Resistance-guided treatment of Mycoplasma genitalium: Observations from a UK sexual health centre

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Declarations

- SpeeDx Ltd provided the kit and all reagents free of charge
- SpeeDx were not involved with the analysis or interpretation of data

Mgen: **Underdiagnosed** & **hard-to-treat…**

- Causes **NGU** and **PID**[1]
- Rx choice: uncomplicated vs. complicated infection[2]
- **Uncomplicated**
  - 1st **Azithromycin**
  - 2nd **Moxifloxacin**

  Complicated
  - 1st **Moxifloxacin**
- High rates of macrolide resistance in UK & globally
- Poor patient satisfaction & clinic resource intensive
- ∴ increasing use of quinolones

Overuse of single dose azithromycin 1g

+

Underdiagnosis of Mgen in UK

=

High macrolide resistance

- UK 41%
- Worldwide 30-100%

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↑ QR is seen with ↑ quinolone use

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Limited future options

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Increasing quinolone use

Overuse of single dose azithromycin 1g + Underdiagnosis of Mgen in UK = High macrolide resistance
- UK 41%
- Worldwide 30-100%

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An untreatable STI? = ↑ dual resistance + ? Moxifloxacin induces resistance + Increasing quinolone use

Limited future options

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↳ Resistance-guided treatment

5.2	All *M. genitalium* positive specimens should be tested for macrolide resistance mediating mutations	1B
6.2	Treatment regimens for uncomplicated infection: Doxycycline 100mg two times daily for 7 days followed by azithromycin 1g orally as a single dose then 500mg orally once daily for 2 days Moxifloxacin 400mg orally once daily for 10 days	 1D 1B
6.3	Treatment regimens for complicated infection: Moxifloxacin 400mg orally once daily for 14 days	 1D
6.5	Alternative treatment regimens: Doxycycline 100 mg two times daily for 7 days followed by pristinamycin 1g orally four times daily for 10 days Pristinamycin 1g orally four times daily for 10 days Doxycycline 100mg orally twice daily for 14 days Minocycline 100mg orally twice daily for 14 days	 2C 2C 2C 2D

Resistance-guided treatment

Does this help **patients**?

Does this help **clinics**?

Is this ”worth it”?

Taken from 2018 BASHH *Mycoplasma genitalium* guidelines[2]

Aims

- To measure **macrolide** and **quinolone resistance** in Mgen infection across attendees of a UK sexual health centre
- Clinically evaluate **resistance-guided treatment** of Mgen infection

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1. Antibiotic failure rate
2. Time to microbiological cure
3. Time to symptom resolution

Methods: **Evaluation of RGT in Brighton**

- Across 3 months: +ve Mgen NAAT → Also tested for **macrolide-resistance mutations** (ResistancePlus® MG)
- Azithromycin avoided if macrolide resistance mutations detected

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- Across 3 months: +ve Mgen NAAT → Also tested for **macrolide-resistance mutations** (ResistancePlus® MG)
- Azithromycin avoided if macrolide resistance mutations detected
- ‘Microbiological cure’ = -ve test 5 weeks after Rx
- ‘Antibiotic failure’ = positive test at TOC
- Comparison: those not given RGT (Year preceding)
- Batch tested stored samples using SpeeDx **ParC (beta) assay**

Results: **48** patients tested positive for Mgen

Macrolide resistance: 35/48 **(73%)**

Quinolone resistance: 3/32 **(9%)**

Results: **48** patients tested positive for Mgen

- **34** given RGT
- **21** patients return for f/u
  - 11 Males with NGU
  - 7 Females with PID
  - 3 Asymptomatic contacts

Pre-RGT comparison

- **85** patients return for f/u
  - 54 Males with NGU
  - 34 Females with PID
  - 20 Asymptomatic contacts

- Only demographic difference = higher proportion of **unknown HIV serostatus** in prospective cohort

1 Antibiotic failure rate

Overall

RGT	Pre-RGT	p
1/21 (5%)	24/85 (28%)	0.023

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Failure with azithromycin

Pre-RGT: **33%** vs 0% with moxifloxacin (p=0.017)

RGT: **20%*** vs 0% with moxifloxacin (p=0.238) → More appropriate use of azithromycin

2 Time to microbiological cure

Overall

RGT	Pre-RGT	p
63.7 days (95% CI 50.4 - 76.9)	**85.1 days** (95% CI 73.5 - 96.7)	0.122

Males with NGU

RGT	Pre-RGT	p
54.7 days (95% CI 40.9 - 68.5)	**88.4 days** (95% CI 73.7 - 103.0)	0.036

Females with PID = 0.607

3 Time to symptom resolution

Overall

RGT	Pre-RGT	p
64.2 days (95% CI 54.7 - 73.6)	**58.6 days** (95% CI 49.3 - 67.9)	0.200

What does this mean?

- **Higher MR** than 5 years previously (41%)[3]
- Higher QR than previous estimates[2]
- **Lower** antibiotic failure rate
  - better for patients and clinics
- Shorter time to microbiological cure (NGU)
  - RGT is particularly good for the treatment of urethritis
- **No effect** on time to symptom resolution
- RGT preserves the efficacy of moxifloxacin
  - Curbs increase in patients requiring expensive additional Rx

Limitations & future development

- Single centre & small sample size
- High rate of lost-to-follow-up
- Wide confidence interval
- Data for analysis was limited by what was reported in records
  - Cumbersome EPR
- Project extended by 3 months – data analysis on going
- Publication later this year

Thank you

Any questions?

References

1. Taylor-Robinson D, Jensen JS. Mycoplasma genitalium: from Chrysalis to Multicolored Butterfly. *Clin Microbiol Rev* 2011;24:498–514.

2. Soni S, Horner P, Rayment M, et al. British Association for Sexual Health and HIV national guideline for the management of infection with Mycoplasma genitalium. [Online]. 2018. [accessed 9 Jan 2019]. Available from: https://www.bashhguidelines.org/media/1198/mg-2018.pdf

3. Pond MJ, Nori A V., Witney AA, et al. High prevalence of antibiotic-resistant mycoplasma genitalium in nongonococcal urethritis: The need for routine testing and the inadequacy of current treatment options. *Clin Infect Dis* 2014;58(5):631-7

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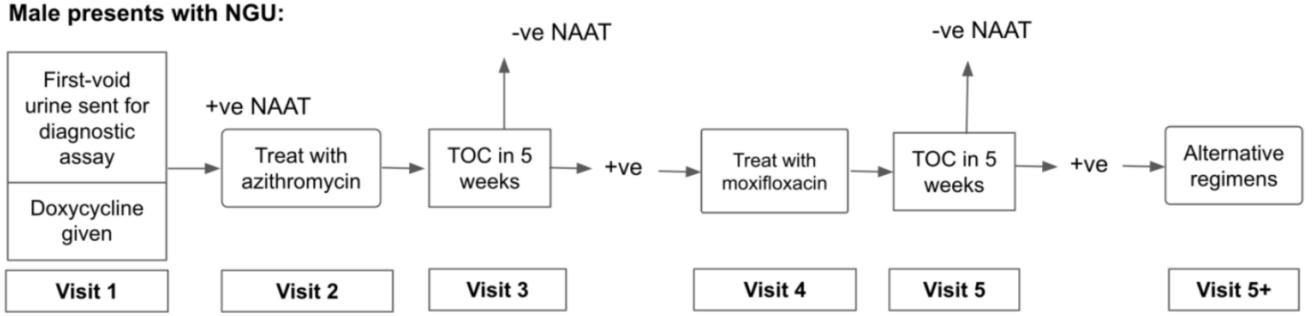
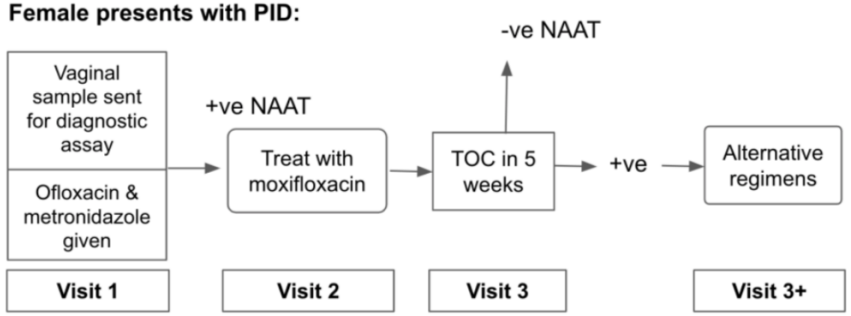
Pre-Resistance-guided therapy

Male presents with NGU:

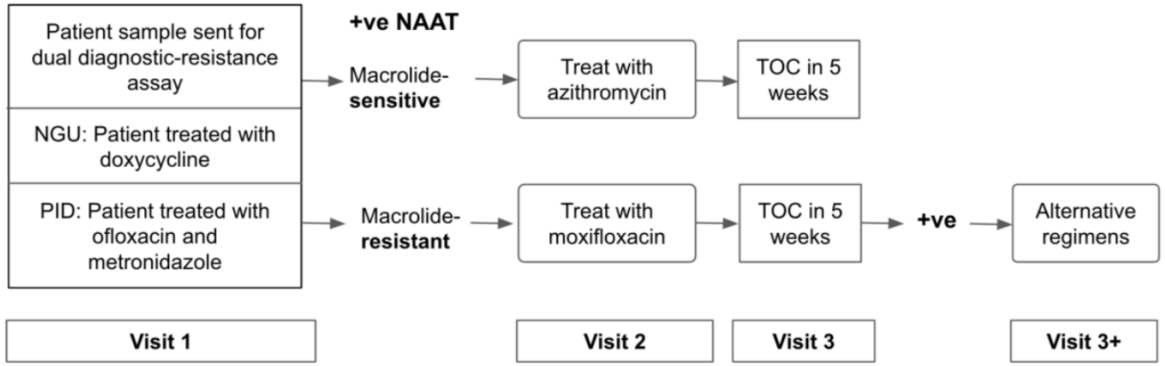


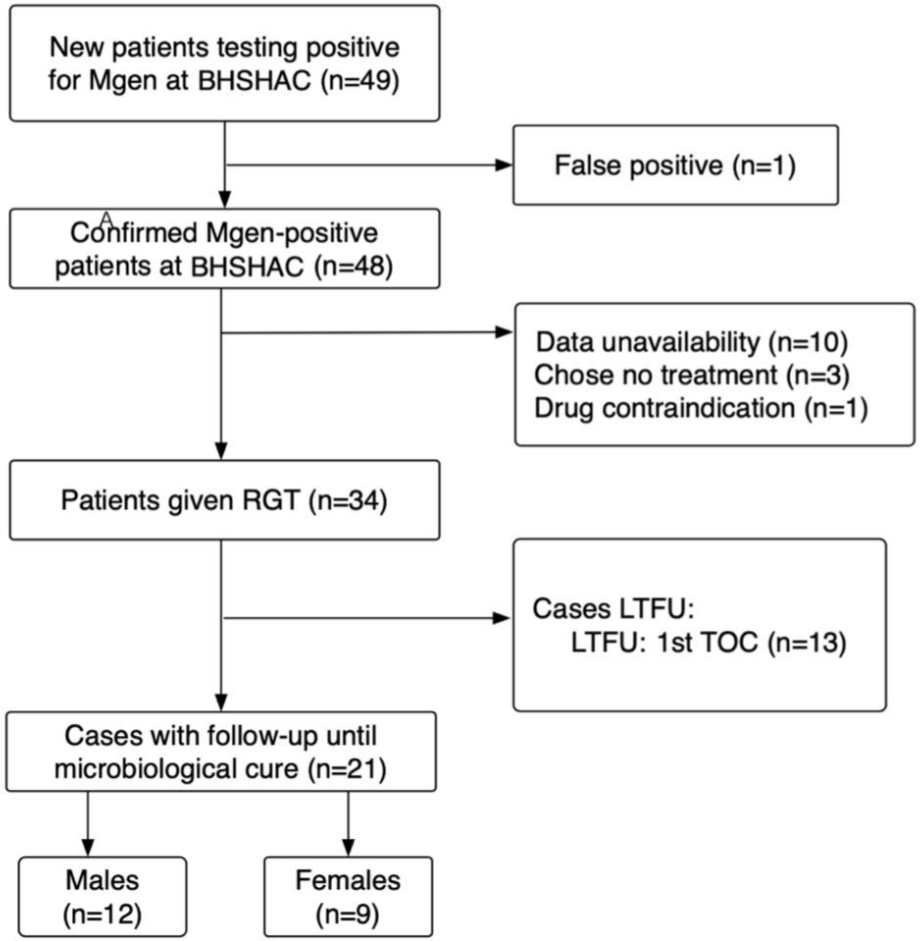
Female presents with PID:



Resistance-guided therapy

Patient presents with NGU/PID:




New patients testing positive for Mgen at BHSHAC (n=49)
False positive (n=1)
Confirmed Mgen-positive patients at BHSHAC (n=48)
Data unavailability (n=10)
Chose no treatment (n=3)
Drug contraindication (n=1)
Patients given RGT (n=34)
Cases LTFU:
LTFU: 1st TOC (n=13)
Cases with follow-up until microbiological cure (n=21)
Males (n=12)
Females (n=9)

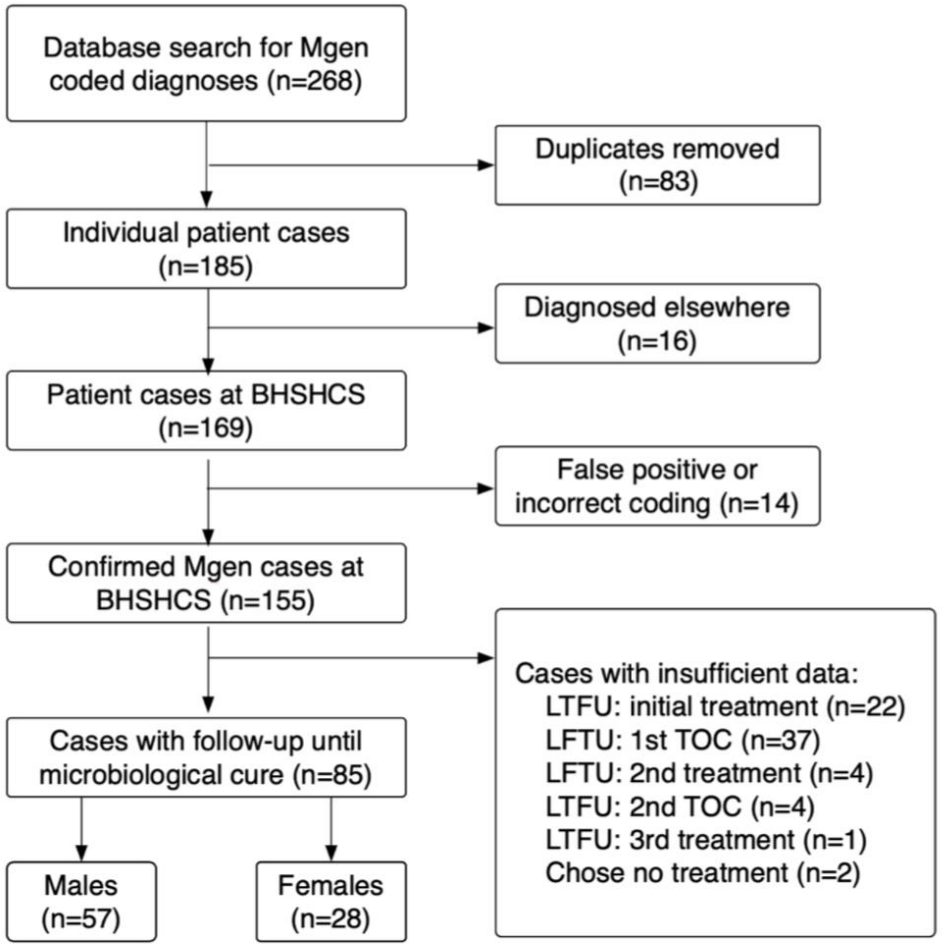

Database search for Mgen coded diagnoses (n=268)
Duplicates removed (n=83)
Individual patient cases (n=185)
Diagnosed elsewhere (n=16)
Patient cases at BHSHCS (n=169)
False positive or incorrect coding (n=14)
Confirmed Mgen cases at BHSHCS (n=155)
Cases with insufficient data:
LTFU: initial treatment (n=22)
LFTU: 1st TOC (n=37)
LFTU: 2nd treatment (n=4)
LTFU: 2nd TOC (n=4)
LTFU: 3rd treatment (n=1)
Chose no treatment (n=2)
Cases with follow-up until microbiological cure (n=85)
Males (n=57)
Females (n=28)

Table 2 Antibiotic treatment failure, by first antibiotic treatment and diagnostic category.

	RGT		Pre-RGT		p*
	n	Failure, n (%)	n	Failure, n (%)	
Overall	21	1 (5)	85	24 (28)	0.023
Antibiotic					
Azithromycin	4	1 (20)	73	24 (33)†	n/a
Moxifloxacin	16	0	12	0 †	n/a
Diagnostic category					
Males with NGU	11	0	54	17 (31)	0.054
Females with PID	7	1 (14)	18	3 (17)	n/a
Asymptomatics	3	0	13	4 (31)	n/a

*calculated using Fisher's exact test; †p=0.017; n/a indicates the p value was incalculable.

RGT, resistance-guided therapy; TOC, test of cure; NAAT, nucleic acid amplification test

Table 3 Time to microbiological cure.

	RGT			Pre-RGT			p*
	n	Mean days (SD)		n	Mean days (SD)		
From initial presentation	21	63.7	(29.2)	85	85.1	(53.8)	0.122
Males with NGU	11	54.7	(20.5)	54	88.4	(53.5)	0.036
Doxycycline given	3	-		34	92.2	(59.9)	-
No doxycycline	8	-		20	81.8	(40.9)	-
Adherent	10	-		47	87.7	(55.2)	-
Non-adherent	1	-		7	92.4	(43.7)	-
Females with PID	7	84.9	(36.0)	18	87.5	(60.4)	0.607
Asymptomatics	3	47.0	(9.2)	13	68.3	(45.5)	0.544
From specific treatment	21	45.3	(22.6)	85	67·5	(53.2)	0.289
Males with NGU	11	34.8	(15.1)	54	68.2	(52.5)	0.088
Doxycycline given	3	-		34	70·1	(60.2)	-
No doxycycline	8	-		20	65·1	(37.0)	-
Adherent	10	-		47	67.9	(54.6)	-
Non-adherent	1	-		7	70·3	(38.3)	-
Females with PID	7	58.3	(31.8)	18	68·1	(61.6)	0.832
Asymptomatics	3	42.3	(3.1)	13	63·5	(47.7)	0.893

*calculated using Mann-Whitney test.

SD, standard deviation; RGT, resistance-guided therapy; NGU, non-gonococcal urethritis; PID, pelvic inflammatory disease

Table 5 Time to symptom resolution, by diagnostic category.

	RGT			Pre-RGT			p*
	n	Mean days (SD)		n	Mean days (SD)		
From initial presentation	18	64.2	(19.0)	72	58.6	(39.6)	0.200
Males with NGU	11	57.3	(18.6)	54	56.7	(42.9)	0.451
Doxycycline given	3	-		34	46.6	(35.4)†	-
No doxycycline	8	-		20	73.9	(49.5)†	-
Adherent	10	-		47	54.4	(40.1)	-
Non-adherent	1	-		7	72.1	(60.1)	-
Females with PID	7	75.0	(14.7)	18	64.2	(27.7)	0.203
From specific treatment	18	43.5	(27.8)	72	39.2	(40.0)	0.173
Males with NGU	11	40.4	(13.4)	54	37.1	(42.1)	0.229
Doxycycline given	3	-		34	24.5	(36.6)‡	-
No doxycycline	8	-		20	58.7	(48.2)‡	-
Adherent	10	-		47	35.2	(39.4)	-
Non-adherent	1	-		7	50.0	(59.6)	-
Females with PID	7	48.4	(17.6)	18	45.3	(27.8)	0.505

*calculated using Mann-Whitney test; †p=0.017; ‡p=0.007.

SD, standard deviation; RGT, resistance-guided therapy; NGU, non-gonococcal urethritis, PID, pelvic inflammatory disease