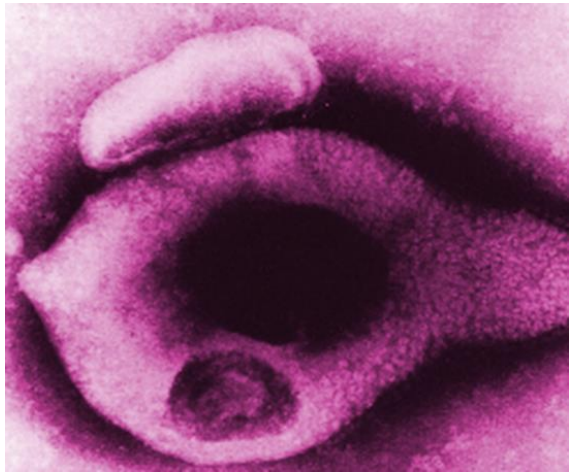
Non-quinolone options for the treatment of *Mycoplasma genitalium* in the era of increased resistance



Authors:

Doyle M[1], Vodstrcil L A[1,2], Plummer E L[1,2], Aguirre I[1], Fairley C K[1,2], Bradshaw C S[1,2]

[1] Melbourne Sexual Health Centre, Alfred Health, Carlton, Victoria, Australia

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Declaration

- CKF and CSB are supported by Australian NHMRC Leadership Investigator Grants (GNT1172900 and GNT1173361, respectively).
- Potential conflicts of interest: Melbourne Sexual Health Centre have received institutional funding from Speedx Pty Ltd to support research assistant salary while undertaking investigator-initiated studies on M. genitalium

Background

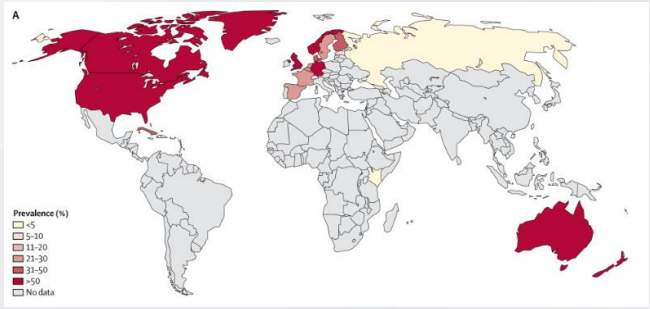
- Established cause of NGU; MG responsible for 15-30% of NGU cases
- PID
- Cervicitis
- Pre-term birth
- Spontaneous abortion
- Tubal factor infertility

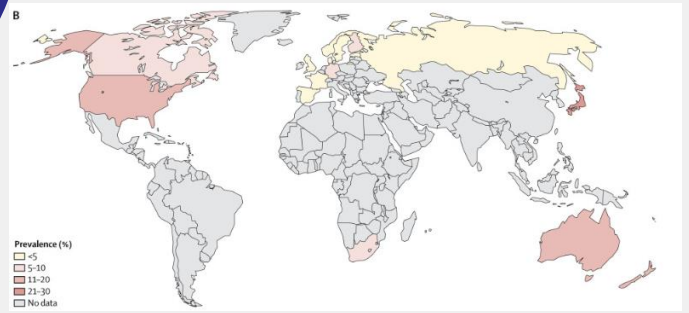
Jensen et al., 2016
Jensen & Taylor-Robinson, 2011
Lis et al CID 2015

Background

Mycoplasma genitalium (MG) is becoming increasingly difficult to treat

- Options within existing licenced drugs are limited
- Limited options in pregnancy
- Macrolide resistance now exceeds 50% in many regions
- Concern regarding the safety profile of quinolones
- Quinolone resistant-mutations also increasing ~ 20% in Asia Pacific
- Contraindications to quinolones





Manhart & Jensen, 2020
Gesink et al., 2012
Bradshaw, Jensen & Waites, 2017
Machalek et al., 2020
Deguchi et al., 2017
Read et al., 2018
Read et al., 2019

Background

- Two older oral agents displayed favorable MICs against MG

Pristinamycin

Minocycline

Emergence of *Mycoplasma genitalium* with clinically significant fluoroquinolone resistance conferred by amino acid changes both in GyrA and ParC in Japan

Takashi Deguchi, Shin Ito, Mitsuru Yasuda, Hiromi Kondo, Yoshiteru Yamada, Keita Nakane, Kosuke Mizutani, Tomohiro Tsuchiya, Shigeaki Yokoi and Masahiro Nakano

Journal of Infection and Chemotherapy, 2017-09-01, Volume 23, Issue 9, Pages 648-650, Copyright © 2017 Japanese Society of Chemotherapy and The Japanese Association for Infectious Diseases

Two cases of multidrug-resistant genitourinary Mycoplasma genitalium infection successfully eradicated with minocycline

Allison M Glaser [1], William M Geisler [2], Amy E Ratliff [3], Li Xiao [4], Ken B Waites [3], Michael Gaisa [1]

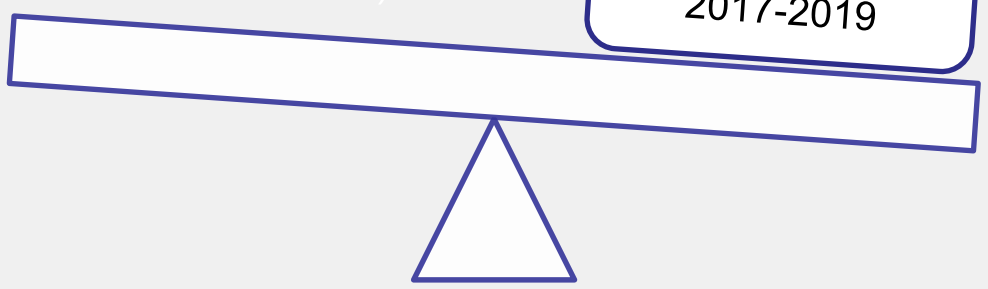
Affiliations + expand

PMID: 30999836 DOI: 10.1177/0956462418816757

Limited adherence data

75% cure rate reported in 2012-2014 data (n=114)

Only two prior case reports published 2017-2019



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Read et al., 2018
Glaser et al., 2019

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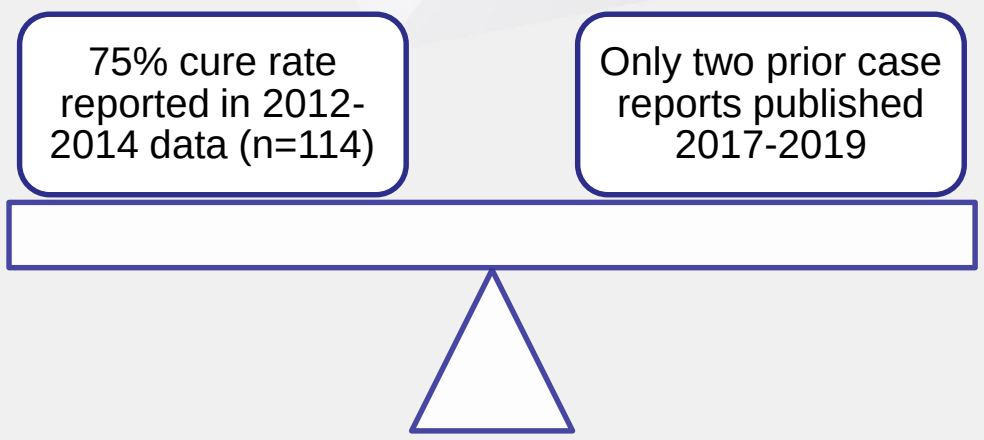
Pristinamycin

Minocycline

Emerg Infect Dis. 2018 Feb; 24(2): 328–335. PMCID: PMC5782881
doi: 10.3201/eid2402.170902 PMID: 29350154

Use of Pristinamycin for Macrolide-Resistant *Mycoplasma genitalium* Infection

Tim R.H. Read, Jørgen S. Jensen, Christopher K. Fairley, Mieken Grant, Jennifer A. Danielewski, Jenny Su, Gerald L. Murray, Eric P.F. Chow, Karen Worthington, Suzanne M. Garland, Sepehr N. Tabrizi, and Catriona S. Bradshaw



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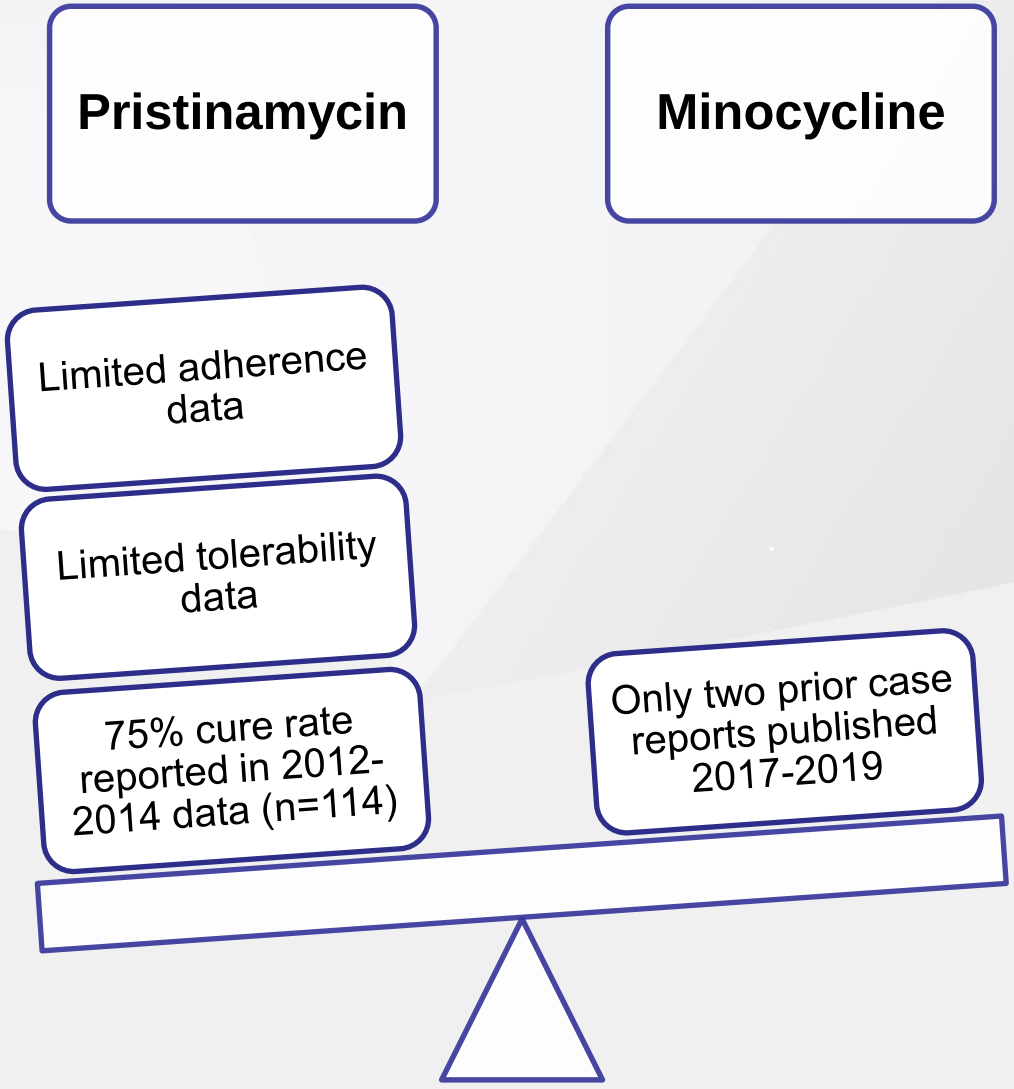

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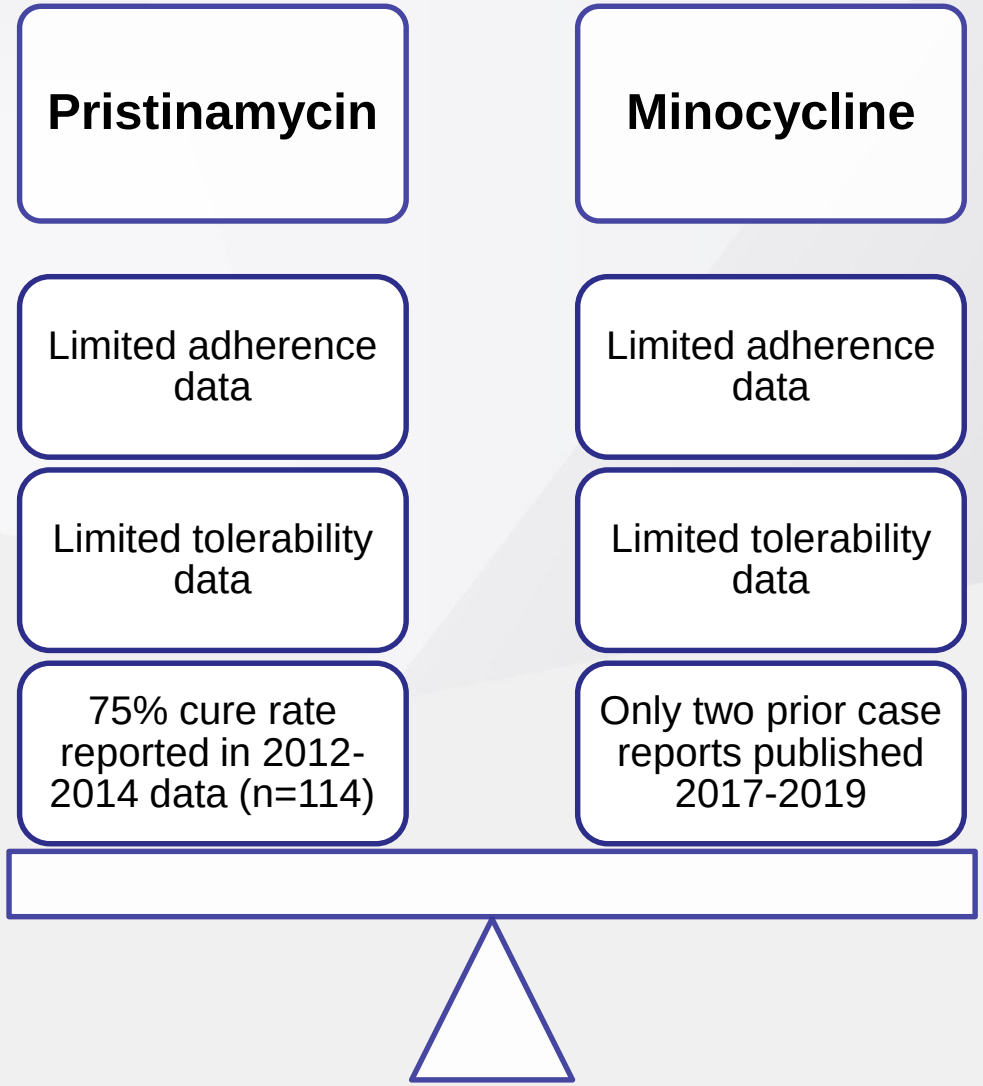

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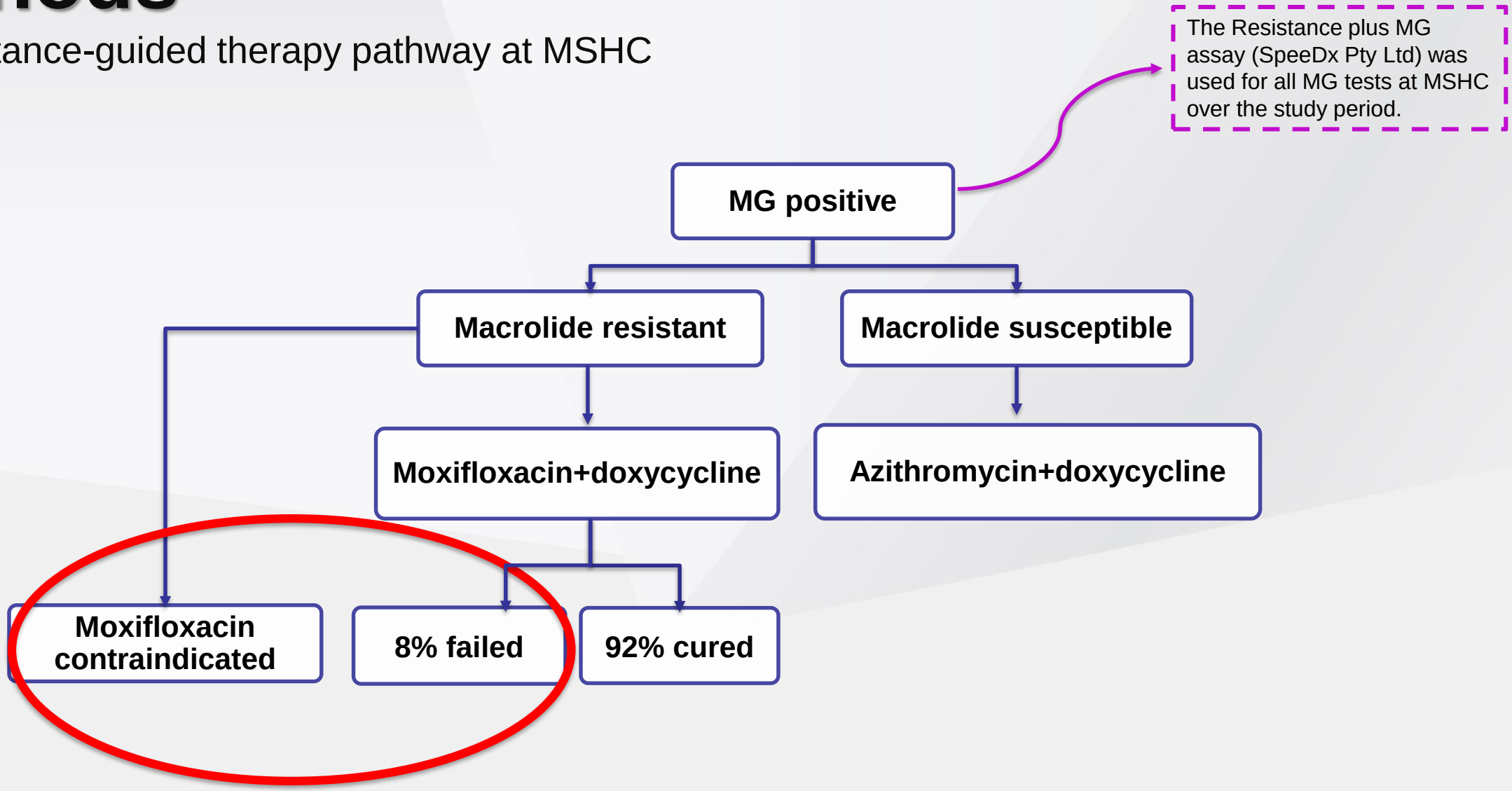
Aims

- To report the efficacy and tolerability of two treatment regimens;
  - pristinamycin+doxycycline
  - minocycline
- To provide more precision around proportion cured and adverse effects to assist clinicians making management decisions with complex cases.

Methods

MG resistance-guided therapy pathway at MSHC



Durukan et al., 2019
Read et al., 2019

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Methods

In December 2019, there was a global pristinamycin shortage and so we were unable to continue to use this for second line treatment

Macrolide resistant MG cases that failed treatment with doxycycline +moxifloxacin

OR

Macrolide resistant MG cases where moxifloxacin was contraindicated

Case series 1 (n=73)

Pristinamycin+doxycycline

Pristinamycin 1g three times daily in combination with doxycycline 100mg twice a day for 10 days

September 2018-December 2019

Case series 2 (n=35)

Minocycline

Minocycline 100mg twice daily for 14 days

May 2018-Febuary 2020

TOC 14-28 days after completing treatment

At the TOC appointment clinicians used a standardised electronic performa to capture data on adherence, tolderability, and any sex since treatment

Excluded:

- Failure to attend for TOC
- Unprotected sex with an ongoing, untreated partner

Prior to December 2019, minocycline had only been used in 7 patients who had exhausted all other available treatment options.

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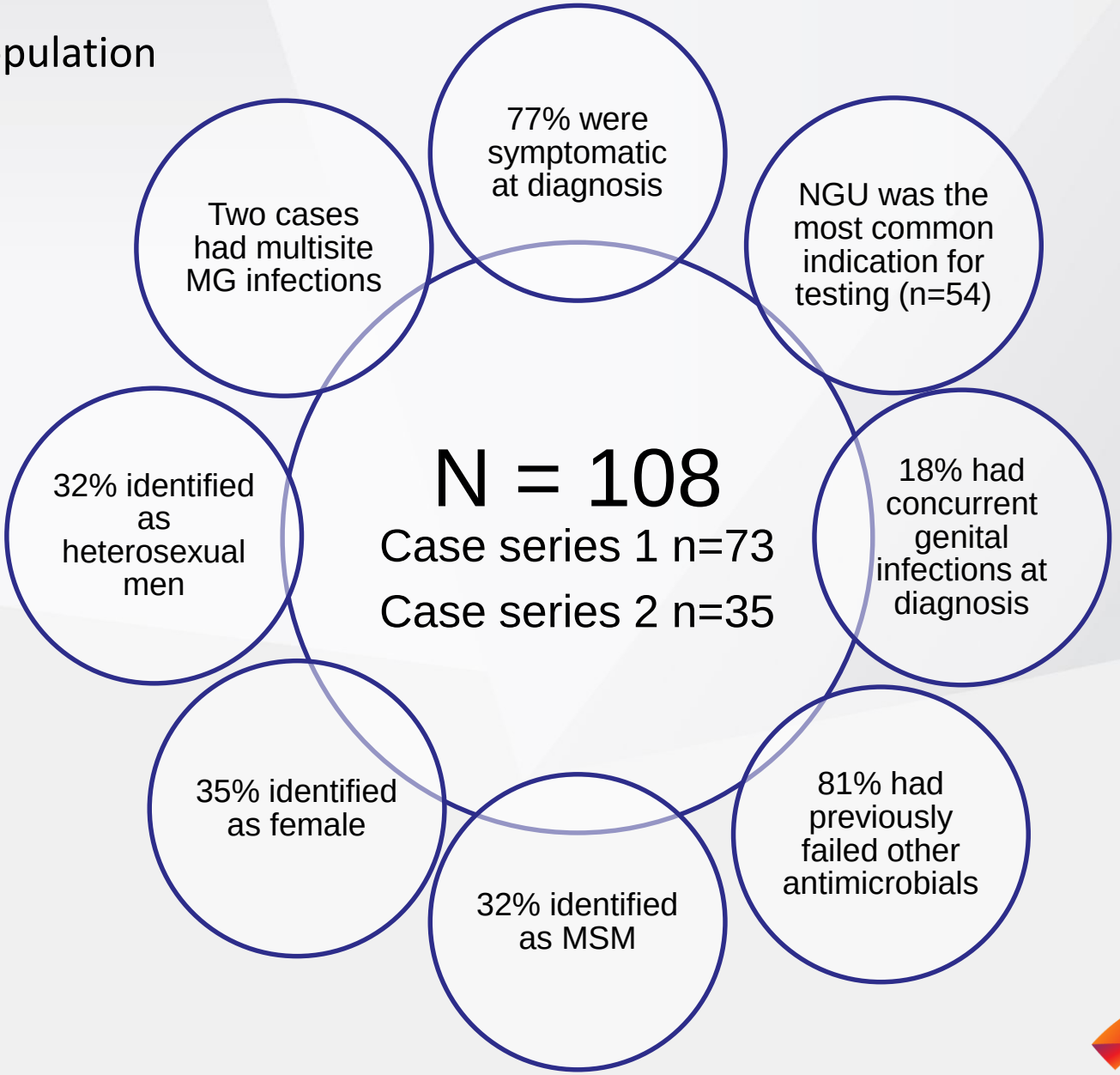
Results

Characteristics of study population



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Results

Microbiological Cure

Case series 1

Pristinamycin+doxycycline

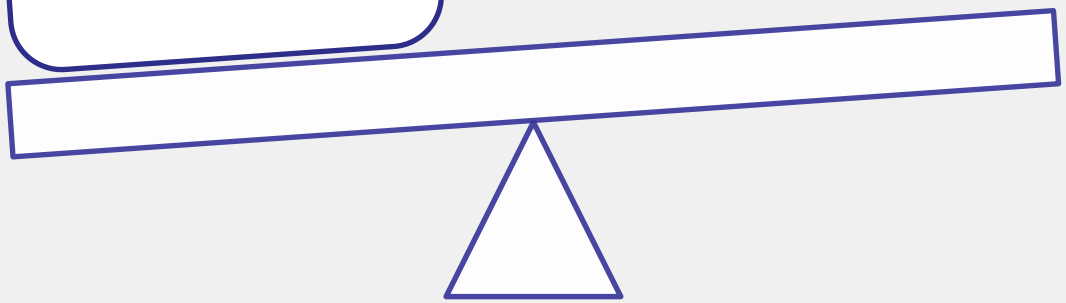
N=73

55 (75%) cured

(95% CI,64%-85%)

18 (25%) failed

(95% CI,15%-36%)



This did not change significantly from our 2012-2014 data (74%; 95% CI 64-85%)

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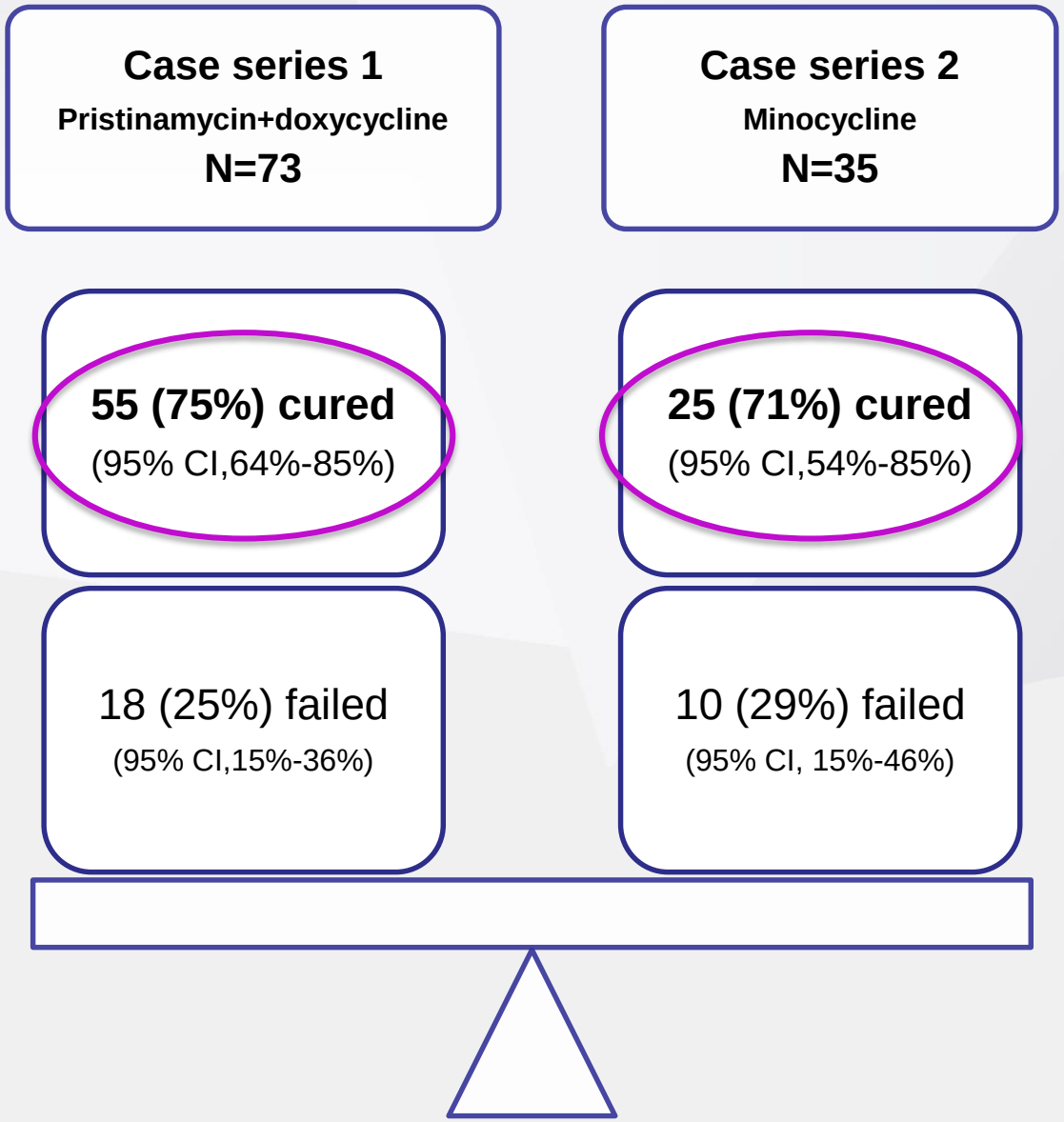

Being symptomatic at TOC was significantly associated with both pristinamycin and minocycline failure

OR 3.76 & 7.33 respectively

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Results

Adherence & side effects

		Pristinamycin+doxycycline(n=61-63[a])	Minocycline (n=33[b])
Adherence			
	Took all doses	55 (90%)	30 (91%)
	Missed 1-5 doses	6 (10%)	3 (9%)
Side effects to medication (any)		38 (60%)	15 (46%)
	Headache	4 (6%)	5 (14%)
	Diarrhoea	21 (33%)	2 (6%)
	Rash	1 (2%)	0
	Vomiting	1 (2%)	0
	Nausea	10 (16%)	2 (6%)
	Insomnia	2 (3%)	N/A
	Fatigue/lethargy	5 (8%)	2 (6%)
	Reflux/indigestion	N/A	2 (6%)
	Dizziness/light headedness	3 (5%)	7 (20%)

[a]Adherence and side effect data was available for 61 & 63 of the 73 patients prescribed pristinamycin+doxycycline, respectively

[b] Adherence and side effect data was available for 33 of the 35 patients prescribed minocycline

Limitations

- Adherence, reinfection risk and side effect data were all self-reported
- Results may not be generalisable to the community as participants were all recruited from MSHC; the only free sexual health service in Melbourne
- LTFU occurred in 20% of patients, which may have resulted in a higher proportion of failures.

Conclusion

- Macrolide and quinolone failures are becoming increasingly more common
- Concerns regarding the safety profile of quinolones is increasing
- 75% of macrolide resistant MG was cured with pristinamycin+doxycycline
- 71% of macrolide resistant MG was cured with minocycline
- Both of these regimens appear to have similar efficacy
- While side effects were common, they were mostly mild and tolerable
- Alternative licensed agents with known safety profiles are needed to effectively treat MG

Publication

Nonquinolone Options for the Treatment of *Mycoplasma genitalium* in the Era of Increased Resistance

Michelle Doyle ✉, Lenka A Vodstrcil, Erica L Plummer, Ivette Aguirre, Christopher K Fairley, Catriona S Bradshaw

Open Forum Infectious Diseases, Volume 7, Issue 8, August 2020, ofaa291, https://doi.org/10.1093/ofid/ofaa291

Email: mdoyle@mshc.org.au

ON-DEMAND Program
#87 Doxycycline and Sitafloxacin Combination Therapy for Treating Highly Resistant Mycoplasma genitalium
Duygu Durukan

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- Professor Christopher Fairley
- Ivette Aguirre and all of the MSHC pharmacy staff
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