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Screening for STIs is one of the main drivers of macrolide consumption in PrEP users

Dear Editors

A recent publication by Forster et al. explored the demographic and behavioural factors associated with antimicrobial susceptibility to ceftriaxone and azithromycin of *Neisseria Gonorrhoeae* (NG). This article showed an alarming increase in NG geometric mean azithromycin minimum inhibitory concentration (MIC) between 2014/2015 and 2017/2018. Moreover they found a higher geometric mean azithromycin MIC in men who have sex with men (MSM) compared with other groups. Given the emergence of antimicrobial resistance in NG, the authors emphasize the need for interventions in order to reduce the inappropriate use of azithromycin.[1]

In our clinic, we made use of a natural experiment, where we changed from triple-site, 3-monthly to single-site 6-monthly screening to assess the impact of screening intensity on macrolide consumption.

From October 2015 until May 2018 PrEP was provided to 197 MSM and 3 transgender women via an open-label prospective cohort study that served as implementation trial for PrEP in Antwerp, Belgium (the Be-PrEP-ared study).[2] Participants underwent 3-site 3-monthly screening for *Chlamydia trachomatis* (CT) and NG for at least 18 months' follow-up. A retrospective analysis of macrolide prescriptions during this study revealed a macrolide consumption of 12.05 defined daily doses/1000 individuals/day (DID) which is 4–7 times higher than thresholds associated with inducing macrolide resistance in a range of bacterial species.[3,4]

By the end of the study, PrEP was re-imbursed in Belgium and participants of the Be-PrEP-ared study were invited to routine PrEP care after study completion, along with new PrEP patients. During routine care, screening for CT/NG was performed at a single site every 6 months, due to Belgian testing reimbursement regulations. The antimicrobial treatment of CT/NG followed the then contemporary IUSTI guidelines.[5–7] CT was typically treated with azithromycin or doxycycline and NG with ceftriaxone and azithromycin. Based on clinical records, WHO standard methodology was used to calculate screening intensity and macrolide consumption (in DID) in a period of 'routine PrEP', between October 2019 and December 2020, which was compared to the results from the Be-PrEP-ared period.

A total of 1305 patients attended the PrEP clinic during this routine PrEP period, 1297 were male and 8 were female. We performed 2060 CT/NG nucleic acid amplification tests (NAATs), representing 2.16 tests/person/year, whereas during the Be-PrEP-ared study 12 tests were performed per person per year (Table 1).

Macrolide consumption was 3.27 DID during the routine PrEP period. To assess the impact of COVID-19 restrictions we repeated the same calculation for two different periods: 10/2019-03/2020 and 04/2020-12/2020. Macrolide consumption declined slightly from 3.61 DID in the first period to 3.17 DID in the second period.

In the routine PrEP period, macrolide consumption was thus almost four-fold lower than during Be-PrEP-ared. The main driver of macrolide prescriptions in PrEP cohorts with 3-site, 3-monthly screening is the treatment of asymptomatic CT/NG infections.[3,8] Most guidelines still recommend 3-site 3-monthly screening among PrEP users although the evidence supporting this is scarce. In particular, more intense screening for CT/NG has not been shown to reduce the prevalence of these infections compared to less intense screening.[9,10] We conclude that less intensive screening of CT/NG in PrEP cohorts offers a way to reduce macrolide consumption. Alternative antimicrobial regimens, including those limiting the use of azithromycin, could also be considered.[7] The dramatic increases in macrolide resistance in *Neisseria gonorrhoeae, Mycoplasma genitalium* and other bacteria in Belgium and elsewhere suggest the urgent need to

Table 1. Screening intensity for *Chlamydia trachomatis* (CTs)/*Neisseria gonorrhoeae* (NG) and macrolide consumption during the 'routine PrEP' and Be-PrEP-ared periods.

	Be-PrEP-ared period	Routine PrEP period
Screening intensity CT/NG	12 tests/patient/year	2.16 tests/patient/year
Macrolide consumption	12.05 DID	3.27 DID

CT: Chlamydia trachomatis; NG: Neisseria gonorrhoeae; DID: doses/1000 individuals/day.

incorporate this type of stewardship into plans of how intensively to screen for CT/NG in PrEP and other populations.

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