

# Surveillance of Gonococcal Infection Treatment Failures 2015-2018 in Quebec, Canada

## Authors

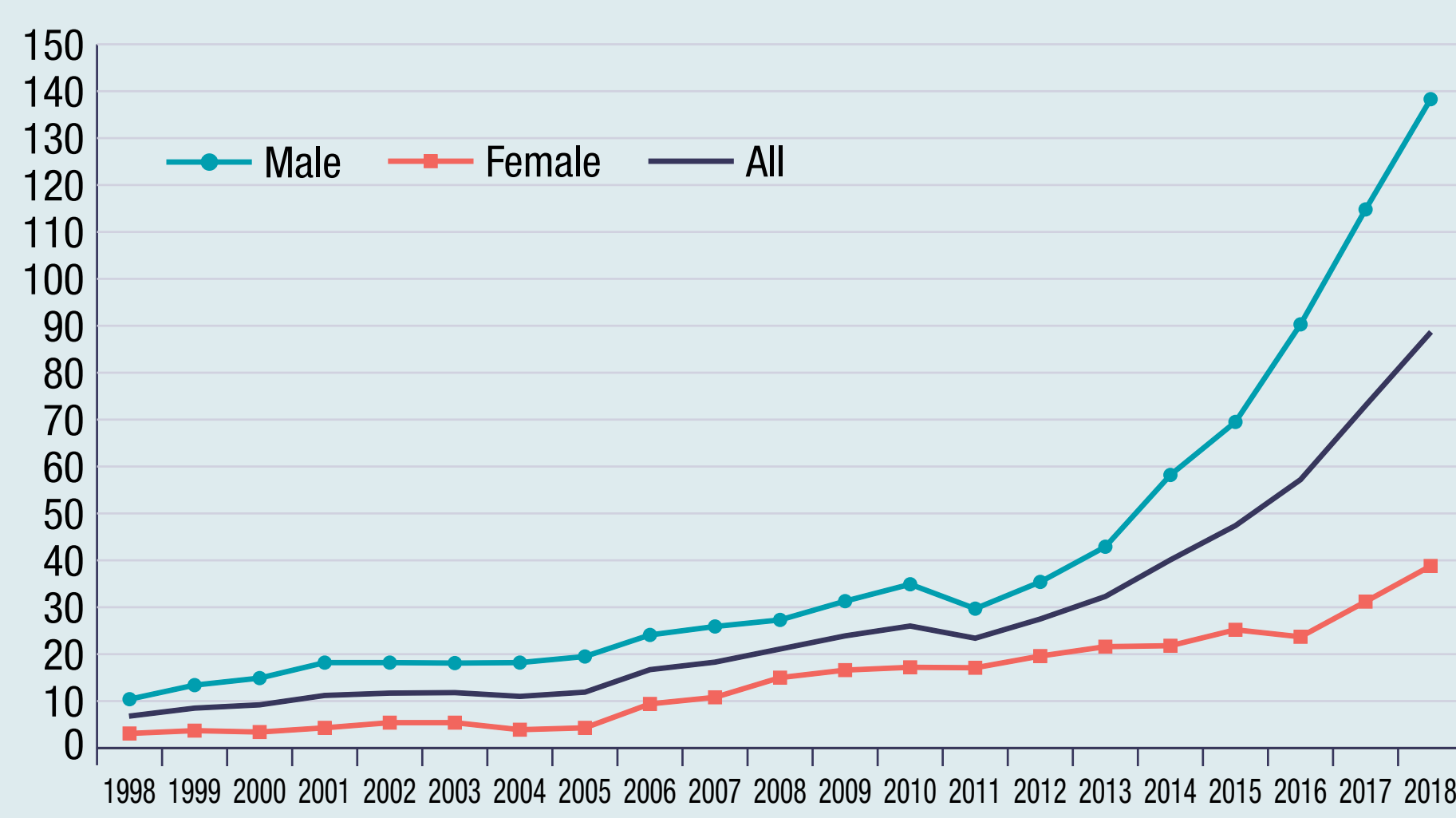
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## Background

Incident cases of gonococcal infection are increasing. Antibiotic resistance may compromise the effectiveness of treatment. In 2017, the proportion of azithromycin-resistant strains reached 31% in Québec and a first strain non-susceptible to ceftriaxone and cefixime was detected. Antimicrobial Susceptibility Testing (AST) is available for 24% of reported gonococcal infection as most infections are detected by Nucleic Acid Amplification Testing (NAAT) only.

**Figure 1: Gonococcal Infection, Reported cases, rates/100000 persons, by sex, Québec, 1998-2018**



Data extracted May 21<sup>st</sup>, 2019 from Portail Info-Centre, Institut national de santé publique

**Table 1: *Neisseria gonorrhoeae* antimicrobial resistance, Quebec, 2017 (N = 1478 strains tested)**

Azithromycin resistance	30,9%
Ciprofloxacin resistance	67,3%
Cefixime resistance	0,2%
Reduced susceptibility to cefixime	0,9%
Ceftriaxone and cefixime resistance	First case

Laboratoire de santé publique du Québec, *Neisseria gonorrhoeae* Antimicrobial surveillance program

## Methods

Since November 2014, public health departments are invited to report possible cases of treatment failure. Clinical and epidemiological information are collected with a standardized form for each case of gonococcal infection occurring < 42 days following a previous episode in the same person. AST is conducted at the provincial reference laboratory (Laboratoire de santé publique du Québec) and the NG-MAST typing is performed at the National Microbiology Laboratory. Cases are classified as retained or suspected. Case definitions are consistent with those of the Québec and Canadian sentinel surveillance networks for gonococcal infection.

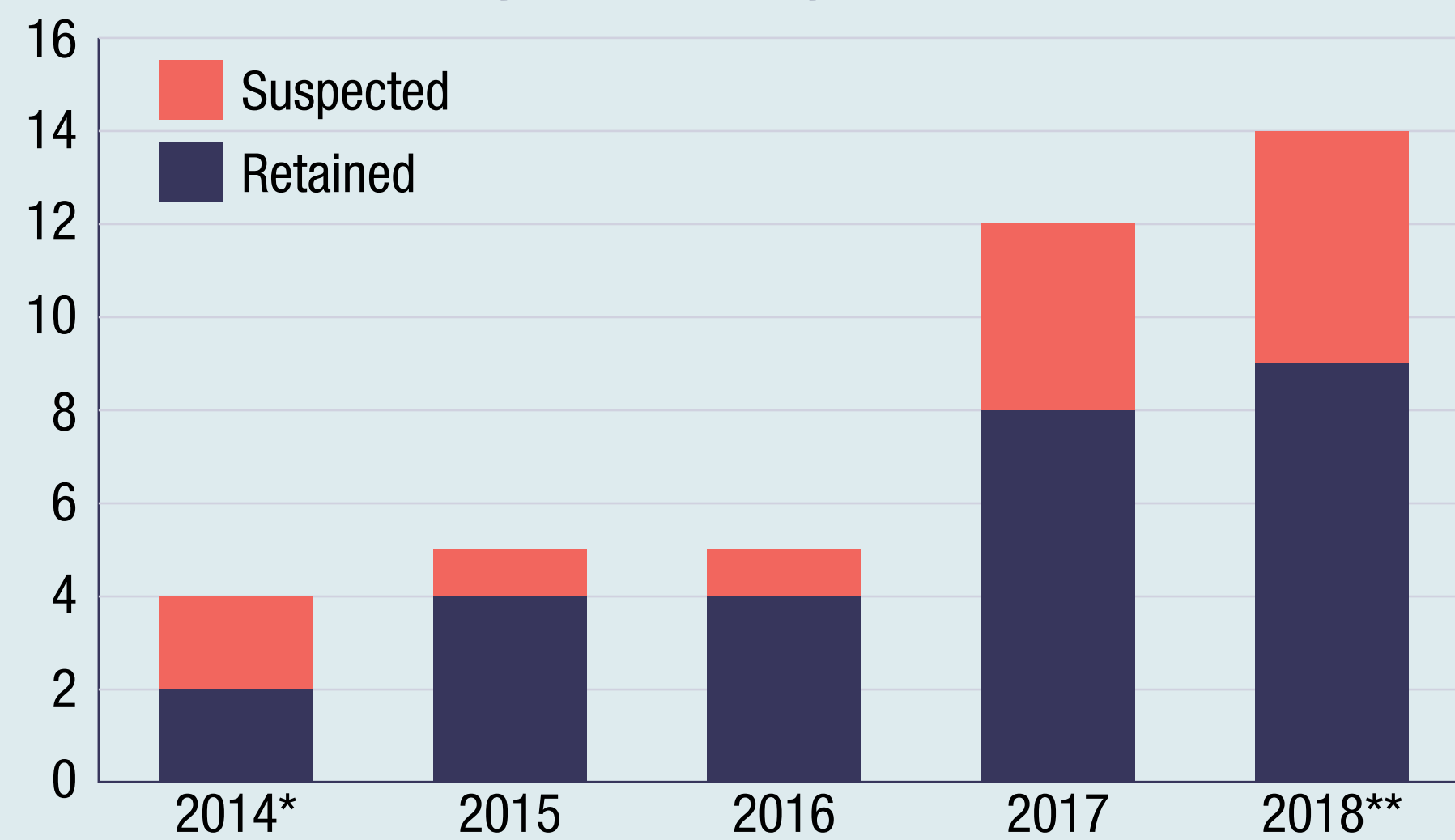
**Table 2: Definitions**

Retained cases: all criteria met	
1	Gonococcal infection confirmed by laboratory test, regardless of site of infection AND documented treatment
2	Positive test of cure using one of the following <i>N. gonorrhoeae</i> detection tests, even if the site is different from the initial site:  Isolation of <i>N. gonorrhoeae</i> by culture from a specimen obtained ≥ 72 hours post-treatment OR a positive NAAT from a specimen obtained ≥ 2 weeks post-treatment  The maximum period between the first and the second detection test is 42 days (6 weeks).
3	Subject reports no sexual contact between the start of treatment and the second positive result
4	When available, strain of bacteria is of the same type as the first culture, according to the NG-MAST genotypic analysis
Suspected cases: criteria not all met but case not considered as a new infection	
	Sexual contact reported but new infection seems unlikely: e.g., occurred after seven days of abstinence posttreatment, always using condom with a treated partner and no other sexual partner since start of treatment

## Results

Between November 2014 and December 2018, 51 cases of possible treatment failure were reported. After excluding 11 cases not meeting definition criteria, 40 were analyzed (27 classified as retained and 13 as suspected). There were 12 women, 27 men (69% MSM) and one trans person. Three cases (10%) had sexual exposure outside Québec. Most of the cases (62%) reported fewer than three sexual partners during the 60 days before the initial infection.

**Figure 2: Number of reported Gonococcal infection treatment failures by status and year**



\* beginning November 24th \*\* One region stopped reporting as of October 2018

**Table 3: Site(s) of treatment failure by gender**

[site(s) of treatment failures refers to site(s) of a positive test of cure within the appropriate delays]

	Female (N=12)	Male (N=27)	Trans (N=1)	Total (N=40)
Genital site only (urethra, urine, cervix, vagina)	9	13		22
Pharynx only	2	13		15
Pharynx and genital site	1			1
Anal and genital site		1	1	2

Pharynx was identified as a site of treatment failure for 16 cases (40%). Among those, eight (50%) were detected by culture at the test of cure (TOC). For six other cases (38%), TOC was positive by NAAT without culture performed or negative culture. A false positive result induced by cross-reaction with other *Neisseria* was not likely as the clinical context favored a true positive result: for example, other site were also TOC positive, or treatment was azithromycin monotherapy with initial strain showing azithromycin resistance.

Among cases for which AST was available, 90% showed intermediate susceptibility or resistance to tetracycline, 78% were resistant to ciprofloxacin and 41% were resistant to azithromycin. All strains were susceptible to third generation cephalosporin (3GC), but one strain showed decreased susceptibility to cefixime.

**Table 4: Antimicrobial susceptibility, Retained or suspected Treatment failure Québec November 2014-December 2018**

Susceptibility profile	Total (N=27)
R Cipro, I/R Tetra, S Azi, S 3GC	9 (33%)
R Azi, R Cipro, I/R Tetra, S 3GC	8 (30%)
R Azi, R Cipro, S 3GC, (Tetra NA)	1 (4%)
S Azi, S Cipro, S 3GC, (Tetra S or NA)	3 (11%)
S Azi, S Cipro, S 3GC, R Tetra	1 (4%)
R Cipro, S Azi, S 3GC (Tetra NA)	2 (7%)
R Cipro, DS Cefixime, S Azi, S cef, (Tetra NA)	1 (4%)
R Azi, S 3GC, S Cipro, (Tetra NA)	1 (4%)
R Azi, S 3GC, S Cipro, (I Tetra)	1 (4%)

Antimicrobial susceptibility was available for 27/40 cases of treatment failure; 13 cases were detected only by NAAT

Legend:

3GC Third Generation Cephalosporin (ceftriaxone and cefixime)  
S Susceptible  
I Intermediate  
R Resistant  
DS Decreased susceptibility (WHO criteria)

Eleven cases (28%) received azithromycin monotherapy as initial therapy.

Among genital treatment failures, seventeen (17/24, 71%) received first option therapy recommended in Québec for genital infection (cefixime 800 mg or ceftriaxone 250 mg, with azithromycin 1 g). Among 16 pharyngeal treatment failures, only three had received the recommended option of ceftriaxone 250 mg/azithromycin 1 g as initial therapy. In many cases, the infection at pharyngeal site was not known when therapy was initiated and was not adjusted before TOC.

Among cases with available antimicrobial susceptibility results (N=27), resistance or decreased susceptibility to at least one of the antibiotics used for initial therapy was detected for 13 cases (48%).

**Table 5:**

Initial therapy and Antimicrobial susceptibility Retained or suspected Genital infection Treatment failure Quebec, November 2014-December 2018

	R or DS*	S**	AS not available	Total (N=24)
Cefixime 800 mg and Azithromycin 1 g	2	3	8	13
Azithromycin 2 g	1	2		3
Azithromycin 1 g	1			1
Ceftriaxone 250 mg IM and Azithromycin 1 g	1	3		4
Other therapy with Ciprofloxacin				
• Ciprofloxacin 500 mg bid 10 days + Metronidazole 500 mg bid 7 days			1	3
• Ciprofloxacin 2 g and Azithromycin 1 g	2			
• Ciprofloxacin 1 g 7 days and Azithromycin 1 g				
All cases genital infection treatment failure N=24	7/24 (29%)	8/24 (33%)	9/24 (38%)	24
Cases with AST available N=15	7/15 (47%)	8/15 (53%)		

Initial therapy and Antimicrobial susceptibility Retained or suspected Pharynx infection Treatment failure Quebec, November 2014-December 2018

	R or DS*	S**	AS not available	Total (N=16)
Cefixime 800 mg and Azithromycin 1 g	2	1		3
Cefixime 800 mg		1		1
Azithromycin 2 g	2	3	1	6
Azithromycin 1 g	1			1
Azithromycin 1 g + TMP-SMX		1		1
Ceftriaxone 250 mg IM and Azithromycin 1 g			3	3
Cefixime 800 mg, Doxycycline 100 mg bid 7 days and Ceftriaxone 250 mg IM	1			1
All cases pharynx infection treatment failure N=16	6/16 (38%)	6/16 (38%)	4/16 (25%)	16
Cases with AST available N=12	6/12 (50%)	6/12 (50%)		

Notes:

\* to at least one antibiotic used for initial therapy

\*\* to all antibiotics used for initial therapy

## Conclusion

Treatment failures are not always related to documented resistance. For treatment failures at the genital site, most (71%) have received recommended therapy and, among them, 18% had documented antibiotic resistance to at least one of the antibiotics used for initial therapy. For treatment failure at the pharyngeal site, most (82%) did not receive the appropriate therapy as initial therapy. Cultures are not always done even when it is clearly indicated (for example, persistent symptoms, positive NAAT at TOC).

## Limitations

This analysis probably underestimates the real extent of treatment failures since TOC are not systematically performed. On the other hand, overestimation is possible: reinfection cannot be completely excluded as exposure is self-reported by cases and false-positive results can occur.

## References

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Keywords: Gonococcal infection, treatment failure, antibiotic resistance