Sexually Transmitted Infections

Managing bacterial sexually transmitted infections (STIs) and preventing HIV/STIs in Europe

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HIV, viral hepatitis, and other sexually transmitted infections (STIs) are major public health threats worldwide, and the WHO European Region is no exception. The WHO estimates that in 2020 there were 374 million new infections globally of four curable STIs in women and men aged 15–49 years–*Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Treponema pallidum*, and trichomoniasis—with 23 million infections in the WHO European region alone.[1] Although the WHO has no data on *Mycoplasma genitalium*, its prevalence is second only to *C. trachomatis* in most studies.[2] Furthermore, in the WHO European Region, an estimated 319,000 people were newly infected with Hepatitis B and C virus in 2019 and 170,000 were newly infected with HIV in 2020.[1] In light of these figures, improved screening, surveillance in key populations, access to treatment and vaccination are crucial to meet the WHO's 2030 goals of ending HIV, viral hepatitis and STIs.[3]

Two papers published in *The Lancet Regional Health - Europe* for the Series on "Sexually Transmitted Infections" address the treatment strategies for bacterial STIs[4] and the prevention approaches for HIV, viral hepatitis and STIs in Europe.[5]

Mitjà et al.[4] discuss the state of the art in the treatment of bacterial STIs—*N. gonorrhoeae*, *M. genitalium* and *T. pallidum*—and explore the new challenges that have emerged alongside with it. In particular, the increasing incidence of antimicrobial resistance (AMR) in *N. gonorrhoeae* and *M. genitalium*, which has been identified as a priority by the WHO and the US Centers for Disease Control[6]; and the supply-chain shortages of commonly used antibiotics for *T. pallidum*.

The spread of extensively drug-resistant *N. gonorrhoeae* clones combining ceftriaxone-resistance and low- or high-level azithromycin resistance in several WHO regions including Europe is of concern and challenges the recommended combined therapy in Europe. Rapid expansion of *M. genitalium* resistance to first-line macrolide and second-line fluoroquinolone treatment especially in key populations, like men who have sex with men, has led to the implementation of resistance-guided therapy (RGT) to treat only symptomatic patients.[7]

To mitigate AMR in *N. gonorrhoeae* and *M. genitalium*, Mitjà et al. have identified a number of strategies that can be implemented: rapid identification of drug-resistant pathogens by molecular assays; development of point-of-care assays to reduce the overuse and misuse of antibiotics and reduce the selection pressure exerted by frequent broad-spectrum antimicrobials[8]; contact tracing to break the chain of transmission; and reducing empirical treatment in asymptomatic contacts of cases with *N. gonorrhoeae* or narrowing screening for *M. genitalium* to symptomatic patients.

Another approach discussed by Mitjà et al., is the use of older antibiotics, which are repurposed either to reduce *N. gonorrhoeae* exposure to ceftriaxone, as a third-line treatment for multi-resistant *M. genitalium*, or as an alternative treatment for *T. pallidum* in response to benzathine penicillin shortages. In addition to existing therapies, the development of new antimicrobials is currently promising only for *N. gonorrhoeae* with gepotidacin and zoliflodacin in phase 3 development, while new molecules against *M. genitalium* or *T. pallidum* are still lacking.

Gökengin et al.[5] highlight the remarkable inequality in the implementation of prevention strategies for STIs, HIV, and viral hepatitis when comparing Western Europe with Central and Eastern regions. For HIV prevention, the only strategy that has gained validation in Europe is oral pre-exposure prophylaxis (PrEP) using lamivudine and tenofovir disoproxil fumarate, mostly

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used in men who have sex with men. Still, its equitable distribution across European countries remains a challenge, with cost and stigma being significant barriers. Gökengin et al. also discuss the next promising FDA-approved strategy, injectable PrEP administered every two months, combining long-acting cabotegravir and rilpivirine, and the ongoing development of vaginal rings.

In the realm of bacterial STIs prevention using doxycycline as post-exposure prophylaxis (doxy-PEP), recent studies have demonstrated a reduction of about two-thirds in STIs incidence among men who have sex with men, particularly for *C. trachomatis* and *T. pallidum* infections. Gökengin et al. identify two major concerns with this approach: (i) the potential emergence of AMR in STI pathogens as evoked for *N. gonorrhoeae*,[9] given that the risks of resistance in *C. trachomatis* and *T. pallidum* appear to be lower,[10] and (ii) the impact of doxy-PEP on the composition of different microbiota.[11] Consequently, doxy-PEP is not currently recommended in Europe, and further research is essential to define the specific patient profiles eligible for such a strategy.

When it comes to vaccines, the landscape is promising yet uneven. Hepatitis A and B vaccines have been widely adopted across European regions. It is imperative to broaden and standardize access to the human papillomavirus vaccine, emulating Australia's approach of vaccinating young individuals regardless of gender. Although limited data suggests a reduction in gonococcal infections with the serogroup B meningococcal vaccine, it is crucial to sponsor further studies before endorsing this costly vaccine on a wider scale. Emerging strategies for an HIV vaccine, especially those leveraging the mRNA platform and heterologous prime–boost combinations,[12] are showing preliminary promise, lighting the path toward the "holy Grail".

While these two papers highlight the commendable advances in HIV and STIs treatment–including innovative technologies to detect antimicrobial resistance–and in STIs prevention strategies, it is a fact that Europe is still lagging behind on the road to meeting HIV, viral hepatitis and STIs elimination targets by 2030—an urgent political commitment is needed.

Contributors
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Declaration of interests
The authors have no competing interests to declare.

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