

PLAN FOR PREVENTION AND CONTROL OF TUBERCULOSIS IN SPAIN

EXECUTIVE SUMMARY

December 2019



1. INTRODUCTION

In 2017, tuberculosis (TB) was the tenth cause of death globally and the leading cause from a single infectious agent, even though its incidence had been declining since 2000. Among the major current challenges are the drug resistance, the innovation, availability, and equitable access to diagnosis and treatment, as well as the annual fall in incidence rate at global level.

In low incidence countries (<10 cases/100,000 inhabitants) TB is mainly concentrated within vulnerable populations and a large proportion of incident cases are a reactivation of previous TB infection.

In 2014, the “End TB” strategy was approved by World Health Assembly, which envisaged the following global targets by 2035: a 95% reduction in mortality rates, a 90% reduction in incidence rates, and that no households experience catastrophic costs due to TB.

In Spain, once the Plan for the Prevention and Control of TB was approved in 2007, the efforts made by involved partners have resulted in a decrease in the estimated incidence rate from 17.9/100,000 in 2007 to 9.4/100,000 in 2017 and from 12.6/100,000 to 6.8/100,000 in 2017 for estimated incidence rate of pulmonary TB. The treatment success rate in 2017 was around 85%. According to available data, the incidence of TB drugs resistance is relatively low in Spain, between 20 and 30 MDR-TB strains and 1-2 XDR-TB have been identified annually. In terms of diagnosis, there have been several advances in the study of the activity carried out by microbiology laboratories, the availability of molecular techniques as well as the creation of a network of Laboratories for TB diagnosis. In terms of epidemiological surveillance, a situation analysis has been elaborated covering the situation in the CCAA (Autonomous Communities in Spanish) and common indicators for monitoring progress have been defined.

The current context of international commitment and agreed scenario of to end the TB epidemic places the update of the Spanish Plan for TB prevention and control (Plan TB) at an opportune momentum. The Plan TB is aimed at the detection and control of the transmission of TB, especially pulmonary forms of disease, likewise the detection and control of MDR/XDR TB. It incorporates elements and actions for territorial and inter-sectorial coordination with the explicit aim of ensuring that ‘no one is left behind’.

2. OBJECTIVES

Alongside the ‘End TB’ Strategy and the action plan for the WHO European Region 2016-2020, this plan proposes a working timescale until 2030 with two intermediate points, the first in 2020 and the second in 2025. It includes specific goals and milestones to be reached by 2020, the year in which an evaluation will be carried out, in order to assess, inform and readjust the goals and targets for the following period.

Overall Aim

To halt the transmission of TB in Spain through universal access to prevention, diagnosis and treatment.

Specific goals

- 1. To consolidate the TB incidence rate below 10 cases/100.000 inhabitants maintaining the downward trend at, at least, 4% per year for pulmonary TB.***

Strategic courses of action will be focussed on improving early diagnosis, identifying latent infection in specific people, improving the implementation of contact tracing and incorporating vulnerable people and groups.

Milestones for 2020 (using data from 2015)

- To reduce the incidence of TB by 15-25%, achieving a rate of between 9 and 7.9 cases/100,000 population.
- To reduce the incidence of pulmonary TB at least 4% per year, achieving a rate of 6.8 cases/100,000 population.

2. To improve the treatment success rate, in all forms of TB, irrespective of the presence of drug-resistance.

The strategic courses of action will focus on the improvement in microbiological diagnosis and identification of drug resistances the provision of supervised and directly observed treatment, and the introduction of a Case Management Protocol to be developed by every CCAA.

Milestones for 2020

- To reach a treatment success rate of 95% in sensitive cases.
- To reach a treatment success rate of 75% in MDR/XDR cases.

3. To improve knowledge and information regarding TB cases and outbreaks.

Lines of action will be aimed at the improvement of epidemiological surveillance, including microbiological information and fulfilled information at Surveillance and Case Management Protocols.

Milestones for 2020

- The National Network of Epidemiological Surveillance (RENAVE in Spanish) will receive comprehensive and quality information regarding TB cases and outbreaks, at CCAA and National level.
- Information for indicators will be available at National level in the first 6 months of the following year; those relating to treatment will correspond to year before closure.

3. STRATEGIC LINES

3.1. Improvement in early diagnosis

3.1.1. Reducing TB diagnosis delay

The observed median of diagnosis delay in some CCAA had a wide range, between 35 and 81.5 days. The objective is to reach a median below 30 days between the appearance of symptoms and the starting of treatment in TB pulmonary cases.

It is compulsory to suspect and proceed to diagnosis in patients who present relevant signs and symptoms, as well as in some clinical and socioeconomic circumstances (overcrowding, homelessness, or recent migration from TB high incidence countries and limited access to health services) which increases vulnerability.

The clinical signs of TB in children can be scarce. TB in children is considered a 'sentinel event' of recent TB transmission.

For any patient with suspected pulmonary TB, a chest x-ray must be carried out within a maximum of 24-48 hours.

A complete microbiological diagnosis would include a sputum-smear microscopy and culture, identification of tuberculosis complex, and drug-susceptibility testing. In drug-resistant strains, a second-line drug-susceptibility testing must be carried out.

The result of the sputum-smear microscopy must be available in less than 24 hours. For microbiological diagnosis, the simultaneous use of liquid and solid culture mediums is recommended. WHO recommends the use of rapid molecular tests as soon as possible and the Xpert MTB/RIF for the simultaneous detection of TB and resistance to rifampicin.

To confirm the *Mycobacterium Tuberculosis* complex, rapid 15-minute immunochromatographic tests are recommended, as they provide definitive identification of all species of the complex (excluding *M. Bovis*-BCG).

The carrying out of an antibiogram for first-line drugs for all diagnosed patients, regardless of previous treatments, must be guaranteed. If there is resistance to any of these drugs, the antibiogram must be repeated for second or expanded line of treatment, and genetic study must be included. It's essential to confirm resistance, either by repeating the study or referring to a reference laboratory.

In resistant strains, molecular typing using the MIRU technique and whole genome sequencing should be carried out by laboratories with sufficient capacity in at least the RR/MDR/XDR strains. Laboratories without sufficient capacity can send the strains to the National Centre for Microbiology reference laboratory.

3.1.2. Reinforcing the identification of latent TB infection

Between 5-10% of patients with latent TB infection (LTBI) will develop the active illness over the course of their lives, usually in the first 5 years following infection and depending on the presence of risk factors.

An infection diagnosis must be carried out on all TB patient's contacts, people with HIV infection, and those at starting of biological or immunosuppressive therapies, dialysis, organ transplant candidates, hematopoietic progenitors, silicosis, or fibrotic changes in chest X-ray that may suggest TB.

An assessment of TB exposure and infection diagnosis should be considered in professional facilities such as: health centres, microbiology laboratories, prisons, homeless shelters, centres for recently arrived migrants, as well as humanitarian workers and military staff in countries with TB high incidence. Minors (children) who have visited these countries should be tested 10 weeks after their return.

Individualised assessment will be carried out on persons with risk factors derived from socioeconomic conditions, in particular homeless ones, and children in the process of adoption or migration from countries with a high incidence of TB.

For diagnosis of infection, the Tuberculin Skin Test (TST) must be carried out, using the Mantoux technique and/or IGRA (*Interferon-Gamma Release Assay*).

In all cases in which the infection is diagnosed, the active illness will be ruled out and following professional criteria they will be treated. Adherence to treatment will be assessed, using the case management protocol to be developed as proposed in Plan TB.

3.1.3. Actions by sector of intervention

A focus on inter-institutional and intersectoral collaboration is needed for actions developed by organisations outside the health sector, such as those attending people at risk of social exclusion (vulnerable migrants, prisoners and homeless people).

The plan proposes actions such the identification of specific teams, professionals responsible for TB Programmes/Units in CCAA and information sharing with relevant partners.

TB plan also includes a variety of actions related to training, information and coordination to improve early diagnosis. These are to be carried out in healthcare facilities, in occupational health sector, in social services facilities and units and migrant shelters. In addition, the plan suggests the standardization of action, criteria and protocols, the boosting of early TB diagnosis and fluent communication among involved actors.

3.2. Surveillance

TB surveillance in Spain is carried out by RENAVE. In every CCAA once notified epidemiological and microbiological case information is integrated by public health services, and afterward aggregated at national level by National Centre of Epidemiology (CNE in Spanish).

For this strategic line the objectives aimed to contribute to the knowledge of the disease epidemiology and strengthen the information in MDR/XDR-TB cases.

3.2.1. Cases Notification

Every TB case will be notified to Public Health authorities in CCAA from where such information will be transmitted on weekly basis to the CNE.

Information about LTBI cases will be collected from now in an aggregated way.

The file of notified cases in a year in each CCAA will be updated during the first three months of the following year. The information regarding treatment outcome in notified cases will be updated in the first six months from the previous two years. The sensitivity of surveillance system must be improved using as much sources of information as possible.

For cases requiring national or international coordination for their management, CCAA must notify to the Coordination Centre for Health Alerts and Emergencies (CCAES in Spanish) and CNE. CCAES, CNE and CCAA affected will jointly decide on measures to take and if necessary, to notify the Early Warning and Response System (European Union) and/or WHO, in accordance with European Directive and International Health Regulations 2005 (IHR-2005).

Regarding the notification of cases or suspected cases in travellers, both the IHR-2005 and Decision 1082/2013 is the regulatory framework for surveillance and control and international public health. Establishment of measures after TB diagnosis in an air traveller must consider some criteria such duration of the flight, time between flight and diagnosis, and evidence of transmission to other contacts. In cases of diagnosis of-MDR/XDR-TB, contacts must be identified, regardless of the length of the flight.

3.2.2. Outbreaks, detection, investigation and notification.

An outbreak is defined as a group of 2 or more cases where there is clear evidence of active transmission. A cluster is defined as 2 or more active cases with identified epidemiological links and the same genotype of *M. Tuberculosis*.

The outbreak study should be completed, wherever possible, with the genetic study of the *M. Tuberculosis* isolates. Microbiological support for this activity can be obtained from the Network of Laboratories for TB diagnosis and the CNM-National Reference Laboratory.

The public health authorities of involved CCAA must be notified immediately after the detection of any cluster or outbreak. The results of the investigation must be sent to CNE in maximum 3 months once proper study is finished.

Outbreaks requiring coordinated action either national or international level, must be urgently communicated to CCAES and CNE. Occupational Health Units in CCAA must also be notified of all clusters or outbreaks identified in the workplace to properly react.

3.2.3. Actions by areas of intervention

TB cases must be officially notified and all health centres, regardless of their level of care or property (private or public) are obliged to report it, following the protocol of RENAVE.

In case of suspected cases at social and assistance to migrant services and facilities, cases should be referred in adequate manner and reported to the public health services in CCAA. For that, appropriate networks need to be established.

In case of TB cases detected at workplace, it must also be notified. It should be considered, where applicable, as an occupational illness or work-related accident, by occupational health professionals at preventive services or National Health System professionals, in accordance with current regulations.

3.3. Conventional Contact Investigation

The objective of this line of action is to carry out a conventional contact investigation (ECC in Spanish initials) in 100% of cases of pulmonary and pleural TB. Those cases with a greater probability of transmission will be prioritised. It will always be carried out in childhood TB, even in cases of extra-pulmonary TB.

The implementation of the ECC will be based on the procedure described in the Protocol of RENAVE, which includes a census of contacts, the anamnesis and classification, the carrying out of a TST or IGRA test and chest x-rays in cases where applicable. In the full document of Plan TB, these interventions are detailed according to the characteristics of each contact.

The public health services in each CCAA should coordinate the contact studies, evaluate the results and provide the indicators at a central level, so that it can be incorporated into the annual figures.

The plan proposes a series of activities related to awareness, training, notification and coordination in order to improve the implementation of ECC in health care services, to coordinate with other actors involved as well as to give a decisive boost to activities in the workplace, if needed.

3.4. Prevention and Treatment

Effective treatment is the most important and decisive measure for TB control. As basic principles which sustain anti-tuberculosis therapies, it is essential to combine drugs to avoid resistance, treatments to reduce the likelihood of recurrences, and the simultaneous administration and in one single dose, where possible.

The objectives are to ensure treatment of LTBI for the 100% of cases that require it and to reach a treatment success rate of 95% in cases of sensitive TB and of 75% in cases of MDR/XDR -TB.

3.4.1. BCG Vaccine

Systematic BCG vaccination is not recommended. Vaccination in children and young people with close and prolonged contact with bacilliferous TB, and health workers in frequent contact with tuberculosis patients and their biological tests, should be assessed individually.

With the objective of the control and prevention of imported TB, the administration of the BCG should be assessed individually for minors up to the age of five who are going to countries with an incidence of ≥ 40 cases per 100,000 inhabitants and to live with the local population from more than three months or repeatedly during their infancy, if no other control measures can be applied.

3.4.2. Preventive treatment

Treatment must be managed by medical staff with an appropriate level of knowledge and experience.

3.4.2.a) Chemoprophylaxis

This treatment is indicated as long as the exposed person presents a negative TST or IGRA and a normal chest x-ray, in children (principally under-fives) who are contacts of an infectious TB case, people living with HIV or immunosuppressed, and people who belong to a cluster or outbreak, based on clinical criteria.

Chemoprophylaxis consists of the administration of 300 mg/day of isoniazid (H) in adults and 10 mg/day in children, for a period of 8-12 weeks, after which the TST should be repeated. If it is negative, the treatment is stopped, and if it is positive, it should be continued until the course is completed.

3.4.2.b) Treatment of Latent TB Infection

The objective is to avoid an infected patient developing the clinically active illness. The treatment should be used once tuberculosis and TB drugs contraindications have been ruled out. It should be used only once for the same infection and usually has a duration of six months.

The medicine used is isoniazid (H). The recommended dose is 10 mg/kg/day in children (between 7 and 15 mg/kg/day but no higher than 300 mg daily) and 300 mg/day in adults.

3.4.3. Treatment of New Cases

Treatment must be managed by medical staff with an appropriate level of knowledge and experience. Fixed-dose combinations are recommended. Currently, combinations of two (RH) three (RHZ) and four (RHZE) drugs are available.

The standard treatment regimen for all patients without drug resistance is an initial intensive phase of two months with rifampicin (R), isoniazid (H), pyrazinamide (Z) and ethambutol (E), followed by a continuation phase of four months with R and H. E should be stopped when the antibiogram results are available and these show sensitivity to the other medicines.

If intolerance, toxicity or resistance to habitual medicines appears, the introduction of streptomycin (S) or quinolones should be considered.

3.4.4. Retreatment

In cases of relapse, treatment failure or abandonment, a second treatment will be carried out. This requires a non-standard regimen based on the medical history, a wide antibiogram, the administration of at least three or four effective medicines, the avoidance of short term regimes, and strict monitoring.

3.4.5. Treatment of multi-resistant (MDR) and extensively-resistant (XDR) cases.

The plan proposes that teams of medical experts are established in every CCAA, given that these treatments must be managed by medical professionals with an appropriate level of qualification and experience.

In order to choose the most useful treatment plan, the most up to date recommendations- those that classify the medicines available and puts them in order, balancing effectivity and security- should be followed. The choice of a conventional or short term regime should be done at an individual level. Following the WHO treatment guides, a shortened scheme of 9-12 months with strict monitoring can be recommended for those patients with specific characteristics, as set out in the Plan.

3.4.6. Monitoring and Treatment Control

The establishment of treatment for both the infection and the illness must be combined with an assessment of the potential adherence of the patient, the accompanying measures and the necessary monitoring, bearing in mind the clinical and socioeconomic circumstances of the patient.

3.4.7. Directly observed and supervised treatment

The indication for the establishment of a directly observed (TDO in Spanish initials)/ or supervised treatment (TS in Spanish initials) are previous non-compliance with treatment, retreatment, TB/MDR or TB/XDR, harmful use of alcohol or drugs, children and older patients, homeless patients, specific socioeconomic or medical conditions and the prison population.

The plan recommends actions to promote flexibility of attendance, patient accompaniment, and the elimination of economic or administrative barriers to facilitate adherence to the treatment.

This must be carried out by professionals who are appropriately trained in this type of treatment monitoring.

4. RESOURCES

For the implementation of the plan, material and human resources of the National Health System will be used. The Autonomous Communities will develop pertinent care and coordination facilities and structures. The Health Authorities must provide the necessary material and human resources in their own competencies in order for the Plan's objectives to be met. As well, they must ensure the provision of prevention and treatment to those who have been identified with limited compliance with treatment due to economic conditions

An analysis of the costs of prevention and control of TB will allow specifying measures for the accessibility and the universal and free of charge treatment coverage, and its impact on the budget.

5. COMMUNICATION AND INFORMATION

Plan TB proposes that information about TB is provided on the Ministry of Health website and those of the autonomous communities with updated information, events to publicise the plan and its advances, and the diffusion of information leaflets about the prevention and control of TB.

Regarding communication and promotion of the Plan, its results will be presented annually, and there will be information sessions in coordination with the CCAA and other agents, national and international forums, and the promotion of institutional relationships with other plans, programs and sectors involved.

6. EVALUATION OF THE PLAN

Without compromising the annual monitoring indicators, the evaluation in the first semester of 2021, 2026 and 2031 should be prioritised.

The evaluation scheduled for 2021 will be carried out on the basis of information provided from RENAVE and the indicators of monitoring process, along with the information generated and provided by the CCAA. For the evaluation of new actions, such as the identification of LTBI and intersectoral coordination, we will include new indicators and qualitative information related to the activity and the process, in order to later assess their inclusion as indicators.

In relation to this, the report 'Monitoring Indicators of the Plan for the Prevention and Control of TB in Spain' has been revised and updated in order to progressively converge towards the framework proposed by the ECDC (European Centre for Disease Prevention and Control) and WHO European Region in the context of the 'End TB 'strategy. Indicators that allow the continuance of the available series of relevant variables will be maintained alongside new ones and the inclusion of indicators for TB in paediatrics will be considered. The indicators can be consulted in the Plan.