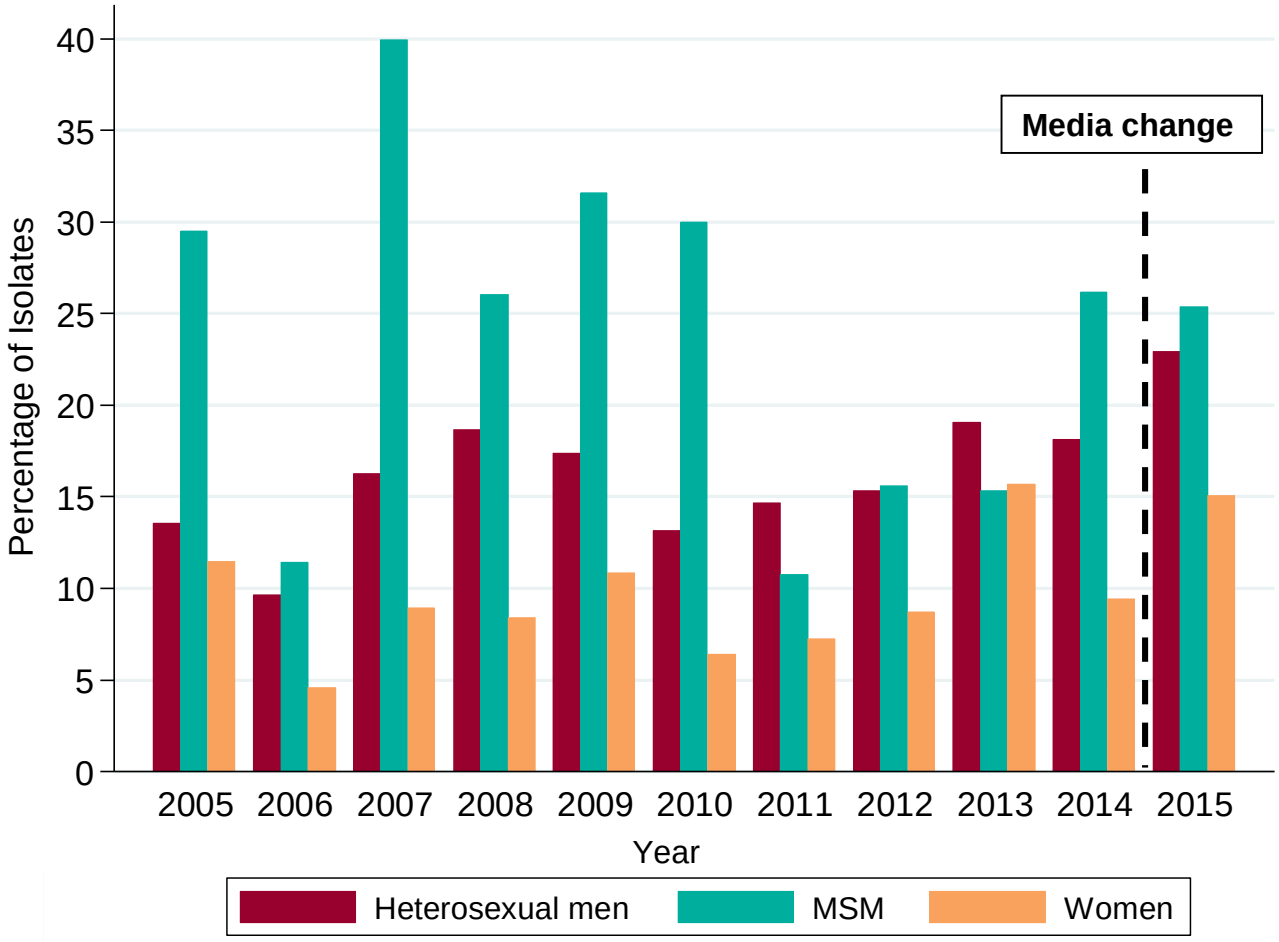
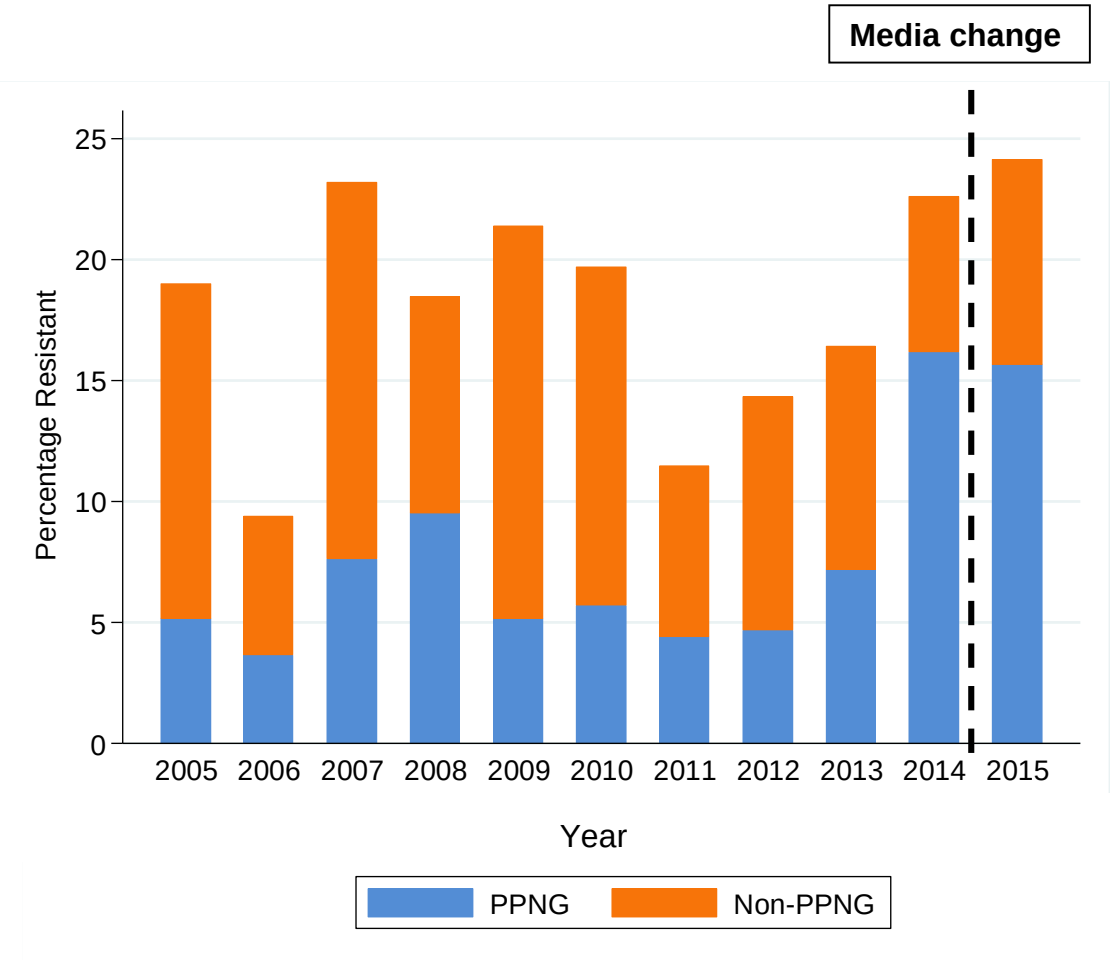


Figure 15: Percentage of gonococcal isolates resistant to penicillin by type (PPNG, Non-PPNG) within the sentinel surveillance system: 2005 - 2015

**Note: due to changes in the DST medium used to test antimicrobial susceptibility in the sentinel surveillance system 2015 isolates, penicillin resistance prevalence in 2015 cannot be compared with resistance prevalence in previous years*



4.7 Tetracycline

Sentinel surveillance system (July-September 2015)

The prevalence of tetracycline resistance (MICs ≥2 mg/L) in 2015 was 39%.

Due to changes in the DST medium used to test antimicrobial susceptibility of sentinel surveillance 2015 isolates, tetracycline resistance prevalence in 2015 cannot be compared with resistance prevalence in previous years. The apparent fall in resistance will almost entirely arise from this change.

SGSS voluntary laboratory reports (January-December 2015)

Susceptibility testing coverage
In 2015, 53% (10,329/19,372) of gonococci reported to SGSS had a tetracycline susceptibility result (Table 2). Testing of tetracycline susceptibility varied by PHE centre areas, ranging between 37% and 86%.

Susceptibility results
Of those tested, 21% (2,159/10,329) were reported to have resistance to tetracycline (Table 3). Isolates reported as tetracycline-resistant by primary diagnostic laboratories were not all confirmed by PHE's national reference laboratory.

4.8 Spectinomycin

Sentinel surveillance system (July-September 2015)

In 2015, there were no isolates exhibiting resistance to spectinomycin (MICs >64 mg/L).

SGSS voluntary laboratory reports (January-December 2015)

Susceptibility testing coverage
In 2015, 68% (13,088/19,372) of gonococci reported to SGSS had a spectinomycin susceptibility result (Table 2). Testing of spectinomycin susceptibility varied by PHE centre areas, ranging between 2% and 92%.

Susceptibility results
Of those tested, 0.2% (30/13,088) were reported to have resistance to spectinomycin (Table 3). Isolates reported as spectinomycin-resistant by primary diagnostic laboratories were not all confirmed by PHE's national reference laboratory.

5. Prescribing practice

Antimicrobial prescription data were available for 91% of patients in the sentinel surveillance sample (1,552/1,699). Of these, 91% received the recommended treatment of ceftriaxone (500 mg IM) in combination with azithromycin (1 g oral). For comparison, 87% of patients received the recommended treatment in 2014 (Figure 16). In 2015, 93% of heterosexual men received the recommended treatment, compared with 90% of MSM and 91% of women.

Of those patients not prescribed the recommended treatment (n=141) 5% (7/141) received combination therapy with antimicrobials other than azithromycin (Figure 18). Combinations prescribed included 1% (1/141) cefixime and doxycycline, 1% (1/141) ciprofloxacin and doxycycline and 3% (5/141), four of them MSM, received ceftriaxone and doxycycline. There was a decline in the number of patients receiving the combination of ceftriaxone and doxycycline compared with 2014.

Among those not prescribed the recommended treatment, 32% (45/141) patients received combination therapy with azithromycin plus an antimicrobial that was not ceftriaxone. These included cefixime (n=8), doxycycline (n=2), ciprofloxacin (n=3), spectinomycin (n=16), spectinomycin and doxycycline (n=4), cefotaxime (n=2), and unspecified (n=10). Of these, four patients had isolates that were resistant to azithromycin. Overall, 23% (33/141) were prescribed monotherapy, of which 25 received azithromycin, one received cefixime, four received doxycycline, three received ceftriaxone and one received ciprofloxacin. Out of the 25 patients, three (12%) receiving azithromycin monotherapy were resistant to azithromycin. The remaining 55 patients, 39% (55/141) were prescribed an unspecified antibiotic

Figure 16: Antimicrobial prescribing practice within the sentinel surveillance system: 2005 - 2015

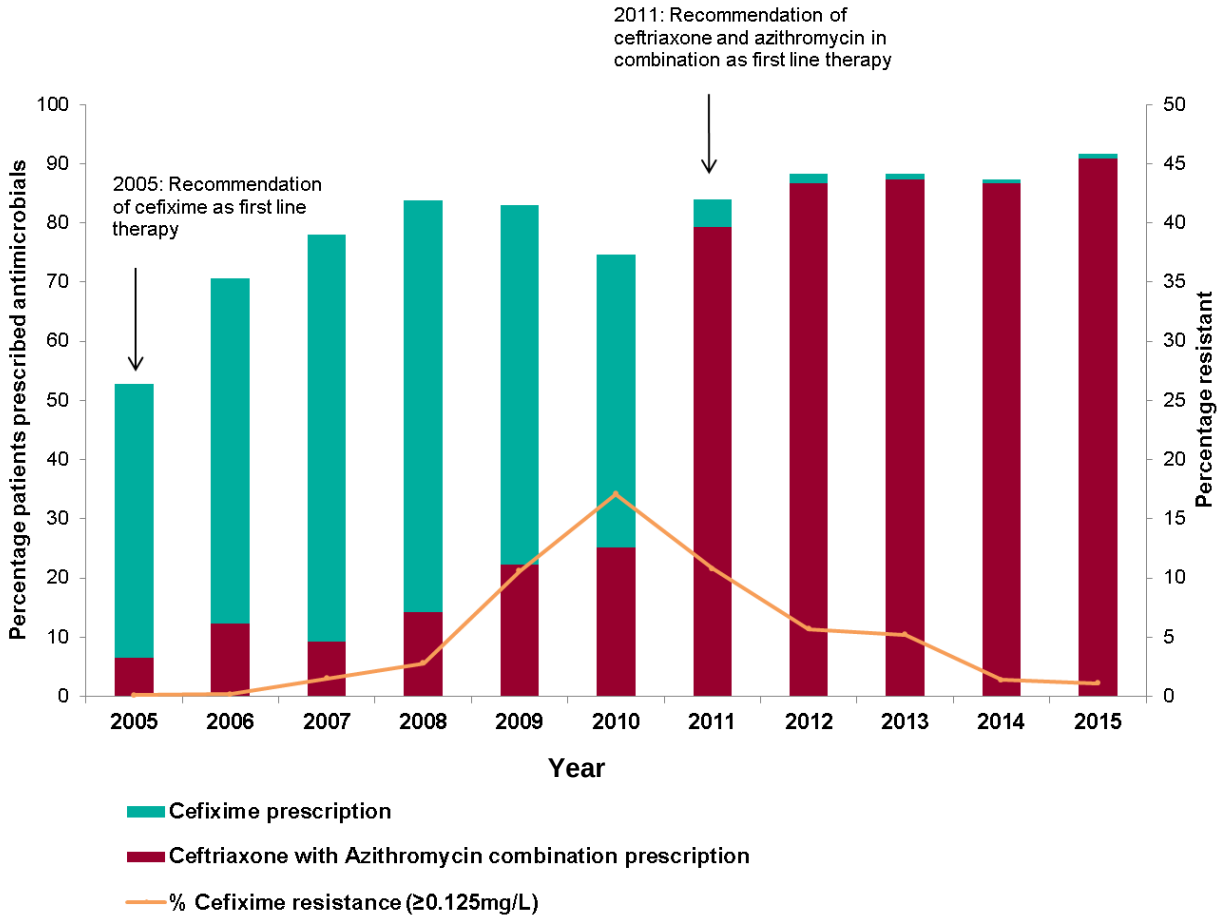


Figure 17: Percentage of patients prescribed ceftriaxone with doxycycline by gender and male sexual orientation within the sentinel surveillance system: 2005 - 2015

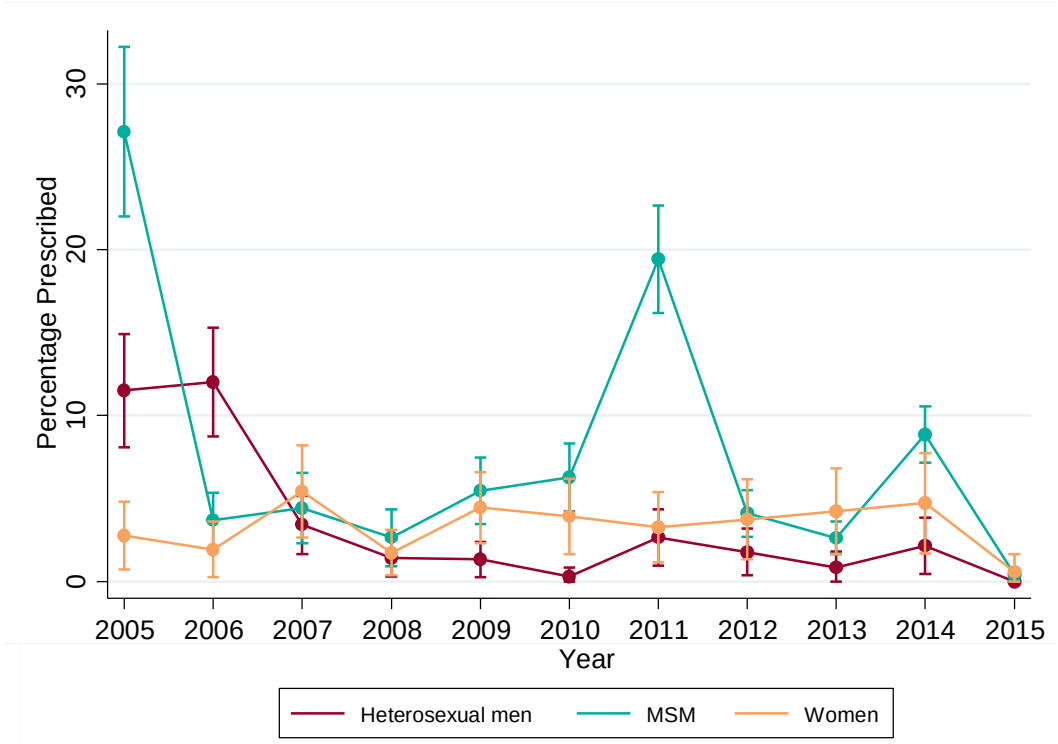
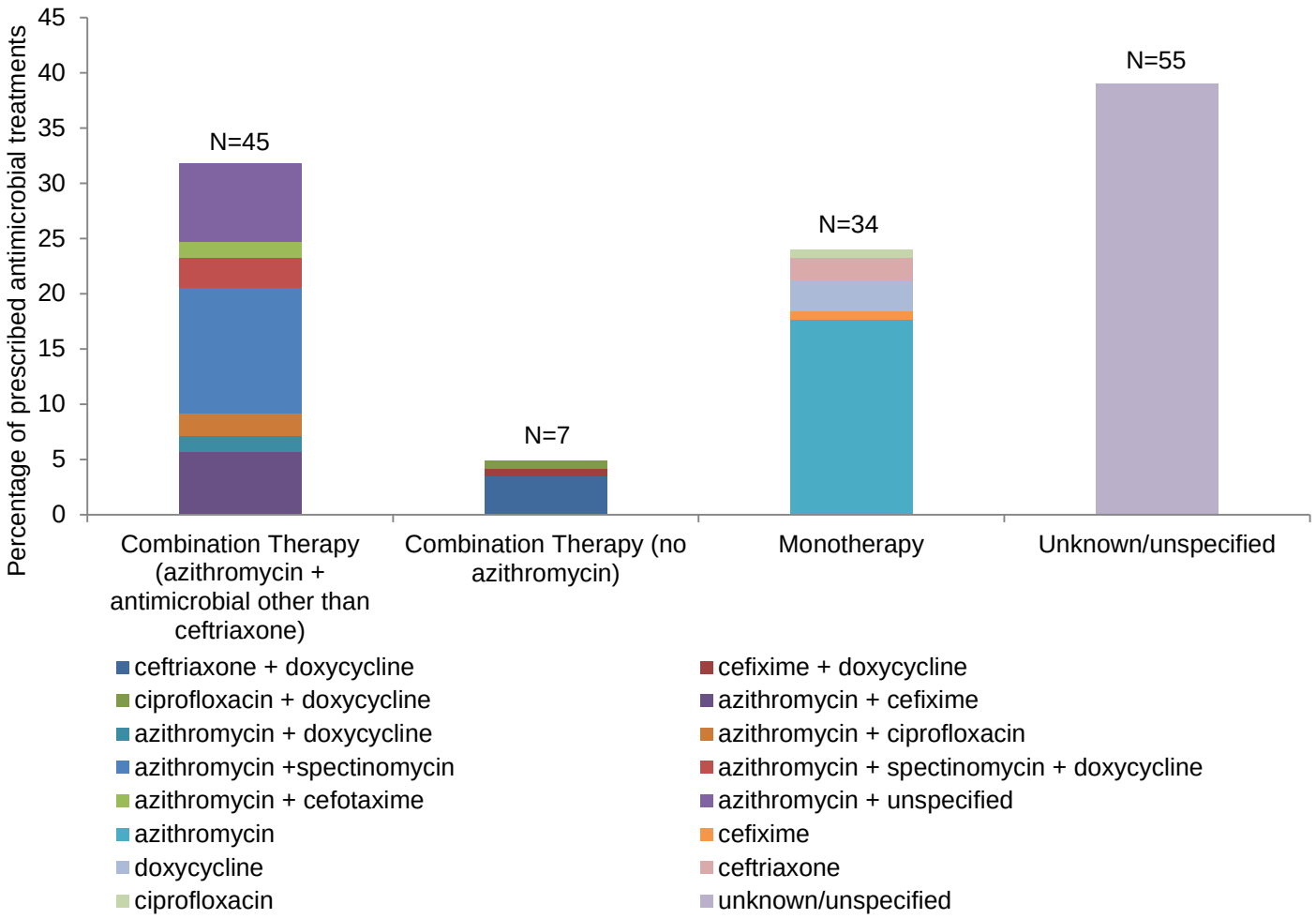


Figure 18: Antimicrobial prescriptions of non-recommended treatments (N=141), 2015



6. Discussion

6.1 Resistance to first-line therapies

The first globally documented treatment failure to dual antimicrobial therapy using ceftriaxone and azithromycin was reported in England in 2015. Although this patient was infected abroad and no further cases were identified in the UK, this case demonstrates that dual therapy treatment failure is possible. Sensitive surveillance and timely clinical action is essential to identify and delay the spread of *N. gonorrhoeae* resistant to dual therapy across the UK.

Of immediate concern, is the high prevalence of azithromycin resistant *N. gonorrhoeae,* particularly high-level resistance (≥256mg/L MIC). The outbreak of high-level azithromycin resistant *N. gonorrhoeae* continues to spread both geographically across England and between heterosexual and MSM sexual networks. The majority of cases linked to the Leeds outbreak (clade 1) share a recent common ancestor, but there are two other linked clades that share a more distant common ancestor (ie outside the timeframe of the outbreak investigation) with the clade 1 samples. Two of the three clades include heterosexuals and MSM. Further results from WGS analysis are awaited on recent cases. If this continues, high-level azithromycin resistance could undermine the rationale of front-line dual treatment as azithromycin is very unlikely to remain effective against any of these isolates that also develops ceftriaxone resistance.

In the sentinel surveillance system, the prevalence of azithromycin resistant *N. gonorrhoeae* is the highest it has ever been in England and Wales at nearly 10% of all cases, which is well above the WHO recommended resistance threshold of 5%. However, it is important to note the MIC distribution of the sample, as the great majority (91%) of the azithromycin resistant isolates had an azithromycin MIC of 1 mg/L, which is just above the breakpoint for resistance (0.5 mg/L). It is difficult to determine how much of this increase is due to a true increase in azithromycin resistance, and how much is due to the change in the medium used for antimicrobial susceptibility testing, which may have increased the azithromycin MICs by up to two dilutions. In addition, there is insufficient evidence to determine the likelihood of azithromycin treatment being effective (as part of dual therapy) against isolates with azithromycin MICs >0.5 mg/L, particularly as this susceptibility breakpoint is based on a 2 g single dose in monotherapy[2]. In contrast, in the primary diagnostic laboratories, *N. gonorrhoeae* azithromycin resistance prevalence was much lower (2%) but these laboratories generally use the disc diffusion method for antimicrobial susceptibility testing which is not directly comparable to susceptibility methods that result in an MIC, such as agar dilution or Etests.

To prevent further dissemination of high-level azithromycin resistant gonorrhoea, PHE is leading a national incident response with the support of PHE centres and health protection teams to enhance data collection, raise awareness among local communities affected and sexual health clinics to ensure all cases are reported to PHE, thoroughly investigated and treated according to national guidelines. A National Resistance Alert was issued to all microbiologists in October 2015 (available here) to ensure that all gonococcal isolates are tested for azithromycin and ceftriaxone susceptibility, and that all resistant isolates (MIC >0.5 mg/L for azithromycin, and >0.125 mg/L for ceftriaxone) are referred to PHE's national reference laboratory for confirmation and follow-up.

The sentinel surveillance system within GRASP provides an invaluable and unique resource to explore associations between AMR and patient characteristics. The key population groups for detecting emerging AMR belong to distinct sexual networks where emergence of AMR may proceed rapidly and result in treatment failures before disseminating into (and therefore becoming detectable in) the broader population. MSM are the most important sub-group for gonococcal AMR trend analyses, as this group has the highest number of gonorrhoea diagnoses. Gonococcal isolates from MSM continue to be less susceptible to first-line therapy with ceftriaxone and azithromycin than isolates from heterosexual men and women. While the highest rates of gonorrhoea in men occur in older age-groups, young heterosexuals aged 15 and 24 years are also an important risk group, as STI diagnoses are highest amongst this group and the outbreak of high-level azithromycin resistant *N. gonorrhoeae* was first identified in this population. The sentinel surveillance system in GRASP found AMR was equally distributed across age groups.

6.2 Prescribing of first-line therapies

Good antimicrobial stewardship is essential for retaining gonorrhoea as a treatable infection. Overall, prescribing in GUM clinics complies with the national treatment guideline and the proportion of patients treated appropriately has increased year on year. However, 25 patients identified by the sentinel surveillance system received azithromycin monotherapy and, of these, three were infected with an azithromycin resistant strain of *N. gonorrhoeae*. This is concerning, as these patients may have remained infected after treatment, which increases the likelihood of onward transmission of a resistant *N. gonorrhoeae*.

Action taken to promote the use of dual therapy for gonorrhoea, particularly for patients with a concurrent rectal chlamydial infection, has been successful. Recommended therapy for patients with concurrent rectal chlamydia is ceftriaxone and azithromycin for gonorrhoea, plus doxycycline for rectal chlamydia.[8] There is still concern regarding sub-optimal prescribing in some non-specialist settings such as general practice and through online pharmacies.[9,10,11] Sub-optimal prescribing increases the likelihood of treatment failure and raises the risk of complications and onward transmission of

resistant infections. Practitioners are urged to comply with national treatment guidelines and be alert to changes in antimicrobials recommended for front-line use.

6.3 Worldwide context

Antimicrobial susceptibility testing programmes are now common in many regions of the world. There is a global trend of low ceftriaxone and cefixime resistance as presented by the 2014 data from Europe[13], the USA[14], Canada[15] and Australia[16] (7.7 Table 7). More than 97% of circulating *N. gonorrhoeae* isolates were susceptible to first-line therapy, ceftriaxone, using the 0.064 mg/L breakpoint, and very few isolates with an MIC of >0.12 mg/L were detected in 2014. The highest levels of cefixime resistance were detected in the European region, which was still low at 2%. As in England and Wales in 2015, azithromycin resistance levels increased globally in 2014 with >7% of isolates displaying azithromycin resistance in the USA and Europe. However, it should be noted that the level of azithromycin resistance in Canada using the breakpoint of >0.5 mg/L is unknown, and in Australia azithromycin resistance ranged from 0% to 9% across the Australian states or territories. Ciprofloxacin resistance remains very high globally.

6.4. Conclusion and key recommendations

Effective gonorrhoea treatment remains threatened by antimicrobial resistance. Resistant to azithromycin is of particular concern given the ongoing outbreak of high-level azithromycin resistant *N. gonorrhoeae* in England and the increase in azithromycin resistance identified by the sentinel surveillance system above the WHO recommended threshold. Although there has been an improvement in antimicrobial susceptibility testing of clinical samples within primary diagnostic laboratories, some areas are still testing less than half of the culture samples they receive. All primary diagnostic laboratories should test gonococcal isolates for susceptibility to first-line antimicrobials and refer suspected azithromycin- and/or ceftriaxone-resistant isolates to the PHE reference laboratory for confirmation and follow-up. Practitioners should ensure all patients with gonorrhoea are treated and managed according to national guidelines and be alert to changes in antimicrobials recommended for front-line use. Sexual health services should report possible cases of treatment failure to PHE via the online HIV and STI web-portal. Anyone having sex with new or casual sexual partners should be advised to use condoms consistently and correctly and test regularly for sexually transmitted infections.

7. Appendix

7.1 Sentinel surveillance methodology

Isolates from consecutive patients attending 25 GUM clinics (23 in England, two in Wales) between July and September 2015 were submitted by local laboratories to PHE's national reference laboratory for antimicrobial susceptibility testing. Where more than one isolate was collected from a patient, the following hierarchy of isolates for collection was applied: 1. male rectal, 2. male urethral, 3. female cervical, 4. any other site. Demographic, clinical and behavioural data for each patient were extracted from the national genitourinary medicine clinic dataset (GUMCADv2).[1] Additional behavioural and antibiotic prescribing data were submitted by GUM clinics electronically. Data for patients from the clinic in Wales were collected using paper-based forms. The antimicrobial susceptibility and clinical data were linked using the patient's unique identifier number, the unique clinic code and the patient's date of attendance. Isolates that were retrieved, tested for antimicrobial susceptibility and matched to clinical data were included in the final sentinel surveillance system.

7.2 SGSS data extraction methodology

Data on N. gonorrhoeae isolates tested for antimicrobial susceptibility in 2014-Q2 2016 were extracted from SGSS by a member of the SGSS Information Management team. There are two sub-repositories within SGSS that hold data on antimicrobial susceptibility: the communicable disease reporting (CDR) repository and the antimicrobial resistance (AMR) repository. By extracting all available data from both the CDR and AMR repositories, the dataset included duplicate records within and across repositories (ie the same record is found in both the CDR and AMR repository). Furthermore, for a single episode of infection, defined as having a susceptibility test no more than once within a six week period, multiple specimens were tested. The data were restricted to one isolate per episode of infection (six week period). If more than one isolate was collected from a patient, where resistance profiles differed, the resistant code was preferentially kept for the entire episode and only one specimen site was analysed per six week episode period. Isolates with an ocular specimen site were removed prior to restricting isolates to one episode per six week period.

In primary diagnostic labs, ceftriaxone and cefixime susceptibility is often inferred by testing cefuroxime as a proxy cephalosporin. If a gonococcus is found susceptible to cefuroxime it may be reported susceptible to ceftriaxone or cefixime. However, if the isolate is resistant to cefuroxime, resistance to ceftriaxone or cefixime cannot be inferred and labs should perform an E-test to determine the ceftriaxone or cefixime MIC. Hence, when ceftriaxone or cefixime susceptibility results were missing and cefuroxime

was reported susceptible, the ceftriaxone or cefixime result was recorded as susceptible. However, when ceftriaxone or cefixime susceptibility results were missing and cefuroxime was reported resistant, the ceftriaxone or cefixime result was recorded as missing since there was no way to verify whether a ceftriaxone resistance confirmatory E-test was done or the result.

7.3 DST medium

The testing protocol for the sentinel surveillance system includes the use of Oxoid DST for MIC testing. This methodology provided satisfactory growth to read MIC results for over 90% of the isolates submitted to the sentinel surveillance system for ten years. However, it was noted that some clinical isolates submitted in later years did not grow satisfactorily. A retrospective analysis of results from 2013 and 2014 indicated that an increasing percentage of isolates successfully retrieved from storage then failed to produce the satisfactory growth on Oxoid DST media needed to perform MIC determination. A review of the 2014 Internal Quality Controls (IQC), performed with reference strains, revealed that there were a few occasions when the MICs of IQCs were lower than expected, particularly for azithromycin. This indicates that the media does not provide consistent optimal growth conditions or the pH of the media is not always optimal for all the antimicrobials tested.

Subsequent testing different batches of media supplements produced satisfactory results on IQC strains, but did not improve efficiency of MIC testing for the more fastidious isolates. The manufacturer's technical support team assert that no formula preparation changes had been introduced, though, like all media, it contains biological peptones and agars that may subtly vary over time. It was concluded that a subset of *N. gonorrhoeae* strains seemed to have higher physiological demands, and were fastidious growers. Evaluation of a DST agar from a different manufacturer (HiMedia) followed.

New DST Media Validation Methodology

An initial comparison was carried out using a selection of isolates with known MIC results from the 2015, 2014 and 2012 collections. Reliably good growth was obtained on the new HiMedia DST for all strains and including those that did not grow on the 'traditional' Oxoid DST during 2014.

Comparison of MICs determined on DST agars from our traditional (Oxoid) and new supplier (HiMedia) indicated differences for some antimicrobials (as outlined in the main body of this report), most notably affecting azithromycin and tetracycline; MICs of tetracycline decreased, whereas the MICs of azithromycin increased when determined on the new HiMedia DST. For this reason, MICs for the 2015 collection are not directly comparable to those from previous years, and trends must be interpreted with caution.

After changing the DST supplier, only 37 isolates from the 2015 collection were unable to grow on the new DST. The newly sourced HiMedia DST seemingly provided better pH and physiological conditions for growth of fastidious strains of *N. gonorrhoeae* in the sentinel surveillance system, and will be used for MIC testing of future collections.

7.4 Table 4: Characteristics of patients in the sentinel surveillance system compared with all patients diagnosed with gonorrhoea in the same GUM clinics and all gonorrhoea diagnoses made in England, 2015

Characteristics	Sentinel surveillance^ (col %)	All diagnoses in English sentinel surveillance clinics (col %)	All gonorrhoea diagnoses in English GUM clinics (col %)
Total (N)	**1,699**	**5,140**	**39,696**
Gender/Male Sexual Orientation			
Women	10.5	13.4	21.3
Heterosexual Men	14.9	13.1	21.3
MSM*	72.2	72.1	55.2
Not reported	2.4	1.4	3.1
Ethnicity			
White	72.8	71.8	72.6
Black Caribbean	5.5	4.9	4.7
Black African	3.1	2.8	3.5
Black Other	1.2	1.8	2.0
Asian	3.6	3.7	4.1
Other ethnic group (including Chinese)	3.2	4.0	3.3
Mixed ethnic group	7.5	6.7	5.6
Not reported	3.1	4.2	4.3
Age Group (years)			
13-19	6.2	6.1	10.7
20-24	20.3	19.8	24.5
25-34	44.1	42.8	38.0
35-44	19.8	20.5	17.0
>=45	9.6	10.7	9.6
Not reported	0.1	0.0	0.3
Symptoms			
Discharge and/or Dysuria	43.9	31.5	-
No Discharge and/or Dysuria	26.7	39.7	-
Not reported	29.5	28.9	-
Previously Diagnosed With Gonorrhoea			
Yes	28.7	30.5	23.9
No	65.9	69.0	76.1
Not reported	5.4	0.5	0.0
Concurrent STI**			
Syphilis	2.5	1.1	1.4
Chlamydia	19.5	18.6	20.0
Herpes	1.0	0.6	0.9
Warts	1.5	1.1	1.3
LGV	1.5	1.1	0.5
Hepatitis B	0.1	0.1	0.1
Hepatitis C	0.2	0.3	0.2
New HIV diagnoses	1.6	1.0	0.8
HIV Status			
Negative	37.1	37.0	62.2
Positive	18.4	17.9	11.7
Not reported	44.5	45.1	26.0
Multiple Site Infection			
Yes	34.3	25.1	7.5
Not reported	21.2	23.3	0.0
Total Partners (past 3 months)			
0-1	19.4	18.4	-
2-5	32.9	30.7	-
6-10	6.2	7.0	-
11+	4.9	5.1	-
Not reported	36.5	38.9	-
Sex Abroad			
Yes	4.8	4.8	-
No	58.7	56.3	-
Not reported	36.5	38.9	-
Geographical Location			
London	62.4	62.4	47.7
Outside London	36.8	30.0	49.6
Not reported	0.8	7.6	2.7

Total (N) is the number of patients or isolates included in the data for analysis
^ Sentinel surveillance sample includes gonorrhoea diagnoses for which an isolate was tested for antimicrobial susceptibility
* Men who have sex with men
** Numerator: patients in sentinel surveillance 2015 dataset with specified concurrent STI, Denominator: all patients in sentinel surveillance 2015 dataset. Not all patients are tested for each STI.
Not all variables are not routinely collected through GUMCAD

7.5 Table 5: Characteristics of patients in the sentinel surveillance system, by gender and sexual orientation, 2015

	Women	Heterosexual Men	MSM*	Not reported	Total
Total (N)	**179**	**253**	**1,226**	**41**	**1,699**
Patient residence			**%**		
London	29.6	42.3	72.0	41.5	62.4
Outside London	68.2	55.3	27.7	58.4	36.8
Not reported	2.2	2.4	0.2	0.0	0.8
Ethnicity					
White	59.2	50.2	80.1	52.7	72.8
Black Caribbean	7.8	17.4	2.4	17.1	5.5
Black African	5.0	6.3	2.1	2.4	3.1
Black Other	2.8	2.0	0.7	2.4	1.2
Asian	2.2	3.9	3.7	4.9	3.6
Other ethnic group (including Chinese)	2.2	4.7	3.1	1.0	3.2
Mixed ethnic group	12.3	10.3	6.2	7.3	7.5
Not reported	8.4	4.7	1.8	9.8	3.1
Age Group (years)					
13-19	26.3	9.9	2.3	12.2	6.2
20-24	32.4	26.5	17.3	19.5	20.3
25-34	31.3	39.1	47.2	36.6	44.1
35-44	7.8	14.6	22.4	24.4	19.8
≥45	2.2	9.9	10.8	4.9	9.6
Not reported	0.0	0.0	0.0	2.4	0.1
Symptoms					
Discharge and/or Dysuria	44.7	80.6	37.0	19.5	43.9
No Discharge and/or Dysuria	33.0	11.9	29.2	15.6	26.7
Not reported	22.3	7.5	33.9	65.9	29.5
Previously Diagnosed With Gonorrhoea					
Yes	13.4	9.5	35.7	7.3	28.7
No	78.2	87.8	60.5	39.0	65.9
Not reported	8.4	2.8	3.9	53.7	5.4
Concurrent STI**					
Syphilis	0.6	1.2	3.0	2.4	2.5
Chlamydia	31.8	24.5	16.8	17.1	19.5
Herpes	1.7	1.2	1.0	2.4	1.0
Warts	0.7	4.0	1.1	0.0	1.5
LGV	0.0	0.4	2.0	0.0	1.5
Hepatitis B	0.0	0.8	0.0	0.0	0.1
Hepatitis C	0.0	0.3	0.0	0.0	0.2
New HIV diagnoses	0.0	2.3	0.0	0.0	1.6
Site of Infection***					
Genital	86.0	87.0	37.0	24.4	49.3
Rectal	9.9	49.7	16.2	19.5	39.5
Throat	37.9	27.4	10.7	12.2	32.1
Other (not specified)	3.3	9.9	2.1	0.0	3.3
Not reported	11.7	6.7	24.2	61.0	21.2
Multiple site of infection	15.8	38.8	34.6	12.2	34.3
HIV Status					
Positive	0.6	2.4	24.4	17.1	18.4
Negative	54.8	31.7	56.1	2.4	37.1
Not reported/Unknown	44.7	41.5	43.9	80.5	44.5
Total Partners (past 3 months)					
0-1	41.3	28.5	14.5	12.2	19.4
2-5	31.8	46.2	31.0	12.2	32.9
6-10	0.0	3.2	8.0	0.0	6.2
11+	2.2	1.6	6.1	2.4	4.9
Not reported	24.6	20.5	40.4	73.2	36.5
Sex Abroad					
Yes	7.5	4	7.3	0	4.8
No	68.2	71.9	55.6	26.8	58.7
Not reported	24.6	20.5	40.4	73.2	36.5

** Men who have sex with men
** Numerator: patients in sentinel surveillance 2015 dataset with specified concurrent STI, Denominator: all patients in sentinel surveillance 2015 dataset. Not all patients are tested for each STI.
*** Numerator: patients in sentinel surveillance 2015 dataset infected at site specified, Denominator: all patients in sentinel surveillance 2015 dataset. Not all patients are tested for gonorrhoea at each site. Data reported are for patients being infected with at least the specified site, not exclusively this site.

7.6 Table 6: Antimicrobial resistance (MICs) by patient characteristic, sentinel surveillance system, 2015

Characteristics	Total N†	Azithromycin ≥1 mg/L row %	Cefixime ≥0.125 mg/L row %	Ciprofloxacin ≥1 mg/L row %	Penicillin ≥2 mg/L row %	Tetracycline ≥1 mg/L row %
Age Group	1,699	9.8	1.1	39.1	24.1	39.4
13-24	450	11.1	0.7	34.2	23.6	39.6
25-34	749	9.5	0.9	42.5	23.0	38.6
35-44	336	9.8	1.5	38.7	24.7	39.0
>=45	163	7.4	1.8	38.0	29.5	43.6
Sexual Orientation						
Heterosexual Men	253	9.9	2.0	38.7	22.9	37.5
MSM	1,226	10.3	0.8	42.7	25.4	41.6
Women	179	6.7	1.7	18.4	15.1	27.4
Ethnicity						
White	1,237	10.8	1.1	40.1	24.8	40.3
Black Caribbean	94	6.4	0.0	28.7	17.0	31.9
Black African	52	1.9	0.0	46.2	28.9	40.4
Black Other	20	5.0	5.0	20.0	10.0	40.0
Asian	61	8.2	0.0	44.3	23.0	44.3
Other ethnic group (including Chinese)	55	9.1	1.8	41.8	29.1	45.4
Mixed ethnic group	127	7.1	0.8	36.2	20.5	33.9
Total Partners (past 3 months)						
0-1	329	13.1	1.5	33.4	22.2	33.7
2-5	559	7.7	0.7	40.4	26.8	40.8
6+	190	10.0	0.5	39.5	19.5	41.0
Sex Abroad						
No	997	9.7	0.8	36.9	23.7	37.9
Yes	81	9.9	2.5	53.1	29.6	48.1
Symptoms						
No	453	10.6	0.9	36.9	20.8	39.7
Yes	745	9.7	1.2	39.6	26.3	38.5
Previously diagnosed with gonorrhoea						
No	1,120	9.2	0.9	39.0	24.6	39.1
Yes	487	10.5	1.4	42.1	22.8	41.1
HIV Status						
Negative	630	8.9	1.3	38.7	25.2	37.6
Positive	313	9.0	0.6	40.3	26.8	41.2
Patient residence						
Outside London	626	10.9	0.8	31.5	25.4	37.7
London	1,060	9.2	1.2	44.1	23.5	40.6

†N is the number of patients for which information was reported for the particular characteristic

7.7 Table 7: Percentage of gonococcal isolates that were resistant to selected antimicrobials from Europe, Canada, Australia and the USA surveillance programmes

	Cefixime (MIC >0.12mg/L)	Ceftriaxone (>0.064mg/L)	Azithromycin (MIC >0.5 mg/L)	Ciprofloxacin (MIC >0.5 mg/L)
GRASP (2015)	0.4%	0%	9.8%	39.1%
GRASP (2014)[12]	0.1%	0.0%	1.0%	37.2%
Euro-GASP (2014)[13]	2%	2.8%	7.8%	50.7%
USA GISP (2014)[14]	0.8%	0.1%	7.1%	19.2%
Canada (2014)[15]	1.1%	2.7%	3.3%*	No data
Australia AGSP (2014)[16]	No data	0.6%	2.5%	36%

*Resistance MIC >0.1 mg/L

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