

Comparison of patients diagnosed with gonorrhoea through community screening with those self-presenting to the genito-urinary medicine clinic

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Title:
Comparison of patients diagnosed with gonorrhoea through community screening with
those self-presenting to the genito-urinary medicine clinic.
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ABSTRACT

Objectives: To compare the clinical, socioeconomic and demographic characteristics of individuals diagnosed with Neisseria gonorrhoea (NG) in the community using concomitant a Nucleic Acid Amplification Test (NAAT, AptimaCombo2) testing as part of the (community-based) United Kingdom Chlamydia Screening Programme (CSP), with those diagnosed in hospital–based Genitourinary Medicine (GUM) services.

Design: A retrospective case note review of all 643 patients treated for NG at a GUM in north west England (01/2007—04/2009).

Participants: All 643 treated for NG (including CSP cases, since all cases were referred to GUM for treatment). Limited data were available for 13 CSP cases who failed to attend GUM.
Primary outcome measure: Whether the case was detected in the community or GUM.
Predictors were demographics (age, gender, postcode for deprivation analysis), sexual history (e.g. number of partners) and clinical factors (e.g. culture positivity).

Results: 131 cases were diagnosed by CSP (13 of whom did not attend GUM). A further 4 cases were contacts of these. The GUM caseload was thus inflated by 23% (from 521 to 643). Community cases were overwhelmingly female (85% vs 27% in GUM, P<0.001) and younger (87% females were <25y vs 70% GUM females, p=0.001). Logistic regression analysis restricted to the target age of the CSP (<25y) revealed that CSP cases, compared to GUM cases, were more likely to reside in deprived areas (adjusted OR =5.6, 95%CI 1.4—21.8 and 5.3, CI 1.7—16.6 for the most and second most deprived group respectively, compared to the averagely deprived group, p= 0.037) and be asymptomatic (adjOR=1.9,CI 1.1—3.4, 0.02).

Conclusion

Community screening for NG led to a 79% increase in the number of infections detected in women aged <25y. Screening is targeted at young people, and tends to disproportionately attract young women, a group under-represented at GUM. Screening also contributed further to case detection in deprived areas.

ARTICLE SUMMARY

Strengths and limitations of this study

- Little attention has been paid to the possibility that screening programmes improve diagnosis in populations that would not traditionally attend GUM. This study fills a gap in knowledge about the socioeconomic status of those identified in the different settings.
- NG cases were over-represented in particular relatively deprived areas of the study area, as shown by geodemographic profiling (the Mosaic tool).
- Community screening for NG contributed extra female cases, asymptomatic male cases and cases from relatively more deprived areas, which may have otherwise remained undetected.
- As a retrospective review of cases, there were no controls, limiting the conclusions from this study.
- The deprivation results and Mosaic groups should be interpreted with caution, since such area-level measures of deprivation may not represent the characteristics of individuals.

INTRODUCTION

Nucleic acid amplification tests (NAATs) have greater sensitivity than culture and are now widely used to diagnose sexually transmitted infections (STIs), including *Neisseria gonorrhoeae* (NG) using non-invasive and easily transportable samples. However, in low prevalence populations where an NG NAAT might not display a positive predictive value exceeding 90%, positive samples are now recommended to be subjected to confirmatory testing.[1]

The UK national Chlamydia Screening Programme (CSP) is an opportunistic screening programme which uses NAATs for *Chlamydia trachomatis* (CT). The programme is targeted at all young people aged under 25 years (although tends to be predominantly taken up by women[2]), and based in community settings such as pharmacies, community contraception clinics, primary care, schools and colleges. Concomitant NAAT screening for both CT and NG (Aptima Combo 2 assay, Gen-Probe Inc, San Diego, CA, USA) using either self-taken or clinician samples was introduced into the study area CSP in 2004 at the same cost as a CT test alone. Cases of NG identified are subsequently referred to the specialist Genitourinary Medicine (GUM) service for parenteral treatment, specialist partner notification and antibiotic sensitivity testing. The overall detection of NG has increased in areas where such an approach has been implemented.[3-5]

Previous studies of NG epidemiology have been based on GUM clinic populations [6-8] and therefore less is known about the characteristics of cases that are detected outside GUM. Such analysis that does exist confirms the characteristics that would be expected based on the target and settings of the screening programme (i.e. young women)[5]. Little attention has been paid to

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the possibility that screening programmes improve diagnosis in populations that would not traditionally attend GUM. This study compares the demographic and clinical profile of NG cases detected by the CSP with that of a GUM clinic population with a specific aim to fill the gap in knowledge about the socioeconomic status of those identified in the different settings.

METHODS

A cross-sectional retrospective case note review was completed of all cases of complicated and uncomplicated NG attending a GUM service between 01/01/07 and 31/03/09, identified from GUM clinic records (using the Sexual Health and HIV Activity Property Type—SHHAPT surveillance report codes). The GUM is located in a large city, adjacent to some of the most deprived areas in England. The referral route was recorded as follows: diagnosed in the openaccess GUM clinic; referred from the CSP; a contact of an NG case; referred from general practice. Demographic data collected included: postcode (to allow allocation of an area-based deprivation measure and use of a postcode classification tool, Mosaic, that uses over 400 data indicators to classify all UK citizens into fifteen population types, 'Mosaic groups'), gender, age (either <25 years, the target age for the CSP, or ≥ 25 years) and ethnicity. Clinical data were: symptoms of NG; NG culture results; CT test result. Clinic policy was for NG culture samples to be recommended as a minimum of one sample per NG from up to four anatomical sites in total: pharynx, rectum, cervix (women only), and urethra. Culture result was recorded as 'positive' if one or more was positive, and 'negative' if all were negative. CT testing was by in-house NAAT on urine samples alone. Sexual history variables included sex between men (although this was poorly completed and thus omitted from the analysis) and number of partners recorded in the previous three months, as per the national guidelines at the time for taking a sexual history [9].

All clinical and behavioural data were collected by the GUM, irrespective of the source of the diagnosis. GUM clinical policy includes routine recommendation of NG culture samples from the urethra and throat in all men with NG, plus a sample from the rectum in men who had sex with men (MSM). For females, NG culture samples are routinely recommended from the cervix, throat and rectum. NG cases were defined as patients who tested positive with NAAT, and adhered to the standards set out by Public Health England [1]. These policies were consistent irrespective of referral route. Patients not referred from the CSP were also tested with the GUM service in house Polymerase Chain Reaction (PCR) NAAT. Basic data (age, gender, postcode) were also available from the CSP for all individuals referred to GUM with a positive NG screening test who then failed to attend for treatment.

Cases were assigned a study number and pseudoanonymised. Postcodes were linked to the lower super output area (LSOA) of residence (a statistical unit representing ~1,500 population) and then to area-level deprivation categories (English quintiles of deprivation, Index of Multiple Deprivation 2007[10]). Only 3% of cases resided in the least deprived two-fifths, so these cases were merged with the averagely deprived category. Firstly, the distribution of NG is displayed by Mosaic group, and compared to the distribution of city's households using chi square goodness of fit tests. Then, the demographic and clinical characteristics of CSP cases were compared with GUM cases using univariate chi square analysis, firstly for all cases and then for <25year-olds (the target age range of the CSP). Cases with missing data were excluded from the analysis (ethnicity missing: 7; missing partner information: 14; symptoms and culture missing: 17. Cases with missing data were predominantly the 13 who were diagnosed by CSP but did not attend the GUM). Logistic regression (SPSS v20), using the source of the cases (CSP or GUM) as the

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outcome, was used to assess independent relationships. The NHS Research Ethics Service approved the study (08/H1002/70).

RESULTS

In total, 656 cases were identified , 131 (20%) of whom were diagnosed as a result of community screening (114 primary cases who attended GUM for treatment, four contacts of primary cases and thirteen who were diagnosed in the community but did not present to GUM for treatment). The community-diagnosed population, and their contacts, together inflated the GUM caseload by 23% (from 521 to 643, not including the 13 who did not present to GUM). Allocation to deprivation group and Mosaic group was possible for 576 (88%) of records. Since the proportion of records with unknown deprivation category was relatively high, and because the probability of missing data in this field is not random (the probability of missing postcode data is related to deprivation and other risk indicators[11]), the missing values were coded as 'deprivation unknown' and retained in the analysis.

Table 1 shows the distribution of NG cases by Mosaic groups. The relatively affluent groups (B, C, D) are at the top of the table (group A, a rural category, does not occur in the study city). The distribution of NG does not follow the expected distribution based on the distribution of all households in the study area (P<0.001 for all cases; P<0.001 for cases in people aged under 25 years). Inspection of the residuals reveals that cases of NG were under represented in the wealthy groups B, C, D and F, and in the average group H. Cases were over-represented in 'N-Young people renting flats in high density social housing' and 'O-Families in low-rise social housing

with high levels of benefit need'. Group O itself is over-represented in the study area (27%) compared to nationally (5%) [12]; in this study, 32% of all cases and 38% of cases in those aged under 25 years of all NG cases resided in 'O'. Numbers of cases in each Mosaic group were too low to compare CSP cases with GUM cases.

Table 1. Distribution of cases of Neisseria gonorrhoea by Mosaic residential category, compared to the distribution of the general
population of the city

Mosaic category		All cases (n=578	3)	Age	Aged under 25y (n=340)			
	N (%)	Expected N (%) ^a	Standardised Residual ^b	N (%)	Expected N ^a	Standardised Residual ^c		
B Residents of small and mid- sized towns with strong local roots	5 (0.86)	11.2 (1.94)	7.69	4 (1.2)	6.6 (1.94)	1.02		
C Wealthy people living in the most sought after neighbourhoods	3 (0.52)	9.7 (1.67)	14.96	3 (0.9)	5.7 (1.67)	1.26		
D Successful professionals living in suburban or semi-rural homes	7 (1.2)	14.4 (2.49)	7.82	5 (1.5)	8.5 (2.49)	1.42		
E Middle income families living in moderate suburban semis	55 (9.45)	61.8 (10.69)	0.84	35 (10.3)	36.3 (10.69)	0.05		
F Couples with young children in comfortable modern housing	6 (1.03)	11.9 (2.05)	5.8	2 (0.6)	7 (2.05)	3.54		
G Young, well-educated city dwellers	66 (11.34)	77.7 (13.45)	2.07	33 (9.7)	45.7 (13.45)	3.55		
H Couples and young singles in small modern starter homes	5 (0.86)	14.5 (2.5)	18.05	3 (0.9)	8.5 (2.5)	3.56		
I Lower income workers in urban terraces in often diverse areas	66 (11.34)	60.2 (10.42)	0.51	39 (11.5)	35.4 (10.42)	0.36		
J Owner occupiers in older-style housing in ex-industrial areas	23 (3.95)	26.8 (4.63)	0.63	14 (4.1)	15.7 (4.63)	0.19		
K Residents with sufficient incomes in right-to-buy social houses	48 (8.25)	43.3 (7.49)	0.46	23 (6.8)	25.5 (7.49)	0.24		

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M Elderly people reliant on state support	23 (3.95)	29.8 (5.16)	2.01	9 (2.6)	17.5 (5.16)	4.16
N Young people renting flats in high density social housing	76 (13.06)	50.9 (8.8)	8.29	35 (10.3)	29.9 (8.8)	0.86
O Families in low-rise social housing with high levels of benefit need	188 (32.3)	155.5 (26.9)	5.62	128 (37.6)	91.5 (26.9)	14.59
U Unclassified	7 (1.2)	10.4 (1.8)	1.65	7 (2.1)	6.1 (1.8)	0.13

 ^aExpected number of cases in each Mosaic category if cases were proportionally distributed to the general population distribution in the city where the clinic is located. Data taken from [12], which cites the Experian Mosaic Public Sector Tool.

^bChi square goodness of fit of observed distribution (cases of gonorrhoea) against expected (general population)=46.9; df=13, P<0.001

^cChi square goodness of fit of observed distribution (cases of gonorrhoea in those aged under 25 years) against expected (general population)=34.9, df =13, P=0.001

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Including all cases, whether attending the GUM for treatment or not (N=656), there were more males diagnosed with NG than females (404 vs 252). The CSP predominantly contributed female cases (111, 85% of cases vs 27% female in GUM, chi square=148.4, P<0.001), leading to a 79% increase on the number of female cases that would have been detected in the absence of the CSP (from 141 to 252). The community cases and their contacts were labelled as 'CSP' to represent the additional cases (n=131). Cases labelled as 'GUM' (n=525) represent those diagnosed at GUM (i.e. 465 self-referrals to the open access clinic, 19 referrals from general practice and 41 contacts). Similar numbers of females were identified by GUM and CSP (table 2). Not surprisingly, given the target age of the screening programme (those under 25 years), the CSP group was younger (87% were aged under 25 years vs 70% GUM, p=0.001). CSP females were more likely to reside in deprived areas compared to GUM females (p=0.014). Overall, only 43% of females had symptoms of NG. Not all cases found positive by NAAT were subsequently found to be positive by culture (overall, 10% of NAAT positive cases were not positive by culture, and this was higher for females, 18%, than males, 5%). Cases found positive by NAAT were treated as NG, as per national guidance [1]. In particular, females diagnosed NAAT positive for NG by the CSP (by Aptima Combo2) were more likely to be culture negative than were females identified NAAT positive by the in-house GUM PCR (25% vs 14% GUM, p=0.028). Of the nineteen male CSP cases who subsequently attended GUM, eight had no symptoms (42%). In contrast, only 12% of those identified through the GUM were symptomless (p<0.001). CT positivity was not significantly associated with setting in NG positive patients,

either for males (20.4% positive at GUM vs 31.6% at CSP; p=0.243) or females (29.8% positive at GUM vs 41.4% positive at CSP, p=0.064).

	Males					Femal	les	Multivariate predictors of those aged <25years being diagnosed by CSP ^d Adj OR (95%		
	GUM	CSP	Chi	Р	GUM	CSP	Chi	Р	CI)	Р
Gender										
Male		-	-	-	-	-	-	-	1	< 0.00
Female	_	-	-	-	-	-	-	-	9.5 (4.7—19.2)	
Age^a (N)	384	20			141	111				
<25 (%)	50.3	85.0	9.2	0.002	69.5	86.5	10.1	< 0.001	e_	
=>25 (%)	49.7	15.0			30.5	13.5				
Ethnicity (N)	379	20			141	109				
Not white (%)	9.8	10.0	< 0.1	1.000	14.9	10.1	1.3	0.34	0.9 (0.4-2.1)	0.86
White (%)	90.2	90.0			85.1	89.9			1	
$IMD \ quintile^b \ (N)$	384	20			141	111				
Average deprivation (%)	7.8	0	1.9	0.577	15.6	3.6	16.4	< 0.001	1	0.03
Fourth most deprived (%)	12.8	10.0			7.8	10.8			5.6 (1.4-21.8)	
Most deprived (%)	67.4	75.0			69.5	66.7			5.3 (1.7—16.6)	
Unknown (%)	12.0	15.0			7.1	18.9			5.6 (1.3–23.8)	
No. Partners ^c (N)	384	19			141	<i>98</i>				
One (%)	21.6	31.6	1.9	0.384	63.8	54.1	3.6	0.165	1	0.24
Two (%)	56.5	57.9			31.2	42.9			1.4 (0.8–2.6)	
Three or more (%)	21.9	10.5			5	3.1			1.0 (0.3—3.1)	
Symptoms (N)	381	19			141	98				
No (%)	11.8	42.1	14.5	< 0.001	53.2	63.3	2.4	0.121	1.9 (1.1—3.4)	0.02
Yes (%)	88.2	57.9			46.8	36.7			1	
Culture (N)	384	18			140	97				
Negative (%)	4.9	0	0.9	0.334	13.6	24.7	4.8	0.028	1	0.37
					15					

Table 2 Demographic and clinical characteristics of cases of Neisseria gonorrhoea diagnosed in the genitourinary medicine (GUM)

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Positive (%)	95.1	100			86.4	75.3			0.7 (0.3—1.5)	
CT status (N)	382	19			141	99				
Negative (%)	79.6	68.4	1.4	0.243	70.2	58.6	3.5	0.064	1	0.442
Positive (%)	20.4	31.6			29.8	41.4			1.3 (0.7–2.2)	

CSP includes primary cases diagnosed in the community and 4 partners diagnosed as a result of contact tracing

GUM includes primary cases, self-referrals, referrals from general practice and partners of primary GUM cases

^aChi square analysis was repeated restricting to <25 year-olds, and results were similar (see text).

^bLeast deprived and second least deprived quintiles were merged with the average deprivation category

^cNumber of partners in previous 3 months

 ^dLogistic regression analysis with source of case as the outcome (CSP=1; GUM=0), restricted to those aged under 25years (n=404) who have complete data for partner number, symptoms and culture history (n=385). Predictor variables: gender, ethnicity, IMD, number of partners, CT status, symptoms (yes or no) and culture (negative or positive). AdjOR are adjusted odds ratios of being diagnosed by the CSP, with 95% confidence intervals.

^eAge was excluded from multivariate analysis because analysis was restricted to <25years.

The CSP targets younger persons aged under 25 years and therefore the univariate chi-square comparisons were repeated restricting to this younger age group in order to compare the profile of younger persons accessing the GUM with those using opportunistic screening. Results were similar to the all-age comparisons: there was no significant difference in the probability of being culture negative between the two settings (chi square=1.714, p=0.130); there was no significant association between CT positivity and setting (chi square=0.2, p=0.650); and men diagnosed in the community remained significantly less likely to have symptoms than younger men diagnosed in the GUM (chi square=4.996, p=0.037). Young females diagnosed in the community remained more likely to reside in deprived areas compared to young female GUM patients (chisquare=16.3, p=0.001). Findings from the univariate analysis were confirmed using multivariate analysis to find independently significant predictors of young people being detected by CSP rather than GUM (table 2). Analysis was restricted to this younger age group and confirmed that CSP cases were much more likely to be female (adjusted OR=9.9, 95% CI 4.9—19.8, P<0.001). After statistically controlling for the effect of gender, CSP cases had a two times higher odds (95% CI 1.1—3.6, P=0.021) of being symptomless and a five times higher odds of residing in the fourth or fifth most deprived quintiles compared to GUM cases (fourth: adj OR=5.4, 95% CI1.4—20.9; fifth: adj OR=5.3, 95% CI 1.7—16.6; P=0.038).

DISCUSSION

As a retrospective review of cases, there were no controls, limiting the conclusions from this study. Data recorded were variable in quality, and in particular there were only restricted data on those who were diagnosed by CSP but did not attend GUM. P-values of the univariate tests should be interpreted with caution since many tests were carried out, thereby increasing the risk of type I errors. The deprivation results and Mosaic groups should be interpreted with caution, since such area-level measures of deprivation may not represent the characteristics of individuals. An example of where area-level descriptors may be less helpful is the excess of cases of NG in those aged under 25 years (i.e. a young group) in areas typified by containing more older residents (the Mosaic group 'M-older people reliant on state support': table 1).

Despite these limitations, we have shown that use of NAATs can greatly increase the number of NG cases detected outside of clinic settings and have obtained epidemiological evidence of the demographic characteristics associated with these additional cases. This study confirms the association of NG with poverty that has been noted in the USA[13] and UK[7], and adds further insight by mapping to the 15 Mosaic groups. More than one third of cases came from a single Mosaic group, which represented deprived communities, and these were disproportionately represented compared to the study area as a whole. Community screening for NG contributed an additional 23% to the GUM caseload. Testing targeted was those aged under 25years, and predominantly attracts women. Although not surprising, this has resulted in a doubling of NG infections detected in women in that age category, and these cases may have remained undetected in the absence of community screening.

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Compared to the age-matched GUM women, the women detected by the CSP were qualitatively different, being yet more likely to reside in deprived areas, suggesting that community screening had accessed a yet more vulnerable population. CSP cases (especially males) were less likely to have symptoms, and therefore presumably less likely to present to clinical services. Although only statistically significant in the small number of males, we found a higher proportion of the community sample were culture negative. NG culture samples were obtained at the GUM clinic according to a strict policy based on gender and sexual history rather than route of referral and thus differences in culture results are unlikely to be the result of different testing practice. Our results support the notion that NG positive samples originating from community sites might more often represent low bacterial load or asymptomatic infection [14 15] although this conclusion is limited by the low sensitivity of bacterial culture for gonorrhea.

Since the data collection for this study was carried out, public policy on CT screening has been updated. The new Public Health Outcome Framework (PHOF) is used to monitor targets to increase the number of diagnoses (in the first instance, with the expectation that the target will be eventually to reduce prevalence)[16]. The major overarching aim of the PHOF is to reduce inequalities in health[17]. Although there are no specific NG targets, our data show that opportunistic CT/NG screening may contribute to reductions in health inequality by disproportionately benefitting lower SES groups. This is in direct contrast to other opportunistic screening programmes, which risk increasing such inequalities (e.g. for breast and cervical cancer[18]). The opportunity, within the CSP, to use low cost testing to detect low level, asymptomatic infections in a wider population has the potential to be an important influence on NG control and may contribute to the government's target to reduce health inequalities.

AUTHOR CONTRIBUTIONS

FA, HM and SS initiated the project. FA, LH-B, MW, KJ and JE-J collected the data. JE-J prepared the ethical review submission. PAC and HM analysed the data. JE-J, PAC and HM interpreted the results and compiled the first draft. All authors contributed to the revision of the manuscript.

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COMPETING INTERESTS

JE-J and HM have received free testing kits from Gen Probe for previous small scale studies (using the *Trichomonas vaginalis* assay). None of the authors have a financial interest in the product or company, and none of the authors have received grants or fees from the company.

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Title:

Comparison of patients diagnosed with gonorrhoea through community screening with those self-presenting to the genito-urinary medicine clinic.

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Running head: Testing for gonorrhoea in the community

Key words: Neisseria gonorrhoeae, Mass Screening, Residence Characteristics,

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ABSTRACT

Objectives: To compare the clinical, socioeconomic and demographic characteristics of individuals diagnosed with Neisseria gonorrhoea (NG) in the community using concomitant a Nucleic Acid Amplification Test (NAAT, AptimaCombo2) testing as part of the (community-based) United Kingdom Chlamydia Screening Programme (CSP), with those diagnosed in hospital–based Genitourinary Medicine (GUM) services.

Design: A retrospective case note review of all 643 patients treated for NG at a GUM in north west England (01/2007—04/2009).

Participants: All 643 treated for NG (including CSP cases, since all cases were referred to GUM for treatment). Limited data were available for 13 CSP cases who failed to attend GUM.
Primary outcome measure: Whether the case was detected in the community or GUM.
Predictors were demographics (age, gender, postcode for deprivation analysis), sexual history (e.g. number of partners) and clinical factors (e.g. culture positivity).

Results: 131 cases were diagnosed by CSP (13 of whom did not attend GUM). A further 4 cases were contacts of these. The GUM caseload was thus inflated by 23% (from 521 to 643).

Community cases were overwhelmingly female (85% vs 27% in GUM, P<0.001) and younger (87% females were <25y vs 70% GUM females, p=0.001). Logistic regression analysis restricted to the target age of the CSP (<25y) revealed that CSP cases, compared to GUM cases, were more likely to reside in deprived areas (adjusted OR =5.6, 95%CI 1.4—21.8 and 5.3, CI 1.7—16.6 for the most and second most deprived group respectively, compared to the averagely deprived group, p= 0.037) and be asymptomatic (adjOR=1.9,CI 1.1—3.4, 0.02).

Conclusion

Community screening for NG led to a 79% increase in the number of infections detected in women aged <25y. Screening is targeted at young people, and tends to disproportionately attract young women, a group under-represented at GUM. Screening also contributed further to case detection in deprived areas.

ARTICLE SUMMARY

Strengths and limitations of this study

- Little attention has been paid to the possibility that screening programmes improve diagnosis in populations that would not traditionally attend GUM. This study fills a gap in knowledge about the socioeconomic status of those identified in the different settings.
- NG cases were over-represented in particular relatively deprived areas of the study area, as shown by geodemographic profiling (the Mosaic tool).
- Community screening for NG contributed extra female cases, asymptomatic male cases and cases from relatively more deprived areas, which may have otherwise remained undetected.
- As a retrospective review of cases, there were no controls, limiting the conclusions from this study.
- The deprivation results and Mosaic groups should be interpreted with caution, since such area-level measures of deprivation may not represent the characteristics of individuals.

INTRODUCTION

Nucleic acid amplification tests (NAATs) have greater sensitivity than culture and are now widely used to diagnose sexually transmitted infections (STIs), including *Neisseria gonorrhoeae* (NG) using non-invasive and easily transportable samples. However, in low prevalence populations where an NG NAAT might not display a positive predictive value exceeding 90%, positive samples are now recommended to be subjected to confirmatory testing.[1]

The UK national Chlamydia Screening Programme (CSP) is an opportunistic screening programme which uses NAATs for *Chlamydia trachomatis* (CT). The programme is targeted at all young people aged under 25 years (although tends to be predominantly taken up by women[2]), and based in community settings such as pharmacies, community contraception clinics, primary care, schools and colleges. Concomitant NAAT screening for both CT and NG (Aptima Combo 2 assay, Gen-Probe Inc, San Diego, CA, USA) using either self-taken or clinician samples was introduced into the study area CSP in 2004 at the same cost as a CT test alone. Cases of NG identified are subsequently referred to the specialist Genitourinary Medicine (GUM) service for parenteral treatment, specialist partner notification and antibiotic sensitivity testing. The overall detection of NG has increased in areas where such an approach has been implemented.[3-5]

Previous studies of NG epidemiology have been based on GUM clinic populations [6-8] and therefore less is known about the characteristics of cases that are detected outside GUM. Such analysis that does exist confirms the characteristics that would be expected based on the target and settings of the screening programme (i.e. young women)[5]. Little attention has been paid to

the possibility that screening programmes improve diagnosis in populations that would not traditionally attend GUM. This study compares the demographic and clinical profile of NG cases detected by the CSP with that of a GUM clinic population with a specific aim to fill the gap in knowledge about the socioeconomic status of those identified in the different settings.

METHODS

A cross-sectional retrospective case note review was completed of all cases of complicated and uncomplicated NG attending a GUM service between 01/01/07 and 31/03/09, identified from GUM clinic records (using the Sexual Health and HIV Activity Property Type-SHHAPTsurveillance report codes). The GUM is located in a large city, adjacent to some of the most deprived areas in England. The referral route was recorded as follows: diagnosed in the openaccess GUM clinic; referred from the CSP; a contact of an NG case; referred from general practice. Demographic data collected included: postcode (to allow allocation of an area-based deprivation measure and use of a postcode classification tool, Mosaic, that uses over 400 data indicators to classify all UK citizens into fifteen population types, 'Mosaic groups'), gender, age (either <25 years, the target age for the CSP, or ≥ 25 years) and ethnicity. Clinical data were: symptoms of NG; NG culture results; CT test result. Clinic policy was for NG culture samples to be recommended as a minimum of one sample per NG from up to four anatomical sites in total: pharynx, rectum, cervix (women only), and urethra. Culture result was recorded as 'positive' if one or more was positive, and 'negative' if all were negative. CT testing was by in-house NAAT on urine samples alone. Sexual history variables included sex between men (although this was poorly completed and thus omitted from the analysis) and number of partners recorded in the previous three months, as per the national guidelines at the time for taking a sexual history [9].

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All clinical and behavioural data were collected by the GUM, irrespective of the source of the diagnosis. GUM clinical policy includes routine recommendation of NG culture samples from the urethra and throat in all men with NG, plus a sample from the rectum in men who had sex with men (MSM). For females, NG culture samples are routinely recommended from the cervix, throat and rectum. NG cases were defined as patients who tested positive with NAAT, and adhered to the standards set out by Public Health England [1]. These policies were consistent irrespective of referral route. Patients not referred from the CSP were also tested with the GUM service in house Polymerase Chain Reaction (PCR) NAAT. Basic data (age, gender, postcode) were also available from the CSP for all individuals referred to GUM with a positive NG screening test who then failed to attend for treatment.

Cases were assigned a study number and pseudoanonymised. Postcodes were linked to the lower super output area (LSOA) of residence (a statistical unit representing ~1,500 population) and then to area-level deprivation categories (English quintiles of deprivation, Index of Multiple Deprivation 2007[10]). Only 3% of cases resided in the least deprived two-fifths, so these cases were merged with the averagely deprived category. Firstly, the distribution of NG is displayed by Mosaic group, and compared to the distribution of city's households using chi square goodness of fit tests. Then, the demographic and clinical characteristics of CSP cases were compared with GUM cases using univariate chi square analysis, firstly for all cases and then for <25year-olds (the target age range of the CSP). Cases with missing data were excluded from the analysis (ethnicity missing: 7; missing partner information: 14; symptoms and culture missing: 17. Cases with missing data were predominantly the 13 who were diagnosed by CSP but did not attend the GUM). Logistic regression (SPSS v20), using the source of the cases (CSP or GUM) as the

outcome, was used to assess independent relationships. The NHS Research Ethics Service approved the study (08/H1002/70).

RESULTS

In total, 656 cases were identified , 131 (20%) of whom were diagnosed as a result of community screening (114 primary cases who attended GUM for treatment, four contacts of primary cases and thirteen who were diagnosed in the community but did not present to GUM for treatment). The community-diagnosed population, and their contacts, together inflated the GUM caseload by 23% (from 521 to 643, not including the 13 who did not present to GUM). Allocation to deprivation group and Mosaic group was possible for 576 (88%) of records. Since the proportion of records with unknown deprivation category was relatively high, and because the probability of missing data in this field is not random (the probability of missing postcode data is related to deprivation and other risk indicators[11]), the missing values were coded as 'deprivation unknown' and retained in the analysis.

Table 1 shows the distribution of NG cases by Mosaic groups. The relatively affluent groups (B, C, D) are at the top of the table (group A, a rural category, does not occur in the study city). The distribution of NG does not follow the expected distribution based on the distribution of all households in the study area (P<0.001 for all cases; P<0.001 for cases in people aged under 25 years). Inspection of the residuals reveals that cases of NG were under represented in the wealthy groups B, C, D and F, and in the average group H. Cases were over-represented in 'N-Young people renting flats in high density social housing' and 'O-Families in low-rise social housing

with high levels of benefit need'. Group O itself is over-represented in the study area (27%) compared to nationally (5%) [12]; in this study, 32% of all cases and 38% of cases in those aged under 25 years of all NG cases resided in 'O'. Numbers of cases in each Mosaic group were too low to compare CSP cases with GUM cases.

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Table 1. Distribution of cases of Neisseria gonorrhoea by Mosaic residential category, compared to the distribution of the general population of the city

Mosaic category		All cases (n=578) Age				=340)
	N (%)	Expected N (%) ^a	Standardised Residual ^b	N (%)	Expected N ^a	Standardised Residual ^c
B Residents of small and mid- sized towns with strong local roots	5 (0.86)	11.2 (1.94)	7.69	4 (1.2)	6.6 (1.94)	1.02
C Wealthy people living in the most sought after neighbourhoods	3 (0.52)	9.7 (1.67)	14.96	3 (0.9)	5.7 (1.67)	1.26
D Successful professionals living in suburban or semi-rural homes	7 (1.2)	14.4 (2.49)	7.82	5 (1.5)	8.5 (2.49)	1.42
E Middle income families living in moderate suburban semis	55 (9.45)	61.8 (10.69)	0.84	35 (10.3)	36.3 (10.69)	0.05
F Couples with young children in comfortable modern housing	6 (1.03)	11.9 (2.05)	5.8	2 (0.6)	7 (2.05)	3.54
G Young, well-educated city dwellers	66 (11.34)	77.7 (13.45)	2.07	33 (9.7)	45.7 (13.45)	3.55
H Couples and young singles in small modern starter homes	5 (0.86)	14.5 (2.5)	18.05	3 (0.9)	8.5 (2.5)	3.56
I Lower income workers in urban terraces in often diverse areas	66 (11.34)	60.2 (10.42)	0.51	39 (11.5)	35.4 (10.42)	0.36
J Owner occupiers in older-style housing in ex-industrial areas	23 (3.95)	26.8 (4.63)	0.63	14 (4.1)	15.7 (4.63)	0.19
K Residents with sufficient incomes in right-to-buy social houses	48 (8.25)	43.3 (7.49)	0.46	23 (6.8)	25.5 (7.49)	0.24

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M Elderly people reliant on state support	23 (3.95)	29.8 (5.16)	2.01	9 (2.6)	17.5 (5.16)	4.16
N Young people renting flats in high density social housing	76 (13.06)	50.9 (8.8)	8.29	35 (10.3)	29.9 (8.8)	0.86
Families in low-rise social housing with high levels of benefit need	188 (32.3)	155.5 (26.9)	5.62	128 (37.6)	91.5 (26.9)	14.59
U Unclassified	7 (1.2)	10.4 (1.8)	1.65	7 (2.1)	6.1 (1.8)	0.13

^aExpected number of cases in each Mosaic category if cases were proportionally distributed to the general population distribution in the city where the clinic is located. Data taken from [12], which cites the Experian Mosaic Public Sector Tool.

^bChi square goodness of fit of observed distribution (cases of gonorrhoea) against expected (general population)=46.9; df=13, P<0.001

^cChi square goodness of fit of observed distribution (cases of gonorrhoea in those aged under 25 years) against expected (general population)=34.9, df =13, P=0.001

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Including all cases, whether attending the GUM for treatment or not (N=656), there were more males diagnosed with NG than females (404 vs 252). The CSP predominantly contributed female cases (111, 85% of cases vs 27% female in GUM, chi square=148.4, P<0.001), leading to a 79% increase on the number of female cases that would have been detected in the absence of the CSP (from 141 to 252). The community cases and their contacts were labelled as 'CSP' to represent the additional cases (n=131). Cases labelled as 'GUM' (n=525) represent those diagnosed at GUM (i.e. 465 self-referrals to the open access clinic, 19 referrals from general practice and 41 contacts). Similar numbers of females were identified by GUM and CSP (table 2). Not surprisingly, given the target age of the screening programme (those under 25 years), the CSP group was younger (87% were aged under 25 years vs 70% GUM, p=0.001). CSP females were more likely to reside in deprived areas compared to GUM females (p=0.014). Overall, only 43% of females had symptoms of NG. Not all cases found positive by NAAT were subsequently found to be positive by culture (overall, 10% of NAAT positive cases were not positive by culture, and this was higher for females, 18%, than males, 5%). Cases found positive by NAAT were treated as NG, as per national guidance [1]. In particular, females diagnosed NAAT positive for NG by the CSP (by Aptima Combo2) were more likely to be culture negative than were females identified NAAT positive by the in-house GUM PCR (25% vs 14% GUM, p=0.028). Of the nineteen male CSP cases who subsequently attended GUM, eight had no symptoms (42%). In contrast, only 12% of those identified through the GUM were symptomless (p<0.001). CT positivity was not significantly associated with setting in NG positive patients,

either for males (20.4% positive at GUM vs 31.6% at CSP; p=0.243) or females (29.8% positive
at GUM vs 41.4% positive at CSP, p=0.064).
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		Males				Fema	les	Multivariate predictors of those aged <25years being diagnosed by CSP ^d Adj OR (95%		
	GUM	CSP	Chi	Р	GUM	CSP	Chi	Р	CI)	Р
Gender										
Male	_	-	-	-	-	-	-	-	1	< 0.001
Female	-	-	-	-	-	-	-	-	9.5 (4.7—19.2)	
Age^{a} (N)	384	20			141	111				
<25 (%)	50.3	85.0	9.2	0.002	69.5	86.5	10.1	< 0.001	e_	
=>25 (%)	49.7	15.0			30.5	13.5				
Ethnicity (N)	379	20			141	109				
Not white (%)	9.8	10.0	<0.1	1.000	14.9	10.1	1.3	0.34	0.9 (0.4-2.1)	0.866
White (%)	90.2	90.0			85.1	89.9			1	
$IMD \ quintile^b \ (N)$	384	20			141	111				
Average deprivation (%)	7.8	0	1.9	0.577	15.6	3.6	16.4	< 0.001	1	0.037
Fourth most deprived (%)	12.8	10.0			7.8	10.8			5.6 (1.4-21.8)	
Most deprived (%)	67.4	75.0			69.5	66.7			5.3 (1.7—16.6)	
Unknown (%)	12.0	15.0			7.1	18.9			5.6 (1.3–23.8)	
No. Partners ^c (N)	384	19			141	98				
One (%)	21.6	31.6	1.9	0.384	63.8	54.1	3.6	0.165	1	0.244
Two (%)	56.5	57.9			31.2	42.9			1.4 (0.8–2.6)	
Three or more (%)	21.9	10.5			5	3.1			1.0 (0.3-3.1)	
Symptoms (N)	381	19			141	98				
No (%)	11.8	42.1	14.5	< 0.001	53.2	63.3	2.4	0.121	1.9 (1.1-3.4)	0.02
Yes (%)	88.2	57.9			46.8	36.7			1	
Culture (N)	384	18			140	97				
Negative (%)	4.9	0	0.9	0.334	13.6	24.7	4.8	0.028	1	0.370
					15					

Table 2. Demographic and clinical characteristics of cases of Neisseria gonorrhoea diagnosed in the genitourinary medicine (GUM) service compared with those identified as a result of the Chlamydia Screening Programme (CSP), by gender.

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Positive (%)	95.1	100			86.4	75.3			0.7 (0.3—1.5)	
CT status (N)	382	19			141	<i>99</i>				
Negative (%)	79.6	68.4	1.4	0.243	70.2	58.6	3.5	0.064	1	0.442
Positive (%)	20.4	31.6			29.8	41.4			1.3 (0.7–2.2)	

CSP includes primary cases diagnosed in the community and 4 partners diagnosed as a result of contact tracing

GUM includes primary cases, self-referrals, referrals from general practice and partners of primary GUM cases

^aChi square analysis was repeated restricting to <25year-olds, and results were similar (see text).

^bLeast deprived and second least deprived quintiles were merged with the average deprivation category

^cNumber of partners in previous 3 months

^dLogistic regression analysis with source of case as the outcome (CSP=1; GUM=0), restricted to those aged under 25years (n=404) who have complete data for partner number, symptoms and culture history (n=385). Predictor variables: gender, ethnicity, IMD, number of partners, CT status, symptoms (yes or no) and culture (negative or positive). AdjOR are adjusted odds ratios of being diagnosed by the CSP, with 95% confidence intervals.

^eAge was excluded from multivariate analysis because analysis was restricted to <25years.

The CSP targets younger persons aged under 25 years and therefore the univariate chi-square comparisons were repeated restricting to this younger age group in order to compare the profile of younger persons accessing the GUM with those using opportunistic screening. Results were similar to the all-age comparisons: there was no significant difference in the probability of being culture negative between the two settings (chi square=1.714, p=0.130); there was no significant association between CT positivity and setting (chi square=0.2, p=0.650); and men diagnosed in the community remained significantly less likely to have symptoms than younger men diagnosed in the GUM (chi square=4.996, p=0.037). Young females diagnosed in the community remained more likely to reside in deprived areas compared to young female GUM patients (chisquare=16.3, p=0.001). Findings from the univariate analysis were confirmed using multivariate analysis to find independently significant predictors of young people being detected by CSP rather than GUM (table 2). Analysis was restricted to this younger age group and confirmed that CSP cases were much more likely to be female (adjusted OR=9.9, 95% CI 4.9—19.8, P<0.001). After statistically controlling for the effect of gender, CSP cases had a two times higher odds (95% CI 1.1—3.6, P=0.021) of being symptomless and a five times higher odds of residing in the fourth or fifth most deprived quintiles compared to GUM cases (fourth: adj OR=5.4, 95%) CI1.4—20.9; fifth: adj OR=5.3, 95% CI 1.7—16.6; P=0.038).

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DISCUSSION

As a retrospective review of cases, there were no controls, limiting the conclusions from this study. Data recorded were variable in quality, and in particular there were only restricted data on those who were diagnosed by CSP but did not attend GUM. P-values of the univariate tests should be interpreted with caution since many tests were carried out, thereby increasing the risk of type I errors. The deprivation results and Mosaic groups should be interpreted with caution, since such area-level measures of deprivation may not represent the characteristics of individuals. An example of where area-level descriptors may be less helpful is the excess of cases of NG in those aged under 25 years (i.e. a young group) in areas typified by containing more older residents (the Mosaic group 'M-older people reliant on state support': table 1).

Despite these limitations, we have shown that use of NAATs can greatly increase the number of NG cases detected outside of clinic settings and have obtained epidemiological evidence of the demographic characteristics associated with these additional cases. This study confirms the association of NG with poverty that has been noted in the USA[13] and UK[7], and adds further insight by mapping to the 15 Mosaic groups. More than one third of cases came from a single Mosaic group, which represented deprived communities, and these were disproportionately represented compared to the study area as a whole. Community screening for NG contributed an additional 23% to the GUM caseload. Testing targeted was those aged under 25years, and predominantly attracts women. Although not surprising, this has resulted in a doubling of NG infections detected in women in that age category, and these cases may have remained undetected in the absence of community screening.

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Compared to the age-matched GUM women, the women detected by the CSP were qualitatively different, being yet more likely to reside in deprived areas, suggesting that community screening had accessed a yet more vulnerable population. CSP cases (especially males) were less likely to have symptoms, and therefore presumably less likely to present to clinical services. Although only statistically significant in the small number of males, we found a higher proportion of the community sample were culture negative. NG culture samples were obtained at the GUM clinic according to a strict policy based on gender and sexual history rather than route of referral and thus differences in culture results are unlikely to be the result of different testing practice. Our results support the notion that NG positive samples originating from community sites might more often represent low bacterial load or asymptomatic infection [14 15] although this conclusion is limited by the low sensitivity of bacterial culture for gonorrhea.

Since the data collection for this study was carried out, public policy on CT screening has been updated. The new Public Health Outcome Framework (PHOF) is used to monitor targets to increase the number of diagnoses (in the first instance, with the expectation that the target will be eventually to reduce prevalence)[16]. The major overarching aim of the PHOF is to reduce inequalities in health[17]. Although there are no specific NG targets, our data show that opportunistic CT/NG screening may contribute to reductions in health inequality by disproportionately benefitting lower SES groups. This is in direct contrast to other opportunistic screening programmes, which risk increasing such inequalities (e.g. for breast and cervical cancer[18]). The opportunity, within the CSP, to use low cost testing to detect low level, asymptomatic infections in a wider population has the potential to be an important influence on NG control and may contribute to the government's target to reduce health inequalities.

AUTHOR CONTRIBUTIONS

FA, HM and SS initiated the project. FA, LH-B, MW, KJ and JE-J collected the data. JE-J prepared the ethical review submission. PAC and HM analysed the data. JE-J, PAC and HM interpreted the results and compiled the first draft. All authors contributed to the revision of the manuscript.

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COMPETING INTERESTS

JE-J and HM have received free testing kits from Gen Probe for previous small scale studies (using the *Trichomonas vaginalis* assay). None of the authors have a financial interest in the product or company, and none of the authors have received grants or fees from the company.

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	Item No	Recommendation	Reported on page #
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or	4
		the abstract	
		(b) Provide in the abstract an informative and balanced summary of what	4
Introduction		was done and what was found	
Background/rationale	2	Explain the scientific background and rationale for the investigation being	6
Background/rationale	2	reported	0
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of	7
		recruitment, exposure, follow-up, and data collection	
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection	7
		of participants	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders,	7-8
		and effect modifiers. Give diagnostic criteria, if applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of methods	7-8
measurement		of assessment (measurement). Describe comparability of assessment	
		methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	8
Quantitative	11	Explain how quantitative variables were handled in the analyses. If	8
variables		applicable, describe which groupings were chosen and why	
Statistical methods	12	(<i>a</i>) Describe all statistical methods, including those used to control for confounding	8-9
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	8
		(<i>d</i>) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers	9 and
I		potentially eligible, examined for eligibility, confirmed eligible, included	Tables
		in the study, completing follow-up, and analysed	1 and 2
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical,	8 and
*		social) and information on exposures and potential confounders	Tables
			1 and 2
		(b) Indicate number of participants with missing data for each variable of	8 and
		interest	Table 2
Outcome data	15*	Report numbers of outcome events or summary measures	8 and
			Table 2
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted	Table 2

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		estimates and their precision (eg, 95% confidence interval). Make clear	
		which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were	Table 2
		categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute	N/A
		risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	18—19
Limitations	19	Discuss limitations of the study, taking into account sources of potential	18
		bias or imprecision. Discuss both direction and magnitude of any potential	
		bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives,	18—19
		limitations, multiplicity of analyses, results from similar studies, and other	
		relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study	20
		and, if applicable, for the original study on which the present article is	
		based	

*Give information separately for exposed and unexposed groups.

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.