

***Neisseria gonorrhoeae* antimicrobial resistance surveillance report of Belgium – 2024**



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1. Rationale – Background

The Institute of Tropical Medicine (ITM) is the National Reference Centre of Sexually Transmitted Infections (NRC-STI) of Belgium since 2010. Besides chlamydia, gonorrhoea is the second most detected bacterial STI in Belgium.¹ However, more worrying is the fact that *Neisseria gonorrhoeae*, the causative agent of gonorrhoea, is evolving into a superbug. It acquired resistance to all classes of antimicrobials used for treating infections.² Given the extraordinary capacity of *N. gonorrhoeae* to acquire resistance mechanisms, it is likely that *N. gonorrhoeae* may become untreatable in the not-too-distant future. As such, an important surveillance activity of the NRC-STI is the monitoring of antimicrobial resistance of *N. gonorrhoeae* to anticipate its resistance to specific antimicrobials. The results may lead to an adaptation of the treatment guidelines when necessary. Here, we present the data from 2024 along with historical data spanning the past decade up to 2015.

2. Methods

Laboratories from all districts in Belgium voluntarily send presumptive *N. gonorrhoeae* isolates to the NRC-STI. At the NRC-STI, confirmation of the identification of *N. gonorrhoeae* is performed by Gram stain, oxidase test, and confirmation via molecular detection or MALDI-TOF MS. When *N. gonorrhoeae* is confirmed, additional antimicrobial susceptibility testing is performed to determine the minimal inhibitory concentration or MIC to a certain antibiotic. The MIC allows interpretation of resistance to a specific antibiotic based on breakpoints available in the EUCAST guidelines version 14.0. Since 2023, the breakpoint of tetracycline was adapted from >1mg/L to >0.5mg/L. **Table 1** lists the antibiotics tested, the method, the resistance breakpoints, and the frequency of antimicrobial susceptibility testing (AST). Penicillin, Spectinomycin, and Gentamycin are only performed every three years (snapshot years). Multidrug resistance is defined to be resistant to azithromycin, ciprofloxacin, and ceftriaxone. Resistance to azithromycin can be low-level (LL) resistant (MIC 1.5-3 mg/L), intermediate-level (IL) resistant (MIC 4-192 mg/L), or high-level resistant (MIC ≥256 mg/L).³

Table 1: Antibiotic susceptibility testing of *N. gonorrhoeae* at the NRC-STI

Antibiotic	Test method	Resistance breakpoint (EUCAST)	AST frequency
Azithromycin	Etest (Biomerieux, France)	>1 mg/L	Yearly
Ciprofloxacin	Etest (Biomerieux, France)	> 0.064 mg/L	Yearly
Ceftriaxone	Etest (Biomerieux, France)	>0.125 mg/L	Yearly
Cefixime	Agar dilution method	>0.125 mg/L	Yearly*
Penicillin	Agar dilution method	>1 mg/L	Every three years - 2025
Tetracycline	Agar dilution method	>0.5 mg/L	Yearly*
Spectinomycin	Agar dilution method	> 64 mg/L	Every three years - 2025
Gentamicin	Agar dilution method	No breakpoint defined	Every three years - 2025

*MIC of cefixime and tetracycline is only tested on a maximum of 200 isolates collected between September and December as required by the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP). AST: Antimicrobial susceptibility testing

3. Results

3.1 Characteristics of *N. gonorrhoeae* isolates

In 2024, the NRC-STI received 935 samples originating from all Belgian regions (Flanders, Brussels, and Wallonia). However, 4.6% (43/935) of the isolates did not survive the transport, three isolates were contaminated (0.3%), and three isolates (0.3%) were not confirmed to be *N. gonorrhoeae*, which brings the number of *N. gonorrhoeae* isolates to 886. Annex one lists the number of *N. gonorrhoeae* isolates by the 67 different laboratories. After review, 12 isolates were found to be duplicates (sampling dates within one month in the same individual) and were not included in the analysis (n=874). The increasing trend that was noted since 2023 is continuing in 2024. Since the start of our surveillance activities, this is the highest number of isolates confirmed, with an observed increase of 7% compared to 2023 (n=874) (**Figure 1**). The isolates were detected in 848 individuals, and 24 individuals had more than one infection in 2024. In 2024, the majority of isolates originated from Flanders (719/874; 82.3%), with fewer from Wallonia (112/874; 12.8%) and Brussels (43/874; 4.9%), reflecting the same regional distribution observed in 2023 (**Figure 2**).



Figure 1: Number of *N. gonorrhoeae* isolates identified by NRC-STI over the years (2014-2024).

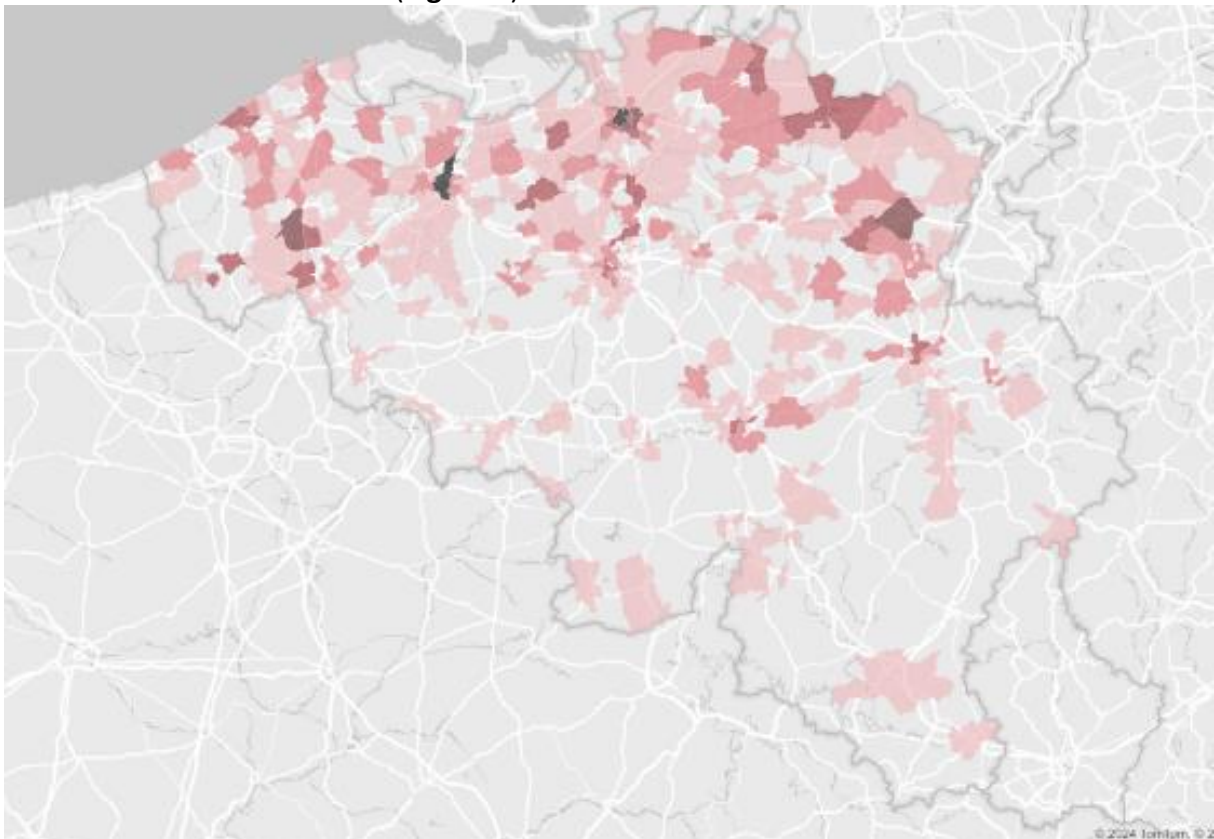


Figure 2: Geographical location of identified gonococcal isolates. The shading intensity indicates the number of isolates, ranging from pink for 1-3 isolates to very dark red for 20-30 isolates. Black areas represent more than 30 gonococcal isolates).

The majority of the samples was taken from men (709/874; 81.1%). Almost one-fifth of the isolates were detected among women (164/874; 18.8%), and one was detected in a trans woman. **Figure 3** shows the number of isolates received per semester from 2014 to 2024, stratified by sexual transmission. The number of isolates from women did not increase since the previous year (168 in 2023; 164 in 2024).

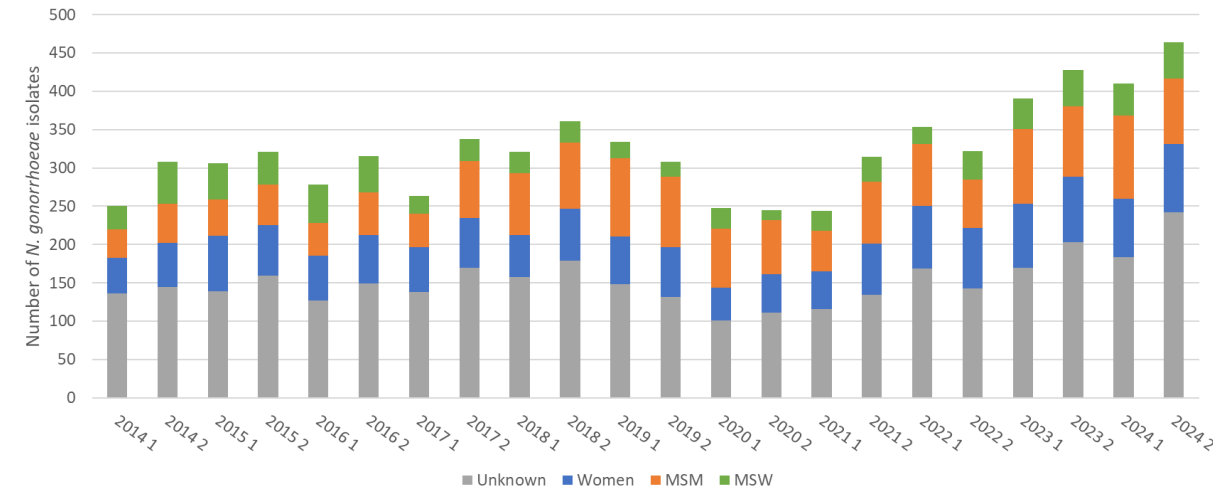


Figure 3: Percentage of *N. gonorrhoeae* isolates received by the NRC-STI from 2014 to 2024 per semester, stratified by sexual transmission. MSM: Men who have sex with men and including all anorectal male samples. MSW: Men who have sex with women. Unknown: Unknown gender or men with unknown sex of sex partners

Table 1 presents the locations of infection for *N. gonorrhoeae* isolates in 2024. Most isolates originated from the urogenital anatomical sites, followed by the anorectum.

Table 1: Infection site of the *N. gonorrhoeae* isolates of 2024

Body site	Female (n=164)		Male (n=709)		Trans woman (n=1)		Total (n=874)	
	N	%	N	%	N	%	N	%
Urogenital	157	95.7	613	86.5	1	100	771	88.2
Anorectal	2	1.2	52	7.3	0	0	54	6.2
Throat	0	0	1	0.1	0	0	1	0.1
Pooled Sample (urine, anorectal & throat)	0	0	23	3.2	0	0	23	2.6
Eye	2	1.2	3	0.4	0	0	5	0.6
Articular origin	1	0.6	9	1.3	0	0	10	1.1
Blood	0	0.0	2	0.3	0	0	2	0.3
Other	2	1.2	2	0.3	0	0	4	0.4
Unknown	0	0.0	4	0.6	0	0	4	0.5

Other includes: 1 cerebrospinal fluid, 1 ascites fluid, and two pus from wounds (hand and unknown)

Interestingly, 16 isolates were associated with disseminated gonococcal infection or DGI, a rare condition caused by untreated *N. gonorrhoeae* infections (16/874; 1.8%).

3.2 Disseminated gonococcal infections

DGI is a rare complication, occurring in approximately 0.5–3% of untreated gonorrhoea cases. It is characterised by bacteraemia, often accompanied by arthritis or skin lesions, and may infrequently lead to more severe manifestations such as endocarditis and meningitis.^{4,5} **Figure**

4 shows the number of *N. gonorrhoeae* isolates associated with DGI over time. Between 2013 and 2022, an average of four *N. gonorrhoeae* isolates from suspected DGI cases were reported annually (range: 0–6). Since 2023, a marked increase in DGI cases has been observed, prompting the implementation of additional genomic surveillance. Whole genome sequencing (WGS) of 2023 isolates revealed that most were classified as PorB1a, carried multiple resistance mechanisms, and predominantly belonged to sequence types ST-1583 or ST-1588 (8 out of 14 isolates).⁶ Enhanced surveillance is ongoing for all received DGI-associated isolates, including the systematic collection of additional clinical data to improve DGI characterisation.

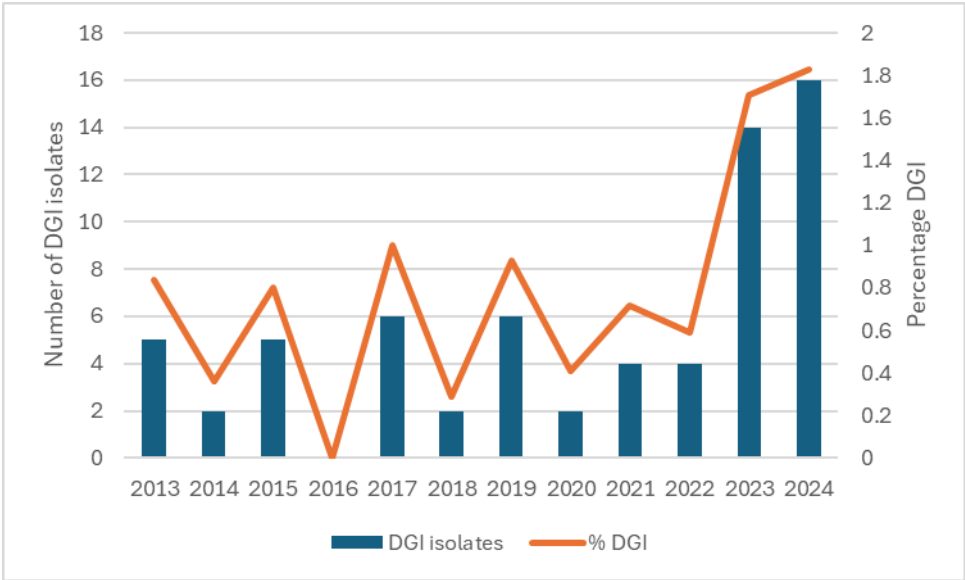


Figure 4: Number and % of *N. gonorrhoeae* isolates associated with disseminated gonococcal infection (DGI) from 2013 to 2024

3.3 Antimicrobial resistance of *N. gonorrhoeae*

Table 2 lists the MICs of the *N. gonorrhoeae* isolates of 2024 for the following antibiotics: azithromycin, ciprofloxacin, ceftriaxone, cefixime, and tetracycline.

Table 2: Minimal Inhibitory Concentration (MIC) and final interpretation of the *N. gonorrhoeae* isolates 2023

	S		MIC limit value mg/L	I		MIC limit value mg/L	R		MIC limit value mg/L
	N	%		N	%		N	%	
Azithromycin (n=874)	661	75.6	≤ 1	-	-	-	213	24.4	> 1
Ciprofloxacin (n=874)	276	31.6	≤ 0.032	8	0.9	0.047- 0.064	590	67.5	> 0.064
Ceftriaxone (n=874)	874	100	≤ 0.125	-	-	-	-	-	> 0.125
Cefixime (n=199)	198	99.5	≤ 0.125	-	-	-	1	0.5	> 0.125
Tetracycline (n=197)	29	14.6	≤ 0.5	-	-	-	170	85.4	> 0.5

MIC Breakpoints according to EUCAST guidelines. S: Susceptible; I: Susceptible, Increased Exposure; R: Resistant

Figures 5 shows the antimicrobial resistance of *N. gonorrhoeae* to the different antibiotics over ten years.

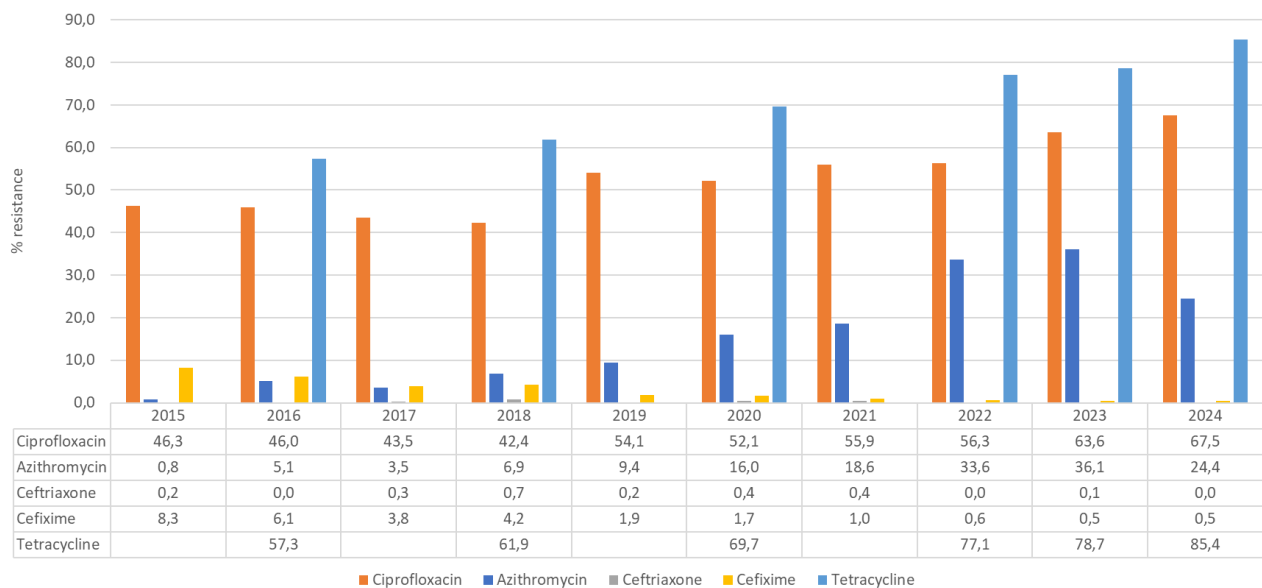


Figure 5: Antimicrobial resistance of *N. gonorrhoeae* to ciprofloxacin, azithromycin, ceftriaxone, cefixime, and tetracycline over 10 years (2015-2024) in Belgium.

3.3.1 Azithromycin resistance of *N. gonorrhoeae*

After a decade-long increase in azithromycin resistance, we are now observing a decline in *N. gonorrhoeae* resistance to azithromycin (24.4% in 2024 vs 36.1% in 2023). Although one in four isolates remains resistant, this trend is encouraging. Interestingly, the decline is seen across all populations, with the most pronounced decrease among MSM. The discontinued use of azithromycin to treat *N. gonorrhoeae* and other STIs may have contributed to the overall reduction in resistance (Figure 6).

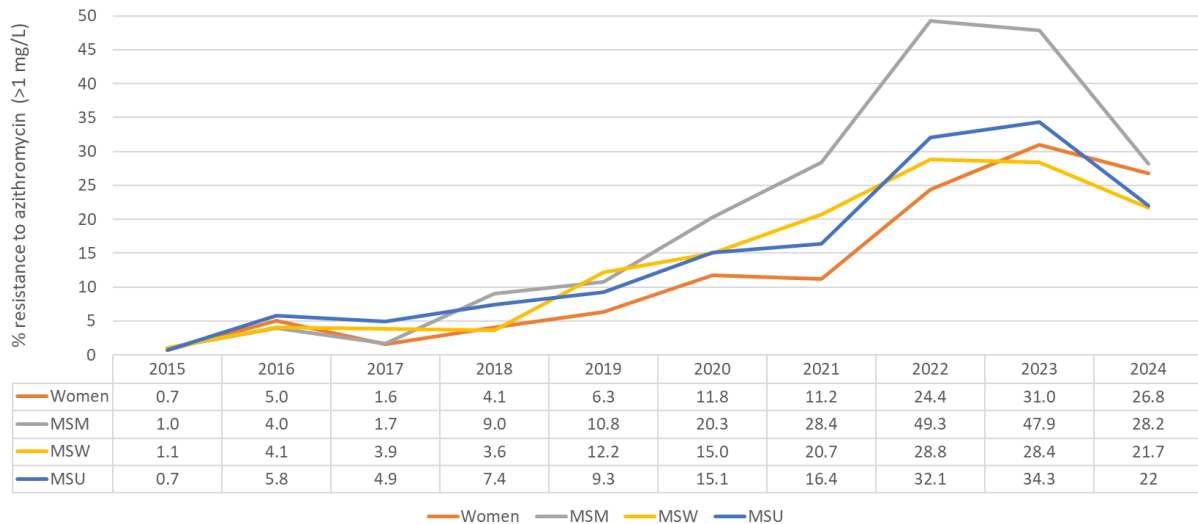


Figure 6: Resistance to azithromycin of *N. gonorrhoeae* stratified by gender and sexual transmission over 10 years. MSM: Men who have sex with men. MSW: Men who have sex with women. MSU: Unknown gender or men with unknown gender of sex partners

When stratifying by azithromycin MIC, we observe an increase in isolates that are highly susceptible (≤ 0.125 mg/L) compared to 2023. This trend is most pronounced among MSM

(Figure 7). Overall, resistant isolates were predominantly low-level resistant (199/213; 93.4%; MIC 1.5 – 3 mg/L), with only one isolate showing high-level resistance (≥ 256 mg/L). This high-level resistant isolate was identified in a man who reported sex with men and presented with urethritis. The isolate remained susceptible to both ciprofloxacin and ceftriaxone.

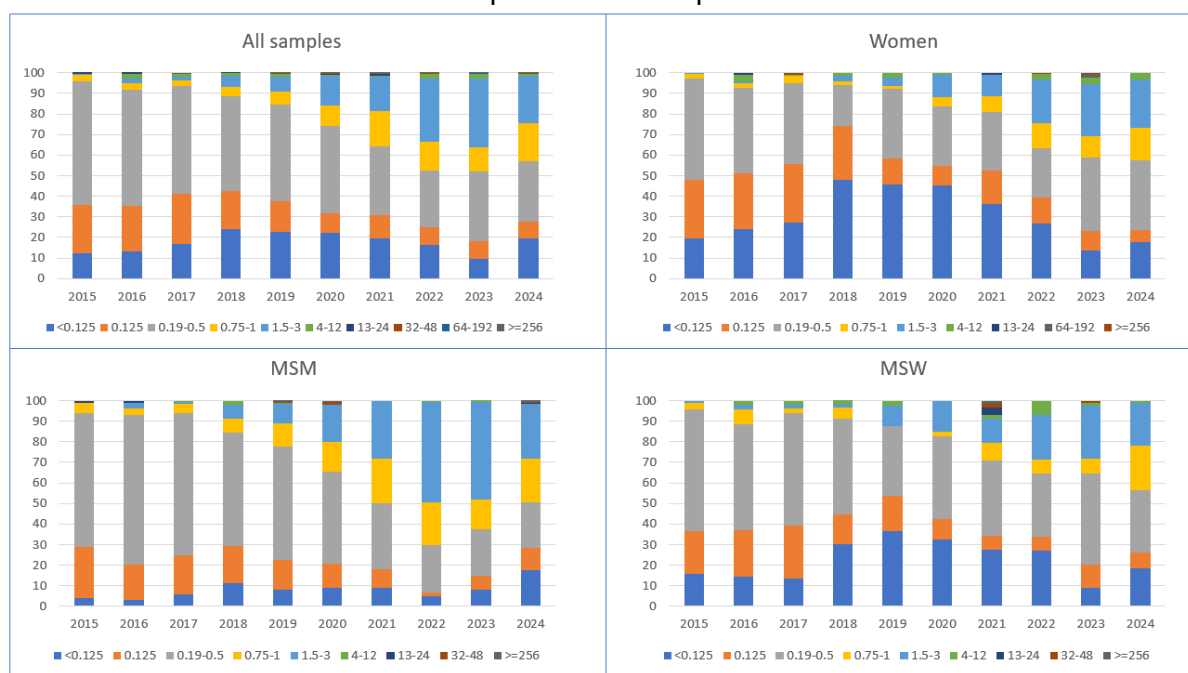


Figure 7: Minimal inhibitory concentration (MIC) distribution (mg/L) for azithromycin over ten years for all *N. gonorrhoeae* isolates and stratified per sexual transmission. MSM: Men who have sex with men. MSW: Men who have sex with women

3.3.2 Ciprofloxacin resistance of *N. gonorrhoeae*

Resistance to ciprofloxacin has continued to rise since 2021, with two out of three isolates showing resistance. When stratified by mode of sexual transmission, resistance approaches 70% among men, regardless of sexual orientation. Although resistance among isolates from female origin is lower (60%), this group shows the largest increase since 2021, and the only statistically significant one (Figure 8). The ciprofloxacin MIC distribution over time, stratified by population group, is shown in Figure 9.

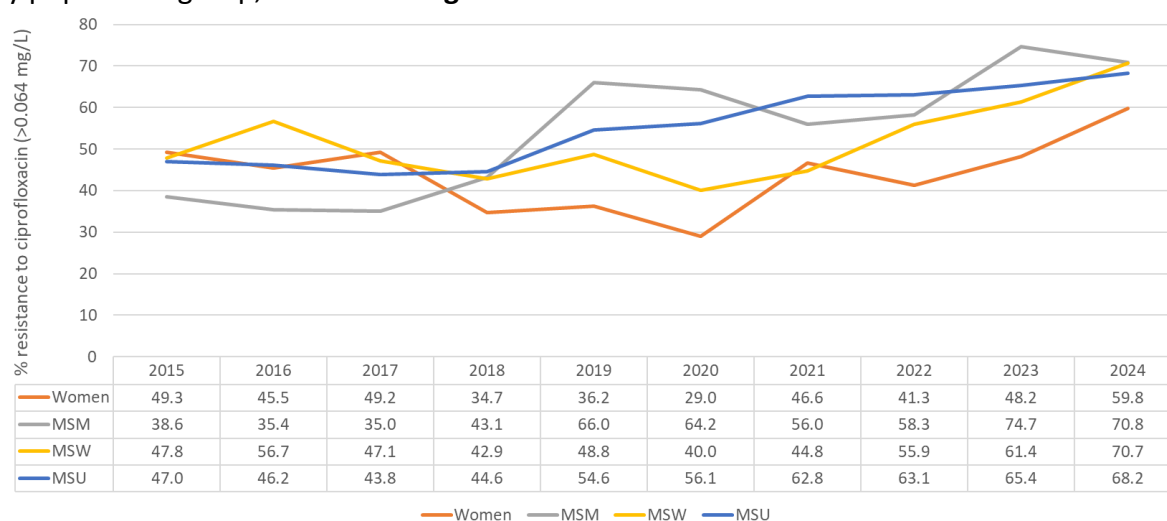


Figure 8: Resistance to ciprofloxacin of *N. gonorrhoeae* stratified by gender and sexual transmission. MSM: Men who have sex with men. MSW: Men who have sex with women. MSU: Unknown gender or men with unknown gender of sex partners

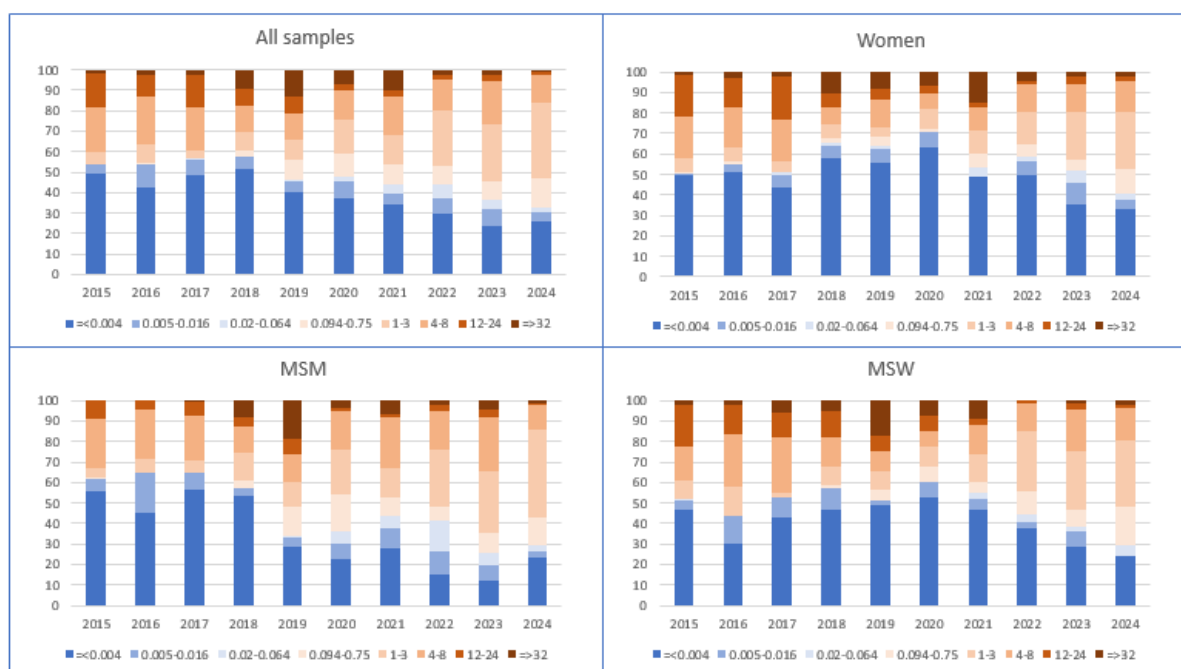


Figure 9: Minimal inhibitory concentration (MIC) distribution (mg/L) for ciprofloxacin over the last ten years for all *N. gonorrhoeae* isolates and stratified per sexual transmission. MSM: Men who have sex with men. MSW: Men who have sex with women

3.3.3 Cephalosporin resistance of *N. gonorrhoeae*

Since 2013, resistance to **ceftriaxone** has been identified in 14 cases, with no additional cases detected in 2024. We did not observe any increase in ceftriaxone MICs (**Figure 10**).



Figure 10: Minimal inhibitory concentration (MIC) distribution (mg/L) for ceftriaxone over the years for all *N. gonorrhoeae* isolates and stratified per sexual transmission. MSM: Men who have sex with men. MSW: Men who have sex with women

Importantly, since May 2023 we introduced new E-test strips with an extended lower detection limit (from <0.016 mg/L to <0.002 mg/L) to better capture shifts from highly susceptible to less susceptible *N. gonorrhoeae* isolates. As a result, data from 2024 cannot be directly compared to those from 2018 to 2023. However, when compared to the period 2013–

2017, during which agar dilution was used, we observe a shift toward more susceptible isolates, which is reassuring.

Resistance to **cefixime** is only measured in a maximum of 200 *N. gonorrhoeae* isolates, as this antibiotic is not used anymore in Belgium. In 2024, only one isolate was found to be resistant (MIC 0.25 mg/L). This isolate was susceptible to ceftriaxone (MIC 0.047 mg/L) and azithromycin (MIC 1 mg/L), but resistant to ciprofloxacin (MIC 24 mg/L).

3.3.4 Tetracycline resistance of *N. gonorrhoeae*

With the introduction of doxycycline post-exposure prophylaxis (doxy-PEP) to prevent STIs among MSM in several countries (defined as a 200 mg dose of doxycycline taken within 72 hours after condomless sex) and the use of doxycycline to treat other STIs, tetracycline susceptibility testing is now conducted annually on a subset of up to 200 *N. gonorrhoeae* isolates. This aims to monitor potential changes in resistance patterns and to evaluate the possible future impact of doxy-PEP on gonorrhoea incidence, which may be influenced by existing levels of tetracycline. In 2024, tetracycline resistance reached 85%, representing an 8.6% increase compared to 2023. As shown in **Figure 11**, resistance exceeds 80% among all male groups and approaches 80% in isolates from females. The MIC distribution, stratified by transmission group, is presented in **Figure 12**, showing a clear shift toward higher MICs across all categories. However, interpretation should be cautious due to the limited sample sizes. Notably, 36.5% (62/170) of tetracycline-resistant isolates exhibited MICs above 4 mg/L.

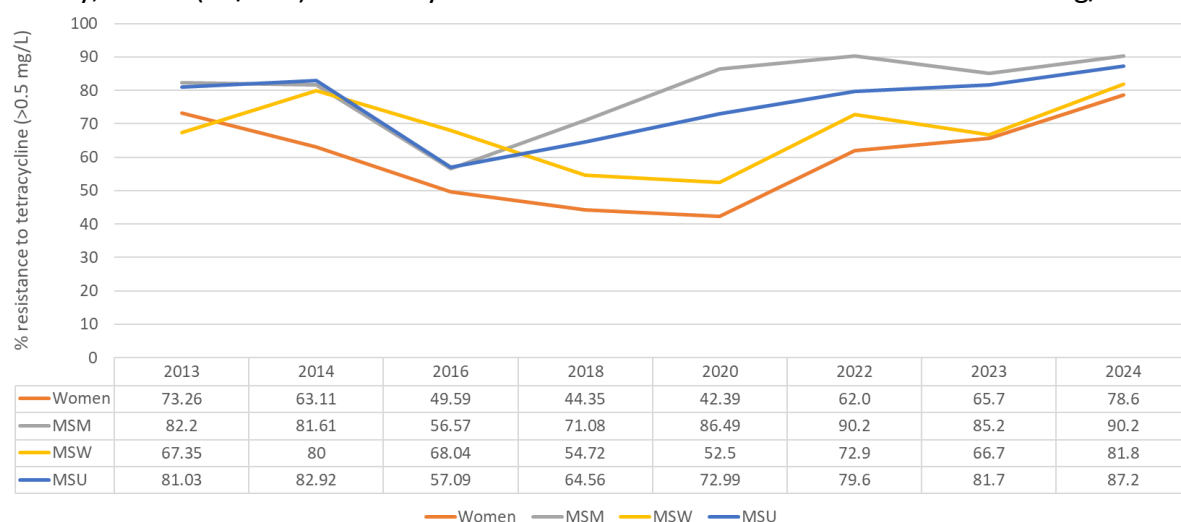


Figure 11: Resistance to tetracycline (breakpoint >0.5 mg/L) of *N. gonorrhoeae* stratified by gender and sexual transmission. MSM: Men who have sex with men. MSW: Men who have sex with women. MSU: Unknown gender or men with unknown gender of sex partners

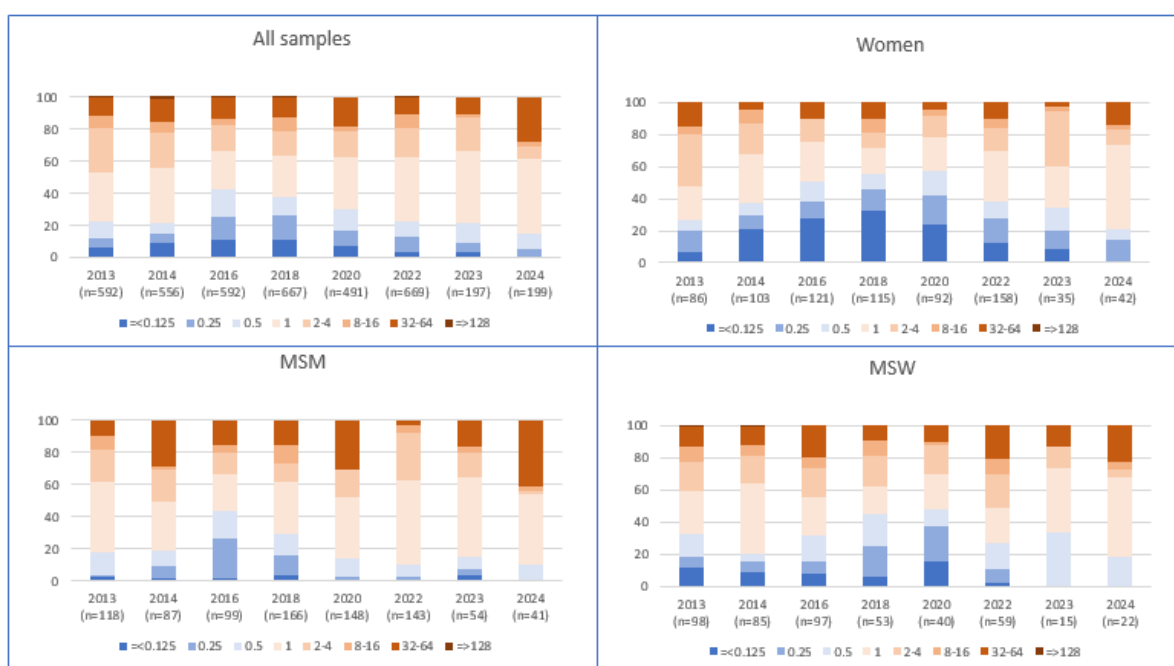


Figure 12: Minimal inhibitory concentration (MIC) distribution (mg/L) for tetracycline over the years for all *N. gonorrhoeae* isolates and stratified per sexual transmission using breakpoint >0.5mg/L. MSM: Men who have sex with men. MSW: Men who have sex with women

3.4 Multidrug resistance of *N. gonorrhoeae*

No isolate was resistant to ceftriaxone, azithromycin, and ciprofloxacin in 2024. However, **Figure 13** shows the number of isolates resistant to both azithromycin and ciprofloxacin, stratified by sexual transmission route over time. Notably, after a continuous increase in dual resistance in previous years, a decline was observed in 2024, from 24.3% in 2023 to 17.7%. This decrease was exclusively observed among isolates from male patients, with the most pronounced drop among MSM, where dual resistance declined from 34.2% to 20.6%. In contrast, one in five isolates from female patients (20.0%) remained resistant to both antibiotics.

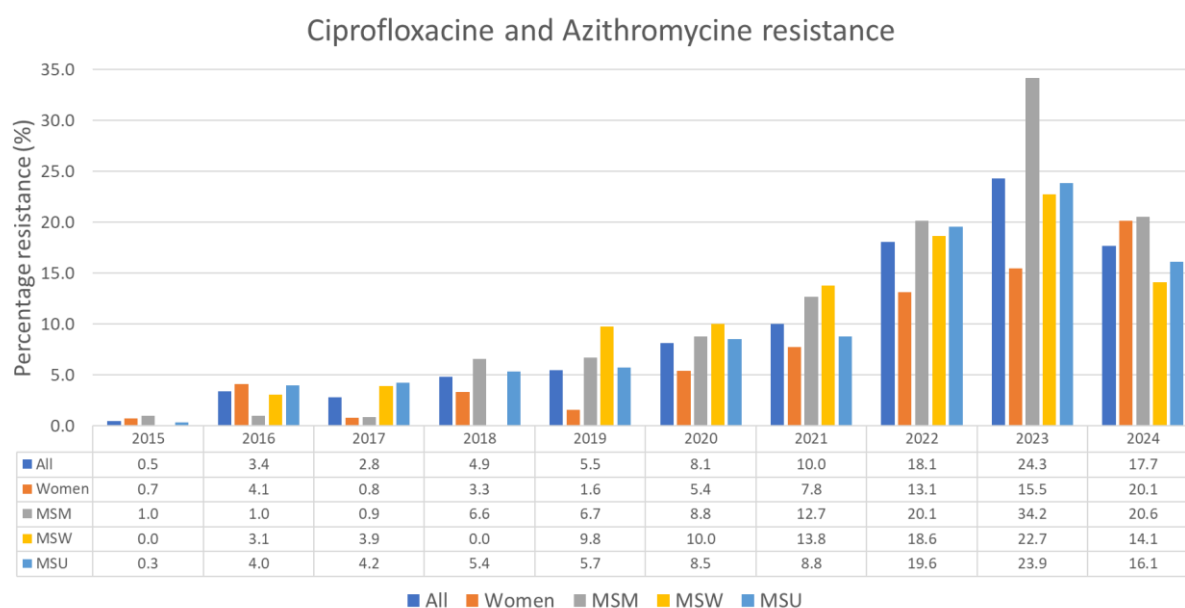


Figure 13: *N. gonorrhoeae* isolates resistant to ciprofloxacin and azithromycin stratified by gender and sexual transmission. MSM: Men who have sex with men. MSW: Men who have sex with women. MSU: Men with unknown sexual orientation or unknown gender

4. Discussion

The **number of *N. gonorrhoeae* isolates received by the NRC-STI continued to increase in 2024**, corroborating the observed rise in *N. gonorrhoeae* incidence reported in Belgium in 2023.¹ This upward trend has also been documented in neighbouring countries since 2022, including the Netherlands.⁷

Notably, there was no increase in the number of isolates from women (164 vs. 168 in 2023); the entire increase was attributable to samples from men, which rose by 9.4% (709 vs 648 in 2023). Among these, 209 were from MSM, representing a 10% increase compared to 2023 (209 vs. 190). Intriguingly, this rise in *N. gonorrhoeae* isolates was confined to Flanders. A plausible hypothesis is increased awareness around the importance of culturing *N. gonorrhoeae* for antimicrobial resistance surveillance in Flanders. However, no additional public health campaigns or changes in testing practices were implemented to explain this increase. A survey is planned among Belgian microbiology laboratories to better understand their referral practices of *N. gonorrhoea* to the NRC-STI.

In addition to the absolute rise in cases, there has been an **increase in confirmed cases of DGI** since 2023. The uptick in DGI cases may reflect a concerning trend in *N. gonorrhoeae* infections in Belgium. Among the DGI cases identified in 2024, three were identified in women and thirteen in men, including two MSM. Cases were distributed across regions: 3 in Brussels, 8 in Flanders, and 5 in Wallonia, reported by different laboratories. Further investigation, including WGS, is ongoing to assess the genetic diversity of these isolates and to explore the potential association between DGI and specific virulence factors. **Increasing clinical awareness of DGI, particularly among healthcare providers outside of sexual health settings, will be essential.**

Interestingly, **the trend of increasing azithromycin resistance appears to be reversing** after a decade-long increase, with resistance decreasing from 36.1% to 24.4%. This decline was observed across all populations, but was most pronounced among MSM. A likely explanation is a shift in treatment practices, with azithromycin now used less frequently for STIs. Most resistant *N. gonorrhoeae* isolates demonstrated low-level resistance (93.4% of the resistant isolates had MICs between 1.5–3 mg/L), and there was a noticeable increase in isolates highly susceptible to macrolides ($\text{MIC} \leq 0.125$ mg/L).

A similar trend was seen for **ceftriaxone, with a shift toward highly susceptible isolates**. This pattern has also been reported in Ireland.⁸ In contrast, the Netherlands has documented an increase in isolates with slightly reduced susceptibility to ceftriaxone ($\text{MIC } 0.008\text{--}0.047$ mg/L).⁷ Ceftriaxone monotherapy is currently the first-line treatment for *N. gonorrhoeae* in Belgium.⁹

Despite these encouraging trends for azithromycin and ceftriaxone, **resistance to ciprofloxacin (67.5%) and tetracycline (85.4%) is rising. Ciprofloxacin resistance is now nearly 70% among male patients and 60% among female patients.** Although tetracycline resistance was assessed in only a subset of 200 isolates, increases were seen across all groups, with rising MIC values. Doxycycline has largely replaced azithromycin as the first-line treatment for chlamydia and *Mycoplasma genitalium*, and is also used to prevent the acquisition of STIs among MSM (doxy-PEP), although this is not recommended by Europe and supported by Belgian experts.^{10,11} A 2024 survey among MSM in Belgium indicated that doxy-PEP use remains limited, with only 10% of participants reporting its use.¹² Importantly, our results show that **tetracycline resistance among MSM now stands at 90%**, suggesting that doxy-PEP is unlikely to be effective for preventing *N. gonorrhoeae* infections. Moreover, one in three tetracycline-resistant isolates had MICs > 4 mg/L. These findings suggest that doxy-

PEP may not only be ineffective against *N. gonorrhoeae* but could also drive the selection of highly resistant strains. Notably, tetracycline resistance mutations and genes are often linked to resistance mechanisms against other antibiotic classes.¹³ Therefore, the implementation of doxy-PEP warrants close monitoring for its impact on both individual- and population-level antimicrobial resistance across bacterial species, including *N. gonorrhoeae*, as recommended by the ECDC.¹¹

The evolving antimicrobial resistance landscape of *N. gonorrhoeae* demonstrates the bacterium's remarkable ability to adapt to changes in treatment practices. This underscores the critical importance of continued phenotypic resistance surveillance and reinforces the recommendation to culture *N. gonorrhoeae* detected via molecular assays.⁹ **Sustained surveillance efforts are essential to guide treatment guidelines and public health responses.**

5. Acknowledgements

We would like to thank Dominique Van Beckhoven, Jessika Deblonde, and Thibaut Vanbaelen for their feedback.

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7. Annexes

7.1 Number of *N. gonorrhoeae* isolates received per laboratory

Laboratory	Number
11601 AZ KLINA BRASSCHAAT	3
11603 UZ ANTWERPEN	4
11642 AZ MONICA DEURNE	8
11653 AML ANTWERPEN	20
11677 GZA CAMPUS ST AUGUSTINUS ST VINCENTIUS ST JOZEF WILRIJK	13
11704 ITG ANTWERPEN	146
11791 ZNA CAMPUS MIDDELHEIM ANTWERPEN	4
12609 AZ ST MAARTEN MECHELEN	4
12616 SOMEDI HEIST OP DEN BERG	8
12647 AKL LIER	14
13608 AZ ST DIMPNA GEEL	4
13618 AZ TURNHOUT CAMPUS ST JOZEF TURNHOUT	5
13656 CMA HERENTALS	134
23604 AZ JAN PORTAELS VILVOORDE	8
24650 MCH LEUVEN	11
24700 UZ KUL CAMPUS GASTHUISBERG LEUVEN	4
25607 LIMS LOUVAIN LA NEUVE OTTIGNIES	1
25611 LIMS CLIN ST PIERRE LOUVAIN LA NEUVE OTTIGNIES	3
26678 LHUB ULB BRUSSEL	15
26726 CEBIODI SITE DU JARDIN BOTANIQUE BRUSSEL	6
27729 ULB INSTITUT DE BIOLOGIE CLIN BRUSSEL	2
28612 CHIREC SITE DELTA OUDERGEM	1
28667 HOP IRIS SUD SITE ETTERBEEK BRUSSEL	4
29636 UZ BRUSSEL	13
31639 AML WEST ARDOOIE	67
31669 AZ ZENO CAMPUS KNOKE HEIST	2
33606 RZH JAN YPERMAN IEPER	19
34612 AZ GROENINGE KORTRIJK	6
35607 AZ DAMIAAN OOSTENDE	1
36609 AZ DELTA ROESELARE	4
41658 OLV ZH AALST	5
42609 MEDINA DENDERMONDE	110
43620 AZ ALMA CAMPUS EKKLO	3
44610 LABO NUYTINCK EVERGEM	9
44624 MEDILAB GENT	4
44673 AZ MARIA MIDDELARES GENT	5
44696 AZ ST LUCAS GENT	23
44700 UZ GENT	10
44711 CERBA HEALTHCARE BELGIUM BVBA CRI ZWIJNAARDE	8
46615 VITAZ ST NIKLAAS	3
52610 SYNLAB HEPPIGNIES	4
52616 GHDC SITE ST JOSEPH GILLY	1

Laboratory	Number
52626 CHU DE CHARLEROI HOP CIVIL MARIE CURIE LODELINSART	3
53606 CHU HELORA NIMY	1
53639 EPICURA HORNU	5
55604 CH DE TIVOLI LA LOUVIERE	1
55614 CHR HAUTE SENNE SITE CH DE SOIGNIES	2
55624 CH DE JOLIMONT SITE DE JOLIMONT LA LOUVIERE	1
56603 CENTRE DE SANTÉ DES FAGNES CHIMAY	2
57606 CHWAPI LABO SITE NOTRE DAME TOURNAI DOORNIK	3
61602 CH RÉGIONAL DE HUY	1
62654 SYNLAB LABO COLLARD LIEGE LUIK	1
62668 CLIN MONTLEGIA LIEGE LUIK	32
62700 HU DU SART TILMAN LIEGE LUIK	4
71604 LKO LMC ST TRUIDEN	21
71615 JESSA ZH CAMPUS VIRGA JESSE HASSELT	6
71622 ZH OOST LIMBURG GENK	17
71725 KLIN LABO RIGO GENK	13
81602 VIVALIA SITE ST JOSEPH ARLON AARLEN	2
84609 VIVALIA CHA LIBRAMONT	4
91605 CHU UCL NAMUR YVOIR	5
92611 CHR SAMBRE ET MEUSE SITE MEUSE NAMUR NAMEN	3
92613 CLIN MATERNITÉ ST ELISABETH NAMUR NAMEN	7
92629 CLIN ST LUC BOUGE	21
Grand Total	874