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Clinical Features of Mycoplasma Genitalium Associated Pelvic Inflammatory Disease and Response to Moxifloxacin: A Case Series

1st November 2018

Rosie Latimer

Background

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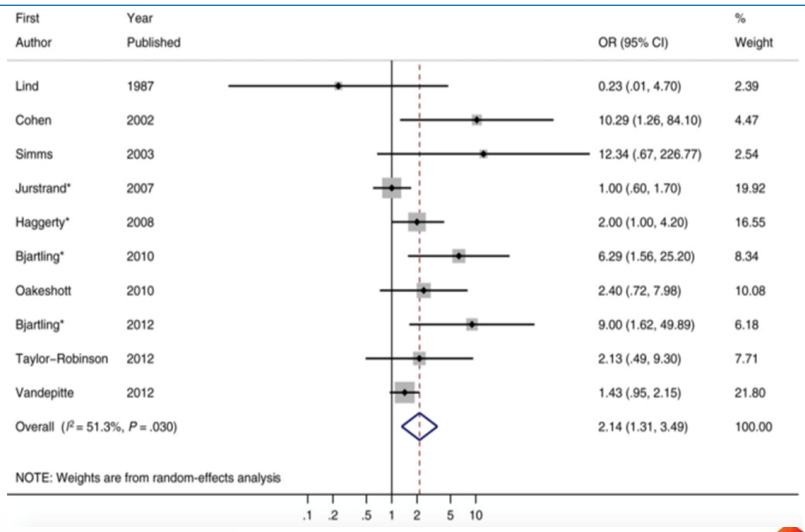
Role in Pelvic Inflammatory Disease



Reference: Lis, R., Manhart, L. et al. Clinical Infectious diseases 13/05/15

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MG PID compared with other PID

- There is very little on the clinical characteristics of MG-associated PID
- 1 study compared MG-PID to gonorrhea-PID
  - Less inflammatory markers
  - Less mucopurulent cervicitis
  - Lower pain scores
- No study that directly compares chlamydial and MG-PID

Reference: Short, V. Clinical Infectious Diseases 2009

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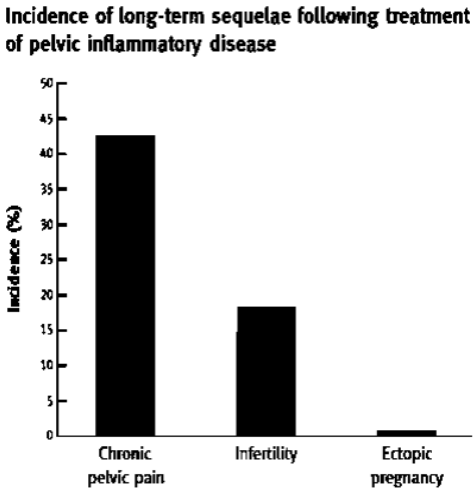
Sequelae following PID



Adapted from Ross JD, Pelvic inflammatory disease, Medicine: Elsevier; 2014(119)

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Antibiotics for PID

- Antibiotic guidelines for PID do not contain an effective agent for MG
- The following regimen is used for the presumptive treatment of outpatient PID.

Antibiotic	Dose	Duration	Efficacy
Azithromycin	1g	stat	
Doxycycline	100mg	bd 14/7	
Metronidazole	400mg	bd 14/7	

Reference: ASHA PID Guidelines, Gov Dept Health 2016; Bissessor et. al Clin Infect Dis 2015, Haggerty CL et. al Infect Dis Obstet Gynecol 2006

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Antibiotic	Dose	Duration	Efficacy
Azithromycin	1g	stat	Less than 60%
Doxycycline	100mg	bd 14/7	
Metronidazole	400mg	bd 14/7	

Reference: Manhart Mycoplasma genitalium: should we treat and how? Clin Infect Dis. 2011

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Azithromycin	1g	stat	Less than 60%
Doxycycline	100mg	bd 14/7	~20-40%
Metronidazole	400mg	bd 14/7	

Reference: Bissessor M. Clin Infect Dis. 2015;60(8):1228-36

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Antibiotic	Dose	Duration	Efficacy
Azithromycin	1g	stat	Less than 60%
Doxycycline	100mg	bd 14/7	~20-40%
Metronidazole	400mg	bd 14/7	Does not work (mechanism of action at bacterial cell wall)

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Antibiotics for MG & PID

- Azithromycin is currently first line treatment for MG itself
- One RCT of moxifloxacin in uncomplicated PID (all causes)
  - Three patients had MG; 100% cure rate
  - This study had various limitations
- 2006- MSHC first to implement treatment with moxifloxacin for MG failing azithromycin
- 2011- MSHC implemented 14 days of moxifloxacin for MG-PID
- Moxifloxacin recommended for PID caused by MG according to the CDC

Reference: ASHA PID Guidelines, Gov Dept Health 2016; Ross et al Sex Transm Infect 2006; Bissessor et. al Clin Infect Dis 2015, Haggerty CL et. al Infect Dis Obstet Gynecol 2006

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MG-PID treatment at MSHC

Presentation
- Diagnosed with PID and treated with azithromycin 1g stat, doxycycline 100mg bd 14/7, metronidazole 400mg bd 14/7. Tested for a range of STIs- mycoplasma genitalium, chlamydia, gonorrhoea, trichomoniasis, bacterial vaginosis.

8-14 days
- MG test returned positive; recalled to MSHC. Other antibiotic regimen ceased. Prescribed 14 days of moxifloxacin.

1 month
- Return for test of cure. Symptoms documented.

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Project Outline

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Aims

1) Describe the clinical characteristics of MG-PID and to determine how they differ from those associated with Chlamydial trachomatis (CT)-PID.

2) To determine the proportion of women:
   a) Microbiologically cured of MG-PID following 14 days of moxifloxacin (i.e. MG not detected by nucleic acid amplification assay at test of cure).
   b) Clinically cured of MG-PID following 14 days of moxifloxacin (i.e. asymptomatic following treatment).

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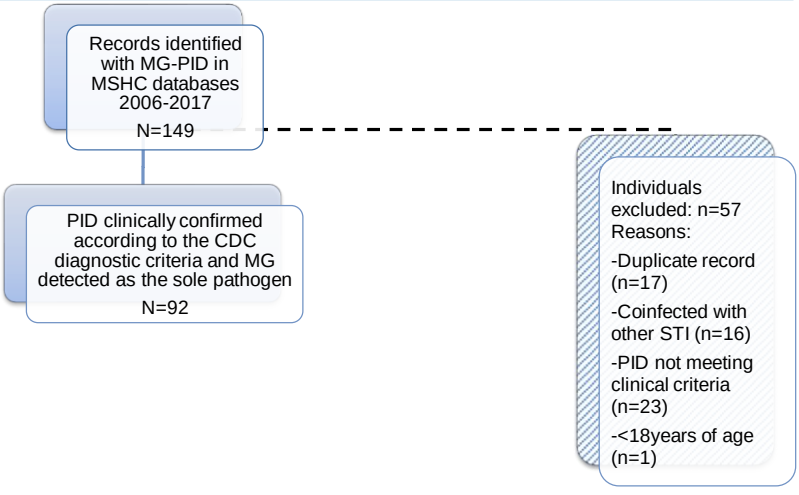
Methods



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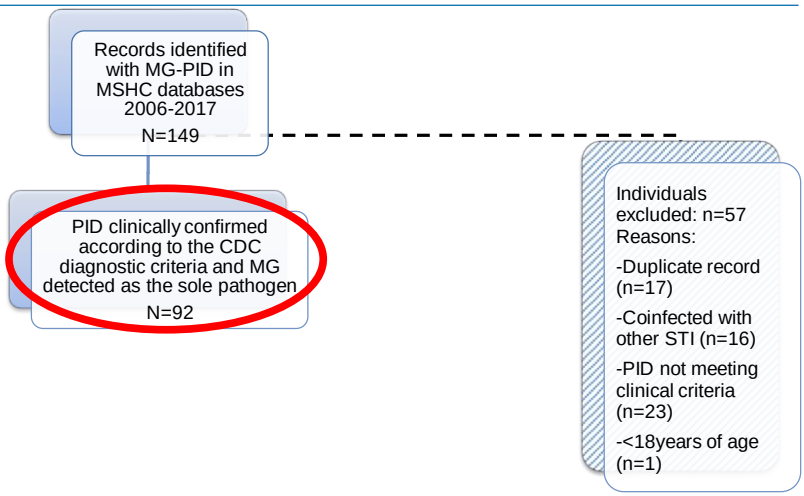
Methods

Compared to 92 patients with CT-PID, with CT the sole pathogen detected



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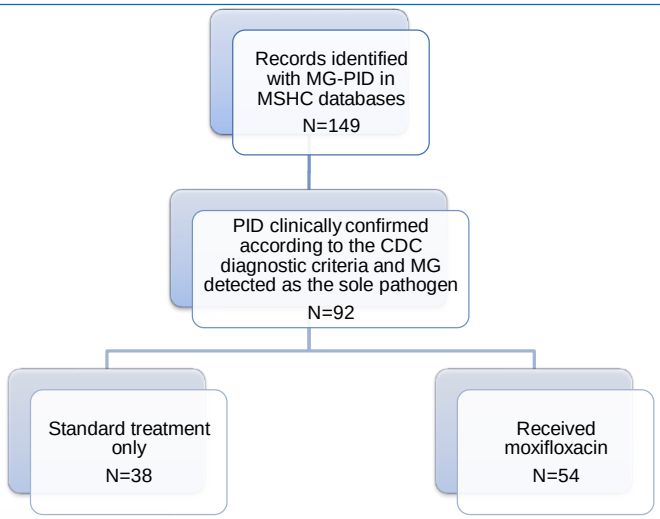

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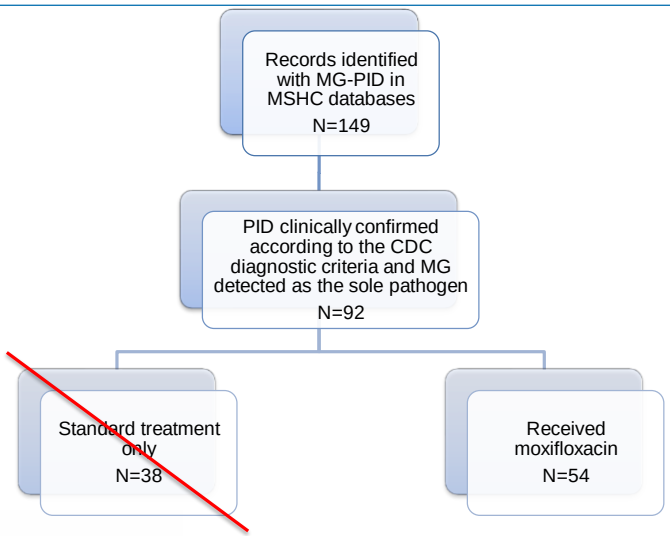

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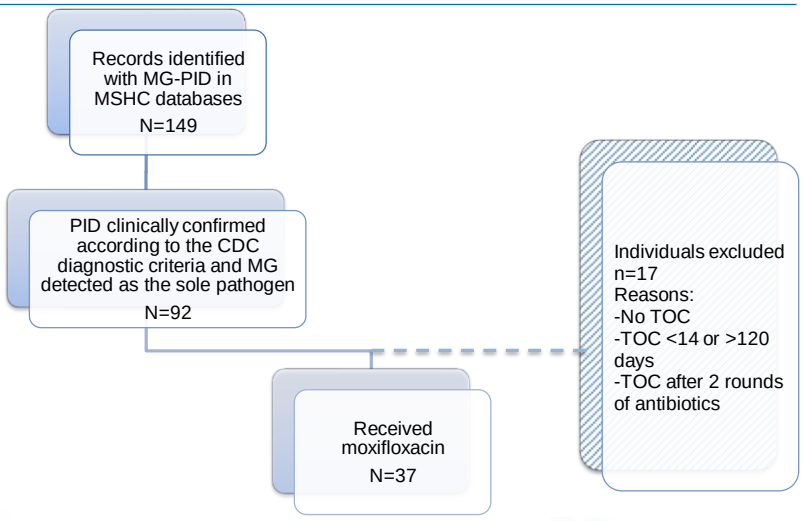

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Results

Demographics of *Mycoplasma genitalium* PID cases compared to *Chlamydia Trachomatis* PID cases (N=184)						
	Chlamydia PID cases n=92 (%, 95% CI) or median (IQR)	Mycoplasma genitalium PID cases n=92 (%, 95% CI) or median (IQR)	Unadjusted Odds Ratios (95%CI)	P-value	Adjusted[a] Odds Ratio (95%CI)	P-value
Age	24 (21-28)	25 (21-29)				
Number of MSP last 3months[bc]						
≤1	35 (38, 28-49)	49 (53, 43-64)	1.0		1.0	
>1	57 (62, 51-72)	43 (47, 36-57)	0.54 (0.30-0.97)	0.039	0.54 (0.27-1.06)	0.071
Consistency of condom usage[b]						
Not always	79 (94, 87-98)	72 (85, 75-92)	1.0			
Always	5 (6, 2-13)	13 (15, 8-25)	2.85 (0.97-8.40)	0.057		
Current sex worker						
No	83 (90, 82-95)	69 (75, 65-83)	1.0		1.0	
Yes	9 (10	23 (25, 17-35)	3.07 (1.33-7.08)	0.008	1.92 (0.75-4.97)	0.176
Sex within Australia only[b]						
No	36 (42, 32-54))	23 (28, 19-39)	1.0			
Yes	49 (58, 46-68)	59 (72, 61-81)	1.88 (0.99-3.60)	0.054		

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Symptoms of *Mycoplasma genitalium* PID compared to *Chlamydia Trachomatis* PID (N=184)

	Chlamydia PID cases n=92 (%, 95% CI) or median (IQR)	Mycoplasma genitalium PID cases n=92 (%, 95% CI) or median (IQR)	Unadjusted Odds Ratios (95%CI)	P-value	Adjusted[a] Odds Ratio (95%CI)	P-value
Abdominal pain						
No	23 (25, 17-35)	13 (14, 8-23)	1.0			
Yes	69 (75, 65-83)	79 (86, 77-92)	2.03 (0.95-4.30)	0.066		
Dyspareunia						
No	43 (47, 36-57)	45 (49, 38-60)	1.0			
Yes	49 (53, 43-64)	47 (51, 40-62)	0.92 (0.51-1.63)	0.768		
Post-coital bleeding						
No	73 (79, 70-87)	83 (90, 82-95)	1.0		1.0	
Yes	19 (21, 13-30)	9 (10, 5-18)	0.42 (0.18-0.98)	0.044	0.40 (0.15-1.12)	0.082
Intermenstrual bleeding						
No	77 (84, 75-91)	71 (77, 67-85)	1.0			
Yes	15 (16, 9-25)	21 (23, 15-33)	1.52 (0.73-3.17)	0.267		
Dysuria						
No	64 (70, 59-79)	72 (78, 68-86)	1.0			
Yes	28 (30, 21-41)	20 (22, 14-32)	0.63 90.33-1.23	0.181		
Urinary frequency						
No	72 (78, 68-86)	82 (89, 81-95)	1.0		1.0	
Yes	20 (22, 14-32)	10 (11, 5-19)	0.44 (0.19-1.00)	0.050	0.56 (0.22-1.46)	0.234
Vaginal discharge (symptom)						
No	36 (39, 29-50)	40 (43, 33-54)	1.0			
Yes	56 (61, 50-71)	52 (57, 46-67)	0.84 (0.46-1.50)	0.549		

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Signs of *Mycoplasma genitalium* PID compared to *Chlamydia Trachomatis* PID (N=184)

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Lower abdominal tenderness						
No	49 (53, 43-64)	30 (33, 23-43)	1.0		1.0	
Yes	43 (47, 36-57)	62 (67, 57-77)	2.36 (1.29-4.28)	0.005	2.29 (1.14-4.60)	0.020
Cervical or adnexal motion tenderness						
No	15 (16, 9-25)	13 (14, 8-23)	1.0			
Yes	77 (84, 75-91)	79 (86, 77-92)	1.18 (0.53-2.65)	0.682		
Mucopurulent cervicitis						
No	57 (62, 51-72)	62 (67, 57-77)	1.0			
Yes	35 (38, 28-49)	30 (33, 23-43)	0.79 (0.43-1.44)	0.441		
Cervical contact bleeding						
No	78 (95, 76-91)	81 (88, 80-94)	1.0			
Yes	14 (15, 9-24)	11 (12, 6-20)	0.76 (0.32-1.77)	0.520		
Vaginal discharge (sign)						
No	42 (46, 37-56)	43 (46, 37-56)	1.0			
Yes	50 (54, 44-63)	49 (54, 44-63)	0.96 (0.54-1.71)	0.882		
Bacterial Vaginosis						
Not detected	49 (53, 43-64)	51 (55, 45-66)	1.0			
Detected	33 (36, 26-47)	32 (35, 25-45)	0.93 (0.50-1.74)	0.824		
Vaginal PMN count						
< 1	23 (28, 19-39)	38 (46, 35-58)	1.0			
1-4	19 (23, 15-34)	12 (15, 8-24)	0.38 (0.16-0.93)	0.034	0.34 (0.13-0.89)	0.027
≥5	40 (49, 38-60)	32 (39, 28-50)	0.48 (0.24-0.97)	0.041	0.72 (0.34-1.54)	0.400
Cervical PMN count						
<5	5 (11, 4-25)	9 (24, 12-41)	1.0			
5-8	6 (14, 5-27)	14 (38, 22-55)	1.29 (0.30-5.54)	0.726		
>8	33 (75, 60-87)	14 (38, 22-55)	0.24 (0.24-0.15)	0.024		

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Yes	77 (84, 75-91)	79 (86, 77-92)	1.18 (0.53-2.65)	0.682		
Mucopurulent cervicitis						
No	57 (62, 51-72)	62 (67, 57-77)	1.0			
Yes	35 (38, 28-49)	30 (33, 23-43)	0.79 (0.43-1.44)	0.441		
Cervical contact bleeding						
No	78 (95, 76-91)	81 (88, 80-94)	1.0			
Yes	14 (15, 9-24)	11 (12, 6-20)	0.76 (0.32-1.77)	0.520		
Vaginal discharge (sign)						
No	42 (46, 37-56)	43 (46, 37-56)	1.0			
Yes	50 (54, 44-63)	49 (54, 44-63)	0.96 (0.54-1.71)	0.882		
Bacterial Vaginosis						
Not detected	49 (53, 43-64)	51 (55, 45-66)	1.0			
Detected	33 (36, 26-47)	32 (35, 25-45)	0.93 (0.50-1.74)	0.824		
Vaginal PMN count						
< 1	23 (28, 19-39)	38 (46, 35-58)	1.0			
1-4	19 (23, 15-34)	12 (15, 8-24)	0.38 (0.16-0.93)	0.034	0.34 (0.13-0.89)	0.027
≥5	40 (49, 38-60)	32 (39, 28-50)	0.48 (0.24-0.97)	0.041	0.72 (0.34-1.54)	0.400
Cervical PMN count						
<5	5 (11, 4-25)	9 (24, 12-41)	1.0			
5-8	6 (14, 5-27)	14 (38, 22-55)	1.29 (0.30-5.54)	0.726		
>8	33 (75, 60-87)	14 (38, 22-55)	0.24 (0.24-0.15)	0.024		

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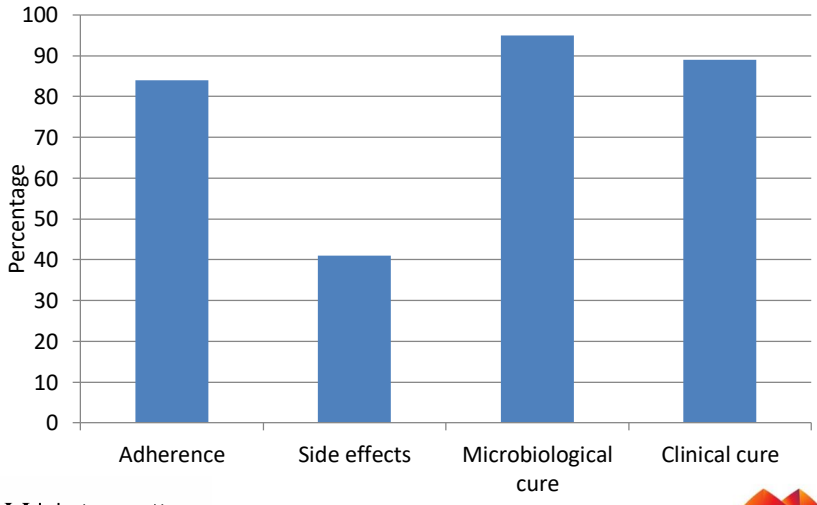
Moxifloxacin Treatment Outcomes (n=37)



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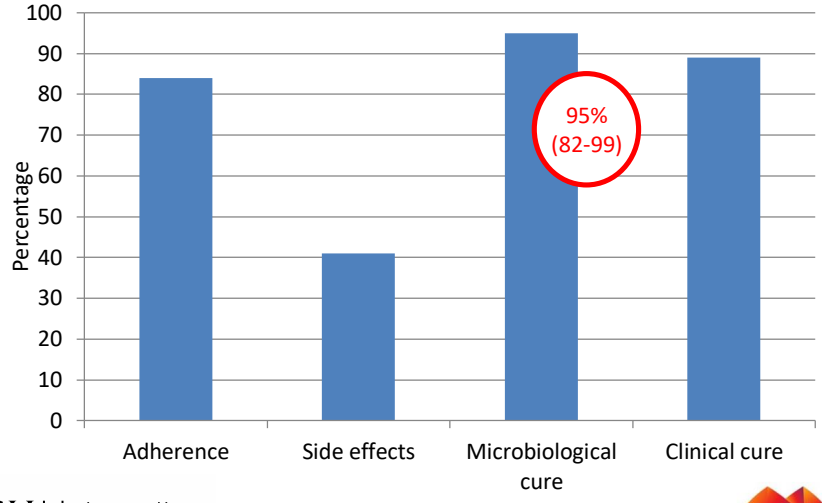
Moxifloxacin Treatment Outcomes (n=37)



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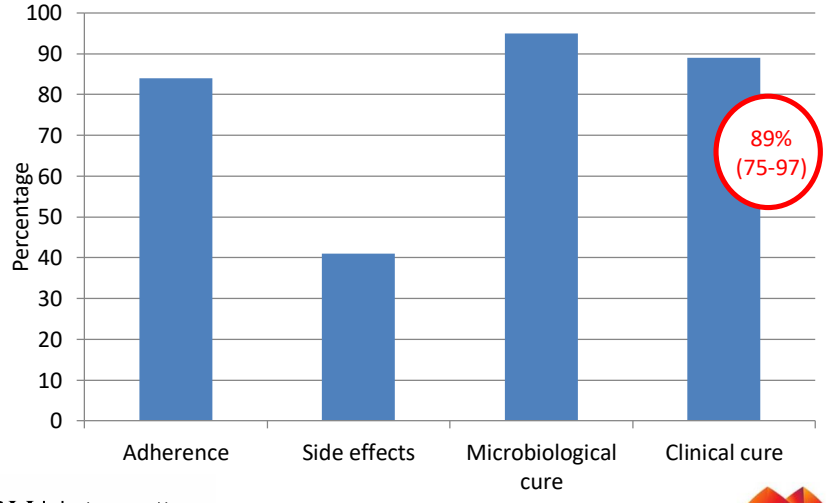
Moxifloxacin Treatment Outcomes (n=37)



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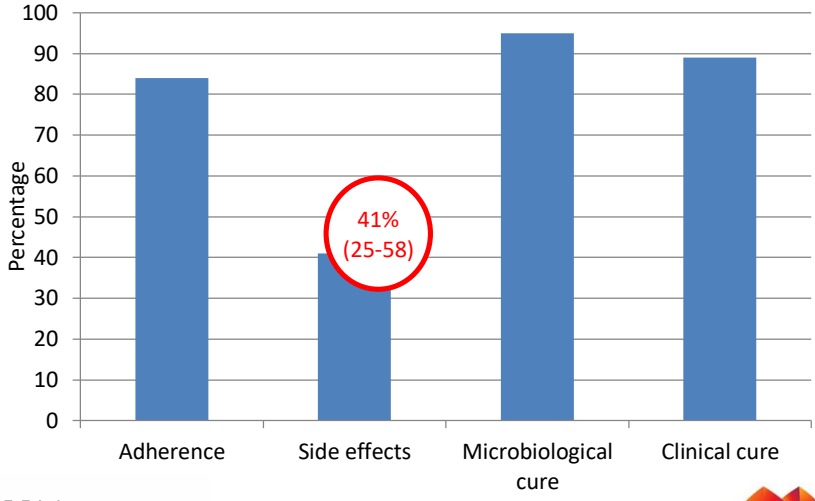
Moxifloxacin Treatment Outcomes (n=37)



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Implications

- Largest data set of MG-PID cases
- It did not find clinically meaningful differences between women with MG-PID and CT-PID.
- Moxifloxacin is highly effective in achieving microbiological cure of MG in women with PID (>95%)
  - 2 in 5 women will experience predominately mild adverse effects
- Moxifloxacin should be used in patients with established MG-PID
  - No other antibiotic classes available currently
  - PID is serious and warrants treatments over the risk of side effects.

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Acknowledgments

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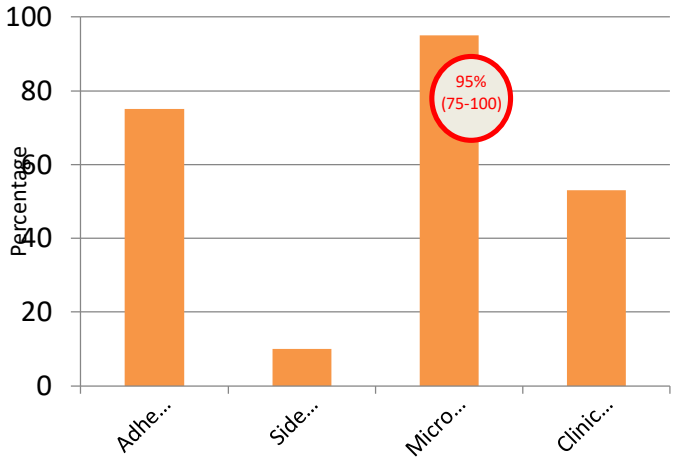
Standard treatment n=



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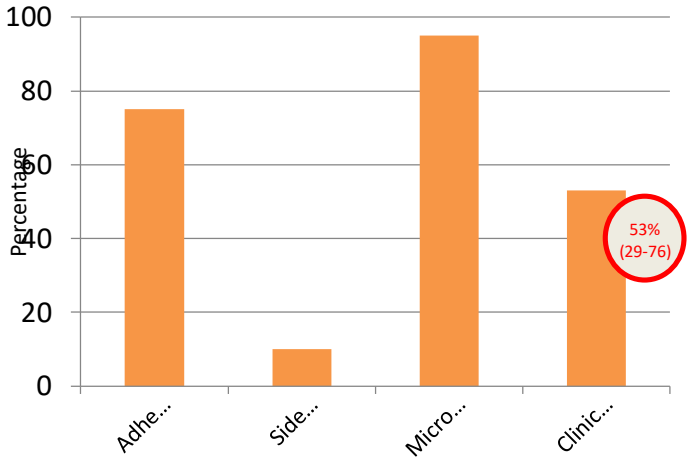
Standard treatment



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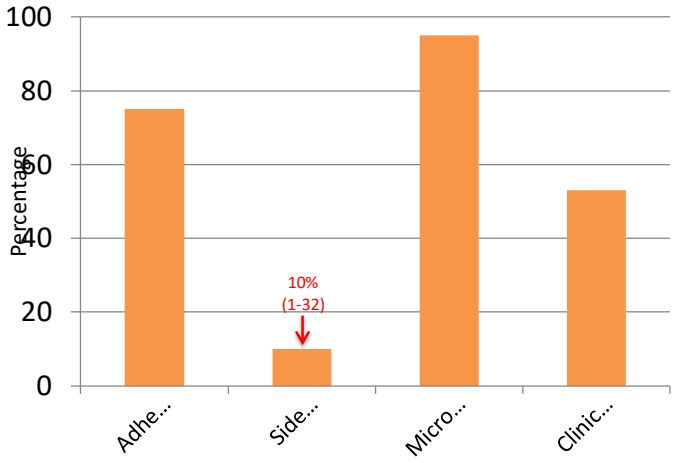
Standard treatment



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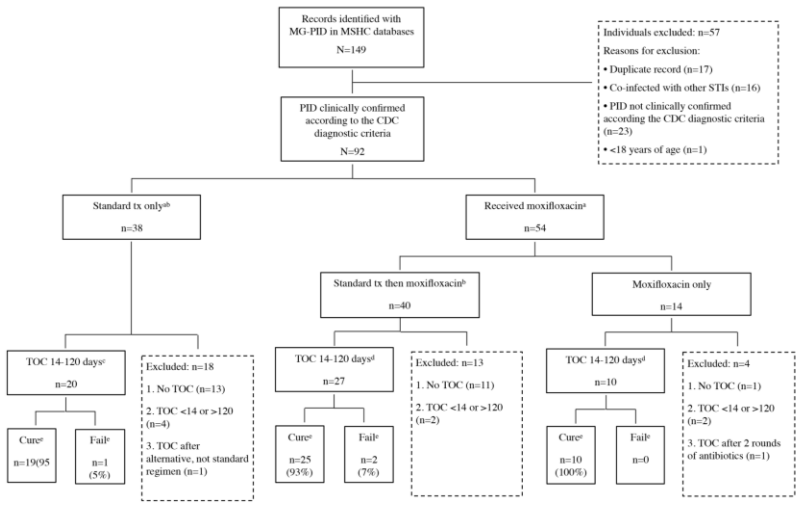

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MG-PID cases were women with presumptive PID at presentation (87%), who underwent STI testing and were commenced on recommended therapy for PID (henceforth standard treatment). In a minority of cases (13%), women developed symptoms and signs following testing, and were diagnosed with presumptive PID at the following visit.

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Treatment outcomes were not compared between women treated with moxifloxacin versus standard treatment for the following reasons: i) all women treated with standard treatment only received azithromycin; ii) a significant proportion of women receiving standard treatment only were treated earlier in the study (60% treated before 2013), when macrolide resistance was less common and azithromycin was highly effective for MG,917 18 while the majority of those in the moxifloxacin group were treated later in the study timeframe (85% after 2013); iii) a marked increase in macrolide resistance occurred during the

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