Benefits of POC sexual health testing

A recently published study has highlighted the economic and clinical benefits of incorporating a point-of-care nucleic acid amplification test for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* into genitourinary medicine clinics.[1] In this article, some of the paper's authors highlight the advantages over traditional immunoassay techniques for point-of-care detection.

Chlamydia trachomatis and *Neisseria gonorrhoeae* are responsible for a significant number of sexually transmitted infections (STIs), with genitourinary medicine (GUM) clinics diagnosing 100,647 cases of *chlamydia* and 20,964 of gonorrhoea in England alone in 2011.[2] Currently, patients with symptoms indicating possible *chlamydia* or gonorrhoea infection usually undergo 'presumptive treatment' for *chlamydia* prior to diagnosis being confirmed by laboratory testing.[3,4] As symptoms are often non-specific – and may be due to other infections, such as *Mycoplasma genitalium* – this 'syndromic' management strategy can lead to sub-optimal, inappropriate or unnecessary treatment,[5,6] resulting in unnecessary costs, delays in patients receiving appropriate treatment and poor antimicrobial stewardship.[5-7] Asymptomatic infection is also a common problem, and patients remain untreated until the laboratory diagnosis is available, increasing the risk of complications or additional individuals becoming infected and further increasing the overall cost of care.

Under current best-practice guidelines, off-site laboratories should provide clinicians with results of diagnostic testing within seven days. However a 2011 audit identified that only 75% of GUM clinics received this level of service, leading to further delays in patients receiving appropriate treatment.[8] This issue is compounded by difficulties in contacting many patients to arrange follow-up appointments, as well as non-attendance at these appointments,[9] highlighting a place for rapid and robust point-of-care (POC) diagnosis.

Laboratory standards at the point of care

POC tests for *C. trachomatis* and *N. gonorrhoeae* can broadly be divided into immunoassay methods and DNA-based techniques. Early POC *chlamydia*/gonorrhoea tests based on antibody/antigen binding have had limited application, due to lower sensitivity and specificity compared with nucleic acid amplification tests (NAATs) performed in laboratories.[10-12]

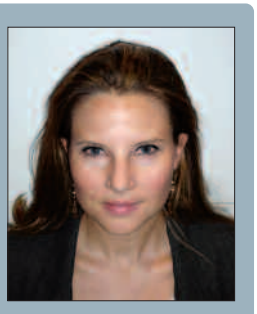
Dr Patrick Horner, consultant senior lecturer in the School of Social and Community Medicine at the University of Bristol, explained: "Unlike many other areas of medicine, there can be significant non-medical consequences of being diagnosed with an STI for the individual – particularly for those in long-term relationships – and so it is extremely important for diagnoses to be accurate. Even the best POC enzyme immunoassays only offer around 80%-85% sensitivity and less than 99% specificity,[12] meaning that a significant number of infections will be missed and, more importantly, there will also be false positives. This lack of performance compared with the laboratory gold standard of nucleic acid-based testing has resulted in poor uptake of POC testing, as clinicians simply did not have confidence in the technology."

Recent advances in POC technology have enabled the latest generation of in-clinic analysers – such as Cepheid's GeneXpert series – to offer rapid, PCR-based testing at the point of patient care. This new generation of POC assays can provide laboratory quality results within 90 minutes (Cepheid Xpert CT/NG), while significantly reducing the space and staff training required for operation.[13, 14]

The development of an easy-to-use NAAT for *C. trachomatis* and *N. gonorrhoeae* represents a significant development for STI diagnosis in GUM clinics, helping to transform patient management and treatment strategies. Dr Horner continued: "Nucleic acid-based POC testing for STIs is a quantum leap from previous methods, potentially offering same day results for the patient. This has the potential to substantially change the way we manage patients, leading to better-informed clinical decisions and helping to reduce patient anxiety."

Dr Elisabeth Adams, director and founder of Aquarius Population Health, added: "There has recently been a move towards offering

'The introduction of POC technologies represents a very good opportunity to overhaul services in a way that will benefit patients and clinics alike.'



Dr Elisabeth Adams.

rapid sexual health screens for asymptomatic patients in the UK's GUM clinics, and high performance, accurate POC tests fit really well into that model. Traditionally, patients attending GUM clinics would have blood samples drawn by a nurse on arrival at the clinic, then see a doctor. Clinicians have reported that both waiting times and consultations could be fairly lengthy, with many patients being examined, including those reporting no symptoms. This model is now changing, with more clinics offering a rapid screening pathway for asymptomatic patients, avoiding the potentially long wait to see a doctor for patients who have more generalised concerns about their sexual health. Many of these patients will have attended the clinic due to anxiety, and so rapid turnaround of results is particularly important in these cases."

> 'Replacing standard laboratory testing for *chlamydia* and gonorrhoea with a POC test could save costs while improving diagnostic accuracy and reducing unnecessary or inappropriate treatments.'

A new way of working

The availability of reliable POC tests for *C. trachomatis* and *N. gonorrhoeae* offers significant potential benefits for patients, GUM clinics and the entire health service. Dr Horner commented: "From a clinician's perspective, the best option would be to have the test results available before seeing the patient, as the consultation and patient's care can then be based on their known *chlamydia*/gonorrhoea status. This would obviously lead to better informed patient management decisions, helping to eliminate presumptive treatment strategies and avoid the need for follow-up consultations once the results are received from the laboratory."

"For example, if a patient was a *chlamydia* contact, but the results of a POC test were negative, then that patient would probably not need treatment. Previously, we would not have been able to make this decision, and so the patient would have been treated as a precaution until results were available. This not only increases the patient's anxiety while they are awaiting the test results, it also raises concerns around antimicrobial stewardship, potentially increasing the likelihood of antimicrobial resistance. Alternatively, if a male patient presents with urethritis, the treatment strategy will vary depending on whether it is due to *chlamydia*, gonorrhoea or neither of these micro-organisms, as different antimicrobials are needed for optimal treatment of these conditions. Being able to rule out *chlamydia* or gonorrhoea at the time of the consultation would allow a better informed clinical decision to be made regarding treatment, helping to improve outcomes."[15]

To fully realise these benefits, GUM clinics will need to develop new patient care pathways to accommodate this novel technology. Dr Adams explained: "Redesigning care pathways can be a daunting prospect, and often causes logistical issues for services. Increasing cost pressures mean that many clinics are having to rethink how they deliver sexual health care, in order to be as efficient and effective as possible. The introduction of POC technologies represents a good opportunity to overhaul these services in a way that will benefit patients and clinics alike."

An economic argument

While improving patient outcomes is the main driver for implementation of POC testing, there are also considerable estimated cost-savings which can be realised by redesigning care pathways to take advantage of this new technology. The recently published paper presents an early, pragmatic decision analysis of introducing a POC NAAT for *chlamydia* and gonorrhoea into GUM clinics in England, comparing the testing and treatment costs with current practice.[1]

Dr Adams continued: "One of the biggest potential areas of savings is the elimination of inappropriate and unnecessary treatments. A large number of patients currently receive sub-optimal or inappropriate treatment due to epidemiological or presumptive care while awaiting the results of laboratory testing. The availability of POC testing results when patients are seen ensures the most appropriate antimicrobial is used, or avoids treatment altogether for those who do not have an infection. This can yield significant savings on prescriptions, while contributing to improve antimicrobial stewardship. Introduction of same-day testing also avoids the need to culture negative samples for antimicrobial susceptibility testing, further reducing the average cost of laboratory services per patient.

"These benefits could more than offset the slightly higher cost per assay for POC NAATs compared with off-site laboratory-based testing, and free up both clinic time and administrative resources by avoiding the need for many follow-up appointments. As well as the savings which can be achieved through reducing the testing and consultation workload, there are also a number of potential indirect effects of reducing the time between test and treatment, including preventing onward transmission and the progression to complications such as pelvic inflammatory disease. Overall, the study suggests that savings of around

'Currently, patients with symptoms indicating possible infection usually undergo 'presumptive treatment' prior to diagnosis being confirmed by laboratory testing.'

£11.75 m per annum could be realised across the UK if all GUM clinics adopted a POC testing pathway for *chlamydia* and gonorrhoea."

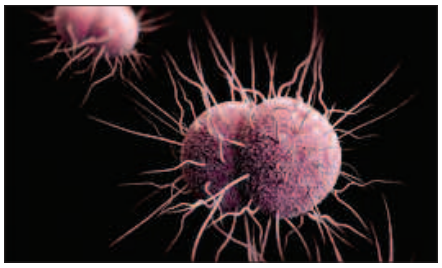
Quality control in a POC environment

As with any POC diagnostic service, quality assurance must be central to the successful adoption of POC *chlamydia*/gonorrhoea NAATs, to avoid reliability issues which may hinder the widespread adoption of the technology. Dr Horner said: "Introduction and oversight of POC tests are complex issues for any clinic. In Bristol, we work closely with our microbiology laboratory, and that is certainly something I would advocate. Trained laboratory staff bring a certain skill set and technical expertise to diagnostic testing, and so are best placed to oversee operation of POC analysers. Ideally, a POC analyser should be straightforward to operate and involve minimal sample preparation, and a rigorous, reproducible and practical approach to training and instrument use should be adopted. There is no reason why the clinic staff cannot be trained to use the equipment effectively, but laboratory staff are best placed to oversee this, as they have the in-depth knowledge and experience of laboratory-based quality assurance procedures, helping to ensure the highest standards are maintained."

Listening to the evidence

The conclusions of this early study suggest that POC *chlamydia*/gonorrhoea testing has the potential to significantly alter the way GUM clinics manage patients, leading to better patient flow and improved outcomes, while offering significant cost savings. The study is based on the published performance data of the existing POC NAAT (Cepheid Xpert CT/NG)[13] and expert opinions as to the likely 'best approach' to patient care, with further data needed to confirm the findings once the test is implemented in clinics.

Dr Horner explained: "Early findings suggest that this technology offers laboratory quality testing within the clinic, but we can currently only forecast its likely impact on patient care and clinic management; as yet, there is no randomised control data to support its adoption. This evidence is vital whenever a new technology is introduced and the more rigorous the evaluation, the stronger the argument for its adoption. I would welcome such an evaluation of POC NAATs for *chlamydia*/gonorrhoea, as I firmly believe that it will confirm the benefits of this approach, accelerating its widespread adoption."



CDC/ Melissa Brower

A computer-generated image of *Neisseria gonorrhoeae*.

Conclusions

Replacing standard laboratory testing for *chlamydia* and gonorrhoea with a POC test could save costs while improving diagnostic accuracy and reducing unnecessary or inappropriate treatments. Overtreatment currently accounts for around one-tenth of all reported *chlamydia* and gonorrhoea treatments, and POC NAATs would effectively eliminate the need for presumptive treatment. "Based on the evidence available, if you could introduce POC testing as part of your sexual health screening and diagnostic pathways, then you could offer a more efficient and effective service," Dr Adams concluded.

'The conclusions of this early study suggest that POC testing has the potential to significantly alter the way GUM clinics manage patients, leading to better patient flow and improved outcomes.'

References

1 Turner KME, Round J *et al*. An early evaluation of clinical and economic costs and benefits of implementing point of care NAAT tests for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in genitourinary medicine clinics in England. *Sex Transm Infect* 2013; 0: 1-8.
2 Health Protection Agency. STI Data Tables. 2012. http://www.hpa.org.uk
3 Horner PJ, Boag FC. *2006 UK National Guideline for the Management of Genital Tract Infection with Chlamydia trachomatis*. British Association of Sexual Health & HIV, 2006.
4 Bignell CJ, FitzGerald M. UK national guideline for the management of gonorrhoea in adults, 2011. *Int J STI AIDS* 2011; 22: 551-47.
5 Manhart LE, Broad JM, Golden MR. Mycoplasma genitalium: should we treat and how? *Clin Infect Dis* 2011; 53(Suppl 3): S129-42.
6 Anagrius C, Loré B, Jensen J. Treatment of Mycoplasma genitalium. Observations from a Swedish STD Clinic. *PLoS One* 2013; 8: e61481.
7 Horner PJ. Azithromycin antimicrobial resistance and genital *Chlamydia trachomatis* infection: duration of therapy may be the key to improving efficacy. *Sex Transm Infect* 2012; 88: 154-6.
8 2011 Audit against the Key Performance Indicators in the BASHH MedFASH STI Management Standards. BASHH National Audit Group. H McClean. http://www.bashh.org/documents/3786.xls
9 NCSP quality assurance 2010 Turnaround times audit 2010. http://www.chlamydiascreening.nhs.uk/ps/resources/quality/Nov_2010_QA_repor_turnaround_times_Final_V1.1.pdf
10 Hislop J, Quayyum Z *et al*. Systematic review of the clinical effectiveness and cost-effectiveness of rapid point-of-care tests for the detection of genital *chlamydia* infection in women and men. *Health Technol Assess* 2010; 14: 1-iv.
11 Watchirs Smith LA, Hillman R *et al*. Point-of-care tests for the diagnosis of *Neisseria gonorrhoeae* infection: a systematic review of operational and performance characteristics. *Sex Transm Infect* 2012; 89: 3206.
12 Mahilum-Tapay L, Laitila V *et al*. New point of care *Chlamydia* Rapid Test – bridging the gap between diagnosis and treatment: performance evaluation study. *BMJ* 2007; 335: 1190-4.
13 Gaydos CA, Van Der PB *et al*. Performance of the Cepheid CT/NG Xpert Rapid PCR Test for the Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. *J Clin Microbiol* 2013; 51: 166672.
14 Goldenberg SD, Finn J *et al*. Performance of the GeneXpert CT/NG assay compared to that of the Aptima AC2 assay for detection of rectal *Chlamydia trachomatis* and *Neisseria gonorrhoeae* by use of residual Aptima Samples. *J Clin Microbiol* 2012; 50: 3867-9.
15 Horner P, Blee K, Adams E. Time to manage *Mycoplasma genitalium* as an STI: but not with azithromycin 1 g! *Curr Opin Infect Dis* 2014; 27(1): 68-74.