



MISSION REPORT



Tuberculosis in the Netherlands

Report of the joint ECDC and WHO review of the tuberculosis prevention and care system in the Netherlands

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Report of the joint ECDC and WHO review of the tuberculosis prevention and care system in the Netherlands, 24–28 June 2019



This joint report of the European Centre for Disease Prevention and Control (ECDC) and the World Health Organization (WHO) was coordinated by Senia Rosales Klintz and Marieke J. van der Werf.

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Abbreviations

BCG	Bacillus Calmette–Guérin
Cib	Centre for Infectious Disease Control (of the RIVM)
COA	Central Agency for the Reception of Asylum Seekers
CPT	Committee for Practical Tuberculosis Control
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EU	European Union
GGD	Municipal Health Service
GGD GHOR Nederland	Association of GGDs and GHOR-offices in the Netherlands
GHOR	Regional Medical Emergency Preparedness and Planning Offices
H	Isoniazid
HIV	Human Immunodeficiency Virus
IGJ	Health and Youth Care Inspectorate
IGRA	Interferon gamma release assays
KNCV	KNCV Tuberculosis Foundation [<i>Koninklijke Nederlandse Centrale Vereniging tot bestrijding der tuberculose</i>]
LTBI	Latent tuberculosis infection
MDR	Multidrug-resistant
NSPOH	Netherlands School for Public and Occupational Health
NTCP	National Tuberculosis Control Plan
R	Rifampicin
REC	Regional Expertise Centre
RIVM	National Institute for Public Health and the Environment
TB	Tuberculosis
TST	Tuberculin skin testing
WHO	World Health Organization

Executive summary

Rationale and purpose of the country visit

The Netherlands is a low tuberculosis (TB) burden country in western Europe which in the last two decades has achieved significant progress in reducing its TB notification rate from 9.8 per 100 000 in 1999 to 4.7 per 100 000 in 2018. Since 77% of all reported TB cases in the Netherlands are of foreign origin, current TB strategies focus mainly on active case finding by screening among certain population groups at risk for TB (including migrants and asylum seekers), contact investigation and management of latent TB infection (LTBI) and TB patients with active disease. Since 2004, favourable treatment outcomes for drug-susceptible TB have exceeded 85%, which has contributed to the overall decline in TB incidence and mortality. Over the past few years a low number of cases with drug-resistant TB have been registered (10–15 patients annually) and all have had access to therapy in accordance with the latest World Health Organization guidelines.

The Centre for Infectious Disease Control of the National Institute for Public Health and the Environment (RIVM), the KNCV Tuberculosis Foundation (KNCV) and the National Association of Municipal Health Services and Regional Medical Emergency Preparedness and Planning Offices (GGD GHOR Nederland) requested an external review of the TB prevention and care activities in the Netherlands. The European Centre for Disease Prevention and Control (ECDC) and the World Health Organization's Regional Office for Europe (WHO) then jointly conducted a country visit to provide expert advice on sustaining the accessibility, quality, effectiveness and efficiency of TB prevention and care measures. A team of six experts visited the Netherlands between 24 and 28 June 2019 to perform the external review, in collaboration with national counterparts. The external review focused on LTBI screening among migrants and retention of knowledge and expertise on TB prevention and control in a country with declining TB incidence. The progress made on the recommendations from the 2013 international review was also assessed.

Technical reports, surveillance data, national guidelines and epidemiological data were reviewed in preparation for the country visit. During the visits to health authorities, health services and a TB hospital, the review team met healthcare personnel. Interviews were held with key informants representing public health authorities and professional organisations involved in the provision of TB services. The review team then suggested options to further strengthen TB prevention and care based on findings and the latest WHO and ECDC policy guidance on TB prevention and care.

Key findings

Screening of LTBI in migrants

- The Committee for Practical Tuberculosis Control has issued national guidelines for LTBI diagnosis, LTBI treatment, and LTBI/TB screening in persons infected with HIV. The Dutch Thoracic Society has developed a set of guidelines on LTBI/TB screening prior to immunosuppressive medication.
- Targeted diagnosis and treatment of LTBI among people at risk of TB is performed and monitored routinely in the Netherlands, along with active TB case finding.
- Since December 2015, screening and treatment for LTBI has been recommended for migrants under the age of 18 years. Other migrants are not targeted unless they have concomitant risk factors.
- There are some system barriers to accessing TB services, including LTBI screening and treatment, for certain population groups, particularly asylum seekers, undocumented migrants and other vulnerable populations (i.e. compulsory deductible payment).
- Several treatment regimens are recommended for LTBI treatment.
- Since 1993, municipal health services (GGDs) and hospitals can voluntarily report LTBI cases to an anonymised, nationwide, case-based register. The LTBI register is linked to the national TB register and enables the monitoring of treatment initiation, treatment completion and reasons for interrupting treatment among those with a positive LTBI test.

Human resources

- Healthcare professionals working in TB prevention and care at municipal health service (GGD) level have a well-established collaboration with the clinical sector and other GGDs.
- There is a good networking and linkage between the relevant institutions involved in TB prevention and care (RIVM, KNCV, GGDs, hospitals, sanatoria and the penitentiary system) and many of these organisations are involved in training and capacity building.
- The changes in TB epidemiology in the country (i.e. an overall decrease in TB case numbers) have an impact on the volume and the nature of TB activities.
- The number of trained TB physicians and nurses is decreasing and in some areas, the number of trained professionals is insufficient.

- Continuous education is required for re-registration as a TB public health physician and it is also necessary for other professionals working in TB prevention and care. Medical technical assistants do not have a mandatory system of registration. However, a TB refresher training day is organised on an annual basis.

Options

Screening of LTBI in migrants

- To consider extending the policy of systematic testing and treatment for LTBI to all migrants and asylum seekers from countries with a high TB burden who have entered Europe during the last five years or less. This policy change could be considered after a feasibility analysis, including the human resource and cost-effectiveness aspects.
- To operationalise systematic LTBI testing and treatment of at-risk migrants and asylum seekers by:
 - providing information on LTBI and LTBI treatment to all immigrants recommended for testing and treatment;
 - assessing whether the GGDs could act as the primary entry point for systematic testing and treatment of LTBI in migrants;
 - screening migrants for LTBI as soon as possible after their settlement in the Netherlands. General practitioners may facilitate linkage to LTBI screening for newly-arrived immigrants with residence permits as a result of family reunification.
- To continue offering a range of different LTBI treatment regimens so that each person can be treated with the most appropriate treatment. Shorter regimens should be prioritised.
- To continue the monitoring of the programmatic management for LTBI by using indicators already implemented (e.g. treatment acceptance among those eligible and LTBI treatment completion) and by introducing new indicators (e.g. number of people eligible for LTBI screening and number of people screened for LTBI) to allow for the monitoring of WHO-recommended indicators.

Human resources

- To establish an inclusive stakeholder platform for the development of a capacity building plan and to steer the implementation.
- To develop a flexible and adjustable competency framework for TB prevention and care activities for GGDs, taking into account the diversity in the different GGD areas.
- To give greater emphasis to TB-related topics in general infectious disease public health training for doctors, nurses and medical technical assistants.
- To ensure that adequate training, mentoring and supervision is provided when tasks are shifted to healthcare workers not previously involved in TB prevention and care activities.
- To consider developing international collaboration with high-TB burden countries or settings. TB professionals in the Netherlands would benefit from capacity building and training activities in settings with more TB patients than in the Netherlands, especially for diagnosis and treatment of TB. If necessary, relevant national and international stakeholders could also be involved, with the possible support of the KNCV, RIVM, ECDC and WHO.

Conclusions

The Netherlands is achieving significant progress towards eliminating TB and implementing the National TB Control Plan for 2016–2020. With focus on implementing a combination of strategies for LTBI screening among migrants and management of active TB, the Netherlands National TB Programme is setting an example in achieving targets and milestones under the global End TB Strategy and the WHO Regional TB Action Plan for Europe, 2016–2020. Retaining knowledge and expertise among public health TB professionals on TB prevention and care should be one of the priorities of the Netherlands' National TB Programme on its path towards TB elimination.

1 Background

In recent decades the Netherlands has made significant progress in reducing the tuberculosis (TB) notification rate from 9.8 per 100 000 in 1999 to 4.7 per 100 000 in 2018 (806 TB cases registered) [1,2]. With 77% of all reported TB cases in the Netherlands of foreign origin (619 TB cases) [2], current TB strategies have been mostly focused on active case finding among at-risk population groups, including migrants and asylum seekers. The main activities conducted are contact investigation, screening and management of both latent TB infection (LTBI) and active TB disease, and Bacillus Calmette–Guérin (BCG) vaccination of child risk groups. Since 2004, favourable treatment outcomes for drug-susceptible TB have been exceeding 85%, which has contributed to the overall decline in TB incidence and mortality [1]. Over the past few years the registered number of cases with drug-resistant TB has been low (10–15 patients annually) and all have access to therapy in accordance with the latest guidelines from the World Health Organization (WHO) [3,4].

The last country visit to the Netherlands in 2013 resulted in specific recommendations [5] and contributed to the development of the National TB Control Plan (NTCP) for 2016–2020 [6], which was developed in line with the End TB Strategy [7] and WHO's Regional TB Action Plan for Europe for 2016–2020 [8]. The aim of the Dutch NTCP is to reduce TB incidence by 25% (3.7 per 100 000) and TB transmission by 25% by 2019.

The Centre for Infectious Disease Control (Cib) of the National Institute for Public Health and the Environment (RIVM), together with the KNCV Tuberculosis Foundation (KNCV) and the National Association of Municipal Health Services and Regional Medical Emergency Preparedness and Planning Offices (GGD GHOR Nederland), requested an external review of national TB control activities in the Netherlands. The European Centre for Disease Prevention and Control (ECDC) Tuberculosis Disease Programme and WHO's Regional Office for Europe then jointly conducted a country visit between 24 and 28 June 2019, in accordance with the agreed terms of reference (Annex 1). The purpose of the review was to provide expert advice on sustaining the accessibility, quality, effectiveness and efficiency of TB services in the Netherlands.

The specific objectives of the external review were:

- to review the progress made on the recommendations of the international review 2013;
- to review and advise on prioritisation and extent of latent TB infection screening of migrants to achieve the set targets;
- to review and advise on the conditions and measures necessary for the retention of knowledge and expertise in the Netherlands, a country with declining TB incidence.

The review team consisted of:

- Marieke J. van der Werf, Head of ECDC's TB Disease Programme, and country mission leader
- Askar Yedilbayev, TB Unit Lead, WHO Regional Office for Europe
- Senia Rosales Klintz, ECDC Expert in TB
- Martin van den Boom, Technical Officer, WHO Regional Office for Europe
- Delphine Antoine, ECDC external expert in human resources and training, Santé publique France [French National Public Health Agency]
- Alberto Matteelli, ECDC external expert in LTBI screening, University of Brescia, Brescia Spedali Civili General Hospital and WHO Collaborating Centre for TB/HIV and TB Elimination.

At national level, the visit was organised and coordinated by Gerard de Vries and Cindy Schenk (RIVM).

Before the country visit, the team members reviewed relevant documents provided by the national counterparts. These documents included national guidelines, technical reports (including peer-reviewed scientific publications), epidemiological data and training curricula describing various aspects of the TB prevention and care activities conducted in the Netherlands. During the country visit, the review team visited national authorities and TB health services. Selected stakeholders were interviewed to gain a deeper understanding of the current situation in the Netherlands. Annex 2 describes the programme followed during the visit and Annex 3 summarises the people and organisations met.

The collected evidence was discussed within the review team and observations and recommendations were agreed. On 28 June 2019, the review team held a debriefing meeting with national stakeholders.

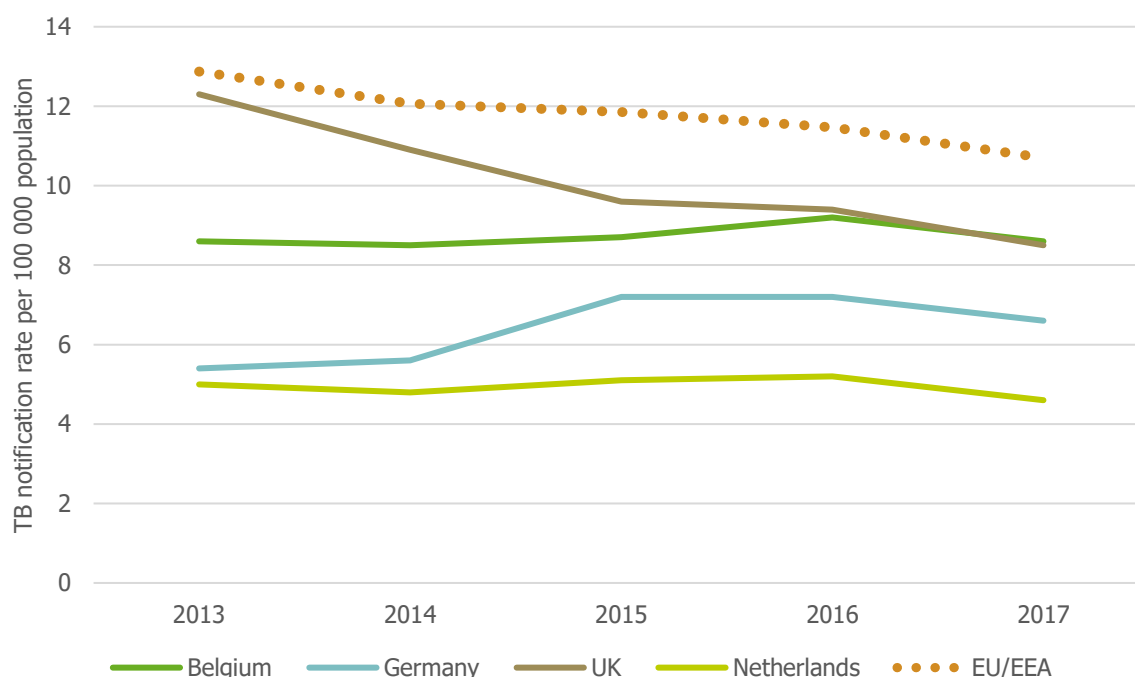
2 Overview of the TB situation in the Netherlands

Epidemiological information

In 2018, the Netherlands had a population of 17.2 million [9], 23% of which had a migrant background [10]. In the Netherlands, life expectancy of the male population was 80 years in 2016, and life expectancy for females was 83 years [11]. The three main causes of death are heart disease, Alzheimer's disease and other dementias, and lung cancer [12].

In 2018, 806 TB patients were notified [2]. Of these, 469 (58%) had pulmonary TB and 337 (42%) extrapulmonary TB. The notification rate decreased slightly between 2013 and 2017 (-2.2%) but increased again in 2018 [13]. The notification rate in the Netherlands is below the European Union and European Economic Area (EU/EEA) average and also lower than in three neighbouring countries (Belgium, Germany, and the United Kingdom [UK]) (see Figure 1.)

Figure 1. Trend in TB notification rate in the Netherlands compared with three neighbouring countries and the European Union and European Economic Area (EU/EEA), 2013–2017



Source: ECDC/WHO [13]

The majority of TB patients in the Netherlands are of foreign origin, 77% in 2018, with the main countries of birth being Eritrea, Morocco, India, Somalia and Indonesia (in order of decreasing number of patients) [2]. High proportions of TB patients of foreign origin are also observed in other countries in western and northern Europe (Figure 2).

In 2018, six patients were diagnosed with multidrug-resistant (MDR) TB [14]. Between 2013 and 2018, the number of MDR TB patients ranged from six to 16 [13,14]. The percentage of patients diagnosed with MDR TB is similar to that for Belgium and the UK and lower than the EU/EEA average [13] (Figure 3).

The percentage of TB patients with known human immunodeficiency virus (HIV) status increased between 2014 and 2018 from 61% to 76% in the Netherlands [14]. The percentage with known HIV status is slightly lower than or equal to the EU/EEA average for the countries that reported on HIV status [13] (Figure 4).

Figure 2. TB in persons of foreign origin in the European Union and European Economic Area (EU/EEA), 2017

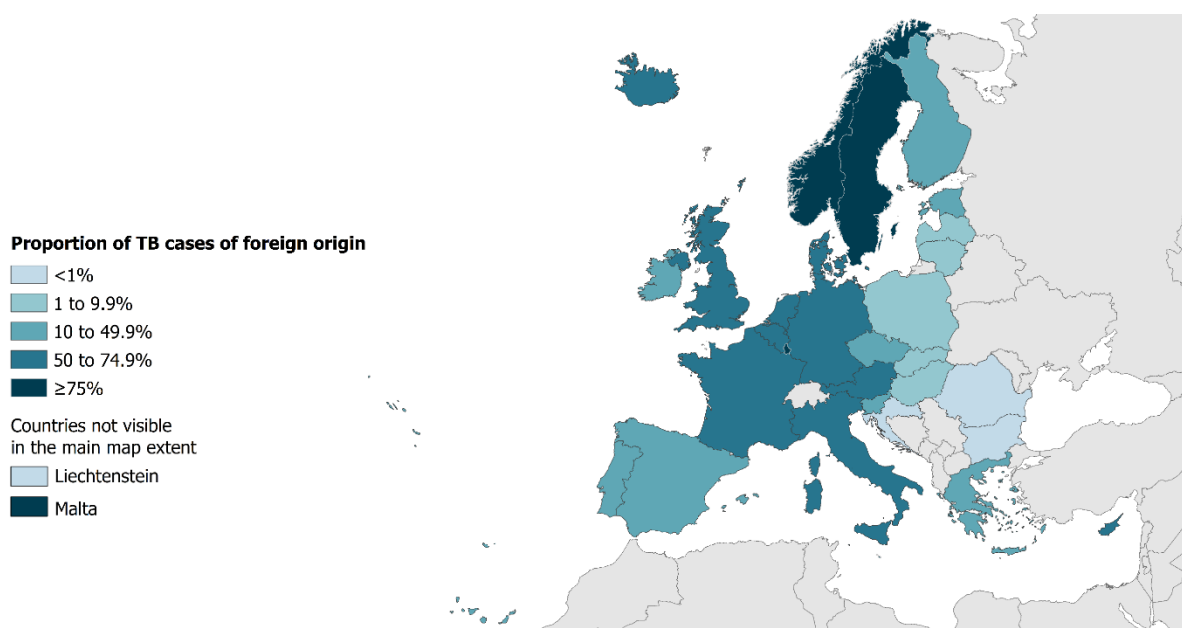
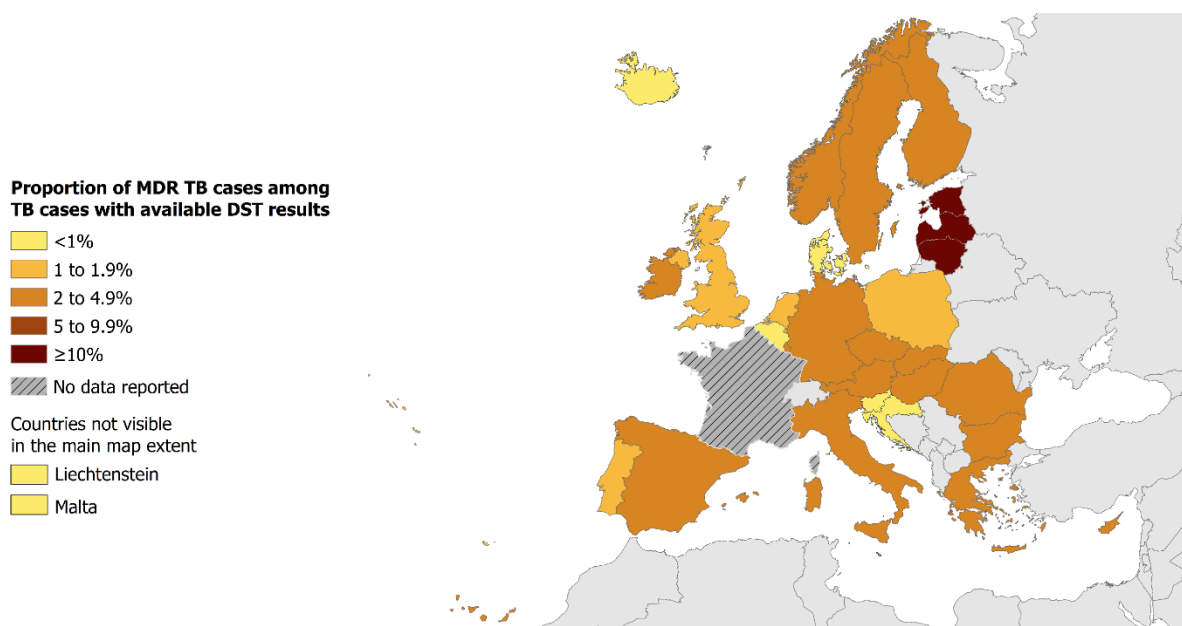


Figure 3. Multidrug-resistant (MDR) TB in patients with available drug susceptibility testing (DST) results in the European Union and European Economic Area (EU/EEA), 2017

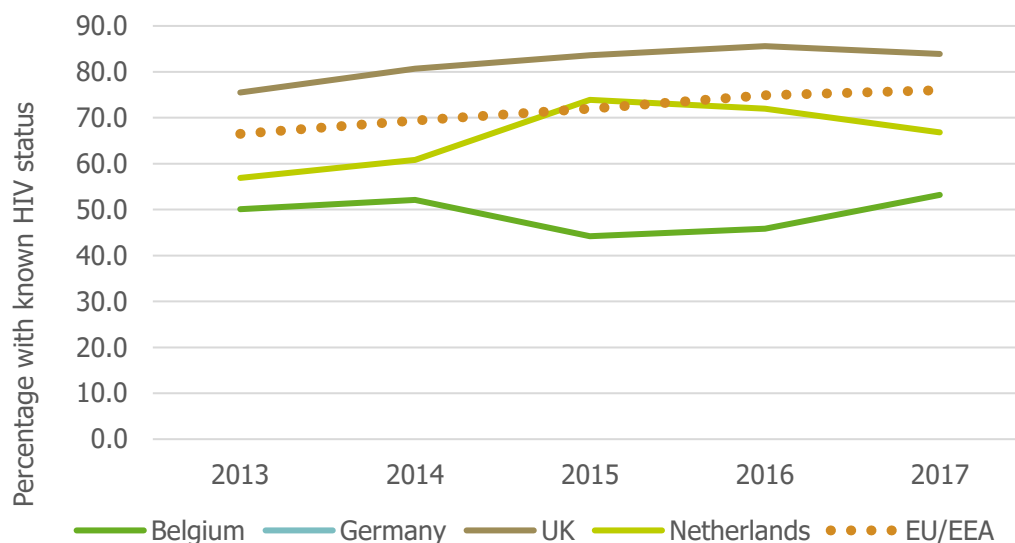


Source: ECDC/WHO [13]

In 2017, 22 (4.2%) of 787 TB patients in the Netherlands with a known HIV status were co-infected with HIV [13]. This was similar to the EU/EEA average of 3.9%, when compared with data from the 23 EU/EEA countries that reported on HIV status in 2017 (Figure 5).

Compared to the neighbouring country Belgium, the percentage of TB cases co-infected with HIV is lower (Figure 6). The trend in the Netherlands is comparable to the trend in the UK and for the EU/EEA as a whole.

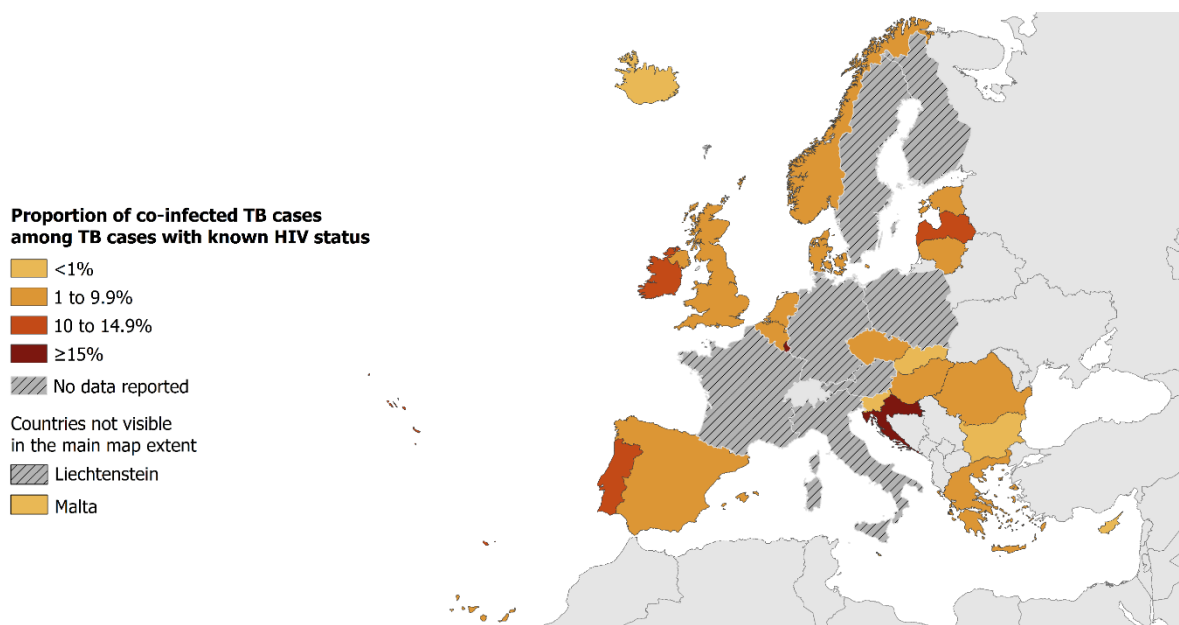
Figure 4. Trend in percentage of TB patients with known HIV status in the Netherlands* compared with three neighbouring countries (Germany reported no data) and the European Union and European Economic Area (EU/EEA), 2013-2017



Source: ECDC/WHO [13]

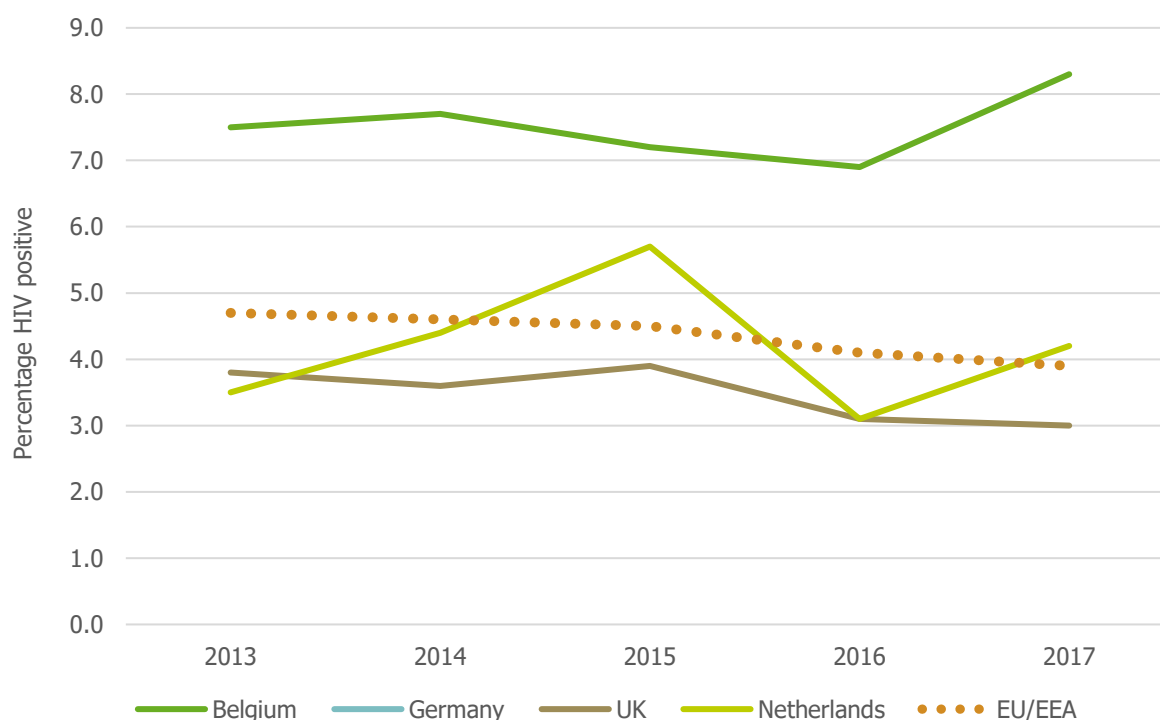
*The 2019 TB surveillance report from the Netherlands indicates that the actual number of recorded TB cases with HIV testing was 78% in 2017 and 76% in 2018 [14].

Figure 5. Proportion of co-infected patients among TB patients with known HIV status in the European Union and European Economic Area (EU/EEA), 2017



Source: ECDC/WHO [13]

Figure 6. Trend in percentage of HIV-positive TB patients among TB patients with known HIV status in the Netherlands compared with three neighbouring countries (Germany reported no data) and the European Union and European Economic Area (EU/EEA), 2013–2017



Source: ECDC/WHO [13]

Organisation of TB prevention and care services

The Netherlands is divided into 12 provinces, which are divided in 355 municipalities and three special municipalities (Bonaire, Saba, St Eustatius). Healthcare is provided by around 10 000 general practitioners, 88 hospitals and 25 municipal health services ('Gemeentelijke Geneeskundige Dienst', GGD) [15]. The GGDs are responsible for public health activities. A director of public health leads each GGD.

Since 2014, the 25 GGDs have organised themselves into four Regional Expertise Centres for TB Control (REC). The tasks of the GGDs in relation to TB include TB/LTBI diagnosis and treatment, contact investigation, outbreak management, screening of groups at-risk, provision of BCG vaccination and coordination of activities to prevent TB transmission [16,17].

In addition, there are two modern sanatoria, Beatrixoord and Dekkerswald, which are affiliated with the university hospitals in Groningen and Nijmegen, respectively. These TB hospitals provide care for patients with complex clinical presentations, such as MDR TB, vertebral TB, TB/HIV co-infection and TB combined with social problems requiring long-term care. They also serve as expert centres providing advice and capacity building on TB clinical management [15,16].

Legal basis

The legal framework for the provision of TB prevention and care services in the Netherlands is extensive [16]. This section refers to the most relevant legislation for the purposes of this external review.

The Dutch health system is based on managed competition in the markets for health insurance, health services provision and healthcare purchasing, as defined in the Health Insurance Act ('Zorgverzekeringswet') and the Health Care Market Regulation Act ('Wet Marktordening Gezondheidszorg') [18]. Dutch residents must acquire a basic health insurance package with the insurance provider of their choice. The health insurance covers aspects such as the cost of medical care and treatment for TB, but the insurance policyholders must pay a compulsory deductible fee (EUR 385, 2019 [19]) on an annual basis. TB and LTBI treatment costs are not exempt from the deductible payment. Children and adolescents <18 years of age are insured free of charge and exempted from the deductible payment.

The Public Health Act ('Wet Publieke Gezondheid'), includes TB control as a public health care task [6]. National policy, national surveillance, and participation in international policy development are defined, organised and implemented at national level. Several stakeholders are involved in the provision of TB prevention and care services:

- Ministry of Health, Welfare and Sports (VWS) has a regulatory role and participates in international policy development.
- Health and Youth Care Inspectorate (IGJ), is an independent advisory body to the VWS.
- RIVM is an independent advisory body to the VWS and holds the TB national reference laboratory.
- The municipalities have executive responsibility for TB. This executive responsibility is carried out by the 25 GGDs.
- GGD GHOR Nederland represents the interests of its members; promotes quality in public health services; and facilitates cooperation between GGDs.
- KNCV is a knowledge centre that monitors and evaluates TB control interventions, supports and coordinates professional reviews of the RECs and develops/provides educational materials and professional training on TB.
- The Committee for Practical Tuberculosis Control (CPT) develops scientific guidelines and associated protocols.

The Population Screening Act ('Wet op het Bevolkingsonderzoek') aims to regulate screening with the intention of limiting the negative effects of population screening. Consequently, TB and LTBI screening policy is regularly evaluated and adapted when necessary. The evaluations are jointly conducted by KNCV and the GGDs. Annual reports on the results of screening in penal institutions are provided by the GGD GHOR Nederland [16].

The Immigration Act ('Vreemdelingenwet') stipulates that foreign nationals are expected to cooperate in TB medical investigations. The GGDs are in a position to screen for TB among foreign nationals (including immigrants and asylum seekers from certain non-EU countries) intending to stay in the country for longer than three months. EU/EEA residents, as well as citizens from countries with a WHO-estimated TB incidence <50/100 000 (for asylum seekers and refugees) and <100/100 000 (for other migrants) are exempt from TB screening. The Immigration and Naturalization Service can suspend expulsion of a foreign national and his/her family members if they are suspected of having or have been diagnosed with TB. An exception applies when the foreign national has previously applied for asylum in another EU Member State [20]. This exception is often referred as a 'Dublin claim'¹.

¹ The Dublin regulation is accessible at the following link: <https://eur-lex.europa.eu/legal-content/en/ALL/?uri=celex%3A32013R0604>

3. Progress in implementation of previous TB country review recommendations

During the external review conducted in 2013, the ECDC/WHO review team issued 33 specific recommendations, covering six thematic areas. Annex 4 provides a detailed description of their implementation status. Table 1 summarises the progress in implementing the 12 key recommendations proposed in the 2013 external review. Given the scope of the current external review, the review team could not assess the extent to which all recommendations from the previous external review had been implemented.

Table 1. Implementation status of key recommendations from TB programme review in the Netherlands, 2013

	Recommendation	Status
1	Establish a formal laboratory network structure linking a defined national reference laboratory with few regional laboratories, clearly stating which test is performed at each level, to optimise TB diagnosis.	RIVM is the national reference laboratory (NRL). No formal laboratory network available. The mycobacteriology working group of the Dutch Association for Medical Microbiology (NVMM) has: <ul style="list-style-type: none"> issued two national guidance documents, one on diagnosis of mycobacterial diseases (2015) and another on the application of direct testing for MDR tuberculosis (2018); conducted a survey to assess the implementation of the guidance documents and the type and number of TB tests performed (2019). The response rate was 96% (46 of 48 invited laboratories). Thirty-one laboratories performed mycobacterial culturing.
2	Ensure that culturing and drug susceptibility testing for <i>M. tuberculosis</i> complex strains only takes place in a few nationally and internationally quality-assured biosafety level-3 facilities with internal and external quality assurance systems in place (for all diagnostic procedures performed).	RIVM performs drug susceptibility testing for <i>M. tuberculosis</i> complex. All 31 laboratories performing mycobacterial culturing have appropriate biosafety level-3 [21]. External quality assurance was performed by 94% of the laboratories participating in the NVMM survey.
3	Send the first positive culture from any person with TB immediately to the NRL for genotyping and if any resistance is reported, conduct phenotypic drug susceptibility testing verification, including that previously detected by molecular methods (to improve the timely delivery of results).	A total of 94% of the laboratories participating in the NVMM survey reported PCR testing done directly on patient samples to detect drug resistance. All isolates are sent to the NRL for genotyping [1].
4	Develop a comprehensive TB-relevant human resources plan corresponding to current and any planned service delivery model(s), also taking into account the projected trend of TB epidemiology, including TB expertise with children.	Three models of care have been developed and proposed to the GGDs. However, a comprehensive development plan for human resources is not yet in place.
5	Raise and maintain awareness and knowledge of TB among relevant first-line healthcare personnel (such as general practitioners).	Not observed.
6	Facilitate and harmonise the preparation and communication of TB-related training curricula and courses (including web-based tools).	E-learning and training materials available through KNCV Tuberculosis Foundation. The TB handbook [16] is widely used.
7	Discuss implementing LTBI screening for high-risk groups in the light of TB elimination, even though LTBI screening is not cost-effective using the ceiling for the cost-effectiveness of healthcare interventions.	Generally there is compliance with international guidelines for LTBI management [22,23]. Migrants < 18 years of age are screened for LTBI, but this has not yet been implemented for asylum seekers < 18 years. Decision on extending LTBI screening to other migrants is pending.
8	Consider scaling up implementation of LTBI detection and preventive treatment of eligible children, especially among the children of migrants on entry, second-generation migrants and in contacts born outside of the Netherlands.	Foreign-born TB contacts are screened for LTBI. Non-BCG vaccinated children, with a parent born in a country with estimated TB incidence of > 50/ 100 000, and who have a positive TST are offered LTBI treatment.
9	Evaluate coverage of entry screening for migrants and assess whether using a residence permit should be linked to proof of TB screening.	Not observed.
10	Boost and improve the implementation of TB screening, including assessing whether the current follow-up screening by chest X-ray should be replaced by screening of LTBI and offer treatment to certain groups with this condition.	The research project TB END point is ongoing (Phase I – Implementation project of LTBI screening among high-risk migrants. Phase II – models for cost effectiveness and impact analysis). As of March 2019, the radiological follow-up can be replaced by LTBI screening and treatment [24].
11	Develop an implementation plan for the new contact investigation guidelines and monitor implementation, including assurance of optimal contact tracing, also in migrant populations, as well as contact tracing and source finding for all childhood cases.	Implementation plan was not observed, but many activities are being put into practice.
12	Apply innovative information and communication technology solutions to support adherence to LTBI, especially if the distance between the contact's home and the relevant care-providing health facility is considerable.	Mobile application introduced for directly observed treatment (observed in Amsterdam).

GGDs= municipal health services; LTBI= latent tuberculosis infection; PCR= Polymerase chain reaction; RIVM= National Institute for Public Health and the Environment; TB= tuberculosis

4. Screening of LTBI in migrants

Diagnosis and treatment of LTBI has been a cornerstone of TB control in the Netherlands for more than 25 years. In the Netherlands, LTBI screening is recommended for contacts of bacteriologically confirmed pulmonary TB patients, certain clinical risk groups, occupational risk groups and travellers returning from high-incidence countries [10]. The Committee for Practical Tuberculosis Control has issued national guidelines for LTBI diagnostics [25], LTBI treatment [26], and TB/HIV co-infection [27,28]. Since 2015 screening for LTBI has also been recommended for certain migrant groups [24]. The Dutch Thoracic Society (NVALT) has developed a guideline on LTBI/TB screening prior to immunosuppressive medication [27].

LTBI is diagnosed using a two-step approach - i.e. an initial tuberculin skin test (TST), followed by an interferon gamma release assay (IGRA) if the TST result is ≥ 5 mm and active TB has been excluded. In clinical risk groups (e.g. people living with HIV, patients starting tumour necrosis factor (TNF)-alpha blocking medication and candidate organ transplant patients) both tests are recommended simultaneously. A positive result for either of the tests represents a need for treatment.

Several treatment regimens are used for LTBI treatment: three-month regimen of isoniazid/rifampicin (3HR), six-month regimen isoniazid (6H), or four-month regimen rifampicin (4R). Patients with immunosuppressive disorders or starting immunosuppressive medication and those with pulmonary fibrotic lesions are treated with 4HR or 9H [26]. The shorter regimens 3HR and 4HR are the most widely used [29]. An email from Gerard de Vries (dated 29 November 2019) reported that 2017 data from the NTR indicated that 88% of treatment prescriptions for LTBI were for 3HR or 4HR. Currently rifapentine is not available in the Netherlands and thus the 12-dose three-month regimen of rifapentine and isoniazid (3HP) cannot be offered.

Key findings

Migrant screening

Since 2013 there have been policy changes relating to target groups for TB and LTBI screening upon entry to the Netherlands. These developments, which were informed by the evaluation of screening policies and epidemiological data [30-35], are summarised below.

TB screening: mandatory chest X-ray screening at entry was limited to migrants originating from countries with a TB incidence of >50 per 100 000 in January 2015. The same screening policy was implemented for all asylum seekers in April 2016. In April 2019 the screening threshold for migrants was changed to a TB incidence of >100 per 100 000 in the country of origin [24]. For asylum seekers the threshold remains at a TB incidence of >50 per 100 000.

Radiological follow-up screening is offered on a voluntary basis to migrants originating from countries with a TB incidence $>200/100\ 000$ and for other migrants if the chest X-ray is abnormal upon entry screening. The radiological follow-up is conducted every six months over a two-year period. As of March 2019, the radiological follow-up can be replaced with LTBI screening and treatment [24].

The TB screening pathways differ for newly arrived migrants and asylum seekers because the immigration procedures upon arrival are different. For newly arrived migrants, TB screening procedures would normally take place within three months after applying for a residence permit. For asylum seekers, TB screening will take place within 48 hours after registration in a reception centre [31,33].

A recent analysis of TB screening data from more than 34 000 asylum-seeking children, collected between 2013 and 2017, suggests that:

- Chest X-ray screening should be indicated only for asylum-seeking children aged 12 to 17 years, originating from countries with an estimated TB incidence rate of $>100/100\ 000$;
- LTBI screening at entry should be considered for asylum-seeking children originating from countries with an estimated TB incidence rate of $>50/100\ 000$, irrespective of age [32].

A new information system for management of patients' information was introduced in 2018. This cloud-based national platform, called iTBC, allows public health physicians to access chest X-ray images remotely, irrespective of their work location [36]. As was demonstrated during the review team visits to different health facilities, this technical development contributes to clinicians' work flexibility and the provision of high-quality services.

LTBI screening: From December 2015, migrants and asylum seekers <18 years of age are eligible for LTBI screening at entry [24]. All GGDs are carrying out LTBI screening for migrants <18 years, but only a few are screening asylum seekers <18 years. The countrywide implementation of the LTBI screening for asylum seekers <18 years is still pending a practical proposal, which has so far been difficult to design due to the process and infrastructure for asylum seeking in the Netherlands [5,31,37].

In 2018, an increase in the number of TB cases among unaccompanied minor asylum seekers (i.e. <18 years of age) from Eritrea was detected in the Ter Apel reception centre. This event triggered the implementation of outbreak management activities. Upon request from GGD Groningen, all GGDs were asked to conduct targeted LTBI screening for Eritrean unaccompanied minors who arrived in 2018 and were relocated to different municipalities [38].

During the visit to GGD Hollands Noorden, the review team was informed of some of the operational challenges and achievements of the outbreak management work. For example, the size of the GGD's catchment area and the long distances between the localities where targeted people resided and the GGD was a logistical challenge. Another challenge reported was the difficulty in accessing personal information for the target group due to data protection regulations. For instance, newly arrived immigrants who have a residence permit granted for family reunification are more difficult to locate and contact. In such cases, only municipal authorities can provide contact information. Among the achievements reported was the provision of directly observed LTBI treatment for asylum seekers because of the good collaboration between the GGD staff and the social workers at the asylum centres. Similarly, the availability of educational materials, produced as part of a pilot study (see section on operational research), facilitated the provision of information concerning LTBI screening and treatment. The education activities targeted both the staff and the at-risk migrants in the reception centres. As a result of this experience, GGD Hollands Noorden is systematically performing LTBI screening among unaccompanied minor asylum seekers who are considered to be at greater risk of TB (e.g. if their travel route to Europe included known hot-spots for TB transmission).

The complexity of the health system governance, as well as the intricate organisation and interactions of all actors involved in TB control activities has been acknowledged during this visit. Through the visits to the GGDs and the interactions with healthcare staff, the review team gained a deeper understanding of structural barriers to accessing TB services. For example, the compulsory deductible payments were reported as one concrete barrier preventing vulnerable populations from accessing TB/LTBI care. For asylum seekers, the cost of TB screening is covered through an agreement between GGD GHOR Netherlands and the Central Agency for the Reception of Asylum Seekers (COA) [6]. However, the perceived increase in the number of 'Dublin-claims' (as reported by GGD staff) contributes to a more complex scenario. It was also reported that EU migrants from medium/high TB incidence countries are often uninsured. A similar situation applies to homeless people, who are referred to GGDs by non-governmental organisations. The review team was informed that these challenges are often overcome by the determination and individual commitment of the GGD healthcare staff, and arrangements for urgent medical care for the uninsured.

Despite the achievements obtained and the potential for further progress towards TB elimination in the Netherlands, some informants have expressed their hesitancy to endorse further expansion of LTBI screening efforts. Several factors may influence such hesitancy:

- satisfaction with the current situation of TB prevention and care activities;
- the fact that no major threats to TB control have been identified;
- concern about the additional financial, human resources and organisational requirements. GGD doctors carry out screening activities. There are uncertainties as to whether the system will be maintained as the number of TB cases is decreasing and the competence of GGD doctors may be adversely affected in the near future, as the disease becomes increasingly rare. This problem may arise first in rural areas, where there are lower numbers of migrants.

Operational research

The Netherlands Organization for Health Research and Development (ZonMw) has sponsored an operational research project entitled 'TB elimination through disease prevention optimization in the Netherlands' (TB-ENDPoint). The purpose of the TB-ENDPoint project is to assess how to best implement LTBI screening among at-risk migrants. Cost-effectiveness and impact analyses are also included in the project.

During the first phase of the TB-ENDPoint project, between 2016 and 2018, three pilot studies were conducted. The target groups were newly arrived migrants, asylum seekers and Eritrean migrants. Table 2 provides an overview of the methodology and results of the pilot studies. A number of observations that can be derived from these data appear below.

- LTBI screenings completion is very high among newly arrived migrants and asylum seekers. Acceptance of LTBI screening was less favourable among resident Eritrean migrants (who were tested ≥ 6 months to 10 years after arrival). Given that most of the foreign-born TB cases notified in 2018 were Eritreans [2], strategies are clearly required to capture this at-risk population.
- LTBI prevalence was 12%, 17% and 25% among resident Eritrean immigrants, newly arrived migrants, and asylum seekers, respectively. Moderate prevalence rates probably reflect the level of the TB epidemic in the country of origin.
- The rates of LTBI treatment initiation and treatment completion are low among newly arrived migrants. Understanding the reasons for these observations and developing interventions to increase the uptake and completion of LTBI treatment should be considered a priority.

- In contrast, the LTBI treatment initiation and completion rates among asylum seekers and at-risk Eritrean migrants are high.

Preliminary results of the cost-effectiveness analysis performed within the TB-ENDPoint project indicate that:

- LTBI screening of newly arrived migrants is cost-effective if a high willingness-to-pay threshold (EUR 80 000 per quality-adjusted life year [QALY]) is chosen (as used in curative medicine);
- LTBI screening of asylum seekers is more cost-effective than screening of migrants, but is still not cost-effective if using the threshold commonly applied for preventive intervention (EUR 20 000 per QALY);
- LTBI screening of other at-risk migrant groups is probably not cost-effective [37].

Table 2. Overview of the TB-ENDPoint pilot studies

	Pilot 1 Newly arrived migrants	Pilot 2 Asylum seekers	Pilot 3 Eritrean migrants
TB incidence in the country of origin	>50/100 000	>200/100 000	Not applicable
Age	All	≥ 12 years	All
Type of screening	Mandatory entry TB and LTBI screening	Voluntary follow-up TB and LTBI screening	Voluntary TB and LTBI screening (community approach)
Screening tests	TST and IGRA IGRA only	IGRA	IGRA
Number of GGDs	5	8	4
Target population (absolute numbers)	588	1055	779
Number of people screened	566 (96%)	719 (68%)	246 (32%)
LTBI prevalence	94 (17%)	178 (25%)	30 (12%)
LTBI treatment uptake	49 (52%)	149 (84%)	29 (97%)
LTBI treatment completion	34 (69%)	129 (87%)	28 (97%)

Adapted from [37,39]. GGDs= Municipal Health Services; IGRA= interferon gamma release assays; LTBI= latent tuberculosis infection; TB= tuberculosis; TST= tuberculin skin test.

The TB-ENDPoint project also produced educational materials as a complement to the activities conducted for the pilot studies. These materials provided general information about the LTBI screening procedures in different languages. Similar educational initiatives have been supported by the KNCV, in collaboration with civil society organisations [40,41]. Moreover, KNCV is involving multidisciplinary teams (comprising of digital health consultants, medical illustrators and social scientists) and exploring cross-border collaboration (with NHS England and TB Alert) to develop or adapt audio-visual educational materials [41]. The challenges related to medical illiteracy among target groups for LTBI interventions were brought to the attention of the review team. The review team acknowledges the importance of developing and implementing educational initiatives which are both linguistically and culturally adapted to the needs of at-risk groups.

Contact investigation

The most recent evaluation of contact investigation practices (2011–2016 data), showed that contacts of 3 216 (61%) of notified TB patients had been investigated; contact investigation had been done in 91% of smear-positive pulmonary TB patients and in 70% of culture-positive pulmonary TB patients. Of 52 983 contacts examined, 48 467 (92%) were tested for LTBI, either using tuberculin skin tests (TST) or interferon gamma release assays (IGRA). Overall, the prevalence of active TB among TB contacts was 664/100 000 and the LTBI prevalence was 8.8%. The number of foreign-born TB contacts who were tested for LTBI as part of contact investigations increased compared to the previous evaluation period (2006–2010). Similarly, the proportion of foreign-born persons who had a positive LTBI test among TB contacts had also increased (Table 3) [42].

Table 3. Proportion of Dutch-born and foreign-born contacts tested for latent tuberculosis infection in the context of contact investigations

	Dutch born	Foreign born
	Number (% of all Dutch-born contacts examined)	Number (% of all foreign-born contacts examined)
2006–2010*	22 926 (83%)	20 595 (65%)
2011–2016	19 559 (95%)	28 147 (89%)

* Excluding Rotterdam

The risk of progression to active TB was consistently lower for TB contacts with LTBI who had completed LTBI treatment [43].

LTBI monitoring

LTBI cases are registered in the Netherlands TB Register (NTR), an anonymised nationwide web-based case-based surveillance system for TB and LTBI. Voluntary LTBI reporting started in 1993. The following data are recorded: patients' demographic characteristics, target group, diagnostic method and patient management (preventive treatment regimen or radiological follow-up), completion of preventive treatment, and reason for interrupting preventive treatment (adverse events, development of active TB or non-adherence) [20].

Between 1993 and 2013, 37 729 LTBI cases were notified to the Netherlands TB Register. Of those, 28 931 (77%) initiated LTBI treatment. Treatment results were registered for 27 748 persons (96%), 85% of whom completed the LTBI treatment. Multivariable analysis of these data showed that children and immunosuppressed people were more likely to initiate LTBI treatment. Among those initiating LTBI treatment, children, immunosuppressed people and people treated with regimens containing rifampicin (alone or in combination with isoniazid), were more likely to complete treatment [29]. The analysis of surveillance data (2005–2013) has shown that the highest TB incidence occurs in the first year after LTBI diagnosis [43].

The review team noted that LTBI reporting is not compulsory, thus completeness and reliability of reported data may not be optimal. For example, substantial hospital LTBI data are probably missing in the notification registry. Over the last 10 years the number of notifications has increased (probably due to a larger list of conditions being notifiable and an improved attitude towards notification). No survey has ever been conducted to define the level of underreporting.

Options

- To consider extension of systematic testing and treatment for LTBI to all migrants and asylum seekers from countries with a high TB burden who have entered Europe within the last five years or less. This recommendation is in agreement with ECDC public health guidance and WHO guidelines for programmatic management of LTBI [22,23]. This policy change could be considered after a feasibility analysis of aspects such as human resources and cost-effectiveness.
- To operationalise the extension of LTBI screening among high-risk migrants (described above) by planning and implementing activities to provide information on LTBI and treatment for LTBI for all immigrants who are recommended for screening and treatment.
- GGDs could act as the primary entry point for systematic testing and treatment of LTBI in migrants. An analysis of the resources required could be conducted separately or included in ongoing operational research (such as the ZonMW TB-EndPoint projects).
- To screen migrants for LTBI as soon as possible after their settlement into the Netherlands, in order to secure high coverage of the intervention. General practitioners may play a role linking newly arrived migrants to LTBI screening. In particular, newly arrived migrants with a residence permit due to family reunification could benefit from this approach as they are already settled in a municipality.
- To continue offering a range of different treatment regimens for LTBI, as recommended by the current and forthcoming WHO guidance [22,44]. This ensures that each person can be treated with the most appropriate treatment regimen. Shorter regimens should be prioritised compared to other regimens.
- To continue the monitoring of the programmatic management for LTBI by using indicators that have already been implemented (e.g. treatment acceptance among those eligible for LTBI treatment and LTBI treatment completion) and introducing new indicators (e.g. number of people eligible for LTBI screening and number of people screened for LTBI) to allow for the monitoring of WHO recommended indicators.
- To explore the usefulness of a proxy indicator for LTBI screening coverage. The number of migrants screened for LTBI during a certain period (derived from the GGD client register iTBC) could be used as the numerator. The number of newly arrived immigrants/asylum seekers eligible for LTBI screening, as per current national guidelines, (derived from the national census) could serve as denominator.
- To develop measures to mitigate the impact of having implemented the General Data Protection Regulation [45] for the sake of information sharing between relevant institutions (i.e. RIVM, GGD).

5 Human resources

The tasks related to TB prevention and care are performed by different types of healthcare workers (e.g. TB public health doctors, infectious disease public health doctors, pulmonologists, TB public health nurses, and medical technical assistants.) In 2016, the GGDs employed 19.1 full time equivalent (FTE) TB public health doctors, 44.0 FTE TB public health nurses, and 90.6 FTE medical technical assistants (According to an email from Gerard de Vries from 9 May 2019).

Since 2014, the 25 GGDs have organised themselves into four Regional Expertise Centres for TB Control (REC):

- North-East, including five provinces (Groningen, Friesland, Drenthe, Overijssel and Gelderland) and eight GGDs;
- North-West, consisting of three provinces (Utrecht, North Holland and Flevoland) and seven GGDs;
- South Holland, comprising one province (South Holland) and four GGDs;
- South, including three provinces (Zeeland, North Brabant and Limburg) and six GGDs [17].

The purpose of the RECs is to concentrate and maintain an appropriate level of TB knowledge and expertise [6]. GGD GHOR Nederland has the task of facilitating the debate among RECs, professional associations and other stakeholders regarding the organisation of TB services in the near future (5–10 years) [6].

Three models of care, defined as 'the organizational form that a GGD region chooses to meet the statutory tasks for TB control, including the Population Screening Act and the Public Health Act' [46], were developed in 2018. These models are based on risk profiles defined using the incidence of TB and LTBI, the source and contact investigation performed by the GGDs and the nature and extent of the risk populations that visit the GGD.

The three models of care proposed to the GGDs and accepted by their directors are:

- **Autonomous TB care model ('Autonome Tuberculose Zorgmodel', ATZ):** intended for high-risk GGD regions. In this model the GGD continues to play the role it currently has. It is assumed that the workload is sufficient; allowing the GGD to function independently, while maintaining an appropriate level of expertise.
- **Mobile TB teams ('Mobiele Tuberculose Teams', MTT):** intended for low-risk GGD regions. This model proposes that the GGD purchases the necessary expertise and capacity from an autonomous (ATZ) region.
- **Local care arrangement ('Lokaal Zorg Arrangement', LZA):** intended for low-risk GGD regions. This model suggests that the GGD purchases care from different organisations and other divisions of the GGD [46].

The three different models or parts of them can also be combined, depending on the specific needs of the setting the GGDs serve. This acknowledges the diversity in organisation of TB prevention and care activities among GGD regions due to various factors such as epidemiological situation; structure of population; rural or urban location; size of the area; organisation and structure of staff.

Key findings

Roles and tasks of GGDs in TB prevention and care

The GGDs are responsible for the implementation of TB prevention and care activities. Hospital pulmonologists or infectious disease specialists also provide diagnosis and treatment of TB and LTBI. TB professional staff of GGDs participate in the CPT, the TB policy and guideline committee of the Netherlands.

The 'Handbook tuberculosis' published by the KNCV includes a list of services that need to be provided by the GGD. This TB Handbook offers professionals involved in TB prevention and care, and others, an up-to-date overview of the TB situation in the Netherlands and of the current guidelines for diagnostics, treatment, active detection in risk groups and prevention of TB [16].

Healthcare professionals working in TB prevention and care at GGD level (TB public health doctors, infectious disease public health doctors, pulmonologists, TB public health nurses, and medical technical assistants) have a well-established network with the clinical sector (TB coordinators, pulmonologists) and the other GGDs.

The contribution of hospitals to TB control (including diagnosis, treatment and hospitalisation of TB patients, if required) is organised through TB coordinators. In each hospital, a TB coordinator is the person designated for dealing with TB-related questions. The TB coordinator, who is usually a pulmonologist, has followed a short master class for TB coordinators and may participate in a short TB training course on an annual basis [47].

Most TB control-relevant institutions seem to be well interlinked: RIVM, KNCV, GGDs, hospitals, the modern sanatoria Dekkerswald and Beatrixoord, the asylum seeker reception centres, the penitentiary system, etc.

Models of TB care

The GGDs of the urban, more densely populated regions South Holland and North-West are all using the same model of care (autonomous TB care model). In other regions, GGDs are exploring one of the other models of care.

The RECs are to retain knowledge and expertise in TB control and have a role in trying to harmonise the management and staff organisation.

Roles and tasks of healthcare professionals involved in TB prevention and care

Usually, staff working in TB prevention and care are employed by a GGD and dedicated to TB (physicians, nurses and technical medical assistants).

TB physicians are public health physicians and their duties related to TB control include public health activities (screening, contact investigation, treatment follow-up), but also clinical activities such as diagnosis and treatment (prescription and clinical follow-up) of active TB and LTBI. These clinical activities are not part of the activities covered by infectious disease public health physicians.

TB nurses are involved in public health activities (screening, contact investigation, treatment follow-up), are usually in charge of the directly observed therapy (DOT), and provide patient support to ensure treatment adherence.

Medical technical assistants are working under the responsibility of the physician. They conduct vaccination, TST, take blood samples and make chest X-rays. The role of medical technical assistants in TB control seems to be unique and does not exist as such in other areas of infectious disease control covered by the GGD. However, their role is similar to the 'dokterassistent', a trained medical assistant practicing in clinical care under the responsibility of a general practitioner.

The GGDs have the option to contract hospital pulmonologists for specific tasks. Some TB activities may also be shifted to professionals historically not involved in TB prevention and care, such as infectious disease public health doctors or nurses working in infectious diseases control. This was observed in Eindhoven, where the GGD contracted pulmonologists from the hospital for TB diagnosis (e.g. chest X-ray screening) and treatment. Public health doctors and nurses specialising infectious disease performed the public health activities (contact investigation, treatment follow-up). In Groningen, one TB public health doctor and one infectious disease doctor (trained in TB) perform clinical and public health TB activities.

For the future, it is envisaged that the clinical and public health activities for TB prevention and care remain the same in all GGDs. However, the staff involved in these activities may differ depending on the choices made by the individual GGDs (see Table 4).

Table 4. Examples of diversity of organisation for TB control activities

TB control activities	Den Haag	Eindhoven	Groningen
Diagnosis	TB physicians	Hospital pulmonologist	TB physicians and public health physicians specialising in infectious disease (trained in TB and infectious disease)
Active TB treatment (prescription)	TB physicians	Hospital pulmonologist	TB physicians or public health physicians specialising in infectious diseases and TB
Public health activities (screening, contact investigation, treatment follow-up)	TB physicians and TB nurses	Public health physicians and nurses specialising in infectious disease and TB	TB physicians or public health physicians specialising in infectious diseases and TB and TB nurses
DOT (Directly Observed Therapy)	TB nurses	Nurses	Nurses
Vaccination, TST, taking blood samples, making chest X-rays.	Technical medical assistant	Technical medical assistant	Technical medical assistant

TB= tuberculosis; TST= Tuberculin Skin Test

Training of healthcare professionals involved in TB prevention and care

A wide range of stakeholders involved in TB prevention and care are also involved in training and capacity-building for TB prevention and care, including the Netherlands School for Public and Occupational Health (NSPOH), professional associations, the KNCV, GGDs and RIVM.

The initial TB training for physicians, consisting of a two-year specialisation in public health, TB prevention and control, is a well-structured and recognised specialisation with a registration system. An additional two years training will qualify the person as a registered specialist in public health/social medicine. Nurses performing public health tasks in TB prevention and care are usually not trained specifically in public health and TB control. Public health training is not required to work in TB prevention and care and access to public health training for nurses may be limited due to training costs and the perceived time investment required. Nurses and technical medical assistants receive the introductory TB training mainly as on-the-job training, complemented by some days of theoretical training organised by the KNCV (Table 5).

The changes in TB epidemiology in the country (i.e. an overall decrease in TB case numbers) have an impact on the volume and nature of TB activities. The heterogeneity of the TB burden has increased - i.e. some regions have relatively high notification rates and others low - and there are differences in the characteristics of TB cases. In addition, the management of TB is complex, due to the long treatment and additional social and psychological issues in the patient population, including stigma. Due to the decrease in the number of TB cases there are fewer sites available for training since training sites should have a sufficient number of TB cases to ensure that doctors and nurses in training gain enough experience.

The number of trained TB physicians and nurses is decreasing and in some areas the number of trained professionals is insufficient. In addition, the TB physician 'population' is ageing and retirements can be anticipated. The training capacity for TB physicians is 1–2 physicians per year, and currently two physicians are in training.

To address this situation, there is already some discussion regarding the training of physicians and a more integrated training for infectious diseases and TB control is being considered. This would allow more flexibility.

Continuous education is required for re-registration as a TB public health physician and it is also necessary for other professionals working in TB prevention and care. Specific courses are organised and coordinated by the KNCV, by RIVM or by some TB professionals. When GGDs are contracting pulmonologists from hospital, it is advised that the contract not only focuses specifically on TB prevention and care tasks but also includes training. Medical technical assistants do not have a mandatory system of registration. However, a refresher training day on TB is organised on an annual basis.

Table 5. Tuberculosis training for GGD staff working in TB prevention and care

	GGD Physician	GGD Nurse	GGD Medical technical assistant
Professional association	VvAwT (Dutch Association of Tuberculosis Control Physicians)	V&VN/Tuberculosis Committee (Dutch Association of TB Nurses)	MTMBeve (Association of medical technical assistant)
Initial TB training	Specific four-year public health TB control profile (NSPOH) including 6–8 months clinical training	KNCV seven days training + on-the-job training	KNCV training (five days) + on-the-job training
Public health training	TB training is one specialisation of public health	Usually not trained in public health (not required, and access to public health training limited due to costs)	
Continuous TB education	Refresher training (two days/year)	Refresher training (two days/year)	Refresher training day (one day/year)

Options

- To establish an 'all-stakeholder'/all-inclusive platform for the development of a capacity-building plan and to steer implementation, including GGD GHOR Nederland, GGDs, RIVM, the KNCV, sanatoria (Beatrixoord and Dekkerswald), professional associations and the NSPOH.
- To develop a competency framework for TB control activities for GGDs which is flexible and adjustable to also cater for future changes, and to take into account the diversity of different epidemiological situations and models of care. A competency framework can support the identification of training needs and the development of training material and methodology. Its development consists mainly of defining the tasks and the purpose of these tasks; describing the key skills required; describing the knowledge required. A

competency framework is usually developed with the support of professionals in training and education [48], and it is essential to involve the people doing the work (here TB control).

- Training of physicians:
 - to give greater emphasis to TB-related topics in public health infectious disease training (the current ongoing revision of public health education provides a good opportunity) and to involve all parties contributing to training and capacity building for physicians working in public health;
 - to ensure that in contracts between GGDs and hospitals the training aspects are explicitly stipulated/included;
 - to consider exchange of interns between GGDs and hospitals (to increase mutual understanding of the work).
- Training of nurses:
 - to consider increasing the minimum standards for training of TB public health nurses by establishing a system for nurses to take post-graduate public health training that could include TB and infectious diseases.
- Training of medical technical assistants:
 - to consider the possibility of developing training that merges TB and infectious disease public health aspects;
 - to review the role for the KNCV in developing further capacity building on TB control for nurses and medical technical assistants.
- To ensure that adequate training, mentoring and supervision is provided when tasks are moved to become the responsibility of healthcare workers who were not previously involved in TB control.
- To consider developing international collaboration with high TB burden countries or settings. TB professionals in the Netherlands would benefit from capacity building and training activities in settings with a larger number of TB patients (i.e. outside of the Netherlands), especially for diagnosis and treatment of TB. If necessary, other relevant national and international stakeholders could also be involved, with the possible support of the KNCV, RIVM, ECDC and WHO.

6 Conclusions and implications

The Netherlands has invited an international team to review the Dutch national tuberculosis prevention and care system every five years since 2003. The reviews are conducted in close collaboration with national TB experts. The options and recommendations provided by the review team are included in the NTCP for the Netherlands. This cycle of review and updating of the NTCP ensures that TB prevention and care is continuously adjusted and updated, taking into account the latest developments and guidelines.

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Annex 1. Terms of reference

Goal

To provide expert advice on how to sustain - and where possible to improve - the accessibility, quality, effectiveness and efficiency of tuberculosis (TB) services in the Netherlands.

The review will focus on the TB prevention and care system (hospitals, laboratories, public health services) and the country visit team will discuss and advise which changes could be made in the next decade, anticipating a further decline in the number of TB cases (806 cases in 2018; 4.7/100,000), current changes in TB screening policies and activities (more focus on screening for latent TB infection, a reduction in the number of screening chest X-rays) and increased pressure on human and financial resources.

Specific objectives

- To review the progress made on the recommendations of the international review 2013;
- To review and advise on prioritisation and extent of latent TB infection screening of migrants to achieve the set targets; and
- To review and advise on the conditions and measures necessary for the retention of knowledge and expertise in the Netherlands/a country with declining TB incidence.

Ad 1

In 2013, the World Health Organization Regional Office for Europe and the European Centre for Disease Prevention and Control conducted a programme review of the national TB control programme in the Netherlands. During the country visit the team will follow up on the recommendations included in the report of the programme review.

Ad 2

The Netherlands is currently implementing screening for latent TB infection in several risk groups, for example, the guideline for screening of migrants and asylum seekers, advises to screen persons <18 years of age for latent TB infection. The RIVM holds a database where data on latent TB infections and treatment are collected. Not all guidelines are rigorously implemented and the effectiveness of latent TB infection screening is sometimes questioned. Specific questions for the country visit are:

- Is the current screening, addressing persons most benefiting from the LTBI screening, the most efficient and effective approach to meet the set targets in the national plan, or need other groups to be prioritized?
- Is the current monitoring and evaluation for latent TB infection screening sufficient or does this need to be strengthened?

Ad 3

The directors of the municipal health services (GGDs) have decided on three types of models for the organization of TB public health prevention and control activities, i.e. 1) 'Autonome Tuberculose Zorgmodel' (ATZ) ('autonomous TB model'. The current situation in most GGDs), 2) 'Mobiele Tuberculose Teams' (MTT) ('mobile TB teams'). The ATZ provides capacity and specialized expertise to the ATZ; the GGD provides capacity (e.g. TB nurses, infectious disease doctors) and other services), 3) 'Lokaal Zorg Arrangement (LZA)' ('local care arrangements'. The GGD contracts services e.g. from the hospital). These models are implemented in different parts of the country. With the country visit it is aimed to advice the Netherlands on:

- What expertise and skills are needed at regional and national level for the different actors involved (doctors, nurses and allied professionals)
- What training is needed?
- How can skills and expertise and quality of the work be monitored and evaluated?

Expected outputs

- Debriefing presentation with key observations and suggested actions at the end of the country visit
- Detailed visit report within three months after the visit

Team members

- Marieke J. van der Werf (ECDC), team leader
- Askar Yedilbayev (WHO EURO)
- Senia Rosales-Klintz (ECDC)
- Martin van den Boom (WHO EURO)
- Delphine Antoine (public health training, scientific and international office of Santé publique France)
- Alberto Matteelli, expert on latent TB infection screening.

Team 1 (latent TB infection screening): Alberto Matteelli, Senia Rosales-Klintz and Askar Yedilbayev (The Netherlands: Connie Erkens, Cindy Schenk)

Team 2 (Human resources skills and expertise for TB prevention and care): Delphine Antoine, Marieke van der Werf and Martin van den Boom (The Netherlands: Gerard de Vries, Chantal Laurent).

Annex 2. Programme

Monday, 24 June 2019

Venue: Ministry of Health, The Hague

Time	Activity	Responsible
14.15-14.30	Welcome/introduction	
14.30-14.50	Epidemiological situation of TB in the Netherlands	Erika Slump (RIVM)
14.50-15.10	National plan: current state of implementation	Gerard de Vries (RIVM)
15.10-15.30	Organisation of TB public health	Chantal Laurent (GGD GHOR Nederland)
15.30-15.50	Laboratory issues	Ed Kuiper (LUMC)
15.30-16.00	Short break	
16.00-16.30	LTBI screening of migrants	Connie Erkens (KNCV Tuberculosis Foundation)
16.30-16.45	Clinical care issues (MDR, HIV, etc.)	Martin Boeree (NVALT)
16.45-17.00	TBD	
17.00-17.15	Closure	

Tuesday, 25 June 2019

Team 1 (LTBI)		Team 2 (Human resources)	
Time		Time	Topic
9.30-12.30	LTBI policy and practice, and LTBI health education issues Venue: TB Department, GGD Amsterdam	9.00-11.00	Models and human resources Venue: TB Department, GGD The Hague
14.30-16.30	LTBI practice Venue: TB Department, GGD Alkmaar	14.00-16.00	Models and human resources Venue: TB Department, GGD Eindhoven

Wednesday, 26 June 2019

Team 1 (LTBI)		Team 2 (Human resources)	
Time	Topic	Time	Topic
9.00-11.00	LTBI practice Venue: TB Department, GGD Rotterdam	10.00-13.00	Models and human resources Venue: TB Department, GGD Groningen
12.30-16.00	LTBI data base Venue: RIVM	13.30-14.30	Visit to Beatrixoord TB Centre Place: Groningen (Haren)

Thursday, 27 June 2019

Time	Activity (venue)
8.30-10.30	Interviews (IGJ and RIVM)
10.30-12.00	Debriefing preparation (RIVM)
13.00-14.00	Interviews (NSPOH, pulmonologist)
14.00-16.00	Debriefing preparation (RIVM)

Friday, 28 June 2019

Time	Activity (venue)
10.00-12.00	Debriefing meeting (Jaarbeurs MeetUp conference centre, Utrecht)

Annex 3. People met

Monday, 24 June 2019

Name	Position, Organisation
1. Ciska Scheidel	Director Public Health, Ministry of Health, Den Haag
2. Stephanie Wiessenhaan	Policy advisor, Department of Public Health, Ministry of Health, Den Haag
3. Jaap van Dissel	Director Centre for Infectious Disease Control (CIb), National Institute for Public Health and the Environment (RIVM), Bilthoven
4. Cindy Schenk	Policy advisor, RIVM-CIb, Bilthoven
5. Gerard de Vries	National coordinator TB control, RIVM-CIb, Bilthoven
6. Dick van Soelingen	Head Mycobacteriology Reference Laboratory, RIVM-CIb, Bilthoven
7. Erika Slump	Epidemiologist, TB surveillance unit, RIVM-CIb, Bilthoven
8. Kitty van Weezenbeek	Director, KNCV Tuberculosis Foundation, Den Haag
9. Connie Erkens	Head team The Netherlands & Elimination, KNCV Tuberculosis Foundation, Den Haag
10. Chantal Laurent	Policy advisor, GGD GHOR Nederland, Utrecht
11. Martin Boeree	Pulmonologist, TB Sanatorium Dekkerswald, Radboud UMC, Nijmegen, on behalf of NVALT (Dutch Thoracic Society)
12. Ed Kuiper	Medical microbiologist, LUMC, Leiden, on behalf of NVMM (Dutch Society Medical Microbiologists)
13. Wieneke Meijer	Head of TB department, GGD Amsterdam and Chair Committee for Practical TB Control (CPT)
14. Mariska Petrignani	Infectious Disease Public Health Doctor, GGD Amsterdam, on behalf of NVIB (Dutch Association for Infectious Disease Public Health Doctors)

Tuesday, 25 June 2019

Name	Position, Organisation
15. Wieneke Meijer	Head of TB department, GGD Amsterdam and CPT Chair
16. Niesje Jansen,	Senior nurse consultant, KNCV Tuberculosis Foundation
17. Connie Erkens	Senior TB consultant, KNCV Tuberculosis Foundation and CPT secretary
18. Gabriëlle Geerdink	Deputy-director, GGD Hollands Noorden (Alkmaar)
19. Sytze Keizer	TB public health physician, GGD Hollands Noorden (Alkmaar)
20. Marja Karels	TB public health Nurse, GGD Hollands Noorden (Alkmaar)
21. Ruth Tsegay	TB public health Nurse, GGD Hollands Noorden (Alkmaar)
22. Ilja Tijm	Medical technical assistant, GGD Hollands Noorden (Alkmaar)
23. Mirjam van Kralingen	Medical technical assistant, GGD Hollands Noorden (Alkmaar)
24. Therese Claassen	REC region manager, GGD Haaglanden
25. Erik Huisman	TB public health physician, GGD Haaglanden
26. Hewan Teshome	TB public health nurse, GGD Haaglanden
27. Arthur van Iersel	Senior policy advisor, GGD GHOR Nederland
28. Elske Beintema	Team manager, GGD Brabant-Zuidoost (Eindhoven)
29. Jacques Creemers	Pulmonologist Catharina Hospital and GGD Brabant-Zuidoost (Eindhoven)
30. Pascal Wielders	Pulmonologist Catharina Hospital and GGD Brabant-Zuidoost (Eindhoven)
31. Pierre Rutten	TB public health nurse and infectious disease public health nurse, GGD Brabant-Zuidoost (Eindhoven)
32. Viola Koppelmans	TB public health nurse and infectious disease public health nurse, GGD Brabant-Zuidoost (Eindhoven)
33. Melissa de Gooijer	TB public health nurse, GGD Brabant-Zuidoost (Eindhoven)
34. Ronald ter Schegget	Infectious disease public health physician, GGD Brabant-Zuidoost (Eindhoven)

Wednesday, 26 June 2019

Name	Position, Organisation
35. Dennis van Leeuwen	Pulmonologist/ TB public health physician, GGD Rotterdam-Rijnmond
36. Erika Slump	consultant TB surveillance, RIVM
37. Henriëke Schimmel	Data manager TB, RIVM
38. Karlijn van Beurden	Data manager TB, RIVM
39. Jos Rietveld	Director Public Health; GGD Groningen
40. Tita Klimp	TB team manager, GGD Groningen and GGD Drenthe
41. Bert Wolters	TB public health physician and infectious disease public health physician, GGD Groningen
42. Rob van Hest	TB public health physician, GGD Groningen and GGD Fryslân
43. Mirjam Urban	TB public health nurse, GGD Groningen
44. Yvonne Aartsma	Medical technical assistant, GGD Groningen

Thursday, 27 June 2019

Name	Position, Organisation
45. Jaap van Dissel	Director, RIVM-CIB
46. Arthur van Iersel	Senior Advisor, GGD GHOR Nederland
47. Robbin Westerhof	Senior Inspector Infectious Disease Control, Health and Youth Care Inspectorate (IGJ)
48. Marleen Bakker	Pulmonologist, Erasmus MC
49. Jeannette de Boer	Netherlands School for Public and Occupational Health (NSPOH)
50. Cecile de Ruiter	NSPOH

Annex 4. Status of implementation of the recommendations from the country review 2013

Recommendation		Status
1. Organization of laboratory services		
1	<p>Culturing and drug susceptibility testing for <i>M. tuberculosis</i> complex strains should only take place in a few nationally and internationally quality assured BSL III facilities. The quality assurance should include:</p> <ul style="list-style-type: none"> - Guidance on the minimum number of specimens processed to maintain high quality and, at the same time, be cost-effective; - Mandatory accreditation (quality measurement system) of an international standard, such as ISO 15189:2012 (1); - Regular internal and external quality schemes, preferably with accessible results available in the public domain (2), and - Guidance on BSL III standards (2, 3), including regular inspection and accreditation visits in all BSL III facilities. 	<p>46 laboratories are performing mycobacterial diagnostics. The number of samples processed by each laboratory annually differs widely. RIVM is performing drug susceptibility testing for <i>M. tuberculosis</i> complex. All 31 laboratories performing mycobacterial culturing have appropriate biosafety level-3 for performing mycobacterial diagnostics (15 out of 46 responding to the NVMM survey were not performing cultures). External quality assurance was performed by 94% of the laboratories participating in the NVMM survey.</p>
2	<p>A formal laboratory network structure should be established between a national reference laboratory and the few regional laboratories, and local laboratories, clearly stating which tests are performed at which level (local, regional, national), to optimize TB diagnostics. The following should apply:</p> <ul style="list-style-type: none"> - A suitable high-quality laboratory should be recognized as the national reference laboratory (such as the currently acting one), to head the network and provide guidance on methods and optimizing diagnostic procedures. - Duties and responsibilities within the network should be clearly specified. - Important information from the national reference laboratory should transparently reach the Ministry of Health, Welfare and Sport. - A suggestion for diagnostic structure could be: (a) local level: microscopy and commercially available polymerase chain reaction for species identification; (b) regional level: addition of culture, genotypic drug susceptibility testing and phenotypic drug susceptibility testing for first-line drugs; and (c) national reference laboratory: addition of phenotypic drug susceptibility testing for second-line drugs and verification of "resistance" found at other levels. 	<p>RIVM is the national reference laboratory. No formal laboratory network available.</p> <p>The mycobacteriology working group of the Dutch Association for Medical Microbiology (NVMM) has:</p> <ul style="list-style-type: none"> • Issued two national guidance documents, one on diagnosis of mycobacterial diseases (2015) and another on the application of direct testing for MDR tuberculosis (2018). • Conducted a survey to assess the implementation of the guidance documents (2019). The response rate was 96% (46 of 48 invited laboratories)
3	<p>For timely delivery of results, the first positive culture from any new person with TB should immediately (the same day) be sent to the national reference laboratory for genotyping and, if any resistance is reported, phenotypic drug susceptibility testing verification (4), including that previously detected by molecular methods. In addition:</p> <ul style="list-style-type: none"> - TB diagnosis based on nucleic acid testing results only should always be confirmed by culture (4); - Turnaround time for all diagnostic tests performed should be agreed on, put in writing and monitored. 	<p>94% of the laboratories participating in the NVMM survey reported PCR testing done directly on patient samples to detect drug resistance. Rapid molecular diagnosis is available and used for diagnosis of TB. Whether first positive cultures are sent to the national reference laboratory was not observed.</p>
2. Governance and human resources		
4	Continue to compile and use strategic plans and action plans to ensure horizontal and vertical cooperation for all stakeholders.	In progress.
5	Set up a comprehensive performance assessment framework that would include measuring the efficiency of the programme. This framework could also synthesize the outputs from the monitoring activities of other main actors, including RIVM, KNCV and GGDs.	Not observed

	Recommendation	Status
6	Organize a platform or national committee for partnership to improve vertical collaboration in the form of transparent and regular consultation by involving all main stakeholders such as the Ministry of Health, Welfare and Sport, RIVM, Committee on Practical Tuberculosis Control, GGDs, KNCV and professional associations. The platform would help to speed up the feedback between the stages of the policy cycle and to improve the alignment between the functions of the programme, such as service delivery, stewardship, regulation, planning, monitoring and evaluation. This platform would assess the annual progress based on the comprehensive performance reports and would initiate actions for correction and/or for improvement. The KNCV as knowledge centre and the RIVM being the responsible actor for health system performance assessment and for managing surveillance could jointly prepare the performance assessment of the TB programme. The platform could discuss and approve action plans to implement the strategies and realize the visions for the TB programme, but the Ministry of Health, Welfare and Sport would have the right to veto issues of funding and regulation.	Not observed
3. Developing human resources		
7	Develop a feasible, costed, SMART (specific, measurable, attainable, relevant and time-bound) human resources plan for TB that includes and consults all stakeholders covering a suggested five- to six-year period (2015–2020) in accordance with the overall health policy in place and the TB regionalization processes. The plan should be jointly developed by planning specialists from the Ministry of Health, Welfare and Sport, microbiologists from the national reference laboratory, GGDs and from all relevant professional associations, containing the following regional and peripheral laboratories' personnel, public health physicians, nurses and technical assistants, pulmonologists, infectious disease specialists and hospital managers (list not necessarily exhaustive).	Not observed.
8	For the TB human resources plan, revisit and revise the terms of reference of all the stakeholders for which the plan is made (of associations and bodies and those mentioned above who should be involved developing it). It is recommended that TB public health personnel (physicians, nurses and technical assistants) should have possibly adjusted terms of reference in the future. This would mean to take account of dwindling numbers of people with TB in some areas (particularly rural areas in the eastern parts of the country), which could result in adding responsibilities that are not solely TB related or else consider reorganizing and reallocating human resources to spots with higher need (such as cities in the western parts of the country).	See section on human resources
9	Train TB public health regional physician and nurse coordinators (trained specifically for the field in which they work) and enable at least one TB nurse per region to develop further competencies in coordinating treatment and in academic research, possibly to the nurse-practitioner level. The tasks, responsibilities, training requirements and minimum TB caseloads should be clearly specified.	E-learning and training materials were developed by KNCV Tuberculosis Foundation and are available for training purposes. The TB handbook ² is widely used and addressed the TB health care workers' tasks and responsibilities, improving their competencies. See section on human resources
10	Assess and evaluate yearly the patient numbers seen and cared for by all types of health personnel per region (both in hospitals, GGDs and laboratories, the latter for samples processed) on an annual basis and cater for flexible reorganization schemes, creating economically feasible enablers for personnel to relocate or retrain when deemed necessary by the regional health administration (it is important to maintain sufficient staff levels at sufficient quality). This is to include the two existing TB specialized institutions of Dekkerswald and Beatrixoord.	Three models of care have been defined. GGDs can choose the model that best fits their local situation including the considerations of changing patient numbers.
11	Consider mobile outreach units in very rural areas with very low numbers of people with TB, to compensate for the increasing distance of people with TB and people suspected of having TB, also with regard to contact investigation, to TB relevant health facilities, thus facilitating access to services and maintaining sufficient service efficiency.	Conducted according to needs, i.e. in the Northern Region of the Netherlands, through regular visits from the GGD Groningen to low population density islands, for example.
12	Clearly and formally link the pulmonologists in hospitals with their infectious disease specialist colleagues and the ambulatory GGD services, including strengthening joint case discussions and conferences.	Networks linking pulmonologists and the GGDs are in place. Hospitals have TB coordinators.

² Commissie voor Praktische Tuberculosebestrijding. Handboek Tuberculose 2019. Den Haag: KNCV Tuberculosefonds; 2019. Available from: <https://www.kncvtbc.org/uploaded/2019/06/Handboek-Tuberculose-Nederland-2019-def.pdf>.

	Recommendation	Status
4. Funding		
13	Establish a comprehensive and coherent data collection and reporting mechanism for the funding and costs of TB control.	Not observed.
14	Ensure that TB services by hospitals are classified in the A segment of the services in which the insurer can negotiate only volume and quality aspects while the Health Care Authority establishes the prices.	Not observed.
15	Analyze carefully how the compulsory deductible influences the utilization of TB services. If there is evidence for delayed utilization, stop charging the deductible for people suspected of having TB and people diagnosed with TB.	Not observed.
16	Create sustainable funding conditions with appropriate payment mechanisms for the laboratory functioning as the national TB reference laboratory to maintain the current high-level services to other laboratories and to initiate quality control programmes (see more in the section on laboratory).	Not observed.
17	Perform detailed efficiency analysis for active detection of TB and latent TB infection cases along with the planning process for the new service delivery model of the GGDs.	The operational research project TB ENDpoint is ongoing (Phase I – Implementation project of LTBI screening among high-risk migrants. Phase II – models for cost effectiveness and impact analysis).
5. TB among children		
18	Ensure implementation of BCG vaccination policy to increase coverage in risk groups.	Completed. The BCG vaccination is targeted to new-born children with a parent born in a country with estimated TB incidence >50 per 100,000 population. Non-BCG-vaccinated children with a positive TST are offered preventive treatment for LTBI.
19	Source finding and contact investigation must be ensured for all children with TB.	Source finding and contact investigation procedures are in place.
20	Scale up the implementation of latent TB infection detection and provision of preventive treatment to eligible children, especially among migrants upon entry, and among children born in the Netherlands to parents born outside the Netherlands and children born outside the Netherlands upon contact tracing or where latent TB infection testing of the children is indicated.	Foreign-born TB contacts are screened for LTBI. LTBI screening at entry is offered for asylum-seeking children originating from countries with an estimated TB incidence rate of >50/100,000, irrespective of age.
21	Child-friendly drug formulations should be made available.	Only Rifampicin syrup is available for paediatric patients.
22	Ensure sustainable numbers of pediatricians with sufficient experience and exposure to childhood TB cases.	Not observed.
6. Screening and contact investigation		
23	Consider initial screening for latent TB infection, applying appropriate diagnostic tools for asylum-seeker and migrant children 0–11 years old.	From December 2015, migrants and asylum seekers <18 years of age are eligible for LTBI screening at entry.
24	Discuss the implementation of latent TB infection screening for high-risk groups in the light of TB elimination even though latent TB infection screening is not cost-effective using the ceiling for cost-effectiveness of health care interventions.	Generally there is a compliance with international guidelines for LTBI management ³ . Migrants < 18 years of age are screened for LTBI. Decision on extending LTBI screening to other migrants is pending.
25	Evaluate the effect and cost-effectiveness of the change in the screening policy for prisoners.	Not observed.
26	Evaluate the coverage of entry screening for migrants and assess whether permits should be linked again to proof of TB screening.	Not observed.
27	Consider engaging general practitioners in following up TB screening among migrants.	Not observed.
28	Adopt a consistent nationwide approach to TB screening with regard to costs for migrants.	Mandatory chest X-ray screening at entry for migrants and asylum seekers originating from countries with a TB incidence of >50-100 per 100,000 in the country of origin was initiated during 2015-2016.
29	Ensure the implementation of TB screening, including systematic follow-up screening for migrants and other high-risk groups (finding the best way to ensure high participation).	Mandatory chest X-ray screening at entry for migrants and asylum seekers originating from countries with a TB incidence of >50-100 per 100,000 in the country of origin was initiated during 2015-2016. The follow-up screening has been evaluated. As of March 2019, the radiological follow-up can be replaced by LTBI screening and treatment.
30	Develop an implementation plan for the new contact investigation guidelines and monitor implementation.	Implementation plan is not observed, but many activities are being implemented.
31	Secure optimal contact tracing, including in the migrant population.	In progress.

³ World Health Organization. Latent tuberculosis infection: updated and consolidated management for programmatic management. Geneva: WHO; 2018. Available from: <https://www.who.int/tb/publications/2018/latent-tuberculosis-infection/en/>
European Centre for Disease Prevention and Control. Programmatic management of latent tuberculosis infection in the European Union. Stockholm: ECDC; 2018. Available from: <https://www.ecdc.europa.eu/en/publications-data/programmatic-management-latent-tuberculosis-infection-european-union>.

Recommendation		Status
32	Establish a mobile screening clinic for screening contacts who live far from the nearest health care facility with a TB department.	Completed.
33	Use innovative IT solutions to support adherence to latent TB infection treatment, especially if the distance to the health facility is considerable.	Mobile application introduced for directly observed treatment (observed in Amsterdam). A new information system for management of patients' information was introduced in 2018. This cloud-based national platform, called iTBC, allows clinicians to access chest X-ray images independently of their work location.

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