The use and efficacy of moxifloxacin for *Mycoplasma genitalium* infection 2015 - 2024

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Australasian Sexual & Reproductive Health Conference

September 18, 2025
Tarndanya, Kaurna Country

Acknowledgement of Country

I am privileged to be able to work and live on Wurundjeri Country, and to be visiting Tarndanya on Kaurna Country this week.

Sovereignty of these lands has never been ceded and will always firmly belong to Wurundjeri and Kaurna peoples.

Disclosures of Interest

None to declare

Mycoplasma genitalium (MG)

Bacterial sexually transmitted infection (STI)[1]

Associated with STI syndromes: urethritis, cervicitis, pelvic inflammatory disease (PID)[1,2]

Sequelae include miscarriage, preterm birth, infertility[1,2]

[**1**] Jensen, J.S. & Bradshaw, C. (2015). Management of *Mycoplasma genitalium* infections – can we hit a moving target? *BMC Infect Dis 15*(343)
[**2**] Htaik, K., et al., (2024). Systematic review and meta-analysis of the association between *Mycoplasma genitalium* and pelvic inflammatory disease (PID). *Clin Infect Dis*

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Highly mutable genome conferring antimicrobial resistance

Macrolide-resistance mutation (MRM) now present in >65% of MG infections in Australia, >80% among men-who-have-sex-with-men[3]

[**1**] Jensen, J.S. & Bradshaw, C. (2015). Management of *Mycoplasma genitalium* infections – can we hit a moving target? *BMC Infect Dis 15*(343)
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[**3**] Machalek, D.A., et al., (2020). Prevalence of mutations associated with resistance to macrolides and fluoroquinolones in *Mycoplasma genitalium*: a systematic review and meta-analysis. *Lancet Infect Dis. 20*(11)

Moxifloxacin

Fluoroquinolone antibiotic

Introduced for MG in 2006 in response to azithromycin failure

Dual binding: DNA Topoisomerase IV and DNA Gyrase

ParC, ParE *and* ***GyrA, GyrB*** *subunits*

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Fluoroquinolone antibiotic

Introduced for MG in 2006 in response to azithromycin failure

Dual binding: DNA Topoisomerase IV and DNA Gyrase

ParC, ParE *and* ***GyrA, GyrB*** *subunits*

Only one systematic review of moxifloxacin efficacy for MG[4]

100% *pre-2010*
89% *post-2010*

[**4**] Li Y et al. (2017). Meta-analysis of the efficacy of moxifloxacin in treating *Mycoplasma genitalium* infection. Int J STD AIDS. 28(11)

Fluoroquinolone-resistant MG

Number of mutations identified in ***parC*** (TopoIV) and ***gyrA*** (Gyr) genes

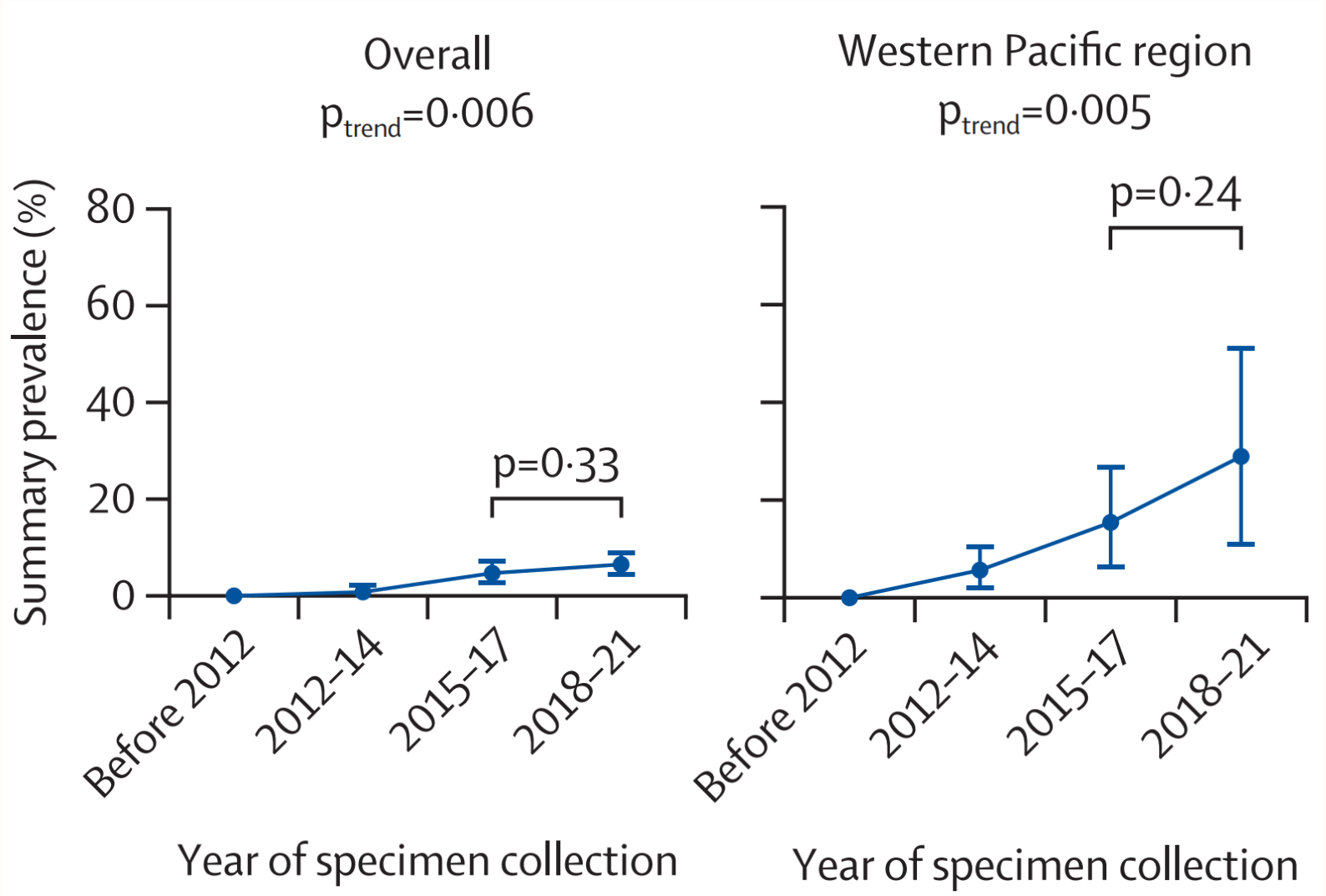
parC G248T mutation conferring **ParC S83I phenotype** most common

Clinical study found **ParC S83I** associated with 60% moxifloxacin failure[5]

[**5**] Vodstrcil, L.A., et al., (2022). Combination Therapy for *Mycoplasma genitalium*, and New Insights Into the Utility of parC Mutant Detection to Improve Cure. *Clin Infect Dis, 75*(5)

Prevalence of dual MRM & ParC mutation

Chua, 2025[6]



WHO Western Pacific region global hotspot for ParC and dual-class mutation

29% carrying dual-class mutation
(2018-21)

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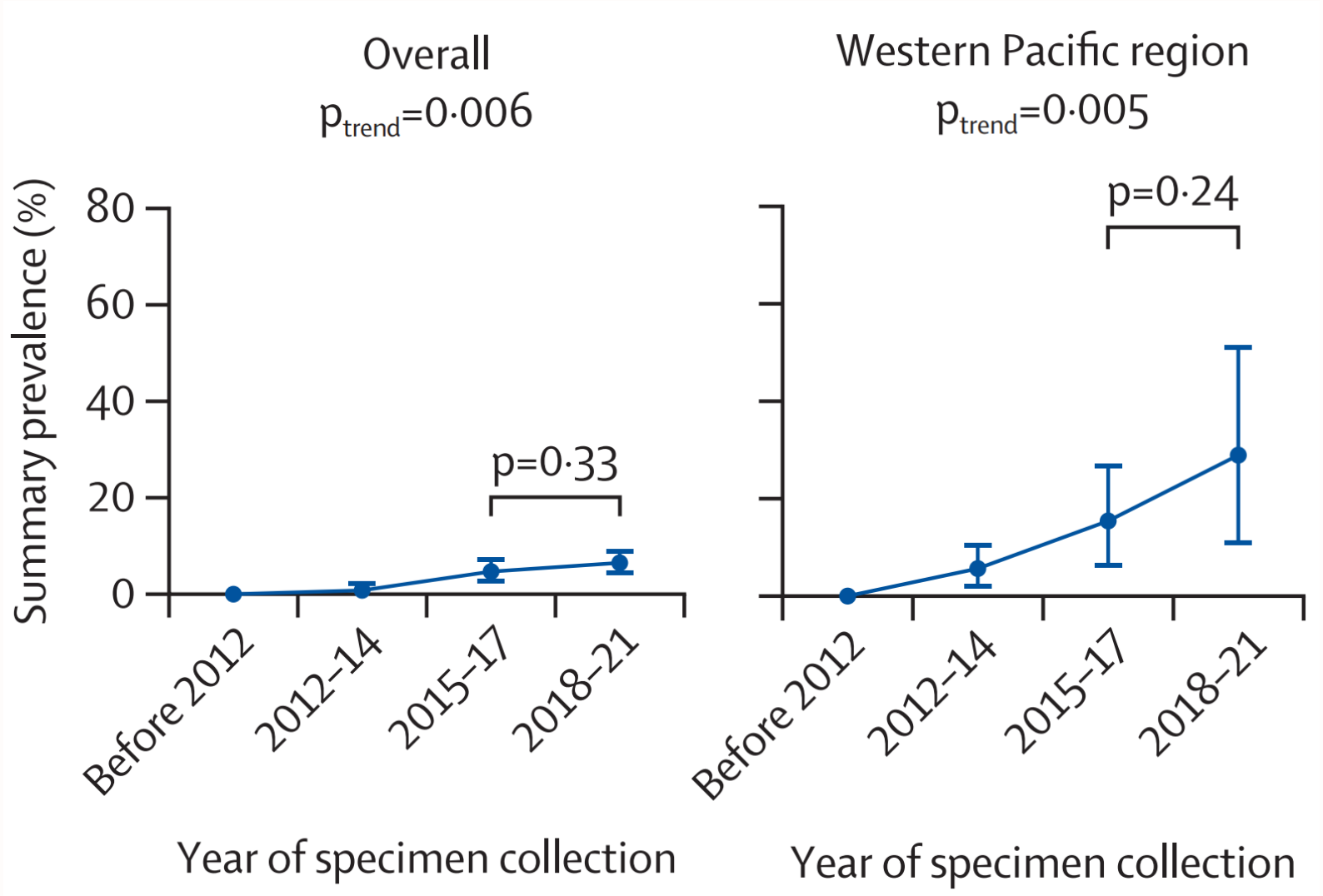

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29% carrying dual-class mutation (2018-21)

We need more longitudinal data & drug surveillance

Aims

Examine trends in the use and efficacy of moxifloxacin for MG infection at Melbourne Sexual Health Centre (MSHC) from 2015–2024

Secondary aims:

- Assess moxifloxacin efficacy by site of infection and coinfection status
- Assess the impact of MSHC's introduction of ParC assay on moxifloxacin use and efficacy

The Study

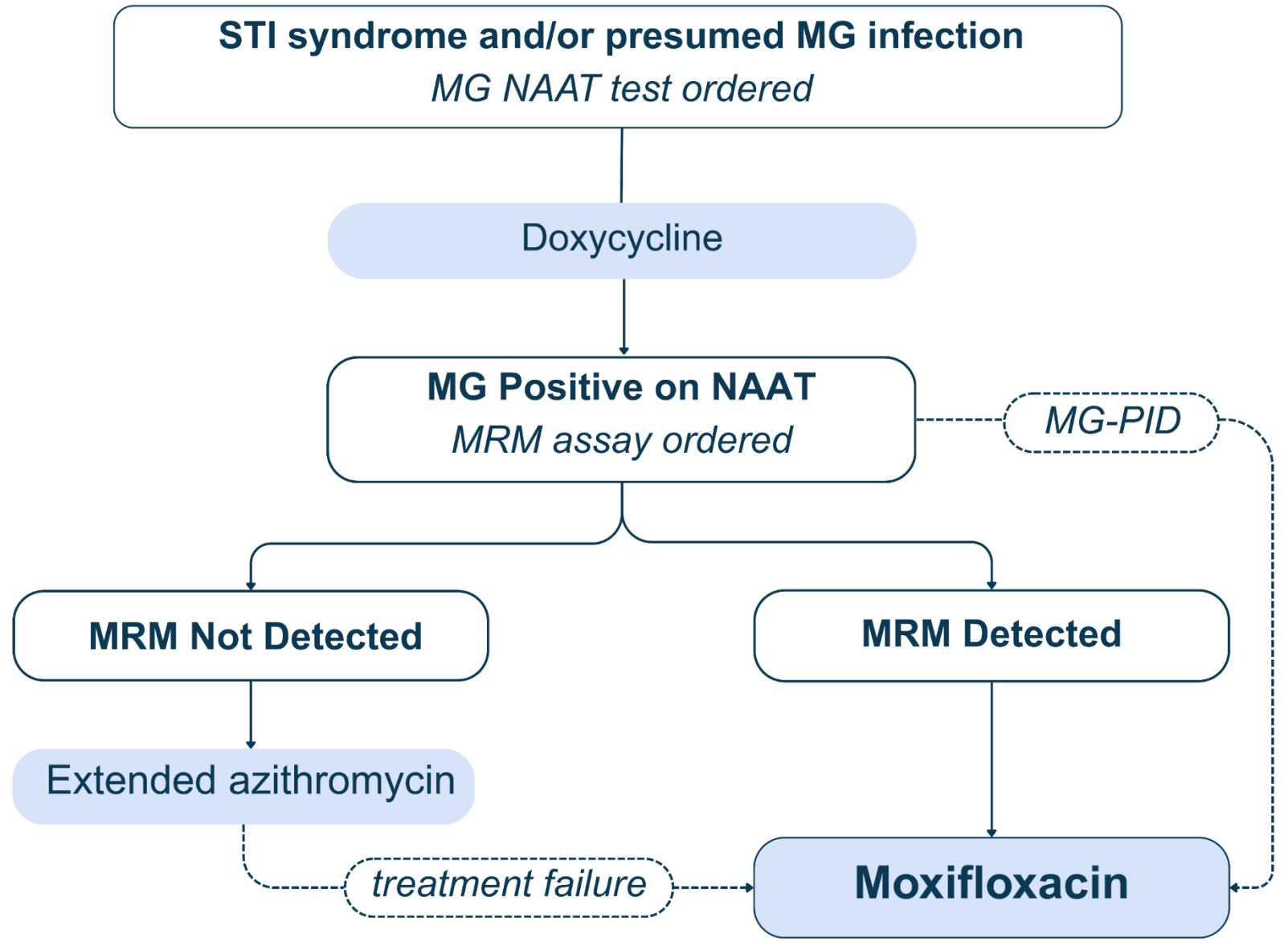
Retrospective audit of every MG infection diagnosed and managed at MSHC from 2015-2024

Large, urban sexual health service

Extraction of epidemiological, clinical, treatment data from electronic client records

Ethics Approval - Alfred Hospital Ethics Committee 232/16

Resistance-Guided Therapy (RGT)



NAAT: nucleic acid amplification test
MRM: macrolide-resistance mutation
PID: pelvic inflammatory disease

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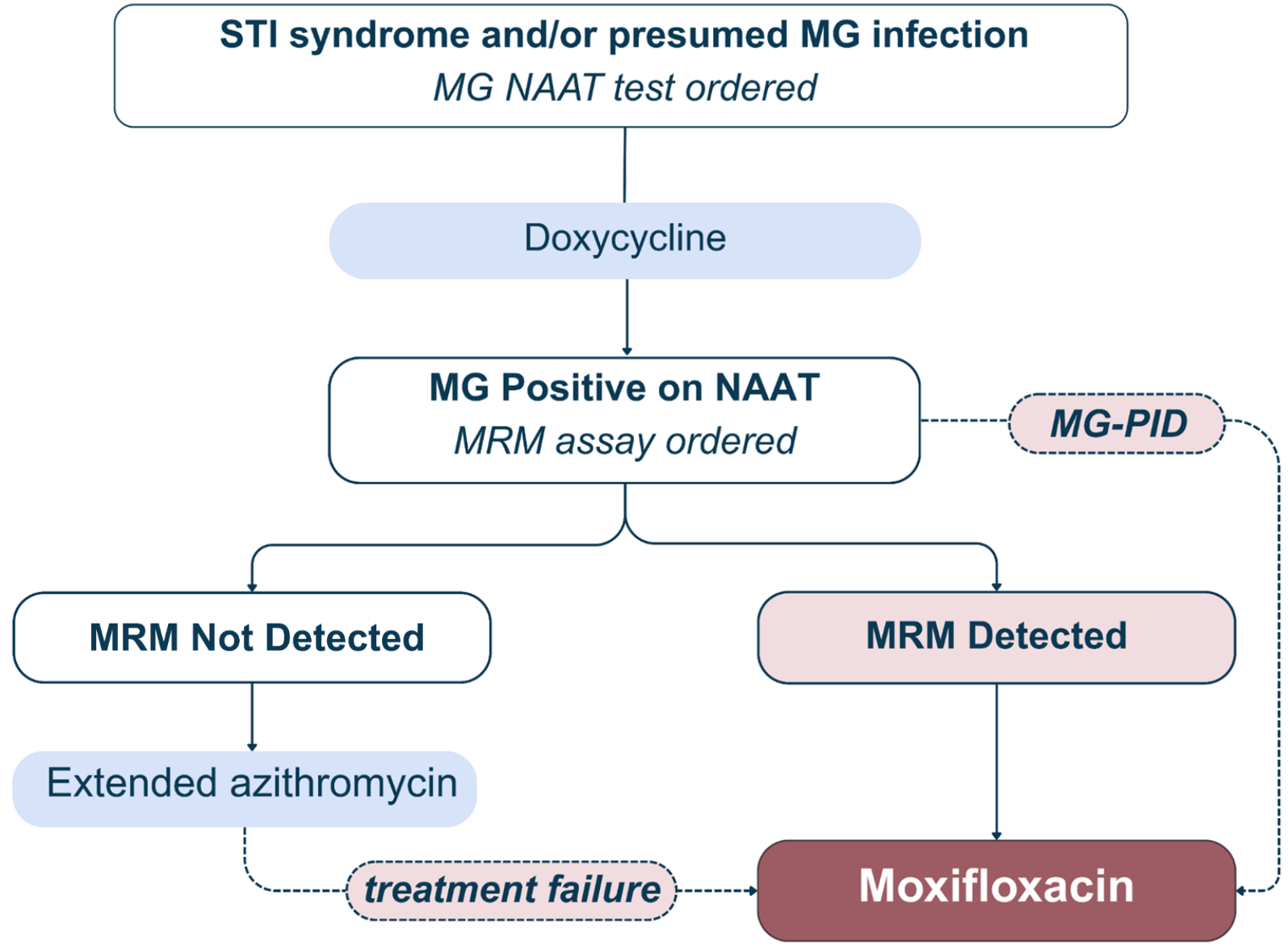

NAAT: nucleic acid amplification test
MRM: macrolide-resistance mutation
PID: pelvic inflammatory disease

MRM+	7 days
MG-PID	14 days

Outcomes

Eligible for use analyses

- MG diagnosed at MSHC 2015 – 2024
- Received moxifloxacin from MSHC pharmacy within 14 days of diagnosis or failed azithromycin
- No prior fluoroquinolone/minocycline/pristinamycin treatment for same infection

Eligible for efficacy analyses

- Treated with moxifloxacin *(as above)*
- Test of cure (TOC) at MSHC 14-90 days after completion of moxifloxacin
- Conclusive treatment outcome

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  - **Cure:** TOC was negative at all sites diagnosed and no inconclusive/invalid results
  - **Treatment failure:** TOC was positive at any site

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Conclusive treatment outcome

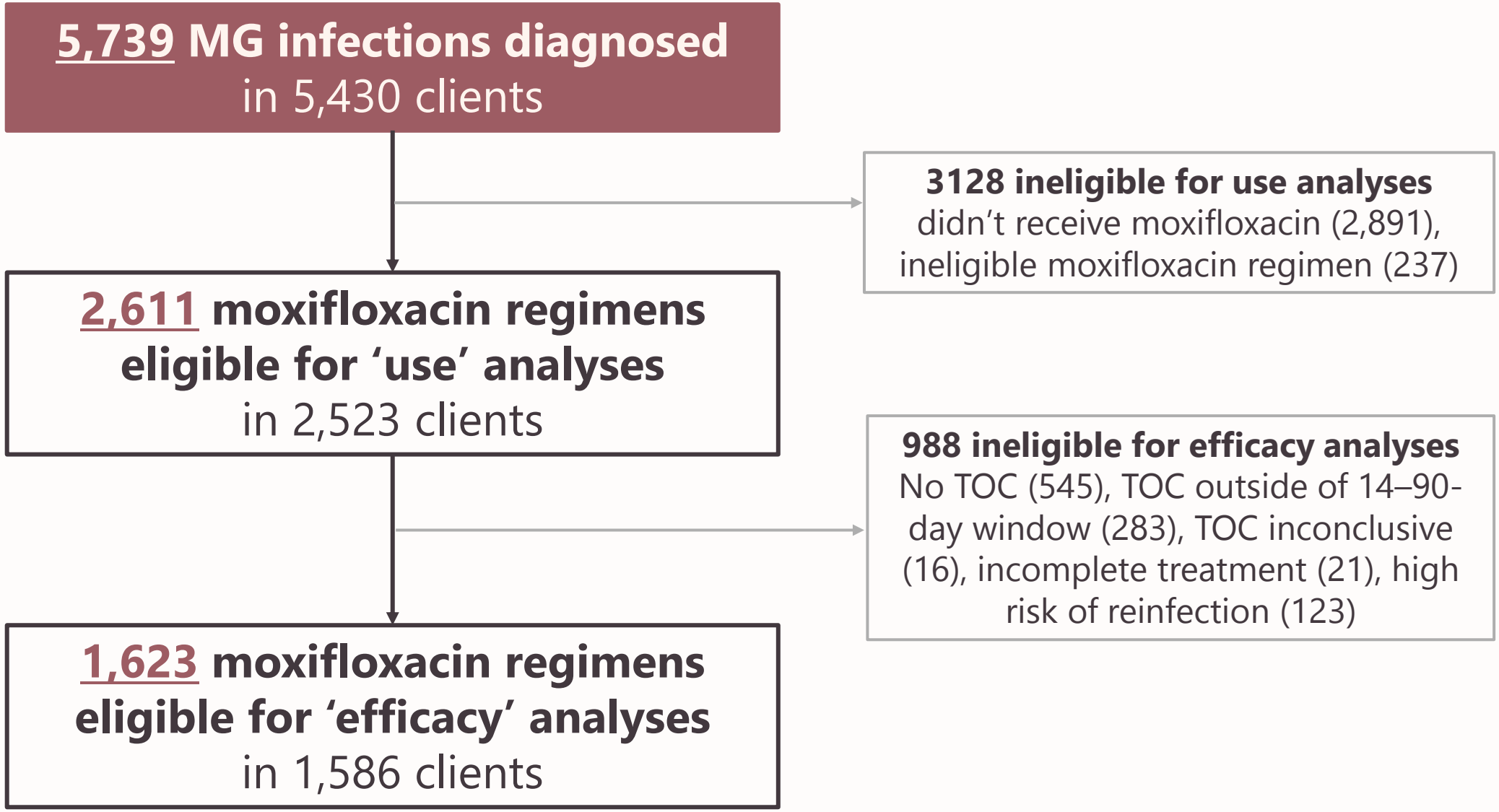
→ **Cure:** TOC was negative at all sites diagnosed and no inconclusive/invalid results

→ **Treatment failure:** TOC was positive at any site

Ineligible for efficacy analyses

- Did not return for TOC, returned outside of 14-90-day window, or TOC inconclusive
- Reported taking <50% prescribed doses of moxifloxacin (incomplete treatment)
- Clients reported condomless sex with an untreated ongoing partner (high risk of reinfection)

Overview of study population



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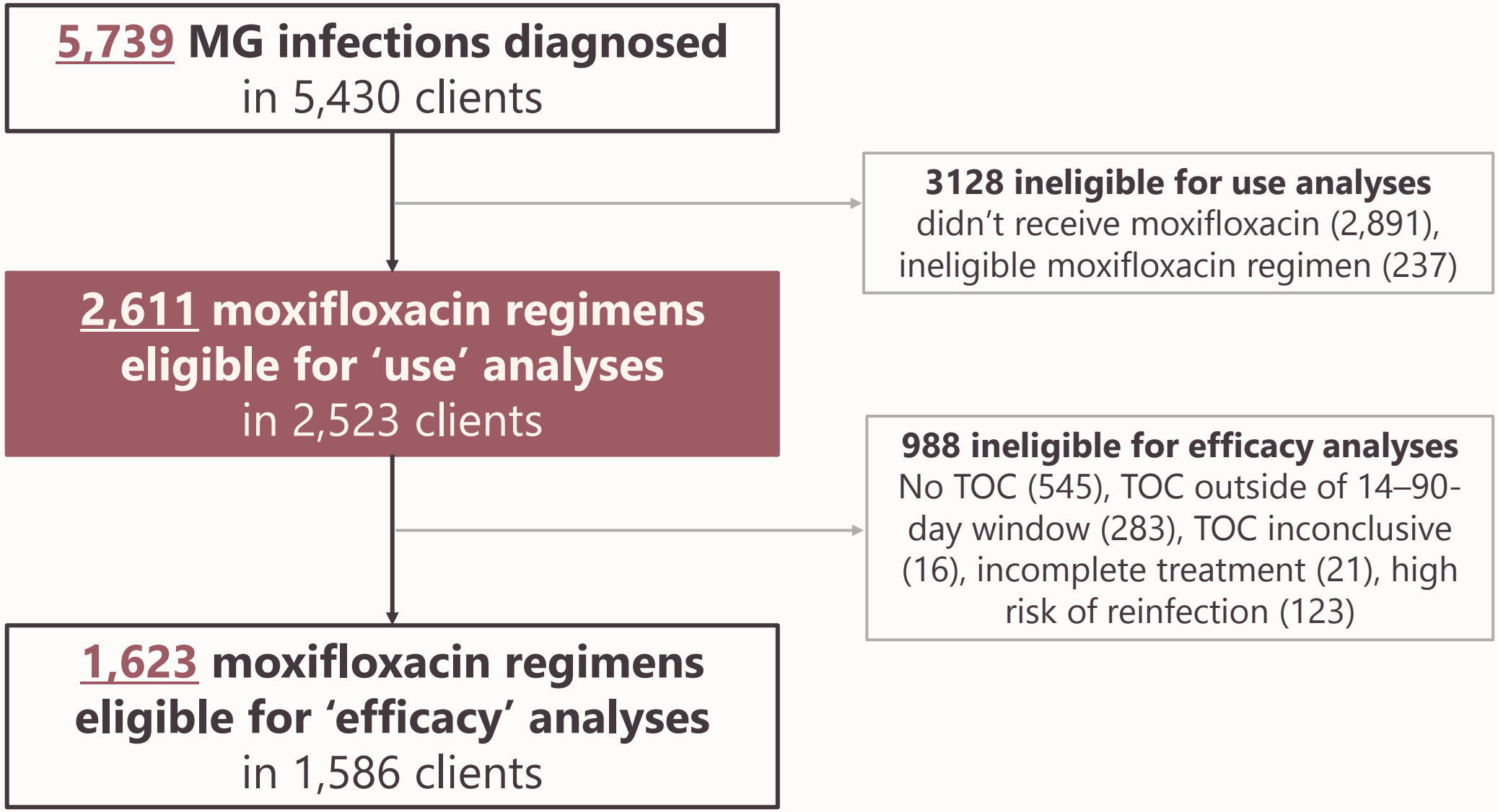

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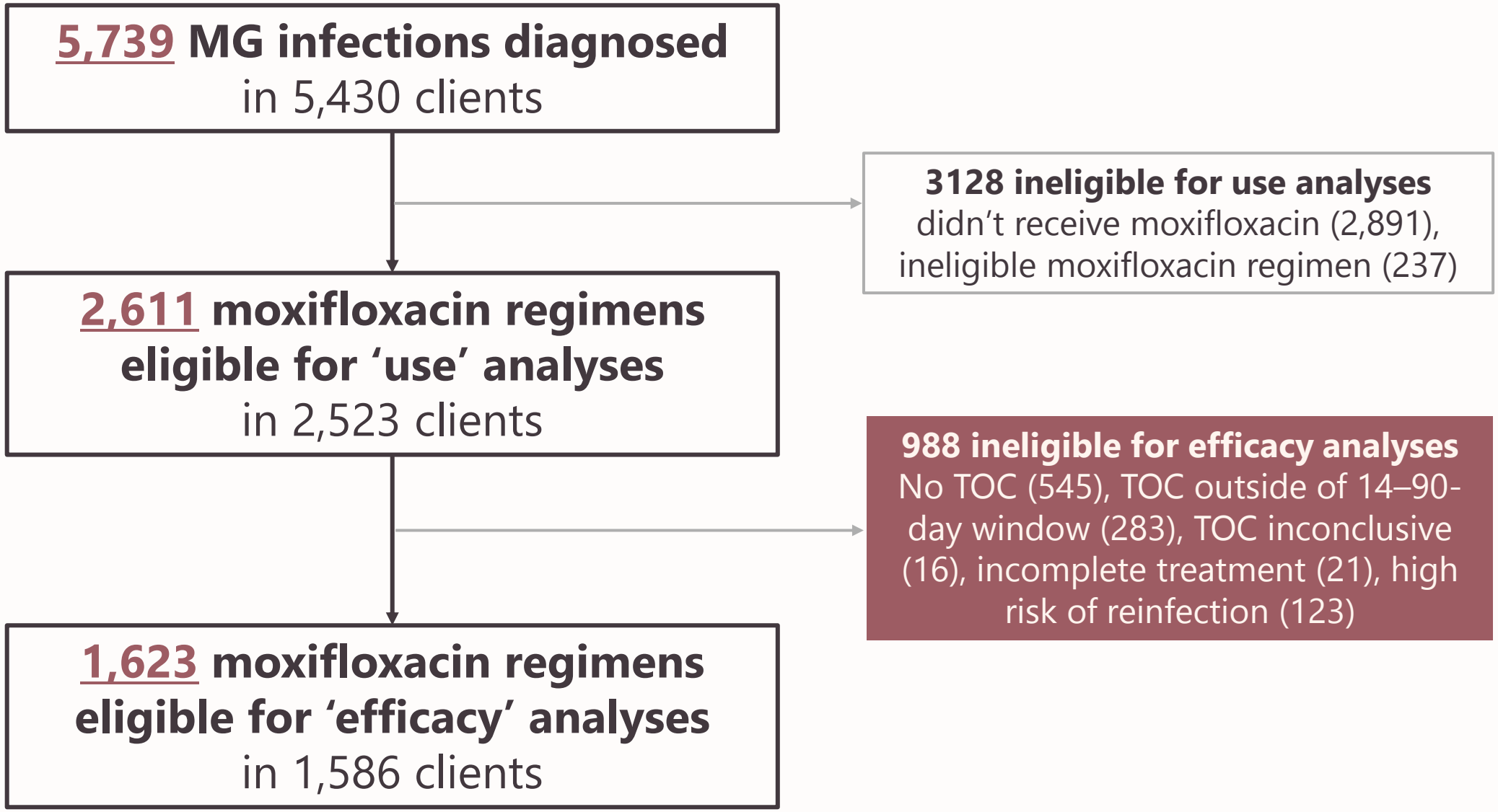

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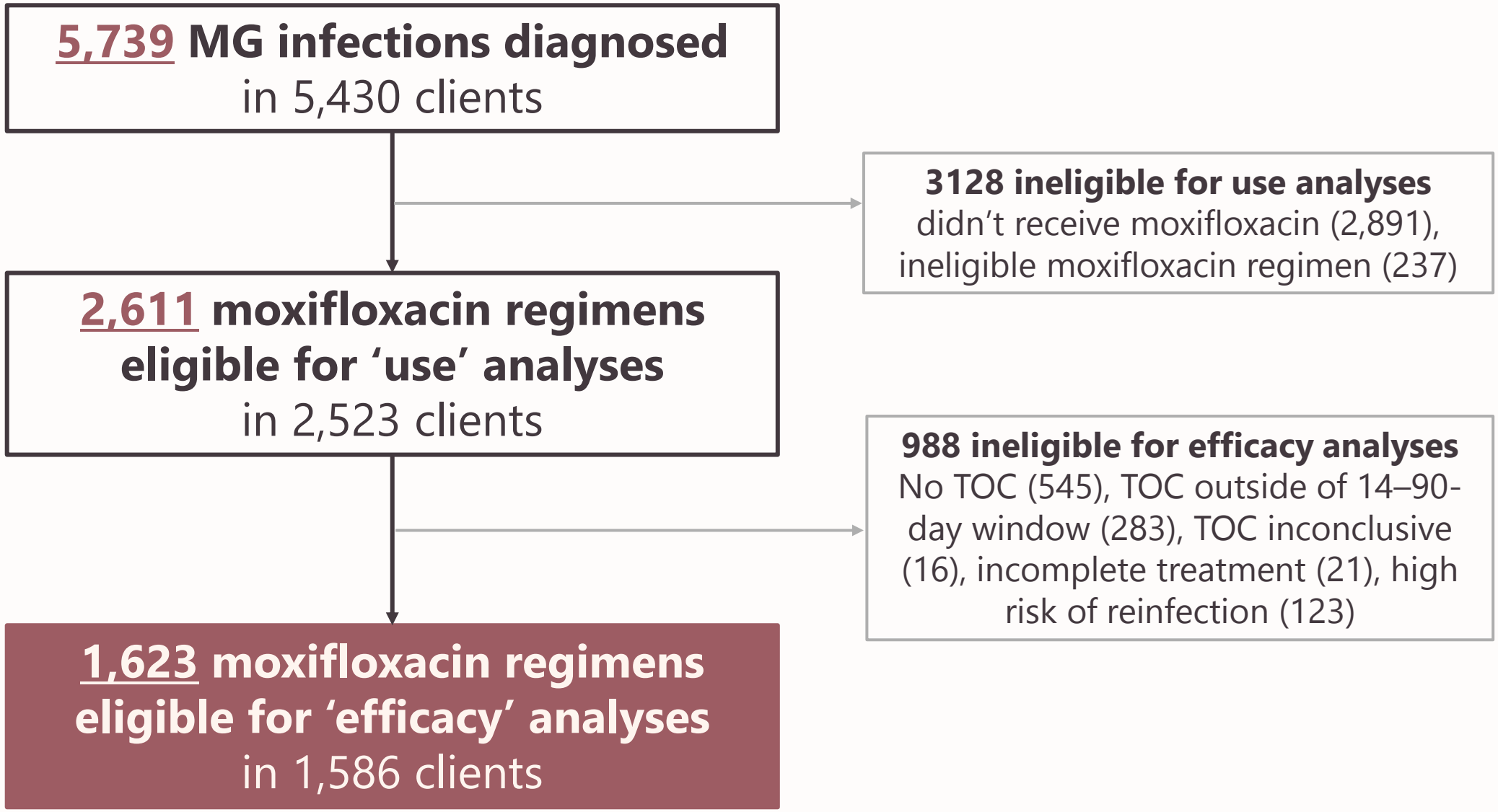

Characteristics of moxifloxacin-treated population

Characteristic	n (%) N=2611
Age, median [range]	28 [16-69]
People living with HIV	102 (3.91)
Gender & Sexuality	
Cisgender women	**863** (33.05)
Cisgender men (no male partners)	**633** (24.24)
Cisgender men (male partners)	**1043** (39.95)
Gender Diverse people	**72** (2.76)
Site of Infection	
Urine/urethral	**1565** (59.94)
Cervicovaginal	**699** (26.77)
Anorectal	**322** (12.33)
Multisite (anorectal + another)	**25** (0.96)

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**significantly ($p<0.05$) higher in infections receiving moxifloxacin compared to total study population (36% MSM and 1.5% GD)*

Characteristics of moxifloxacin-treated population

Characteristic	n (%) N=2611
Indication for Moxifloxacin	
MRM+ detected	**2,236** (85.64)
Failed azithromycin	**144** (5.52)
MG-PID	**231** (8.85)
Moxifloxacin Duration (days)	
7	**2,312** (88.55)
10*	**56** (2.14)
14	**243** (9.31)

**period in 2015/16 where 10-day regimen was used instead of 7-day*

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CT/NG Coinfection	
Neither detected	**2263** (86.67)
CT detected	**205** (7.85)
NG detected	**109** (4.17)
CT+NG detected	**34** (1.30)
BV Coinfection (N = 1124, 59% of women)	
BV detected (Nugent's ≥7)	**407** (36.21)
BV not detected (Nugent's <7)	**717** (63.79)

CT: *Chlamydia trachomatis*
NG: *Neisseria gonorrhoeae*
BV: Bacterial vaginosis

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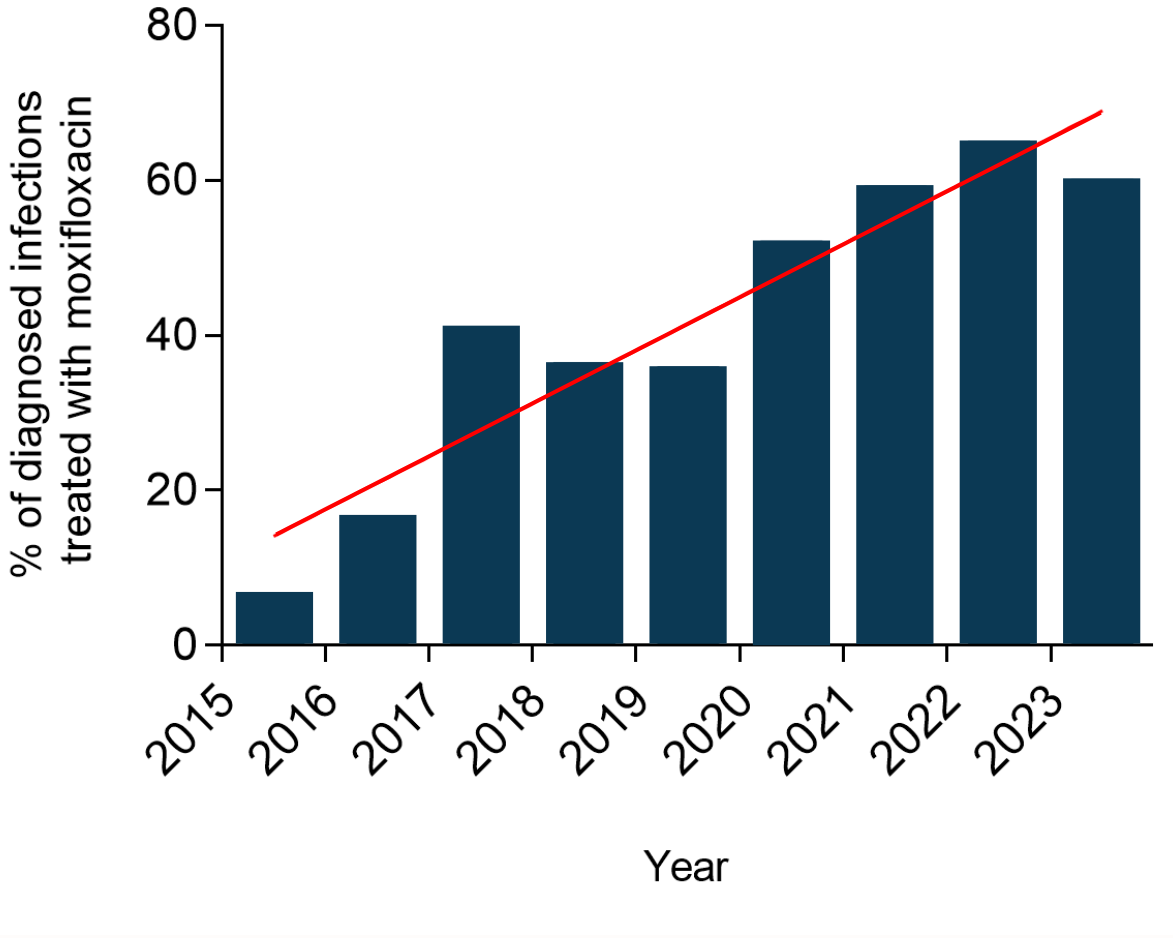
Moxifloxacin use by year, 2015-2023

Year	n regimens / N diagnoses	Use, % [95% CI]
2015	19/282	**6.74 [4.10-10.32]**
2016	72/433	16.63 [13.24-20.48]
2017	204/496	41.13 [36.76-45.60]
2018	263/719	36.58 [33.05-40.22]
2019	222/616	36.04 [32.24-39.97]
2020	255/488	52.25 [47.72-56.76]
2021	269/453	59.38 [54.70-63.94]
2022	368/565	65.13 [61.04-69.06]
2023	482/800	**60.25 [56.76–63.66]**
TOTAL	2,154/4,852	44.39 [42.99-45.81]



p_{trend} <0.0001

Year-on-year changes to moxifloxacin use

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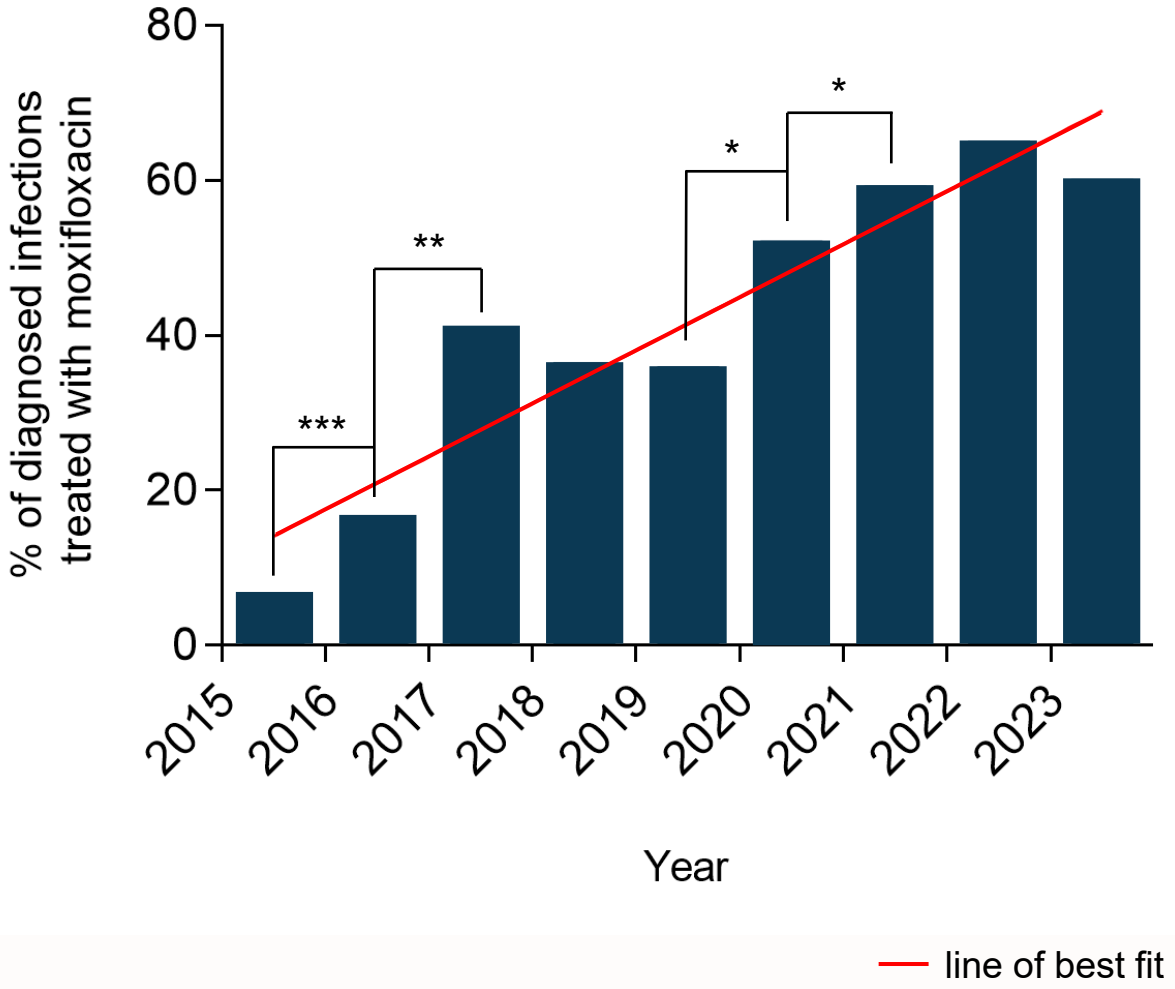
Significant increase from year prior

** p<0.05* *** p<0.01* ****p<0.0001*



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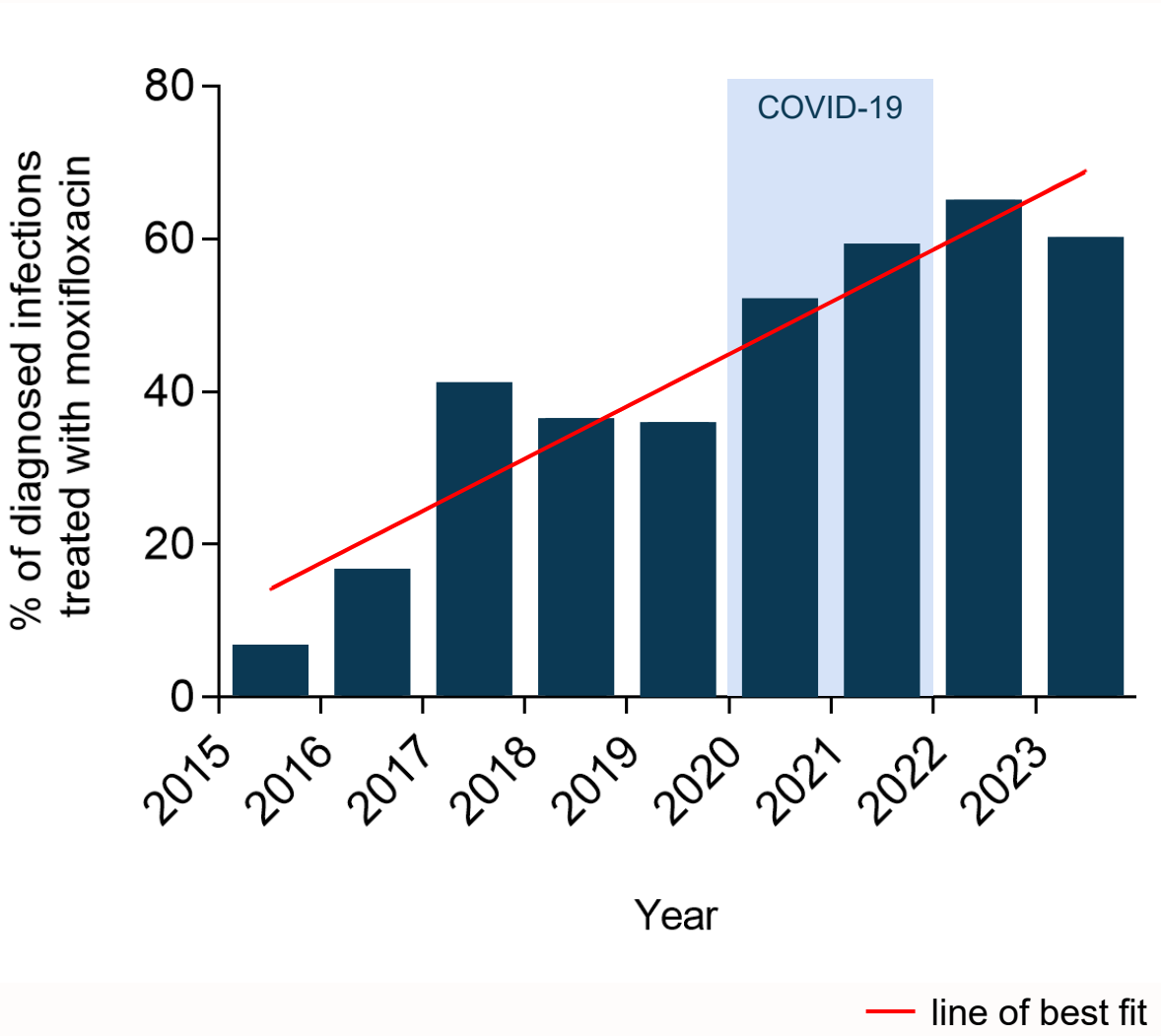
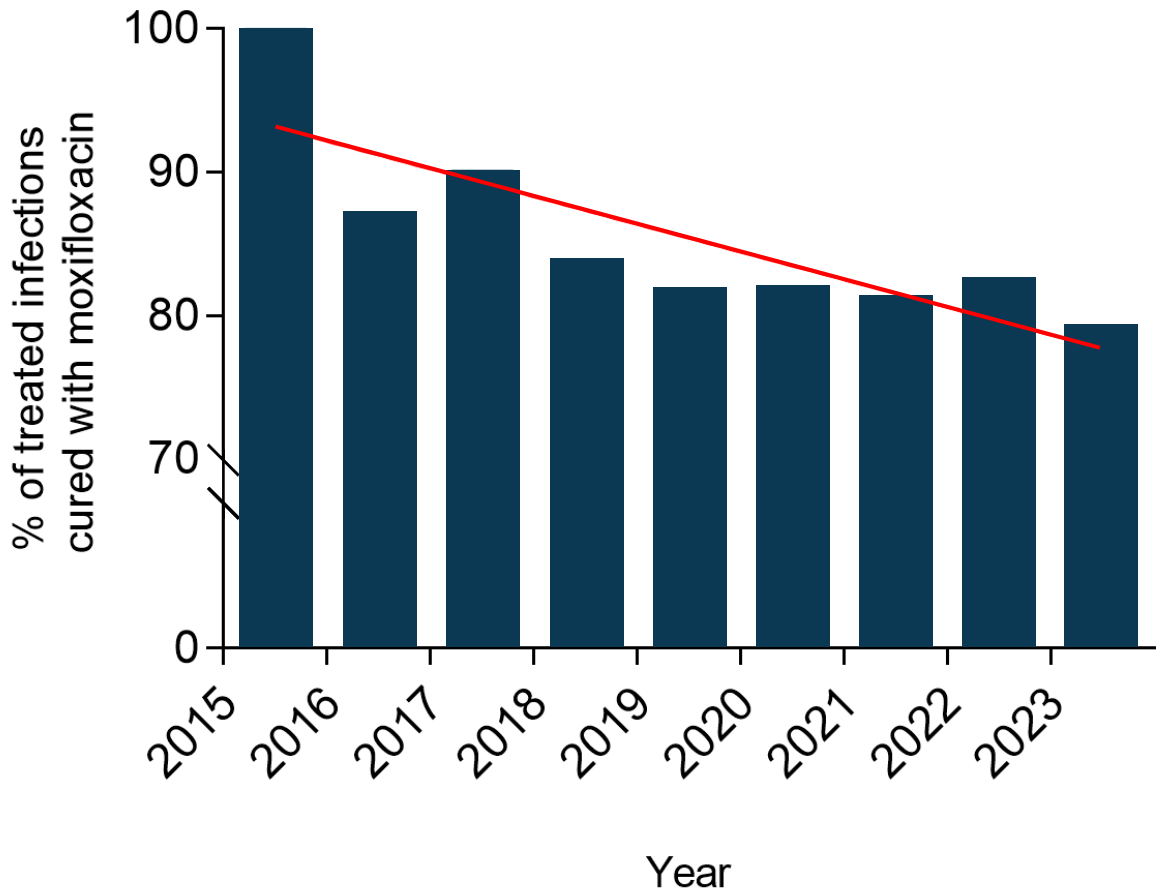


Moxifloxacin efficacy by year, 2015-2023

Year	n cures / N eligible regimens	Efficacy, % [95% CI]
2015	11/11	**100 [71.51-100]**
2016	34/39	87.18 [72.57-95.70]
2017	110/122	90.16 [83.45-94.81]
2018	141/168	83.93 [77.49-89.13]
2019	116/140	81.86 [75.58-88.70]
2020	142/173	82.08 [75.54-87.49]
2021	144/177	81.36 [74.83-86.81]
2022	190/230	82.61 [77.08-87.28]
2023	238/300	**79.33 [74.30-83.77]**
TOTAL	1,126/1,360	**82.79 [80.68-84.76]**



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No significant increase in LTFU (p>0.05)

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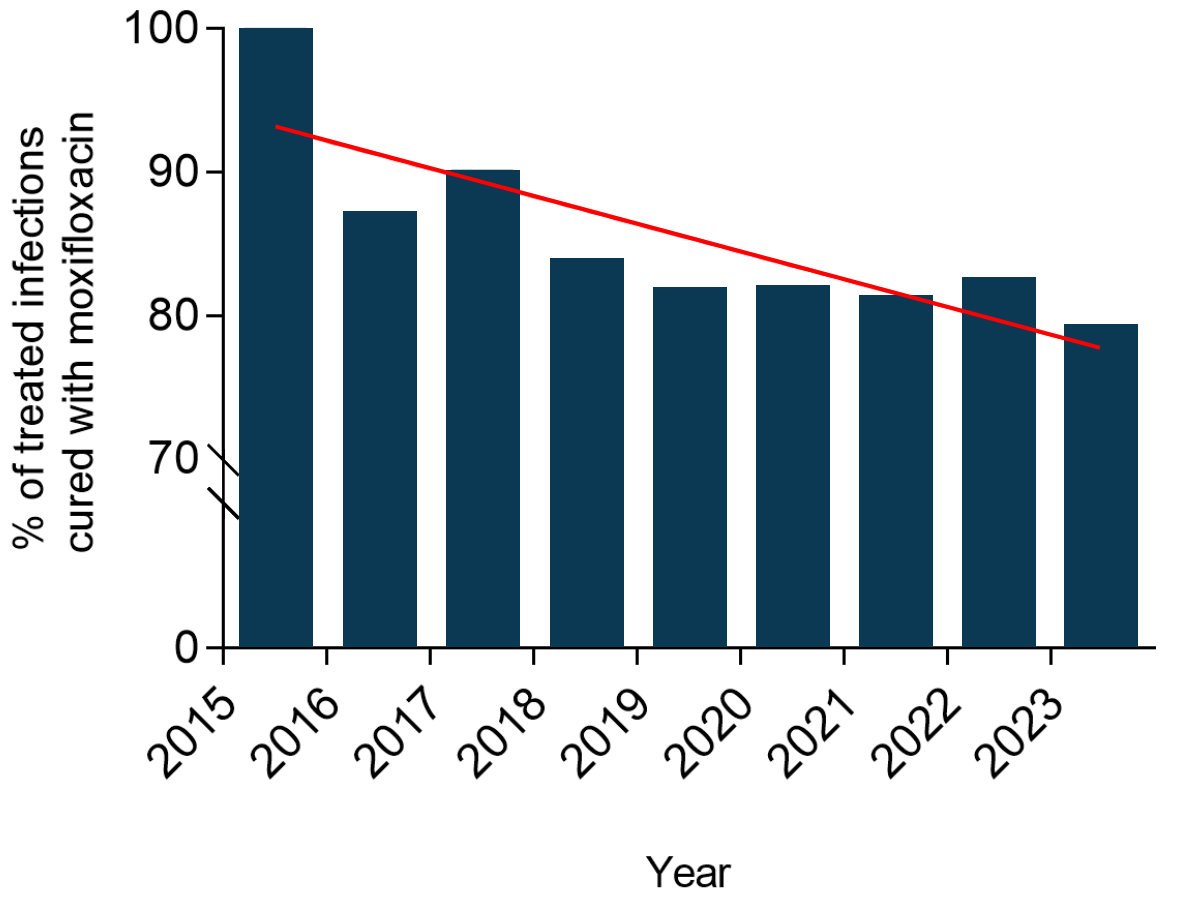

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Introduction of ParC Assay, 2024

In early 2024, ParC PCR resistance assay introduced to MSHC practice

All MRM+ samples undergo assay

Assay targets: **ParC S83** (wildtype) and **ParC S83I** (mutant)

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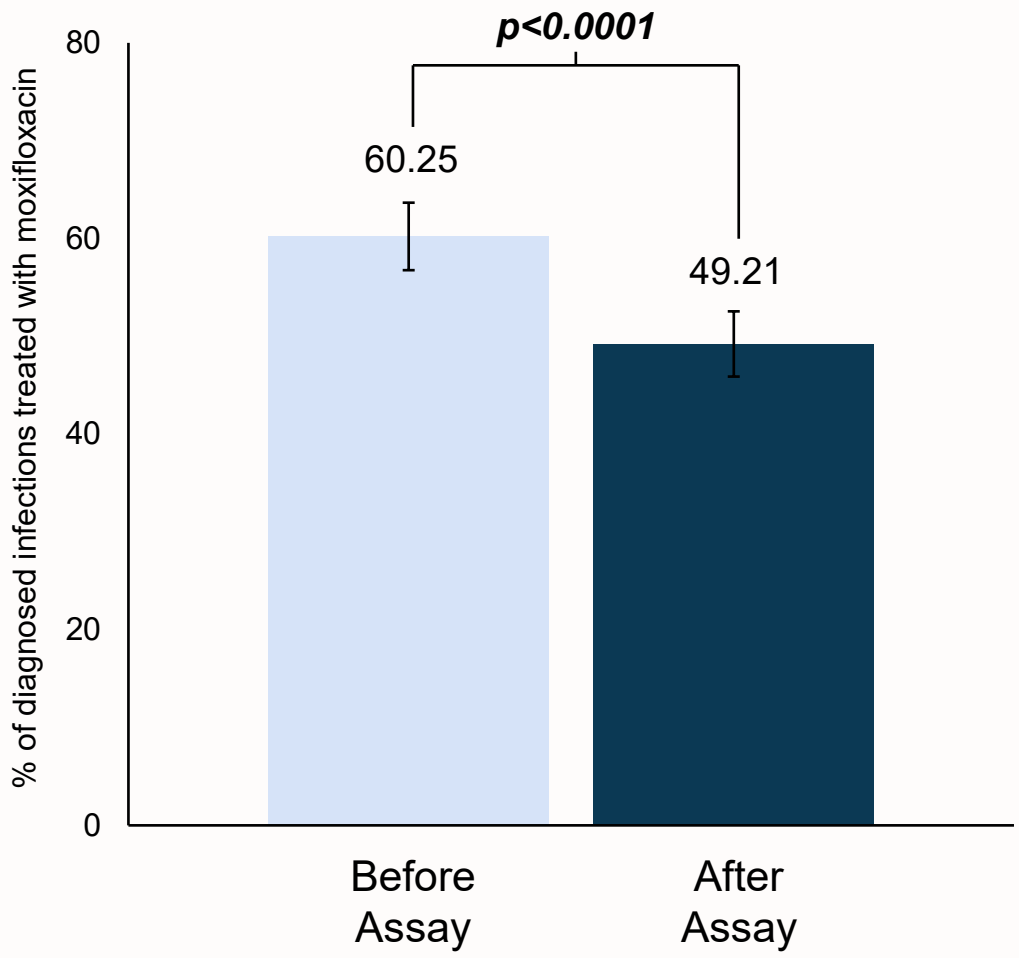
Assay targets: **ParC S83** (wildtype) and **ParC S83I** (mutant)

Assay result	Interpretation	Curative antibiotics
ParC S83I mutant	Reduced susceptibility to moxifloxacin	Metronidazole + Minocycline *OR* Sitafloxacin
ParC S83 wildtype	susceptible to moxifloxacin	**Moxifloxacin**
No result	below limit of detection of assay, or another mutation (*e.g. S83R*) detected	
Invalid test	assay unable to be performed (*i.e.* due to inhibition or sample contamination)	

Moxifloxacin use after introduction of ParC assay

	n regimens / N diagnoses	Use, % [95% CI]
Before Assay	482/800	**60.25** [56.76–63.66]
After Assay*	438/890	**49.21** [45.88-52.55]

p *< 0.0001*

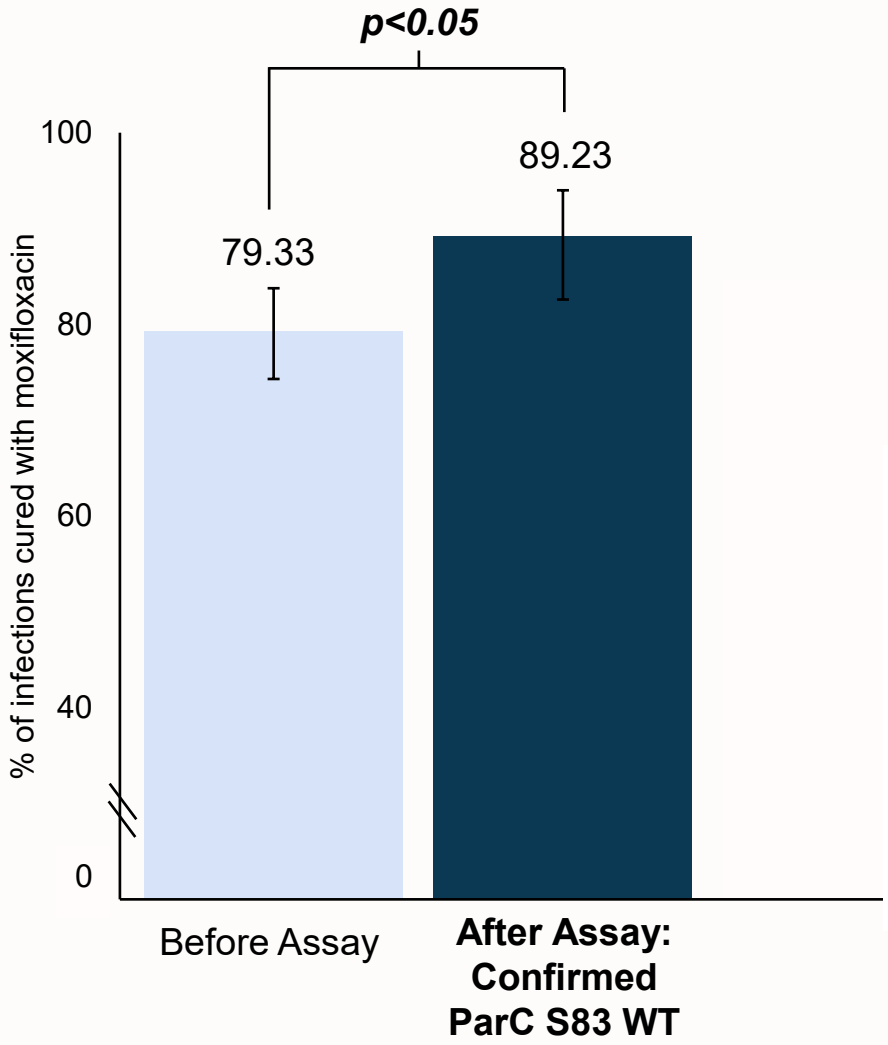


**1 May 2024 – 1 May 2025, accounting for roll-out period*

Moxifloxacin efficacy after introduction of ParC assay

	n cured / N eligible regimens	Efficacy, % [95% CI]
Before Assay	238/300	**79.33** [74.30–83.77]
After Assay: ParC S83 WT infections	116/130	**89.23** [82.59-93.99]

***p* = 0.013**



Infections treated with moxifloxacin, by ParC result

Assay Result	Number of infections treated with moxifloxacin, n N=241	Efficacy, % [95% CI]
ParC S83 WT	**130**	**89.23** [82.59-93.99]
No result	**63**	80.95 [69.09-89.75]
Invalid test	**19**	68.42 [43.45-87.42]
ParC assay not performed (no MRM+ result)	**29**	82.76 [64.23-94.15]

Only **54%** of moxifloxacin-treated infections were **confirmed** ParC S83 wildtype

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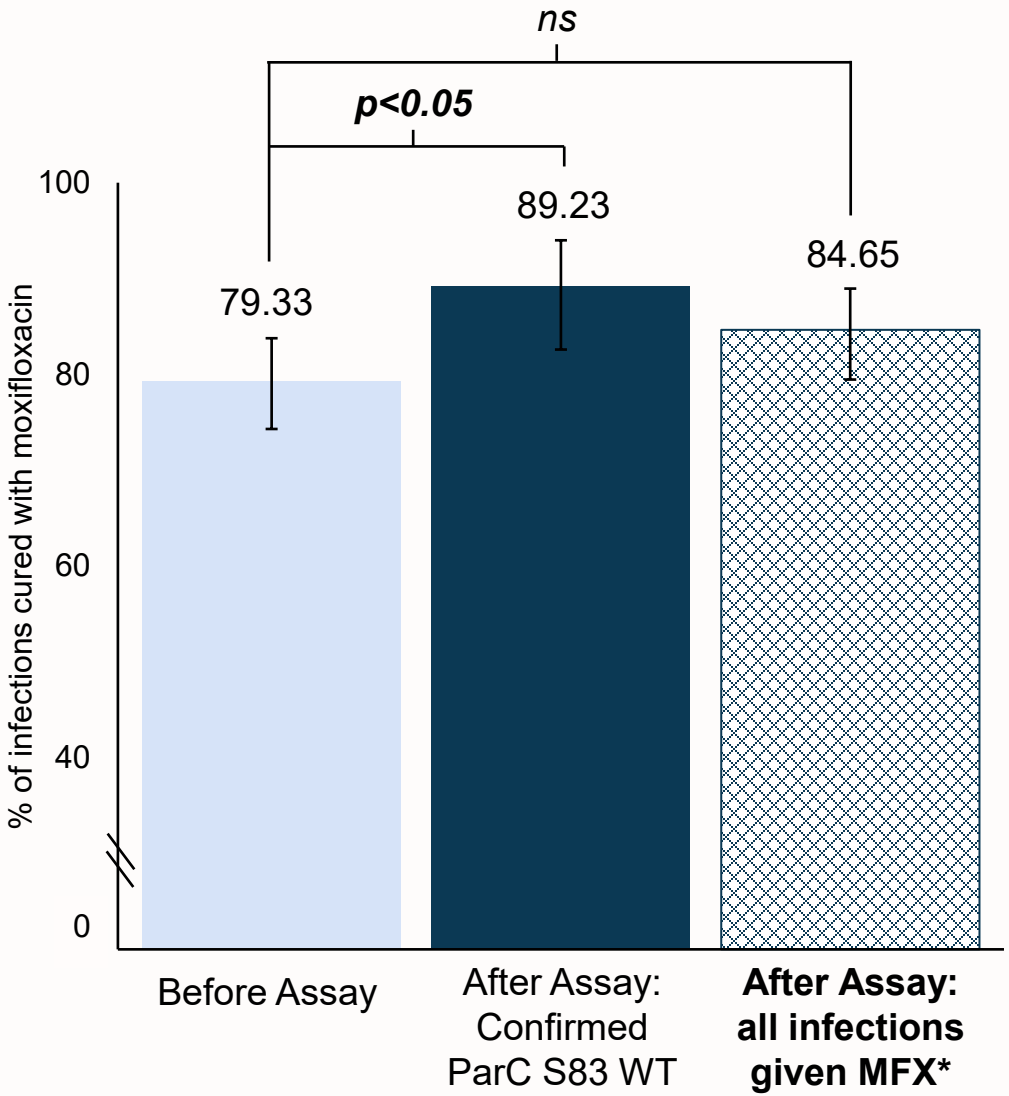
Only **54%** of moxifloxacin-treated infections were **confirmed** ParC S83 wildtype

Moxifloxacin efficacy after introduction of ParC assay

	n cured / N eligible regimens	Efficacy, % [95% CI]
Before Assay	238/300	**79.33** [74.30–83.77]
After Assay: ParC S83 WT infections	116/130	**89.23** [82.59-93.99]
After Assay: all infections given MFX*	204/241	**84.65** [79.46-88.95]

Overall moxifloxacin efficacy impacted by high proportion of infections with indeterminate ParC assay results, some of which would be resistant



**i.e.* including ParC S83 WT, No Result, Invalid, MRM not detected

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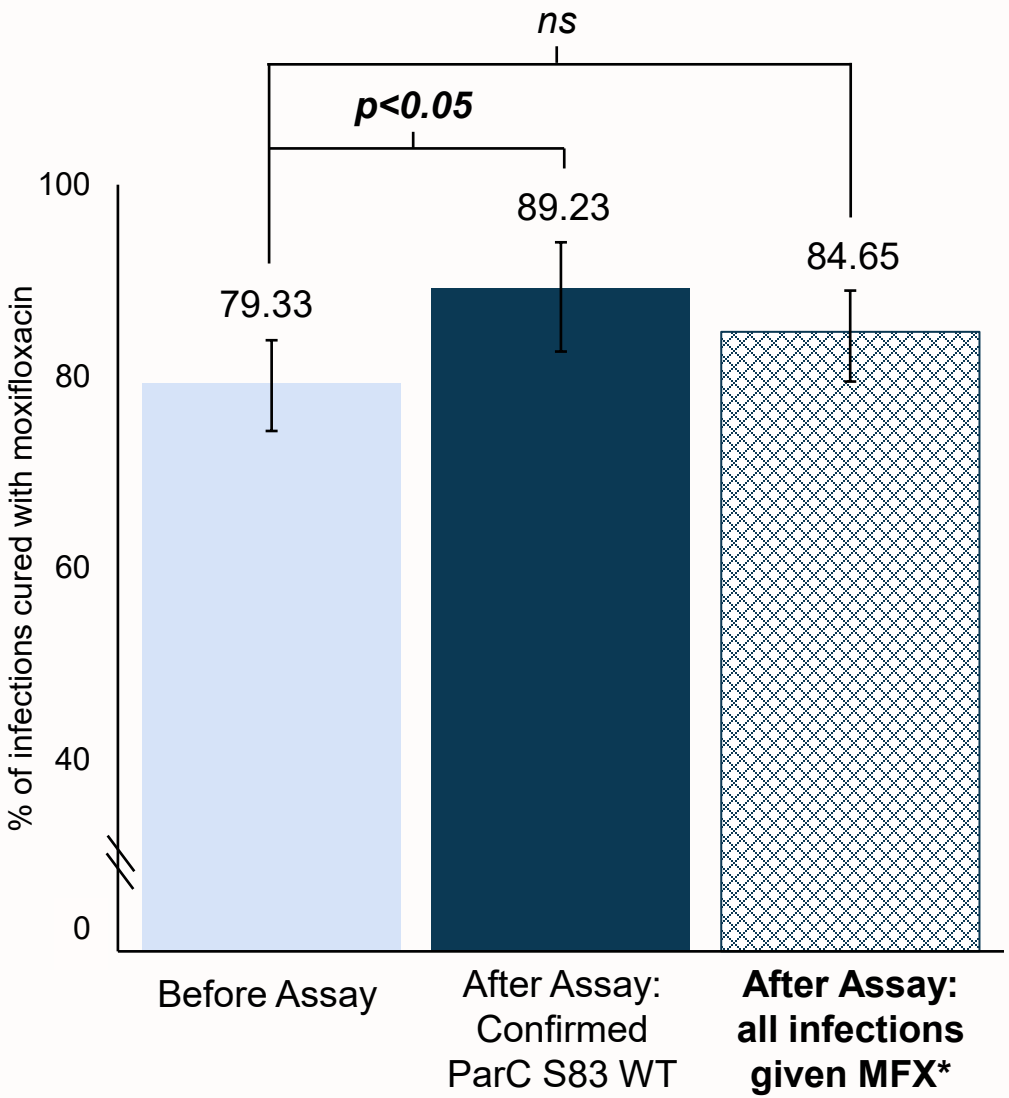
Loss to follow-up increased after assay introduction, from 38% to 45% ($p<0.05$) which likely impacted findings (selection bias for unresolved infections)



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- Large sample size
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- No ParC data, 2015-2023
- Loss to follow up affecting efficacy estimates
- Population with high antimicrobial consumption, drug-resistant STIs
- More “no result” and “invalid” ParC results than anticipated

  Low load infections, and differences in test sensitivity ⟶ **‘resistance gap’**

In Summary: Trends in Moxifloxacin Use and Efficacy

Moxifloxacin now the most common curative antibiotic for MG at MSHC, surpassing azithromycin due to increasing MRM

Efficacy is in decline:

- 2023 estimate of 79% is lowest reported MFX efficacy from MSHC
- 2015-23 estimate of 83% lower than Li's meta-analysis (100% 2003-09, 89% 2010-17)

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"trigger point" for MRM assay (2006): **~75% AZI efficacy**

efficacy of moxifloxacin (2023): **79%**

Time for Next-Gen RGT?

MSHC's introduction of ParC assay in 2024 significantly reduced our use of moxifloxacin

Cure was significantly improved for confirmed ParC S83 wildtype infections

ParC assay shows great promise for MG management, but technology remains new and imperfect at this stage

Time for Next-Gen RGT?

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for further investigation…

Previous MSHC study reported moxifloxacin cure ≥96% for ParC wildtype[5]

Mutations to GyrA binding site? Other factors driving moxifloxacin failure?

How do we manage ParC S83I infections safely and effectively?

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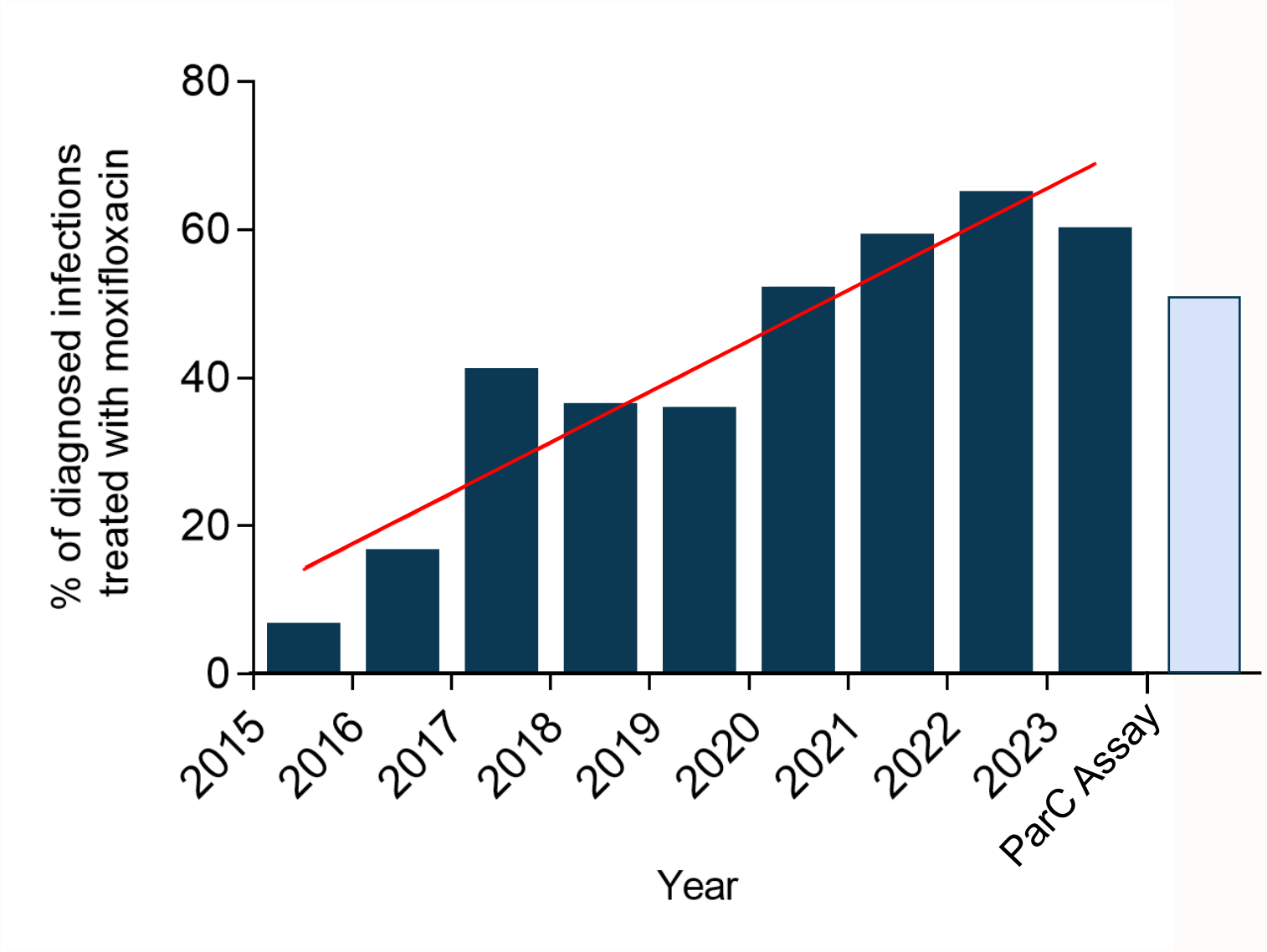
Moxifloxacin use by year



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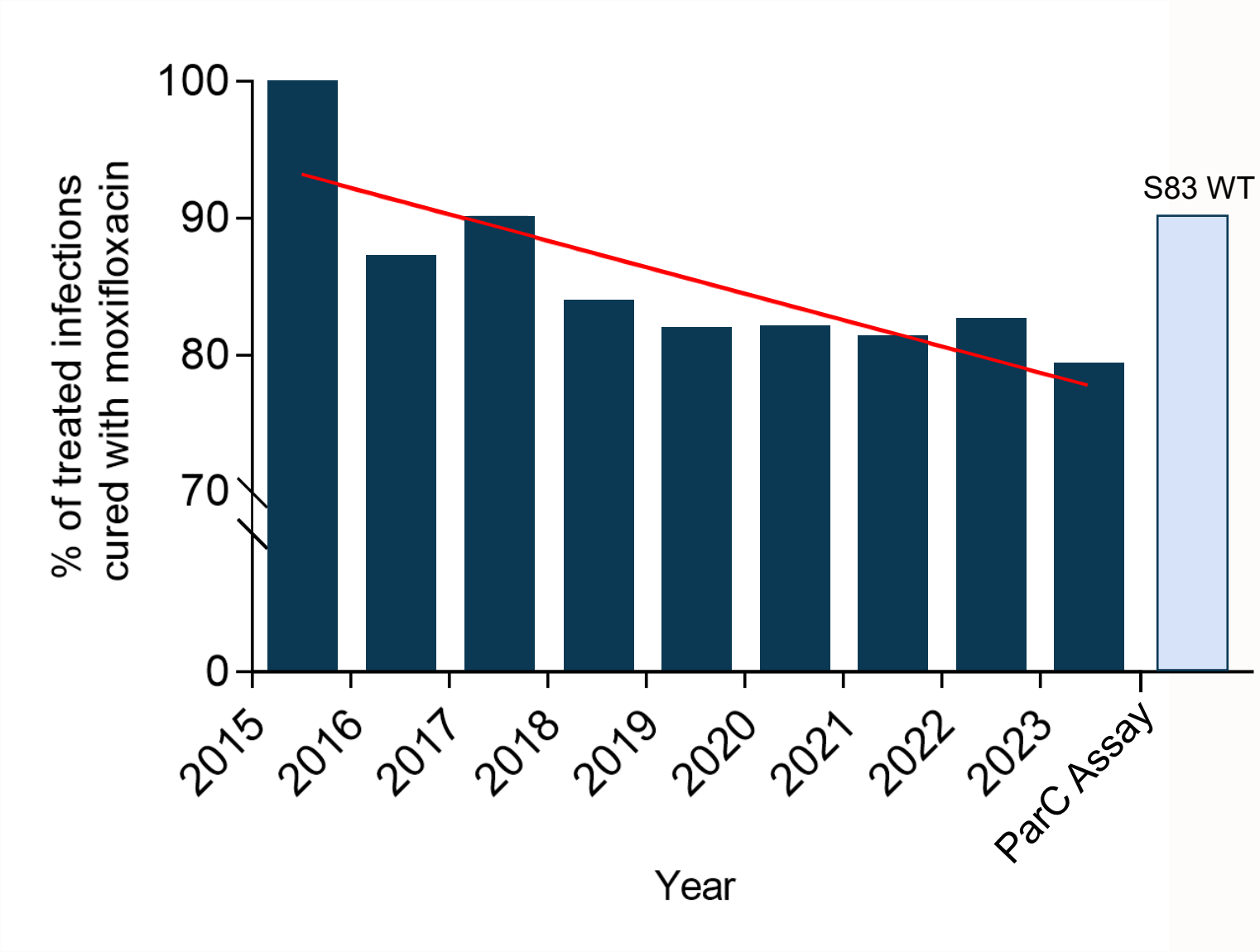

Appendix: Secondary Outcomes