





Moving towards tuberculosis elimination: a call for action from Italy and a possible model for other low tuberculosis incidence countries

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Consensus document to advocate and ensure proper implementation of WHO recommendations on TB elimination in Italy <http://ow.ly/BHJC307S2U4>

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In 2014 the World Health Assembly endorsed the new End Tuberculosis Strategy that aims at reducing the global incidence of the disease by 90% within 2035 [1].

The World Health Organization (WHO) published, in 2015, a framework for tuberculosis (TB) elimination, *e.g.* a roadmap on how to reach TB elimination (less than one TB case per million population) in low TB incidence countries (those where TB incidence is lower than 10 cases per 100 000 population) [2]. The document had been jointly promoted by WHO and the European Respiratory Society in Rome in July 2014, followed by a consultation with representatives of low TB incidence countries and partner organisations. In this editorial, we present a roadmap for Italy which could also be used as a model for other low TB incidence countries in Europe.

In order to reach TB elimination by 2050, Italy first needs to lower TB incidence to reach the TB pre-elimination threshold (<10 cases per million population) by 2035 [2].

Over the past 70 years, TB incidence (as derived from TB notifications) in Italy has remained rather stable at around seven cases per 100 000 population [3], or 70 cases per million inhabitants. The rapid decline of

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TB cases among native Italians and the slower decline among foreign-born individuals has slowly modified the epidemiology of TB in Italy. According to a survey done by Istituto Superiore di Sanità, Rome (unpublished data), aimed at ensuring quality control in reference laboratories, out of 13030 strains examined between 2008 and 2014, 47% belonged to native Italians (6161) and 53% to foreign-born individuals (6869). Interestingly, out of 410 multidrug-resistant TB (MDR-TB) strains, 77 were identified among native Italians (19%) and 333 among foreign-born individuals (81%).

In Italy and other low TB incidence countries in Europe, the goal of TB elimination is plausible [2]; it requires that the Ministry of Health identifies priority interventions and promotes a budgeted national plan for TB control and elimination with appropriate indicators [4–6].

TABLE 1 Summary of the main interventions to eliminate tuberculosis (TB) in Italy

Political commitment with quality anti-TB services

- Convening a national team of experts supporting the Ministry of Health to plan and evaluate TB control and elimination interventions.
- The team needs to rely on a budget to fund the necessary activities and to be able to have dialogue with regional authorities to facilitate coherence in TB plans.
- Redesign the funding system for TB services. The current DRG (Disease Related Group) system is focused on the management of drug-susceptible cases in the hospital environment. The new system needs to consider clinical-based care (the main stay of case holding in TB treatment) as well as fund reference laboratories and MDR-TB centres.
- Adopt social protection elements necessary to prevent catastrophic TB-related costs for TB patients and their families.
- Fostering the quality control plan for mycobacteriology laboratories.
- Implementing rapid molecular test at programmatic level.

Improvement of surveillance allowing quality monitoring and evaluation of the programme

- Upgrading the national surveillance system with better integration with the regional systems to allow timely notifications to WHO and ECDC according to existing requirements.
- Publishing and disseminating the annual national TB report to allow monitoring and evaluation activities at regional and national level.
- Funding of a systematic national plan for epidemiological surveillance.
- Making LTBI a notifiable condition.

Focus on groups at higher risk of developing TB

- Defining groups and procedures to ensure a public health impact in terms of reduction of the “reservoir” of latently infected individuals
- Strengthening collaborative activities for optimal management of TB/HIV co-infected individuals.
- Defining mechanisms to coordinate management of TB outbreaks and micro-epidemics.

Implementing a plan to manage migration-related issues

- Implementing the Ministry of Health recommendations to control TB in migrant populations, defining the standards for screening, diagnosis and treatment of both TB and LTBI.
- Including all the necessary social protection elements necessary to prevent catastrophic TB-related costs for TB patients and their families.

Priority to LTBI diagnosis and treatment particularly in risk groups

- Creating and implementing a register and a surveillance system for LTBI.
- Identifying the groups at higher risk to develop TB disease given infection.
- Planning the necessary training for the different categories of health staff to implement this activity.

Prevention and treatment of MDR-TB

- Implementing an Italian version of the ERS/WHO TB Consilium [18] based on the ERS platform. The platform is free-cost, multi-language, and allows adequate management of difficult-to-treat MDR-TB cases through the support of leading world TB experts. This service is particularly important for correct management of the new anti-TB drugs delamanid and bedaquiline.
- Standardising the rapid diagnosis of drug-resistant TB.
- Implementing a comprehensive surveillance system for new drugs.
- Designing and implementing a national register of MDR-TB cases and monitoring MDR-TB treatment outcome.
- Identifying MDR-TB reference centres[#].
- “Ad hoc” funding for reference clinical and laboratory services supporting MDR-TB management[¶].
- Releasing second-line anti-TB drugs directly through reference centres.

Fostering of research on new vaccines, diagnostics and drugs

- Launching a national TB research plan.

Global and European coordination of TB elimination efforts

- Supporting, and coordinating the international anti-TB activities (human resource development, control and elimination) managed by the Italian Centres of Excellence.

MDR-TB: multidrug-resistant tuberculosis; WHO: World Health Organization; ECDC: European Centre for Disease Prevention and Control; LTBI: latent tuberculosis infection; ERS: European Respiratory Society. [#]: reference centres need to be defined based on 1) documented experience (number and outcomes of cases managed, adoption of international guidelines, etc.); 2) support of a reference mycobacteriology laboratory; 3) availability of second-line anti-TB drugs; and 4) availability of adequate infection control practices. [¶]: as an example, in the Lazio Region the DRG (Disease Related Group) refund for TB cases ranges from €4422 (DRG 80: non-complicated TB) to a maximum of €5744 (DRG 79: TB with complications that do not include MDR-TB), which far from covers the cost of MDR-TB management.

Mathematical modelling indicates that, in order to reach TB elimination by the fixed deadline, the present annual incidence decline in Europe (2–5%) should gradually increase to approach the level of 20% [2, 3, 7]. According to WHO, this is possible if available prevention, diagnostic and treatment weapons are optimally implemented [2, 8, 9]. These include new generation rapid diagnostics and shorter regimens to treat TB disease (including its resistant forms) and latent TB infection (LTBI) [10, 11].

Examples are available of settings where an “aggressive approach”, based on TB control and elimination interventions, resulted in a rapid reduction in the incidence of TB and an advance towards the pre-elimination phase [12, 13].

This consensus (and call for action) document is aimed at promoting discussion between TB experts, administrators and policymakers in order to ensure that WHO recommendations on TB elimination are implemented in Italy.

In agreement with the principles of the TB elimination framework, we summarise eight core interventions and activities to be included in a roadmap for TB elimination in Italy, which were developed by consensus of representatives of different Italian and international organisations (including the European Respiratory Society) in a meeting organised by the Italian Respiratory Society (SIP/IRS) in Milan on October 5, 2016 (table 1).

- 1) Political commitment with quality anti-TB services. TB control in Italy is presently based on 21 regional plans, which are not necessarily consistent among themselves and with the latest WHO policy documents. The main areas for further work are the management of LTBI and the use of rapid diagnostic tests outside reference centres. TB control and elimination activities need to be adequately funded.
- 2) Improvement of surveillance allowing quality monitoring and evaluation of the programme. Italy should optimise its capacity to submit complete surveillance data to WHO and the European Centre for Disease Prevention and Control in a timely manner, while implementing a consistent plan for national molecular epidemiological surveillance.
- 3) Focus on groups at higher risk of developing TB. A periodic identification of the groups where targeting TB elimination efforts is necessary, based on surveillance data.
- 4) Development of a plan to manage migration-related issues. The number of TB cases among foreign-born individuals has increased and is, today, higher than that of native Italians. In addition, the important migration flow to Europe *via* land or sea (Italy is among the main migrants' host countries) needs a coherent and coordinated approach [14–16].
- 5) Prioritisation of LTBI testing and treatment in high-risk groups. Diagnosis and treatment of LTBI is the core intervention needed to achieve TB elimination, as it will reduce the “reservoir” of infected individuals from which future cases will be generated [2].
- 6) Prevention and treatment of MDR-TB. Although the absolute number of these cases is not high [17], the complexity and costs of their management, and the potentialities for further nosocomial transmission, call for a targeted approach [2]. Treatment outcome monitoring of MDR-TB should be implemented.
- 7) Fostering of research on new vaccines, diagnostics and drugs. Italy needs to contribute to the global effort towards the acquisition of basic knowledge leading to the development of new anti-TB tools (basic research) and on their optimal implementation (implementation research).
- 8) Global and European coordination of TB elimination efforts. It is common experience that TB does not respect borders and the best way to maintain future generations of TB experts is to actively cooperate in international TB control and elimination activities.

We are confident that TB elimination can be within reach if Italy, together with the other low TB incidence countries in and outside Europe, will seriously embark in a comprehensive plan that incorporates all the core activities discussed above.

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