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National Chlamydia Screening Programme

External Peer Review: Review Panel Report

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Abbreviations

BAME	Black and Minority Ethnic
BASHH	British Association for Sexual Health and HIV
BV	bacterial vaginosis
CTAD	Chlamydia Testing Activity Dataset
DH	Department of Health
DRI	detection rate indication
EP	ectopic pregnancy
GP	general practitioner
GUM	genitourinary medicine
GUMCAD	Genitourinary Medicine Clinical Activity Dataset
HPV	Human papilloma virus
HSE	Health Survey for England
LARC	Long-acting reversible contraception
LSOA	lower layer super output area

MSOA	medium layer super output area
PID	pelvic inflammatory disease
PN	partner notification
QALY	quality-adjusted life years
SEU	Seroepidemiology Unit
STI	sexually transmitted infection
TFI	tubal factor infertility

Introduction

Public health budgets continue to come under pressure although the sexual health needs of the population have not decreased. Sexual health services therefore need to demonstrate value for money and cost effectiveness. The National Chlamydia Screening Programme (NCSP) is central to the PHE strategy to improve sexual health. NCSP invited an external group of experts to review the evidence and provide a report of how best to improve chlamydia control activities in England.

An evidence pack (National Chlamydia Screening Programme External Peer Review: Evidence Pack) was assembled by the NCSP team and distributed to the members of the review panel prior to the review meeting. The panel agreed that the evidence review presented was excellent and was a fair and unbiased review of the evidence. It was also agreed, however, that some elements had been omitted such as: evidence from population studies outside the UK; the influence of antibiotics used to treat chlamydial infections, particularly azithromycin, in terms of resistance in *Mycoplasma genitalium* and gonorrhoea; the impact of contraceptives, particularly hormonal contraceptives, on both chlamydia and pelvic inflammatory disease (PID) and how both may have changed over time. Panel members agreed to suggest specific information for inclusion within the evidence review.

A two-day review meeting was held on 24-25 October 2017 at which the NCSP team gave presentations under the following headings: History of the NCSP; PHE's role in screening; natural history of chlamydia; data collection; surveillance outputs; evaluating the impact of the NCSP; health economics; stakeholder feedback. The peer review panel was then asked to address specific questions and this report is a summary of the expert review panel's discussion during the review meeting.

Recommendations for the programme policy

1. Aims of the programme

1.1 The principal aim of the programme should be re-stated as:

- to prevent the adverse consequences of untreated chlamydia infection

1.2 Secondary aims of the programme:

- to reduce re-infections and onward transmission of chlamydia
- to raise awareness of good sexual health

Rationale

There is evidence that detecting and treating chlamydia infections can prevent subsequent harm in asymptomatic women. There is no strong empirical evidence that chlamydia screening of women and men has resulted in a fall in prevalence (evidence pack page 80). Currently there is no accurate method for monitoring the incidence or prevalence of chlamydia at the local level. Although mathematical modelling had originally indicated that screening and treating infected individuals would reduce the prevalence of chlamydia and that the scale of this reduction was dependent upon the number of infections identified, this reduction has not been observed in practice (evidence pack page 7). To date the development of realistic chlamydia models that can fit observed data has proven problematic (evidence pack page 79).

The goals of chlamydia screening globally have always been poorly articulated, complicating retrospective justification. This review is a suitable point to clearly articulate the goals of the NCSP. Prevention of ongoing transmission is unlikely to be realistic, whereas prevention of harm from sequelae of chlamydia infection is likely to be more measurable and appropriate. Re-framing the programme objectives should enable a clearer understanding of what changes are required to better target at-risk populations, produce better data, generate more up to date health economic benefit models and achieve true evaluation of the impact of the programme.

A national chlamydia control programme would be best incorporated with health promotion and good sexual health education programmes to better inform people that the best way to control chlamydia is through condom use. Health promotion should continue to be offered to people requesting or being offered a chlamydia test.

2. Who should be offered testing

2.1 Opportunistic screening of young women should continue.

2.2 Young men should be offered tests if they are identified as partners or at risk, if they have symptoms, if they are undergoing other sexual health screening or if they request a test.

Rationale

There is good evidence from randomised controlled trials that detection and treatment of chlamydia can reduce the risk of pelvic inflammatory disease (PID) in women (evidence pack page 90). However, only a minority of PID cases are attributable to chlamydia, with an estimated population excess fraction (PEF) <10% for treated chlamydia, 26% untreated, (Davies et al 2017), 29% overall (Price et al 2016). Around 1 in 5 cases of TFI and 1 in 20 ectopic pregnancies are attributable to chlamydia (Price et al 2016).

The overall impact of the costs and benefits of chlamydia screening on the cost-effectiveness of a national screening programme are not easy to judge (evidence pack page 112). A reliable cost effectiveness analysis cannot be undertaken until either empirical evidence of the impact of screening on prevalence is obtained or transmission dynamic models are developed that can fit available data on screening activity and diagnosis rates, as well as data on the frequency of sequelae (evidence pack page 115).

Removing the opportunistic testing of men will improve the health economic benefit of the programme. Young men should continue to be offered tests if they are identified as partners of people with chlamydia or otherwise at risk, if they have symptoms, if they are undergoing other sexual health screening or if they request a test.

The programme should increase awareness in young women about chlamydia at the point they seek contraceptive advice, along with providing information about testing on partner change. The NCSP seems well placed to offer a significant contribution to national campaigns about good sexual health and this opportunity should be further developed.

2.3 Partner notification should be enhanced with the incorporation of new technologies and with better support for partner notification in primary care.

Rationale

Most partner notification currently depends on individuals who test positive contacting their partners directly. Partner notification is a key element of quality care for people with an STI and it should be retained as part of the programme and further developed. The diversity of testing settings has resulted in the loss of the opportunity to create central partner notification systems. There is evidence that the use of enhanced partner notification methods is effective but it was noted that there was limited investment in such systems as they tend to be resource-intensive.

Better partner notification systems would enable more areas, including rural areas with few positive cases, to meet their detection rate indicators. Partners may seek testing at some distance from index cases and systems could help ensure that data are captured.

2.4 Health promotion should continue to be offered to people requesting or being offered a chlamydia test.

Rationale

As per text in Recommendation 1

3. Where testing should be offered

3.1 Tests should continue to be offered to women and available to men in a variety of settings:

- testing through the national chlamydia programme should continue to be provided through sexual health clinics, GPs, pharmacies, first point of contact services and termination of pregnancy services etc, with appropriate outreach programmes considered for high risk populations
- online
- at all services which provide contraception

Rationale

As a general guide, provision of contraceptive services should be linked to provision of chlamydia testing. Given the relatively high case finding rates, testing through the national chlamydia programme should continue to be provided through sexual health clinics, GPs, pharmacies, first point of contact services and termination of pregnancy

services etc, with appropriate outreach programmes considered for higher risk areas and sub-populations.

For online testing, PHE should consider the roll-out of a chlamydia testing delivery model equivalent to the service which is currently provided for HIV testing and which has been shown to work well. If the delivery model option does not prove possible, then PHE should consider introducing mandatory minimum quality standards and service specifications for online testing services to ensure that appropriate tests are offered and provided.

Local commissioners should consider targeting of particular at risk populations. Current programme data indicates variation in test positivity by area, sociodemographic and behavioural characteristics. Improved analytic tools could be developed to identify sub-populations most likely to benefit from targeted screening. National targets should be broad to allow local targeting where necessary.

3.2 For online testing, PHE should consider the roll-out of a chlamydia testing delivery model equivalent to the service which is currently provided for HIV testing and which has been shown to work well. If the delivery model option does not prove possible, then PHE should consider introducing mandatory minimum quality standards.

Rationale

The HIV self-sampling service enables the procurement of an online service at a larger scale. This has the advantage of materially reducing the cost per test.

4. When else should testing be offered

4.1 The focus for offering screening should shift from "annual" to "on partner change."

4.2 Everyone who tests positive for chlamydia should be encouraged to have a re-test at 3 months.

Rationale

Modelling estimates that detection and treatment of incident infection would have a greater impact on cases of pelvic inflammatory disease averted, compared to detection and treatment of prevalent infections (Price et al, 2012b and Price et al, 2016). It was agreed that to minimise the duration of infection the best time to test for chlamydia is at partner change. There is limited evidence to reinforce annual testing as a programme recommendation but regular retesting is logical and there is strong evidence to support

retesting after 3 months for infected individuals as there is evidence of a higher rate of progression to PID for subsequent infections (Davies et al 2014, Davies et al 2016).

5. Treatment

5.1 Test results should be available within 7 days, and treatment within another 7 days.

Rationale

The current programme recommendation of treatment within 6 weeks where positive is too long and may result in avoidable transmissions, it should be changed to test results being available within 7 days and treatment within another 7 days, with the expectation that the majority of treatment initiations would be delivered within this two-week period. It was also noted that there is evidence which indicates that women who are treated for pelvic pain within 3 days have better fertility outcomes and that swift treatment could be a recommended public health intervention.

Recommendations for PHE activity

1. Support and delivery of NCSP and wider sexual health

1.1 The potential to combine NCSP data with information on teenage pregnancies as a possible indicator of areas of local need should be investigated.

Rationale

There are current separate data collection programmes for chlamydia screening and teenage pregnancy which report at different geographical scales. The panel questioned if information from these could be better managed by PHE and used to help inform the new sexual health education programme which is just starting within schools.

1.2 The NCSP team were also asked to consider if chlamydia testing could be linked to subsequent STI diagnosis (i.e. are people who access chlamydia testing more likely to be subsequently diagnosed with other STIs).

1.3 The panel recommended that consideration was given to whether the national programme could be used as an indicator for integrated sexual health services, perhaps through pathway analytics to determine the percentage of people accessing contraception who also receive a chlamydia test.

Rationale

Changes in such figures could prove useful for providing evidence of the benefits of health promotion advice.

2. Data collection for monitoring and supporting programme delivery

2.1 Data at MSOA with levels of positivity by deprivation, ethnicity and linked to other sexual health indicators should be available to local public health leads, sexual health commissioners and sexual health service providers.

2.2 Where possible, an indicator for the reason for testing (i.e. partner notification, new partner, annual test, re-test, symptoms) should be added and incorporated into existing test data.

2.3 PHE should produce geo-maps to MSOA level which also incorporate teenage pregnancy and Long Acting Reversible Contraception data.

Rationale

Such information, if available at L/MSOA level (see Q9) is likely to better inform targeting of testing at individuals at greater risk of infection by local providers, would be of value in identifying areas of poor sexual health which enable better targeting of scarce public health resources and would help improve local sexual relationship education in schools.

2.4 The NCSP should continue to make the most of current and improving ethnicity data to see if such trends can be identified, as they would also provide useful evidence of the impact of the programme.

Rationale

There is evidence that common vaginal microbiome populations in women of African heritage tend to be associated with higher prevalence and transmission of sexually transmitted infections hence targeted testing in such populations could have a greater impact in terms of prevention of harm from chlamydia infections.

3. Evaluation of outcomes

3.1 The panel recommended the continuation of surveillance of all-cause PID, with EP as a secondary objective.

3.2 The panel recommended that study of biomarkers of *all* PID (including chlamydia associated PID) should continue.

3.3 The panel recommended age-specific monitoring of NHS IVF clinics for possible changes in the aetiology of infertility. Case control studies of chlamydia-associated TFI should be possible using serology.

Rationale

It was acknowledged that the failure to incorporate a reliable measure of success for the programme at its inception was unfortunate but that it was essential not to be in a similar position in another 5 years – hence attempts to address this should be made now. This might include setting up enhanced sampling systems now and storing samples for when better analytic methods become available.

The panel agreed that evaluation of the programme would necessarily involve evaluating the impact of PID, including chlamydia-associated PID, but recognised that this was currently difficult. Demonstrating a reduction in PID, and its chronic sequelae such as tubal factor infertility (TFI) and ectopic pregnancy (EP), as a result of screening through the NCSP has not proved possible in practice (evidence pack page 90). This probably reflects the lack of robust outcome measures, together with recent evidence that chlamydia only causes around 20% of PID in women aged 16-44yrs (evidence pack page 89-90).

While the data are currently difficult to interpret, (hospital outpatient data on PID is currently not reliable enough for routine collection; it is likely that contraceptive use over time, particularly hormonal contraceptives, will have had some influence on both the natural history of chlamydia and on PID) the panel recommended that it still be collected in the hope that new methods of interpretation will be developed.

The difficulties of using PID levels as a measure of success of the programme were acknowledged and ways of improving the diagnosis of PID were discussed, including a pilot study in Bristol where PID diagnosis is further broken down to probable and possible PID. More reliable PID coding on test results was considered likely to improve the data collected to measure success of the programme.

The use of sentinel surveillance sites for improved PID diagnosis is recommended. It was noted that strong and defined case management processes would be required for sentinel sites. While initially better clinically defined PID cases are likely to have a range of causes, a collection of cases would then allow further work to be undertaken to ascertain which were due to chlamydia. If successful and if suitable for national roll-out, this would allow PID to be a suitable measure of success for the national programme in terms of chlamydia control.

In addition the NCSP should investigate the sentinel sites approach for undertaking linked follow-up studies to assess the risk of chronic pelvic pain following a diagnosis and treatment of PID, particularly if patients can be categorised into possible versus probable PID. This could link to the finite mixture modelling using serology (Ades et al, 2017).

4. Evaluation of incidence and prevalence

4.1 The NCSP should measure the prevalence of antibodies against *C. trachomatis* as a measure of past exposure.

4.2 Sentinel surveillance sites to monitor positivity levels from chlamydia testing should be considered.

Rationale

Over the lifetime of the programme, there has been no obvious impact on the prevalence of chlamydia but this is not unique to the UK. There are no metrics of prevalence which would allow inferences about impact of supplying opportunistic screening or lack of it. High income countries all have some level of testing. Further research work may provide methods to use seroprevalence data to estimate incidence and prevalence.

Work is on-going on dynamic transmission models but none has so far been shown to model chlamydia transmission effectively. Accurate metrics of changes in prevalence would enable validation of these models and evaluation of the impact of screening.

Recommendations for local authorities

1. Local commissioners should consider targeting of particular at risk populations.

Rationale

It was noted that the data presented suggested that testing coverage within quintile 1 is lower than for the other quintiles and that increased targeting of testing within quintile 1 might be useful.

Recommendations for externals

2. BASHH could consider reviewing the statement and recommendation on chlamydia management when testing occurs within 2 weeks of last intercourse.

Rationale

There is no empirical evidence for a two-week window period for the detection of chlamydia. Evidence indicates that about 25% of women and one-third of men with incident detectable infection only remain positive for on average 3-7 days respectively (Price et al, 2012b and Lewis et al, 2017). This conflicts with the interpretation that some health care professionals may have of the two-week window period in the BASHH chlamydia guidelines i.e. it is better to wait 2 weeks after sexual intercourse to reliably detect infection. Waiting 2 weeks before testing would reduce the efficacy of partner notification in identifying chlamydia-positive partners. BASHH should consider reviewing this statement and recommendation.

3. The BASHH bacterial specialist interest group could be asked to review the evidence for reflex testing of all chlamydia positives for gonorrhoea and *M. genitalium* or use of first line doxycycline, with the NCSP guidelines then updated accordingly.

Rationale

Antimicrobial resistance in gonorrhoea with azithromycin 1g is mentioned in the evidence pack but not *Mycoplasma genitalium* which is an emerging pathogen (see JID special issue: sti.bmj.com/content/93/Suppl_2). Given that *M. genitalium* is detected in 3-9% of women with chlamydia (bmjopen.bmj.com/content/4/2/e003947) and azithromycin 1g is associated with the emergence of macrolide resistance (sti.bmj.com/content/early/2017/07/17/sextrans-2017-053164), it could be argued that treatment of STIs with azithromycin 1g may have unknowingly resulted in increasing macrolide resistance in the *M. genitalium* population (sti.bmj.com/content/93/2/85).

Recommendations for future research

- 1 The impact of harm from chlamydia infections, potentially also chlamydia testing if positive, remain unclear, particularly on mental health impacts and on relationships. There appears to be very little research in this area and more should be encouraged.
- 2 Social media has changed sexual behaviour and may mean that the youngest women are no longer the most at risk. The panel recommends research focussing on assessing risk across the life course, and on the impact of social media/dating apps on this risk.
- 3 Proteomic and metabolomics research, working back from TFI to determine how much is related to PID and then how much of the PID can be related to chlamydia, should be encouraged.
- 4 Research is required to ascertain if risk prediction models can be improved.
- 5 It is unclear if changes in the vaginal microbiome with age influence susceptibility to chlamydia infection. Small initial studies have indicated that the vaginal microbiome can change after infection with chlamydia and gonorrhoea but the causality and significance are unclear. Further research would be useful to a comprehensive understanding of the risk of chlamydia transmission.
- 6 Evidence from serology suggests that repeat infections lead to higher antibody levels. Single point in time serology studies can be confounded by passive infections which would clear naturally and may not elicit an antibody response, hence data on antibody levels over time may be more informative. Whether women with higher antibody levels may be at higher risk of infertility should be investigated.

References and other relevant evidence highlighted by the review panel

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