

## Tuberculosis in London – why has it not reduced during the COVID-19 pandemic?

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The rate of tuberculosis (TB) in London has not reduced during the COVID-19 pandemic. This may be surprising given that TB is airborne, and suggests important lessons about the transmission and treatment of the disease.

Although TB has been declining in the UK since 2011, incidence before the COVID-19 pandemic remained relatively high in London at 16 cases per 100,000 residents in 2020, double the UK average, and as high as 43 per 100,000 among residents of the relatively deprived and ethnically diverse borough of Newham in East London.<sup>1</sup> The WHO considers a country to have a ‘high’ incidence of TB if more than 40 people per 100,000 per year are diagnosed with TB.

When non-pharmaceutical interventions and “lockdowns” were introduced to limit COVID-19 in March 2020, we expected TB cases to reduce. Other respiratory infections were profoundly affected.<sup>2</sup> The usual influenza season did not happen in winter 2020/21 – in London in December 2020 there were 19 confirmed cases of influenza, compared to 1,947 in December 2019. This is likely due to reduced transmission rather than a lack of testing for influenza during the COVID-19 pandemic.<sup>3</sup> Similarly, in winter 2020/21 there were few cases of respiratory syncytial virus, a common cause of hospitalisation of infants.

We expected that TB would also be affected for two reasons. First, TB transmission might be reduced due to restrictions on social mixing, closure of workplaces, bars, and restaurants, and limitations on local and international travel. These changes might reduce the number cases that result from recent exposure. Such an effect would likely be lagged because TB has a latent (or incubation) period, which varies widely between patients and settings but is usually less than two years,<sup>4</sup> and after onset of symptoms there is often a delay of several months before diagnosis.<sup>1</sup> The distribution of these periods is skewed: some individuals have short periods between exposure and diagnosis (for example 3-6 months), while for some this period may be many years. If COVID-19 restrictions affected incidence of TB, we would expect some difference in the rate of diagnoses by summer 2021; more than a year after non-pharmaceutical interventions were first introduced.

Second, all health services have worked differently during the pandemic and many have been less accessible. This may have meant people with TB are less likely to seek help for symptoms such as coughing and fatigue, while TB specialists and general practitioners may be less accessible with longer waiting lists. There has been international concern that COVID-19 would reduce access to TB diagnosis and treatment.<sup>5</sup> The World Health Organization reported that the number of TB diagnoses globally reduced from 7.1 million in 2019 to 5.8 million in 2020, with these reductions concentrated in India, Indonesia, and the Philippines, while conversely the number of deaths increased.<sup>6</sup> The WHO concluded that “for the first time in over a decade, TB deaths have increased because of reduced access to TB diagnosis and treatment in the face of the COVID-19 pandemic”. At the start of the pandemic, many TB specialists were concerned that something similar would happen in the UK, with fewer but more severe cases presenting to services, and an increasing number of undiagnosed cases in the community.

However, TB is a very different disease to respiratory viruses such as influenza and respiratory syncytial virus. It is much less seasonal; it has a long latent period (months or years rather than days), and is closely associated with social deprivation.<sup>7</sup> It is possible that COVID-19 interventions have a different impact on groups most affected by TB in London, such as those living in larger households, people experiencing homelessness,<sup>8</sup> and communities that often visit countries with

high incidence of TB. These groups may be unable to avoid social mixing or work in jobs that cannot be done at home. The potential impact of COVID-19 on TB was therefore uncertain.

The London TB Register (LTBR), a surveillance database maintained by the UK Health Security Agency, shows the number and characteristics of all TB cases diagnosed in London. This data shows that an average of 4.1 cases of TB were diagnosed per day in London during the first lockdown (March – June 2020); only slightly lower than 4.7 per day over the previous 12 months. This slight reduction may be part of a decade-long decline in TB. There is some evidence that this trend reversed after the first lockdown, reaching an average 5.0 cases per day in summer 2021. More time will be needed before this trend becomes clear. There has evidently not been the dramatic reduction in cases seen for other respiratory infections.

The clinical and demographic characteristics of cases during the pandemic has also been similar to patients before the COVID-19 pandemic, with an average age of approximately 40 years, 6-in-10 being male, and approximately 5% of infections being resistant to the first-line antibiotics. Most importantly, the duration between reported symptom onset and diagnosis has remained at approximately three months, suggesting that people with TB are not waiting until symptoms are more severe before seeking help.

This appears different to the global pattern of fewer patients treated for TB. It suggests that TB services in London have remained accessible during the COVID-19 pandemic. Like many health services, TB services in London struggled during COVID-19 due to staff shortages and the need to limit face-to-face contact. They used more remote assessments, reduced home visits, and reduced 'directly observed therapy', in which patients take antibiotics at regular in-person clinic visits, allowing clinicians to monitor treatment regimens and the patient's general health. Despite these changes, TB services in London have diagnosed similar numbers of cases each day.

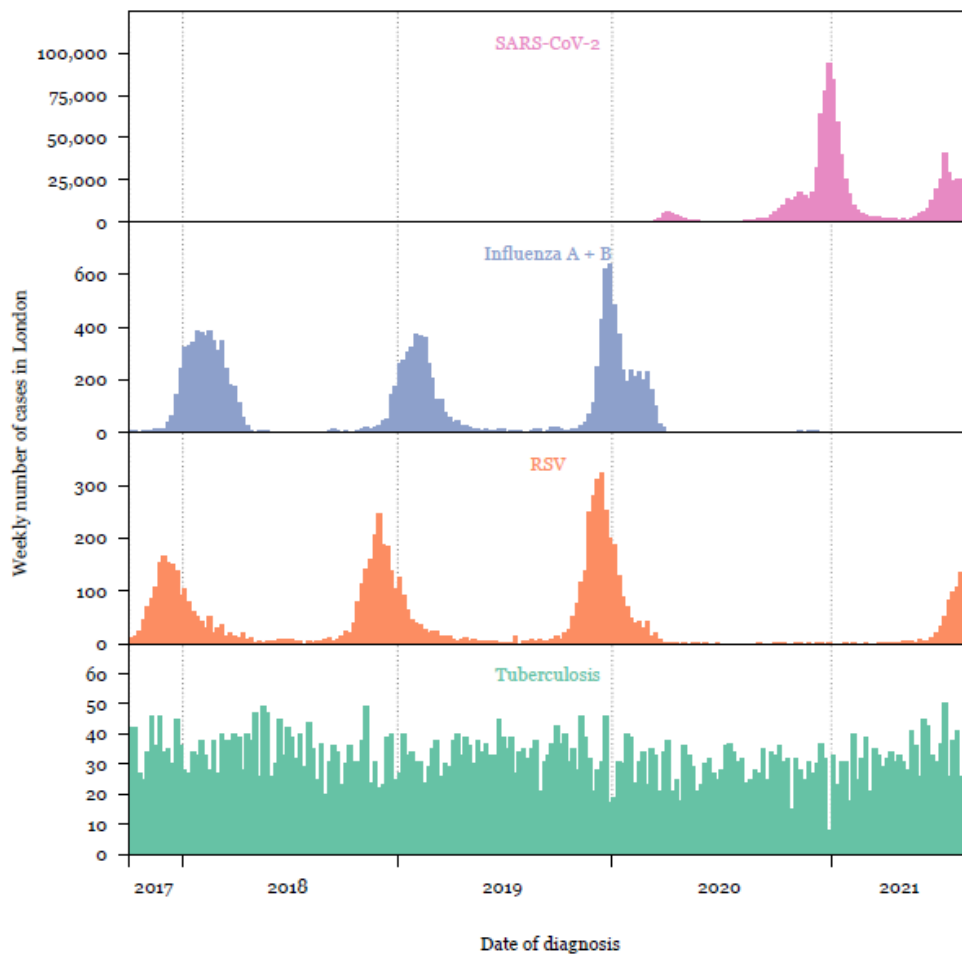
One possible reason for the continued incidence of TB during COVID-19 is that most cases arise from long-term latent infections. The balance of active TB cases attributable to recent exposure compared to reactivation of long-term latent infection is unclear, and may be changing over time and varying with local TB incidence. Studies in England suggest that a small proportion of cases (4% and 11% in two studies<sup>9,10</sup>) are attributable to recent local transmission. This may suggest that most active infections are attributable to latent infections acquired long ago; possibly explaining the continued incidence of TB in London despite reduced social contact during the pandemic.

Another possible reason is that TB transmission continued during the pandemic in settings and communities most affected by TB, such as multigenerational households and those experiencing homelessness. TB cases during the COVID-19 pandemic had similar characteristics to those before the pandemic, including similar prevalence of homelessness, problematic drug use, and mental health problems, suggesting that the continued incidence of TB is not explained by increased concentration of the disease in these populations.

Most surprisingly, the London TB Register shows that the rate of TB diagnosis might now be increasing. Possible reasons for a gradual increase in TB diagnoses during COVID-19 include: (a) more mixing in private homes during lockdowns, which may also be higher risk settings for TB transmission than public places and workplaces; (b) co-infection with COVID-19 may increase the infectiousness of TB, for example through increased coughing; (c) COVID-19 infection may increase susceptibility to TB infection or reactivation; (d) increased help-seeking for more severe or long-term respiratory symptoms due to awareness of COVID-19. Some of these theories could be investigated by linking patient-level data on TB or latent TB testing with COVID-19 testing or hospital data.

TB's long incubation period means that changes in incidence happen much more slowly than for influenza and other diseases with rapid onset. The full impact of COVID-19 lockdowns on TB in London may not yet be clear. However, it is already clear that patients have continued presenting to services and are being diagnosed at a similar rate to before the pandemic. This suggests it is possible to operate TB services during COVID-19 restrictions in high-income settings. Countries in Africa and South and South-East Asia, with less resources and higher incidence of TB, will need international support to continue treating people with TB.

Figure: Number of diagnosed cases per week in London for selected respiratory infections (TB, SARS-CoV-2, RSV, and influenza A + B), October 2017 - August 2021



Data for RSV and Influenza A+B are from the Second Generation Surveillance System ([https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/926838/PHE\\_Laboratory\\_reporting\\_guidelines\\_October-2020-v3.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/926838/PHE_Laboratory_reporting_guidelines_October-2020-v3.pdf)) and for SARS-CoV-2 are publicly available data from the UK Coronavirus data portal (<https://coronavirus.data.gov.uk/>). The number of SARS-CoV-2 cases reported in the 'first wave' (approximately March-June 2020) is low due to limited availability of tests.

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