

# Factors associated with *Neisseria gonorrhoeae* azithromycin resistance in the Quebec sentinel network, 2015-2017

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## Background

In Quebec, the rate of reported gonococcal infection has increased three-fold from 2011 to 2017 (23.4 to 72.9 per 100 000 persons), reaching 6 142 cases in 2017 (1). The emergence of *N. gonorrhoeae* azithromycin resistance (MIC  $\geq$  2mg/L) has been very abrupt (2013 : 1,7%, 2014 : 6,7% , 2015 : 12,4%, 2016 : 19,9%, 2017 : 30,9%)(2). In response to this well-recognized public health issue, a sentinel network was established in the province in 2015.

The Quebec sentinel network for the surveillance of gonococcal infection, antibiotic resistance and treatment failures aims to:

1. Maintain a sufficient number of cultures for antimicrobial resistance surveillance;
2. Cross-link antimicrobial susceptibility data to epidemiological and clinical information;
3. Monitor treatment failures.

## Objective

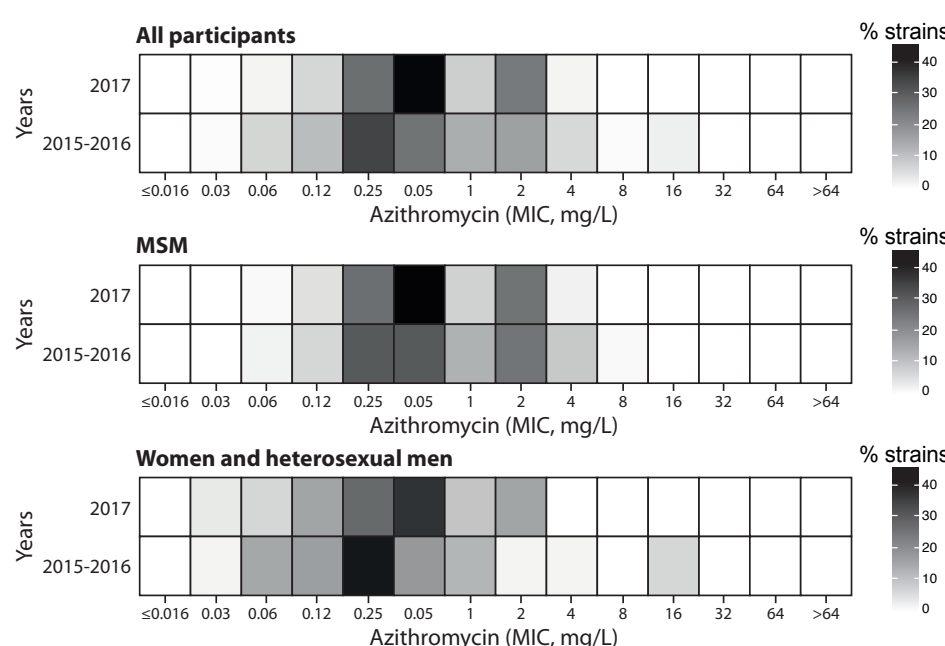
Examine associations between *N. gonorrhoeae* azithromycin resistance and epidemiological/clinical characteristics of cases in the Quebec sentinel network.

- Between September 2015 and December 2017, 68% of episodes (840/1 240) had a culture performed and 571 strains were obtained, including all duplicates.
- Figure 1 shows azithromycin minimal inhibitory concentrations (MIC) of all strains. Higher values were observed for MSM compared to women/heterosexual men. There is a shift to the right in 2017 vs. 2016 for women/heterosexual men.

Figure 1

### Azithromycin minimal inhibitory concentrations (MIC) by year, globally and stratified for MSM and heterosexual men/women

(for all strains, including duplicates), Quebec sentinel network, 2015-2017. Darker colors indicate a higher proportion for a given MIC in a given year.



## Associations

Azithromycin resistance was significantly associated with:

- MSM vs. women and heterosexual men in 2016 (PR=6.39, 95 % CI [2.05-19.86],  $p<0.01$ ), but not in 2017 (PR=1.69 [0.72-3.93],  $p=0.23$ )
- Reporting a sex partner outside Quebec in 2016 (PR=2.28, 95 % CI [1.19-4.34],  $p=0.01$ ), but not in 2017 (PR=0.99, 95 % CI [0.48-2.07],  $p=0.98$ )
- Reporting previous sexually transmitted and blood-borne infections (STBBIs), globally in 2016 and 2017 (similar for both years)
  - HIV vs. no STBBIs (PR=2.57, 95 % CI [1.25-5.27],  $p<0.01$ )
  - STBBIs other than HIV vs. no STBBIs (PR=3.68, 95 % CI [1.71-7.91],  $p=0.01$ )

In multivariate analyses, azithromycin resistance remained significantly associated with MSM in 2016 and with previous STBBIs in 2016-2017 - adjusted for age, year, region of residency, anatomical site, number of sex partners and sex with a partner usually residing outside Quebec.

## References

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## Methods

### Three regions participated in the sentinel network:

- **Montréal**: two clinics recruiting mostly men having sex with men (MSM);
- **Montréal**: 22 clinics recruiting mostly heterosexuals;
- **Nunavik**: two health centers recruiting mainly heterosexual Inuit people (their participation ended in 2017).

Data collection started in September 2015. History and sex behaviors were collected through a self-administered questionnaire or by file review.

All *N. gonorrhoeae* strains isolated in clinical laboratories throughout the province of Quebec were submitted to the *Laboratoire de santé publique du Québec* (LSPQ) where antimicrobial susceptibility analyses were performed using the agar dilution method according to Clinical and Laboratory Standards Institute (3).

### Statistical analyses:

One strain per clinical episode was selected (except for figure 1) prioritizing resistance first, then difficult to treat anatomical sites (pharynx>anus-rectum>urogenital site>other). The first episode per year, per individual was then selected, except otherwise stated. Proportion rates (PR) and 95% confidence intervals (95 % CI) were computed using generalized estimating equations (robust Poisson regression). Analyses were performed using SAS 9.4 and figure 1 was produced using R 3.5.3 and the ggplot2 package.

## Results

Table 1

Proportion of azithromycin resistance (MIC  $\geq$  2 mg/L) according to sociodemographic information, sex behaviors and previous history of STBBIs, by year, Quebec sentinel network, 2015-2017

Variables		n: number of cases with azithromycin resistance/ N: number of strains tested within variable category					
		2016		2017		2015-2017 <sup>3</sup>	
		n/N=190	%	n/N=272	%	n/N=470	%
Sex <sup>1</sup>	Men	39 / 150	26.0	58 / 257	22.6	93 / 408	22.8
	Women	2 / 40	5.0	2 / 15	13.3	6 / 62	9.7
Age (years)	< 25	13 / 48	27.1	9 / 46	19.6	20 / 100	20.0
	25-34	12 / 70	17.1	22 / 110	20.0	34 / 182	18.7
	$\geq$ 35	16 / 72	22.2	29 / 116	25.0	45 / 188	23.9
Region of residency	Montréal	33 / 92	35.9	43 / 190	22.6	74 / 278	26.6
	Outside Montréal	8 / 98	8.2	17 / 82	20.7	25 / 192	13.0
Sex partners (last year) among male cases	Heterosexual men	1 / 21	4.8	3 / 21	14.3	4 / 49	8.2
	MSM	38 / 121	31.4	55 / 235	23.4	89 / 350	25.4
Number of sex partners (previous two months)	0-4	18 / 104	17.3	36 / 154	23.4	54 / 268	20.2
	5 or more	10 / 31	32.3	11 / 76	14.5	20 / 104	19.2
	Missing	13 / 55	23.6	13 / 42	31.0	25 / 98	25.5
Anatomical site	Urogenital	23 / 127	18.1	42 / 190	22.1	63 / 329	19.2
	Anus-rectum	13 / 38	34.2	11 / 55	20.0	24 / 90	26.7
	Pharynx	5 / 25	20.0	7 / 27	25.9	12 / 51	23.5
Previous gonorrhoea	No	15 / 84	17.9	11 / 82	13.4	26 / 175	14.9
	Yes	21 / 68	30.9	41 / 156	26.3	61 / 223	27.4
	Missing	5 / 38	13.2	8 / 34	23.5	12 / 72	16.7
Previous STBBIs <sup>2</sup>	No	5 / 45	11.1	3 / 38	7.9	7 / 86	8.1
	Yes, other than HIV	25 / 95	26.3	39 / 177	22.0	67 / 279	24.0
	Yes, HIV	8 / 24	33.3	16 / 45	35.6	21 / 67	31.3
	Missing	3 / 26	11.5	2 / 12	16.7	4 / 38	10.5
	Yes, other than syphilis	22 / 82	26.8	37 / 163	22.7	60 / 251	23.9
Sex with a partner usually residing outside Quebec (2 last months)	Yes, syphilis	11 / 37	29.7	18 / 59	30.5	28 / 95	29.5
	No	16 / 96	16.7	28 / 131	21.4	43 / 236	18.2
	Yes	11 / 29	37.9	7 / 33	21.2	15 / 58	25.9
	Missing	14 / 65	21.5	25 / 108	23.2	41 / 176	23.3

<sup>1</sup> Cases of unknown sex and trans persons are excluded; <sup>2</sup> STBBIs : sexually transmitted and blood-borne infections

<sup>3</sup> When proportions were presented for the entire period 2015-2017, the most recent strain per individual was retained. For separate years, the first episode per year was retained.

## Conclusions

- Recommendations to perform cultures appear to be relatively well implemented (68% of episodes) but there is scope for improvement.
- Azithromycin resistance seems to be well established in Quebec, particularly but not exclusively in cases who reported previous STBBIs and in MSM.
  - Association between azithromycin resistance and MSM was observed in 2016 but not in 2017. This is consistent with the results of the surveillance program for all strains detected in Quebec, where the proportion of azithromycin resistance was higher in men than in women (21% vs.12%,  $p=0.003$ ) in 2016, while in 2017, the observed proportions of azithromycin resistance were the same (30.9% in men and 31.2% in women).

- These results also suggest a possible declining contribution of travel-acquired resistant infection between 2016 and 2017.
- The main limits include moderate sample size, high proportion of missing information for some variables and sampling bias (i.e. over-representation of MSM). Thus, these results would not be representative of the entire province.

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