UK Health Security Agency

Antimicrobial resistance in *Neisseria gonorrhoeae* in England and Wales

Key findings from the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP 2021)

Data to June 2022

Contents

Foreword

The Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) is run by the UK Health Security Agency (UKHSA), formerly known as Public Health England (PHE). The UKHSA is an executive agency sponsored by the Department of Health and Social Care and became operational on 1 October 2021.

Key points

Between 2020 and 2021 *Neisseria gonorrhoeae* isolates collected through GRASP showed:

- a decrease in reduced susceptibility (minimum inhibitory concentration (MIC) >0.03 mg/L) to ceftriaxone, the current first-line therapy, from 1.4% in 2020 to 0.07% in 2021
- the modal ceftriaxone MIC increased to 0.015 mg/L after having remained stable at 0.008 mg/L since 2018
- the modal ceftriaxone MIC for isolates from gay, bisexual, and other men who have sex with men (GBMSM) remained higher (0.015 mg/L) than those from both women and heterosexual men (0.008 mg/L)
- there were 11 cases of ceftriaxone resistance (MIC >0.125 mg/L) confirmed by the UKHSA Antimicrobial Resistance in Sexually Transmitted Infections (AMRSTI) national reference laboratory on direct referral from January 2021 to June 2022 compared to no cases in 2020 and 3 cases in 2019
- azithromycin resistance (MIC >0.5 mg/L) increased from 8.7% to 15.2%
- cefixime resistance (MIC >0.125 mg/L) decreased from 0.6% to 0.3%
- ciprofloxacin resistance (MIC >0.06 mg/L) increased from 44.3% to 46.9%
- penicillin resistance (MIC >1.0 mg/L) increased from 9.6% to 14.1%
- tetracycline resistance (MIC >1.0 mg/L) increased from 65.1% to 75.2%

The continual decreases in reduced susceptibility (MIC >0.03 mg/L) to ceftriaxone and resistance to cefixime between 2019 and 2021 represent a reversal in trends relative to 2016 to 2018. The increase in azithromycin resistance (MIC >0.5 mg/L) was driven by an increase in isolates with MICs at 1.0 mg/L. However, the proportion of isolates with azithromycin MIC >1.0 mg/L remained stable at 4.2% in 2020 and 5.0% in 2021. Penicillin resistance has remained stable with some fluctuation over recent years. Tetracycline and ciprofloxacin resistance have continued to increase rapidly since 2016. As in previous years, no spectinomycin resistance (MIC >64 mg/L) was detected in 2021 and the modal gentamicin MIC remained low (4 mg/L).

Prescribing data demonstrated excellent adherence to the UK guideline for managing infection with *N. gonorrhoeae*, with 97.1% of individuals receiving the recommended first-line of ceftriaxone 1g intramuscular (IM) monotherapy in 2021 (1).

The effectiveness of first-line treatment for gonorrhoea continues to be threatened by the development of antimicrobial resistance, particularly in light of the recent reports of mainly travel associated ceftriaxone resistance in England. The ongoing decline in reduced ceftriaxone susceptibility and cefixime resistance are encouraging developments. However, increases in the ceftriaxone modal MIC and the number of referred resistant isolates to AMRSTI national reference laboratory show that increases in susceptibility are not universal and require continual monitoring.

Recommendations

All primary diagnostic laboratories should test gonococcal isolates for susceptibility to ceftriaxone and refer suspected resistant isolates (MIC >0.125 mg/L, European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoint) to the UKHSA AMRSTI national reference laboratory for confirmatory testing and follow-up. Primary diagnostic laboratories are encouraged to report test results and antimicrobial resistance data to the Second-Generation Surveillance System (SGSS) to facilitate real-time monitoring of trends in *N. gonorrhoeae* diagnoses and antimicrobial resistance in England.

Sexual health practitioners should ensure that all individuals diagnosed with gonorrhoea are treated and managed according to national guidelines, including the need to perform a test-of-cure, and should be alert to changes in recommended first-line therapies. Possible cases of treatment failure should be reported to the UKHSA via the HIV and STI Data Exchange.

Consistent and correct use of condoms can significantly reduce the risk of gonorrhoea and other sexually transmitted infections (STIs). Regular testing for HIV and STIs is also essential for good sexual health among the sexually active population. Similarly, open access to rapid treatment and partner notification at sexual health services is vital to reducing the risk of complications and further transmission.

Anyone having condomless sex with new or casual partners should have an STI screen annually, including an HIV test (2). In addition:

- women and other people with a womb or ovaries under the age of 25 who are sexually active should have a chlamydia test annually and on change of sexual partner
- GBMSM should have an annual test for HIV and STIs or every 3 months if having condomless sex with new or casual partners

Introduction

Gonorrhoea, caused by the bacterium *Neisseria gonorrhoeae*, is the second-most commonly diagnosed STI in England. If untreated, gonorrhoea can lead to complications, such as chronic pelvic pain, pelvic inflammatory disease, ectopic pregnancy and infertility.

Gonorrhoea diagnoses in England increased by 164% between 2012 and 2019 (from 26,840 to 70,908) (3). A 29% reduction was observed in 2020 (50,233), which coincided with a 25% decrease in sexual heath screens in 2020 caused by the disruption in service provision during the coronavirus (COVID-19) pandemic. Although the number of sexual health screens was closer to pre-pandemic levels in 2021 (an 11% decrease in 2021 relative to 2019), the number of gonorrhoea diagnoses in 2021 (51,074) remained similar to the previous year. This reduced positivity may reflect changes in behaviour leading to a reduction in transmission overall. Nevertheless, gonorrhoea remains concentrated among specific population groups; GBMSM and people of Black Caribbean ethnicity continue to experience disproportionately high rates of gonorrhoea diagnoses (3).

Ceftriaxone is an extended-spectrum cephalosporin (ESC) that is currently recommended in the UK as the first-line therapy for gonorrhoea (1g intramuscular (IM) monotherapy) (1). Where antimicrobial susceptibility is known prior to treatment, ciprofloxacin, a fluoroquinolone, is recommended as an alternative first-line therapy (500 mg orally as a single dose). These antibiotics were recommended as first-line treatments in January 2019 in the UK by the British Association for Sexual Health and HIV (BASHH) in an effort to delay the emergence of antimicrobial resistance (AMR). The updated guidance represented a major change from the 2011 guidelines, which advised using dual therapy with ceftriaxone 500 mg IM and azithromycin 1g orally as first-line treatment. ESCs are among few remaining antimicrobials that can be effectively used as first-line monotherapy for gonorrhoea.

Ongoing monitoring of AMR, comprising the culture of isolates, test-of-cure and the maintenance of comprehensive and enhanced surveillance is vital for the detection of emerging trends and to ensure that first-line treatments for gonorrhoea remain effective. Ineffective treatment facilitates onward transmission and the development of sequelae.

This report presents trends in gonococcal susceptibility to therapeutically relevant antimicrobials and explores the recent epidemiology of *N. gonorrhoeae* AMR in England and Wales. The Gonococcal Resistance to Antimicrobial Surveillance Programme (GRASP) includes a suite of surveillance systems to detect and monitor AMR in *N. gonorrhoeae* and to record potential treatment failures; these include the GRASP sentinel surveillance system, analysis of real-time laboratory data and reports of suspected treatment failure.

The GRASP sentinel surveillance system

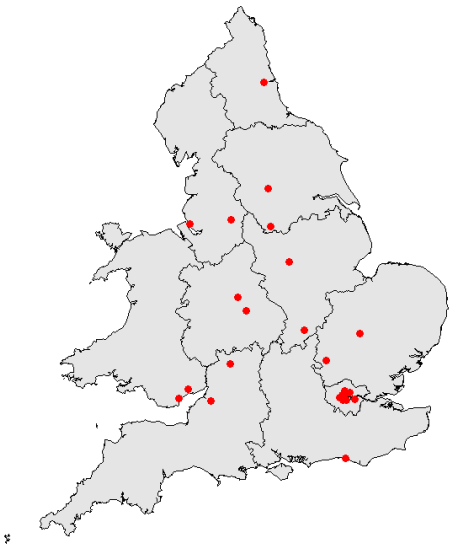
GRASP sentinel surveillance data is obtained annually from a network of sexual health services (SHSs) across England and Wales and their associated laboratories. In 2021, 26 SHSs (24 in England, 2 in Wales) and 20 laboratories participated in the programme. The geographical distribution of the 26 participating SHSs is shown in Figure 1.

Participating laboratories are requested to collect consecutive *N. gonorrhoeae* isolates over a 3-month period (usually between July to September). All collected *N. gonorrhoeae* isolates are sent to the UKHSA AMRSTI national reference laboratory for antimicrobial susceptibility testing. Antimicrobial susceptibility results are linked securely to pseudonymised GUMCAD STI Surveillance System data to obtain demographic and clinical details. The GUMCAD STI Surveillance System is a disaggregated, patient-level data set of all STI tests and diagnoses at SHSs in England (3). In addition, enhanced demographic, clinical and behavioural data is submitted by participating SHSs to supplement GUMCAD data. Two statistical sample tests of proportion and Chi-square tests for trend are used to define recent and longitudinal antimicrobial susceptibility trends, respectively. All analyses are performed with Stata V.15.1 (StataCorp LP, College Station, Texas, USA).

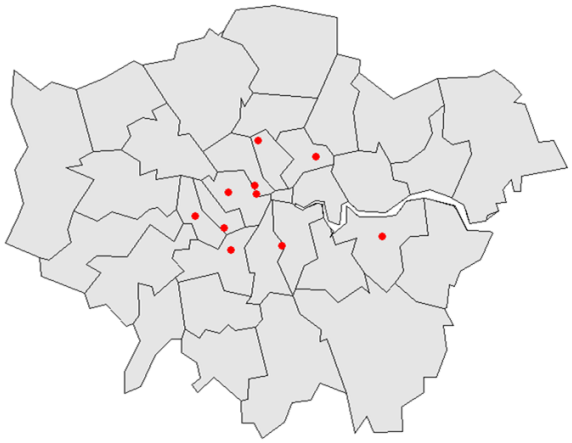
Full details on the data sets and methodology used for the GRASP sentinel surveillance system are available online (4).

Figure 1. Map showing 26 sentinel sexual health services participating in GRASP 2021 across a. England and Wales and b. London (shown at larger scale)

a. England and Wales



b. London



Real-time laboratory data

Data from the GRASP sentinel surveillance system is supplemented year-round by real-time laboratory data, reported through the Second-Generation Surveillance System (SGSS) and by the UKHSA AMRSTI national reference laboratory (Appendix 1).

Second-Generation Surveillance System

SGSS is an application that stores and manages laboratory data and notifications, capturing routine surveillance data on infectious diseases and antimicrobial resistance. Positive test results and antimicrobial resistance data is submitted on a voluntary basis from 147 laboratories who receive specimens from a range of healthcare providers, including SHSs, general practitioners and hospitals across England, Wales and Northern Ireland (5). Within GRASP, SGSS data is used to monitor real-time trends in *N. gonorrhoeae* diagnoses and antimicrobial resistance in England.

Antimicrobial Resistance in STIs national reference laboratory

Laboratories are asked to refer *N. gonorrhoeae* isolates with suspected ceftriaxone resistance (MIC >0.125 mg/L, EUCAST breakpoint) to the UKHSA AMRSTI national reference laboratory for antimicrobial susceptibility testing and confirmation. The UKHSA AMRSTI national reference laboratory primarily acts as a reference and diagnostic service for laboratories in England, but also receives samples from Wales and Northern Ireland.

Treatment failures

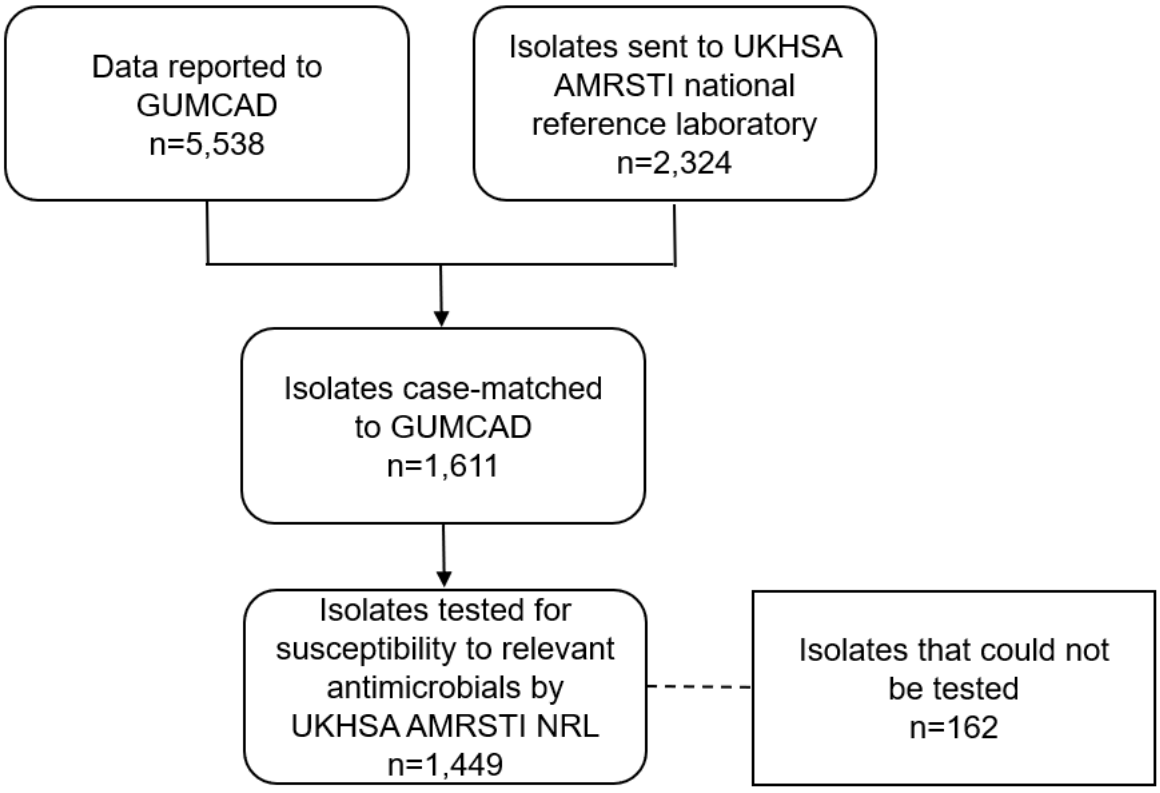
Information on suspected treatment failures is reported to UKHSA via the HIV and STI Data Exchange.

Sentinel surveillance sample

Sampling frame

The 2021 GRASP collection took place between 1 July to 30 September 2021 during which a total of 5,538 gonorrhoea diagnoses were reported to GUMCAD by the 24 SHSs in England participating in GRASP, as shown in Figure 2. Over the same period, 2,324 *N. gonorrhoeae* isolates were sent to the UKHSA AMRSTI national reference laboratory for antimicrobial susceptibility testing from these clinics. Isolates were included in analyses if they, a) could be case-matched to a GRASP participating SHS within the GUMCAD STI surveillance system (n=1,611), and b) had been successfully tested for susceptibility to 8 therapeutically relevant antimicrobials by the UKHSA AMRSTI national reference laboratory (n=1,449). In 2021, 62.3% (1,449 out of 2,324) of isolates submitted to the UKHSA AMRSTI national reference laboratory were included in the GRASP analysis compared to 65.5% (1,534 out of 2,341) in 2020.

Figure 2. Sentinel surveillance sampling frame flowchart in GRASP 2021



Where more than one isolate was collected from an individual, a hierarchy for testing was applied as shown in Table 1. Of note, the 2021 GRASP collection was the first time that pharyngeal isolates have been prioritised ahead of all other sites due to concerns that resistance is most likely to emerge in this site (4). In 2020 and prior years, pharyngeal isolates

had the same prioritisation as 'any other site' and were thus only tested if no other specimen sites (1 to 4) were available. Among the 1,449 tested and case-matched isolates, the anatomical site of specimen collection was most commonly urethral (43.5%), followed by rectal (24.2%) and pharyngeal (20.3%). Prior to the new prioritisation of pharyngeal isolates, pharyngeal isolates constituted only 7.7% of those included in the 2020 GRASP analysis. Cervical isolates accounted for only 9.5% of isolates included in the 2021 analysis, compared to 14.1% in 2020.

Table 1: Anatomical site of specimen collection hierarchy and percentages by year of GRASP collection, 2020 to 2021

	Percentage of all isolates within respective GRASP collections	
Site of specimen collection	**2020**	**2021**
1. Pharyngeal	7.7%	20.3%
2. Male rectal	27.1%	24.2%
3. Male urethral	47.0%	43.5%
4. Female cervical	14.1%	9.5%
5. Any other site	4.2%	2.5%

Sentinel surveillance sample

Among 1,449 individuals with a *N. gonorrhoeae* isolate included in the sentinel surveillance sample, 1,249 (86.2%) were male, of whom 71.6% (894 out of 1,249) were GBMSM (Table 2). Most individuals were White (52.7%), and the modal age group was 25 to 34 years (41.4%), with age ranging from 15 to 82 years old across all those in the sample. Just over half (54.9%) were resident in London.

Among all individuals, 12.1% were living with HIV, and 94.9% (166 out of 175) of these were GBMSM. Over a quarter (29.3%) had been diagnosed with gonorrhoea previously and 21.2% were diagnosed with chlamydia at the time of their gonorrhoea diagnosis. Individuals most commonly reported having sex with 2 to 5 sexual partners in the 3 months prior to their gonorrhoea diagnosis, with 1.8% of all individuals reporting having had a sexual partner abroad (outside the UK) in the same time interval. However, information on the number of sexual partners was not reported for 32.6% of individuals.

Just over half (54.4%) of individuals were reported to have received a test-of-cure, compared to 44.1% in 2020, however this was similar to previous years (ranging from 50.1% to 62.2% from 2015 to 2019).

When GRASP SHSs were compared to all individuals diagnosed with gonorrhoea nationally at all SHSs over the same period (July to September 2021), women were under-represented in GRASP (13.8% vs 20.1%; p<0.001), while GBMSM were over-represented (61.7% vs 53.0%; p<0.001). There was no evidence supporting a difference in the proportion of heterosexual men included in the sentinel system relative to all SHSs (16.8% vs 15.8; p=0.32). London residents were over-represented in the sentinel system relative to all diagnoses nationally (54.9% vs 50.8%; p=0.003). These findings correspond with wider analysis of the representativeness of the GRASP sentinel system data between 2015 and 2018 (Appendix 3).

Table 2. Characteristics of individuals in the GRASP sentinel surveillance system, by gender and sexual orientation, 2021

	GBMSM	Hetero-sexual men	Women	Not reported†	Total
Number of individuals	894	243	200	112	1,449
	n (% of N)	**n (% of N)**	**n (% of N)**	**n (% of N)**	**n (% of N)**
Age group (years)					
15 to 19	17 (1.9%)	22 (9.1%)	32 (16.0%)	10 (8.9%)	81 (5.6%)
20 to 24	115 (12.9%)	47 (19.3%)	70 (35.0%)	23 (20.5%)	255 (17.6%)
25 to 34	387 (43.3%)	98 (40.3%)	65 (32.5%)	50 (44.6%)	600 (41.4%)
35 to 44	223 (24.9%)	53 (21.8%)	21 (10.5%)	18 (16.1%)	315 (21.7%)
45 or over	152 (17.0%)	23 (9.5%)	12 (6.0%)	11 (9.8%)	198 (13.7%)
Ethnicity					
White	584 (65.3%)	70 (28.8%)	90 (45.0%)	20 (17.9%)	764 (52.7%)
Black Caribbean	30 (3.4%)	24 (9.9%)	14 (7.0%)	24 (21.4%)	92 (6.3%)
Black African	23 (2.6%)	21 (8.6%)	10 (5.0%)	4 (3.6%)	58 (4.0%)
Black Other	6 (0.7%)	8 (3.3%)	3 (1.5%)	2 (1.8%)	19 (1.3%)
Asian	46 (5.1%)	16 (6.6%)	12 (6.0%)	7 (6.3%)	81 (5.6%)
Other Ethnic Group	28 (3.1%)	7 (2.9%)	3 (1.5%)	2 (1.8%)	40 (2.8%)
Mixed Ethnic Group	53 (5.9%)	17 (7.0%)	17 (8.5%)	5 (4.5%)	92 (6.3%)
Not Known	124 (13.9%)	80 (32.9%)	51 (25.5%)	48 (42.9%)	303 (20.9%)
Residence					
Outside London	264 (29.5%)	138 (56.8%)	149 (74.5%)	102 (91.1%)	653 (45.1%)
London	630 (70.5%)	105 (43.2%)	51 (25.5%)	10 (8.9%)	796 (54.9%)

	GBMSM	Hetero-sexual men	Women	Not reported†	Total
HIV status					
Negative	710 (79.4%)	207 (85.2%)	169 (84.5%)	107 (95.5%)	1193 (82.3%)
Positive	166 (18.6%)	3 (1.2%)	3 (1.5%)	3 (2.7%)	175 (12.1%)
Not reported	18 (2.0%)	33 (13.6%)	28 (14.0%)	2 (1.8%)	81 (5.6%)
Site of infection (a)					
Genital (male urethral; female cervical)	351 (39.3%)	234 (96.3%)	179 (89.5%)	102 (91.1%)	866 (59.8%)
Rectal	543 (60.7%)	4 (1.6%)	31 (15.5%)	10 (8.9%)	588 (40.6%)
Pharyngeal	479 (53.6%)	14 (5.8%)	65 (32.5%)	6 (5.4%)	564 (38.9%)
Other site	9 (1.0%)	13 (5.3%)	1 (0.5%)	0 (0.0%)	23 (1.6%)
Multiple sites‡	394 (44.1%)	22 (9.1%)	66 (33.0%)	6 (5.4%)	488 (33.7%)
Symptoms					
No	483 (54.0%)	24 (9.9%)	84 (42.0%)	22 (19.6%)	613 (42.3%)
Yes	411 (46.0%)	219 (90.1%)	115 (57.5%)	89 (79.5%)	834 (57.6%)
Not reported	0 (0.0%)	0 (0.0%)	1 (0.5%)	1 (0.9%)	2 (0.1%)
Any concurrent STI (b)					
Chlamydia	184 (20.6%)	46 (18.9%)	50 (25.0%)	27 (24.1%)	307 (21.2%)
Syphilis	4 (0.4%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	5 (0.3%)
Herpes	6 (0.7%)	1 (0.4%)	1 (0.5%)	0 (0.0%)	8 (0.6%)
Warts	2 (0.2%)	1 (0.4%)	0 (0.0%)	2 (1.8%)	5 (0.3%)
LGV	6 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (0.4%)
Previously diagnosed with gonorrhoea (ever)					
No	258 (28.9%)	119 (49.0%)	110 (55.0%)	34 (30.4%)	521 (36.0%)
Yes	348 (38.9%)	36 (14.8%)	21 (10.5%)	19 (17.0%)	424 (29.3%)
Not reported	288 (32.2%)	88 (36.2%)	69 (34.5%)	59 (52.7%)	504 (34.8%)
Total sexual partners (past 3 months)					
0 to 1	132 (14.8%)	100 (41.2%)	113 (56.5%)	72 (64.3%)	417 (28.8%)
2 to 5	286 (32.0%)	105 (43.2%)	54 (27.0%)	23 (20.5%)	468 (32.3%)
6 to 10	45 (5.0%)	7 (2.9%)	2 (1.0%)	3 (2.7%)	57 (3.9%)
11 or more	28 (3.1%)	1 (0.4%)	2 (1.0%)	3 (2.7%)	34 (2.3%)
Not reported	403 (45.1%)	30 (12.3%)	29 (14.5%)	11 (9.8%)	473 (32.6%)
Sex abroad (past 3 months)					
No	474 (53.0%)	209 (86.0%)	168 (84.0%)	99 (88.4%)	950 (65.6%)
Yes	17 (1.9%)	4 (1.6%)	3 (1.5%)	2 (1.8%)	26 (1.8%)
Not reported	403 (45.1%)	30 (12.3%)	29 (14.5%)	11 (9.8%)	473 (32.6%)
Test-of-cure					
No	274 (30.6%)	89 (36.6%)	44 (22.0%)	55 (49.1%)	462 (31.9%)
Yes	487 (54.5%)	121 (49.8%)	130 (65.0%)	50 (44.6%)	788 (54.4%)

	GBMSM	Hetero-sexual men	Women	Not reported†	Total
Not reported	133 (14.9%)	33 (13.6%)	26 (13.0%)	7 (6.3%)	199 (13.7%)

† 'Not reported' refers to instances where information was unknown or not stated.

Notes: (a) Numerator: individuals in GRASP 2021 data set infected at site specified (by gender and sexual orientation).

Denominator: all individuals in GRASP 2021 data set (by gender and sexual orientation). Not all individuals are tested for gonorrhoea at each site. Data reported is for individuals infected with at least the specified site, not exclusively this site.

Percentages do not add to 100% as individuals can be infected at more than one site. Also note that these numbers differ to isolates tested by specimen site as only one site is tested per individual.

‡ For individuals with multiple sites of infection, the isolate sample tested followed the hierarchy described above.

(b) Numerator: individuals in GRASP 2021 data set with any diagnosed concurrent STI (by gender and sexual orientation).

Denominator: all individuals in GRASP 2021 data set (by gender and sexual orientation). Not all individuals are tested for each STI.

Antimicrobial resistance

N. gonorrhoeae has developed resistance to all classes of antimicrobials recommended to treat the infection. Table 3 outlines the antimicrobial resistance definitions used in GRASP. Antimicrobial susceptibility results were interpreted using the EUCAST breakpoints (6). Figure 3 and Table 4 show trends in the percentage of gonococcal isolates collected through the GRASP sentinel surveillance system with resistance to selected antimicrobials since the inception of the programme (2000 to 2021) then with a focus on more recent trends (2017 to 2021), respectively. Appendix 2 shows resistance to selected antimicrobials by individuals' characteristics for GBMSM, heterosexual men, and women.

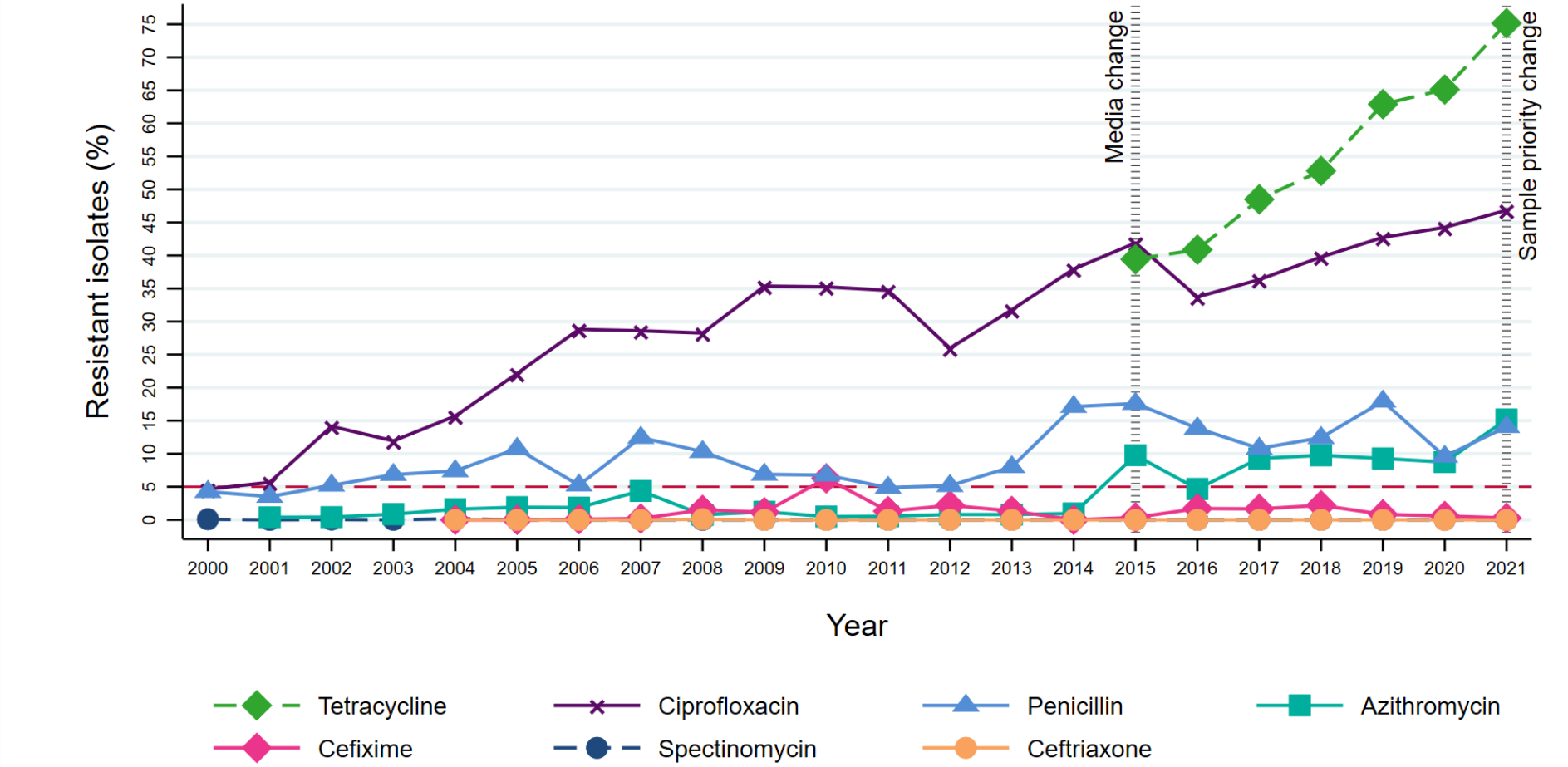
Table 3. Antimicrobial resistance definitions

Antimicrobial	Minimum inhibitory concentration breakpoint for resistance (mg/L)
Ceftriaxone	>0.125
Azithromycin (a)	>0.5
High-level azithromycin (b)	≥256.0
Cefixime	>0.125
Ciprofloxacin	>0.06
Penicillin	>1.0 and/or β-lactamase positive
Tetracycline	>1.0
Spectinomycin	>64.0
Gentamicin	N/A

Notes: (a) Until 2018, EUCAST had set a breakpoint of MIC 0.5 mg/L for *N. gonorrhoeae* azithromycin resistance. This has since been replaced with an 'epidemiological cut-off' of 1.0 mg/L (6). For continuity with previous GRASP reports, the previous breakpoint of 0.5 mg/L is retained as a historic reference point here.

(b) High-level azithromycin resistance is not defined by EUCAST, but the definition of ≥256 mg/L is internationally recognised.

Figure 3. Percentage of *N. gonorrhoeae* isolates in the GRASP sentinel surveillance system that were resistant to selected antimicrobials, England and Wales, 2000 to 2021†



† Due to changes in the diagnostic sensitivity medium used to test antimicrobial susceptibility of sentinel surveillance isolates, MICs for the 2015 to 2021 collections are not directly comparable with those from previous years. Trends from 2000 to 2014 compared to 2015 to 2021 must be interpreted with caution (point of change indicated by vertical dashed black line), particularly for azithromycin and tetracycline (data for tetracycline is only included from 2015 onwards due to this issue) (7). The 5% threshold (≥5% of infections resistant to the first-line therapy) at which the WHO recommends that first-line monotherapy guidelines should be changed is indicated by the horizontal dashed red line. In 2021, pharyngeal isolates were prioritised ahead of all other sites for the first time, resulting in a substantial change in the distribution of specimen sites included in the 2021 sample.

Table 4. Percentage of *N. gonorrhoeae* isolates in the GRASP sentinel surveillance system that were resistant to selected antimicrobials, England and Wales, 2017 to 2021

Antimicrobial MIC (a) resistance breakpoint (mg/L)		Number of resistant isolates (%) (b)				
		2017	2018	2019	2020	2021
		N=1,268	N=1,456	N=1,701	N=1,534	N=1,449
Ceftriaxone (>0.125)†		0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Azithromycin (c)	(>0.5)	117 (9.2%)	142 (9.8%)	158 (9.3%)	134 (8.7%)	220 (15.2%)
	(>1.0)	60 (4.7%)	101 (6.9%)	52 (3.1%)	64 (4.2%)	73 (5.0%)
Cefixime (>0.125)		21 (1.7%)	32 (2.2%)	14 (0.8%)	9 (0.6%)	4 (0.3%)
Ciprofloxacin (>0.06)		461 (36.4%)	579 (39.8%)	727 (42.7%)	679 (44.3%)	679 (46.9%)
Penicillin (>1.0)		137 (10.8%)	181 (12.4%)	305 (17.9%)	147 (9.6%)	204 (14.1%)
Tetracycline (>1.0)		615 (48.5%)	769 (52.8%)	1,070 (62.9%)	999 (65.1%)	1,089 (75.2%)
Spectinomycin (>64.0)		0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

† Although no ceftriaxone resistant cases were detected in GRASP, cases have been confirmed through direct referrals to the UKHSA AMRSTI national reference laboratory: 0 in 2017, 3 in 2018, 3 in 2019, 0 in 2020, 2 in 2021, 9 in 2022 (up to June).

Notes: (a) Minimum inhibitory concentration (MIC).

(b) The number of isolates included in the sample may differ from previous reports as, in this report, only data for isolates matched to GRASP clinics is presented.

(c) Until 2018, EUCAST had a resistance breakpoint of 0.5 mg/L for azithromycin against *N. gonorrhoeae* (6). This has since been removed and replaced with an 'epidemiological cut-off' of 1.0 mg/L. For continuity with previous GRASP reports, the previous breakpoint of >0.5 mg/L is retained as a historic reference point here.

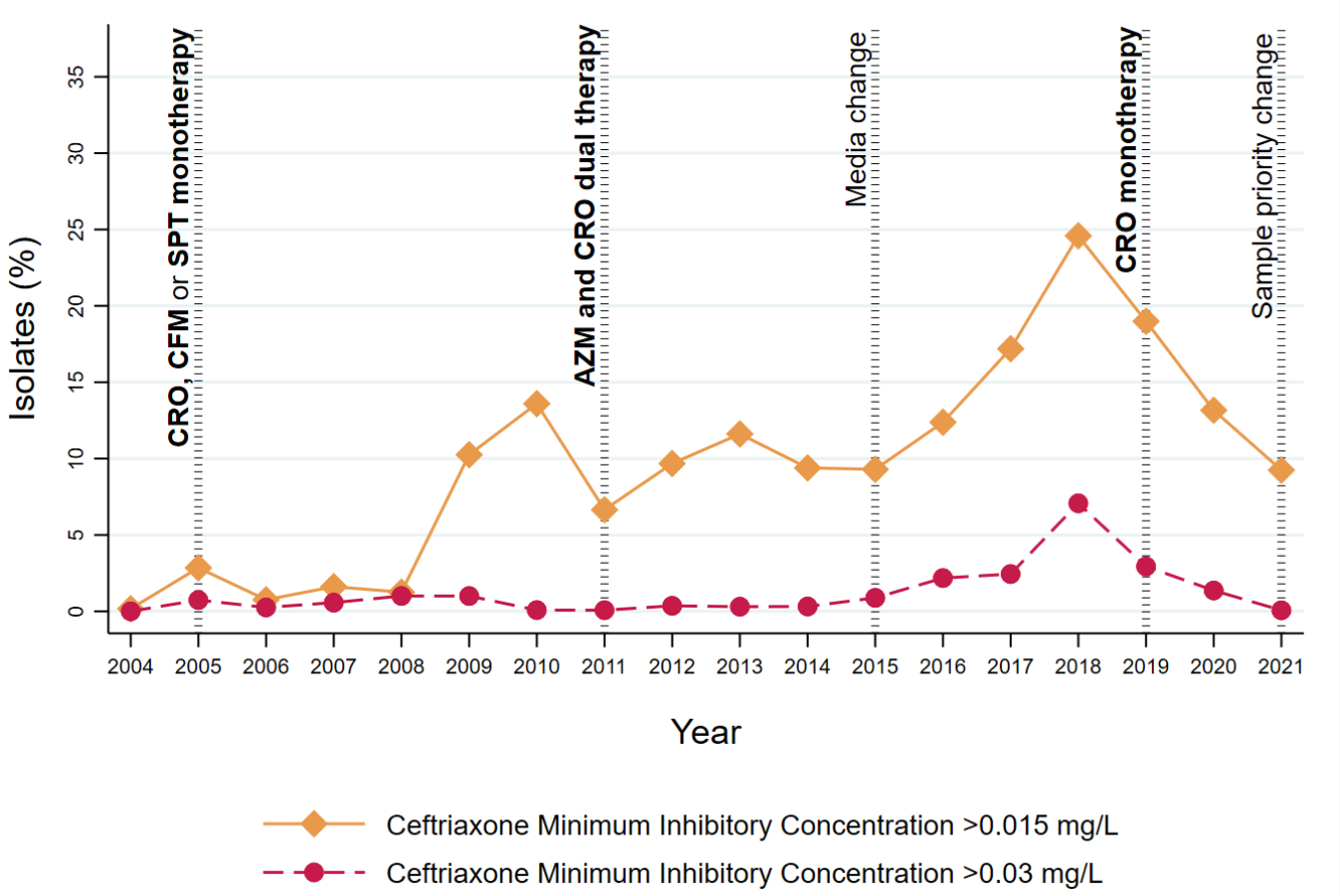
Ceftriaxone

Sentinel surveillance system sample

Among 1,449 isolates included in the sentinel surveillance sample in 2021, none were resistant to ceftriaxone (MIC >0.125 mg/L) (Table 4). The proportion of isolates with reduced susceptibility (defined here as an MIC >0.03 mg/L) to ceftriaxone decreased, for the third successive year, from 1.4% in 2020 to 0.07% in 2021 ($p<0.001$) (Figure 4). A similar trend was observed when using a comparative measure of reduced susceptibility to ceftriaxone (MIC

>0.015 mg/L), decreasing from 13.2% in 2020 to 9.2% in 2021 (p<0.001) continuing the declining trend since 2018 (p<0.001).

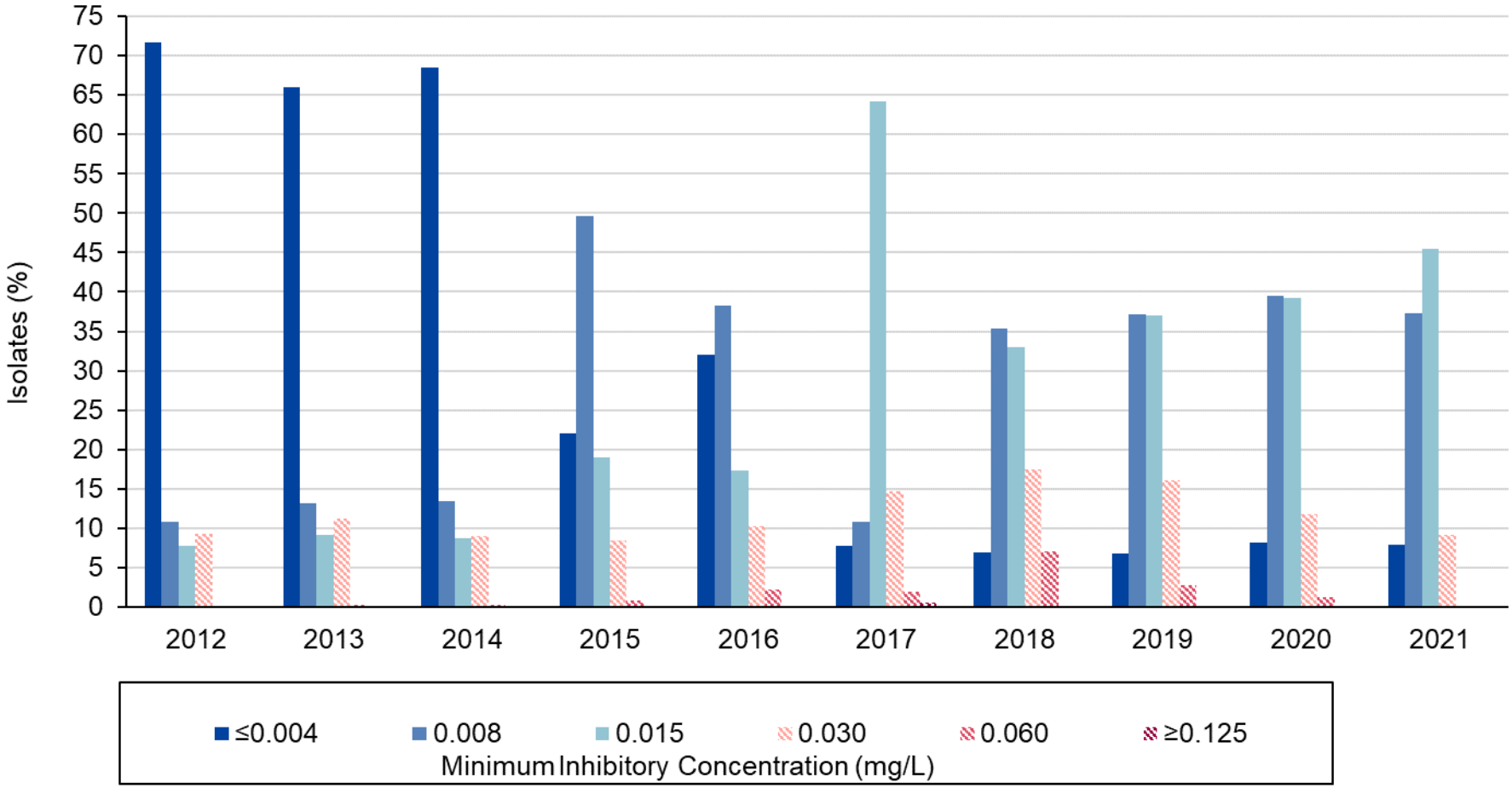
Figure 4. Percentage of *N. gonorrhoeae* isolates in the GRASP sentinel surveillance system with reduced susceptibility to ceftriaxone, England and Wales, 2004 to 2021†



† Due to changes in the diagnostic sensitivity medium used to test antimicrobial susceptibility of sentinel surveillance isolates, MICs for the 2015 to 2021 collections are not directly comparable with those from previous years. Trends from 2004 to 2014 compared to 2015 to 2021 must be interpreted with caution (point of change indicated by vertical dashed black line) (7). Changes to the UK national guidance for the management of infection with *N. gonorrhoeae* are indicated by vertical dashed black lines with bold text. CRO: ceftriaxone; CFM: cefixime; SPT: spectinomycin; AZM: azithromycin. In 2021, pharyngeal isolates were prioritised ahead of all other sites for the first time, resulting in a substantial change in the distribution of specimen sites included in the 2021 sample.

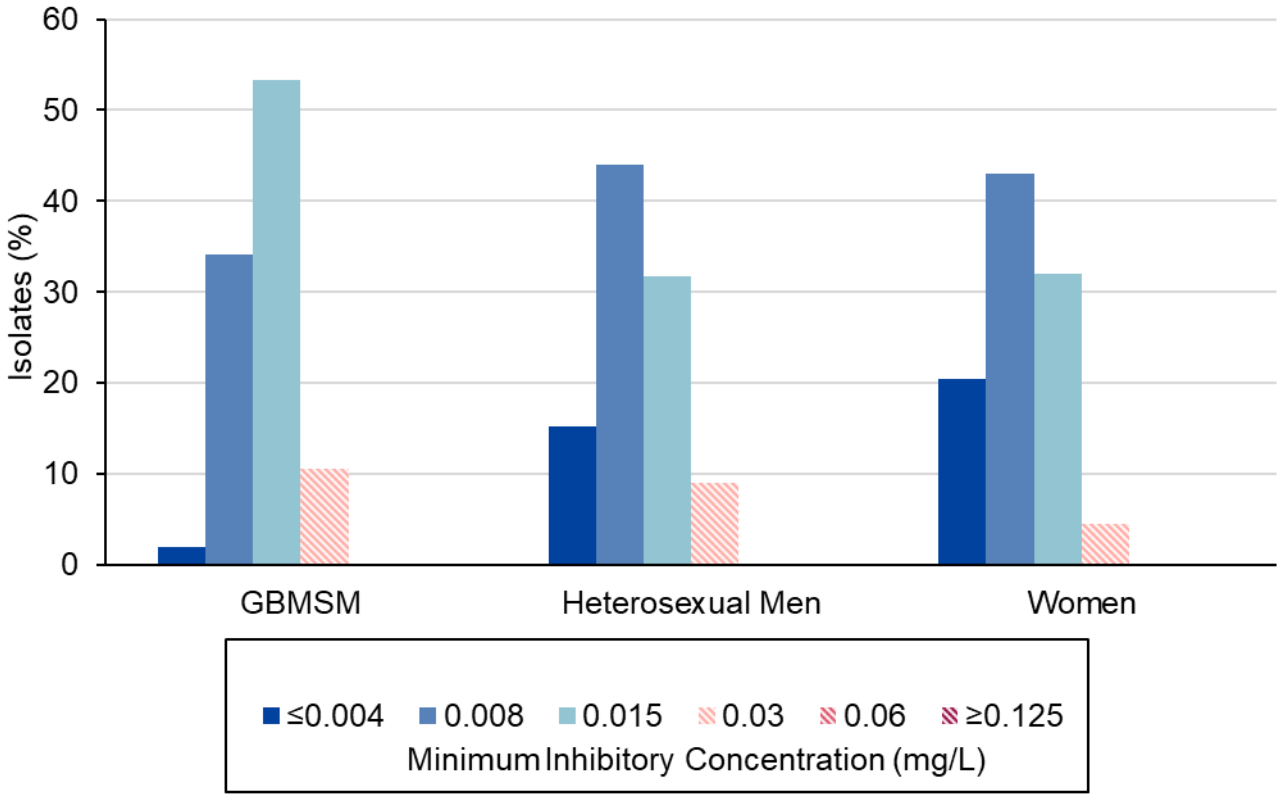
Although ceftriaxone reduced susceptibility (MIC >0.03 mg/L) decreased, for the first time since 2017 the proportion of isolates with a ceftriaxone MIC of 0.015 mg/L surpassed the proportion with an MIC of 0.008 mg/L, indicating an upwards shift in the modal MIC (Figure 5). As was observed in previous years, the modal MIC was higher for isolates from GBMSM (0.015 mg/L) than those from heterosexual men (0.008 mg/L) and women (0.008 mg/L) (Figure 6).

Figure 5. Distribution of ceftriaxone MICs (mg/L) for *N. gonorrhoeae* isolates in the GRASP sentinel surveillance system, England and Wales, 2012 to 2021†



† Due to changes in the diagnostic sensitivity medium used to test antimicrobial susceptibility of sentinel surveillance system isolates, MICs for the 2015 to 2021 collection are not directly comparable with those from previous years. Trends from 2012 to 2014 compared to 2015 to 2021 must be interpreted with caution (7).

Figure 6. Distribution of ceftriaxone MICs (mg/L) for *N. gonorrhoeae* isolates in the GRASP sentinel surveillance system, by gender and sexual orientation, England and Wales, 2021



Real-time laboratory data

From January to June 2022, 11,584 *N. gonorrhoeae* isolates were reported to SGSS by laboratories across England, a 68.3% and 16.4% increase relative to the same period in 2021 and 2020, respectively. The increase in the number of isolates reported may be due to recovery of service provision following the major disruption to SHSs caused by the COVID-19 pandemic response or a result of a genuine increase in gonorrhoea transmission (2).

The proportion of *N. gonorrhoeae* isolates tested for susceptibility to ceftriaxone (or cefuroxime as a proxy, see Appendix 1) in laboratories across England, as reported via SGSS, remained stable between 2018 and the first half of 2022, with at least 99.0% of isolates tested each year (Table 5).

The percentage of isolates that were reported as resistant to ceftriaxone remained stable from 0.14% in 2021 to 0.21% in 2022 (p=0.16) (Table 5). From January to June 2022, only 41.7% of isolates reported as resistant to ceftriaxone by laboratories across England were referred to the UKHSA AMRSTI national reference laboratory for confirmation, despite the recommendation in

the national management guidelines that all isolates with suspected ceftriaxone resistance be referred for confirmation (1). Although this is sub-optimal, it is an improvement from previous years. Follow-up of these isolates has shown that most isolates were misclassified as resistant; in 2022 only one out of 10 referred isolates recorded as resistant in SGSS was confirmed as resistant by the national reference laboratory.

In September 2021, a confirmed case of ceftriaxone-resistant *N. gonorrhoeae* was detected in a male heterosexual who had recently travelled to the Asia Pacific region and was successfully treated with ceftriaxone 1g IM. Upon risk assessment, the individual did not have any further partners upon return to the UK, hence subsequent public health action was not warranted. In December 2021, one further ceftriaxone-resistant *N. gonorrhoeae* case was identified, and subsequently 9 cases were detected in just a 6 month period up to June 2022. For comparison, no cases were detected in 2020 and 3 cases were detected in each of 2018 and 2019 (Table 5). A National Standard Incident Management Team was convened by UKHSA to coordinate the public health response to these cases and contain further transmission.

Most cases confirmed as resistant were associated with travel from the Asia Pacific region, and included 3 partnerships and 4 individuals who were not epidemiologically linked. Although all cases were successfully treated, not all partners of cases could be traced. As such there remains a risk of ongoing transmission of ceftriaxone-resistant gonococcal infection within the UK.

Table 5. Ceftriaxone susceptibility testing and referral of *N. gonorrhoeae* isolates: data from primary diagnostic laboratories reported via SGSS and the UKHSA AMRSTI national reference laboratory, 2018 to 2022

	2018	2019	2020	2021	2022 (a)
Reported to SGSS (Percentage tested for ceftriaxone susceptibility)	24,896 (99.1%)	32,387 (99.5%)	18,308 (99.4%)	16,225 (99.3%)	11,584 (99.0%)
Reported as ceftriaxone resistant in SGSS (Percentage of isolates tested for ceftriaxone susceptibility)	58 (0.24%)	57 (0.18%)	42 (0.23%)	23 (0.14%)	24 (0.21%)
Reported as ceftriaxone resistant in SGSS and referred (Percentage of all reported as resistant)	16 (27.6%)	14 (24.6%)	7 (16.7%)	6 (26.1%)	10 (41.7%)
Referred isolates confirmed as resistant by the AMRSTI national reference laboratory (Percentage of all referred isolates)	2 (12.5%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	1 (10.0%)
All isolates confirmed as resistant by the AMRSTI national reference laboratory (b)	**3**	**3**	**0**	**2**	**9**

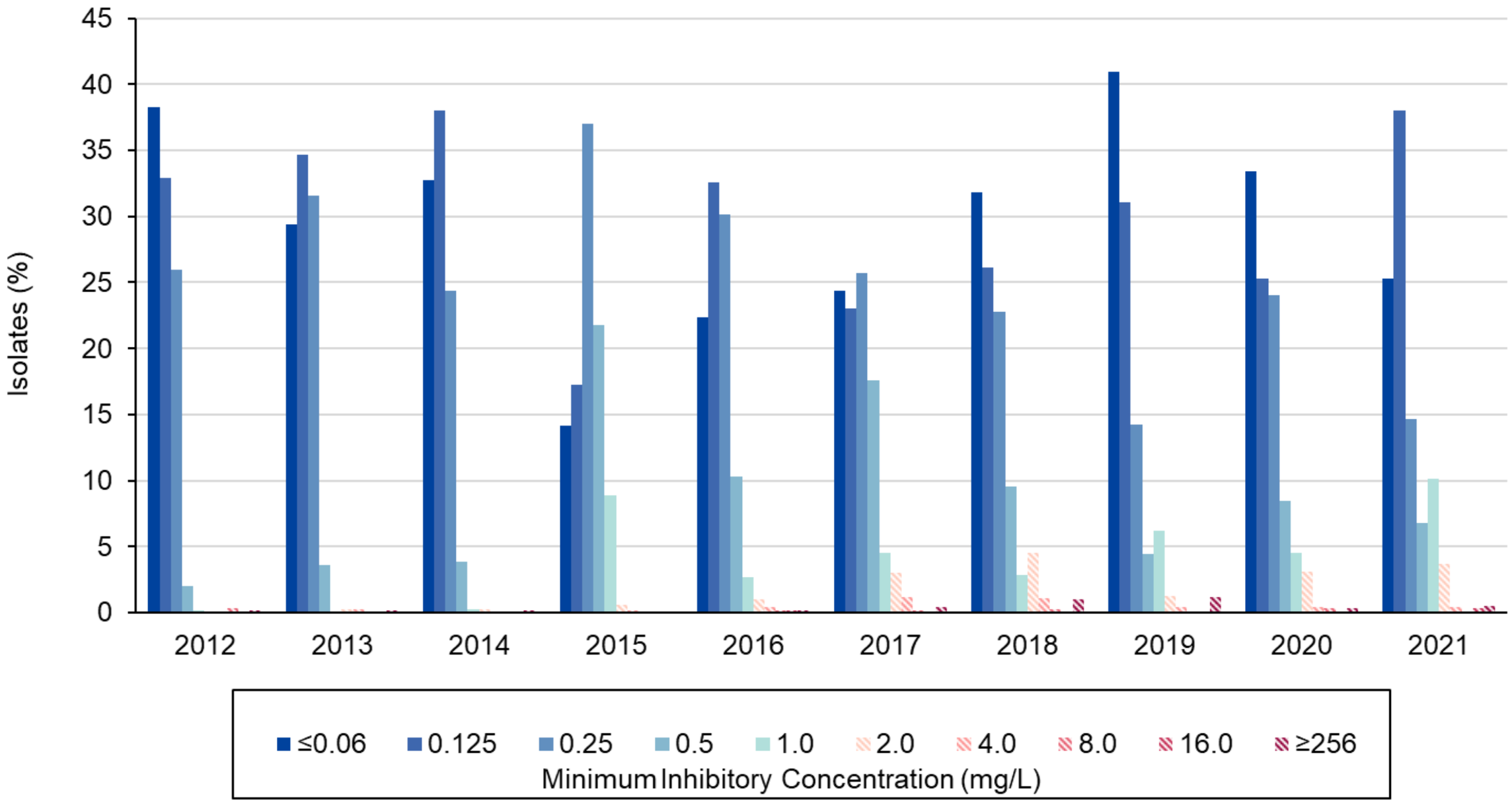
Notes: (a) Data to June 2022. (b) Primary diagnostic laboratories report isolate test results to SGSS on a voluntary basis and therefore not all isolates received at the AMRSTI national reference laboratory have been reported to SGSS. The proportion of all isolates confirmed as resistant by the AMRSTI national reference laboratory is not presented due to the unavailability of an accurate denominator.

Azithromycin

Resistance breakpoints for azithromycin were removed by EUCAST in 2019 and replaced with an epidemiological cut-off of 1.0 mg/L (Table 3) (6). For continuity with previous GRASP reports, the previous breakpoint of 0.5 mg/L is also retained as a historic reference point.

Between 2020 and 2021, the proportion of isolates included in the sentinel surveillance sample with azithromycin MICs >0.5 mg/L increased from 8.7% to 15.2% ($p<0.001$) (Figure 7). Additionally, the modal azithromycin MIC increased to 0.125 mg/L in 2021, having remained stable at the lowest dilution tested (≤0.06 mg/L) between 2018 and 2020. However, the proportion of isolates with azithromycin MICs at the epidemiological cut-off of >1.0 mg/L remained stable from 4.2% in 2020 to 5.0% in 2021 ($p=0.30$). The proportion of isolates with azithromycin MICs ≥256 mg/L, an internationally recognised measure of high-level resistance, remained stable from 0.3% (5 isolates) in 2020 to 0.6% (8 isolates) ($p=0.22$) in 2021, having previously decreased from 1.2% in 2019 (20 isolates). Isolates with high-level resistance were widely geographically distributed and detected at 6 GRASP clinics.

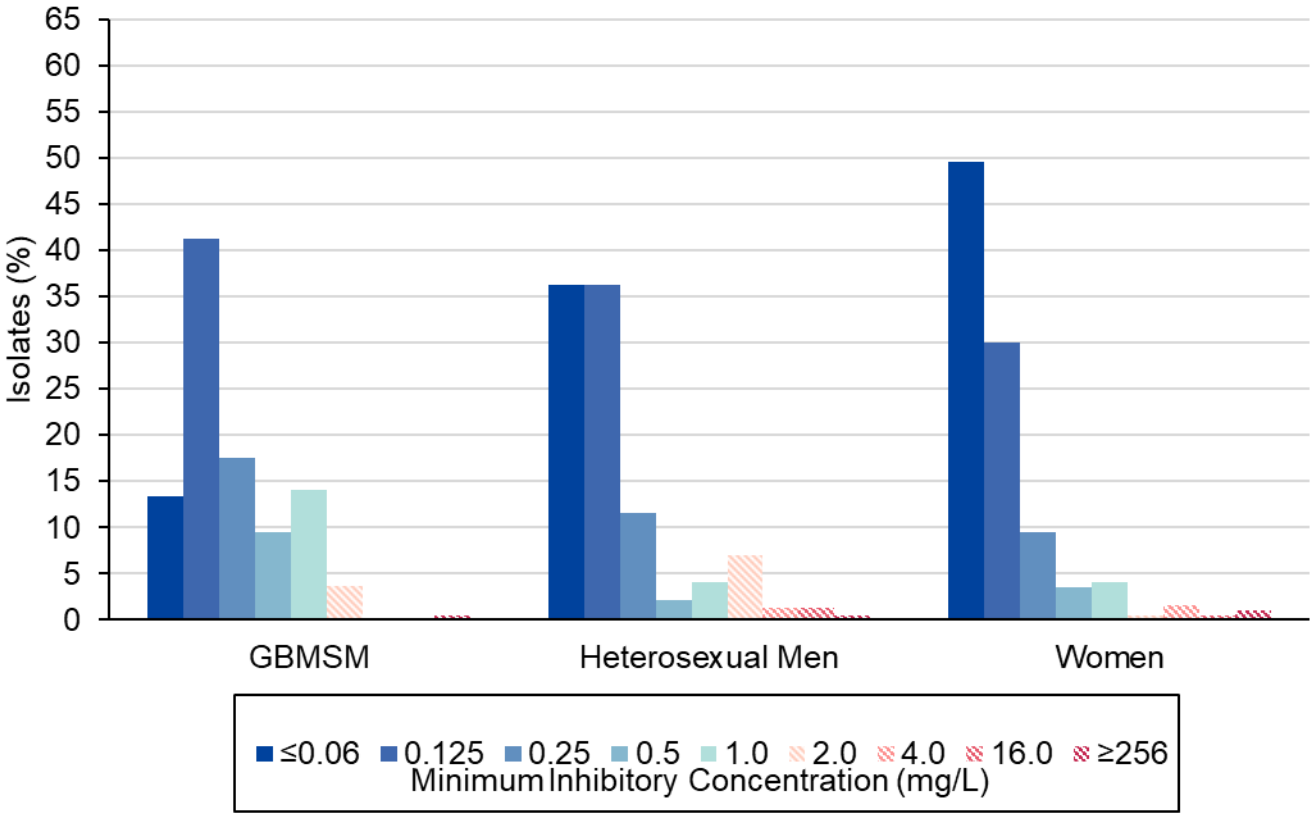
Figure 7. Distribution of azithromycin MICs (mg/L) for *N. gonorrhoeae* isolates in the GRASP sentinel surveillance system, England and Wales, 2012 to 2021†



† Due to changes in the diagnostic sensitivity medium used to test antimicrobial susceptibility of sentinel surveillance system isolates, MICs for the 2015 to 2021 collection are not directly comparable with those from previous years. Trends from 2012 to 2014 compared to 2015 to 2021 must be interpreted with caution, particularly for azithromycin (7).

Azithromycin MICs >0.5 mg/L were more common among isolates from GBMSM (18.3%) compared to those from heterosexual men (14.0%; p=0.002) and women (7.5%; p<0.001) (Figure 8). High-level resistance to azithromycin (MIC ≥256 mg/L) was identified for isolates taken from GBMSM (0.4%; 4 isolates), heterosexual men (0.4%; 1 isolate) and women (1.0%; 2 isolates). The azithromycin MIC distribution was largely positively skewed among isolates from GBMSM, heterosexual men and women, with low modal MICs of either 0.125 mg/L or ≤0.06 mg/L (Figure 8).

Figure 8. Distribution of azithromycin MICs (mg/L) for *N. gonorrhoeae* isolates in the GRASP sentinel surveillance system, by gender and sexual orientation, England and Wales, 2021†

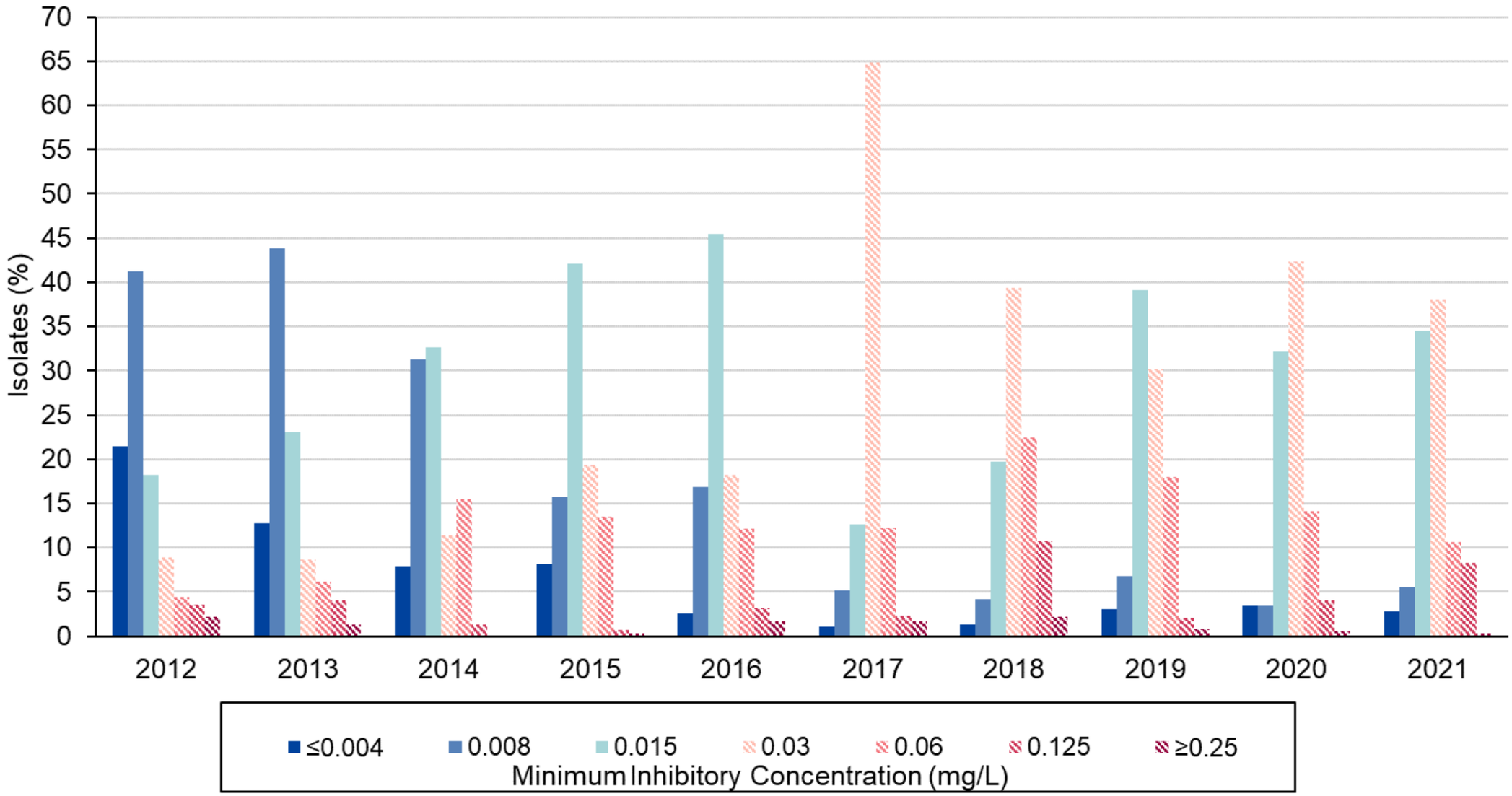


Cefixime

Overall, there has been a continuous decline in cefixime resistant (MIC >0.125 mg/L) isolates since 2018 (2.2%) (p<0.001) (Figure 3; Table 4). The modal cefixime MIC remained stable at 0.03 mg/L in 2021 compared to 2020 (Figure 9). However, the proportion of isolates with a MIC at 0.125 mg/L, only one dilution below the EUCAST threshold for resistance, doubled from 4.0% in 2020 to 8.3% in 2021.

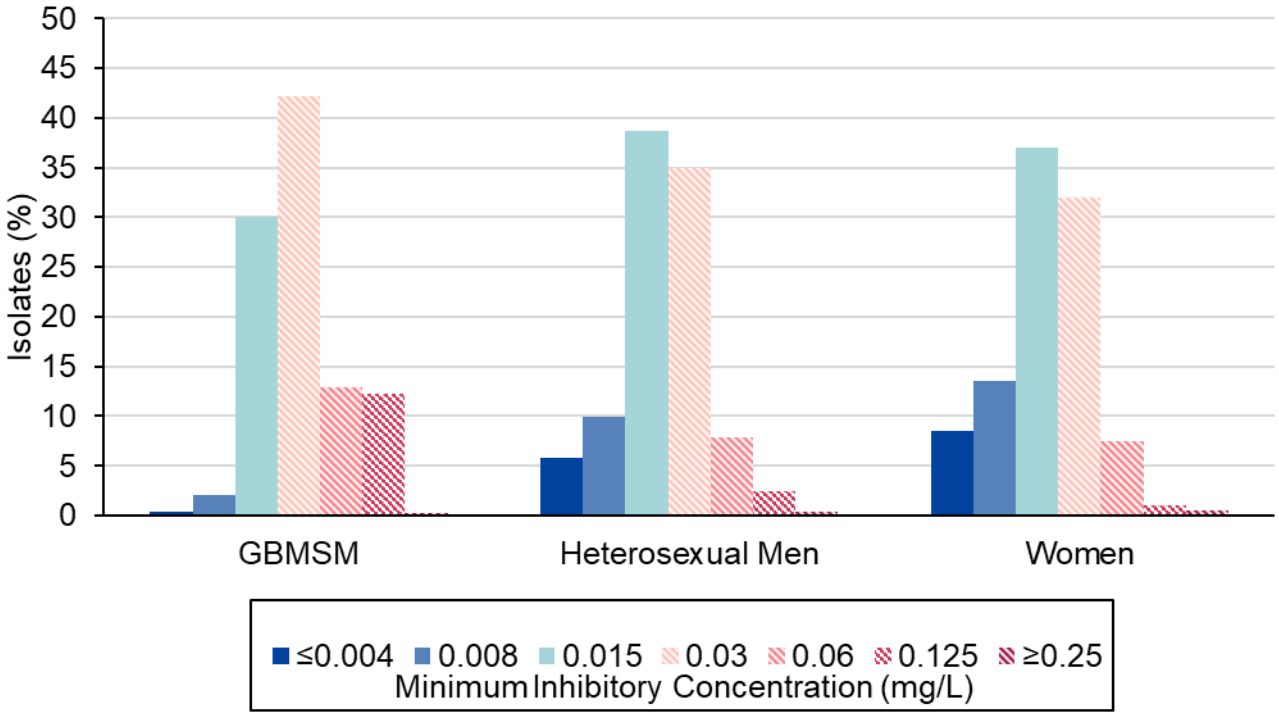
The modal cefixime MIC was higher for isolates from GBMSM (0.03 mg/L) than those from women (0.015 mg/L) for the third successive year, and isolates from heterosexual men (0.015 mg/L) as of 2021 (Figure 10). As only 2 isolates from GBMSM and one from each of women and heterosexual men displayed cefixime resistance (MIC >0.125 mg/L), the proportion resistant among GBMSM (0.2%) was not significantly different from that of women (0.5%) (p=0.17) or heterosexual men (0.4%) (p=0.33).

Figure 9. Distribution of cefixime MICs (mg/L) for *N. gonorrhoeae* isolates in the GRASP sentinel surveillance system, England and Wales, 2012 to 2021†



† Due to changes in the diagnostic sensitivity medium used to test antimicrobial susceptibility of sentinel surveillance system isolates, MICs for the 2015 to 2021 collection were not directly comparable with those from previous years. Trends from 2012 to 2014 compared to 2015 to 2021 must be interpreted with caution (7).

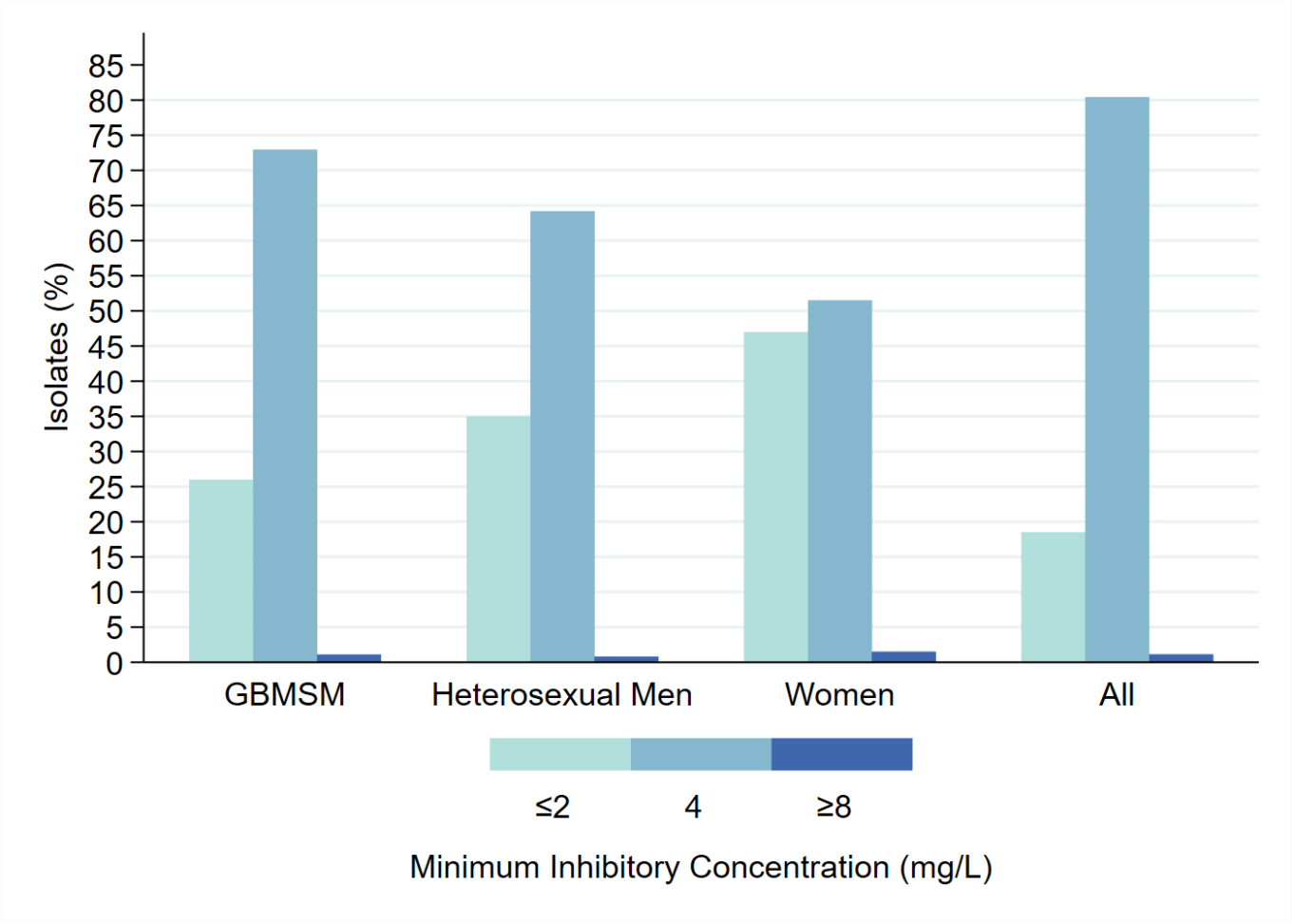
Figure 10. Distribution of cefixime MICs (mg/L) for *N. gonorrhoeae* isolates in the GRASP sentinel surveillance system, England and Wales, 2021



Gentamicin

Antimicrobial susceptibility testing for the sentinel surveillance system included gentamicin for the first time in 2019. Only 1.1% of all isolates had a gentamicin MIC ≥8 mg/L in 2021, a decrease compared to 23.3% and 9.7% of isolates in 2020 and 2019, respectively (Figure 11). The modal MIC for gentamicin has remained stable at 4.0 mg/L between 2019 and 2021. However, a higher proportion of isolates among GBMSM had a gentamicin MIC of 4.0 mg/L, whilst a lower proportion had an MIC of 2 mg/L or less, suggesting lower susceptibility to gentamicin among isolates from GBMSM compared to women and heterosexual men.

Figure 11. Distribution of gentamicin MICs (mg/L) for *N. gonorrhoeae* isolates in the GRASP sentinel surveillance system, England and Wales, 2021

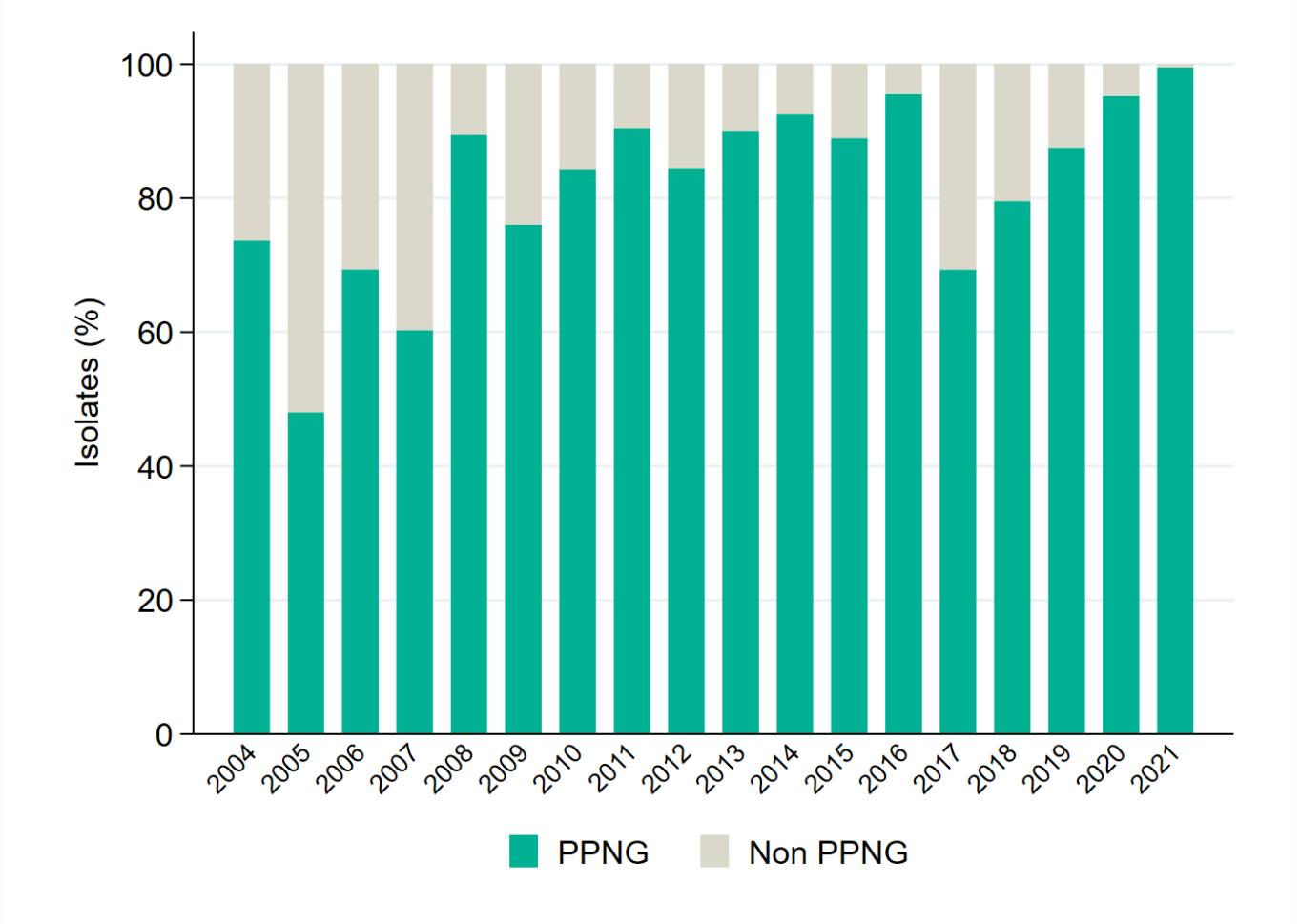


Ciprofloxacin, penicillin, tetracycline and spectinomycin

There was an increase in the proportion of isolates that were resistant to tetracycline (65.1% in 2020 then 75.2% in 2021; p<0.001) and penicillin (9.6% in 2020 then 14.1% in 2021; p<0.001) (Table 4). There has been a continuous incremental increase in ciprofloxacin resistance each year since 2016 (p>0.001), with 46.9% of isolates resistant in 2021 (Figure 3, Table 4). However, ciprofloxacin resistance varied by gender and sexual orientation; among GBMSM 59.1% of isolates were resistant, relative to 33.7% among heterosexual men and 22.0% among women (Appendix 2). Tetracycline resistance (MIC >1 mg/L) has also continuously increased since 2016 (p<0.001). Having decreased from 17.9% to 9.6% between 2019 to 2020, penicillin resistance (MIC >1 mg/L) increased to 14.1% in 2021 (p<0.001). As was the case between 2000 and 2020, no isolates were resistant to spectinomycin in 2021.

Among isolates found to be resistant to tetracycline in 2021, 33.6% (366 out of 1,089) had high-level plasmid-mediated tetracycline resistance (MIC >8 mg/L), similar to 2020 (p=0.14). In 2021, 99.5% (203 out of 204) of penicillin-resistant isolates were penicillinase-producing *N. gonorrhoeae* (PPNG), which have plasmid-mediated resistance, a 4.3% increase from 2020 (p=0.008) (Figure 12).

Figure 12. Percentage of penicillin resistant *N. gonorrhoeae* isolates that were PPNG in the GRASP sentinel surveillance sample, England Wales, 2004 to 2021†



† Due to changes in the diagnostic sensitivity medium used to test antimicrobial susceptibility of sentinel surveillance system isolates, MICs for the 2015 to 2021 collection are not directly comparable with those from previous years. Trends from 2004 to 2014 compared to 2015 to 2021 must be interpreted with caution (7).

Prescribing practices

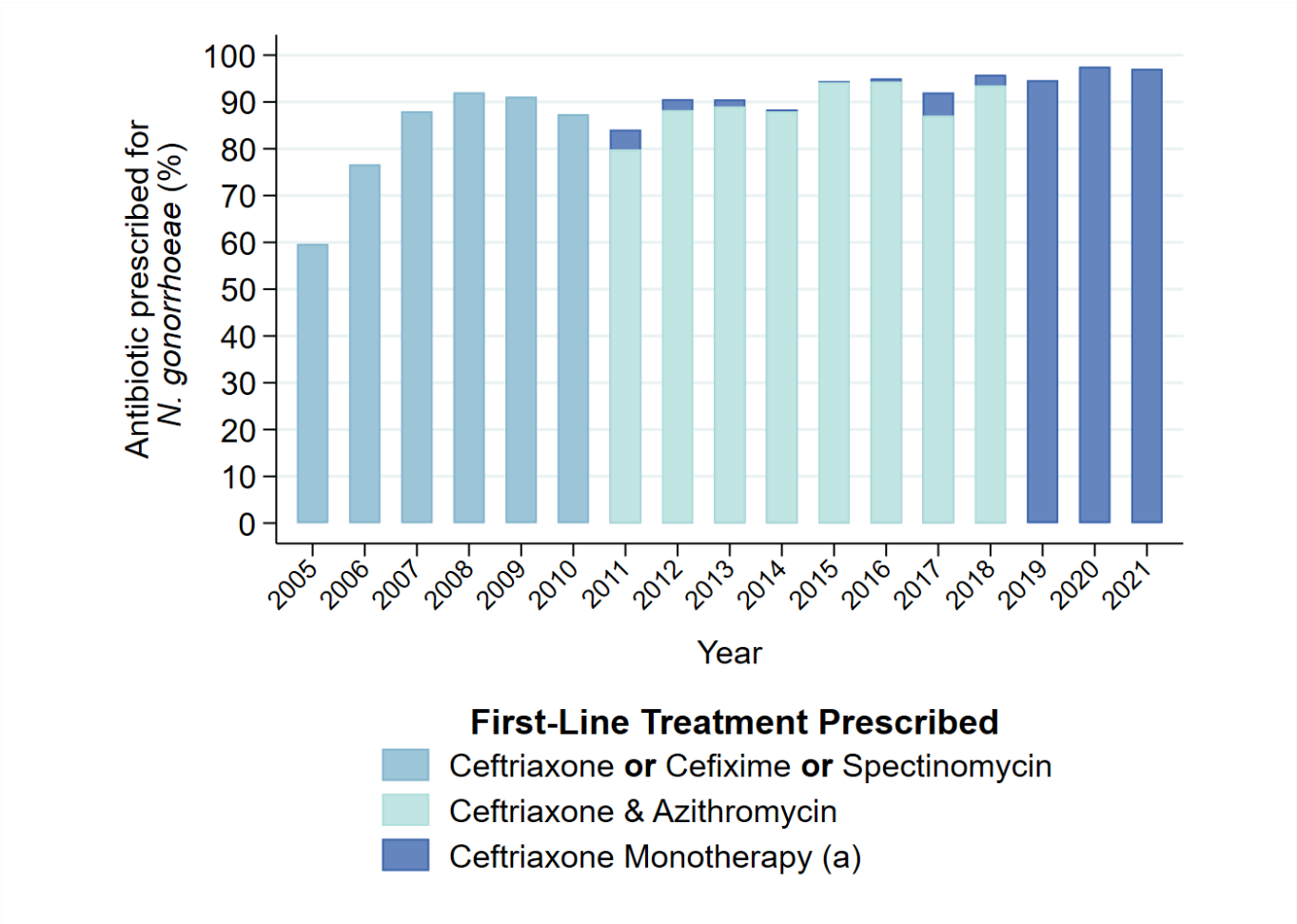
Antimicrobial prescribing data was reported for 1,580 isolates from individuals diagnosed with gonorrhoea at SHSs participating in GRASP in 2021, out of 1,596 isolates with clinical data reported, irrespective of whether a *N. gonorrhoeae* isolate was available for antimicrobial susceptibility testing.

Among individuals with a reported gonorrhoea diagnosis, 97.1% (1,534 out of 1,580) received ceftriaxone (1g IM), in accordance with BASHH first-line treatment recommendations, and was similar for GBMSM (98.2%), heterosexual men (96.5%) and women (92.7%) (Figure 13). For comparison, 97.6% of individuals were prescribed the first-line treatment ceftriaxone 1g monotherapy in 2020 and 94.6% in 2019. Alternatively, ciprofloxacin 500 mg orally is

recommended when antimicrobial susceptibility is known prior to treatment and in 2021, 2 individuals were prescribed ciprofloxacin.

The remaining 43 individuals were prescribed second-line treatments (1). Of these 18 (41.9%) received gentamicin and azithromycin, 8 (18.6%) received azithromycin 2g monotherapy and 8 (18.6%) received cefixime and azithromycin.

Figure 13. Prescribing Practices in England and Wales: Percentage Prescribed Recommended First-Line Treatment, 2005 to 2021†



† Prior to 2016, the denominator includes only isolates within the sentinel surveillance system. Since 2016, the denominator includes all diagnoses made in GRASP clinics (including those without an isolate) where prescription data was available. Individuals prescribed 'other' and 'unknown' antibiotics were categorised based on known treatments given.

Notes: (a) New treatment guidelines for gonorrhoea in the UK were published in January 2019, recommending 1g ceftriaxone monotherapy instead of ceftriaxone (500 mg IM) in combination with azithromycin (1g oral) (1). Although ceftriaxone monotherapy was not recommended as first-line treatment in the guidelines for the period of 2011 to 2018, it is presented to illustrate the use of the main alternative first-line treatment in practice.

Discussion

No cases of ceftriaxone resistance were observed among *N. gonorrhoeae* isolates captured within the GRASP sentinel surveillance system in 2021. We therefore assessed trends in reduced susceptibility to ceftriaxone (MIC >0.03 mg/L), which has decreased for the third successive year, halving from 7.1% in 2018, to 2.9% in 2019, then to 1.4% in 2020 and finally decreasing to 0.07% in 2021, comparable to levels seen in 2011. In contrast, the UKHSA AMRSTI national reference laboratory confirmed 11 cases of ceftriaxone resistance between September 2021 and June 2022 upon direct referral from primary diagnostic laboratories, 9 of which were reported in just the first 6 months of 2022, compared to a total of 9 between 2015 and 2020. Reassuringly, all cases were successfully treated as cultures and NAATs were negative at test-of-cure 2 to 3 weeks after treatment. Most had travel links with the Asia Pacific region, which has been shown to have the highest prevalence of ceftriaxone-resistant *N. gonorrhoeae* globally (8). However, as not all partners could be contact traced in addition to some cases having no travel links, there may be ongoing local transmission within the UK.

Detection and follow-up of these cases of ceftriaxone resistance again highlights the importance of engagement with sexual health clinicians and laboratories; without susceptibility testing in primary diagnostic laboratories, these cases would have gone unreported (9). Recently, laboratories have faced challenges in accessing commercially available media suitable for susceptibility testing. Where media is not widely available, local processes must be employed to prioritise susceptibility testing of first-line recommended therapies (ceftriaxone and ciprofloxacin specifically) to ensure appropriate antibiotic stewardship.

Resistance to cefixime, an ESC recommended in the UK as an alternative regimen for gonorrhoea if IM treatment is contraindicated or refused, continued to gradually decrease to 0.3% in 2021. However, the proportion of isolates with a MIC at 0.125 mg/L, only one dilution below the EUCAST threshold for resistance, doubled from 4.0% in 2020 to 8.3% in 2021. Improvements in ceftriaxone susceptibility, together with decreasing cefixime resistance, are encouraging developments in the effort to maintain the effectiveness of the current first-line gonorrhoea treatment. However, increases in the ceftriaxone modal MIC and the number of referred resistant isolates to the AMRSTI national reference laboratory show that continual vigilance is necessary. With only one out of the 9 cases of ceftriaxone resistance detected in the first 6 months of 2022 reported in SGSS by the primary diagnostic laboratory, increased reporting of test results and antimicrobial resistance data to SGSS could strengthen real-time monitoring of antimicrobial resistance among *N. gonorrhoeae* diagnoses in England.

Although there is no EUCAST resistance breakpoint for azithromycin, a historical breakpoint at >0.5 mg/L has been retained for comparability with previous GRASP data. The proportion of isolates with azithromycin MICs >0.5 mg/L increased by 6.5% to 15.2% in 2021, following

steady levels since 2017. However, as the proportion of isolates with azithromycin MICs >1.0 mg/L (the epidemiological breakpoint) remained stable in 2021, the increase appears to be driven by an increase in the number of isolates with MICs at 1.0 mg/L, just above the historical breakpoint. Additionally, the modal azithromycin MIC increased by one dilution to 0.125 mg/L. While there appears to be some shift in susceptibility to azithromycin, the changes are subtle and require further monitoring.

Tetracycline resistance continues to increase sharply despite its absence as a treatment option for gonorrhoea, possibly due to the use of doxycycline for the treatment of other STIs (10). Ciprofloxacin, penicillin, tetracycline and azithromycin resistance (MIC >0.5 mg/L) continue to be more common among isolates from GBMSM compared to heterosexual men and women.

Prescribing data collected through the sentinel surveillance system demonstrates excellent compliance with the UK guidelines, with nearly all individuals receiving the recommended first-line therapy of ceftriaxone 1g IM monotherapy. The update to UK guidelines in 2019, which replaced dual therapy with ceftriaxone 500 mg IM and azithromycin 1g with a higher dose ceftriaxone 1g IM monotherapy as the recommend first-line treatment, appears to coincide with improving susceptibility to ceftriaxone and cefixime and the overall effectiveness of treatment as no treatment failures were reported in 2021.

Conclusion

Although the effectiveness of first-line treatment for gonorrhoea continues to be threatened by the development and importation of antimicrobial resistance, the decline in reduced susceptibility to ceftriaxone and cefixime resistance are encouraging developments in the effort to maintain these antimicrobials as therapeutic options.

It is important to note however, that the number of ceftriaxone resistant cases thus far in 2022 has already exceeded the total number reported in the 6 years since the first case in 2015. As ceftriaxone resistance has been associated with international travel and COVID-19 restrictions continue to ease in the UK and internationally, a high level of vigilance is required to facilitate the timely detection of emerging trends in resistance and ensure the continued effectiveness of first-line treatments. Culture of isolates and antimicrobial susceptibility testing of isolates, test-of-cure, and partner notification and management of sexual partners remain vital. Continued strong adherence to treatment guidelines and use of the UKHSA AMRSTI national reference laboratory for confirmatory antimicrobial susceptibility testing are also essential.

Appendices

1. Real-time laboratory data

Data on *N. gonorrhoeae* isolates tested for antimicrobial susceptibility from January 2017 to June 2021 was retrieved from SGSS. SGSS is a centralised repository of communicable disease test results for every specimen tested by laboratories in England, Northern Ireland and Wales, including those of *N. gonorrhoeae*. There are 2 sub-repositories within SGSS that hold data on antimicrobial susceptibility: the communicable disease reporting (CDR) repository and the antimicrobial resistance (AMR) repository. Data was extracted from both repositories and duplicate records were removed (where the same record is found in both the CDR and AMR repository). Episodes of infection were defined and enumerated after removing reports for multiple specimens and specimen sites within a 6-week period per patient. If more than one isolate was collected from a patient, where resistance or antimicrobial susceptibility testing profiles differed, the resistant code was preferentially kept. Isolates with an ocular specimen site were removed prior to restricting isolates to one episode per 6-week period.

In primary diagnostic laboratories, ceftriaxone and cefixime susceptibility is often inferred by testing cefuroxime as a proxy cephalosporin. If a gonococcus is found to be susceptible to cefuroxime it may thus be reported susceptible to ceftriaxone or cefixime. If, conversely, the isolate is resistant to cefuroxime, resistance to ceftriaxone or cefixime cannot be inferred and laboratories should use a gradient strip method to determine the ceftriaxone or cefixime IC. Therefore, where the ceftriaxone or cefixime susceptibility results were missing and cefuroxime susceptibility was reported, susceptibility to ceftriaxone or cefixime result was recorded. Where the ceftriaxone or cefixime susceptibility results were missing and resistance to cefuroxime was reported, the ceftriaxone or cefixime result was recorded as missing since there was no way to verify whether ceftriaxone resistance was present.

Isolates reported to SGSS as ceftriaxone resistant by laboratories across England were linked to the UKHSA AMRSTI national reference laboratory database based on available patient information. This was used to calculate the percentage of isolates successfully referred to and confirmed as resistant (or not) by the UKHSA AMRSTI national reference laboratory.

2. Antimicrobial resistance by individuals' characteristics

Table 6. Antimicrobial resistance by individuals' characteristics for GBMSM, sentinel surveillance system, 2021

	Total GBMSM	Azithromycin	Ciprofloxacin	Penicillin	Tetracycline
Resistant isolates	894	164	528	158	769
Age group (years)					
15 to 19	17	3 (17.6%)	9 (52.9%)	4 (23.5%)	15 (88.2%)
20 to 24	115	21 (18.3%)	63 (54.8%)	12 (10.4%)	102 (88.7%)
25 to 34	387	75 (19.4%)	245 (63.3%)	63 (16.3%)	336 (86.8%)
35 to 44	223	41 (18.4%)	126 (56.5%)	51 (22.9%)	190 (85.2%)
45 or more	152	24 (15.8%)	85 (55.9%)	28 (18.4%)	126 (82.9%)
Ethnicity					
White	584	120 (20.5%)	349 (59.8%)	101 (17.3%)	513 (87.8%)
Black Caribbean	30	5 (16.7%)	14 (46.7%)	3 (10.0%)	23 (76.7%)
Black African	23	3 (13.0%)	17 (73.9%)	5 (21.7%)	18 (78.3%)
Black Other	6	0 (0.0%)	5 (83.3%)	1 (16.7%)	3 (50.0%)
Asian	46	6 (13.0%)	26 (56.5%)	8 (17.4%)	38 (82.6%)
Other Ethnic Group	28	4 (14.3%)	20 (71.4%)	9 (32.1%)	24 (85.7%)
Mixed Ethnic Group	53	11 (20.8%)	29 (54.7%)	12 (22.6%)	46 (86.8%)

	Total GBMSM	Azithromycin	Ciprofloxacin	Penicillin	Tetracycline
Not reported	124	15 (12.1%)	68 (54.8%)	19 (15.3%)	104 (83.9%)
Residence					
Outside London	264	49 (18.6%)	121 (45.8%)	27 (10.2%)	224 (84.8%)
London	630	115 (18.3%)	407 (64.6%)	131 (20.8%)	545 (86.5%)
HIV status					
Negative	710	128 (18.0%)	418 (58.9%)	120 (16.9%)	611 (86.1%)
Positive	166	34 (20.5%)	100 (60.2%)	35 (21.1%)	143 (86.1%)
Not reported	18	2 (11.1%)	10 (55.6%)	3 (16.7%)	15 (83.3%)
Symptoms					
No discharge and or dysuria	483	93 (19.3%)	282 (58.4%)	82 (17.0%)	414 (85.7%)
Discharge and or dysuria	411	71 (17.3%)	246 (59.9%)	76 (18.5%)	355 (86.4%)
Previously diagnosed with gonorrhoea					
No	258	50 (19.4%)	152 (58.9%)	31 (12.0%)	217 (84.1%)
Yes	348	72 (20.7%)	206 (59.2%)	80 (23.0%)	308 (88.5%)
Not reported	288	42 (14.6%)	170 (59.0%)	47 (16.3%)	244 (84.7%)
Total sexual partners (past 3 months)					
None to one	132	26 (19.7%)	69 (52.3%)	15 (11.4%)	116 (87.9%)

	Total GBMSM	Azithromycin	Ciprofloxacin	Penicillin	Tetracycline
2 to 5	286	47 (16.4%)	159 (55.6%)	49 (17.1%)	234 (81.8%)
6 to 10	45	9 (20.0%)	25 (55.6%)	8 (17.8%)	42 (93.3%)
11 or more	28	4 (14.3%)	18 (64.3%)	4 (14.3%)	22 (78.6%)
Not reported	403	78 (19.4%)	257 (63.8%)	82 (20.3%)	355 (88.1%)
Sex abroad (past 3 months)					
No	474	85 (17.9%)	260 (54.9%)	75 (15.8%)	403 (85.0%)
Yes	17	1 (5.9%)	11 (64.7%)	1 (5.9%)	11 (64.7%)
Not reported	403	78 (19.4%)	257 (63.8%)	82 (20.3%)	355 (88.1%)

Notes: No isolates were resistant to ceftriaxone or spectinomycin in the 2021 sentinel surveillance collection.

Data is not included for cefixime due to small numbers (n=2).

Percentages are row %.

Table 7. Antimicrobial resistance by individuals' characteristics for heterosexual men, sentinel surveillance system, 2021

	Total heterosexual men	Azithromycin	Ciprofloxacin	Penicillin	Tetracycline
Resistant isolates	243	34	82	27	158
Age group (years)					
15 to 19	22	2 (9.1%)	6 (27.3%)	2 (9.1%)	13 (59.1%)
20 to 24	47	3 (6.4%)	17 (36.2%)	7 (14.9%)	23 (48.9%)
25 to 34	98	15 (15.3%)	27 (27.6%)	9 (9.2%)	60 (61.2%)
35 to 44	53	8 (15.1%)	22 (41.5%)	5 (9.4%)	42 (79.2%)
45 or more	23	6 (26.1%)	10 (43.5%)	4 (17.4%)	20 (87.0%)
Ethnicity					
White	70	5 (7.1%)	22 (31.4%)	6 (8.6%)	43 (61.4%)
Black Caribbean	24	4 (16.7%)	7 (29.2%)	2 (8.3%)	16 (66.7%)
Black African	21	2 (9.5%)	8 (38.1%)	4 (19.0%)	15 (71.4%)
Black Other	8	0 (0.0%)	2 (25.0%)	1 (12.5%)	5 (62.5%)
Asian (including Chinese)	16	1 (6.3%)	7 (43.8%)	3 (18.8%)	10 (62.5%)
Other Ethnic Group	7	0 (0.0%)	5 (71.4%)	4 (57.1%)	6 (85.7%)
Mixed Ethnic Group	17	0 (0.0%)	6 (35.3%)	2 (11.8%)	11 (64.7%)
Not reported	80	22 (27.5%)	25 (31.3%)	5 (6.3%)	52 (65.0%)

	Total heterosexual men	Azithromycin	Ciprofloxacin	Penicillin	Tetracycline
Residence					
Outside London	138	23 (16.7%)	33 (23.9%)	9 (6.5%)	89 (64.5%)
London	105	11 (10.5%)	49 (46.7%)	18 (17.1%)	69 (65.7%)
HIV status					
Negative	207	21 (10.1%)	71 (34.3%)	26 (12.6%)	133 (64.3%)
Positive	3	0 (0.0%)	2 (66.7%)	0 (0.0%)	2 (66.7%)
Not reported	33	13 (39.4%)	9 (27.3%)	1 (3.0%)	23 (69.7%)
Symptoms					
No discharge and or dysuria	24	1 (4.2%)	4 (16.7%)	0 (0.0%)	12 (50.0%)
Discharge and or dysuria	219	33 (15.1%)	78 (35.6%)	27 (12.3%)	146 (66.7%)
Previously diagnosed with gonorrhoea					
No	119	23 (19.3%)	36 (30.3%)	14 (11.8%)	79 (66.4%)
Yes	36	2 (5.6%)	15 (41.7%)	3 (8.3%)	25 (69.4%)
Not reported	88	9 (10.2%)	31 (35.2%)	10 (11.4%)	54 (61.4%)
Total sexual partners (past 3 months)					
None to one	100	17 (17.0%)	30 (30.0%)	6 (6.0%)	67 (67.0%)
2 to 5	105	13 (12.4%)	38 (36.2%)	14 (13.3%)	67 (63.8%)
6 to 10	7	2 (28.6%)	4 (57.1%)	2 (28.6%)	7 (100.0%)

	Total heterosexual men	Azithromycin	Ciprofloxacin	Penicillin	Tetracycline
11 or more	1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Not reported	30	2 (6.7%)	10 (33.3%)	5 (16.7%)	17 (56.7%)
Sex abroad (past 3 months)					
No	209	32 (15.3%)	69 (33.0%)	20 (9.6%)	138 (66.0%)
Yes	4	0 (0.0%)	3 (75.0%)	2 (50.0%)	3 (75.0%)
Not reported	30	2 (6.7%)	10 (33.3%)	5 (16.7%)	17 (56.7%)

Notes: No isolates were resistant to ceftriaxone or spectinomycin in the 2021 sentinel surveillance collection.

Data not included for cefixime due to small numbers (n=2).

Percentages are row %.

Table 8. Antimicrobial resistance by individuals' characteristics for women, sentinel surveillance system, 2021

	Total women	Azithromycin	Ciprofloxacin	Penicillin	Tetracycline
Resistant isolates	200	15	44	11	86
Age group (years)					
15 to 19	32	0 (0.0%)	4 (12.5%)	0 (0.0%)	11 (34.4%)
20 to 24	70	3 (4.3%)	11 (15.7%)	4 (5.7%)	31 (44.3%)
25 to 34	65	6 (9.2%)	16 (24.6%)	4 (6.2%)	25 (38.5%)
35 to 44	21	4 (19.0%)	8 (38.1%)	3 (14.3%)	13 (61.9%)
45 or more	12	2 (16.7%)	5 (41.7%)	0 (0.0%)	6 (50.0%)
Ethnicity					
White	90	5 (5.6%)	22 (24.4%)	5 (5.6%)	42 (46.7%)
Black Caribbean	14	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (35.7%)
Black African	10	1 (10.0%)	4 (40.0%)	1 (10.0%)	6 (60.0%)
Black Other	3	0 (0.0%)	2 (66.7%)	0 (0.0%)	1 (33.3%)
Asian (including Chinese)	12	2 (16.7%)	5 (41.7%)	3 (25.0%)	7 (58.3%)
Other Ethnic Group	3	0 (0.0%)	2 (66.7%)	0 (0.0%)	2 (66.7%)
Mixed Ethnic Group	17	2 (11.8%)	0 (0.0%)	1 (5.9%)	5 (29.4%)
Not reported	51	5 (9.8%)	9 (17.6%)	1 (2.0%)	18 (35.3%)
Residence					

	Total women	Azithromycin	Ciprofloxacin	Penicillin	Tetracycline
Outside London	149	10 (6.7%)	23 (15.4%)	8 (5.4%)	58 (38.9%)
London	51	5 (9.8%)	21 (41.2%)	3 (5.9%)	28 (54.9%)
HIV status					
Negative	169	13 (7.7%)	39 (23.1%)	11 (6.5%)	76 (45.0%)
Positive	3	1 (33.3%)	1 (33.3%)	0 (0.0%)	2 (66.7%)
Not reported	28	1 (3.6%)	4 (14.3%)	0 (0.0%)	8 (28.6%)
Symptoms					
No discharge and or dysuria	84	8 (9.5%)	20 (23.8%)	5 (6.0%)	45 (53.6%)
Discharge and or dysuria	115	6 (5.2%)	24 (20.9%)	6 (5.2%)	40 (34.8%)
Previously diagnosed with gonorrhoea					
No	110	10 (9.1%)	27 (24.5%)	5 (4.5%)	50 (45.5%)
Yes	21	2 (9.5%)	4 (19.0%)	1 (4.8%)	11 (52.4%)
Not reported	69	3 (4.3%)	13 (18.8%)	5 (7.2%)	25 (36.2%)
Total sexual partners (past 3 months)					
None to one	113	8 (7.1%)	20 (17.7%)	7 (6.2%)	45 (39.8%)
2 to 5	54	3 (5.6%)	12 (22.2%)	2 (3.7%)	23 (42.6%)
6 to 10	2	0 (0.0%)	1 (50.0%)	0 (0.0%)	1 (50.0%)

	Total women	Azithromycin	Ciprofloxacin	Penicillin	Tetracycline
11 or more	2	0 (0.0%)	1 (50.0%)	0 (0.0%)	2 (100.0%)
Not reported	29	4 (13.8%)	10 (34.5%)	2 (6.9%)	15 (51.7%)
Sex abroad (past 3 months)					
No	168	11 (6.5%)	33 (19.6%)	9 (5.4%)	70 (41.7%)
Yes	3	0 (0.0%)	1 (33.3%)	0 (0.0%)	1 (33.3%)
Not reported	29	4 (13.8%)	10 (34.5%)	2 (6.9%)	15 (51.7%)

Notes: No isolates were resistant to ceftriaxone or spectinomycin in the 2021 sentinel surveillance collection.

Data not included for cefixime due to small numbers (n=2).

Percentages are row %.

3. Evaluation of the representativeness of the GRASP sentinel surveillance programme, 2015 to 2018

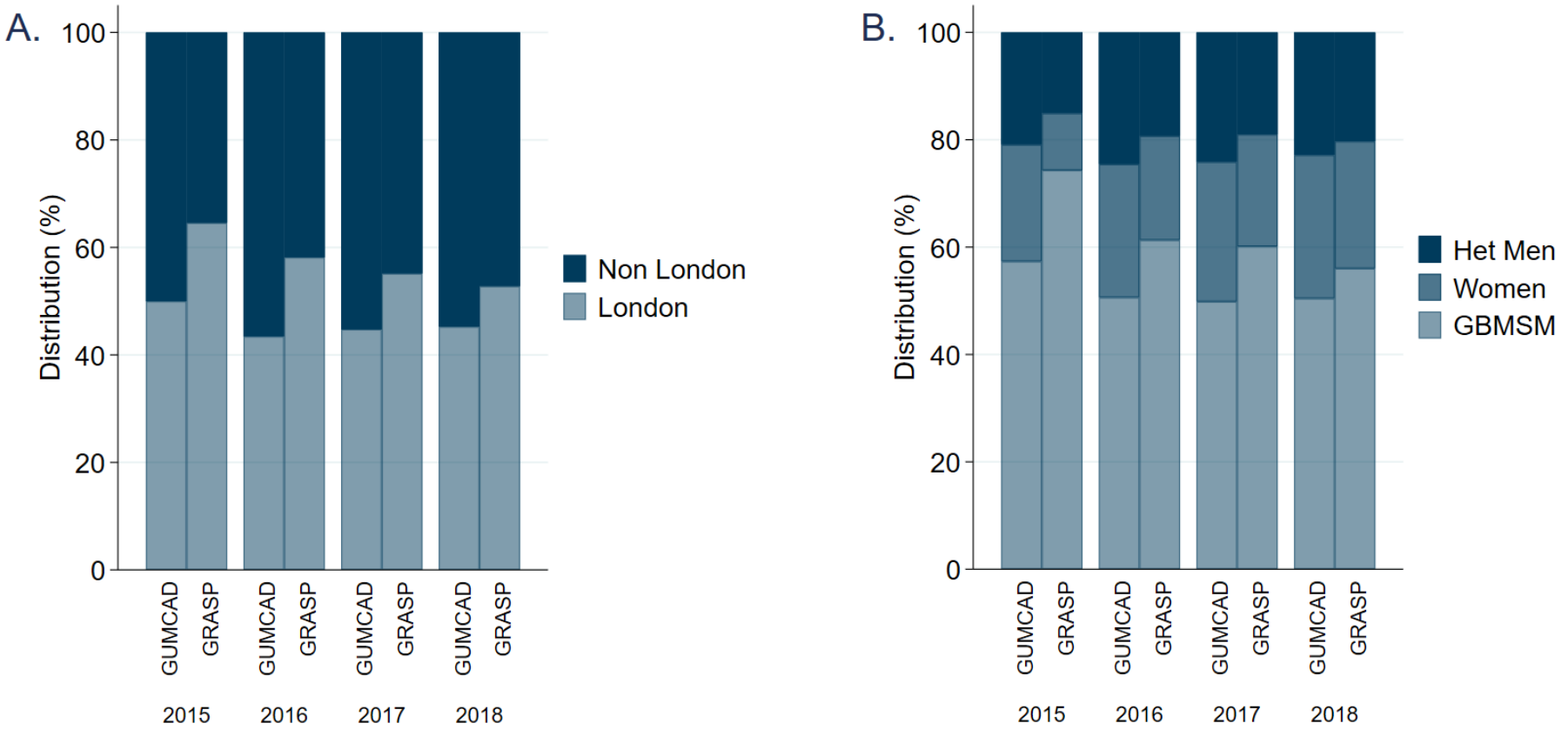
The sexual health services (SHSs) in the GRASP sentinel surveillance programme were purposefully selected to provide wide geographical representation and inclusion of *N. gonorrhoeae* isolates from key populations with higher diagnosis rates of gonorrhoea. Patient-level characteristics, such as gender, sexual orientation, HIV status, and area of residence, may be used to approximate memberships of discrete sexual networks (11). If particular sexual networks are over- or under-represented in the GRASP sentinel sample, the proportion of isolates with resistance may be biased. This analysis aimed to determine how representative the gonorrhoea diagnoses in the GRASP sentinel sample were of gonorrhoea diagnoses at all SHSs in England, and to present adjusted estimates of the proportion of isolates with resistance to therapeutically relevant antibiotics.

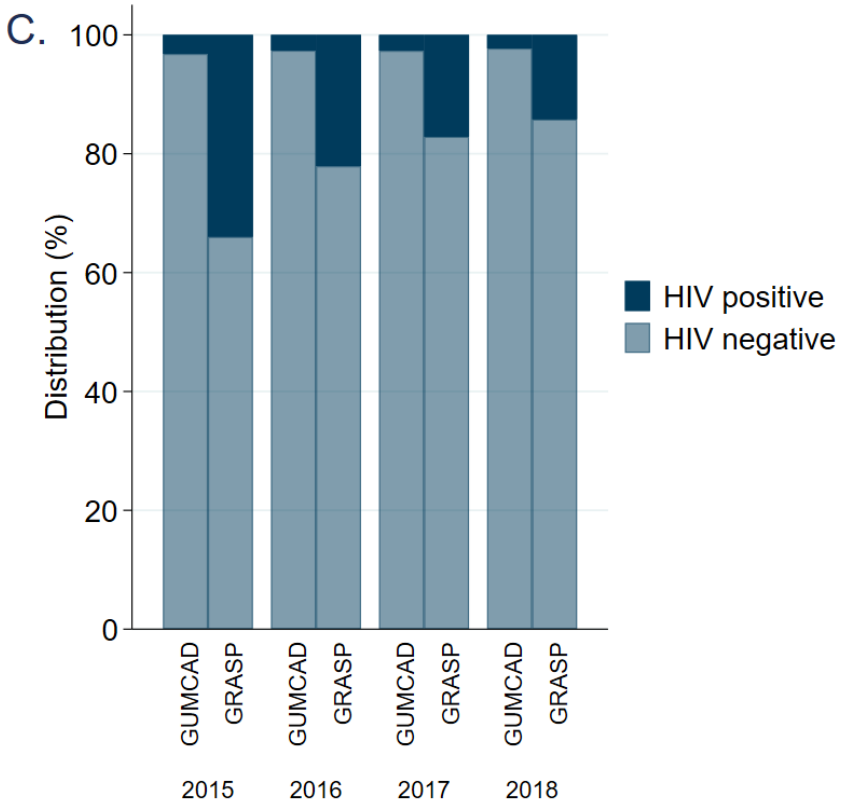
Representativeness of the GRASP sentinel sample

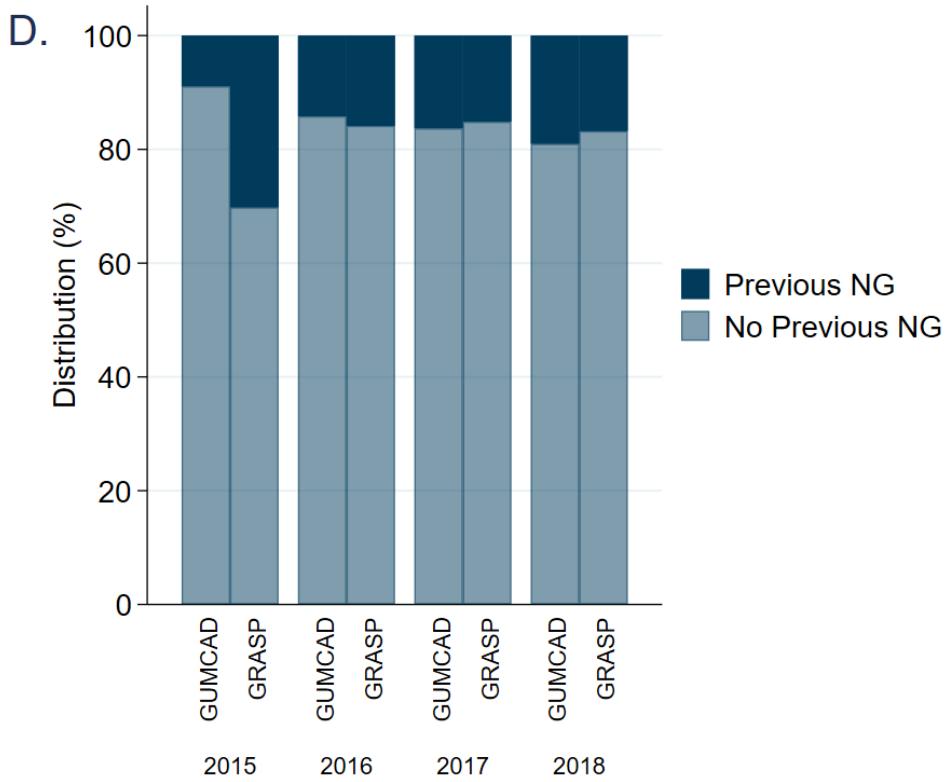
A descriptive analysis was conducted to determine the representativeness of the GRASP sentinel sample in comparison to all gonorrhoea diagnoses at all SHSs in England between 2015 and 2018. Data for the latter was obtained from the GUMCAD STI surveillance system, a data set of all STI tests and diagnoses at SHSs in England; as this does not include data from SHSs in Wales, data from Welsh GRASP clinics was excluded from the analyses. The comparison was limited to variables captured by both GRASP and GUMCAD: age, ethnicity, gender, HIV status, sexual orientation, region of patient residence, and previous gonorrhoea diagnosis (in the past 12 months). Evidence of sampling bias was defined using a pragmatic threshold of a consistent unidirectional difference of 5% or more in the point estimates of each variable in GRASP and GUMCAD between 2015 and 2018.

Gonorrhoea diagnoses among gay, bisexual, and other men who have sex with men (GBMSM), those living in London, and people living with HIV (PLHIV) were consistently overrepresented by at least 5% in GRASP SHSs relative to all SHSs (Figures 14a, 14b, 14c and 15).

Figure 14. Distribution (%) of subgroups in GRASP and GUMCAD between 2015 and 2018 by a) residence, b) gender and sexual orientation (Het = Heterosexual), c) HIV status, d) previous gonorrhoea (NG) diagnosis in the past year, and e) ethnicity




C.
100
80
60
40
20
0
Distribution (%)
HIV positive
HIV negative
GUMCAD
GRASP
2015
2016
2017
2018


D.
100
80
60
40
20
0
Distribution (%)
Previous NG
No Previous NG
GUMCAD
GRASP
2015
2016
2017
2018

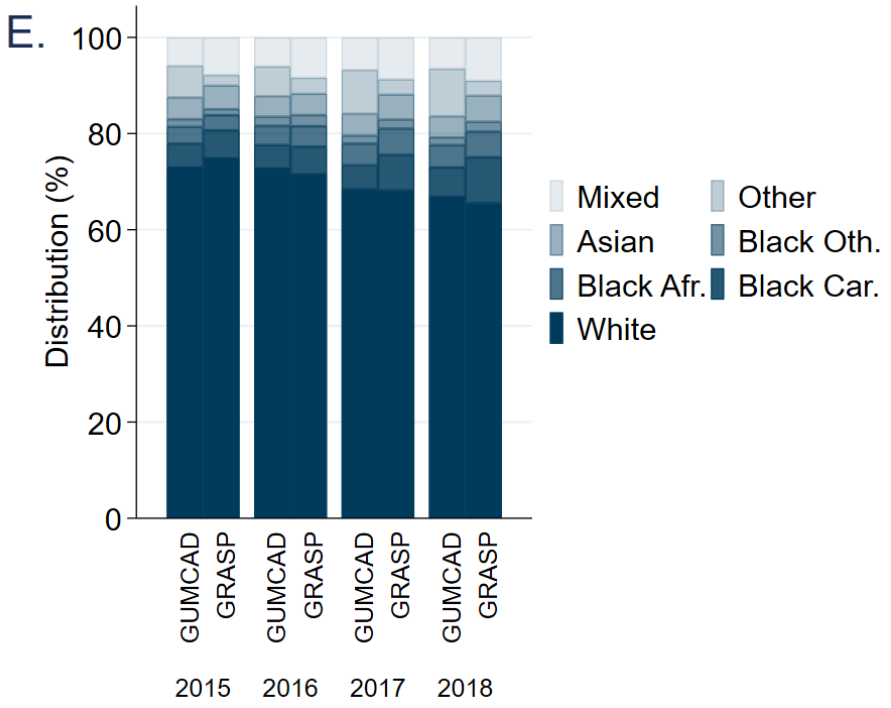
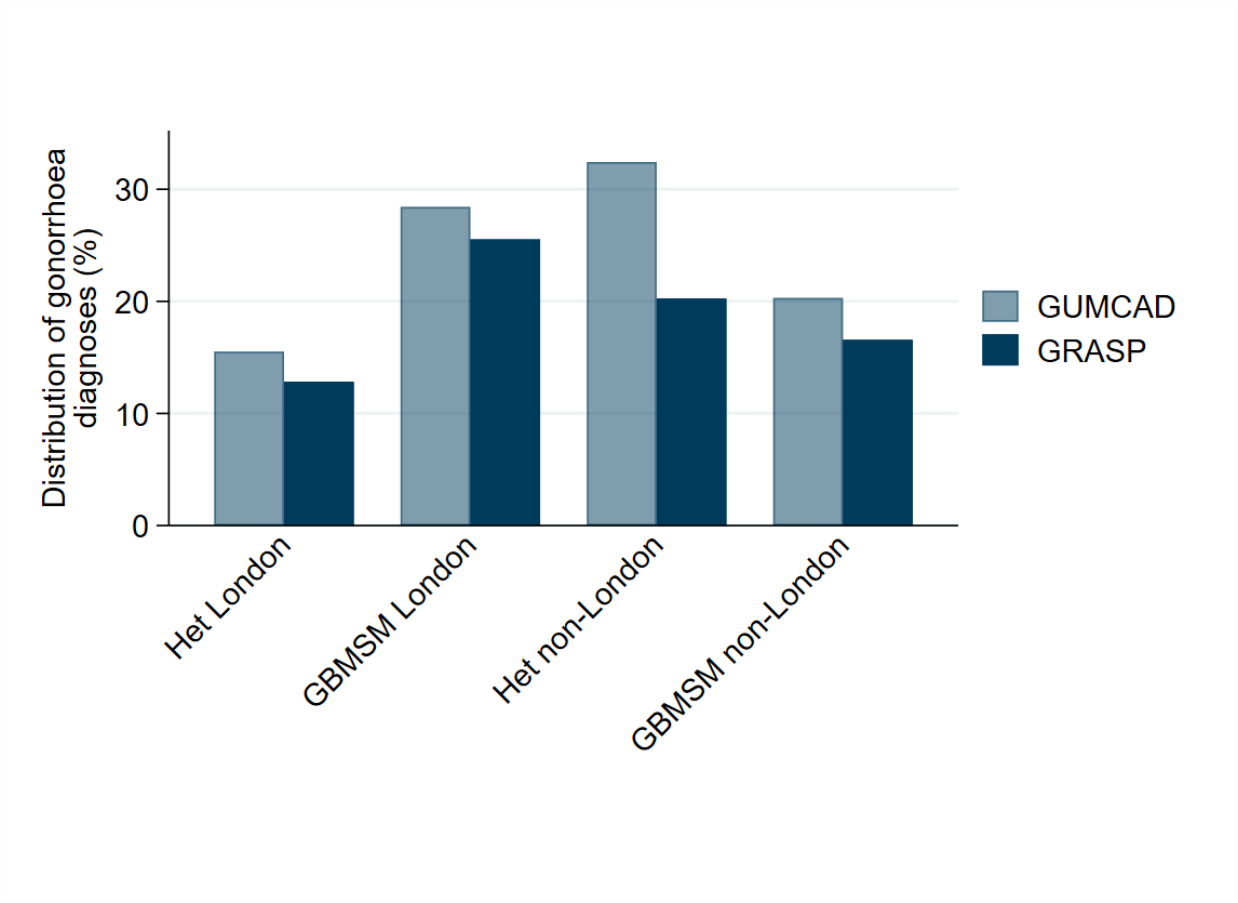
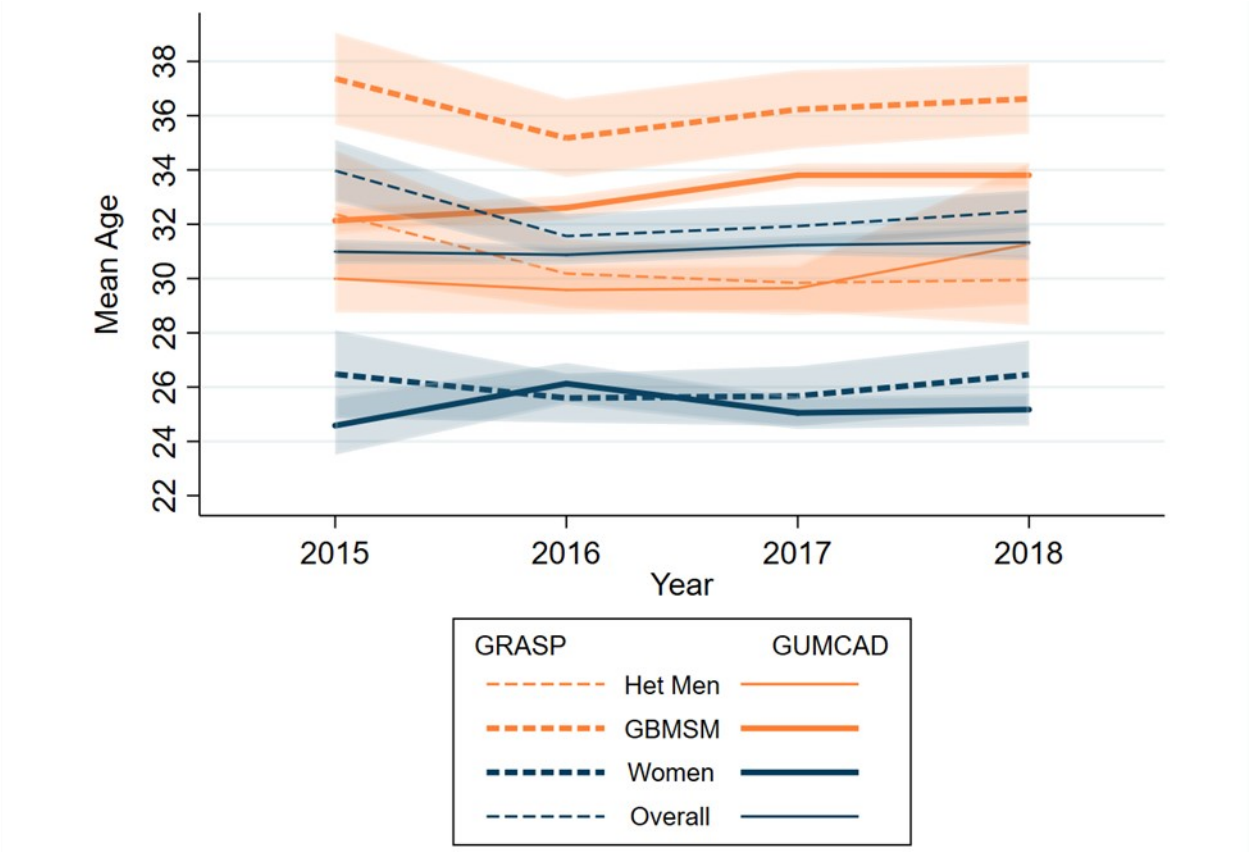


Figure 15. Distribution of gonorrhoea diagnoses by sexual orientation and residence inside or outside of London between GUMCAD and GRASP in 2018. (Het = Heterosexual men and all women)



Overall, there was little variation in ethnicity and the proportion of patients with a previous gonorrhoea diagnosis in the past year between GRASP SHSs and all SHSs (Figure 14d and 14e). Stratification by sexual orientation and gender showed that there was no evidence of differences in the mean ages of heterosexual men and women between GRASP SHSs and all SHSs. However, GBMSM in GRASP had a lower average age than those diagnosed with gonorrhoea at all SHSs (Figure 16).

Figure 16: Mean age of gonorrhoea diagnoses between 2015 and 2018 in GRASP and GUMCAD (all SHSs). 95% confidence intervals shown (shaded); Het Men = Heterosexual men



Comparison of the proportion of *N. gonorrhoea* with resistance using weighted estimates

To determine the effect of sampling bias on the proportion of isolates with resistance determined from the GRASP sentinel sample, weighted estimates were generated accounting for variables considered associated with sexual networks that met the sampling bias criteria. Sampling weights were produced by patient residence (inside or outside of London) and gender and sexual orientation (GBMSM or all women and heterosexual men) for each year between 2015 and 2018 (Equation 1a). HIV status was not included due to data sparsity. The sampling weights were subsequently applied to generate an overall weighted estimate of the proportion of isolates with resistance for each antimicrobial (Equation 1b). Ceftriaxone and spectinomycin were not included as no resistant isolates were reported in GRASP between 2015 and 2018.

Equation 1. (a) Calculation of sample weights (w_i). (b) Calculation of the overall weighted AMR prevalence (W)

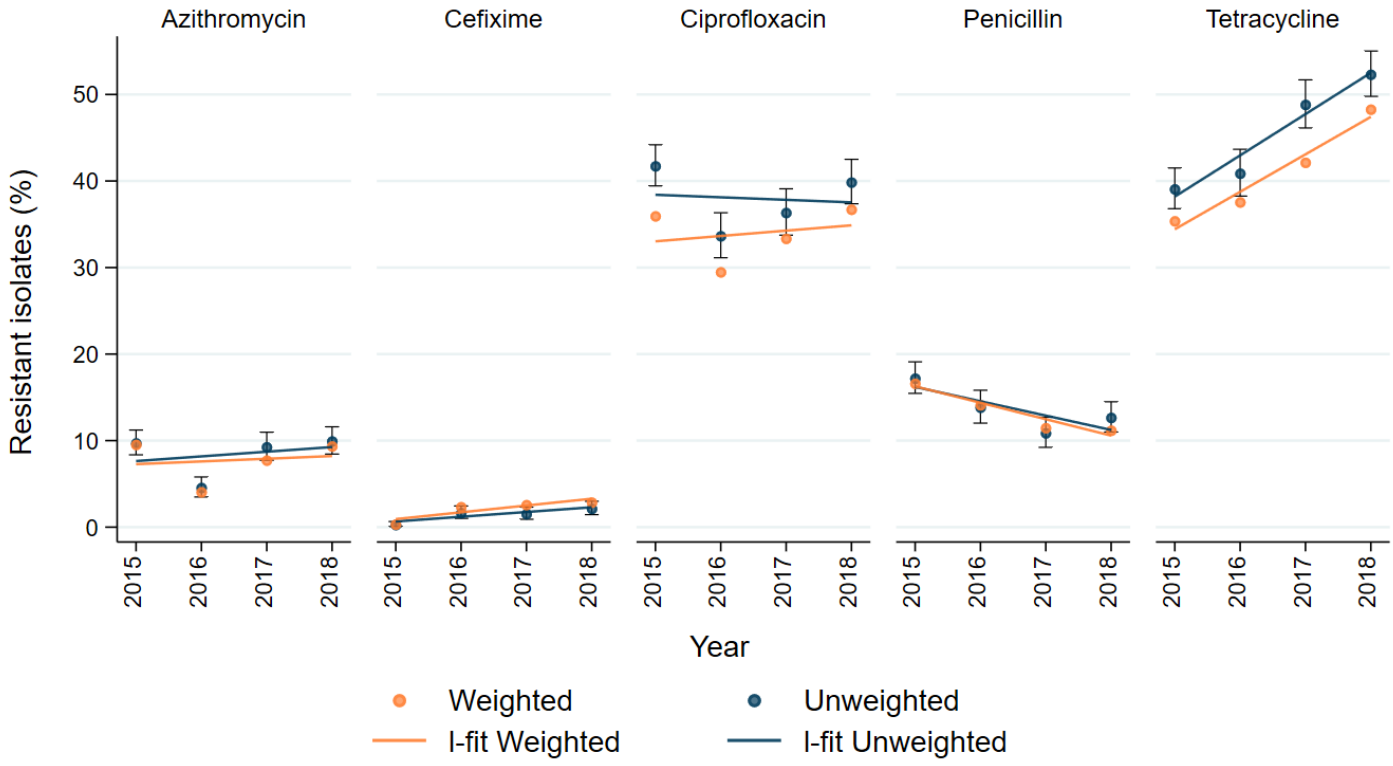
N_{pop}: number of NG diagnoses in all SHSs in one year; N_{sub}: number of NG diagnoses in the substratum in GUMCAD; n_{sample}: number of GRASP isolates in one year; n_{sub}: number of GRASP isolates in the substratum; X_i: substratum AMR prevalence; w_i sampling weight.

$$a)\ w_i = \left(\frac{N_{sub}}{N_{pop}}\right) \Big/ \left(\frac{n_{sub}}{n_{sample}}\right)$$

$$b)\ W = \frac{\sum_{i=1}^{n} w_i X_i}{\sum_{i=1}^{n} w_i}$$

The weighted estimates revealed a lower proportion of isolates with resistance relative to the unweighted data in most cases; ciprofloxacin and tetracycline showed the largest discrepancies between weighted and unweighted proportion of resistant isolates across time (Figure 17). However, the weighted estimates of the proportion of isolates resistant to cefixime were consistently higher relative to the unweighted data and thus closer to, but not exceeding, the 5% threshold (≥5% of infections resistant to the first-line therapy) at which the WHO recommends that first-line monotherapy guidelines should be changed. Notably, no credible interval has been provided for the weighted estimates, a limitation to this analysis.

Figure 17. Weighted and unweighted gonorrhoea AMR prevalence estimates for azithromycin, cefixime, ciprofloxacin, penicillin and tetracycline between 2015 and 2018



Linear regression lines (l-fit) fitted per antimicrobial; unweighted prevalence estimates presented with 95% confidence intervals

Summary

We determined the representativeness of the GRASP sample by comparing the characteristics of people diagnosed with gonorrhoea by SHSs participating in the GRASP sentinel surveillance programme to those diagnosed with gonorrhoea at all SHSs. Between 2015 and 2018, GRASP overrepresented diagnoses among GBMSM, PLHIV and those resident in London. Weighted estimates of the proportion of resistance were generally lower than the unweighted data; the exception was cefixime but the weighted estimate of proportion resistant to this antibiotic did not meet the 5% WHO threshold. The higher weighted estimates for cefixime resistance may also translate to higher ceftriaxone estimates due to similar resistance mechanisms in some strains. This analysis included data until 2018 and precedes the disruption to SHS service delivery during the first 18 months of the COVID-19 pandemic in 2020 and 2021. We concluded that the evidence was not strong enough to justify a change to the current GRASP protocol. Such changes may have included resampling GRASP SHSs or routinely deriving weighted resistance estimates. Ongoing, periodic evaluations of the representativeness of the GRASP sentinel surveillance system should be conducted to reassess the extent and impact of sampling bias on the trends in resistance reported through GRASP.

4. Ethnic categories

The ethnic categories used in this report are as specified by the Office for National Statistics (ONS). Data is presented by disaggregated ethnic groups among people of Black ethnicity to highlight the variability in rates among the ethnic group experiencing the highest rates of the most commonly diagnosed STIs. People of Asian, Mixed, Other and White ethnicity are presented as aggregated ethnic groups for comparison (12). The ethnicities included in each of the aggregated ethnic groups are presented below.

List of ethnicities by ethnic category

White:
- British
- Irish
- any other White background

Mixed:
- White and Black Caribbean
- White and Black African
- White and Asian
- any other mixed background

Asian or Asian British:
- Indian
- Pakistani
- Bangladeshi
- Chinese
- any other Asian background

Black or Black British:
- Caribbean
- African
- any other Black background

Other ethnic groups:
- any other ethnic group

References

1. Fifer H, Saunders J, Soni S, Sadiq ST, and FitzGerald M. '2018 UK national guideline for the management of infection with Neisseria gonorrhoeae'. International Journal of STD and AIDS 2020: volume 31 issue 1, pages 4 to 15
2. UK Health Security Agency. 'Sexually transmitted infections and screening for chlamydia in England: 2021 report' (viewed on 25 October 2022)
3. UK Health Security Agency. 'GUMCAD STI Surveillance System' (viewed on 25 October 2022)
4. UK Health Security Agency. 'Gonococcal resistance to antimicrobials surveillance programme (GRASP) protocol' (viewed on 25 October 2022)
5. UK Health Security Agency. 'Notifiable diseases and causative organisms: how to report' (viewed on 25 October 2022)
6. European Committee on Antimicrobial Susceptibility Testing (EUCAST). 'Clinical breakpoints – breakpoints and guidance' (viewed on 25 October 2022)
7. UK Health Security Agency. 'Surveillance of antimicrobials resistance in Neisseria gonorrhoeae, 2016' (accessed 25 October 2022)
8. Unemo M, Lahra MM, Escher M, Eremin S, Cole MJ, Galarza P and others. 'WHO global antimicrobial resistance surveillance for Neisseria gonorrhoeae 2017-18: a retrospective observational study' Lancet Microbe 2021: volume 2 issue 11, pages e627 to e36
9. Merrick R, Cole M, Pitt R, Enayat Q, Ivanov Z, Day M and others. 'Antimicrobial-resistant gonorrhoea: the national public health response, England, 2013 to 2020' Eurosurveillance 2022: volume 27 issue 40
10. Pitt R, Merrick R, Donaldson H, Rayment M, Day M, Cole M and others. 'P91 Increasing tetracycline resistance in Neisseria gonorrhoeae in England: investigating possible clinic-epidemiological associations' Sexually Transmitted Infections 2022: volume 98, pages A65 to A66.11
11. Town K, Bolt H, Croxford S, Cole M, Harris S, Field N and others. '*Neisseria gonorrhoeae* molecular typing for understanding sexual networks and antimicrobial resistance transmission: A systematic review' Journal of Infection 2018: volume 76 issue 6, pages 507 to 514
12. '2001 to 2011 Census in England and Wales Questionnaire Comparability' December 2012, Office for National Statistics (viewed on 25 October 2022)

Acknowledgements

GRASP would like to thank the collaborating centres and the advisory group for their continued support, SHSs for the prompt submission of clinical data and laboratories for sending isolates to the AMRSTI national reference laboratory at the UKHSA, Colindale. GRASP would also like to thank Oliver Geffen Obregon and Katy Town for their contribution to Appendix 3 (Evaluation of the representativeness of the GRASP sentinel surveillance programme, 2015 to 2018).

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Published: November 2022
Publishing reference: GOV-13627