# Clinical tuberculosis

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## Abstract

Tuberculosis (TB) is an infectious disease transmitted by *Mycobacterium tuberculosis*, which is found in the sputum of patients with pulmonary disease. TB has re-emerged in the cities of Western Europe with a change in its clinical epidemiology to an increased proportion of extrapulmonary disease. It is therefore important that clinicians are aware of its manifestations and treatment. There is increasing concern about drug-resistant TB, but with careful assessment and treatment it appears that drug-resistant TB can be controlled. In sub-Saharan Africa, there is a TB epidemic, driven by co-infection with the human immunodeficiency virus (HIV). The impact of HIV on TB patients needs to be carefully evaluated and management adjusted accordingly.


**Keywords** Acquired immunodeficiency syndrome; central nervous system; HIV; meningeal; multidrug-resistant; tuberculosis

## Key points

- Rates of tuberculosis (TB) have increased in many cities in developed countries. This is largely caused by migration from endemic areas
- Any patient with radiographic consolidation and symptoms for >3 weeks should be considered to have TB until proven otherwise — careful consideration should be given to infection control if the patient is admitted to hospital
- All patients with TB should be supported through treatment and a risk assessment made for default if directly observed therapy is not uniformly employed
- Drug-resistant TB should be suspected in patients who have already undergone treatment for TB or who come from the former Soviet Union
- Co-infection with HIV is common in sub-Saharan Africa, and patients with TB should be offered HIV testing

## Epidemiology

Understanding the epidemiology of the disease is very important when assessing a patient with suspected tuberculosis (TB).

### The global picture

In 2015 the World Health Organization (WHO) estimated that 9.6 million people developed clinical TB and 1.5 million of these died (Figure 1).[1,2] One-third of patients with TB may never have been diagnosed or treated. Approximately 1.2 million TB patients were co-infected with human immunodeficiency virus (HIV) and 74% of these were in sub-Saharan Africa.

The global TB epidemic is on the wane. The incidence of TB is falling and, in 2015, was 18% lower than in 2000. TB mortality fell by 47% in the same time period. It is estimated that effective TB treatment saved 47 million lives between 2000 and 2015. Having said this, it is estimated that one-third of people with TB in 2014 were not reported or treated. Only one-third of patients co-infected with HIV were given anti-retroviral therapy. Having met previous targets, the WHO now seeks to end the TB epidemic. The goal is to reduce TB deaths by 90% and reduce the incidence of TB by 80% between 2015 and 2030.

### The situation in the UK

In the UK, the incidence of TB fell until the early 1990s but increased up to 2011 and is now in decline.[3] This increase has mainly centered on large cities. In London, the largest part of the rise is attributable to immigration from countries where TB is endemic. Molecular epidemiological studies indicate that most cases of clinical disease seen in the UK have resulted from reactivation of infection acquired in the remote past, usually abroad. Eighty per cent of immigrants to the UK developing TB had been in the UK for more than 2 years, and 50% for more than 5 years.[2] The role of vitamin D deficiency as a causal factor in this population has been highlighted. In the minority of cases, where recent transmission has occurred, the roles of homelessness, addictive drug-use and imprisonment have been emphasized.

In areas with high transmission rates, TB is a disease of young adults, most cases occurring in 20—40-year-olds. In the absence of widespread HIV infection, there is a male preponderance, with a ratio of approximately 2:1. In locations with a high HIV prevalence, the sex ratio is more equal as HIV appears to affect women more than men and results in a rapid breakdown from TB infection to clinical disease. Where TB is not being actively transmitted, a greater proportion of clinical cases occur in the elderly.

When considering whether a patient has TB, it is important to consider the underlying risk of the disease in the population they come from. Although factors such as immunosuppression or an increased risk of close contact with TB in homeless or incarcerated populations modify the risk, the risk of infection in the population from which they are derived is the most important factor (Table 1).

### Epidemiology of drug resistance

Anti-tuberculous drug resistance is important because it can render standard anti-tuberculous treatment ineffective and patients then remain infectious for prolonged periods. They become progressively disabled and can die. Drug resistance poses a particular threat to national TB programmes, partly because only 12% of TB patients are tested for TB drug sensitivity and partly because standard regimens are relatively ineffective in treating

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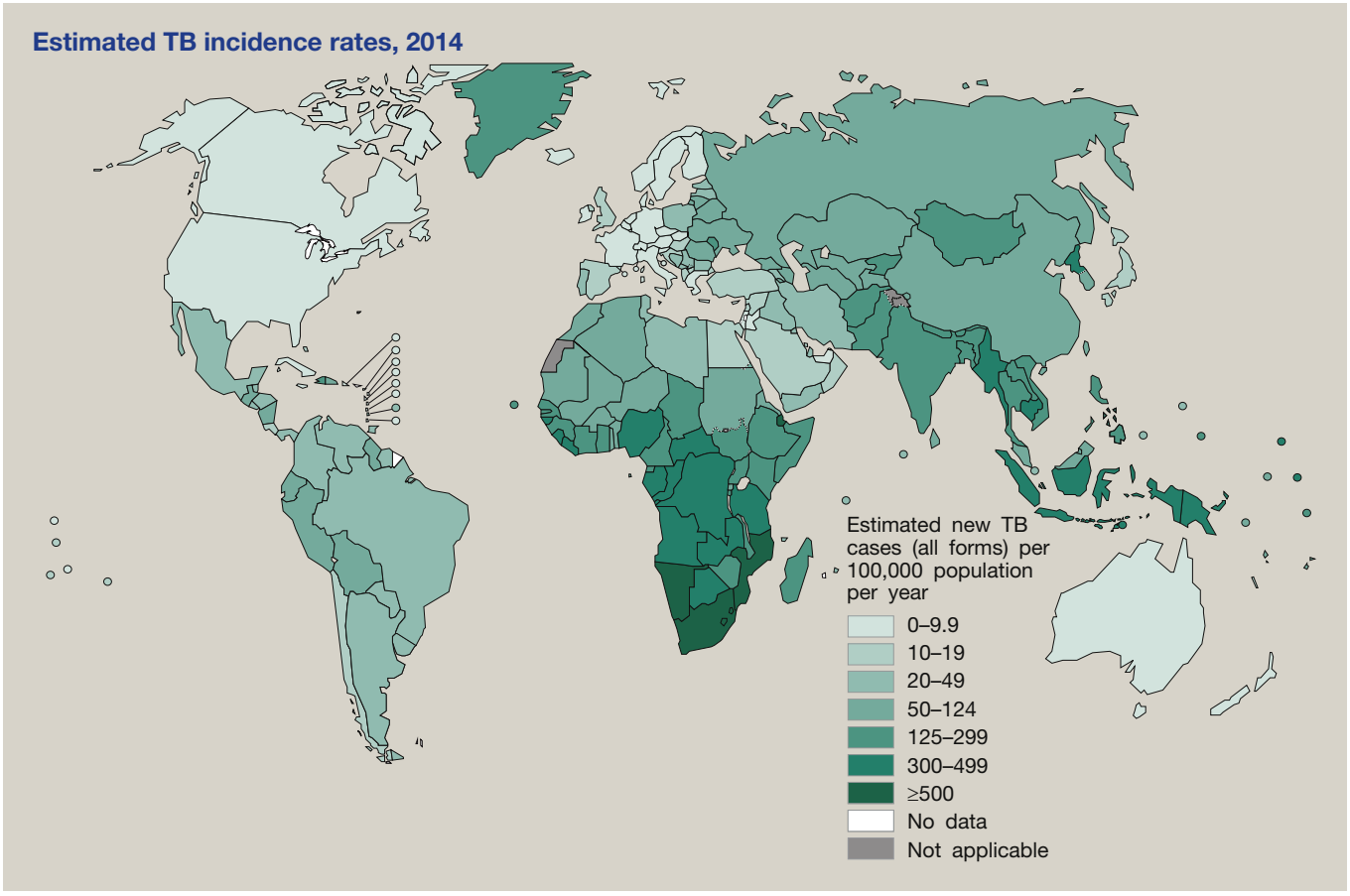


**Figure 1** Republished from World Health Organization. Global Tuberculosis Report 2015 with permission.[1]

drug-resistant TB.[1] With proper concordance between clinician and patient, standardized drug regimens rarely result in drug resistance when treating patients with initially fully sensitive organisms. If proper drug combinations are taken for inappropriately short periods, relapse tends to occur even with fully sensitive organisms. Problems arise when initial (primary) drug resistance is not recognized, inadequate or non-standardized regimens are prescribed or supplies of individual drugs are interrupted.

Of 3880 English patients who were culture-positive for *Mycobacterium tuberculosis* in 2014, 6.9% were resistant to isoniazid, 1.4% were resistant to rifampicin, 1.1% were resistant to ethambutol and 0.8% were resistant to pyrazinamide. Seven per cent were resistant to at least one first-line antibiotic, and 1.3% had multidrug-resistant TB (MDR-TB), with resistance to at least isoniazid and rifampicin.[3] In England, resistance to TB drugs is becoming less common.

The appearance of extensively drug-resistant TB (MDR-TB plus resistance to an aminoglycoside and a fluoroquinolone) in South Africa, and the appearance of widespread drug resistance in eastern Europe, have led to further analyses of the global prevalence of anti-tuberculous drug resistance.[1] In 2014, an estimated 300,000 cases of MDR-TB emerged globally, that is, 3.3% of incident cases and 20% of re-treatment cases.[1] As yet, globally, most MDR-TB cases are thought to be undiagnosed and untreated.[1]

### Incidence and prevalence of TB among different populations

| Population group | Tuberculosis incidence per 100,000/year or per 100,000 population |
|---|---|
| South Africa — gold miners[a] | 1571 |
| Zimbabwe — general population[b] | 278 |
| India — general population[b] | 167 |
| China — general population[c] | 68 |
| London — black African ethnic group[d] | 197 |
| London — problem drug user[d] | 354 |
| London — prisoner[d] | 208 |
| London — homeless[d] | 788 |
| London — white ethnic group[d] | 6 |

[a] Period prevalence.
[b] Estimated incidence.
[c] Reported incidence.
[d] Prevalence.

**Table 1**

## Pathogenesis

TB is usually acquired by inhalation of infected material. The most important risk factor is living for prolonged periods in close proximity to someone with *M. tuberculosis* in their sputum.