

Identification of individuals with gonorrhoea within sexual networks: a population-based study

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Background Molecular typing of *Neisseria gonorrhoeae* and contact tracing provide a combined approach for analysis of sexual networks in metropolitan areas, although there are some difficulties in application. Our aim was to examine the application of high-throughput molecular approaches that can identify individuals in linked sexual networks.

Methods We characterised 2045 isolates of *N gonorrhoeae* from patients presenting at 13 major sexually transmitted infection clinics in London, UK, between June 1 and Nov 30, 2004. All isolates were assigned a sequence type (strain) on the basis of the sequences of internal fragments of two highly polymorphic loci, *por* and *thpB*. These types were matched to demographic and behavioural data obtained at the clinic for each patient. We assessed the congruence in the demographic and behavioural characteristics of individuals infected with the same strain.

Findings We identified 21 prevalent strains in this diverse gonococcal population, each infecting between 20 and 124 individuals. Seven of these strains were predominantly from men who have sex with men; the remaining 14 were predominantly from heterosexual people. No differences were recorded between the strains associated with men who have sex with men in the demographic or behavioural characteristics of infected individuals. By contrast, significant differences in age ($p < 0.0001$), ethnicity ($p = 0.001$), proportion of women ($p = 0.01$), and HIV status ($p = 0.03$) were noted between the 14 prevalent heterosexual-associated strains. Heterosexuals with strains not shared by others in the sample were significantly older ($p = 0.0005$) and more likely to have had sex outside the UK ($p < 0.0001$) than those sharing a strain with at least one other.

Interpretation The discriminatory high throughput strain characterisation method applied here identified localised transmission networks and suggests little bridging between networks of men who have sex with men and heterosexual networks.

Introduction

The incidence of sexually transmitted infections (STIs) has risen substantially in the UK over the past decade, increasing the pressure on genitourinary services and resulting in increased morbidity.¹ This increase has been attributed to changes in sexual behaviour and risk-taking, together with increasing delays in access to treatment due to a crisis in sexual health service provision.^{1,2} The prompt identification of cases of bacterial STIs and the notification and treatment of their sexual contacts (either through provider-led contact tracing or patient-led partner notification) has been the main public-health measure implemented to reduce infection.³ Identification and understanding of the nature of local sexual networks can help to target interventions towards places and people who are most at risk,^{3,4} but is difficult, especially in major cities.^{5,6}

In London, UK, there are 32 genitourinary medicine clinics that are open access, require no referral, and provide free treatment for STIs. These clinics should provide fast and effective diagnosis and treatment to break transmission. However, the incidence of gonococcal infection remains high, and London has a disproportionate burden (45–50%) of all cases diagnosed in England and Wales.¹ Gonorrhoea incidence in London rose sharply from the mid-1990s onwards, and only started to level off from 2003. Overall, gonorrhoea diagnoses fell by 11% from 2003 to 2004, with the most pronounced decrease

occurring in heterosexual men and women. By contrast, diagnoses in men who have sex with men increased by 7% over the same period.¹ Interventions to control STIs in London and many other major metropolitan areas are challenging; exhaustive contact tracing is unrealistic because patients may present to many different clinics, patients are unwilling or unable to identify many sexual partners, some of whom are anonymous, and partner notification in travellers and migrants to identify overseas partners might be difficult. Partner notification data therefore provide incomplete information on the nature and size of the major sexual networks, which limits attempts to control endemic infection.

Molecular epidemiology has been widely used to analyse outbreaks of disease in hospitals and the community⁷ and, for STIs, has the potential to identify individuals within the same sexual network.⁸ Provided that the molecular typing procedure is highly discriminatory, individuals who are not epidemiologically linked should be shown to be infected with different strains, whereas sexual contacts, and those within the same sexual network, should be shown to be infected with the same strain.⁸ For gonorrhoea, valuable information about the nature and size of sexual networks has been obtained by combining molecular typing with epidemiological data on sexual networks obtained through contact tracing, and this approach has elucidated sexual networks that would otherwise remain hidden. This approach has also identified larger networks

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than indicated by epidemiological data alone.^{9–11} However, so far the utility of molecular typing data to inform control has not been tested, mainly because data collection and analysis have been done retrospectively, and has not been attempted in a large metropolitan area with high rates of gonorrhoea.

We report here the use of a highly discriminatory typing method, *Neisseria gonorrhoeae* multi-antigen sequence typing (NG-MAST), which has been shown to identify epidemiologically linked individuals, but to distinguish between patients with no links.¹² The aim of this study was to test the feasibility of characterising isolates from a large proportion of cases of gonorrhoea in a metropolitan area and to identify clusters of linked patients in the absence of contact tracing data.

Methods

Data collection and strain characterisation

Under the auspices of the national Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP), *N gonorrhoeae* isolates and demographic, clinical, and behavioural data were obtained from consecutive patients attending 13 major STI clinics, covering 77% of all reported cases of gonorrhoea in London between June 1 and Nov 30, 2004. Primary isolation and identification of gonococcal isolates was done at each referring laboratory and one isolate from every patient sent to a central laboratory for molecular typing.¹³ NG-MAST was used for precise strain characterisation since it is rapid, highly discriminatory, and allows the unambiguous recognition of indistinguishable isolates in different patients.¹² Isolates were assigned as the same strain (or sequence type) if they had identical nucleotide sequences at the two highly polymorphic loci (*por* and *tbpB*) used in NG-MAST. Epidemiological data were recorded on standardised data collection forms by the individual clinics from case notes and included sex, age, sexual orientation (based on recent reported sexual behaviour), ethnicity, the first four characters of the postcode, HIV status, past history of gonorrhoea, site of infection, information on symptoms, concurrent STIs, antibiotic treatment, numbers of partners in the previous 3 months in the UK and elsewhere, and location of sexual contact outside the UK. The epidemiological data were matched to the isolates with a clinic identifier, clinic number, and date of isolation.

Statistical analysis

The diversity of strains in the sample was calculated with Simpson's index of diversity¹⁴ (*D*) given by:

$$D = 1 - \frac{\sum_{i=1}^{ST} p_i(p_i - 1)}{N(N - 1)}$$

where *p_i* is the proportion of strains with sequence type *i*, *ST* is the number of sequence types, and *N* is the number of isolates. Differences in the epidemiological characteristics between populations of men who have sex with

men, heterosexual men, and women were tested with χ^2 tests for categorical variables and the Wilcoxon rank test for continuous variables.

We focused on the 21 strains recovered from at least 20 individuals (strain clusters), to assess the extent to which epidemiological characteristics were shared by those infected with the same gonococcal strain. The strain clusters were defined as either men who have sex with men associated or heterosexual associated on the basis of the proportion of infected individuals reporting each sexual orientation; 75% or more men who have sex with men were defined as men who have sex with men associated, and 75% or more heterosexual as heterosexual associated. We included all characteristics as categorical variables, with age categorised as the proportion under 25 years and sexual behaviour as the proportion reporting five or more partners in the previous 3 months. Differences in epidemiological characteristics between the clusters were assessed with χ^2 tests.

To further assess the epidemiological significance of the strain clusters, we tested for differences in the characteristics of those who shared their strain with one or more other patients in the sample compared with those with unique strains. Since sexual orientation proved to be associated with differences in all other characteristics, the data were analysed separately for populations of men who have sex with men (including some men identifying as bisexual), heterosexual men, and women (including a few women reported as bisexual). We did univariate and multivariate analyses using logistic regression. All statistical analyses were undertaken with SAS (version 9; Cary, NC, USA).

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

A total of 2891 isolates of *N gonorrhoeae* were gathered from 13 clinics during 6 months, of which 2345 (81%) were successfully recovered and characterised by NG-MAST. Epidemiological data about the patients were available for 87% of these isolates, resulting in 2045 infections where strain characterisation and epidemiological data could be merged. 1539 cases (75%) were in men, 762 (50%) of whom were men who have sex with men. The demographic characteristics of the population (table 1) mirror those recorded in previous studies, with most cases in young heterosexual men and women of black ethnicity and in older white men who have sex with men.¹ The most common concurrent STI was chlamydia, which was most frequent in the

	MSM/bisexual	Heterosexual men	Women	Men of unknown sexual orientation	Test for difference between MSM and heterosexuals (p value)*	Test for difference between heterosexual men and women (p value)*
Number	762	724	506	53		
Median age (years, range)	32 (16–72)	26 (16–68)	22 (13–59)	32 (14–57)	<0.0001	<0.0001
Ethnicity					<0.0001	0.0002
Black Caribbean/black African/other black	66 (9%)	443 (61%)	252 (50%)	22 (42%)		
White British/white Irish/other white	576 (76%)	145 (20%)	127 (25%)	7 (13%)		
Other†	70 (9%)	57 (8%)	38 (8%)	4 (8%)		
Not recorded	50 (7%)	79 (11%)	89 (18%)	20 (38%)		
Concurrent STI (excluding HIV)‡					<0.0001§	0.56§
Chlamydia	42 (6%)	164 (23%)	143 (28%)	6 (11%)		
Syphilis	13 (2%)	4 (1%)	4 (1%)	1 (2%)		
Herpes	2 (0.3%)	4 (1%)	5 (1%)	0		
Genital warts	6 (1%)	7 (1%)	4 (1%)	0		
Other	72 (9%)	58 (8%)	20 (4%)	2 (4%)		
None	537 (71%)	441 (61%)	266 (53%)	31 (59%)		
Not recorded	91 (12%)	54 (8%)	74 (15%)	11 (21%)		
Previous gonorrhoea					<0.0001	<0.0001
Yes	323 (42%)	207 (29%)	79 (16%)	14 (26%)		
No	369 (48%)	450 (62%)	367 (73%)	19 (36%)		
Not known	70 (9%)	67 (9%)	60 (12%)	20 (38%)		
Discharge/dysuria at presentation					0.54	<0.0001
Yes	552 (72%)	618 (85%)	278 (55%)	32 (60%)		
No	164 (22%)	68 (9%)	179 (35%)	4 (8%)		
Not known	46 (6%)	38 (5%)	49 (10%)	17 (32%)		
HIV status					<0.0001	0.05
Positive	198 (26%)	8 (1%)	0	11 (21%)		
Negative	369 (48%)	334 (46%)	247 (49%)	12 (23%)		
Unknown	195 (26%)	382 (53%)	259 (51%)	30 (57%)		
Median number of UK partners in previous 3 months (range)	2 (0–720)	2 (0–30)	1 (0–100)	2 (0–22)	<0.0001	<0.0001
Median number of overseas partners in previous 3 months (range)	0 (0–600)	0 (0–120)	0 (0–700)	0 (0–8)	<0.0001	0.004

MSM=men who have sex with men. *p values for univariate comparisons between populations of men who have sex with men and heterosexuals, and the heterosexual men and women populations. p values are reported from χ^2 tests for categorical variables and Kruskal-Wallis rank tests for continuous variables. †Other ethnicity includes Bangladeshi, Chinese, other Asian, Indian, Pakistani, and other ethnic groups. ‡More than one concurrent STI in some individuals. §p value reports test for reporting some vs no concurrent STIs. Percentages do not add up to 100% because of rounding.

Table 1: Demographic, behavioural, and clinical characteristics of all patients where strain characterisation and epidemiological data were available (n=2045)

heterosexual population. HIV prevalence in the overall population was 11% with significantly higher prevalence in the men who have sex with men than in heterosexual men and women (table 1).

There were 449 distinct gonococcal strains in the 2045 patient isolates, with 252 strains (56%) only recorded once in 6 months. Simpson's index of diversity (the probability that two randomly selected isolates differ in genotype) was 0.98. There was a strong correlation between the sexual orientation of those sharing a strain, with 71% of the 197 strains shared by two or more individuals recovered exclusively from either men who have sex with men or heterosexuals (86% of these were from groups of individuals who were at least 80% of a single sexual orientation), with the remaining 29% of strains seen in both men who have sex with men and heterosexuals (figure 1).

21 strains were shared by 20 or more individuals and represent 956 cases (47% of total cases; table 2). Individuals sharing these prevalent strains were divided by sexual orientation, with seven strain clusters almost exclusively from men (96–100%) with 77% or more declaring themselves men who have sex with men, and the remaining 14 clusters containing 94% or more individuals reported as heterosexual (table 2). In clusters associated with men who have sex with men, there were no differences in the demographic, clinical, or behavioural characteristics of individuals infected with different strains (table 2), illustrating the homogeneous population of men who have sex with men that acquire gonorrhoea. However, in the heterosexual population there were significant differences between strain clusters in the proportion of women, white ethnicity, under 25 years of age, and of unknown HIV status (table 2). Although the larger clusters

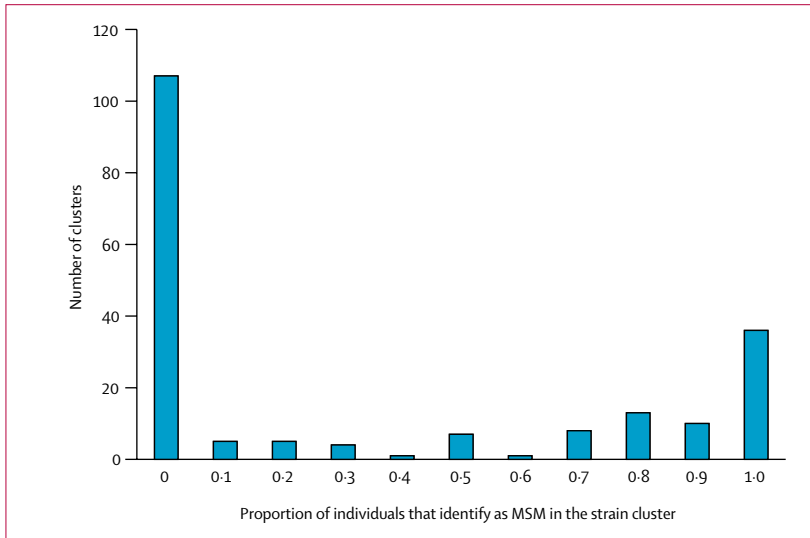


Figure 1: The proportion of patients who are men who have sex with men for each strain cluster
 For values of 0 all individuals within a strain cluster are heterosexual while for values of 1 all individuals are men who have sex with men (or bisexual men). All 197 strains infecting at least two individuals were included; 103 strains were exclusively from heterosexuals and 36 exclusively from men who have sex with men. MSM=men who have sex with men.

generally persist over the 6 months of the study and hence may represent endemic gonorrhoea, other smaller clusters appear and disappear within a shorter time and may represent local outbreaks (figure 2).

No significant differences were recorded between patients with unique strains and those in larger clusters in the men who have sex with men population (table 3). However, in the heterosexual population, being aged 25 years or over and reporting sex outside the UK significantly increased the odds of having a unique strain (table 3). Additionally, those of black ethnicity were significantly less likely to have a unique strain than were those of white ethnicity, and those known to be HIV negative were significantly more likely to have a unique strain compared with those whose HIV status was unknown (table 3). Patients reporting no symptoms were significantly less likely to have a unique strain compared with those reporting symptoms.

Discussion

We have shown that large clusters and newly emerging strains can be identified in a timely manner with the use of discriminatory strain typing in a major metropolitan area with high rates of gonorrhoea. Receipt of sample by

	Number	Women	MSM	Under 25 years	White ethnicity	Five or more partners in previous 3 months	Past gonorrhoea	Concurrent STI	Known HIV positive	Unknown HIV status	With symptoms	Number of clinics reporting strain
MSM-associated sequence types												
40	71	4.2%	84.5%	15.5%	74.7%	31.0%	43.7%	28.2%	28.2%	28.2%	62.0%	13
64	51	3.9%	78.4%	13.7%	58.8%	29.4%	37.3%	17.7%	17.7%	24.5%	72.6%	11
147	50	0%	86.0%	14.0%	64.0%	28.0%	28.0%	26.0%	28.0%	32.0%	68.0%	10
210	86	0%	89.5%	11.6%	65.1%	22.1%	40.7%	17.4%	18.6%	29.1%	76.7%	12
225	124	2.4%	91.9%	21.0%	75.0%	21.0%	42.7%	18.6%	25.0%	30.7%	73.4%	12
359	30	3.3%	76.7%	23.3%	76.7%	33.3%	43.3%	10.0%	26.7%	30.0%	73.3%	8
547	22	0%	81.8%	13.6%	68.2%	13.6%	31.8%	9.1%	27.3%	18.2%	68.2%	9
χ ² p value	NA	0.41	0.14	0.54	0.27	0.40	0.58	0.21	0.69	0.94	0.54	NA
Heterosexual-associated sequence types												
2	102	43.1%	5.9%	53.0%	30.4%	2.9%	21.6%	40.2%	1.0%	53.0%	72.6%	13
6	27	37.0%	0%	48.2%	14.8%	18.5%	25.9%	25.9%	0%	48.1%	74.1%	8
8	38	50.0%	0%	44.8%	10.5%	7.9%	18.4%	29.0%	0%	73.7%	76.3%	7
19	24	25.0%	0%	83.3%	16.7%	8.3%	25.0%	41.7%	0%	62.5%	70.8%	9
25	35	42.9%	2.9%	60.0%	2.9%	2.9%	20.0%	42.9%	0%	54.3%	74.3%	8
33	20	60.0%	0%	95.0%	25.0%	5.0%	20.0%	20.0%	0%	30.0%	55.0%	9
51	62	46.8%	1.6%	51.6%	11.3%	8.1%	27.4%	35.5%	0%	51.6%	54.8%	10
224	41	41.5%	0%	63.4%	17.1%	0%	29.3%	29.3%	0%	58.5%	78.1%	8
356	35	77.1%	0%	60.0%	11.4%	5.7%	14.3%	37.1%	0%	48.6%	62.9%	11
367	26	26.9%	0%	7.7%	11.5%	11.5%	34.6%	15.4%	0%	57.7%	88.5%	7
374	20	35.0%	0%	65.0%	5.0%	5.0%	20.0%	35.0%	0%	30.0%	75.0%	4
387	42	40.5%	0%	71.4%	4.5%	11.9%	31.0%	26.2%	0%	61.9%	66.7%	6
615	24	37.5%	0%	4.4%	4.2%	4.2%	16.7%	29.2%	0%	70.8%	66.7%	3
619	26	42.3%	3.8%	53.9%	23.1%	3.9%	23.1%	26.9%	0%	38.5%	69.2%	8
χ ² p value	NA	0.01	0.22	<0.0001	0.001	0.21	0.84	0.44	0.99	0.03	0.18	NA

MSM=men who have sex with men. NA=not applicable. Bold type indicates comparisons between strains that are significant at the 5% level.

Table 2: Characteristics of the 21 strains identified by sequence type in 20 or more individuals

the clinic to strain assignment can be achieved within 2 weeks, and the use of NG-MAST provided data that were far easier to analyse than those in previous studies with opa-typing.^{9,15}

NG-MAST showed wide diversity in the gonococcal population, confirming the high level of strain discrimination noted with NG-MAST in previous smaller studies in London.¹² These results are also consistent with previous findings in London with opa-typing.⁹ Clusters of patients infected with the same strain showed similarities in behavioural and demographic features, which lends support to the view that NG-MAST has the appropriate level of discrimination to identify individuals who are part of the same sexual network. The strongest evidence for this assertion is provided by the congruence between sexual orientation of those infected by the same strain, since to find a convincing alternative reason for this highly significant association is hard. This view is also lent support by analysis by NG-MAST of isolates from known sexual contacts that shows they are infected with the same strain, although in some heterosexual and men who have sex with men sexual networks two strains circulate, presumably due to mixed infection (N Bilek, CAI, and BGS, unpublished data). Mixed infections will result in some individuals within a sexual network being missed with molecular methods, but even exhaustive contact tracing only identifies some of the individuals within a sexual network,⁹⁻¹¹ especially in large metropolitan areas.

NG-MAST seems to identify linked individuals in London, and 44% of strains were shared by at least two individuals. Several large strain clusters were identified that presumably represent major endemic strains circulating within networks of men who have sex with men and heterosexuals. About 57% of men who have sex with men were infected with the seven major strains associated with men who have sex with men, with 42% of heterosexuals infected with the 14 major heterosexual-associated strains. The significant demographic and behavioural differences in individuals infected with the different heterosexual-associated strains lend support to the hypothesis that the different strain clusters represent localised transmission clusters and allow distinctive sexual networks to be identified. The variation in the proportion of women in different heterosexual-associated clusters could in some cases indicate selection bias if women attended health-care settings not included in the survey, or sex-work-associated outbreaks, although this second possibility would not be consistent with recent research on the relatively low risk of gonorrhoea in women sex workers in London.¹⁶

Many of the 252 strains recovered only once are probably due to importation, although in some cases partners might have been missed if they attended clinics outside the study or other health-care providers. Attendance at other health-care providers probably does not represent many cases, since about 90% of gonorrhoea is diagnosed in genitourinary medicine

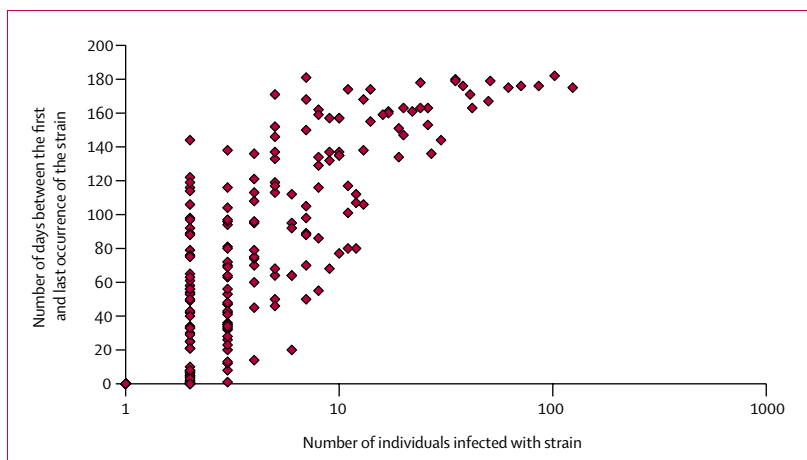


Figure 2: The relation between the number of people infected with a specific strain and the number of days between the first and last occurrence of the strain

Every point represents a strain defined by sequence type. Although some of those strains noted in fewer than ten individuals occur close in time, others are more widely spaced. Strains arising more frequently are generally recorded throughout the study.

clinics in the UK.¹ The tendency of heterosexuals who have sex outside the UK to have unique strains might indicate that novel strains imported into London rarely establish, although this tendency might not apply to strains imported into London by men who have sex with men, since there was no association between sex outside the UK and infection with a unique strain.

Previous studies have not clearly established the amount of overlap between major networks of heterosexuals and men who have sex with men;¹⁷ our data provide strong evidence for the circulation of distinct gonococcal strains in networks of men who have sex with men and heterosexual networks in London. Strain transmission between groups with differing sexual preference seems limited, especially from heterosexuals to men who have sex with men. Only 1.7% of individuals infected with the 14 major heterosexual-associated strains were men who have sex with men, although such men made up 37% of the dataset. Since men who have sex with men and heterosexual networks are dominated by individuals who are white British and black Caribbean, respectively, the major gonococcal strains in London are also being transmitted within different ethnic groups. That gonorrhoea transmission between demographic and behavioural risk groups in London remains restricted is an important conclusion from this study.

The degree to which people's choice of partners is restricted to subgroups of the population affects the rate of spread and determines potential control strategies for STIs.³ For example, bisexuals can potentially act as a bridging group, transmitting strains between men who have sex with men and heterosexuals. Our study shows that bisexual men are usually infected with men who have sex with men-associated strains, suggesting that men reporting themselves as bisexual acquire their

	Unique strains	Non-unique strains	Univariate odds ratio (95% CI)	p value	Adjusted odds ratio (95% CI)	p value
Men who have sex with men						
Number of individuals	89	673				
Aged under 25 years	13	120	0.79 (0.42-1.5)	0.45
Ethnicity						
White British/white Irish/other white	65	511	1.0
Black Caribbean/black African/other black	12	54	2.2 (0.97-4.5)	0.06
Other*	7	63	0.85 (0.52-1.4)	0.54
Not recorded	5	45	0.84 (0.32-2.2)	0.72
Concurrent STI	15	132	0.83 (0.46-1.5)	0.53
Previous gonorrhoea						
Yes	38	285	1.0
No	38	331	0.86 (0.53-1.4)	0.54
Not known	13	57	1.7 (0.86-3.4)	0.13
Discharge/dysuria at presentation						
Yes	67	485	1.0
No	15	149	0.73 (0.40-1.3)	0.29
Not known	7	39	1.3 (0.56-3.0)	0.54
HIV status						
Positive	20	178	1.0
Negative	46	323	1.3 (0.73-2.2)	0.40
Unknown	23	172	1.2 (0.63-2.3)	0.59
Five or more partners reported	21	184	0.82 (0.49-1.4)	0.45
Sex abroad	27	153	1.5 (0.90-2.4)	0.11
Heterosexual men and women						
Number of individuals	157	1073				
Aged under 25 years	62	586	0.54 (0.39-0.76)	0.0005	0.65 (0.45-0.94)	0.021
Ethnicity						
White British/white Irish/other white	50	222	1.0	..	1.0	
Black Caribbean/black African/other black	69	626	0.49 (0.33-0.73)	0.0004	0.58 (0.35-0.96)	0.033
Other*	21	74	1.3 (0.71-2.2)	0.43	1.2 (0.66-2.2)	0.537
Not recorded	17	151	0.50 (0.28-0.90)	0.021	0.64 (0.34-1.2)	0.158
Concurrent STI	46	351	0.86 (0.59-1.2)	0.39		
Previous gonorrhoea						
Yes	34	252	1.0
No	108	709	1.1 (0.75-1.7)	0.56
Not known	15	112	0.99 (0.52-1.9)	0.98
Discharge/dysuria at presentation						
Yes	126	770	1.0	..	1.0	
No	20	227	0.54 (0.33-0.88)	0.014	0.58 (0.35-0.97)	0.04
Not known	11	76	0.88 (0.46-1.7)	0.72	1.3 (0.65-2.7)	0.45
HIV status						
Positive	1	7	1.3 (0.16-10.63)	0.81	0.80 (0.09-7.1)	0.84
Negative	92	489	1.7 (1.2-2.4)	0.002	1.7 (1.2-2.4)	0.004
Unknown	64	577	1.0	..	1.0	
Five or more partners reported	13	59	1.6 (0.83-2.9)	0.17
Sex outside the UK	51	106	4.4 (2.3-6.5)	<0.0001	3.7 (2.5-5.6)	<0.0001
Analyses were done separately for populations of men who have sex with men and heterosexuals. Univariate and adjusted odds ratios, their 95% CIs, and associated p values are shown. *Other ethnicity includes Bangladeshi, Chinese, other Asian, Indian, Pakistani, and other ethnic groups.						
Table 3: Analysis of the odds of having a unique strain						

infections from other men and that transmission to or from women is rare. Individuals infected with strains associated with men who have sex with men did include some men who were recorded as heterosexual (11·8%), some of whom could have had undisclosed sex with other men, but also included a few women (2·1%), which suggests some limited bridging from men who have sex with men to heterosexuals. The fairly low rate of STI transfer between men who have sex with men and heterosexuals suggested by the separate strains circulating in these groups might contribute to the disparity between the incidence of HIV in each of these groups. However, even a small amount of bridging from men who have sex with men could have wider implications for chronic viral infections such as HIV, in which a small number of introductions could lead to wider spread if HIV introduction occurs into dense heterosexual networks. The apparent low level of bridging suggests that public-health campaigns to decrease gonorrhoea incidence in either men who have sex with men or heterosexual populations will not be affected by the frequent introduction of strains from outside the targeted population, and that reduction of infection in one population will have little effect on the incidence in the other.

A limitation of this study is that we were not able to analyse all isolates of *N gonorrhoeae* in London within the 6 month period and as a consequence sexual networks in London could be larger than we observed. Also, inferred sexual networks could not be verified or refuted since partner notification data were not obtained, and behavioural data were from routine clinical interviews, resulting in some missing data and the possibility of data errors.

Our findings indicate that NG-MAST could readily be used for prospective studies of gonorrhoea in large cities that have high rates of disease, allowing the timely identification of individuals within networks of heterosexuals and men who have sex with men, and the targeting of limited public-health resources to high-risk groups, which probably include the core groups that disproportionately contribute to disease transmission and maintenance. Such studies would need to explore the combined utility of knowledge of strain type with routine collection of information on venues of meeting partners to identify targets for public-health interventions. They should be able to distinguish strains that have long been present in the population, and which represent endemic transmission in populations of men who have sex with men or heterosexuals, from new strain clusters that might identify local outbreaks in which different public-health interventions are required.³ Prospective studies can also be used to monitor the spread of antibiotic-resistant strains into high-risk populations¹⁸ and to examine the effects of public-health interventions on the size and nature of sexual networks. Individuals sharing the same strain

typically present to several different clinics, although for heterosexual-associated strains their areas of residence showed pronounced geographic clustering (BP, CLR, ACG, CJB, HW, KAF, CAF, and BGS; unpublished data), highlighting the need to coordinate sexual health prevention programmes across London.

Individuals identified by NG-MAST as sharing the same strain are very likely to be epidemiologically linked, but the closeness of that linkage is still unclear without a better understanding of the rate at which strains defined by NG-MAST diversify. However, the method we describe here identifies individuals who have sufficiently similar behavioural and demographic features to inform public-health interventions and to draw general inferences about the spread of strains within a major city. Molecular methods should be combined with exhaustive contact tracing, but in major metropolitan areas where contact tracing is more difficult, NG-MAST can provide valuable additional data on endemic networks and outbreaks. Analysis of strain type could distinguish sub-epidemics for which different interventions are indicated. The rapid identification of new strains spreading in sub-populations—ie, early epidemic phase—should inform intensified partner notification and outreach at risk venues in an attempt to prevent strains becoming endemic.¹⁹ Similarly, knowledge of the distribution of endemic—ie, later epidemic phase—strains across the city could be used to target health promotion and enhanced case finding.

Contributors

C A Ison, K A Fenton, H Ward, A C Ghani, and B G Spratt designed the study, B Choudhury and C J Bishop did the experimental work, C L Risley and A C Ghani did the statistical analysis, and all authors contributed to the writing of the report.

Conflict of interest statement

We declare that we have no conflict of interest.

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