

GENOME WATCH

Linking an unchained malady

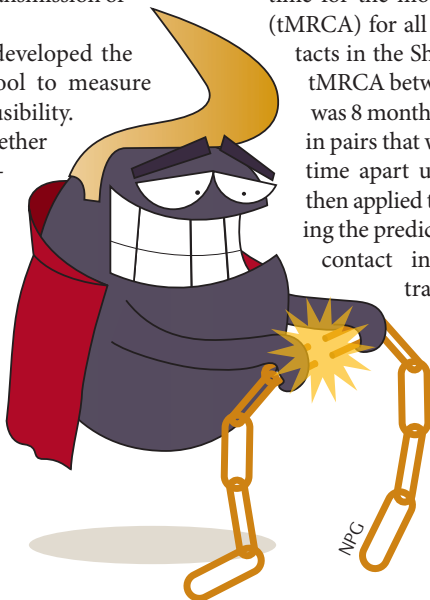
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Whole-genome sequencing (WGS) can be used to track the transmission of *Neisseria gonorrhoeae* in different sexual networks.

Globally, *Neisseria gonorrhoeae* causes more than 78 million cases of gonorrhoea every year¹. Its transmission is driven by human sexual interaction and is linked to particular risk groups, such as sex workers, men who have sex with men (MSM) and young heterosexuals, particularly of black Caribbean ethnicity. The importance of risk groups in the transmission of *N. gonorrhoeae* makes its control different from most other pathogens, as different sexual networks can cause highly disparate pathogen population dynamics. For example, the rise of antimicrobial resistant (AMR) *N. gonorrhoeae*, which is of major concern, is mostly associated with high-risk groups that are more frequently exposed to antibiotic treatment. Whole-genome sequencing (WGS) has been shown to provide the required power of discrimination to study transmission networks for many bacterial pathogens. Now, two new studies use WGS to study the transmission of *N. gonorrhoeae*.

De Silva *et al.*² developed the new 'nomogram' tool to measure transmission plausibility. The tool predicts whether two cases of gonorrhoea are related by comparing the number of SNPs between the infecting strains with the number of SNPs that would be expected to arise between 99% of transmission pairs in the time between the isolation of the samples.



The nomogram was applied to a collection of 1,407 gonococcal isolates from Brighton, UK (2011–2015), which showed that 72% of isolates sampled within a 3-month period were expected to be linked by transmission. Interestingly, 67% of the clusters that contained more than 10 patients were exclusively formed by direct or indirect transmission among males.

Didelot *et al.*³ used a different approach to study transmission in two different settings: 132 isolates of *N. gonorrhoeae* multi-antigen sequence type (NG-MAST) ST12 that were collected in a single clinic in Sheffield, UK (1995–2000), from a mostly heterosexual population, and 105 NG-MAST ST225 isolates that were collected in 13 different clinics in London, UK (June–November 2004), from a mostly MSM population. Traditional typing approaches, such as NG-MAST (which is based on the sequences of two surface proteins), provide little useful information on transmission for isolates that share the same typing profile. Instead, WGS variation in a Bayesian framework was used to estimate the time for the most recent common ancestor (tMRCA) for all pairs of known sexual contacts in the Sheffield data. The maximum tMRCA between pairs of known contacts was 8 months, which makes transmission in pairs that were sampled more than this time apart unlikely. This threshold was then applied to the London dataset, allowing the prediction of links without known contact information. The predicted transmission links were shown to correlate with the available epidemiological information (location, age and sexuality), suggesting that they were accurate.

Gonorrhoea has been estimated to spread two- to three-times faster in MSM than in heterosexual

groups, mainly owing to the higher rate of antibiotic treatment in MSM⁴. Measuring tMRCA values for pairs of isolates that had been sampled within a maximum of 3 months from one another revealed a larger proportion of linked cases in the Sheffield cohort (24%) than in the London cohort (4%)³, despite the much shorter sampling timeframe of the London cohort. This is consistent with an effective population size for ST225 in London that is approximately three-times larger than for ST12 in Sheffield, and a predicted number of infected individuals that is six- to nine-times larger.

Gonorrhoea infections are increasing worldwide and are a major challenge for infection control teams, especially as AMR *N. gonorrhoeae* include strains that are resistant to all known classes of antibiotic, including ceftriaxone and azithromycin, which are currently the most common first-line treatments. However, WGS has proved to be a powerful and versatile tool for revealing transmission dynamics in previously indistinguishable genotype clusters. The use of WGS to track transmission, as well as antimicrobial resistance, in these networks will be of utmost importance to help control the spread of this sexually transmitted superbug.

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Competing interests statement
The authors declares no competing interests.