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Screening for gonorrhoea using samples collected through the English National Chlamydia Screening Programme and risk of false positives: a national survey of Local Authorities

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3 **Screening for gonorrhoea using samples collected through the English National Chlamydia**
4 **Screening Programme and risk of false positives: a national survey of Local Authorities**
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Abstract

Objectives: To investigate use of dual tests for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* on samples collected through the National Chlamydia Screening Programme (NCSP) in England.

Design and setting: During May-July 2013, we delivered an online survey to commissioners of sexual health services in the 152 upper-tier English Local Authorities (LAs) who were responsible for commissioning chlamydia screening in people aged 15-24 years.

Main outcome measures: (1) The proportion of English LAs using dual tests on samples collected by the NCSP; (2) The estimated number of gonorrhoea tests and false positives from samples collected by the NCSP, calculated using national surveillance data on the number of chlamydia tests performed, assuming the gonorrhoea prevalence to range between 0.1-1.0%, and test sensitivity and specificity of 99.5%.

Results: 64% (98/152) of LAs responded to this national survey; over half (53% (52/98)) reported currently using dual tests in community settings. There was no significant difference between LAs using and not using dual tests by chlamydia positivity, chlamydia diagnosis rate, or population screening coverage. Although positive gonorrhoea results were confirmed with supplementary tests in 93% (38/41) of LAs, this occurred after patients were notified about the initial positive result in 63% (26/41). Approximately 450 to 4,500 confirmed gonorrhoea diagnoses and 2,300 false positive screens might occur through use of dual tests on NCSP samples each year. Under reasonable assumptions, the positive predictive value of the screening test is 17%-67%.

Conclusions: Over half of English LAs already commission dual tests for samples collected by the NCSP. Gonorrhoea screening has been introduced alongside chlamydia screening in many low prevalence settings without a national evidence review or change of policy. We question the public health benefit here, and suggest that robust testing algorithms and clinical management pathways, together with rigorous evaluation, be implemented wherever dual tests are deployed.

Article summary

Strengths and limitations of this study

- The English National Chlamydia Screening Programme (NCSP) aims to diagnose and control chlamydia in all sexually active people aged 15-24, but no such community-based screening programme exists for gonorrhoea.
- We undertook a national survey of Local Authority (LA) commissioners of chlamydia screening to investigate use of dual tests, which simultaneously test for chlamydia and gonorrhoea, in community-based settings (excluding special sexual health services).
- Response to the LA survey was high and similar across the geographical regions in England. There was no evidence to suggest participation was associated with IMD or NCSP area-level characteristics.
- The study is limited by the self-reported nature of the survey responses, which might be subject to reporting bias. Our data might underestimate the proportion of LAs using dual tests because commissioners might not always be aware that dual tests are being used for NCSP samples. Most survey questions had item non-response of around 14%.
- In over half of LAs in England, dual tests are already being used on samples collected by the NCSP, and in many areas gonorrhoea test results are returned to patients prior to the result being confirmed.

Introduction

The English National Chlamydia Screening Programme (NCSP) offers sexually active, asymptomatic, women and men, aged 15-24 years old, opportunistic testing to diagnose and control *Chlamydia trachomatis* (chlamydia) infection in England.[1] In 2012, over 1.2 million screening tests were performed for young people in community-based sexual health clinics in England (i.e. outside of specialist sexual health clinics, called genitourinary medicine (GUM) clinics in the UK), with over 80,000 chlamydia infections diagnosed.[4] Screening is offered by a variety of providers, including contraception, sexual health and termination of pregnancy services, pharmacies and primary care, with commissioning undertaken through Local Authorities (LAs) since 2012.[5,6]

The test of choice for chlamydia detection is the nucleic acid amplification test (NAAT), and a range of assays, with extremely high sensitivity and specificity, are available.[7] Many NAATs allow dual detection of chlamydia and *Neisseria gonorrhoeae* (gonorrhoea) using a single specimen and the same assay,[7] and it has become inexpensive and straightforward to simultaneously test for both infections.[8] From a simplistic viewpoint, this technological development may appear advantageous to public health.[8–10] However, current UK guidance on testing for gonorrhoea found only sparse evidence for selective community screening in the UK, and no evidence to support widespread unselected screening in community-based settings.[3] Although chlamydia and gonorrhoea cause similar disease and symptoms, there are important differences in the population distribution and the microbiology of testing for these infections that need consideration.[2] Unlike chlamydia, the prevalence of gonorrhoea is very low in the general population (<0.1% and therefore approximately tenfold lower),[11] and concentrated in specific groups (including those attending specialist GUM clinics).[12] Although the prevalence of gonorrhoea in patients attending community-based services, such as NSCP settings, might be higher than in the general population (ranging from 0.3% to 1.7% outside London,[9,13–15] and up to 4.1% in South London),[16] lack of proper confirmatory strategies means that the available studies might overestimate prevalence.[20] Together, the low prevalence of gonorrhoea and the potential for cross-reaction with non-gonococcal *Neisseria* species mean that high rates of false positive results might occur if gonorrhoea screening is undertaken on NCSP samples.[2]

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3 In 2007, 29% of hospital-based microbiology laboratories in England and Wales were already
4 using dual tests to diagnose chlamydia and gonorrhoea.[17] A recent update of this survey
5 suggests this proportion has increased to 85% (Toby et al, unpublished information).
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7 However, it is not known whether this has led to widespread gonorrhoea screening being
8 undertaken on samples collected by the NCSP. In this study, we (1) undertook a survey of LA
9 commissioners to understand the extent to which dual tests are being deployed for samples
10 collected by the NCSP, (2) collected data about the clinical care pathways used when
11 gonorrhoea is detected, and (3) linked the survey data with national surveillance data to
12 estimate the likely number of gonorrhoea diagnoses and false positive gonorrhoea results
13 occurring in England through the use of dual tests on samples collected by the NCSP.
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22 **Methods**

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24 **Survey methodology:** During May to July 2013, we delivered an online questionnaire (using
25 the Public Health England (PHE) web-based survey tool, 'Select Survey') to commissioners of
26 sexual health services who were responsible for commissioning chlamydia testing in people
27 aged 15-24 years in the 152 upper tier LAs in England. Such web-based surveys are easy to
28 use and maximise response rates.[18] The questionnaire used closed questions and
29 dropdown menus to ask about: use of dual tests outside of GUM settings (i.e. community-
30 based sexual health screening); service setting and sample types; use of confirmatory
31 testing where the screening test was reactive for gonorrhoea; patient information; and
32 consent processes. Since not all commissioners were likely to understand technical
33 molecular definitions used in relation to confirmatory testing, the questionnaire used the
34 following pragmatic definition for a confirmatory test: "a second test used to confirm the
35 diagnosis of gonorrhoea where the initial screening test is positive for gonorrhoea". The
36 questionnaire was piloted to test usability, understanding, clarity, and question flow; it
37 included 29 questions and took approximately 20 minutes to complete. Respondents were
38 recruited by email using a national list of LA sexual health commissioners, which covered the
39 whole of England, and the survey was advertised in the quarterly NCSP newsletter.
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54 **Statistical analysis:** Survey data were extracted to Microsoft Excel and a descriptive analysis
55 was undertaken. The denominator for descriptive analyses was the number of LAs, which
56 varied by item non-response. Using Stata (version 12.1), independent samples t-tests
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3 compared area-level characteristics between LA responders and non-responders and
4 between LAs using and not using dual tests. Chlamydia diagnosis rates (per 100,000
5 population) and chlamydia testing coverage included diagnoses and testing in community-
6 based and GUM settings collected through the Chlamydia Test Activity Dataset (CTAD) and
7 the GUM Clinic Activity Dataset (GUMCAD), and gonorrhoea diagnosis rates (per 100,000
8 population) included diagnoses made in GUM clinics collected through GUMCAD. [4,19]
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15 **Estimating the number of gonorrhoea false positives and confirmed positives:** For each LA
16 using dual tests, PHE Chlamydia Testing Activity Dataset (CTAD)[4] data on the number of
17 chlamydia tests performed outside of GUM clinics in 2012 was used as a proxy for the total
18 number of gonorrhoea tests performed through use of dual tests on samples collected by
19 the NCSP (excluding screening in GUM). Using this figure, and assuming the prevalence of
20 gonorrhoea in most community-based settings to range between 0.1% to 1.0%,[11,20] we
21 estimated the absolute number of unconfirmed reactive tests and the number of confirmed
22 diagnoses, using published specificity estimates for a commercial dual test assay.[21]
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31 **Ethics:** This work was undertaken with data collected and held within the requirements of
32 the data protection act and in accordance with data sharing best practice and PHE
33 guidelines.[22] The study did not use individual patient data and did not require or seek
34 ethical approval.
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39 Results

40 **LA survey response and use of dual tests**

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42 Overall, 64% (98/152) of LAs responded to the survey (Table 1). The proportion of LAs
43 responding was at least 50% in all fifteen PHE centre areas, and the area-level
44 characteristics of responding and non-responding LAs were statistically similar. Comparison
45 between responding and non-responding LAs included area-level Index of Multiple
46 Deprivation (IMD)[23] (mean IMD score 22.9 versus 23.1; $p=0.89$), mean chlamydia
47 positivity among those testing and aged 15 to 24 years (7.9% versus 7.8%; $p=0.63$), mean
48 chlamydia diagnosis rate (2152/100,000 versus 1870/100,000; $p=0.06$), mean chlamydia
49 testing coverage among those aged 15 to 24 years (27% versus 24%; $p=0.06$), and mean
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3 GUM gonorrhoea diagnosis rate estimated from GUM diagnoses (43/100,000 versus
4 39/100,000; $p=0.68$) for each LA area.
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8 Over half (53% (52/98)) of responding LAs reported commissioning use of dual tests for
9 samples collected by the NCSP, 45% (44/98) had never commissioned dual tests, and 2%
10 (2/98) had previously commissioned dual tests or did not know (Table 1). Most LAs (82%
11 (37/45)) reported using dual tests in at least five different non-GUM settings, including
12 Contraception and Sexual Health and Sexual and Reproductive Health services (98% (44/45))
13 and primary care (91% (41/45)) settings, as well as in termination of pregnancy services
14 (87% (39/45)) and through remote sample collection by post or Internet (80% (36/45)).
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18 At an area level, there was no significant difference in IMD, chlamydia positivity among
19 those testing and aged 15 to 24 years, chlamydia diagnosis rate, or mean chlamydia testing
20 coverage among those aged 15 to 24 years, when comparing LAs using and not using dual
21 tests (Table 2). Mean gonorrhoea diagnosis rates based on diagnoses made in GUM clinics
22 were higher (53/100,000 versus 32/100,000; $p=0.03$) in LAs using dual tests compared to
23 those not. Nevertheless, most LAs had low gonorrhoea diagnosis rates that were below 50
24 per 100,000 (Figure 1). We noted three LAs where dual tests were not being used, all in
25 London, where GUM gonorrhoea diagnosis rates were above 100 per 100,000, placing these
26 areas inside the top ten percent nationally.[24]
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39 40 ***Clinical care pathway for gonorrhoea***

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42 Overall, 36% (15/42) of LAs using dual tests reported providing gonorrhoea-specific patient
43 information materials to patients, 45% (19/42) provided no gonorrhoea-specific information
44 materials, and 19% (8/42) did not know. Of those without gonorrhoea-specific patient
45 information materials, 84% (16/19) reported that gonorrhoea was discussed within their
46 NCSP patient information leaflet, while only 5% (1/19) of these LAs reported providing no
47 gonorrhoea information (11% (2/19) did not know). Informed consent for testing of
48 gonorrhoea was reported as assumed (on the basis that information was provided and the
49 testing kit was returned) in 71% (25/35) of LAs, and taken in writing in 14% (5/35). 3% (1/35)
50 of LAs did not obtain consent.
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3 Although confirmatory testing (defined in the survey as a second test confirming the
4 diagnosis of gonorrhoea) was reported as being used in 93% (38/41) of LAs, in practice,
5 confirmation only occurred after referral to specialist sexual health services in most areas.
6
7 63% (26/41) of LAs reported referring patients to sexual health services on the basis of a
8 reactive screening test, 17% (7/41) referred after confirmatory testing, 15% (6/41) did not
9 refer patients to another service, and 10% (4/41) did not know.

Estimating the number of false positive and confirmed positive gonorrhoea tests

10 We used the LA survey data, national surveillance data,[4] and published data on
11 gonorrhoea prevalence in community-based settings[11,20] to estimate the number of
12 confirmed gonorrhoea diagnoses and false positives that might be identified each year
13 through the use of dual tests on samples collected by the NCSP (Table 1). Using CTAD
14 surveillance data from only the 52 LAs that reported using dual tests, we estimated that at
15 least 456,085 screening tests for gonorrhoea might be undertaken per year in non-GUM
16 settings in England, which would lead to around 456 diagnoses of confirmed gonorrhoea per
17 year if the overall prevalence is 0.1%. In this scenario, and assuming test sensitivity and
18 specificity of 99.5%, approximately 2,278 false positive reactive screens would occur and the
19 positive predictive value (PPV) of the screening test would be 17%. If the true prevalence of
20 gonorrhoea was 1%, the number of false positive tests occurring would be 2,258, the
21 number of confirmed diagnoses would be 4,561, and the PPV would be 67%.

Discussion

Statement of principal findings

22 This is the first national study to investigate the use of dual tests for chlamydia and
23 gonorrhoea on samples collected by the NCSP. Although the NCSP does not recommend
24 simultaneous screening for chlamydia and gonorrhoea, our data suggest that over half of
25 LAs in England already commission dual tests for NCSP samples. Thus, in many areas across
26 England, screening for asymptomatic gonococcal infection has been introduced in low
27 prevalence settings without a national evidence review or any change in national screening
28 policy. Furthermore, we found evidence that reactive screening test results are being
29 returned to patients prior to gonorrhoea infection being confirmed. Given that many
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3 reactive screening tests for gonorrhoea will be false positives, this finding raises
4 considerable concerns. We question the public health benefit of introducing the use of dual
5 tests for NCSP samples without careful consideration of the risks. Commissioners and
6 providers may need to undertake appropriately powerful pilot studies to decide whether
7 dual tests are appropriate in their local areas. If dual tests are used, confirmatory tests
8 should be performed before patients are informed about gonorrhoea diagnoses.
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14 ***Strengths and weaknesses of the study***

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16 Response to the LA survey was high and similar across the geographical regions in England.
17 There was no evidence to suggest participation bias associated with IMD or NCSP area-level
18 characteristics. It therefore seems likely that the responding LAs are representative of
19 English LAs in their use of dual tests and that the data are generalisable. However, the study
20 is limited by the self-reported nature of the survey responses, which might be subject to
21 reporting bias. Furthermore, most survey questions had an item non-response of around
22 14%, which may reflect respondents' lack of understanding, lack of knowledge about service
23 specifications or reluctance to answer questions that might reveal sub-optimal practice. Our
24 data might underestimate the proportion of LAs using dual tests because commissioners
25 might not always be aware that dual tests are being used for NCSP samples.
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36 Although LAs using dual tests were more likely to be areas with higher rates of gonorrhoea
37 diagnosis made in GUM clinics, which might indicate evidence-based policy making, this
38 finding might also be explained by increased diagnosis of gonorrhoea in these areas arising
39 from the introduction of dual tests.
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45 ***Meaning of the study: possible explanations and implications for clinicians and*** 46 ***policymakers***

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48 This study has significant implications for commissioners of sexual health services in LAs and
49 for clinical services providing chlamydia screening. While screening for gonorrhoea in
50 community-based settings might be appropriate in some areas where the prevalence is
51 high, we show that dual tests are being used in areas where the prevalence and PPV are
52 likely to be extremely low. Conversely, we also show that dual tests are not being used in
53 some high prevalence areas that might benefit from targeted gonorrhoea screening.
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5 The increased availability, technical ease, and declining cost of dual and, in due course,
6 multiplex molecular testing platforms for STIs make them attractive tools for laboratories
7 that process high specimen volumes. The emergence of antimicrobial resistant (AMR)
8 gonorrhoea is a major threat to global health and these molecular tests offer considerable
9 public health benefits by facilitating detection and control of gonorrhoea.[25] However, for
10 commissioners, policy makers and providers, our study draws attention to the risk of false
11 positive test results and the need to minimise potential distress caused to patients. The
12 harms of misdiagnoses include the direct emotional harm to individual patients arising from
13 incorrect and stigmatising diagnoses and unnecessary partner notification,[25,26] as well as
14 the possibility of physical harm in the rare event that the unnecessary treatment causes side
15 effects. Indirect harm may occur at a population level due to avoidable antibiotic usage
16 (with implications for AMR) and clinical expense. Before any STI screening is introduced, the
17 evidence on potential harms as well as benefits should be rigorously assessed and, wherever
18 screening is introduced, robust testing algorithms and clinical management pathways
19 implemented. Essential pathways include those for obtaining informed consent for testing
20 of gonorrhoea and for performing confirmatory testing (using a supplementary NAAT with a
21 different nucleic acid target) before returning results to patients or initiating management.
22 These steps are likely to improve patient autonomy and safety, and avoid misdiagnosis,
23 unnecessary clinical management, and their associated costs.
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41 ***Unanswered questions and future research***

42 This paper highlights a broader issue that decisions about screening may be driven by the
43 availability of diagnostic testing platforms rather than the evidence base.[25,27] A World
44 Health Organization synthesis of emerging screening criteria, based on the Wilson and
45 Yungner criteria, highlights the importance of identifying and responding to a recognised
46 health need, defining a target population, scientific evidence of screening effectiveness, and
47 ensuring the overall benefits of screening outweigh the potential harms.[28] Molecular-
48 based testing brings considerable public health opportunities through rapid and highly
49 sensitive detection of one or more pathogens simultaneously, often using non-invasive
50 samples, with benefits to individual patients diagnosed with treatable infections, as well as
51 enhancing surveillance and prevention efforts.[27,29] For example, a multiplex point of care
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3 assay has already been developed to detect nucleic acid targets for ten different
4 pathogens.[30] The US Food and Drug Administration cleared multiplex panels for
5 respiratory infections in 2011, indicating a new era for the diagnosis of respiratory
6 infection.[31] However, there is an onus on healthcare commissioners and providers to
7 understand the tests being ordered for individual patients and consider the implications for
8 their deployment at a population level. The risk is that the availability and low costs of
9 testing technologies may drive local policies and lead to inconsistent screening practices
10 that lack an evidence base.
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Contributors

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22 NF contributed to the planning and design of this Article, wrote the first and revised subsequent
23 drafts, designed and piloted the survey, and undertook statistical analyses. IK designed and piloted
24 the survey, contributed to statistical analyses, interpreted data and reviewed successive drafts of the
25 Article. KF contributed to the planning and design of this Article, designed and piloted the survey,
26 interpreted data, and reviewed successive drafts of the Article. SD did statistical analyses and
27 reviewed successive drafts of the Article. KT did statistical analyses and reviewed successive drafts of
28 the Article. CI contributed to the planning and design of this Article, interpreted data, and reviewed
29 successive drafts of the Article. GH led the study team, contributed to the planning and design of this
30 Article, interpreted data, and reviewed successive drafts of the Article. All authors approved the final
31 version of the Article.
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44

Competing interests

45
46 All authors have completed the ICMJE uniform disclosure form at
47 http://www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the
48 submitted work; no financial relationships with any organisations that might have an interest in the
49 submitted work in the previous three years, no other relationships or activities that could appear to
50 have influenced the submitted work.
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Transparency Statement

The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Data sharing

No additional data are available.

Table 1. Local authority (LA) survey response and reported use of dual tests on samples collected by the National Chlamydia (CT) Screening Programme (NCSP) for people aged 15-24 years, with estimated numbers of gonorrhoea (NG) tests performed, confirmed diagnoses, and unconfirmed reactive tests for 2012

PHE Region	Number of LAs	LAs (%) survey response	LAs (%) using dual tests ¹	Non-GUM CT tests ²	If community-based NG prevalence is 0.1%		If community-based NG prevalence is 1.0%	
					Estimated NG diagnoses ³	Estimated unconfirmed reactive NG tests (PPV=17%) ⁴	Estimated NG diagnoses ³	Estimated unconfirmed reactive NG tests (PPV=67%) ⁴
ALL	152	98 (64)	52 (53)	456,085	456	2,278	4,561	2,258
London	33	21 (64)	14 (67)	98250	98	491	983	486
Midlands & East of England	35	26 (74)	6 (23)	67362	67	336	674	333
North of England	50	34 (68)	21 (62)	194321	194	971	1,943	962
South of England	34	17 (50)	11 (65)	96152	96	480	962	476

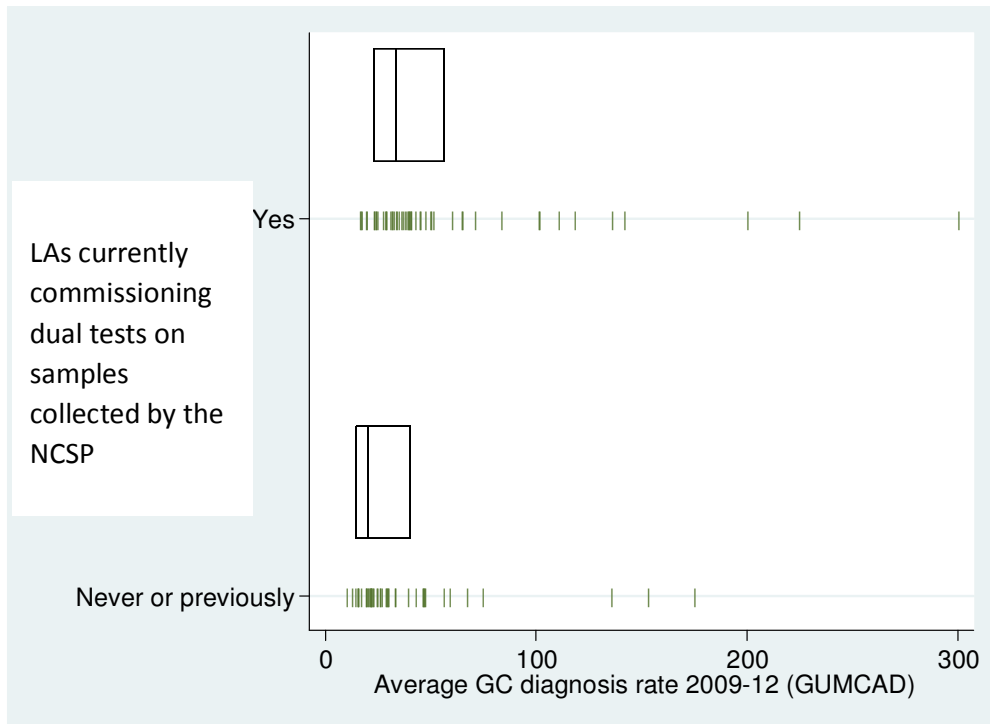
1. Number and percentage of LAs using dual tests out of those responding to the survey
2. Number of non-GUM CT tests performed in all LAs using dual tests as a proxy for the number of gonorrhoea screening tests performed, using data extracted from the Chlamydia Testing Activity Dataset (CTAD) which comprises all chlamydia testing carried out in England
3. Estimated number of confirmed NG diagnoses arising from use of dual tests on samples collected by the NCSP (non-GUM) if NG prevalence is 0.1% or 1.0%
4. Estimated number of reactive but unconfirmed NG tests arising from use of dual tests on samples collected by the NCSP (non-GUM) if NG prevalence is 0.1% or 1.0% and the sensitivity and specificity of test are 99.5%

Table 2. Comparison of area-level characteristics between LAs reporting current commissioning of dual tests and those not¹

	Number of LAs	Mean chlamydia diagnosis rate / 100,000 ²	Mean chlamydia testing coverage ³	Mean gonorrhoea diagnosis rate / 100,000 ⁴
Using dual tests	52	2254.8	28.6%	52.7
Not using dual tests	46	2063.2	26.2%	32.4
<i>p-value difference</i>	-	0.31	0.24	0.03

1. No significant difference was found by NCSP chlamydia positivity rate ($p=0.93$), LA IMD ($p=0.88$), or the proportion of NCSP services provided by GUM or GP, but the proportion of services provided by CSHS was higher in those LAs using dual tests (19.4% vs 8.6%; ($p<0.01$)).
2. Chlamydia diagnosis rates (per 100,000 population) include diagnoses made in community-based and GUM settings collected through the Chlamydia Test Activity Dataset (CTAD) and the GUM Clinic Activity Dataset (GUMCAD)
3. Chlamydia testing coverage includes tests done in community-based and GUM settings collected through CTAD and the GUM Clinic Activity Dataset (GUMCAD)
4. Gonorrhoea diagnoses (per 100,000 population) include diagnoses made in GUM clinics collected through GUMCAD.

Figure 1 – Mean gonorrhoea (NG) diagnoses per 100,000 population (made in GUM clinics) between 2009-2012 by whether Local Authorities (LA) use dual tests on samples collected by the National Chlamydia Screening Programme



1. Each dash represents the four year average (2009-2012) for gonorrhoea diagnoses (per 100,000 population) for the 98 LAs responding to the survey, including diagnoses made in GUM clinics collected through GUMCAD
2. Boxes shows the median and lower and upper quartiles for four year average gonorrhoea diagnoses

References

- 1 National chlamydia screening programme - NCSP home.
<http://www.chlamydia-screening.nhs.uk/> (accessed 25 Feb2011).
- 2 Ison C. GC NAATs: is the time right? *Sex Transm Infect* 2006;**82**:515.
doi:10.1136/sti.2006.022731
- 3 Health Protection Agency and BASHH. Guidance for gonorrhoea testing in England and Wales. 2010.http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1267550166455
- 4 HPA - CTAD: Chlamydia Testing Activity Dataset.
<http://www.hpa.org.uk/sexualhealth/ctad> (accessed 30 May2014).
- 5 DH and cross Government. A Framework for Sexual Health Improvement in England. 2013.https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/142592/9287-2900714-TSO-SexualHealthPolicyNW_ACCESSIBLE.pdf
- 6 Health and Social Care Act 2012, c.7.
<http://www.legislation.gov.uk/ukpga/2012/7/contents/enacted> (accessed 30 May2014).
- 7 British Association for Sexual Health and HIV. Chlamydia trachomatis UK Testing Guidelines. 2010.<http://www.bashh.org/documents/3352.pdf> (accessed 21 Feb2014).
- 8 Bignell, C J. *Sex Transm Infect* 2007;**83**:179–80.
- 9 Lavelle SJ, Jones KE, Mallinson H, *et al*. Finding, confirming, and managing gonorrhoea in a population screened for chlamydia using the Gen-Probe Aptima Combo2 assay. *Sex Transm Infect* 2006;**82**:221–4. doi:10.1136/sti.2005.017616
- 10 Lavelle SJ, Mallinson H, Henning SJ, *et al*. Impact on gonorrhoea case reports through concomitant/dual testing in a chlamydia screening population in Liverpool. *Sex Transm Infect* 2007;**83**:593–4. doi:10.1136/sti.2007.027870
- 11 Sonnenberg P, Clifton S, Beddows S, *et al*. Prevalence, risk factors, and uptake of interventions for sexually transmitted infections in Britain: findings from the National Surveys of Sexual Attitudes and Lifestyles (Natsal). *The Lancet* 2013;**382**:1795–806. doi:10.1016/S0140-6736(13)61947-9
- 12 Public Health England. Health Protection Report. 2013.<http://www.hpa.org.uk/hpr/archives/2013/hpr2313.pdf> (accessed 6 Feb2014).
- 13 Skidmore S, Copley S, Cordwell D, *et al*. Positive nucleic acid amplification tests for *Neisseria gonorrhoeae* in young people tested as part of the National Chlamydia Screening Programme. *Int J STD AIDS* 2011;**22**:398–9. doi:10.1258/ijsa.2011.010378
- 14 Fowler T, Edeghere O, Inglis N, *et al*. Estimating the positive predictive value of opportunistic population testing for gonorrhoea as part of the English Chlamydia Screening Programme. *Int J STD AIDS* Published Online First: 20 March 2013. doi:10.1177/0956462412472443

- 1
2
3 15 Downing J, Cook PA, Madden HCE, *et al.* Management of cases testing positive for
4 gonococcal infection in a community-based chlamydia screening programme. *Sex*
5 *Transm Infect* 2010;**86**:474–7. doi:10.1136/sti.2010.043240
6
7
8 16 Rao GG, Bacon L, Evans J, *et al.* Prevalence of *Neisseria gonorrhoeae* infection in young
9 subjects attending community clinics in South London. *Sex Transm Infect* 2008;**84**:117–
10 21. doi:10.1136/sti.2007.026914
11
12 17 Benzie A, Alexander S, Gill N, *et al.* Gonococcal NAATs: what is the current state of play
13 in England and Wales? *Int J STD AIDS* 2010;**21**:246–8. doi:10.1258/ijsa.2010.010004
14
15 18 Dayan Y, Paine CS, Johnson AJ. Responding to sensitive questions in surveys: A
16 comparison of results from Online panels, face to face and self-completion interviews.
17 2009.[http://www.ipsos-](http://www.ipsos-mori.com/Assets/Docs/Publications/Ops_RMC_Responding_Sensitive_Questions_08_03_10.pdf)
18 [mori.com/Assets/Docs/Publications/Ops_RMC_Responding_Sensitive_Questions_08_03](http://www.ipsos-mori.com/Assets/Docs/Publications/Ops_RMC_Responding_Sensitive_Questions_08_03_10.pdf)
19 [_10.pdf](http://www.ipsos-mori.com/Assets/Docs/Publications/Ops_RMC_Responding_Sensitive_Questions_08_03_10.pdf) (accessed 21 Feb2014).
20
21
22 19 Public Health England. Genitourinary Medicine Clinic Activity Dataset (GUMCADv2).
23 <http://www.hpa.org.uk/gumcad> (accessed 30 May2014).
24
25 20 Fifer H, Ison CA. Nucleic acid amplification tests for the diagnosis of *Neisseria*
26 *gonorrhoeae* in low-prevalence settings: a review of the evidence. *Sex Transm Infect*
27 2014.
28
29 21 APTIMA COMBO 2, APTIMA CT, APTIMA GC, Chlamydia Trachomatis, *Neisseria*
30 *Gonorrhoeae*, TIGRIS DTS system, CT/GC, GC Assay, CT Assay. [http://www.gen-](http://www.gen-probe.com/products-services/aptima-combo)
31 [probe.com/products-services/aptima-combo](http://www.gen-probe.com/products-services/aptima-combo) (accessed 30 May2014).
32
33 22 Hughes, Gwenda, Evans BG, Ncube, F, *et al.* PHE HIV and STI Data Sharing Policy version
34 4. 2014.http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1247816526850
35 (accessed 27 Jun2014).
36
37 23 Payne RA, Abel GA. UK indices of multiple deprivation - a way to make comparisons
38 across constituent countries easier. *Health Stat Q Off Natl Stat* 2012;**53**:22–37.
39
40 24 HPA - STI Annual Data Tables.
41 http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1203348026613
42 (accessed 28 Mar2010).
43
44 25 Low N, Unemo M, Skov Jensen J, *et al.* Molecular Diagnostics for Gonorrhoea:
45 Implications for Antimicrobial Resistance and the Threat of Untreatable Gonorrhoea.
46 *PLoS Med* 2014;**11**. doi:10.1371/journal.pmed.1001598
47
48 26 Katz AR, Effler PV, Ohye RG, *et al.* False-positive gonorrhea test results with a nucleic
49 acid amplification test: the impact of low prevalence on positive predictive value. *Clin*
50 *Infect Dis Off Publ Infect Dis Soc Am* 2004;**38**:814–9. doi:10.1086/381895
51
52 27 Klausner JD. The NAAT Is Out of the Bag. *Clin Infect Dis* 2004;**38**:820–1.
53 doi:10.1086/381897
54
55
56
57
58
59
60

- 1
2
3 28 Andermann A, Blancquaert I, Beauchamp S, *et al.* Revisiting Wilson and Jungner in the
4 genomic age: a review of screening criteria over the past 40 years. *Bull World Health*
5 *Organ* 2008;**86**.<http://www.who.int/bulletin/volumes/86/4/07-050112/en/>
6
7
8 29 Tucker JD, Bien CH, Peeling RW. Point-of-care testing for sexually transmitted infections:
9 recent advances and implications for disease control. *Curr Opin Infect Dis* 2013;**26**:73–9.
10 doi:10.1097/QCO.0b013e32835c21b0
11
12 30 Kriesel J, Bhatia A, Vaughn M, *et al.* P3-S5.05 Rapid point of care testing for ten sexually
13 transmitted diseases. *Sex Transm Infect* 2011;**87**:A294–A295. doi:10.1136/sextrans-
14 2011-050108.472
15
16 31 Russek-Cohen E, Feldblyum T, Whitaker KB, *et al.* FDA Perspectives on Diagnostic Device
17 Clinical Studies for Respiratory Infections. *Clin Infect Dis* 2011;**52**:S305–S311.
18 doi:10.1093/cid/cir056
19
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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract Yes – p.1-2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found Yes
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Yes – p.4
Objectives	3	State specific objectives, including any prespecified hypotheses Yes – p.4-5
Methods		
Study design	4	Present key elements of study design early in the paper Yes – p.5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Yes – p.5
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants Yes – p.5-6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Yes – where applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Yes – see methods and results sections
Bias	9	Describe any efforts to address potential sources of bias N/A
Study size	10	Explain how the study size was arrived at Yes
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Yes – p.5-6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding

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2 (b) Describe any methods used to examine subgroups and interactions

3 N/A

4 (c) Explain how missing data were addressed

5 Yes – p.5

6 (d) *Cohort study*—If applicable, explain how loss to follow-up was addressed

7 *Case-control study*—If applicable, explain how matching of cases and controls was
8 addressed

9 *Cross-sectional study*—If applicable, describe analytical methods taking account of
10 sampling strategy

11 N/A

12 (e) Describe any sensitivity analyses

13 Yes – p.6

14 Continued on next page

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Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed N/A (b) Give reasons for non-participation at each stage Yes – p.6 (c) Consider use of a flow diagram Not required
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Yes – area level characteristics of LAs described (b) Indicate number of participants with missing data for each variable of interest Yes – p.6-8 (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures Yes
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included N/A (b) Report category boundaries when continuous variables were categorized N/A (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses N/A – all data are shown
Discussion		
Key results	18	Summarise key results with reference to study objectives Yes – p. 8-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Yes – p.9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Yes – p.9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results Yes – p.8-11
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

Yes – p.11-12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Screening for gonorrhoea using samples collected through the English National Chlamydia Screening Programme and risk of false positives: a national survey of Local Authorities

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3 **Screening for gonorrhoea using samples collected through the English National Chlamydia**
4 **Screening Programme and risk of false positives: a national survey of Local Authorities**
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Abstract

Objectives: To investigate use of dual tests for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* on samples collected through the National Chlamydia Screening Programme (NCSP) in England.

Design and setting: During May-July 2013, we delivered an online survey to commissioners of sexual health services in the 152 upper-tier English Local Authorities (LAs) who were responsible for commissioning chlamydia screening in people aged 15-24 years.

Main outcome measures: (1) The proportion of English LAs using dual tests on samples collected by the NCSP; (2) The estimated number of gonorrhoea tests and false positives from samples collected by the NCSP, calculated using national surveillance data on the number of chlamydia tests performed, assuming the gonorrhoea prevalence to range between 0.1-1.0%, and test sensitivity and specificity of 99.5%.

Results: 64% (98/152) of LAs responded to this national survey; over half (53% (52/98)) reported currently using dual tests in community settings. There was no significant difference between LAs using and not using dual tests by chlamydia positivity, chlamydia diagnosis rate, or population screening coverage. Although positive gonorrhoea results were confirmed with supplementary tests in 93% (38/41) of LAs, this occurred after patients were notified about the initial positive result in 63% (26/41). Approximately 450 to 4,500 confirmed gonorrhoea diagnoses and 2,300 false positive screens might occur through use of dual tests on NCSP samples each year. Under reasonable assumptions, the positive predictive value of the screening test is 17%-67%.

Conclusions: Over half of English LAs already commission dual tests for samples collected by the NCSP. Gonorrhoea screening has been introduced alongside chlamydia screening in many low prevalence settings without a national evidence review or change of policy. We question the public health benefit here, and suggest that robust testing algorithms and clinical management pathways, together with rigorous evaluation, be implemented wherever dual tests are deployed.

Article summary

Strengths and limitations of this study

- The English National Chlamydia Screening Programme (NCSP) aims to diagnose and control chlamydia in all sexually active people aged 15-24, but no such community-based screening programme exists for gonorrhoea.
- We undertook a national survey of Local Authority (LA) commissioners of chlamydia screening to investigate use of dual tests, which simultaneously test for chlamydia and gonorrhoea, in community-based settings (excluding special sexual health services).
- Response to the LA survey was high and similar across the geographical regions in England. There was no evidence to suggest participation was associated with Index of Multiple Deprivation or NCSP area-level characteristics.
- The study is limited by the self-reported nature of the survey responses, which might be subject to reporting bias. Our data might underestimate the proportion of LAs using dual tests because commissioners might not always be aware that dual tests are being used for NCSP samples. Most survey questions had item non-response of around 14%.
- In over half of LAs in England, dual tests are already being used on samples collected by the NCSP, and in many areas gonorrhoea test results are returned to patients prior to the result being confirmed.

Introduction

The English National Chlamydia Screening Programme (NCSP) offers sexually active, asymptomatic, women and men, aged 15-24 years old, opportunistic testing to diagnose and control *Chlamydia trachomatis* (chlamydia) infection in England.[1] In 2012, over 1.2 million screening tests were performed for young people in community-based sexual health clinics in England (i.e. outside of specialist sexual health clinics, called genitourinary medicine (GUM) clinics in the UK), with over 80,000 chlamydia infections diagnosed.[2] Screening is offered by a variety of providers, including contraception, sexual health and termination of pregnancy services, pharmacies and primary care. Since 2013, commissioning arrangements have been undertaken through Local Authorities (LAs), which are regional local government administrative bodies.[3]

The test of choice for chlamydia detection is the nucleic acid amplification test (NAAT), and a range of assays, with extremely high sensitivity and specificity, are available.[4] Many NAATs allow dual detection of chlamydia and *Neisseria gonorrhoeae* (gonorrhoea) using a single specimen and the same assay,[4] and it has become inexpensive and straightforward to simultaneously test for both infections.[5] From a simplistic viewpoint, this technological development may appear advantageous to public health.[5–7] However, new guidance for England on testing for gonorrhoea found only sparse evidence for selective community screening, and no evidence to support widespread unselected screening in community-based settings.[8,9] Although chlamydia and gonorrhoea cause similar disease and symptoms, there are important differences in the population distribution and the microbiology of testing for these infections that need consideration.[10] Unlike chlamydia, the prevalence of gonorrhoea is very low in the general population (<0.1% and therefore approximately tenfold lower),[11] and concentrated in specific groups (including those attending specialist GUM clinics).[12]

Where prevalence is low, the positive predictive value (PPV) of a single test will also be low, but the problem of low PPV can be resolved by undertaking a supplementary test on samples that initially screen positive. Although the prevalence of gonorrhoea in patients attending community-based services, such as NSCP settings, might be higher than in the general population (ranging from 0.3% to 1.7% outside London,[6,13–15] and up to 4.1% in

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3 South London),[16] lack of proper confirmatory strategies means that the available studies
4 might overestimate prevalence.[9] Together, the low prevalence of gonorrhoea and the
5 potential for cross-reaction with non-gonococcal *Neisseria* species mean that high rates of
6 false positive results might occur if gonorrhoea screening is undertaken on NCSP
7 samples.[10]
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14 In 2007, a laboratory survey found that 29% of hospital-based microbiology laboratories in
15 England and Wales were already using dual tests to diagnose chlamydia and
16 gonorrhoea.[17] A recent repeat of this survey suggests this proportion has increased to
17 85% (Toby et al, Public Health England (PHE), unpublished study). However, it is not known
18 whether this has led to widespread gonorrhoea screening being undertaken on samples
19 collected by the NCSP. In this study, we (1) undertook a survey of LA commissioners to
20 understand the extent to which dual tests are being deployed for samples collected by the
21 NCSP, (2) collected data about the clinical care pathways used when gonorrhoea is
22 detected, and (3) linked the survey data with national surveillance data to estimate the
23 likely number of gonorrhoea diagnoses and false positive gonorrhoea results occurring in
24 England through the use of dual tests on samples collected by the NCSP.
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35 **Methods**

36 **Survey methodology:** During May to July 2013, we delivered an online questionnaire (using
37 the PHE web-based survey tool, 'Select Survey') to commissioners of sexual health services
38 who were responsible for commissioning chlamydia testing in people aged 15-24 years for
39 each of the 152 upper tier LAs in England (upper tier LAs are administrative bodies with a
40 wide range of local government responsibilities, including for public health). Such web-
41 based surveys are easy to use and maximise response rates.[18] The questionnaire used
42 closed questions and dropdown menus to ask about: use of dual tests outside of GUM
43 settings (i.e. community-based sexual health screening); service setting and sample types;
44 use of confirmatory testing where the screening test was reactive for gonorrhoea; patient
45 information; and consent processes. Since not all commissioners were likely to understand
46 technical molecular definitions used in relation to confirmatory testing, the questionnaire
47 used the following pragmatic definition for a confirmatory test: "a second test used to
48 confirm the diagnosis of gonorrhoea where the initial screening test is positive for
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3 gonorrhoea". The questionnaire was piloted to test usability, understanding, clarity, and
4 question flow; it included 29 questions and took approximately 20 minutes to complete.
5 Respondents were recruited by email using a national list of LA sexual health
6 commissioners, which covered the whole of England, and the survey was advertised in the
7 quarterly NCSP newsletter.
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14 **Statistical analysis:** Survey data were extracted to Microsoft Excel and a descriptive analysis
15 was undertaken. The denominator for descriptive analyses was the number of LAs, which
16 varied by item non-response. Using Stata (version 12.1), independent samples t-tests
17 compared area-level characteristics between LA responders and non-responders and
18 between LAs using and not using dual tests. Chlamydia diagnosis rates (per 100,000
19 population) and chlamydia testing coverage included diagnoses and testing in community-
20 based and GUM settings collected through the Chlamydia Test Activity Dataset (CTAD) and
21 the GUM Clinic Activity Dataset (GUMCAD), and gonorrhoea diagnosis rates (per 100,000
22 population) included diagnoses made in GUM clinics collected through GUMCAD. [2,19]
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32 **Estimating the number of gonorrhoea false positives and confirmed positives:** For each LA
33 using dual tests, PHE Chlamydia Testing Activity Dataset (CTAD)[2] data on the number of
34 chlamydia tests performed outside of GUM clinics in 2012 was used as a proxy for the total
35 number of gonorrhoea tests performed through use of dual tests on samples collected by
36 the NCSP (excluding screening in GUM). Using this figure, we estimated the absolute
37 number of unconfirmed reactive tests and the number of confirmed diagnoses, using
38 published specificity estimates for a commercial dual test assay.[20] We did this for two
39 scenarios for the overall prevalence of gonorrhoea in community-based settings, 0.1% and
40 1.0%, which represent plausible minimum and maximum values.[9,11]
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49 **Ethics:** This work was undertaken with data collected and held within the requirements of
50 the data protection act and in accordance with data sharing best practice and PHE
51 guidelines.[21] The study did not use individual patient data and did not require or seek
52 ethical approval.
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Results

LA survey response and use of dual tests

Overall, 98/152 of LAs responded to the survey, which equates to a response rate across England of 64% (Table 1). The proportion of LAs responding was at least 50% in all fifteen PHE centre areas, and the area-level characteristics of responding and non-responding LAs were statistically similar. Comparison between responding and non-responding LAs included area-level Index of Multiple Deprivation [22] (mean Index of Multiple Deprivation score 22.9 versus 23.1; $p=0.89$), mean chlamydia positivity among those testing and aged 15 to 24 years (7.9% versus 7.8%; $p=0.63$), mean chlamydia diagnosis rate (2152/100,000 versus 1870/100,000; $p=0.06$), mean chlamydia testing coverage among those aged 15 to 24 years (27% versus 24%; $p=0.06$), and mean GUM gonorrhoea diagnosis rate estimated from GUM diagnoses (43/100,000 versus 39/100,000; $p=0.68$) for each LA area.

Over half (53% (52/98)) of responding LAs reported commissioning use of dual tests for samples collected by the NCSP, 45% (44/98) had never commissioned dual tests, and 2% (2/98) had previously commissioned dual tests or did not know (Table 1). Most LAs (82% (37/45)) reported using dual tests in at least five different non-GUM settings, including Contraception and Sexual Health and Sexual and Reproductive Health services (98% (44/45)) and primary care (91% (41/45)) settings, as well as in termination of pregnancy services (87% (39/45)) and through remote sample collection by post or Internet (80% (36/45)).

At an area level, there was no significant difference in Index of Multiple Deprivation, chlamydia positivity among those testing and aged 15 to 24 years, chlamydia diagnosis rate, or mean chlamydia testing coverage among those aged 15 to 24 years, when comparing LAs using and not using dual tests (Table 2). Mean gonorrhoea diagnosis rates based on diagnoses made in GUM clinics were higher (53/100,000 versus 32/100,000; $p=0.03$) in LAs using dual tests compared to those not. Nevertheless, most LAs had low gonorrhoea diagnosis rates that were below 50 per 100,000 (Figure 1). We noted three LAs where dual tests were not being used, all in London, where GUM gonorrhoea diagnosis rates were above 100 per 100,000, placing these areas inside the top ten percent nationally.

Clinical care pathway for gonorrhoea

NCSP standards stipulate that patients should be given specific information about any testing that is additional to chlamydia and that informed consent for such testing is obtained.[23] The standards also recommend that laboratories should not test for any infection unless this has been specifically requested, and that patients diagnosed with gonorrhoea in community-based settings should usually be referred to a GUM clinic.[23]

Overall, 36% (15/42) of LAs using dual tests reported providing gonorrhoea-specific patient information materials to patients, 45% (19/42) provided no gonorrhoea-specific information materials, and 19% (8/42) did not know. Of those without gonorrhoea-specific patient information materials, 84% (16/19) reported that gonorrhoea was discussed within their NCSP patient information leaflet, while only 5% (1/19) of these LAs reported providing no gonorrhoea information (11% (2/19) did not know). Informed consent for testing of gonorrhoea was reported as assumed (on the basis that information was provided and the testing kit was returned) in 71% (25/35) of LAs, and taken in writing in 14% (5/35). 3% (1/35) of LAs did not obtain consent.

Although confirmatory testing (defined in the survey as a second test confirming the diagnosis of gonorrhoea) was reported as being used in 93% (38/41) of LAs, in practice, confirmation only occurred after referral to specialist sexual health services in most areas. 63% (26/41) of LAs reported referring patients to sexual health services on the basis of a reactive screening test, 17% (7/41) referred after confirmatory testing, 15% (6/41) did not refer patients to another service, and 10% (4/41) did not know.

Estimating the number of false positive and confirmed positive gonorrhoea tests

We used the LA survey data, national surveillance data,[2] and published data on gonorrhoea prevalence in community-based settings[9,11] to estimate the number of confirmed gonorrhoea diagnoses and false positives that might occur each year through the use of dual tests on samples collected by the NCSP (Table 1). Using CTAD surveillance data from only the 52 LAs that reported using dual tests, we estimated that at least 456,085 screening tests for gonorrhoea might be undertaken per year in non-GUM settings in England, which would lead to around 456 diagnoses of confirmed gonorrhoea per year if the

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3 overall prevalence is 0.1%. In this scenario, and assuming test sensitivity and specificity of
4 99.5% (which is likely to be at the upper end of existing platform specificity), approximately
5 2,278 false positive reactive screens would occur and the PPV of the screening test would be
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8 17%. If the true prevalence of gonorrhoea was 1%, the number of false positive tests
9 occurring would be 2,258, the number of confirmed diagnoses would be 4,561, and the PPV
10 would be 67%.
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13 Discussion

14 *Statement of principal findings*

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18 This is the first national study to investigate the use of dual tests for chlamydia and
19 gonorrhoea on samples collected by the NCSP. Although the NCSP does not recommend
20 simultaneous screening for chlamydia and gonorrhoea, our data suggest that over half of
21 LAs in England already commission dual tests for NCSP samples. Thus, in many areas across
22 England, screening for asymptomatic gonococcal infection has been introduced in low
23 prevalence settings without a national evidence review or any change in national screening
24 policy. Furthermore, we found evidence that reactive screening test results are being
25 returned to patients prior to gonorrhoea infection being confirmed. Given that many
26 reactive screening tests for gonorrhoea will be false positives due to low prevalence, this
27 finding raises considerable concerns. We question the public health benefit of deploying
28 dual tests for NCSP samples without careful consideration of the risks. Commissioners and
29 providers may need to undertake appropriately powered pilot studies to decide whether
30 dual tests are appropriate in their local areas. If dual tests are used, there are important
31 implications for resource allocation in managing unconfirmed reactive tests and for the
32 personal toll on an individual's wellbeing if the test is not confirmed; confirmatory tests
33 should be performed before patients are informed about gonorrhoea diagnoses.
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49 *Strengths and weaknesses of the study*

50 Response to the LA survey was high and similar across the geographical regions in England.
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52 There was no evidence to suggest participation bias associated with Index of Multiple
53 Deprivation or NCSP area-level characteristics. It therefore seems likely that the responding
54 LAs are representative of English LAs in their use of dual tests and that the data are
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3 generalisable. However, the study is limited by the self-reported nature of the survey
4 responses, which might be subject to reporting bias. Furthermore, most survey questions
5 had an item non-response of around 14%, which might reflect respondents' lack of
6 understanding, lack of knowledge about service specifications or reluctance to answer
7 questions that might reveal sub-optimal practice. Our data might underestimate the
8 proportion of LAs using dual tests because commissioners might not always be aware that
9 dual tests are being used for NCSP samples.
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17 Although LAs using dual tests were more likely to be areas with higher rates of gonorrhoea
18 diagnosis made in GUM clinics, which might indicate evidence-based policy making, this
19 finding might also be explained by increased diagnosis of gonorrhoea in these areas arising
20 from the introduction of dual tests.
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26 ***Meaning of the study: possible explanations and implications for clinicians and***
27 ***policymakers***
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30 This study has significant implications for commissioners of sexual health services in LAs and
31 for clinical services providing chlamydia screening. While screening for gonorrhoea in
32 community-based settings might be appropriate in some areas where the prevalence is
33 high, we show that dual tests are being used in areas where the prevalence and PPV are
34 likely to be extremely low. Conversely, we also show that dual tests are not being used in
35 some high prevalence areas that might benefit from targeted gonorrhoea screening.
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42 The increased availability, technical ease, and declining cost of dual and, in due course,
43 multiplex molecular testing platforms for STIs make them attractive tools for laboratories
44 that process high specimen volumes. The emergence of antimicrobial resistant (AMR)
45 gonorrhoea is a major threat to global health and these molecular tests offer considerable
46 public health benefits by facilitating detection and control of gonorrhoea.[24] However, for
47 commissioners, policy makers and providers, our study draws attention to the risk of false
48 positive test results and the need to minimise potential distress caused to patients. The
49 harms of misdiagnoses include the direct emotional harm to individual patients arising from
50 incorrect and stigmatising diagnoses and unnecessary partner notification,[24,25] as well as
51 the possibility of physical harm in the rare event that the unnecessary treatment causes side
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3 effects. Indirect harm may occur at a population level due to avoidable antibiotic usage
4 (with implications for AMR) and clinical expense. Before any STI screening is introduced, the
5 evidence on potential harms as well as benefits should be rigorously assessed and, wherever
6 screening is introduced, robust testing algorithms and clinical management pathways
7 implemented. A PHE toolkit is available to support LA sexual health commissioners in
8 estimating PPVs for gonorrhoea testing in different population groups.[26] Essential
9 pathways include those for obtaining informed consent for testing of gonorrhoea and for
10 performing confirmatory testing (using a supplementary NAAT with a different nucleic acid
11 target) before returning results to patients or initiating management. These steps are likely
12 to improve patient autonomy and safety, and avoid misdiagnosis, unnecessary clinical
13 management, and their associated costs.
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24 ***Unanswered questions and future research***

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26 This paper highlights a broader issue that decisions about screening may be driven by the
27 availability of diagnostic testing platforms rather than the evidence base.[24,27] A World
28 Health Organization synthesis of emerging screening criteria, based on the Wilson and
29 Yungner criteria, highlights the importance of identifying and responding to a recognised
30 health need, defining a target population, scientific evidence of screening effectiveness, and
31 ensuring the overall benefits of screening outweigh the potential harms.[28] Molecular-
32 based testing brings considerable public health opportunities through rapid and highly
33 sensitive detection of one or more pathogens simultaneously, often using non-invasive
34 samples, with benefits to individual patients diagnosed with treatable infections, as well as
35 enhancing surveillance and prevention efforts.[27,29] For example, a multiplex point of care
36 assay has already been developed to detect nucleic acid targets for ten different
37 pathogens.[30] The US Food and Drug Administration cleared multiplex panels for
38 respiratory infections in 2011, indicating a new era for the diagnosis of respiratory
39 infection.[31] However, there is an onus on healthcare commissioners and providers to
40 understand the tests being ordered for individual patients and consider the implications for
41 their deployment at a population level. The risk is that the availability and low costs of
42 testing technologies may drive local policies and lead to inconsistent screening practices
43 that lack an evidence base.
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Contributors

NF contributed to the planning and design of this Article, wrote the first and revised subsequent drafts, designed and piloted the survey, and undertook statistical analyses. IK designed and piloted the survey, contributed to statistical analyses, interpreted data and reviewed successive drafts of the Article. KF contributed to the planning and design of this Article, designed and piloted the survey, interpreted data, and reviewed successive drafts of the Article. SD did statistical analyses and reviewed successive drafts of the Article. KT did statistical analyses and reviewed successive drafts of the Article. CI contributed to the planning and design of this Article, interpreted data, and reviewed successive drafts of the Article. GH led the study team, contributed to the planning and design of this Article, interpreted data, and reviewed successive drafts of the Article. All authors approved the final version of the Article.

Competing interests

All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

Transparency Statement

The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Data sharing

No additional data are available.

For peer review only

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7 **Figure 1 – Mean gonorrhoea (NG) diagnoses per 100,000 population (made in GUM clinics) between 2009-2012 by whether Local**
8 **Authorities (LA) use dual tests on samples collected by the National Chlamydia Screening Programme**
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1. Each vertical dash represents a LA, giving the four year average (2009-2012) for gonorrhoea diagnoses (per 100,000 population) for the 98 LAs responding to the survey, including diagnoses made in GUM clinics collected through GUMCAD
 2. Boxes shows the median and lower and upper quartiles for four year average gonorrhoea diagnoses in each group

References

- 1 National chlamydia screening programme - NCSP home. <http://www.chlamydia-screening.nhs.uk/> (accessed 25 Feb2011).
- 2 HPA - CTAD: Chlamydia Testing Activity Dataset. <http://www.hpa.org.uk/sexualhealth/ctad> (accessed 30 May2014).
- 3 Health and Social Care Act 2012, c.7. <http://www.legislation.gov.uk/ukpga/2012/7/contents/enacted> (accessed 30 May2014).
- 4 British Association for Sexual Health and HIV. Chlamydia trachomatis UK Testing Guidelines. 2010. <http://www.bashh.org/documents/3352.pdf> (accessed 21 Feb2014).
- 5 Bignell, C J. *Sex Transm Infect* 2007;**83**:179–80.
- 6 Lavelle SJ, Jones KE, Mallinson H, *et al*. Finding, confirming, and managing gonorrhoea in a population screened for chlamydia using the Gen-Probe Aptima Combo2 assay. *Sex Transm Infect* 2006;**82**:221–4. doi:10.1136/sti.2005.017616
- 7 Lavelle SJ, Mallinson H, Henning SJ, *et al*. Impact on gonorrhoea case reports through concomitant/dual testing in a chlamydia screening population in Liverpool. *Sex Transm Infect* 2007;**83**:593–4. doi:10.1136/sti.2007.027870
- 8 Guidance for the detection of gonorrhoea in England; including guidance on the use of dual testing for chlamydia and gonorrhoea. Public Health England © Crown copyright (2014).
- 9 Fifer H, Ison CA. Nucleic acid amplification tests for the diagnosis of Neisseria gonorrhoeae in low-prevalence settings: a review of the evidence. *Sex Transm Infect* 2014.
- 10 Ison C. GC NAATs: is the time right? *Sex Transm Infect* 2006;**82**:515. doi:10.1136/sti.2006.022731
- 11 Sonnenberg P, Clifton S, Beddows S, *et al*. Prevalence, risk factors, and uptake of interventions for sexually transmitted infections in Britain: findings from the National Surveys of Sexual Attitudes and Lifestyles (Natsal). *The Lancet* 2013;**382**:1795–806. doi:10.1016/S0140-6736(13)61947-9
- 12 Public Health England. Health Protection Report. 2013. <http://www.hpa.org.uk/hpr/archives/2013/hpr2313.pdf> (accessed 6 Feb2014).

- 1
2
3
4
5 13 Skidmore S, Copley S, Cordwell D, *et al.* Positive nucleic acid amplification tests for *Neisseria gonorrhoeae* in young people tested as part of
6 the National Chlamydia Screening Programme. *Int J STD AIDS* 2011;**22**:398–9. doi:10.1258/ijsa.2011.010378
7
8
9 14 Fowler T, Edeghere O, Inglis N, *et al.* Estimating the positive predictive value of opportunistic population testing for gonorrhoea as part of
10 the English Chlamydia Screening Programme. *Int J STD AIDS* Published Online First: 20 March 2013. doi:10.1177/0956462412472443
11
12 15 Downing J, Cook PA, Madden HCE, *et al.* Management of cases testing positive for gonococcal infection in a community-based chlamydia
13 screening programme. *Sex Transm Infect* 2010;**86**:474–7. doi:10.1136/sti.2010.043240
14
15 16 Rao GG, Bacon L, Evans J, *et al.* Prevalence of *Neisseria gonorrhoeae* infection in young subjects attending community clinics in South
16 London. *Sex Transm Infect* 2008;**84**:117–21. doi:10.1136/sti.2007.026914
17
18 17 Benzie A, Alexander S, Gill N, *et al.* Gonococcal NAATs: what is the current state of play in England and Wales? *Int J STD AIDS* 2010;**21**:246–
19 8. doi:10.1258/ijsa.2010.010004
20
21 18 Dayan Y, Paine CS, Johnson AJ. Responding to sensitive questions in surveys: A comparison of results from Online panels, face to face and
22 self-completion interviews. 2009. [http://www.ipsos-](http://www.ipsos-mori.com/Assets/Docs/Publications/Ops_RMC_Responding_Sensitive_Questions_08_03_10.pdf)
23 [mori.com/Assets/Docs/Publications/Ops_RMC_Responding_Sensitive_Questions_08_03_10.pdf](http://www.ipsos-mori.com/Assets/Docs/Publications/Ops_RMC_Responding_Sensitive_Questions_08_03_10.pdf) (accessed 21 Feb2014).
24
25 19 Public Health England. Genitourinary Medicine Clinic Activity Dataset (GUMCADv2). <http://www.hpa.org.uk/gumcad> (accessed 30
26 May2014).
27
28 20 Gen-Probe products. Aptima Combo 2 product information webpage. <http://www.gen-probe.com/products-services/aptima-combo>
29 (accessed 30 May2014).
30
31 21 Hughes G, Evans BG, Ncube F, *et al.* PHE HIV and STI Data Sharing Policy version 4.
32 2014.http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1247816526850 (accessed 27 Jun2014).
33
34 22 Payne RA, Abel GA. UK indices of multiple deprivation - a way to make comparisons across constituent countries easier. *Health Stat Q Off*
35 *Natl Stat* 2012;**53**:22–37.
36
37
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44
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46
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48
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2
3
4
5 23 National Chlamydia Screening Programme, Health Protection Agency. National Chlamydia Screening Programme Standards (6th Edition).
6 2012. [http://www.chlamydia-screening.nhs.uk/ps/resources/core-](http://www.chlamydia-screening.nhs.uk/ps/resources/core-requirements/NCSP%20Standards%206th%20Edition_October%202012.pdf)
7 requirements/NCSP%20Standards%206th%20Edition_October%202012.pdf
8
9
10 24 Low N, Unemo M, Skov Jensen J, *et al.* Molecular Diagnostics for Gonorrhoea: Implications for Antimicrobial Resistance and the Threat of
11 Untreatable Gonorrhoea. *PLoS Med* 2014;**11**. doi:10.1371/journal.pmed.1001598
12
13 25 Katz AR, Effler PV, Ohye RG, *et al.* False-positive gonorrhea test results with a nucleic acid amplification test: the impact of low prevalence
14 on positive predictive value. *Clin Infect Dis Off Publ Infect Dis Soc Am* 2004;**38**:814–9. doi:10.1086/381895
15
16 26 Guidance for the detection of gonorrhoea in England - Publications - GOV.UK. [https://www.gov.uk/government/publications/guidance-for-](https://www.gov.uk/government/publications/guidance-for-the-detection-of-gonorrhoea-in-england)
17 the-detection-of-gonorrhoea-in-england (accessed 27 Aug2014).
18
19
20 27 Klausner JD. The NAAT Is Out of the Bag. *Clin Infect Dis* 2004;**38**:820–1. doi:10.1086/381897
21
22 28 Andermann A, Blancquaert I, Beauchamp S, *et al.* Revisiting Wilson and Jungner in the genomic age: a review of screening criteria over the
23 past 40 years. *Bull World Health Organ* 2008;**86**.<http://www.who.int/bulletin/volumes/86/4/07-050112/en/>
24
25 29 Tucker JD, Bien CH, Peeling RW. Point-of-care testing for sexually transmitted infections: recent advances and implications for disease
26 control. *Curr Opin Infect Dis* 2013;**26**:73–9. doi:10.1097/QCO.0b013e32835c21b0
27
28 30 Kriesel J, Bhatia A, Vaughn M, *et al.* P3-S5.05 Rapid point of care testing for ten sexually transmitted diseases. *Sex Transm Infect*
29 2011;**87**:A294–A295. doi:10.1136/sextrans-2011-050108.472
30
31 31 Russek-Cohen E, Feldblyum T, Whitaker KB, *et al.* FDA Perspectives on Diagnostic Device Clinical Studies for Respiratory Infections. *Clin*
32 *Infect Dis* 2011;**52**:S305–S311. doi:10.1093/cid/cir056
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Table 1. Local authority (LA) survey response and reported use of dual tests on samples collected by the National Chlamydia (CT) Screening Programme (NCSP) for people aged 15-24 years, with estimated numbers of gonorrhoea (NG) tests performed, confirmed diagnoses, and unconfirmed reactive tests for 2012

PHE Region	Number of LAs	LAs (%) survey response	LAs (%) using dual tests ¹	Non-GUM CT tests ²	If community-based NG prevalence is 0.1%		If community-based NG prevalence is 1.0%	
					Estimated NG diagnoses ³	Estimated unconfirmed reactive NG tests (PPV=17%) ⁴	Estimated NG diagnoses ³	Estimated unconfirmed reactive NG tests (PPV=67%) ⁴
ALL	152	98 (64)	52 (53)	456,085	456	2,278	4,561	2,258
London	33	21 (64)	14 (67)	98250	98	491	983	486
Midlands & East of England	35	26 (74)	6 (23)	67362	67	336	674	333
North of England	50	34 (68)	21 (62)	194321	194	971	1,943	962
South of England	34	17 (50)	11 (65)	96152	96	480	962	476

1. Number and percentage of LAs using dual tests out of those responding to the survey
2. Number of non-GUM CT tests performed in all LAs using dual tests as a proxy for the number of gonorrhoea screening tests performed, using data extracted from the Chlamydia Testing Activity Dataset (CTAD) which comprises all chlamydia testing carried out in England
3. Estimated number of confirmed NG diagnoses arising from use of dual tests on samples collected by the NCSP (non-GUM) if NG prevalence is 0.1% or 1.0%
4. Estimated number of reactive but unconfirmed NG tests arising from use of dual tests on samples collected by the NCSP (non-GUM) if NG prevalence is 0.1% or 1.0% and the sensitivity and specificity of test are 99.5%

Table 2. Comparison of area-level characteristics between LAs reporting current commissioning of dual tests and those not¹

	Number of LAs	Mean chlamydia diagnosis rate / 100,000 ²	Mean chlamydia testing coverage ³	Mean gonorrhoea diagnosis rate / 100,000 ⁴
Using dual tests	52	2254.8	28.6%	52.7
Not using dual tests	46	2063.2	26.2%	32.4
<i>p-value difference</i>	-	0.31	0.24	0.03

1. No significant difference was found by NCSP chlamydia positivity rate ($p=0.93$), LA Index of Multiple Deprivation ($p=0.88$), or the proportion of NCSP services provided by GUM or GP, but the proportion of services provided by CSHS was higher in those LAs using dual tests (19.4% vs 8.6%; ($p<0.01$)).
 2. Chlamydia diagnosis rates (per 100,000 population) include diagnoses made in community-based and GUM settings collected through the Chlamydia Test Activity Dataset (CTAD) and the GUM Clinic Activity Dataset (GUMCAD)
 3. Chlamydia testing coverage includes tests done in community-based and GUM settings collected through CTAD and the GUM Clinic Activity Dataset (GUMCAD)
- Gonorrhoea diagnoses (per 100,000 population) include diagnoses made in GUM clinics collected through GUMCAD.

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3 **Screening for gonorrhoea using samples collected through the English National Chlamydia**
4 **Screening Programme and risk of false positives: a national survey of Local Authorities**
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Abstract

Objectives: To investigate use of dual tests for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* on samples collected through the National Chlamydia Screening Programme (NCSP) in England.

Design and setting: During May-July 2013, we delivered an online survey to commissioners of sexual health services in the 152 upper-tier English Local Authorities (LAs) who were responsible for commissioning chlamydia screening in people aged 15-24 years.

Main outcome measures: (1) The proportion of English LAs using dual tests on samples collected by the NCSP; (2) The estimated number of gonorrhoea tests and false positives from samples collected by the NCSP, calculated using national surveillance data on the number of chlamydia tests performed, assuming the gonorrhoea prevalence to range between 0.1-1.0%, and test sensitivity and specificity of 99.5%.

Results: 64% (98/152) of LAs responded to this national survey; over half (53% (52/98)) reported currently using dual tests in community settings. There was no significant difference between LAs using and not using dual tests by chlamydia positivity, chlamydia diagnosis rate, or population screening coverage. Although positive gonorrhoea results were confirmed with supplementary tests in 93% (38/41) of LAs, this occurred after patients were notified about the initial positive result in 63% (26/41). Approximately 450 to 4,500 confirmed gonorrhoea diagnoses and 2,300 false positive screens might occur through use of dual tests on NCSP samples each year. Under reasonable assumptions, the positive predictive value of the screening test is 17%-67%.

Conclusions: Over half of English LAs already commission dual tests for samples collected by the NCSP. Gonorrhoea screening has been introduced alongside chlamydia screening in many low prevalence settings without a national evidence review or change of policy. We question the public health benefit here, and suggest that robust testing algorithms and clinical management pathways, together with rigorous evaluation, be implemented wherever dual tests are deployed.

Article summary

Strengths and limitations of this study

- The English National Chlamydia Screening Programme (NCSP) aims to diagnose and control chlamydia in all sexually active people aged 15-24, but no such community-based screening programme exists for gonorrhoea.
- We undertook a national survey of Local Authority (LA) commissioners of chlamydia screening to investigate use of dual tests, which simultaneously test for chlamydia and gonorrhoea, in community-based settings (excluding special sexual health services).
- Response to the LA survey was high and similar across the geographical regions in England. There was no evidence to suggest participation was associated with ~~IMD~~ Index of Multiple Deprivation or NCSP area-level characteristics.
- The study is limited by the self-reported nature of the survey responses, which might be subject to reporting bias. Our data might underestimate the proportion of LAs using dual tests because commissioners might not always be aware that dual tests are being used for NCSP samples. Most survey questions had item non-response of around 14%.
- In over half of LAs in England, dual tests are already being used on samples collected by the NCSP, and in many areas gonorrhoea test results are returned to patients prior to the result being confirmed.

Introduction

The English National Chlamydia Screening Programme (NCSP) offers sexually active, asymptomatic, women and men, aged 15-24 years old, opportunistic testing to diagnose and control *Chlamydia trachomatis* (chlamydia) infection in England.[1] In 2012, over 1.2 million screening tests were performed for young people in community-based sexual health clinics in England (i.e. outside of specialist sexual health clinics, called genitourinary medicine (GUM) clinics in the UK), with over 80,000 chlamydia infections diagnosed.[2] Screening is offered by a variety of providers, including contraception, sexual health and termination of pregnancy services, pharmacies and primary care. Since 2013, commissioning arrangements have been undertaken through Local Authorities (LAs), which are regional local government administrative bodies with commissioning undertaken through Local Authorities (LAs) since 2012.[3]

The test of choice for chlamydia detection is the nucleic acid amplification test (NAAT), and a range of assays, with extremely high sensitivity and specificity, are available.[4] Many NAATs allow dual detection of chlamydia and *Neisseria gonorrhoeae* (gonorrhoea) using a single specimen and the same assay,[4] and it has become inexpensive and straightforward to simultaneously test for both infections.[5] From a simplistic viewpoint, this technological development may appear advantageous to public health.[5–7] However, current new UK guidance for England on testing for gonorrhoea found only sparse evidence for selective community screening, and no evidence to support widespread unselected screening in community-based settings.[8,9] Although chlamydia and gonorrhoea cause similar disease and symptoms, there are important differences in the population distribution and the microbiology of testing for these infections that need consideration.[10] Unlike chlamydia, the prevalence of gonorrhoea is very low in the general population (<0.1% and therefore approximately tenfold lower),[11] and concentrated in specific groups (including those attending specialist GUM clinics).[12]

Where prevalence is low, the positive predictive value (PPV) of a single test will also be low, but the problem of low PPV can be resolved by undertaking a supplementary test on samples that initially screen positive. Although the prevalence of gonorrhoea in patients attending community-based services, such as NSCP settings, might be higher than in the

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3 general population (ranging from 0.3% to 1.7% outside London,[6,13–15] and up to 4.1% in
4 South London),[16] lack of proper confirmatory strategies means that the available studies
5 might overestimate prevalence.[9] Together, the low prevalence of gonorrhoea and the
6 potential for cross-reaction with non-gonococcal *Neisseria* species mean that high rates of
7 false positive results might occur if gonorrhoea screening is undertaken on NCSP
8 samples.[10]
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15 In 2007, a laboratory survey found that 29% of hospital-based microbiology laboratories in
16 England and Wales were already using dual tests to diagnose chlamydia and
17 gonorrhoea.[17] A recent update-repeat of this survey suggests this proportion has
18 increased to 85% (Toby et al, Public Health England (PHE), unpublished informationstudy).
19 However, it is not known whether this has led to widespread gonorrhoea screening being
20 undertaken on samples collected by the NCSP. In this study, we (1) undertook a survey of LA
21 commissioners to understand the extent to which dual tests are being deployed for samples
22 collected by the NCSP, (2) collected data about the clinical care pathways used when
23 gonorrhoea is detected, and (3) linked the survey data with national surveillance data to
24 estimate the likely number of gonorrhoea diagnoses and false positive gonorrhoea results
25 occurring in England through the use of dual tests on samples collected by the NCSP.
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36 **Methods**

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38 **Survey methodology:** During May to July 2013, we delivered an online questionnaire (using
39 the Public Health England (PHE) web-based survey tool, 'Select Survey') to commissioners of
40 sexual health services who were responsible for commissioning chlamydia testing in people
41 aged 15-24 years in-for each of the 152 upper tier LAs in England upper tier LAs are
42 administrative bodies with a wide range of local government responsibilities, including for
43 public health. Such web-based surveys are easy to use and maximise response rates.[18]
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49 The questionnaire used closed questions and dropdown menus to ask about: use of dual
50 tests outside of GUM settings (i.e. community-based sexual health screening); service
51 setting and sample types; use of confirmatory testing where the screening test was reactive
52 for gonorrhoea; patient information; and consent processes. Since not all commissioners
53 were likely to understand technical molecular definitions used in relation to confirmatory
54 testing, the questionnaire used the following pragmatic definition for a confirmatory test: "a
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3 second test used to confirm the diagnosis of gonorrhoea where the initial screening test is
4 positive for gonorrhoea". The questionnaire was piloted to test usability, understanding,
5 clarity, and question flow; it included 29 questions and took approximately 20 minutes to
6 complete. Respondents were recruited by email using a national list of LA sexual health
7 commissioners, which covered the whole of England, and the survey was advertised in the
8 quarterly NCSP newsletter.
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15 **Statistical analysis:** Survey data were extracted to Microsoft Excel and a descriptive analysis
16 was undertaken. The denominator for descriptive analyses was the number of LAs, which
17 varied by item non-response. Using Stata (version 12.1), independent samples t-tests
18 compared area-level characteristics between LA responders and non-responders and
19 between LAs using and not using dual tests. Chlamydia diagnosis rates (per 100,000
20 population) and chlamydia testing coverage included diagnoses and testing in community-
21 based and GUM settings collected through the Chlamydia Test Activity Dataset (CTAD) and
22 the GUM Clinic Activity Dataset (GUMCAD), and gonorrhoea diagnosis rates (per 100,000
23 population) included diagnoses made in GUM clinics collected through GUMCAD. [2,19]
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33 **Estimating the number of gonorrhoea false positives and confirmed positives:** For each LA
34 using dual tests, PHE Chlamydia Testing Activity Dataset (CTAD)[2] data on the number of
35 chlamydia tests performed outside of GUM clinics in 2012 was used as a proxy for the total
36 number of gonorrhoea tests performed through use of dual tests on samples collected by
37 the NCSP (excluding screening in GUM). Using this figure, we estimated the absolute
38 number of unconfirmed reactive tests and the number of confirmed diagnoses, using
39 published specificity estimates for a commercial dual test assay.[20] We did this for two
40 scenarios for the overall prevalence of gonorrhoea in community-based settings, 0.1% and
41 1.0%, which represent plausible minimum and maximum values, and assuming the
42 prevalence of gonorrhoea in most community-based settings to range between 0.1% to
43 1.0%,[9,11] we estimated the absolute number of unconfirmed reactive tests and the
44 number of confirmed diagnoses, using published specificity estimates for a commercial dual
45 test assay.[21]
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Ethics: This work was undertaken with data collected and held within the requirements of the data protection act and in accordance with data sharing best practice and PHE guidelines.[21] The study did not use individual patient data and did not require or seek ethical approval.

Results

LA survey response and use of dual tests

Overall, ~~64%~~ (98/152) of LAs responded to the survey, which equates to a response rate across England of 64% (Table 1). The proportion of LAs responding was at least 50% in all fifteen PHE centre areas, and the area-level characteristics of responding and non-responding LAs were statistically similar. Comparison between responding and non-responding LAs included area-level Index of Multiple Deprivation (~~IMD~~)[22] (mean ~~IMD~~Index of Multiple Deprivation score 22.9 versus 23.1; $p=0.89$), mean chlamydia positivity among those testing and aged 15 to 24 years (7.9% versus 7.8%; $p=0.63$), mean chlamydia diagnosis rate (2152/100,000 versus 1870/100,000; $p=0.06$), mean chlamydia testing coverage among those aged 15 to 24 years (27% versus 24%; $p=0.06$), and mean GUM gonorrhoea diagnosis rate estimated from GUM diagnoses (43/100,000 versus 39/100,000; $p=0.68$) for each LA area.

Over half (53% (52/98)) of responding LAs reported commissioning use of dual tests for samples collected by the NCSP, 45% (44/98) had never commissioned dual tests, and 2% (2/98) had previously commissioned dual tests or did not know (Table 1). Most LAs (82% (37/45)) reported using dual tests in at least five different non-GUM settings, including Contraception and Sexual Health and Sexual and Reproductive Health services (98% (44/45)) and primary care (91% (41/45)) settings, as well as in termination of pregnancy services (87% (39/45)) and through remote sample collection by post or Internet (80% (36/45)).

At an area level, there was no significant difference in IMD Index of Multiple Deprivation, chlamydia positivity among those testing and aged 15 to 24 years, chlamydia diagnosis rate, or mean chlamydia testing coverage among those aged 15 to 24 years, when comparing LAs using and not using dual tests (Table 2). Mean gonorrhoea diagnosis rates based on

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3 diagnoses made in GUM clinics were higher (53/100,000 versus 32/100,000; $p=0.03$) in LAs
4 using dual tests compared to those not. Nevertheless, most LAs had low gonorrhoea
5 diagnosis rates that were below 50 per 100,000 (Figure 1). We noted three LAs where dual
6 tests were not being used, all in London, where GUM gonorrhoea diagnosis rates were
7 above 100 per 100,000, placing these areas inside the top ten percent nationally.
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12 ***Clinical care pathway for gonorrhoea***

13 NCSP standards stipulate that patients should be given specific information about any
14 testing that is additional to chlamydia and that informed consent for such testing is
15 obtained.[23] The standards also recommend that laboratories should not test for any
16 infection unless this has been specifically requested, and that patients diagnosed with
17 gonorrhoea in community-based settings should usually be referred to a GUM clinic.[23]
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26 Overall, 36% (15/42) of LAs using dual tests reported providing gonorrhoea-specific patient
27 information materials to patients, 45% (19/42) provided no gonorrhoea-specific information
28 materials, and 19% (8/42) did not know. Of those without gonorrhoea-specific patient
29 information materials, 84% (16/19) reported that gonorrhoea was discussed within their
30 NCSP patient information leaflet, while only 5% (1/19) of these LAs reported providing no
31 gonorrhoea information (11% (2/19) did not know). Informed consent for testing of
32 gonorrhoea was reported as assumed (on the basis that information was provided and the
33 testing kit was returned) in 71% (25/35) of LAs, and taken in writing in 14% (5/35). 3% (1/35)
34 of LAs did not obtain consent.
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43 Although confirmatory testing (defined in the survey as a second test confirming the
44 diagnosis of gonorrhoea) was reported as being used in 93% (38/41) of LAs, in practice,
45 confirmation only occurred after referral to specialist sexual health services in most areas.
46 63% (26/41) of LAs reported referring patients to sexual health services on the basis of a
47 reactive screening test, 17% (7/41) referred after confirmatory testing, 15% (6/41) did not
48 refer patients to another service, and 10% (4/41) did not know.
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56 ***Estimating the number of false positive and confirmed positive gonorrhoea tests***

We used the LA survey data, national surveillance data,[2] and published data on gonorrhoea prevalence in community-based settings[9,11] to estimate the number of confirmed gonorrhoea diagnoses and false positives that might occur each year through the use of dual tests on samples collected by the NCSP (Table 1). Using CTAD surveillance data from only the 52 LAs that reported using dual tests, we estimated that at least 456,085 screening tests for gonorrhoea might be undertaken per year in non-GUM settings in England, which would lead to around 456 diagnoses of confirmed gonorrhoea per year if the overall prevalence is 0.1%. In this scenario, and assuming test sensitivity and specificity of 99.5% (which is likely to be at the upper end of existing platform specificity), approximately 2,278 false positive reactive screens would occur and the ~~positive predictive value (PPV)~~ of the screening test would be 17%. If the true prevalence of gonorrhoea was 1%, the number of false positive tests occurring would be 2,258, the number of confirmed diagnoses would be 4,561, and the PPV would be 67%.

Discussion

Statement of principal findings

This is the first national study to investigate the use of dual tests for chlamydia and gonorrhoea on samples collected by the NCSP. Although the NCSP does not recommend simultaneous screening for chlamydia and gonorrhoea, our data suggest that over half of LAs in England already commission dual tests for NCSP samples. Thus, in many areas across England, screening for asymptomatic gonococcal infection has been introduced in low prevalence settings without a national evidence review or any change in national screening policy. Furthermore, we found evidence that reactive screening test results are being returned to patients prior to gonorrhoea infection being confirmed. Given that many reactive screening tests for gonorrhoea will be false positives due to low prevalence, this finding raises considerable concerns. We question the public health benefit of deploying dual tests for NCSP samples without careful consideration of the risks. Commissioners and providers may need to undertake appropriately powered ~~edful~~ pilot studies to decide whether dual tests are appropriate in their local areas. If dual tests are used, there are important implications for resource allocation in managing unconfirmed reactive tests and for the

personal toll on an individual's wellbeing if the test is not confirmed; confirmatory tests should be performed before patients are informed about gonorrhoea diagnoses.

Strengths and weaknesses of the study

Response to the LA survey was high and similar across the geographical regions in England.

There was no evidence to suggest participation bias associated with Index of Multiple Deprivation or NCSP area-level characteristics. It therefore seems likely that the responding LAs are representative of English LAs in their use of dual tests and that the data are generalisable. However, the study is limited by the self-reported nature of the survey responses, which might be subject to reporting bias. Furthermore, most survey questions had an item non-response of around 14%, which might reflect respondents' lack of understanding, lack of knowledge about service specifications or reluctance to answer questions that might reveal sub-optimal practice. Our data might underestimate the proportion of LAs using dual tests because commissioners might not always be aware that dual tests are being used for NCSP samples.

Although LAs using dual tests were more likely to be areas with higher rates of gonorrhoea diagnosis made in GUM clinics, which might indicate evidence-based policy making, this finding might also be explained by increased diagnosis of gonorrhoea in these areas arising from the introduction of dual tests.

Meaning of the study: possible explanations and implications for clinicians and policymakers

This study has significant implications for commissioners of sexual health services in LAs and for clinical services providing chlamydia screening. While screening for gonorrhoea in community-based settings might be appropriate in some areas where the prevalence is high, we show that dual tests are being used in areas where the prevalence and PPV are likely to be extremely low. Conversely, we also show that dual tests are not being used in some high prevalence areas that might benefit from targeted gonorrhoea screening.

The increased availability, technical ease, and declining cost of dual and, in due course, multiplex molecular testing platforms for STIs make them attractive tools for laboratories

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3 that process high specimen volumes. The emergence of antimicrobial resistant (AMR)
4 gonorrhoea is a major threat to global health and these molecular tests offer considerable
5 public health benefits by facilitating detection and control of gonorrhoea.[24] However, for
6 commissioners, policy makers and providers, our study draws attention to the risk of false
7 positive test results and the need to minimise potential distress caused to patients. The
8 harms of misdiagnoses include the direct emotional harm to individual patients arising from
9 incorrect and stigmatising diagnoses and unnecessary partner notification,[24,25] as well as
10 the possibility of physical harm in the rare event that the unnecessary treatment causes side
11 effects. Indirect harm may occur at a population level due to avoidable antibiotic usage
12 (with implications for AMR) and clinical expense. Before any STI screening is introduced, the
13 evidence on potential harms as well as benefits should be rigorously assessed and, wherever
14 screening is introduced, robust testing algorithms and clinical management pathways
15 implemented. [A PHE toolkit is available to support LA sexual health commissioners in
16 estimating PPVs for gonorrhoea testing in different population groups.](#)[26] Essential
17 pathways include those for obtaining informed consent for testing of gonorrhoea and for
18 performing confirmatory testing (using a supplementary NAAT with a different nucleic acid
19 target) before returning results to patients or initiating management. These steps are likely
20 to improve patient autonomy and safety, and avoid misdiagnosis, unnecessary clinical
21 management, and their associated costs.
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Unanswered questions and future research

40 This paper highlights a broader issue that decisions about screening may be driven by the
41 availability of diagnostic testing platforms rather than the evidence base.[24,27] A World
42 Health Organization synthesis of emerging screening criteria, based on the Wilson and
43 Yungner criteria, highlights the importance of identifying and responding to a recognised
44 health need, defining a target population, scientific evidence of screening effectiveness, and
45 ensuring the overall benefits of screening outweigh the potential harms.[28] Molecular-
46 based testing brings considerable public health opportunities through rapid and highly
47 sensitive detection of one or more pathogens simultaneously, often using non-invasive
48 samples, with benefits to individual patients diagnosed with treatable infections, as well as
49 enhancing surveillance and prevention efforts.[27,29] For example, a multiplex point of care
50 assay has already been developed to detect nucleic acid targets for ten different
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3 pathogens.[30] The US Food and Drug Administration cleared multiplex panels for
4 respiratory infections in 2011, indicating a new era for the diagnosis of respiratory
5 infection.[31] However, there is an onus on healthcare commissioners and providers to
6 understand the tests being ordered for individual patients and consider the implications for
7 their deployment at a population level. The risk is that the availability and low costs of
8 testing technologies may drive local policies and lead to inconsistent screening practices
9 that lack an evidence base.
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Contributors

20 NF contributed to the planning and design of this Article, wrote the first and revised subsequent
21 drafts, designed and piloted the survey, and undertook statistical analyses. IK designed and piloted
22 the survey, contributed to statistical analyses, interpreted data and reviewed successive drafts of the
23 Article. KF contributed to the planning and design of this Article, designed and piloted the survey,
24 interpreted data, and reviewed successive drafts of the Article. SD did statistical analyses and
25 reviewed successive drafts of the Article. KT did statistical analyses and reviewed successive drafts of
26 the Article. CI contributed to the planning and design of this Article, interpreted data, and reviewed
27 successive drafts of the Article. GH led the study team, contributed to the planning and design of this
28 Article, interpreted data, and reviewed successive drafts of the Article. All authors approved the final
29 version of the Article.
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Competing interests

45 All authors have completed the ICMJE uniform disclosure form at
46 http://www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the
47 submitted work; no financial relationships with any organisations that might have an interest in the
48 submitted work in the previous three years, no other relationships or activities that could appear to
49 have influenced the submitted work.
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Transparency Statement

The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Data sharing

No additional data are available.

Table 1. Local authority (LA) survey response and reported use of dual tests on samples collected by the National Chlamydia (CT) Screening Programme (NCSP) for people aged 15-24 years, with estimated numbers of gonorrhoea (NG) tests performed, confirmed diagnoses, and unconfirmed reactive tests for 2012

PHE Region	Number of LAs	LAs (%) survey response	LAs (%) using dual tests ¹	Non-GUM CT tests ²	If community-based NG prevalence is 0.1%		If community-based NG prevalence is 1.0%	
					Estimated NG diagnoses ³	Estimated unconfirmed reactive NG tests (PPV=17%) ⁴	Estimated NG diagnoses ³	Estimated unconfirmed reactive NG tests (PPV=67%) ⁴
ALL	152	98 (64)	52 (53)	456,085	456	2,278	4,561	2,258
London	33	21 (64)	14 (67)	98250	98	491	983	486
Midlands & East of England	35	26 (74)	6 (23)	67362	67	336	674	333
North of England	50	34 (68)	21 (62)	194321	194	971	1,943	962
South of England	34	17 (50)	11 (65)	96152	96	480	962	476

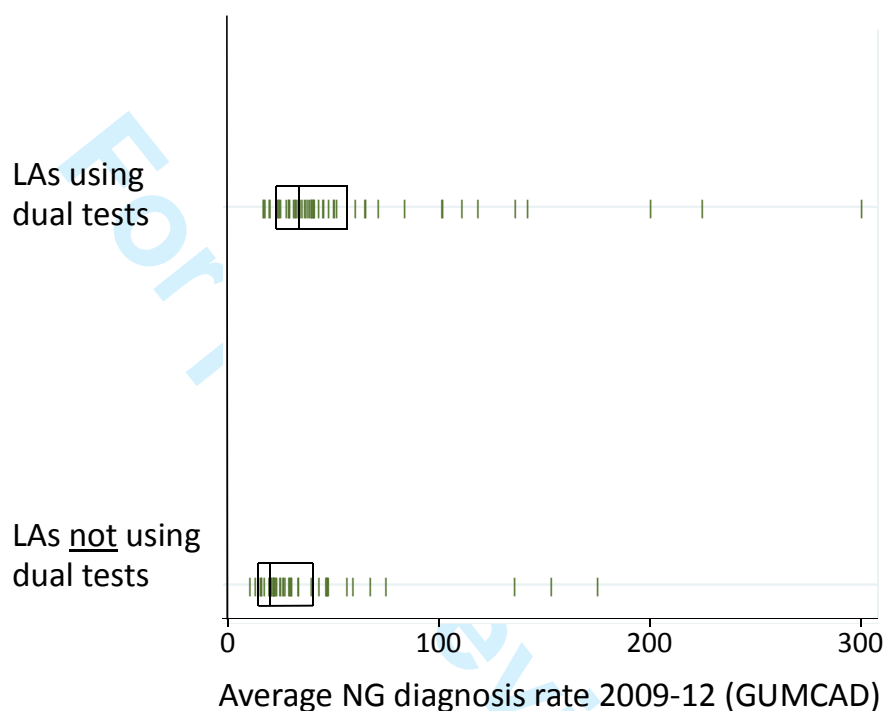
1. Number and percentage of LAs using dual tests out of those responding to the survey
2. Number of non-GUM CT tests performed in all LAs using dual tests as a proxy for the number of gonorrhoea screening tests performed, using data extracted from the Chlamydia Testing Activity Dataset (CTAD) which comprises all chlamydia testing carried out in England
3. Estimated number of confirmed NG diagnoses arising from use of dual tests on samples collected by the NCSP (non-GUM) if NG prevalence is 0.1% or 1.0%
4. Estimated number of reactive but unconfirmed NG tests arising from use of dual tests on samples collected by the NCSP (non-GUM) if NG prevalence is 0.1% or 1.0% and the sensitivity and specificity of test are 99.5%

Table 2. Comparison of area-level characteristics between LAs reporting current commissioning of dual tests and those not¹

	Number of LAs	Mean chlamydia diagnosis rate / 100,000 ²	Mean chlamydia testing coverage ³	Mean gonorrhoea diagnosis rate / 100,000 ⁴
Using dual tests	52	2254.8	28.6%	52.7
Not using dual tests	46	2063.2	26.2%	32.4
<i>p-value difference</i>	-	0.31	0.24	0.03

1. No significant difference was found by NCSP chlamydia positivity rate ($p=0.93$), LA IMD Index of Multiple Deprivation ($p=0.88$), or the proportion of NCSP services provided by GUM or GP, but the proportion of services provided by CSHS was higher in those LAs using dual tests (19.4% vs 8.6%; ($p<0.01$)).
2. Chlamydia diagnosis rates (per 100,000 population) include diagnoses made in community-based and GUM settings collected through the Chlamydia Test Activity Dataset (CTAD) and the GUM Clinic Activity Dataset (GUMCAD)
3. Chlamydia testing coverage includes tests done in community-based and GUM settings collected through CTAD and the GUM Clinic Activity Dataset (GUMCAD)
4. Gonorrhoea diagnoses (per 100,000 population) include diagnoses made in GUM clinics collected through GUMCAD.

Figure 1 – Mean gonorrhoea (NG) diagnoses per 100,000 population (made in GUM clinics) between 2009-2012 by whether Local Authorities (LA) use dual tests on samples collected by the National Chlamydia Screening Programme



1. Each vertical dash represents a LA, giving the four year average (2009-2012) for gonorrhoea diagnoses (per 100,000 population) for the 98 LAs responding to the survey, including diagnoses made in GUM clinics collected through GUMCAD
2. Boxes shows the median and lower and upper quartiles for four year average gonorrhoea diagnoses in each group

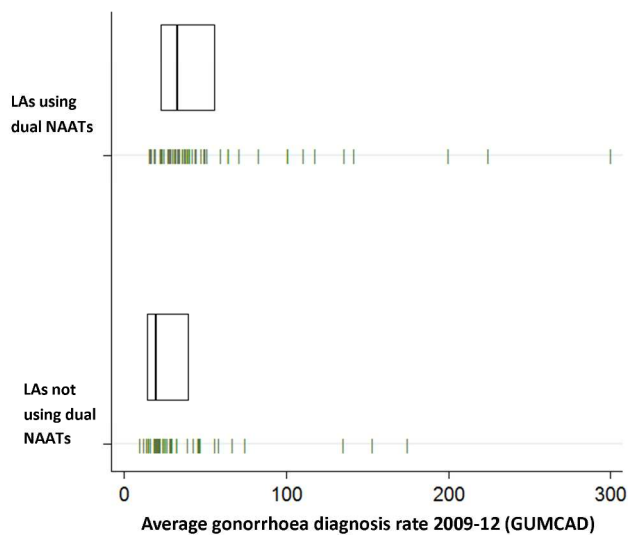
References

- 1 National chlamydia screening programme - NCSP home.
<http://www.chlamydia-screening.nhs.uk/> (accessed 25 Feb2011).
- 2 HPA - CTAD: Chlamydia Testing Activity Dataset.
<http://www.hpa.org.uk/sexualhealth/ctad> (accessed 30 May2014).
- 3 Health and Social Care Act 2012, c.7.
<http://www.legislation.gov.uk/ukpga/2012/7/contents/enacted> (accessed 30 May2014).
- 4 British Association for Sexual Health and HIV. Chlamydia trachomatis UK Testing Guidelines. 2010. <http://www.bashh.org/documents/3352.pdf> (accessed 21 Feb2014).
- 5 Bignell, C J. *Sex Transm Infect* 2007;**83**:179–80.
- 6 Lavelle SJ, Jones KE, Mallinson H, *et al*. Finding, confirming, and managing gonorrhoea in a population screened for chlamydia using the Gen-Probe Aptima Combo2 assay. *Sex Transm Infect* 2006;**82**:221–4. doi:10.1136/sti.2005.017616
- 7 Lavelle SJ, Mallinson H, Henning SJ, *et al*. Impact on gonorrhoea case reports through concomitant/dual testing in a chlamydia screening population in Liverpool. *Sex Transm Infect* 2007;**83**:593–4. doi:10.1136/sti.2007.027870
- 8 Guidance for the detection of gonorrhoea in England; including guidance on the use of dual testing for chlamydia and gonorrhoea. Public Health England © Crown copyright (2014).
- 9 Fifer H, Ison CA. Nucleic acid amplification tests for the diagnosis of Neisseria gonorrhoeae in low-prevalence settings: a review of the evidence. *Sex Transm Infect* 2014.
- 10 Ison C. GC NAATs: is the time right? *Sex Transm Infect* 2006;**82**:515. doi:10.1136/sti.2006.022731
- 11 Sonnenberg P, Clifton S, Beddows S, *et al*. Prevalence, risk factors, and uptake of interventions for sexually transmitted infections in Britain: findings from the National Surveys of Sexual Attitudes and Lifestyles (Natsal). *The Lancet* 2013;**382**:1795–806. doi:10.1016/S0140-6736(13)61947-9
- 12 Public Health England. Health Protection Report. 2013.
<http://www.hpa.org.uk/hpr/archives/2013/hpr2313.pdf> (accessed 6 Feb2014).
- 13 Skidmore S, Copley S, Cordwell D, *et al*. Positive nucleic acid amplification tests for Neisseria gonorrhoeae in young people tested as part of the National Chlamydia Screening Programme. *Int J STD AIDS* 2011;**22**:398–9. doi:10.1258/ijsa.2011.010378
- 14 Fowler T, Edeghere O, Inglis N, *et al*. Estimating the positive predictive value of opportunistic population testing for gonorrhoea as part of the English Chlamydia

- 1
2
3 Screening Programme. *Int J STD AIDS* Published Online First: 20 March 2013.
4 doi:10.1177/0956462412472443
5
6
7 15 Downing J, Cook PA, Madden HCE, *et al.* Management of cases testing positive for
8 gonococcal infection in a community-based chlamydia screening programme. *Sex*
9 *Transm Infect* 2010;**86**:474–7. doi:10.1136/sti.2010.043240
10
11 16 Rao GG, Bacon L, Evans J, *et al.* Prevalence of *Neisseria gonorrhoeae* infection in young
12 subjects attending community clinics in South London. *Sex Transm Infect* 2008;**84**:117–
13 21. doi:10.1136/sti.2007.026914
14
15 17 Benzie A, Alexander S, Gill N, *et al.* Gonococcal NAATs: what is the current state of play
16 in England and Wales? *Int J STD AIDS* 2010;**21**:246–8. doi:10.1258/ijsa.2010.010004
17
18 18 Dayan Y, Paine CS, Johnson AJ. Responding to sensitive questions in surveys: A
19 comparison of results from Online panels, face to face and self-completion interviews.
20 2009. [http://www.ipsos-](http://www.ipsos-mori.com/Assets/Docs/Publications/Ops_RMC_Responding_Sensitive_Questions_08_03_10.pdf)
21 [mori.com/Assets/Docs/Publications/Ops_RMC_Responding_Sensitive_Questions_08_03_](http://www.ipsos-mori.com/Assets/Docs/Publications/Ops_RMC_Responding_Sensitive_Questions_08_03_10.pdf)
22 [10.pdf](http://www.ipsos-mori.com/Assets/Docs/Publications/Ops_RMC_Responding_Sensitive_Questions_08_03_10.pdf) (accessed 21 Feb2014).
23
24
25 19 Public Health England. Genitourinary Medicine Clinic Activity Dataset (GUMCADv2).
26 <http://www.hpa.org.uk/gumcad> (accessed 30 May2014).
27
28
29 20 Gen-Probe products. Aptima Combo 2 product information webpage. [http://www.gen-](http://www.gen-probe.com/products-services/aptima-combo)
30 [probe.com/products-services/aptima-combo](http://www.gen-probe.com/products-services/aptima-combo) (accessed 30 May2014).
31
32 21 Hughes G, Evans BG, Ncube F, *et al.* PHE HIV and STI Data Sharing Policy version 4.
33 2014.http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1247816526850 (accessed
34 27 Jun2014).
35
36
37 22 Payne RA, Abel GA. UK indices of multiple deprivation - a way to make comparisons
38 across constituent countries easier. *Health Stat Q Off Natl Stat* 2012;**53**:22–37.
39
40 23 National Chlamydia Screening Programme, Health Protection Agency. National
41 Chlamydia Screening Programme Standards (6th Edition). 2012.
42 [http://www.chlamydia-screening.nhs.uk/ps/resources/core-](http://www.chlamydia-screening.nhs.uk/ps/resources/core-requirements/NCSP%20Standards%206th%20Edition_October%202012.pdf)
43 [requirements/NCSP%20Standards%206th%20Edition_October%202012.pdf](http://www.chlamydia-screening.nhs.uk/ps/resources/core-requirements/NCSP%20Standards%206th%20Edition_October%202012.pdf)
44
45
46 24 Low N, Unemo M, Skov Jensen J, *et al.* Molecular Diagnostics for Gonorrhoea:
47 Implications for Antimicrobial Resistance and the Threat of Untreatable Gonorrhoea.
48 *PLoS Med* 2014;**11**. doi:10.1371/journal.pmed.1001598
49
50 25 Katz AR, Effler PV, Ohye RG, *et al.* False-positive gonorrhea test results with a nucleic
51 acid amplification test: the impact of low prevalence on positive predictive value. *Clin*
52 *Infect Dis Off Publ Infect Dis Soc Am* 2004;**38**:814–9. doi:10.1086/381895
53
54
55 26 Guidance for the detection of gonorrhoea in England - Publications - GOV.UK.
56 [https://www.gov.uk/government/publications/guidance-for-the-detection-of-](https://www.gov.uk/government/publications/guidance-for-the-detection-of-gonorrhoea-in-england)
57 [gonorrhoea-in-england](https://www.gov.uk/government/publications/guidance-for-the-detection-of-gonorrhoea-in-england) (accessed 27 Aug2014).
58
59
60

- 1
2
3 27 Klausner JD. The NAAT Is Out of the Bag. *Clin Infect Dis* 2004;**38**:820–1.
4 doi:10.1086/381897
5
6 28 Andermann A, Blancquaert I, Beauchamp S, *et al*. Revisiting Wilson and Jungner in the
7 genomic age: a review of screening criteria over the past 40 years. *Bull World Health*
8 *Organ* 2008;**86**.<http://www.who.int/bulletin/volumes/86/4/07-050112/en/>
9
10 29 Tucker JD, Bien CH, Peeling RW. Point-of-care testing for sexually transmitted infections:
11 recent advances and implications for disease control. *Curr Opin Infect Dis* 2013;**26**:73–9.
12 doi:10.1097/QCO.0b013e32835c21b0
13
14 30 Kriesel J, Bhatia A, Vaughn M, *et al*. P3-S5.05 Rapid point of care testing for ten sexually
15 transmitted diseases. *Sex Transm Infect* 2011;**87**:A294–A295. doi:10.1136/sextrans-
16 2011-050108.472
17
18 31 Russek-Cohen E, Feldblyum T, Whitaker KB, *et al*. FDA Perspectives on Diagnostic Device
19 Clinical Studies for Respiratory Infections. *Clin Infect Dis* 2011;**52**:S305–S311.
20 doi:10.1093/cid/cir056
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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract Yes – p.1-2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found Yes
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Yes – p.4
Objectives	3	State specific objectives, including any prespecified hypotheses Yes – p.4-5
Methods		
Study design	4	Present key elements of study design early in the paper Yes – p.5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Yes – p.5
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants Yes – p.5-6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Yes – where applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Yes – see methods and results sections
Bias	9	Describe any efforts to address potential sources of bias N/A
Study size	10	Explain how the study size was arrived at Yes
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Yes – p.5-6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding

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2 (b) Describe any methods used to examine subgroups and interactions

3 N/A

4 (c) Explain how missing data were addressed

5 Yes – p.5

6 (d) *Cohort study*—If applicable, explain how loss to follow-up was addressed

7 *Case-control study*—If applicable, explain how matching of cases and controls was
8 addressed

9 *Cross-sectional study*—If applicable, describe analytical methods taking account of
10 sampling strategy

11 N/A

12 (e) Describe any sensitivity analyses

13 Yes – p.6

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Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed N/A
		(b) Give reasons for non-participation at each stage Yes – p.6
		(c) Consider use of a flow diagram Not required
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Yes – area level characteristics of LAs described
		(b) Indicate number of participants with missing data for each variable of interest Yes – p.6-8
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures Yes
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included N/A
		(b) Report category boundaries when continuous variables were categorized N/A
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses N/A – all data are shown
Discussion		
Key results	18	Summarise key results with reference to study objectives Yes – p. 8-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Yes – p.9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Yes – p.9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results Yes – p.8-11
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

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Yes – p.11-12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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