

Tuberculosis's genetic 'family tree' may hold the key to tackling outbreaks quickly and effectively

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Detailed investigation for one substance abuse cluster. Time of onset of symptoms, diagnosis and treatment. [doi:10.1016/S1473-3099(12)70277-3]

Researchers, led by the NIHR Oxford Biomedical Research Centre, the Health Protection Agency in Birmingham and the Wellcome Trust Sanger Institute in Cambridge, have pioneered the whole genome sequencing (WGS) method through a study of 254 TB cases in the Midlands.

The method, published online in the Lancet Infectious Diseases Wholegenome sequencing to delineate Mycobacterium tuberculosis outbreaks: a retrospective observational study compares the genetic information from the TB germs of each patient to determine with a high degree of accuracy whether cases are isolated, or if there is an outbreak of the



potentially fatal disease.

By genetically mapping the spread of infection it can also show who has given the disease to whom and help identify potential "super spreaders" before any information has been collected from patients.

Armed with this data, public health bodies can assess how much transmission is taking place and thereby target efforts quickly, efficiently and effectively to where it is needed most.

Lead investigator Professor Tim Peto, at the NIHR Oxford Biomedical Research Centre, a partnership between the Oxford University Hospitals NHS Trust and the University of Oxford, said: "This will result in a major rebalancing of the public health approach to the spread of TB.

"It will make them far more focused on where the problems are and make them more efficient and effective."

Co-investigators Drs. Grace Smith and Philip Monk, senior members of the HPA <u>TB control</u> programme, described the research as a "revolution in TB control." Dr Monk added "at present you have to put a lot of work into contact tracing to find links between cases. This is extremely difficult particularly when people often lead such chaotic lives.

"By identifying so-called super spreaders we can target our work effectively. In terms of the public health management of TB, that is a major <u>paradigm shift</u>."

<u>TB cases</u> in the UK remain relatively low. However, the number of cases has risen slightly over the past decade, with 8,963 cases reported in 2011 (source: <u>Health Protection Agency</u>). Many cases are isolated, but there have been numerous outbreaks across the country over recent years.



Current practice sees <u>public health</u> bodies depend on people with TB volunteering information about their movements, family and friends, to identify further cases and piece together the potential spread of the disease. Until now this approach has been aided by limited genetic typing techniques that are only able to rule out transmission between cases, and not reliably confirm transmission.

The process of identifying outbreaks has therefore been time consuming, relying on the information people are able to give and occasionally throwing up "false connections," leading to wasted effort by health bodies.

By sequencing the whole genome the new technique allows linking of cases and the mapping of outbreaks, and has the ability to predict the existence of undiagnosed cases.

WGS is used to measure the genetic distance between TB strains to accurately link cases before any additional patient data has been collected. By analysing the evolving pattern of mutations it is possible to work out the direction of transmission and identify potential "superspreaders."

Prof Peto said: "This work gives a level of certainty you could never have before about who belongs to a transmission chain.

"The information is in the germ, and it speaks for itself."

More information: <u>dx.doi.org/10.1016/S1473-3099(12)70277-3</u>

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