

**23RD IUSTI
WORLD CONGRESS**

ELEPHANT HILLS RESORT, VICTORIA FALLS, ZIMBABWE | 4 - 7 SEPTEMBER 2022

CONFRONTING INEQUITIES IN STI PREVENTION, DIAGNOSTICS AND CARE



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Increasing prevalence and incidence of *Mycoplasma genitalium* infection in PLWH and PrEP users.

Disclosure

Any circumstances that could give rise to a potential conflict of interest related to the conference or topic under discussion	Name of company, organization or institution
Sponsorship	My participation to the 23 rd IUSTI World Congress has been supported by a full Scholarship by the Organization Committee.
Payment or other financial remuneration	None
Shareholder rights	None
Other relations	I served as speaker and consultant for ViiV Healthcare and Gilead Sciences

Background (1).

- *Mycoplasma genitalium* (MG) belongs to the class of *Mollicutes* and is the smallest known self-replicating organism with a genome size of only 580 Kb.
- This flask-shaped organism has a slightly curved terminal organelle. Ability for adhesion, gliding motility, and cell invasion aid it in pathogenesis.
- The organism is small enough to penetrate the surface of the agar medium, hence when viewed microscopically from above, the colonies give the characteristic “fried egg” appearance.

Background (2).

- The organism has been detected in the genitourinary, rectal, and respiratory tract specimens, whilst is very rare in the throat.
- MG is detected in only **1.0-3.3%** of men and women in the general population.
- In contrast, about 15%–20% of NGU cases, 20%–25% of non-chlamydial urethritis, and about **30%** of recurrent or persistent urethritis are caused by MG.
 - Several reports describe a prevalence higher than that of NG but lower than that of CT.
 - The **co-infection with CT** is not uncommon.
- Genital-genital contact is considered the most common route of transmission. Penile-anal transmission has also been reported.
 - Oral sex is not considered to be significant in transmission.
- Younger age group, smoking, dark skin phenotype, and multiple partners are the common risk factors for acquiring this infection.

Taylor-Robinson D, Jensen JS. Clin Microbiol Rev 2011;24:498-514. Andersen B, et al. Sex Transm Infect 2007;83:237-41. Manhart L, et al. Am J Public Health 2007;97:1118-25. Sonnenberg P, et al. Int J Epidemiol 2015;44:1982-94. Edlund M, et al. Int J STD AIDS 2012;23:455-6. Bradshaw C, et al. Sex Transm Infect 2009;85:432-5. 12. Deguchi T, et al. J Infect Chemother 2009;15:410-3. Horner PJ, Martin DH. J Infect Dis 2017;216:S396-405.

Background (3).

- MG lacks the cell wall showing inherent resistance against antibiotics such as beta-lactams and penicillins that target cell wall synthesis.
 - Resistance to **macrolide** is widespread.
 - The prevalence of macrolide-resistant ranges from 30% to 100%.
 - **Doxycycline** as monotherapy is ineffective, but a sequential treatment with doxycycline followed by an extended azithromycin regimen can improve the success rate.
 - **Moxifloxacin** has been found to be very effective in Europe, but resistance is increasing in Asia–Pacific region.
 - **Pristinamycin**, a streptogramin that binds the 50S subunit of the bacterial ribosome, seems an effective third-line regimen.

Aims of the study.

- Aims of the present study are:
 - To describe MG prevalence over time;
 - To describe MG incidence in the overall population and in the subgroups in analysis;
 - To describe factors associated with its presence in urine and cervical samples.

Methods (1).

- This is a monocentric, retrospective analysis that evaluated all urine and cervical swab samples tested for MG from January 2018 up to September 2021.
- Samples that were sent to Microbiological laboratory for the detection of a sexually transmitted infection (STI) were electronically retrieved.
- Demographic characteristics were collected from hospital electronic patients' records.
- All samples were analyzed with Anyplex II STI7 (Seegene). This is a multiplex nucleic acid amplification test that contemporarily search for NG, CT, T. vaginalis, MG, and other Ureaplasma and Mycoplasma spp genomes.
- Samples were grouped in:
 1. People living with HIV (PLWH);
 2. PrEP users;
 3. Subjects presenting for STIs screening;
 4. Women attending Gynecology/Obstetrics (G/O);
 5. Individuals attending the Fertility Clinic;
 6. Samples from other hospital departments (mainly from the Chemical-Clinical and Microbiological Analyses service for outpatient individuals from ours and other hospitals in the area).

Methods (2).

- Descriptive statistics (median and interquartile range for continuous variables, absolute and relative values for categorical variables) were used.
- Nonparametric tests (Wilcoxon rank-sum for continuous and Pearson's Chi-square for categorical variables) were applied to compare groups.
- Time at risk, incidence rates (IR) and incidence rate ratios (IRR) were calculated.
- Unadjusted and adjusted Cox regression analyses were performed to test factors associated to MG infection.
- Two-tailed p -values were calculated and a value below 0.05 was considered statistically significant. Data management and analysis were performed using STATA package, version 16.1 (College Station, TX, StataCorp 2019).
- The study was conducted in accordance with the ethical standards of the Helsinki Declaration. Local Institutional Review Board approval was required. No written informed consent was required given the clinical research design.

Results (1).

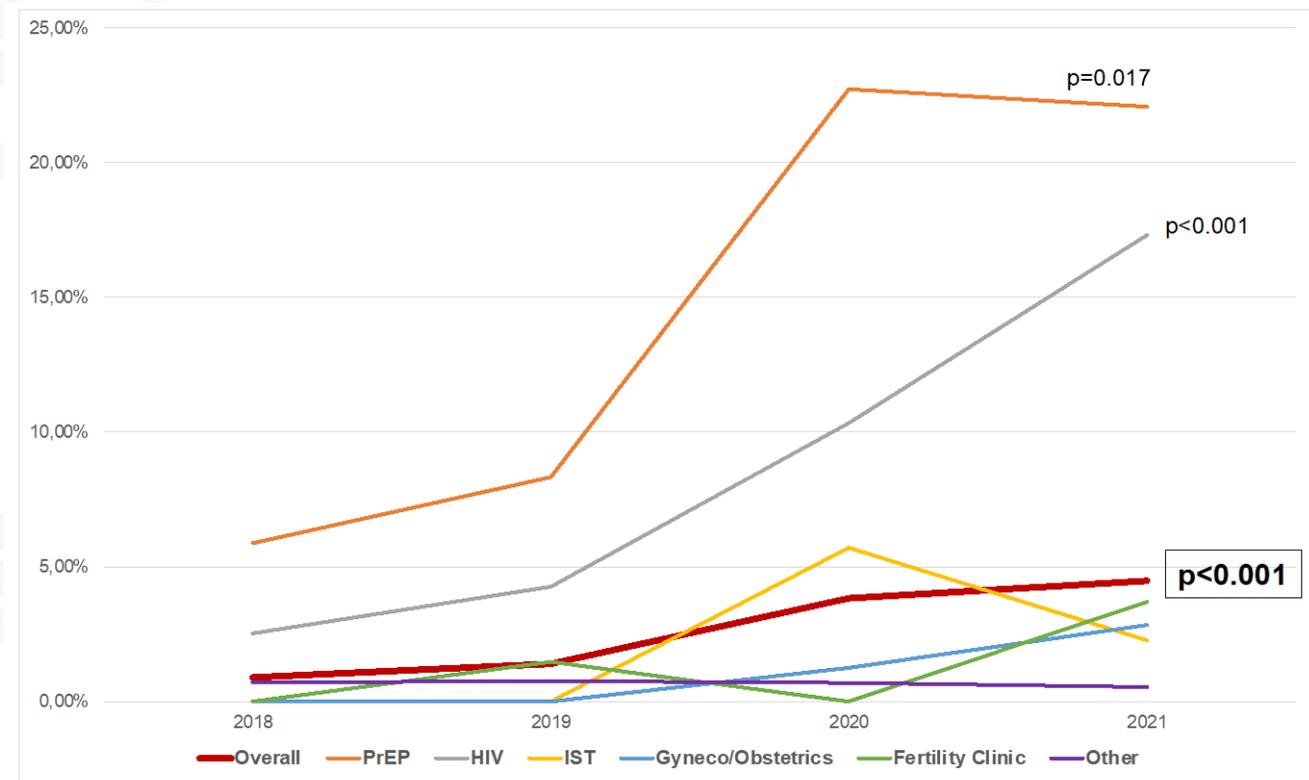
- The analysis included **5,934** individuals for a total number of **9,058** samples.
- The majority (78.5%) presented only one sample, barely 6.6% collected more than 3 samples.

Table 1. Demographic and clinical features of study population.

		Study population (N=5,934)	Negative (N=5,809)	Positive (N=125)	p
Gender, n (%)	Males	2,080 (35.1)	1,978 (95.1)	102 (4.9)	<0.001
	Females	3,810 (64.2)	3,788 (99.4)	22 (0.6)	
	TGW	44 (0.7)	43 (97.7)	1 (2.3)	
Age, years, median (IQR)		37 (31-46)	37 (31-46)	34 (28-41)	<0.001
Origin, n (%)	Italy	4,456 (75.1)	4,359 (97.8)	97 (2.2)	0.868
	Africa	99 (1.7)	98 (99.0)	1 (1.0)	
	Asia	258 (4.3)	254 (98.4)	4 (1.6)	
	Europe	385 (6.5)	379 (98.4)	6 (1.6)	
	South America	453 (7.6)	442 (97.6)	11 (2.4)	
	MENA	283 (4.8)	277 (97.1)	6 (2.1)	
Dept., n (%)	G/O	676 (11.4)	668 (98.8)	8 (1.2)	<0.001
	HIV	592 (10.0)	561 (94.8)	31 (5.2)	
	STI	137 (2.3)	133 (97.1)	4 (2.9)	
	Fertility	247 (4.2)	245 (99.2)	2 (0.8)	
	PrEP	323 (5.4)	266 (82.3)	57 (17.7)	
	Other	3,959 (66.7)	3,936 (99.4)	23 (0.6)	
Number of tests, median (IQR)		1 (1-1)	1 (1-1)	3 (1-7)	<0.001

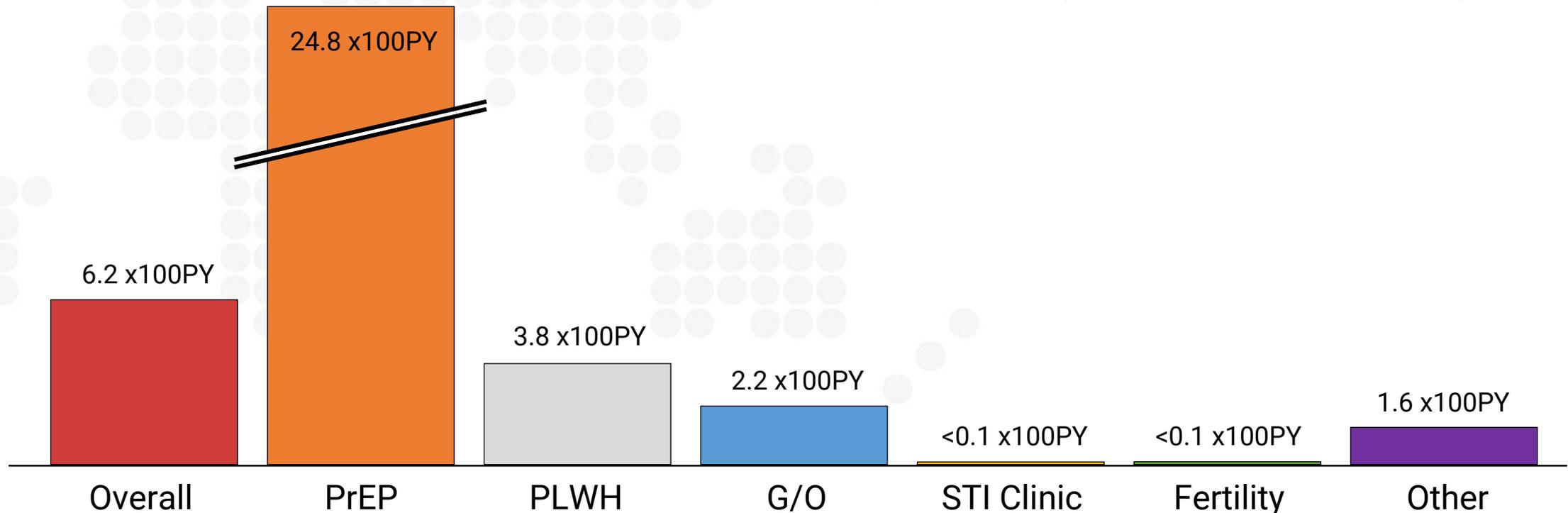
Results (2).

- Cumulative prevalence was **2.1%**.
- Overall prevalence increased over time passing from **0.9%** in 2018 to **4.5%** in 2021 ($p < 0.001$).
- Such rise was mainly due to PLWH (from **2.5%** to **17.3%**, $p < 0.001$) and PrEP users (from **5.9%** to **22.1%**, $p = 0.017$).
- G/O increased from **0%** in 2018 to **2.8%** in 2021 and STI Clinic from **0%** in 2018 to **2.3%** in 2021, but they did not reach the statistical significance ($p = 0.118$ and $p = 0.721$, respectively).



Results (3).

- Total time at risk was **1,311 years**: the cumulative IR was **6.2 per 100PY** (95% CI 5.0-7.7). The highest IR was registered in PrEP users (**24.8 per 100PY**, 95% CI 18.8-32.6) followed by PLWH (**3.8 per 100PY**, 95% CI 2.5-5.6) and G/O (2.2 per 100PY, 95% CI 0.3-16.0).
- IRR for PrEP users was significantly higher compared to the other groups (**9.1**, 95% CI 5.8-14.5, $p < 0.001$).
- IRR for PLWH was significantly higher only after excluding PrEP users (**2.9**, 95% CI 1.2-7.8, $p = 0.006$).



Results (4).

		HR	95%CI	p	aHR	95%CI	p
Gender	Males	1 (ref)			1 (ref)		
	Females	0.11	0.71-0.18	<0.001	0.29	0.13-0.63	0.002
Age, per each year		0.97	0.95-0.98	<0.001	0.96	0.94-0.98	<0.001
Origin	Italy	1 (ref)					
	Africa	0.46	0.06-3.32	0.440			
	Asia	0.71	0.26-1.94	0.501			
	Europe	0.71	0.31-1.63	0.422			
	South America	1.12	0.59-2.10	0.728			
	MENA	0.97	0.42-2.24	0.949			
Department	Other	1 (ref)			1 (ref)		
	G/O	2.05	0.91-4.60	0.082	2.58	1.05-6.37	0.039
	Fertility Clinic	1.40	0.33-5.96	0.651	1.88	0.42-8.46	0.411
	HIV	9.46	5.47-16.33	<0.001	2.20	1.05-4.63	0.037
	PrEP	36.67	22.25-60.45	<0.001	6.56	3.28-13.13	<0.001
	STI Clinic	5.15	1.76-15.09	0.003	2.00	0.63-6.30	0.236
Number of tests performed		1.62	1.52-1.72	<0.001	1.33	1.23-1.43	<0.001
Calendar year	2018	1 (ref)					
	2019	1.57	0.90-27.0	0.756			
	2020	0.76	0.07-7.98	0.820			
	2021	3.71	0.22-63.19	0.364			

Discussion (1).

- In this study, we estimated prevalence and incidence of MG infection in the general population as well as in several at risk groups and identified risk factors for the infection.
- The present analysis enrolled the largest cohort and with the longest follow up described so far.
- The overall prevalence is 2.1% comparable to what reported in existing literature, but with considerably differences among groups.

Discussion (2).

- PrEP users resulted a population at particular risk in terms of prevalence and incidence of MG. Being on PrEP resulted in a risk 6.56 times higher to acquire the infection.
- The same trend in PrEP users was observed also for the other STIs: the available data suggest an overall incidence as high as 91.9 per 100PY (42.0 per 100PY for CT, 37.2 per 100PY for NG, and 9.8 per 100PY for syphilis).
- Incidence of MG infection we found in PrEP users (24.8 per 100PY) is like what observed in these reports.

Limitations.

- Data about symptomatic *versus* asymptomatic infections are not available.
- Samples are collected for routine monitoring in PLWH, PrEP users, STI Clinic clients, and G/O patients, whilst the reason(s) why the tests are performed in most cases (i.e., the “Other” group) were not available.
- We could not gather data about sexual behavior in terms of number of sexual partners, heterosexual *versus* same-sex partners, condom use, chemsex practices, or concomitant co-infections with other pathogens.
- Data about the last quarter of 2021 are not available yet.

Take home messages.

- MG prevalence on urine samples and cervical swabs is increasing especially in key populations such as PLWH and PrEP users. Incidence rate is alarming, especially in the latter population.
- Given the worrying reports about antibiotic resistance and treatment failures, and the high number of unprotected sexual intercourses observed in these patients, additional efforts for MG testing and treatment are necessary to contain this ongoing epidemic.

Acknowledgments.

- Alice Nava, Chiara Baiguera, Federico D'Amico, Elvira Inglese, Carlotta Rogati, Diana Fanti, Leonardo Rezzonico, Chiara Vismara, Francesco Scaglione, Massimo Puoti.
- We wish to thank all subjects who participated to this study.
- The 23rd IUSTI World Congress for the opportunity to participate.
- Thank you all for your attention.