EDITORIAL

What impact will new screening techniques have on the epidemiology of STIs worldwide?

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"Despite the impressive product specifications ... the success of new diagnostics in altering the epidemiology of STIs relies on their effective implementation."

WHO estimates that globally there are over 200 million new cases of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* per year and 10–15% of women with undiagnosed or repeat infection will develop pelvic inflammatory disease (PID) [101].

Syphilis infection has serious consequences in both sexes and it is estimated that approximately 1.4 million pregnant women are infected with syphilis per year globally, of these over 500,000 will experience adverse outcomes of pregnancy: 40% of these stillbirths and 17% neonatal or early infant deaths [1]. All three of these common bacterial STIs are treatable, and their adverse outcomes preventable.

The majority of these cases are asymptomatic, making the need for robust screening strategies a public health priority.

STI screening strategies

■ Who & where to screen?

STI transmission relies on high rates of partner change among members of the population. This transmission is usually not heterogeneous across the population but is driven by a small proportion that have higher than average rates of partner change [2].

■ Core groups

These individuals will often form a small and targetable subset of the overall population (e.g., female sex workers [FSWs]). These groups act as drivers of infection within the general population, transmitting infection through bridging groups.

Reducing STI prevalence in core groups such as FSWs not only reduces adverse outcomes within that group, but impacts upon the prevalence of STIs within the bridging and general populations [3].

These groups are often hard to reach, and screening programs must have high enrollment rates to achieve efficacy. Vulvo–vaginal swabs allow for minimally invasive specimen collection and can be performed by the patient in their own home or community setting, eliminating

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the need for invasive cervical examination at a clinic site. Ostergaard *et al.* provided some of the best data on long-term outcomes following screening, and found that providing minimally invasive home sampling kits to a sexually active student cohort resulted in increased testing uptake over traditional clinic-based screening, and a 50% relative risk reduction in PID at 1 year [4].

Antenatal syphilis screening

It is in antenatal populations that syphilis screening has the largest potential for direct reduction in morbidity and mortality. With the vast majority of women now accessing antenatal care, it is also this population in which screening should be easiest to implement. Unfortunately, this is not being achieved in many settings, with less than 40% of women attending antenatal clinics in sub-Saharan Africa being screened for syphilis [5], and only 60% of those found to have active syphilis receiving timely treatment [6].

How to screen?

For an effective STI screening program, the key requirement of any test is a high sensitivity. This ensures that the maximum number of cases are detected. It is also important that those testing positive then go on to receive treatment.

Traditional laboratory-based screening

Dual (nucleic acid amplification test) NAAT testing platforms for *N. gonorrhoeae* and *C. trachomatis* are highly accurate, with sensitivities between 90 and 100% [7,8]. In countries with advanced laboratory infrastructure NAAT platforms are well suited for generalized screening programs and have a good positive predictive value, even in low prevalence settings.

Despite the obvious advantages of NAAT screening, it requires trained staff, high investment costs and advanced infrastructure. This precludes its use in many low-income settings; and even where available, may not be the most effective diagnostic platform at altering the epidemiology of STIs, due to the length of time between sample collection and result.

Point-of-care testing

The two principle advantages of point-of-care (POC) testing are:

- It provides a rapid result that can guide clinical management at the initial visit;
- It does not require extensive training or laboratory equipment to function effectively.

These points taken together mean that testing can be can be offered in an increased number of settings, without having to invest heavily in infrastructure. It also reduces loss to follow-up rates after testing, as treatment can be offered within the same clinical care visit.

Unfortunately, the diagnostic accuracy of current POC tests is not comparable with NAAT testing platforms as *C. trachomatis* and *N. gonorrhoeae* detection relies on the detection of low amounts of antigen in the mucosa. The *C. trachomatis* Chlamydia Rapid Test has a reported sensitivity of 80% [9]; however, a more recent study in Suriname reported sensitivities as low as 41.2% [10], with POC tests for *N. gonorrhoeae* showing equally disappointing results [11]. These shortcomings call into question the real-world effectiveness of screening with currently available POC tests.

Impact of screening with POC tests

C. trachomatis & *N. gonorrhoeae*

There is evidence, however, that POC testing in its current form can be effective in the right settings. First described by Gift *et al.* as the rapid test paradox, this model showed that use of POC tests resulted in more cases being treated than when reference NAAT testing was used, despite lower sensitivities, as it eliminated loss to follow-up [12].

Similar models have since confirmed this; but only when loss to follow-up rates are relatively high when using NAAT testing and in cohorts with high disease prevalence. While this means that POC testing may not be superior to laboratory-based screening in general populations as found in the UK [9], it could be argued that POC tests could actually make the greatest impact in groups where effective screening is most needed.

POC testing is well suited to the screening of FSWs as STI prevalence is usually high and follow-up rates with traditional screening technologies have been documented to be as low as 50% [13]. Mishra *et al.* found the number of FSWs with active syphilis in Bangalore who received treatment rose from 44.8% with

off-site RPR testing, to 68.3% with the introduction of POC testing with a sensitivity of only 70.8% [13].

Aledort *et al.* published detailed modeling data looking at the disability-adjusted life years that could be saved within an entire population just by introducing regular POC screening for FSWs in low-income settings [14]. They found that the ability to introduce POC testing to clinics in low-income settings would significantly increase access to screening, and that this would result in a 29% increase in disability-adjusted life years saved in areas with minimal infrastructure. This increased to 40% in areas with no infrastructure. These impressive results were based on a test with only 67% sensitivity [14].

Vickerman *et al.*'s 2003 modeling study is unique as it also takes into account the possibility of onward STI transmission in the time between testing and result availability. It showed that the required sensitivity of a POC test is inversely proportional to the waiting time for traditional laboratory results, the prevalence of infection and the rate of partner change. Based on a cohort of South African FSWs, where partner change and STI prevalence was high, the sensitivity of a novel POC test required to decrease the incidence of *C. trachomatis* and *N. gonorrhoeae* was as low as 35 and 23% respectively [15].

Antenatal syphilis screening

Syphilis infection is not confined to the mucosa, but triggers systemic antibody production and detection of these nontreponemal antibodies allows for sensitive immunoassay-based POC tests. Mabey *et al.* provides the most conclusive evidence that POC testing with this existing technology can be both implementable and effective [16].

This study aimed to improve the detection and treatment of maternal syphilis across communities in seven different countries, by introducing a same day testing and treatment approach. The study performed a preintervention survey to determine the proportion of people being screened and treated with the preexisting strategies (most relying on RPR testing) then developed easy to follow guidelines on how the new POC tests should be implemented. By working closely with the local health authorities, impressive and hopefully sustainable results were achieved in each study area. In most settings, both screening of eligible women and same-day treatment rates increased to over 90% [16].

Conclusion

The ability to perform POC testing with no surrounding infrastructure will enable the delivery of effective screening programs to areas where this was previously unthinkable. If POC testing is targeted toward specific populations, the reduction in mortality, morbidity and disease prevalence within populations could exceed results seen even when laboratory testing is available.

This has proved to be successful where sensitive and affordable POC tests are already available, such as in the case of antenatal screening for syphilis. Unfortunately, effective *C. trachomatis* and *N. gonorrhoeae* screening is hindered by POC tests with unreliable sensitivities. However there is optimism surrounding novel POC NAAT testing platforms; The GeneXpert® (Cepheid, CA, USA) allows user friendly simultaneous detection of *C. trachomatis* and *N. gonorrhoeae*. This technology platform has already proved effective in expanding accurate TB detection in much of sub-Saharan Africa. NAAT platforms based on isothermal amplification with real-time detection are in development. These offer the potential of a true POC test with the sensitivity of laboratory-based NAAT platforms that could have a huge impact on the epidemiology of *C. trachomatis* and *N. gonorrhoeae* worldwide [17,18].

Despite the impressive product specifications of these platforms, the success of new diagnostics in altering the epidemiology of STIs relies on their effective implementation. While improving the performance of POC tests is a priority, the appropriate implementation of current POC tests within health systems could represent an incredible opportunity to rectify global health inequalities and impact STI epidemiology worldwide.

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