Sexually transmitted infections: a pressing health issue

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Disclosures

Disclosures from the presenter:

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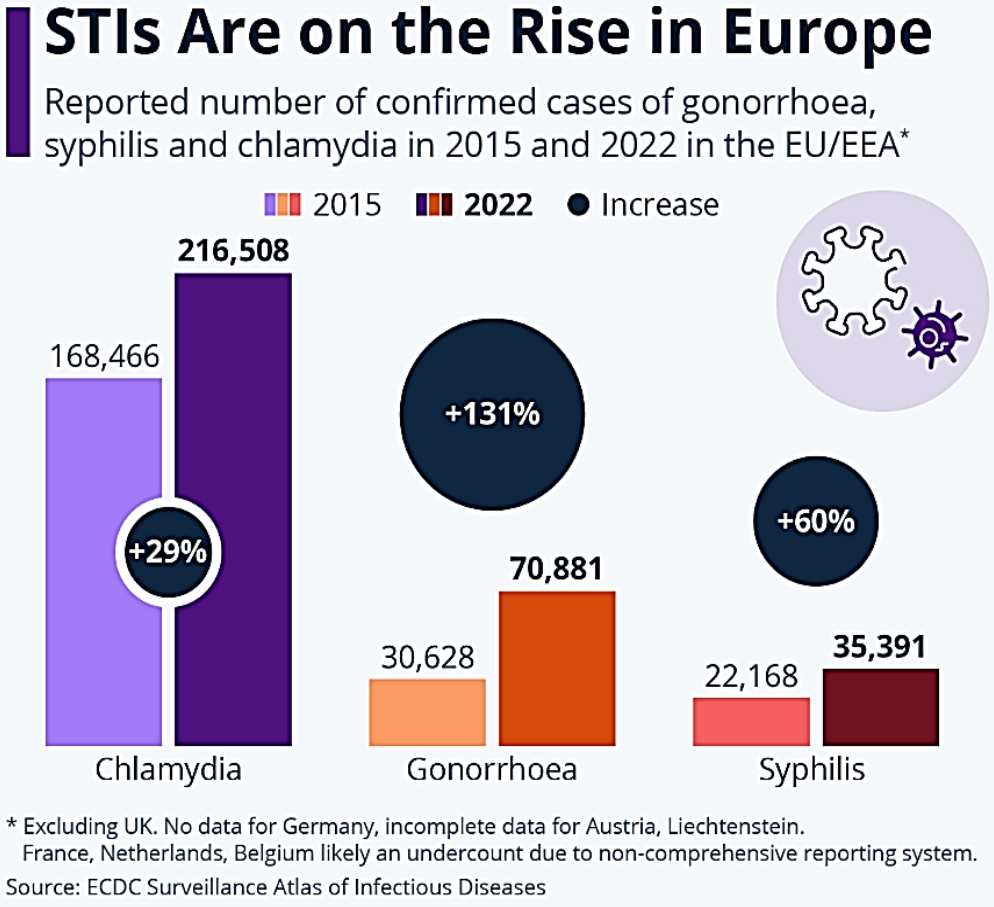
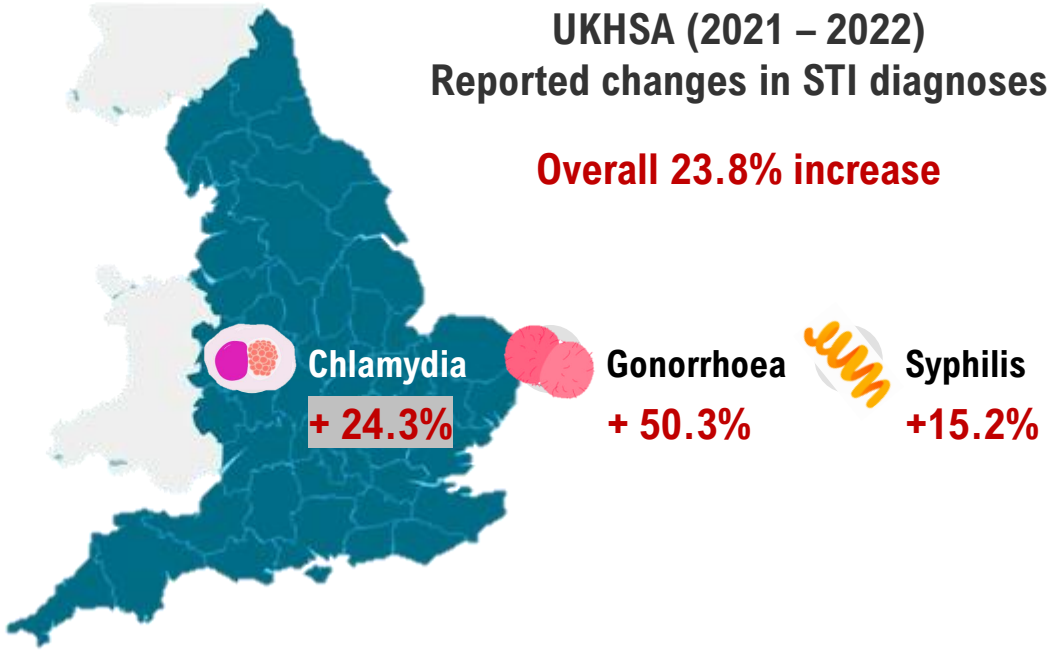
STIs are on the rise - Europe



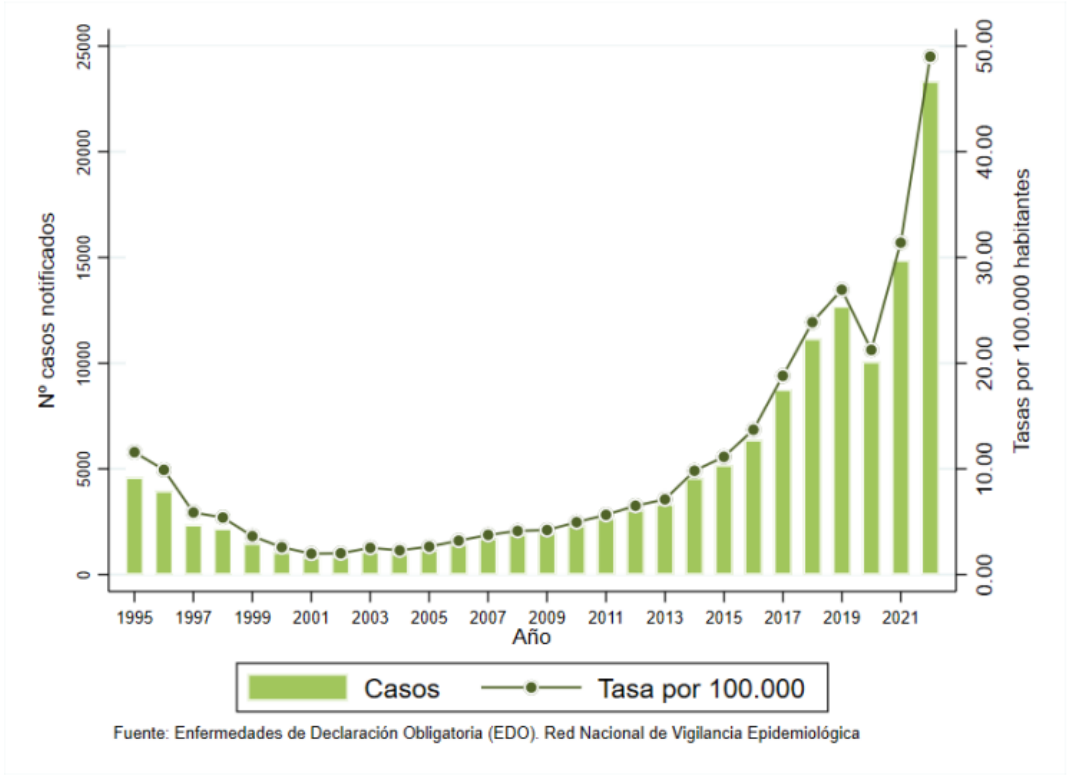


- +13.4% rise in STI testing in 2022 vs 2021
- True increases in transmission, not better case finding from more testing

ECDC Surveillance, 2022 | *BMJ* 2023;381:p1492

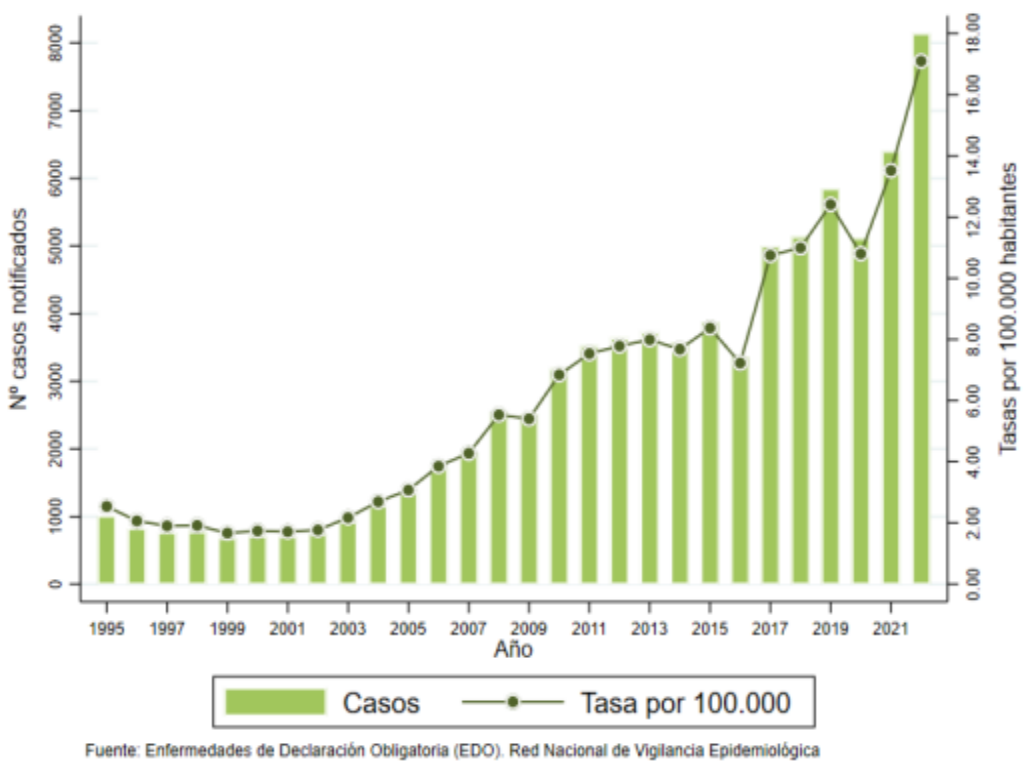
STIs are on the rise - Spain

Figura 1. Incidencia de infección gonocócica
Número de casos y tasas por 100.000 hab. España, 1995-2022



Fuente: Enfermedades de Declaración Obligatoria (EDO). Red Nacional de Vigilancia Epidemiológica

Figura 8. Incidencia de sífilis.
Número de casos y tasas por 100.000 hab. España, 1995-2022



Fuente: Enfermedades de Declaración Obligatoria (EDO). Red Nacional de Vigilancia Epidemiológica

Vigilancia Epidemiológica de las Infecciones de Transmisión Sexual en España, 2022

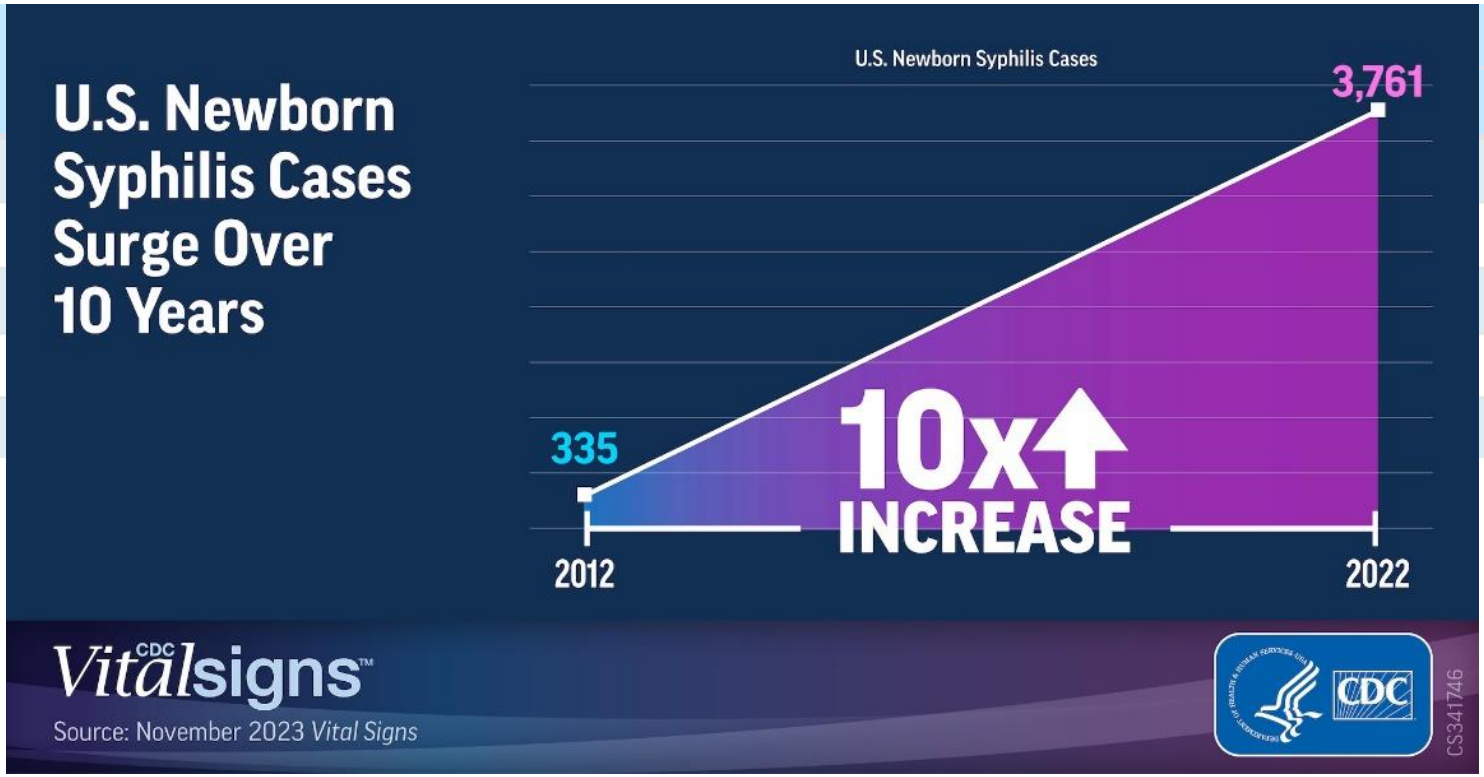
STIs are on the rise globally - US

Disease	Cases					Percent Change
	2018	2019	2020	2021	2022	5 Year
Chlamydia	1,758,668	1,808,703	1,579,885	1,644,416	1,649,716	-6.2
Gonorrhea	583,405	616,392	677,769	710,151	648,056	11.1
Syphilis (All Stages)	113,739	127,943	131,797	173,858	203,500	78.9
Congenital Syphilis	1,325	1,882	2,162	2,875	3,755	183.4
Total Reported STIs	**2,457,137**	**2,554,920**	**2,391,613**	**2,531,300**	**2,505,027**	**1.9**

CDC bulletin, 2023

STIs are on the rise globally - US

Disease	Percent Change 5 Year
Chlamydia	-6.2
Gonorrhea	11.1
Syphilis (All Stages)	78.9
Congenital Syphilis	183.4
Total Reported STIs	**1.9**



CDC bulletin, 2023

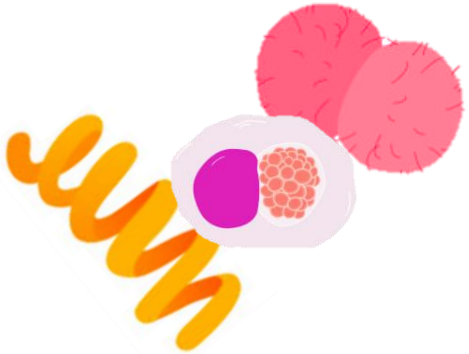
STIs are rising – why is that?

Ultra sensitive testing

Expansion of accessible testing (i.e. online)

MSM account for
- 74% of syphilis
- 60% of gonorrhoea

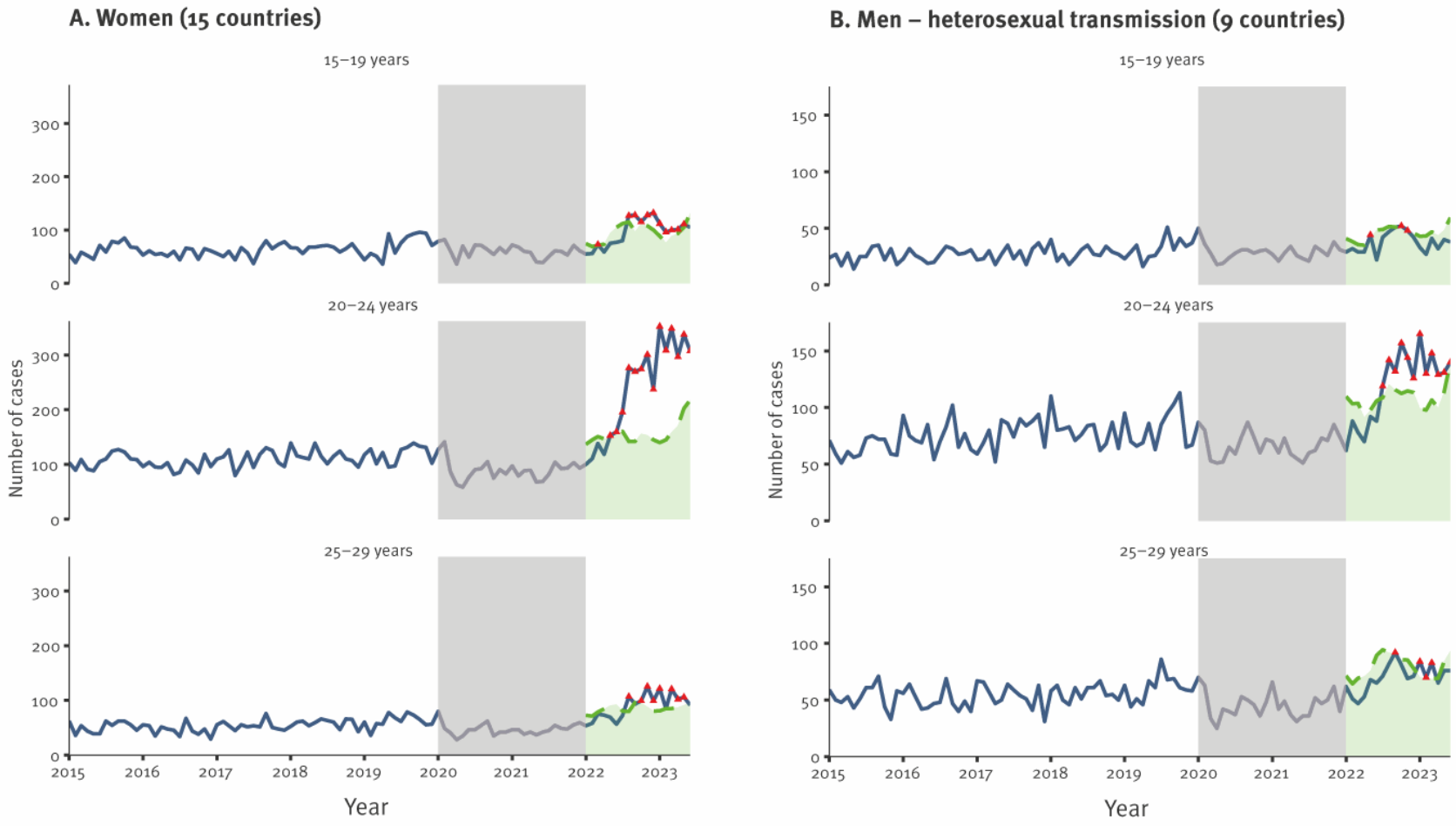
Mostly asymptomatic STI (66%)



Adapted from Tabesh et al. STI 2022 | Kent et al. CID 2005

STIs are rising in young people

Number of gonorrhoea cases (Jan 2015–Jun 2023) compared with the exceedance threshold (Jan 2022–Jun 2023) in EU/EEA



Euro Surveill. 2024;29(10):pii=2400113

Bacterial STIs – Gonorrhoea

Neisseria gonorrhoeae

Gram negative intracellular diplococcus
Infects mucous membranes
Incubation 2-7 days

♀

- Asymptomatic in 50-80%

- Vaginal discharge
- Dysuria
- Pelvic inflammatory disease !!
- Abnormal bleeding
- Rectal discharge
- Pharyngitis

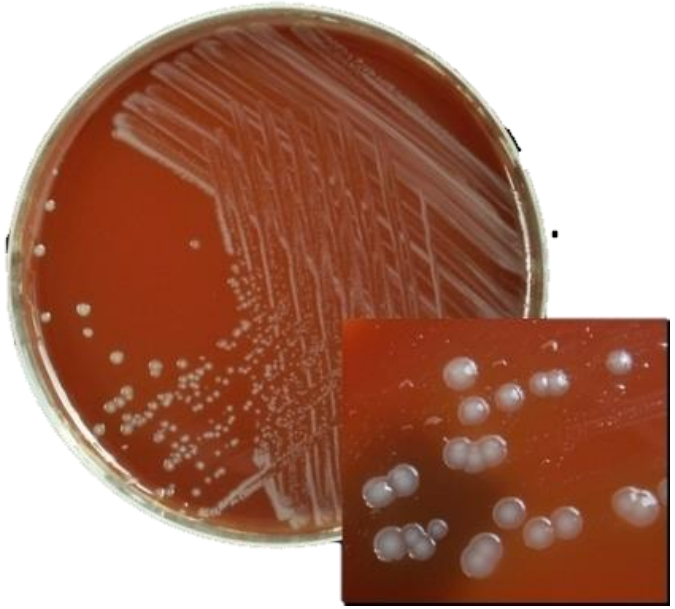
♂♀

- Symptomatic in 90% (urethra)
- Creamy urethral discharge
- Dysuria
- Testicular pain
- Epididymo-orchitis
- Rectal discharge
- Rectal pain/Tenesmus
- Pharyngitis

Bacterial STIs – Gonorrhoea treatment and management

Diagnosis

- Microscopy
- Cultures (pharynx, urethral, rectal, cervical)
- NATs (pharynx, urethral, rectal, cervical)



Management

First line

- Ceftriaxone 1g IM injection
- ± Azithromycin (2g STAT)

Second line

- Spectinomycin 2g IM single dose ± azithromycin 2g STAT
- Ciprofloxacin 500mg STAT
- Gentamicin 240mg IM ± azithromycin 2g STAT

Partner notification

- Abstain from sex for 7 days
- Contact tracing is crucial to break the chain of transmission - ? Test-and-wait in contacts?
- Test of cure

Bacterial STIs – Gonorrhoea treatment and management

- **Diagnosis**
- Microscopy
- Cultures (pharynx, urethral, rectal, cervical)
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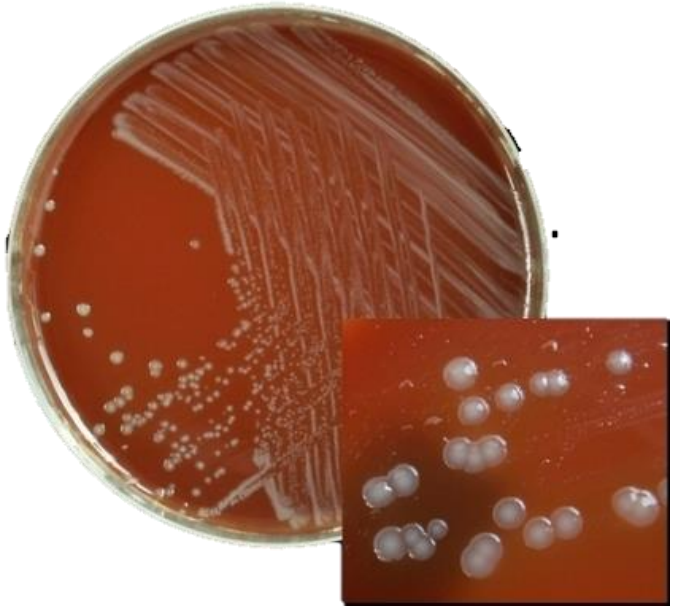

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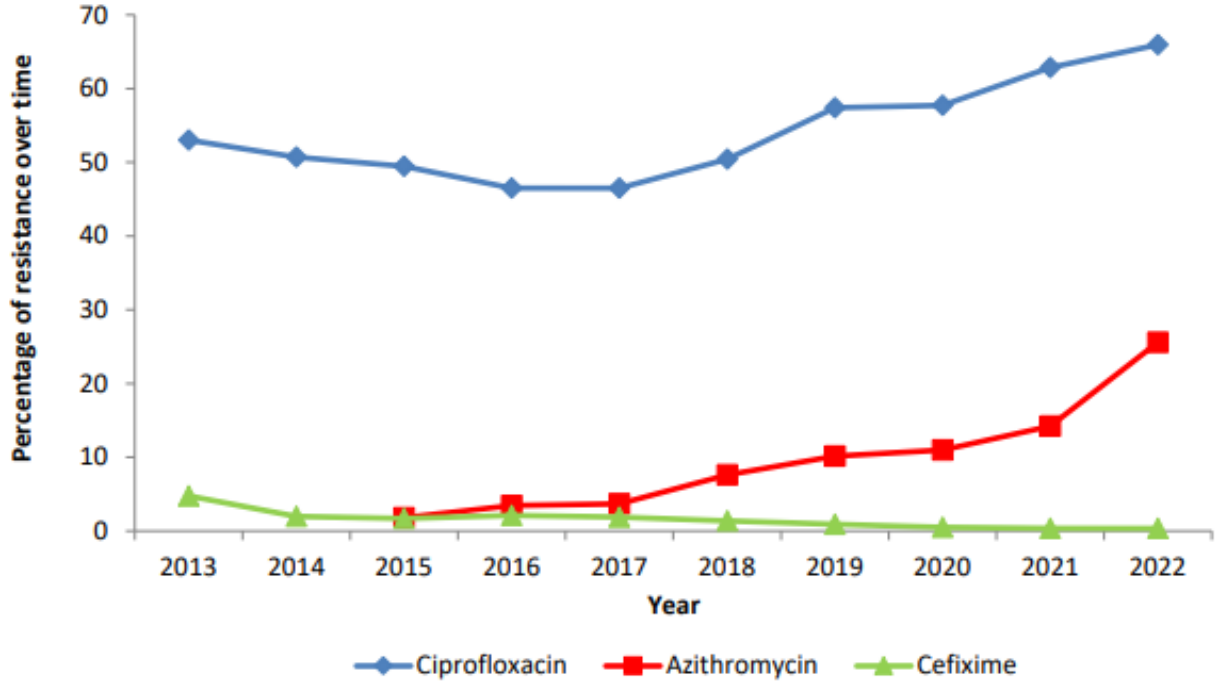
- **Partner notification**
- Abstain from sex for 7 days
- Contact tracing is crucial to break the chain of transmission - ? Test-and-wait in contacts?
- Test of cure

Bacterial STIs – Gonorrhoea concerns

- Growing cephalosporin resistant strains of *N. gonorrhoeae* – fluoroquinolones (60%) and macrolides (10%) have high levels of resistance

Figure 1. Percentage of resistant *Neisseria gonorrhoeae* by antimicrobial and year, Euro-GASP, 2013–2022



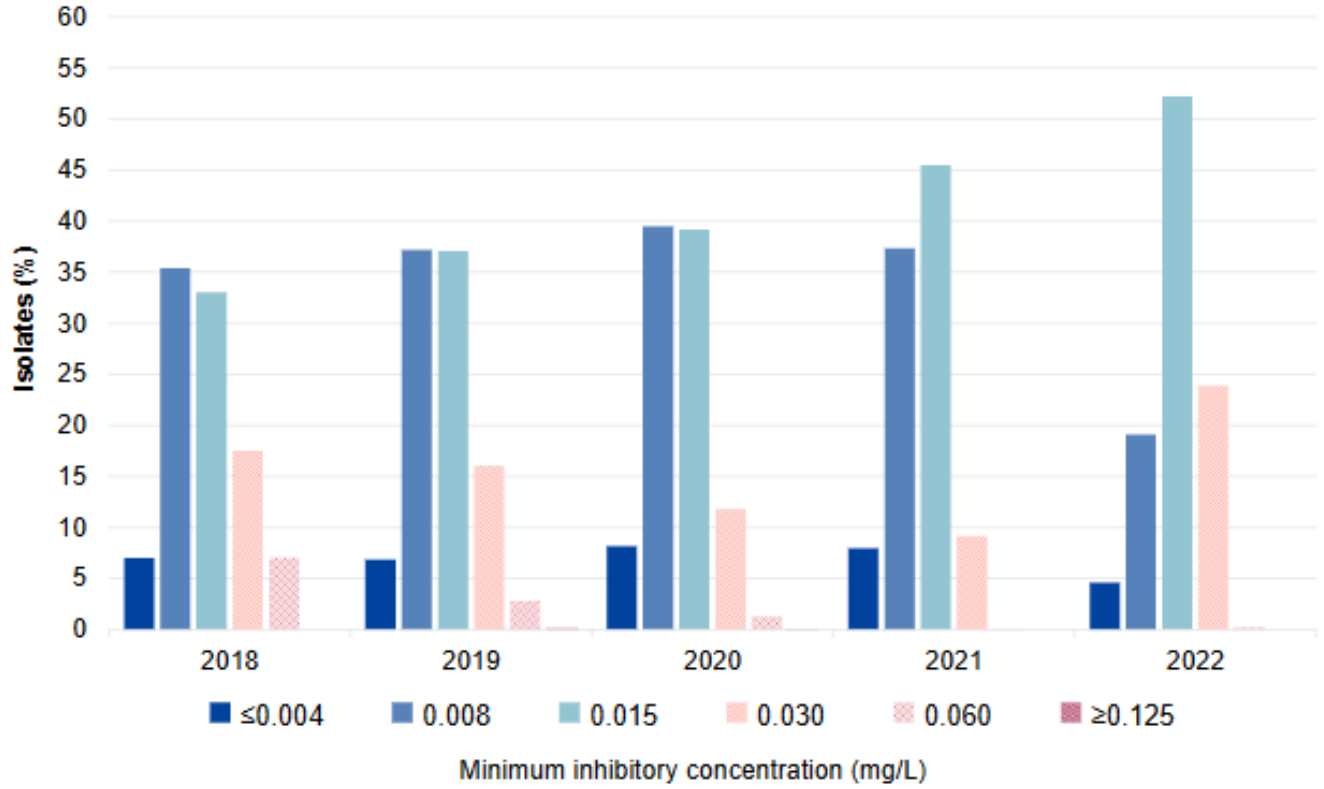
EURO GASP bulletin, ECDC 2023

Euro Surveill. 2024;29(10):pii=2400113

AMR in *Neisseria gonorrhoeae*

Selective pressure for AMR in intensive STI treatment

Figure 6. Distribution of ceftriaxone MICs (mg/L) for N. gonorrhoeae isolates in the GRASP sentinel surveillance system, England and Wales, 2018 to 2022 [note 1]

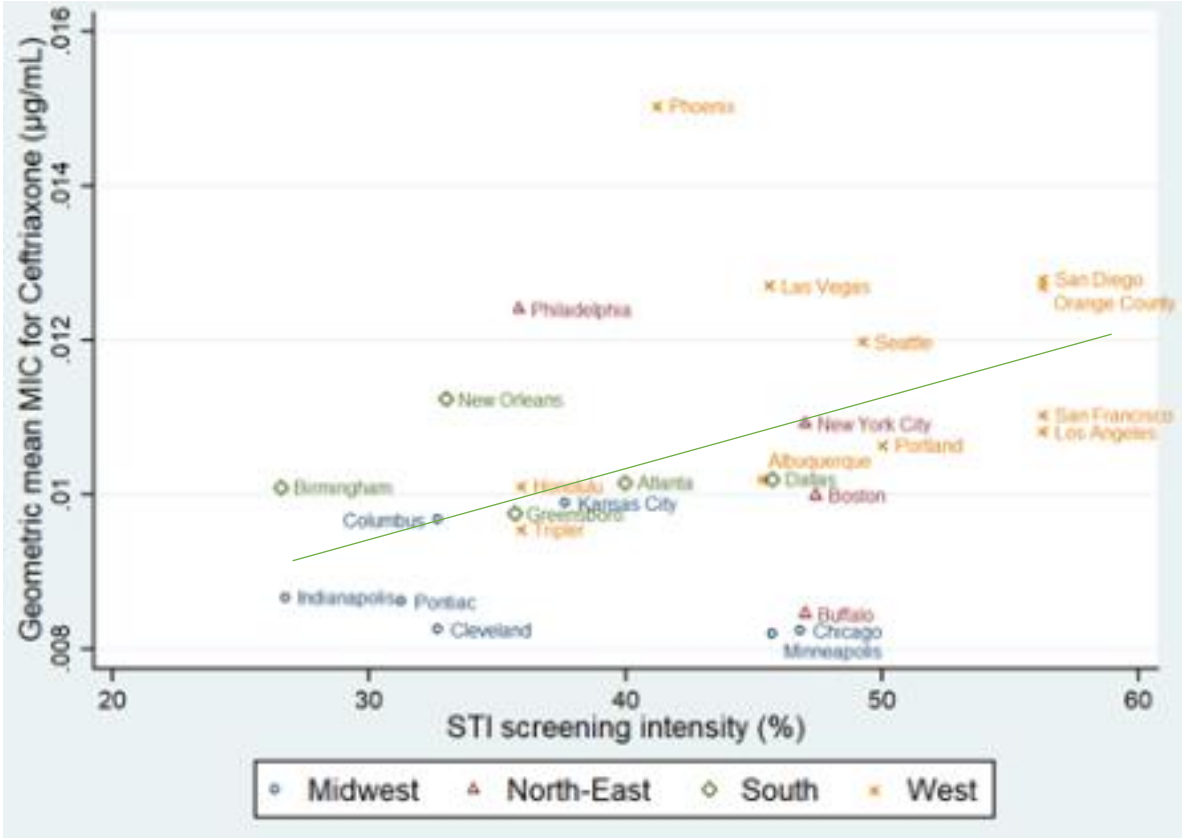


GRASP report. UKHSA 2023

AMR in *Neisseria gonorrhoeae*

Selective pressure for AMR in intensive STI treatment

- STI screening intensity data correlated with gonococcal MICs registered in MSM in 21 USA states in 2015
- Positive ecological association between STI screening intensity and geometric mean gonococcal MIC for ceftriaxone (rho=0.42, *p*=0.03)
- No association between STI screening intensity and gonococcal MIC for azithromycin (rho=0.31, *p*=0.11)



Van Dijck et al. STI BMJ 2020

Bacterial STIs – Gonorrhoea concerns

- Growing cephalosporin resistant strains of *N. gonorrhoeae* –
  fluoroquinolones (60%) and macrolides (10%) have high levels of resistance

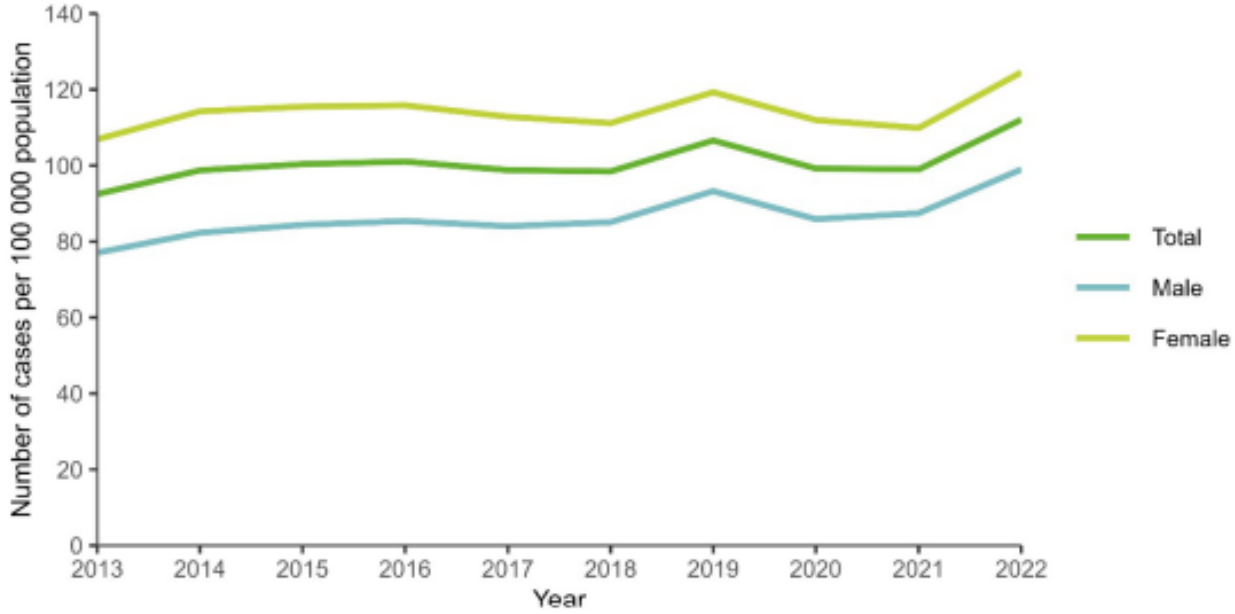
- **Perhaps some hope from new antimicrobials (Zoliflodacin, Lefamulin, Gepotidacin) ?**

Euro Surveill. 2024;29(10):pii=2400113

Bacterial STIs – Chlamydia

- Very common, especially in under 25s
- Serovars D–K cause urogenital infection
- Serovars L1–L3 cause lymphogranuloma venereum (LGV)
- Infection may last many months, often asymptomatic
- Spontaneous clearance possible
- Test with NATs (urine, endocervical/vaginal, rectal, pharyngeal)

Figure 4. Rate of confirmed chlamydia cases per 100 000 population, total and by gender for cases with available data, EU/EEA countries reporting consistently, 2013–2022



ECDC. Chlamydia. Annual Epidemiological Report for 2022; 2024.

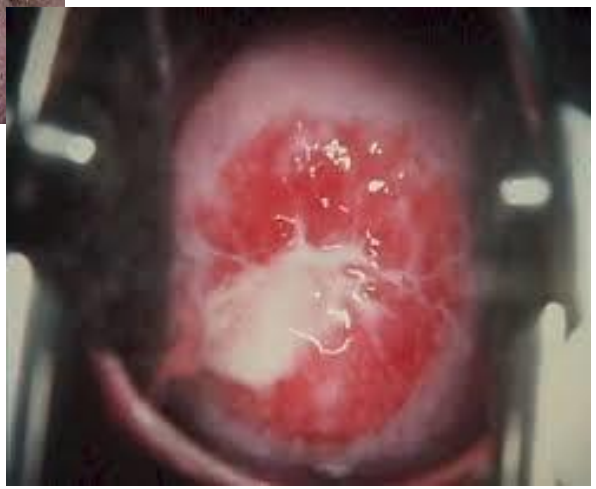
Bacterial STIs – Chlamydia symptoms

♀

Asymptomatic in 80%
Vaginal discharge
Abnormal bleeding
Dysuria
Pelvic pain

♂

Asymptomatic in 50%
Clear urethral discharge
Dysuria
Proctitis



Complications

Pelvic inflammatory disease
- Chronic pelvic pain
- Infertility

Ectopic pregnancy
Perihepatitis (Fitz-Hugh-Curtis syndrome)

Epididymo-orchitis
Prostatitis

Conjunctivitis
Reactive arthritis / Reiters syndrome

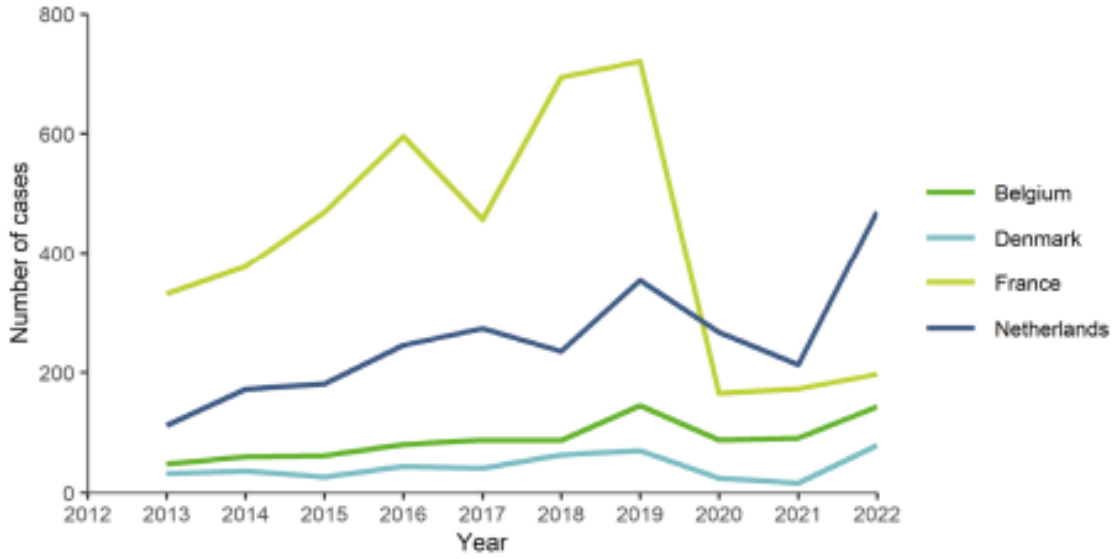
Bacterial STIs – LGV

Nearly all cases are seen in MSM

- LGV infection may cause no symptoms
- Proctitis
- Genital or rectal ulcerations
- Groin lymphadenopathy (2-6 weeks after infection)
- Fever, chills, malaise, muscle and joint pain

BASHH Int J STD AIDS 2013

Figure 1. Number of confirmed lymphogranuloma venereum cases in the four EU/EEA with the highest number of cases in 2022, 2013–2022



Bacterial STIs – Chlamydia treatment

Management

First line

Doxycycline 100mg PO BID for 7 days (21 days for LGV)

Second line (alternatives)

Azithromycin 1g PO STAT or prolonged 3 days course

* **Pregnancy** azithromycin or amoxicillin

treatment failure – 5-23% (gene mutations in 23S rRNA and tet(M) acquisition)

Alternative regimens

Ofloxacin 200 mg PO BID for 7 days
Levofloxacin 500 mg PO QD for 7 days

IUSTI guidelines, JEADV 2019

Bacterial STIs – Syphilis

Treponema pallidum

Approximately one-third of sexual contacts of infectious syphilis will develop the disease

Different clinical manifestations depending on clinical stage at diagnosis

(EARLY) – Primary syphilis (days-weeks)

- Ulcers in mouth or genitals
- Most times painless, usually single chancre (develops from a single papule)
- Anogenital, indurated with clean base, smooth borders
- Can be multiple, painful and purulent (usually extra-genital), especially in PWH
- Resolve over 3-8 weeks

BASHH, syphilis guidelines 2019






Bacterial STIs – Syphilis

Treponema pallidum

(EARLY) Secondary syphilis (4-10 weeks after initial chancre, 25% of cases)

- Widespread mucocutaneous rash, not always itchy
- Can affect palms and soles
- Mucous patches (buccal, lingual and genital)
- Condylomata lata (highly infectious, mainly affecting perineum and anus)

- Can be associated with fever, general malaise, lymphadenopathy
- Can be complicated by arthralgia, alopecia, hepatitis , uveitis, meningitis/meningo-vasculitis, periostitis

Secondary syphilis **will resolve spontaneously** in 3–12 weeks – if untreated – with the disease entering an asymptomatic latent stage

BASHH, syphilis guidelines 2019

Bacterial STIs – Syphilis

Treponema pallidum

EARLY latent vs. LATE latent – cut off used normally is < or > 2 years of latency

- Approximately 25% of patents will develop a recurrence of secondary disease during the early latent stage
- Early latent disease is also infectious
- Late latent disease remains asymptomatic until symptoms and signs of tertiary and quaternary disease occur (and infectiousness is dubious)

BASHH, syphilis guidelines 2019

Bacterial STIs – Syphilis

Treponema pallidum

Tertiary

- Large granulomatous lesions in skin and internal organs including liver, kidneys and brain
- Rare in antibiotic era
- Usually occur many years after infection (average 4-10 years), sooner in PWH

Gummatous syphilis: nodules/plaques or ulcers (skin, mucosae, visceral)

Late neurosyphilis:

- encompasses meningitis, cranial nerve dysfunction
- meningo-vascular syphilis (stroke, myelitis) and parenchymatous
- neurosyphilis (general paresis, tabes dorsalis)

Cardiovascular syphilis:

- aortic regurgitation, stenosis of coronary ostia
- aortic aneurysm (mainly thoracic)

BASHH, syphilis guidelines 2019
IUSTI, syphilis guidelines 2020
Photo credit: NEJM

Bacterial STIs – syphilis diagnosis and treatment

Diagnosis

Dark ground microscopy

PCR from a swab

Syphilis serology

Specific (Treponemal) tests – EIA IgM/IgG, TPPA, TPHA

Remain positive indefinitely after the first infection

Non-Specific (Non-Treponemal) tests – VDRL, RPR

Titre declines after treatment or during latency

Can be used to monitor treatment efficacy or identify re-infection

Treatment - Early syphilis (primary, secondary and early latent)

Benzathine penicillin G 2.4 MU IM single dose *

***not treponemicidal in CSF**

Alternative regimens:

- Procaine penicillin G 600,000 units IM daily 10 days
- Doxycycline 100mg PO BD 14 days
- Ceftriaxone 500mg IM daily10 days
- Amoxycillin 500mg PO QDS plus Probenecid 500mg QDS14 days
- Azithromycin 2g PO STAT or Azithromycin 500mg daily for 10 days

🔮 Linezolid ?

https://www.bashh.org/resources/25/syphilis_2015

Bacterial STIs – syphilis diagnosis and treatment

Diagnosis

Dark ground microscopy

PCR from a swab

Syphilis serology

Specific (Treponemal) tests – EIA IgM/IgG, TPPA, TPHA

Remain positive indefinitely after the first infection

Non-Specific (Non-Treponemal) tests – VDRL, RPR

Titre declines after treatment or during latency

Can be used to monitor treatment efficacy or identify re-infection

Treatment – Late latent

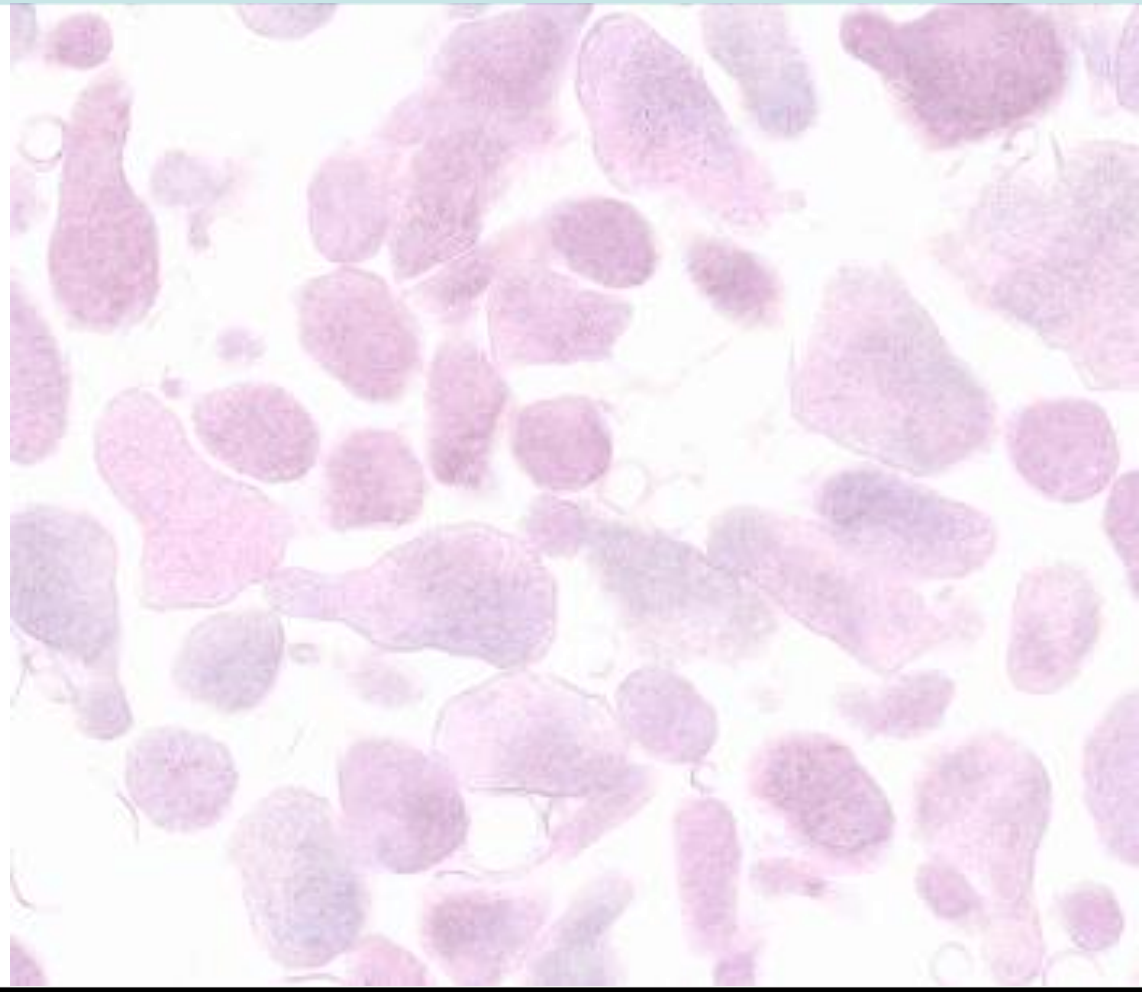
Benzathine penicillin G 2.4 MU IM weekly for three weeks (three doses)

Alternative regimens: Doxycycline 100mg PO BD 28 days

https://www.bashh.org/resources/25/syphilis_2015

Bacterial STIs – Mycoplasma genitalium

- Most people infected with *M. genitalium (MGEN)* in the genital tract do not develop disease
- Cause of **10-20% of non-gonococcal urethritis in male** patients and **40% of persistent or recurrent urethritis**



Bacterial STIs – Mycoplasma genitalium

Signs and symptoms in females

- **None** – the majority are asymptomatic
- Dysuria
- Post-coital bleeding
- Painful inter-menstrual bleeding
- Cervicitis
- Lower abdominal pain (see Complications: PID)

Signs and symptoms in males

- **None** – the majority are asymptomatic
- Urethral discharge
- Dysuria
- Penile irritation
- Urethral discomfort
- Urethritis (acute, persistent, recurrent)

Complications in females

- **Pelvic inflammatory disease**
- Tubal factor infertility (uncertain association)
- Sexually acquired reactive arthritis
- Pre-term delivery

Bacterial STIs – Mycoplasma genitalium – when to test

Based on symptoms

- Individuals with non-gonococcal urethritis
- Individuals with signs and symptoms suggestive of pelvic inflammatory disease
- Women with signs or symptoms of muco-purulent cervicitis, particularly post-coital bleeding

- Consider in people with epididymitis
- Consider in people with sexually-acquired proctitis

Based on risk factors - REGULAR sexual partners of persons infected with MGEN

Specimen choice - first void in cis-men / trans women, vaginal swabs (clinician- or self-taken) in cis-women

All specimens should be **tested for macrolide resistance** mediating mutations (MRAMs)

Soni et al. International Journal of STD & AIDS 2019, 30(10) 938–50

Bacterial STIs – Lessons from MGEN

- 7 day regimen of doxycycline has low efficacy for MGEN with cure in 30-40%
- Rapid increase in macrolide resistance - highly correlates with treatment failure (44-90%)
- Moxifloxacin had a cure rate about 100% and efficacy declined to 90% in the recent years

Mitjà O et al. Lancet Reg Health 2023

Bacterial STIs – Mycoplasma genitalium - treatment

	BASHH	IUSTI	CDC
Uncomplicated urogenital infection	**No macrolide resistance:** **Doxycycline** 100mg BD 7 days followed by **Azithromycin** 1g STAT then 500mg OD for 2 days **Macrolide-resistance:** **Moxifloxacin** 400mg OD for 7 days (also when treatment with azithromycin has failed)	**No macrolide resistance:** **Azithromycin** 500mg on day one, then 250mg on days 2–5 **Macrolide-resistance:** **Moxifloxacin** 400mg OD for 7 days **Persistent M. genitalium infection** after azithromycin and moxifloxacin **Doxycycline** or minocycline 100mg BD for 14 days (cure 40–70%) Pristinamycin 1g QID for 10 days (cure 75%)	**No macrolide resistance:** **Doxycycline** 100mg BD for 7 days, followed by **Azithromycin** 1g STAT, followed by 500mg OD for 3 additional days **Macrolide-resistance:** **Doxycycline**100mg BD for 7 days followed by **Moxifloxacin** 400mg OD for 7 days
Complicated urogenital infection (PID, epididymo-orchitis)	**Moxifloxacin** 400mg OD 14 days	**Moxifloxacin** 400mg OD 14 days	

Bacterial STIs – Lessons from MGEN

- 7 day regimen of doxycycline has low efficacy for MGEN with cure in 30-40%
- Rapid increase in macrolide resistance - highly correlates with treatment failure (44-90%)
- Moxifloxacin had a cure rate about 100% and efficacy declined to 90% in the recent years

✓ Consider **repurposing** old drugs (pristinamycin, minocycline)

✓ Consider **resistance-guided therapy** in STIs

✓ **Mitigate resistance in the community**

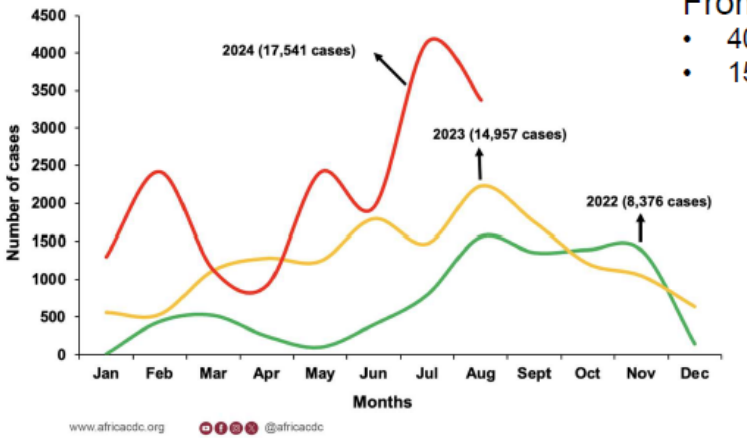
Reducing empirical treatment

Reducing asymptomatic screening **(more evidence needed on the impact at community level)**

Mitjà O et al. Lancet Reg Health 2023

Any other lessons to be learnt from STIs ?

Mpox trends in Africa: 2022 - 2024



From **2022 to date**

- 40,874 cases / 1,512 deaths
- 15 African Union Member States

160% 2023 VS 2024 same period

79% 2023 VS 2022

AfricaCDC Centres for Disease Control and Prevention

Who is getting mpox in the DRC? (WHO survey)

Category	Number of cases	Percentage
Student	932	51.30%
Non-schooled child	319	17.60%
Farmer	214	11.80%
Housekeeper	208	11.40%
Fisherman	55	3.00%
Others	37	2.00%
Teacher/Professor	16	0.90%
Porter	16	0.90%

Equateur, clade Ia

Category	Number of cases	Percentage
Unemployed	519	24.20%
Student	393	18.30%
Sex worker	364	17.00%
Resourceful/Independent	262	12.20%
Others	135	6.30%
Merchant	127	5.90%
Farmer	125	5.80%
Housekeeper	123	5.70%

South Kivu, clade Ib

www.africacdc.org @africacdc

AfricaCDC Centres for Disease Control and Prevention

Cases of clade Ib have recently been reported in CAR, Burundi, Rwanda, Congo, Kenya, Thailand and Sweden

Mpox is highlighting (**AGAIN !**) the consequences of inequitable access to diagnostics, treatments, and vaccines

A coordinated international response is overdue and fundamental to contain a looming epidemic

Take home messages – STIs, a pressing health issue

- STIs are rising among MSM and young adults
  This is not justified entirely by better testing techniques and increased testing volumes

- STI antimicrobial resistance is not a looming threat, it is a reality

- Reducing empirical STI treatment is essential

- We need data on the impact of different screening strategies for *chlamydia* and *gonorrhoea* infections at a population level. Understanding this better would help fighting antimicrobial resistance

- Paying attention to marginalized communities, potentiating sexual health services, coordinating surveillance and policymakers would enable a stronger response to future outbreaks

Contacts

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Thank you !

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