SYPHILIS IS BACK AND IT IS GLOBAL, GENETIC STUDY SUGGESTS

The most comprehensive genomic study of syphilis to date has mapped the recent resurgence of the disease around the world. Researchers at the Wellcome Sanger Institute, the UK Health Security Agency, the London School of Hygiene and Tropical Medicine and their collaborators found almost identical syphilis samples between 14 countries, showing there is widespread international transmission of the disease, particularly within the last 20 years.

The study, published in *Nature Microbiology*, found that the global syphilis population is made up of two lineages, SS14 and Nichols. Detailed analysis of these lineages provides important insights into the genetic diversity of syphilis, with implications for vaccine design and anti-microbial resistance.

Syphilis is caused by the bacterium *Treponema pallidum*. It is one of the most common sexually-transmitted infections (STI) globally, with approximately six million infections each year. Syphilis is easily treatable, though symptoms may fade before an individual realises they are infected or may not appear at all. If left untreated syphilis can cause serious long-term health problems.

Syphilis infections occurring during pregnancy can be passed on to the child, causing congenital syphilis. This is the second leading cause of stillbirth globally and can have severe developmental outcomes for children carried to term. It can be prevented through early screening and treatment during pregnancy[1]. Congenital syphilis is more common in countries without such screening programmes.

For this study, researchers at the London School of Hygiene and Tropical Medicine (LSHTM) and the Wellcome Sanger Institute coordinated the collection of 726 syphilis samples from 23 countries, including well-sampled areas such as the United States and Western Europe as well as poorly sampled regions such as Central Asia, Australia and Africa. Researchers at the Sanger Institute sequenced the genome of each sample and conducted phylogenetic and cluster analyses to map the global syphilis population.

Because DNA changes occur at a known and predictable rate over time, the ancestral relationships between different sequences can be established. The researchers found that all the samples came from just two deeply branching lineages, Nichols and SS14. Both lineages are currently circulating in 12 of the 23 countries sampled, and almost identical samples were present in 14 of these countries.

Dr Mathew Beale, first author of the study from the Wellcome Sanger Institute, said: “The dominant syphilis lineages infecting patients prior to 1983 were not the same as those infecting patients today. Our analysis shows a population bottleneck occurred in the late 1990s that indicates a large decline in the population size of *T. pallidum*, most likely as a result of the HIV/AIDS crisis. The concerning thing from a public health perspective is that the presence of almost identical samples in numerous countries suggests the disease is being transmitted internationally on a regular basis. Syphilis is back and it is global.”

Syphilis incidence declined during the 1980s and 1990s, in part due to safer sexual practices in the wake of the HIV/AIDS epidemic. But in recent decades syphilis has increased again, rising by over 300 per cent in some countries since 2010. Syphilis disproportionately affects men who have sex with men (MSM) in some countries – for example, 90 per cent of UK syphilis cases in 2017 were among MSM[2].

Dr Helen Fifer, a senior author of the paper from the UK Health Security Agency (UKHSA), said: “The explosion of syphilis cases in recent decades is hugely concerning. It is a sexually transmitted infection that can easily go undetected, with a large proportion of cases being diagnosed at the latent stage among men who have sex with men (MSM) in recent years. An increase in syphilis among heterosexuals is also concerning due to the risk of congenital

syphilis. Anyone having sex with new or casual partners should use a condom and get tested – STIs can pose serious consequences to the health of individuals and the health of their current or future sexual partners."

The study is a valuable resource for understanding the genetic diversity of *T. pallidum* that will have implications for vaccine design and drug resistance. Many of the samples sequenced were resistant to macrolides, a class of antibiotics used to treat many STIs – though none showed resistance to the most common syphilis treatment, benzathine benzylpenicillin. Any syphilis vaccine will need to be tailored to the most common lineages of *T. pallidum* currently in circulation.

Professor Nicholas Thomson, senior author of the study from the Wellcome Sanger Institute, said: "It's been a huge logistical effort to bring this study together and we couldn't have done it without our international collaborators. We wanted to build the field of syphilis genomics and these data provide a solid foundation for future research. Combined with the recent ability to culture *T. pallidum* in the lab, there is now a wealth of activity in this field, which is important because syphilis is fast becoming an urgent public health issue."

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Notes to Editors:

[1] For more information on congenital syphilis, see the WHO website

[2] More information on syphilis in the UK is available in this Public Health England report

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Selected websites:

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