Projection of the number of patients with tuberculosis in the Netherlands in 2030

Frank van Leth¹,², Nico A. Kalisvaart¹, Connie G. M. Erkens¹, Martien W. Borgdoff¹,²

Background: The incidence of tuberculosis (TB) in The Netherlands has been declining for many years. For the purpose of planning future TB-control activities we estimated the number of TB patients in The Netherlands up to 2030. Methods: Statistical modelling for 5-year age groups up to 2030 distinguishing among Dutch TB patients infected by a Dutch source (survival model), non-Dutch patients (projection of the proportion of culture-positive patients among first generation immigrants) and Dutch patients infected by a non-Dutch source (fixed relation with the number of non-Dutch patients).

Results: The number of TB patients is expected to decline to 877 in 2030. After 2010 declines may slow due to an increase in non-Dutch TB patients. This increase cancels out the decrease of Dutch TB patients infected by a Dutch source. In 2030, 85% of all TB patients are expected to be non-Dutch. In the four largest counties and the rest of The Netherlands, this will be 89 and 76%, respectively.

Conclusion: The decrease in TB incidence observed over many years may stall from 2010 onwards because of an estimated increase in non-Dutch TB patients. Given their disproportionate burden, future TB-control activities should prioritize the health of first-generation immigrants. Enhanced TB control in the countries of origin and new diagnostic tests to identify those at high risk of developing active TB could help in reducing further the TB incidence in the Netherlands. Future TB-control efforts must be organized in a flexible way to be able to incorporate changing epidemiological situations.

Keywords: immigrants, incidence, the Netherlands, tuberculosis, life table.

Introduction
The incidence of tuberculosis (TB) in the Netherlands declined steadily from the start of registration in 1951 up to 1982. From this time onwards, there was a small increase which peaked in 1993 (1598 patients). Between 1996 and 2006, the incidence of TB (all forms) declined yearly by 4% to 6.2 patients per 100 000 population.¹ The decrease in incidence has been more pronounced in autochthonous Dutch (63% between 1996 and 2006) than in first- (41%) and second-generation immigrants (10%).

The differential decline in the incidence between population groups means that currently the majority of TB patients in The Netherlands is first-generation immigrants (63% of all patients in 2006), while 24% are second-generation immigrants and 8% Dutch.

A substantial percentage of TB patients of foreign descent are also seen in other industrialized countries with marked immigration. In the United States this percentage was 30% in 1993, and increased to 41% in 1998 and 57% in 2006.²³ In Australia in 2003, the incidence of TB was 20 times higher in persons born overseas compared with the non-Indigenous born Australians, accounting for >82% of all TB cases in this country.⁴ In Canada in 2002, 67% of all TB cases were foreign-born.⁵ A similar percentage of foreign-born TB patients was seen in the United Kingdom in the period 2001–03.⁶

The Netherlands is one of the countries with the lowest TB-incidence in the World.¹⁷ Immigrants from high burden countries who wish to stay for 3 months or longer in the Netherlands have to comply with a mandatory screening for active TB. Persons ≥12 years are additionally offered voluntary follow-up screening every 6 months for a period of 2 years. A detailed analysis of the yield of this strategy resulted in a policy change where the voluntary follow-up screening is only offered to immigrants from countries where the TB incidence is reported to be higher than 200/100 000 population.⁸

The objective of the current study is to project the number of TB-patients in the year 2030. This estimate is needed to define future TB-control strategies in a setting with decreasing TB-incidence and the potential for future elimination of TB. Elimination is defined as an incidence of <1 sputum-smear positive case per 1 000 000 population.⁹

Methods
We defined three groups of TB patients: (i) the number of Dutch patients infected by a Dutch source was calculated using a life-table model; (ii) the number of non-Dutch patients was estimated by calculating the proportion of first-generation immigrants with culture-positive TB in 2005 and projecting this proportion onto the expected population of non-Dutch; (iii) the number of Dutch patients infected by a non-Dutch source was based on the assumption that every culture-positive non-Dutch patient would cause one infection in the Dutch population at large. This assumption was derived from a study on TB transmission in the Netherlands using molecular techniques.¹⁰

The information on TB patients was drawn from the Dutch Tuberculosis Register (NTR) that contains surveillance data on all TB patients in the Netherlands. It is provided by all Municipal Health Services in a structured format. Population data from the Netherlands were received from the Central Bureau of Statistics (CBS), whose yearly predictions are validated against observed trends. The assumptions used in the life-table model were those generally used in the literature.

¹ KNCV Tuberculosis Foundation, The Hague, The Netherlands
² Center for Infection and Immunity Amsterdam (CINIMA), Academic Medical Center, University of Amsterdam, The Netherlands

Correspondence: Frank van Leth, KNCV Tuberculosis Foundation, Parkstraat 17, 2514 JD Den Haag, The Hague, The Netherlands, tel: +31 70 4270982, fax: +31 70 3584004, e-mail: vanleth@kncvtb.nl

The life-table model predicted that the number of Dutch TB-patients who are infected by a Dutch source will decrease from 480 in 1995 to 64 [95% confidence interval (CI) 55–71] in 2030 (table 2). The proportion of first-generation immigrants with culture-positive TB in 2005 was 0.00024. Projection of this proportion to the estimated non-Dutch population predicted an increase in the number of non-Dutch TB-patients from 460 in 1995 to 704 [95% CI 619–1218] in 2030. This translates into only a small increase in the number of Dutch TB patients infected by a non-Dutch source; 42 in 1995 and increasing to 64 [95% CI 47–96] in 2030. This is a result of the expected decrease in the absolute number of Dutch in the total population of the Netherlands in the coming years.

The estimated total number of TB patients in the Netherlands from the model is 982 in 1995, decreases to 877 [95% CI 837–946] in 2010, after which it remains relatively constant with 831 (95% CI 619–1218) patients in 2030. This translates to 5 (95% CI 4–7) TB-patients per 100 000 population, and 16 (95% CI 13–21) smear-positive TB-patients per 1 000 000 population. Figure 1 shows that the trend in incidence as predicted by the model fits with the observed number of patients before 1995.

Comparing the incidence of TB in the four largest counties with the rest of the Netherlands is only possible for the years 1996–2025 given the availability of detailed population data from CBS. The total number of TB patients remains constant in the four largest counties between 1996 and 2025 [324 and 325 (95% CI 251–703), respectively], while it decreases with 30% in the rest of the Netherlands [672 and 472 (95% CI 327–557), respectively]. The number of Dutch TB patients infected by a Dutch source decreases in both groups (84% in the four largest counties, and 81% in the rest of the Netherlands). However, in the four largest counties, the number of Dutch TB patients infected by a non-Dutch source, and the number of non-Dutch TB-patients increase. In contrast, the increase in both these groups in the rest of the Netherlands is compensated by the decrease in the number of Dutch patients infected by a Dutch source.

The estimated incidence in 2025 is 15 (95% CI 14–22) per 100 000 population in the four largest counties, and 3 (95% CI 3–3) in the rest of the Netherlands. The estimated incidence of sputum-positive TB-patients is 47 (95% CI 47–72) and 10 (95% CI 9–10) per 1 000 000 population, respectively.

In the primary analysis, the proportion of first-generation immigrants with culture-positive TB was kept constant at the level observed in 2005. This approach can be seen as conservative, because this proportion almost halved in the period 1995–2005 from 41/100 000 population to 24/100 000 population. When this trend of a decrease with 50% every 10 years would continue up to 2030, the total number of TB patients is estimated to be 256 (196–358) which translates to 5 (95% CI 4–7) TB-patients per 100 000 population. When the proportion would increases again to the level of 1995, then the total number of TB patients in 2030

### Results

The life-table model predicted that the number of Dutch TB-patients who are infected by a Dutch source will decrease from 480 in 1995 to 64 [95% confidence interval (CI) 55–71] in 2030 (table 2). The proportion of first-generation immigrants with culture-positive TB in 2005 was 0.00024. Projection of this proportion to the estimated non-Dutch population predicted an increase in the number of non-Dutch TB-patients from 460 in 1995 to 704 [95% CI 619–1218] in 2030. This translates into only a small increase in the number of Dutch TB patients infected by a non-Dutch source; 42 in 1995 and increasing to 64 [95% CI 47–96] in 2030. This is a result of the expected decrease in the absolute number of Dutch in the total population of the Netherlands in the coming years.

The estimated total number of TB patients in the Netherlands from the model is 982 in 1995, decreases to 877

### Table 1 Assumptions used in the life model

<table>
<thead>
<tr>
<th>Assumption</th>
<th>&lt;15 years</th>
<th>16–65 year</th>
<th>&gt;65 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability active TB after infection</td>
<td>0.04</td>
<td>0.14</td>
<td>0.14</td>
</tr>
<tr>
<td>Proportion infectious patients of all infected</td>
<td>0.08</td>
<td>0.08</td>
<td>0.65</td>
</tr>
<tr>
<td>Probability reactivation old infection</td>
<td>0.00005</td>
<td>0.000113</td>
<td>0.0003</td>
</tr>
<tr>
<td>Proportion patients with sputum conversion</td>
<td>0.015</td>
<td>0.015</td>
<td>0.015</td>
</tr>
<tr>
<td>Proportion culture-positive patients of all patients</td>
<td>0.65</td>
<td>0.65</td>
<td>0.65</td>
</tr>
<tr>
<td>Proportion ZN+ patients of all culture-positive patients</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>

### Table 2 Number of TB patients observed (1995) and estimated

<table>
<thead>
<tr>
<th></th>
<th>Total pop.</th>
<th>Four largest counties</th>
<th>Rest the Netherlands</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1995</td>
<td>2030</td>
<td>2025</td>
</tr>
<tr>
<td>Dutch/Dutch</td>
<td>600</td>
<td>64 (55–71)</td>
<td>8 (7–9)</td>
</tr>
<tr>
<td>Dutch/non-Dutch</td>
<td>664</td>
<td>704 (517–1052)</td>
<td>290 (223–411)</td>
</tr>
<tr>
<td>Non-Dutch</td>
<td>1264</td>
<td>832 (619–1218)</td>
<td>325 (351–703)</td>
</tr>
<tr>
<td>Total</td>
<td>1241</td>
<td>984 (719–1618)</td>
<td>357 (351–703)</td>
</tr>
<tr>
<td>Per 10^5 pop.</td>
<td>11</td>
<td>5 (4–7)</td>
<td>15 (14–22)</td>
</tr>
<tr>
<td>ZN+ per 10^5 pop.</td>
<td>33</td>
<td>16 (13–21)</td>
<td>47 (47–72)</td>
</tr>
</tbody>
</table>

Dutch/Dutch = Dutch patient infected by Dutch source
Dutch/non-Dutch = Dutch patient infected by non-Dutch source
Non-Dutch = not born from Dutch parents
Pop. = population
a: Excluding asylum seekers
is estimated to be 1366 (1011–2018), the incidence per 100,000 population 9 (95% CI 6–12) and the incidence of sputum-positive TB-patients 27 (95% CI 20–39) per 1,000,000 population.

The ethnic composition of TB patients changes over the study period due to differential changes in the three groups of patients. Forty-seven percent of all TB-patients in the Netherlands in 1995 were foreign-born or the children of immigrants (figure 2). This proportion increases to 85% in 2030. In the four largest counties, the proportion increased from 76% in 1996 to 89% in 2025. In the rest of the Netherlands the proportion were 34 and 76%, respectively.

Discussion

The progressive decrease in the number of TB patients in the Netherlands over the last decades seems to stall from 2010 onwards. The reason for this is the expected increase in the number of non-Dutch patients. It is estimated that this group will account for 85% of the total number of TB patients seen in 2030. It is unlikely therefore that the target for TB elimination will be reached in the Netherlands in 2030, given the estimated 16 sputum-positive TB patients per 100,000 population.

If the main sending countries change considerably in the near future, then the current model will be no longer valid.

In addition to the uncertain population estimates is the uncertainty of the true number of TB patients. First, the incidence figures of the country derive from notification data. Although notification of TB is mandatory, there is potential for under-reporting. In a recently performed capture-recapture study, it was estimated that the level of underreporting in the NTR could be as high as 13%.

Second, the estimate of the number of non-Dutch TB patients depends primarily on the proportion of culture-positive TB patients amongst first-generation immigrants. This proportion is not stable. A decrease in this proportion is possible when the sending nations change over time, or when improved TB-control in the sending nations reduces the number of immigrants infected with TB. The sensitivity analyses suggest that this proportion has a large influence on the estimated number of TB patients in 2030. However, with the continuation of the trend that the proportion decreases with 50% every 10 years, the target for TB elimination in the Netherlands will not be reached in 2030.

Third, the life-table model assumes a homogenous transmission of TB in all age groups within the Dutch and non-Dutch population, and between these two populations. This is an over-simplification. An earlier study from the Netherlands showed that TB transmission was largely due to TB-patients below the age of 45 years and that transmission occurred mainly between comparable age-groups of the source and contact. Changes in the mean age of first-generation immigrants will therefore translate into changes in TB transmission and the number of TB patients in both the Dutch population and the population of first-generation immigrants.
Despite the limitations, we feel that the estimate of the number of TB patients in the Netherlands in 2030 and the composition of the patient group offers useful information for planning future TB control strategies. These strategies should not be narrowly limited to TB control in the Netherlands itself. Given the large contribution of first-generation immigrants to the incidence of TB, supporting control strategies in the sending nations is a logical approach to curbing TB in the Netherlands. A study conducted in the United States showed that investment in TB control activities in the three major sending countries had a marked effect on TB morbidity and mortality in the United States and was cost-effective.17 Another potential area of intervention can be the development of new diagnostics used at the initial screening of immigrants to more accurately identify those individuals with a high risk of developing TB who would benefit from prophylactic treatment. A study has just started in The Netherlands to assess the predictive value of new immunodiagnostic assays in the immigrant population.

The current study shows that TB is unlikely to be eliminated from The Netherlands in the near future. It is therefore essential that the medical profession remains vigilant in diagnosing the disease without delay in order to start appropriate therapy and interrupt transmission. Adequate training of the medical profession starts with emphasizing the characteristics of the disease in the curriculum of medical students, and continues with regular re-training of health personnel in both the clinical and the public health arena.

The uncertainties around the estimates require that future TB-control strategies should be planned in a flexible way. With a decrease in the number of TB-patients which can occur as a result of changing immigration patterns, centralization of certain aspects of TB-control such as laboratory diagnostics and TB-specialists will be necessary. Case finding and treatment, however, will remain a task of the Municipal Health Services at a decentralized level.

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Conflicts of interest: None declared.

Key points
- The decline in the incidence of tuberculosis (TB) in The Netherlands is predicted to stall from 2010 onwards.
- The incidence of TB in The Netherlands is increasingly defined by TB seen in first-generation immigrants.
- Health professionals should remain alert to diagnose TB and need appropriate (re)training to be able to do so.
- TB-control strategies need to be planned in a flexible way to be able to accommodate uncertainties around the projections of the number of patients.

References

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