Tuberculosis elimination: dream or reality? The case of Cyprus

To the Editor:

The World Health Organization (WHO)-recommended strategy of tuberculosis (TB) control has evolved from the DOTS (directly observed treatment, short course) strategy to the Stop TB strategy [1, 2]. By breaking the chain of transmission through rapid diagnosis and effective treatment of infectious TB cases, this strategy allowed the development of national TB programmes and proved to be highly cost-effective [3, 4].

However, in order to accelerate the decline of the TB pandemic, WHO has planned a post-2015 strategy focusing on the concept of TB elimination [5–8]. To reach elimination (defined as fewer than one sputum smear-positive case per million inhabitants), countries should ensure that diagnosis and treatment of latent TB infection (LTBI) supplements detection and treatment of active TB disease [7–10].

A recent survey conducted by the European Respiratory Society (as part of its 2012–2013 Presidential plan) and WHO in Europe has demonstrated that the majority of countries do not have all the interventions in place to reach elimination [11], and stressed the importance of studying model countries able to demonstrate that TB elimination can be reached [12–14].

The aim of the present study was to show the progress achieved by Cyprus towards the elimination targets. Cyprus has been selected because of its solid TB control programme, the quality of surveillance data and health services, and its small population (865,878 in 2012).

The way Cyprus covered the seven core areas considered essential to reach elimination (commitment, TB awareness and capacity of health systems, surveillance, quality laboratories and care, capacity to manage drug-resistant TB and TB/HIV co-infection, introduction of new tools and operational research, and establishment of international collaborations) are described herein, and the impact indicators (notification of new sputum smear-positive case rates per million population) were analysed between 1995 and 2012 [7, 9].

Surveillance data were made available by the Ministry of Health of Cyprus in Nicosia from 1978 to 2012, based on European Union residents. Although data do not formally cover the whole of the island, Cyprus’ health system offers its services to a large proportion of migrants entering from its northern occupied territory.

Cyprus has a solid TB control programme, and although an elimination plan has not been formalised, much has been done in this direction. Clinical [5] and laboratory [1] reference units have been identified, and civil society and scientific societies are officially collaborating with the national TB programme. Surveillance is regularly conducted including the necessary projection modelling to evaluate progress towards targets [11]. The national reference laboratory performs sputum smear microscopy, culture and drug susceptibility testing (DST) for first-line anti-TB drugs under external quality assurance by a supranational reference laboratory (Pasteur Institute, Athens, Greece), which is in charge of performing DST for second-line drugs. TB diagnostic and treatment services are available for free, while a nominal fee is charged for out-patients services (in 2011 out of 301 patients 255 (85%) were outpatients). Anti-TB drugs are available and no stock-out has ever been described. Multidrug-resistant TB cases are managed in a single reference centre, in isolation wards. Coordination with HIV/AIDS services has been established to ensure a one-stop service for diagnosis and treatment of TB/HIV co-infected individuals.

Screening for LTBI and contact screening are systematically performed as well as LTBI treatment (isoniazid for 6 or 9 months) although completion rates are not being monitored systematically. Impact indicators are summarised in figure 1.

The overall TB notification rate per million population decreased from 85 in 1980 to an historical minimum of 28 in 2002. Among infectious (sputum smear-positive) cases, the decline was from 24 to 11 per million.

In 2003, both the number and incidence of notified cases per million population reached a balance between individuals born in Cyprus and those born abroad. The proportion of cases among migrants to Cyprus has progressively increased, reaching a “plateau” >80% in 2007.

TB notifications and rates (all forms) declined progressively among natives from 31 in 1996 to six per million in 2004, then reaching a plateau around seven to eight per million. Among infectious cases, the
reduction reached two cases per million in 2005, bordering the conventional elimination threshold of one per million. Among foreign-born individuals, the rates of notified cases instead increased to reach 54 overall and nine per million (sputum smear-positive) in 2009.

The analysis of TB trends in Cyprus shows that, under sound control measures, the number of cases had an annual average 9.4% decrease from 1997 to 2002 (from 46 to 20 cases), followed by a mild increase related to contribution of *Mycobacterium tuberculosis* strains from the immigrant population.

Cyprus health services attract more and more foreign-born cases from the Turkish-occupied area of the island [15].

Out of 244 migrants with TB diagnosed between 2007 and 2012, 89 (36.50%) were born in Asia, 91 (37.30%) in eastern Europe, 33 (13.50%) in former Soviet Union countries, 22 (9.00%) in west Europe and nine (3.70%) in Africa. In terms of essential control interventions, Cyprus has developed efficient case-finding (estimated case-detection rate 100% in 2012 and >87% since 1990, diagnostic delay 2–4 days) and treatment services (case success rate >85% since 2006).

This is further testified by the low prevalence of multidrug-resistance (4.4% among new cases and retreatment cases together; 10 cases diagnosed since 2005).

Therefore, Cyprus has virtually reached the elimination phase in its native-born population (fig. 1). Unfortunately, it is difficult to maintain such a low level of *M. tuberculosis* transmission in the population; even a few TB cases deriving from the continuous flow of immigrants are, at the moment, sufficient to prevent further progress.

Thus, several interventions need to be improved to pursue elimination in this country. First of all, focusing on at-risk populations, and especially migrants, is essential: innovative interventions of early and active case detection must be strengthened, accompanied by preventive treatment for persons at high risk. In addition, the Cyprus government needs to implement other measures, including: development of specific targets and plans for TB elimination at the national level accompanied by a well-thought projection model that assesses the potential impact of different measures, including all current, and potential future, new diagnostics and drugs; introduction of rapid molecular diagnostics (a few Xpert MTB/RIF (Cepheid, Sunnyvale, CA, USA) machines could easily cover the entire population of Cyprus) for both native and migrant populations seeking care; surveillance using systematic fingerprinting of all the strains isolated to better identify and contain microepidemics; and implementation of electronic surveillance and mechanisms to ensure validation and quality control of data, and improvement of the existing LTBI register (to allow evaluation of LTBI treatment completion rates). Finally, universal health coverage that translates into easy access to high-quality diagnosis and treatment without catastrophic expenditures, and social protection mechanisms covering for income losses among people with TB during their months-long treatment need also to be introduced to protect the most vulnerable individuals.

The Cyprus model confirms that targeting elimination is feasible although maintaining the TB epidemic below this threshold requires continuous commitment and funding. Among additional core policies and
interventions needed at the national level to accelerate incidence decline, those related to diagnosis and treatment of LTBI are the most important [16].

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Cyprus achieved TB elimination by comprehensive effort but imported cases do not allow it to stay below the threshold http://ow.ly/uWiDB

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