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The impact of immigration on the elimination of tuberculosis in The Netherlands: a model based approach

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SUMMARY

OBJECTIVE: To determine whether elimination of tuberculosis in the Dutch population can be achieved by the year 2030, taking into account the impact of immigration.
METHODS: The incidence of tuberculosis (all forms) in the period 1970 to 2030 was estimated using a life-table model for the Dutch population without the impact of immigration. The influence of immigration on tuberculosis incidence among the Dutch was modelled using four immigrant scenarios, distinguished by the assumed contact rate between immigrants and the Dutch population, and by different projections (middle, upper) of the future size of the immigrant population in The Netherlands.
RESULTS: The incidence of smear-positive tuberculosis among the Dutch is projected to be 1.4 per million in the scenario without the influence of immigrant cases, and ranging from 3.8 to 11.8 per million in the four immigrant scenarios. In all immigrant scenarios, the prevalence of tuberculosis infection will continue to decline and be less than 1% by the year 2030. At least 60% of Dutch tuberculosis cases in the year 2030 are expected to be the result of transmission from a foreign source case.
CONCLUSION: Using a prevalence of tuberculosis infection of less than 1% as the elimination criterion, tuberculosis will probably be eliminated from the indigenous Dutch population by 2030. However, the incidence of smear-positive tuberculosis is expected to remain higher than 1 per million, and the majority of new tuberculosis cases among the Dutch may be attributable to recent infection from a foreign source case.
KEY WORDS: tuberculosis; epidemiology; scenario; projection; immigration; elimination

DURING THE past century, the incidence of tuberculosis has decreased rapidly in many industrialised countries to levels below 10 per 100 000 population. If this trend continues, elimination of tuberculosis as a public health problem may be anticipated within the next few decades.[1] Tuberculosis elimination has been defined as follows: 'elimination has been achieved when the incidence of tuberculosis has fallen to one smear-positive case per million population, and/or the overall prevalence of tuberculous infection in the general population has fallen below one per cent and continues to decrease'.[1]

However, during the last one or two decades, in many of these countries the decrease has levelled off or an increase has been observed.[2–4] Several explanations have been put forward to explain this phenomenon, including the impact of human immunodeficiency virus (HIV) infection, drug abuse, homelessness and immigration of persons from high prevalence countries.[3,4] In The Netherlands, the impact of HIV infection, drug abuse and homelessness can be considered to be of minor importance compared to immigration, as only very few TB cases in the Netherlands belong to any of these categories, and there is no reason to expect this to change. The proportion of tuberculosis patients with a non-Dutch passport rose from approximately 30% in 1980 to almost 60% in 1997.[5] Migration from countries with a high incidence and prevalence of tuberculosis to countries with a low incidence has increased during the last decades, and it seems unlikely that this trend will reverse in the near future. Although some transmission occurs from immigrants to the Dutch population,[6] it is unclear whether this will have a major impact on the elimination of tuberculosis as a public health problem.

The aim of this paper was threefold. First, to project the trend of tuberculosis incidence (all forms) in the Dutch indigenous population until the year 2030 in the absence of transmission from immigrants. Second, to assess the impact of immigration from high prevalence countries on the incidence in the indigenous Dutch population under various immigration scenarios. Third, to determine whether elimination of tuberculosis in the Dutch population can be achieved by the year 2030, taking into account the impact of immigration. We defined as an 'immigrant'

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any first generation non-Dutch person residing in the Netherlands. This is a very heterogeneous group, and comprises individuals from other low prevalence countries. However, the majority of these originate from high prevalence countries.

METHODS

Demography

The demography of the Dutch indigenous population, in the model, was based on Dutch vital statistics and projections. For immigrants, data were too limited to fully model their demography. Therefore, a separate compartment of immigrants (not differentiated by age or sex), interacting with the Dutch indigenous population, was added to the model. The size of this compartment was based on projections made by Statistics Netherlands.

Life-table model for Dutch indigenous population

The incidence of tuberculosis (all forms) in the period 1970 to 2030 was estimated using a life-table model, based on models of Sutherland et al.,[7] Vynnycky et al.[8] and Dye et al.[9] (Figure 1). Table 1 summarises the different states and transition parameters in this model, as well as the parameter values and their sources. Parameter values were used as given by Dye et al., with one exception. Dye et al. consider 65% of all tuberculosis cases to be infectious and assume that these are smear-positive. We consider them as culture-positive tuberculosis, as among the Dutch approximately 65% of patients have culture-positive pulmonary tuberculosis, 50% of which is smear-positive.

Cohort life tables were constructed for 20 5-year age groups (0, 5, 10, 15, . . . , 95), for the years 1970 to 2030. Cohorts are depleted due to age, sex and period specific mortality rates. Depending on the age-period specific risk of tuberculous infection (ARTI), survivors may experience tuberculous infection and either develop clinical tuberculosis or move from the class of susceptibles to the class of latently infected. In any year, new clinical cases also result from reactivations from the pool of latently infected individuals. A spreadsheet programme (Excel) was used to implement the model.

All cases developing tuberculosis are considered to be cured or to die from tuberculosis or other causes in the same year. The effect of defaulting was not considered separately, but incorporated in the average contact rate. Cured cases flow back into the pool of those with latent infection for the next year.

Annual risk of tuberculous infection

Values for the annual risk of tuberculous infection (ARTI) in The Netherlands for the years 1910–1979 were available from tuberculin surveys,[12,13] and were treated as fixed (exogenous) values in the model. Age-specific risks were used as by Styblo et al.,[10] who estimated age-specific relative risks of infection (relative to the age group 0–13) based on a study by Sutherland and Fayers.[14] For example, in the age group 18–25 years, ARTI was estimated to be 1.75 times that in the age group 0–13 years. For the period 1875 to 1910, ARTIs were derived from estimates by Sutherland.[11] For the years 1970 to 1980, we assumed a constant contact rate of 8. This would lead to higher ARTIs than actually measured. The reason for doing this was that ARTI measured in school children was

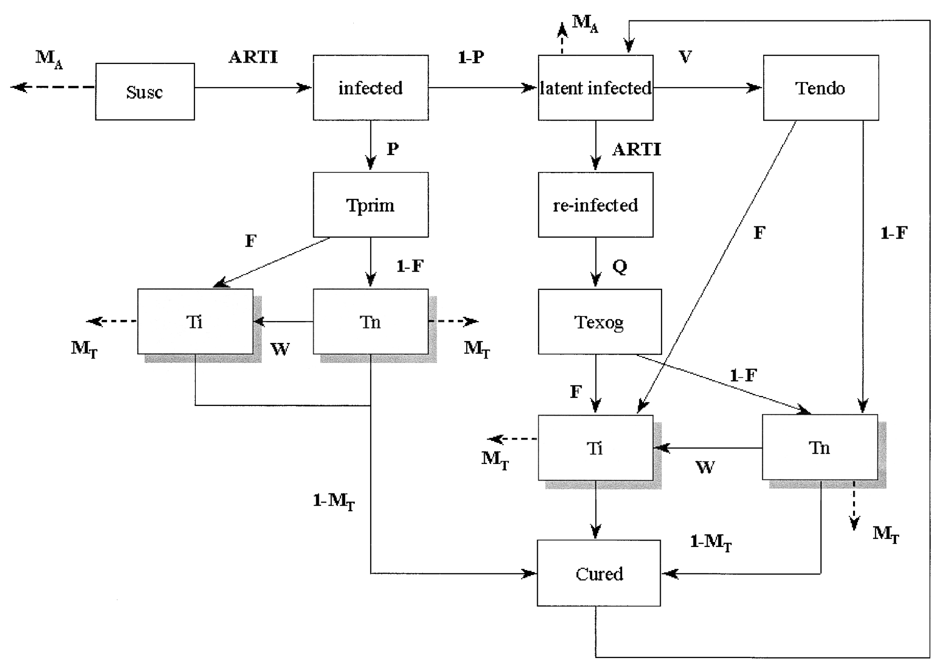

Figure 1 Flow chart of the life-table model. See Table 1 for abbreviations.

Table 1 States and parameters of the life-table model

State	Formula	Description
Infected (a, t)	S (a, t) × ARTI (a, t)	Population infected with tubercle bacillus
S (a+1, t+1)	S (a, t) − Infected (a, t) − M_T × S (a, t)	Population susceptible to tuberculosis infection
Tprim (a, t)	P × infected (a, t)	Primary tuberculosis cases
L (a, t)	(1−P) × infected (a, t)	Latent infected tuberculosis cases
CumL (a, t)	L (a, t) + CumL (a−1, t−1) + (1−M_T) × (Ti + Tn) (a-1, t−1)	Cumulative latent infected tuberculosis cases
Tendo (a, t)	CumL (a, t) × V	Tuberculosis cases as the result of endogenous reactivation
Re-infected (a, t)	CumL (a, t) × ARTI	Re-infected latent infected tuberculosis cases
Texog (a, t)	Re-Infected (a, t) × Q	Tuberculosis cases as the result of exogenous reactivation
Ti (a, t)	Tprim × F + Texog × F + Tendo × F	Infectious tuberculosis cases
Tn (a, t)	Tprim × (F − 1) + Texog × (F − 1) + Tendo × (F − 1)	Non-infectious tuberculosis cases
Cured (a, t)	(Ti + Tn) × (1−M_T) (a, t)	Cured tuberculosis cases
ARTI	Until 1980 based on measured values, (Styblo, 1997)[10] with a correction of the ARTI according to trend of tuberculosis incidence. After 1980 estimated from model (Ti × contact rate)	Annual risk of tuberculosis infection
M_A	Data provided by Statistics Netherlands	All-cause mortality rate
M_T	Data derived from Statistics Netherlands	Tuberculosis mortality rate
P	Age ⩽15 years: 0.04 Age >15 years: 0.14 (Dye, 1998)[9]	Proportion of infected individuals developing tuberculosis (primary cases)
F	Age ⩽15 years: 0.08 Age >15 years: 0.65 (Dye, 1998)[9]	Proportion of infectious tuberculosis cases
W	0.015 (Dye, 1998)[9]	Rate of smear conversion
V	Age ⩽15 years: 5×10^{-5} Age 15–65 years: 1.13×10^{-4} Age >65 years: 3×10^{-4} (Dye, 1998)[9]	Endogenous reactivation latent tuberculosis cases
Q	Age ⩽15 years: 0.04 (Dye, 1998)[9] Age >15 years: 0.07 (Sutherland, 1982)[11]	Proportion of re-infected developing tuberculosis

a = age group; t = calendar year.

subject to measurement bias resulting from an increase in the average age of infectious cases in those years. Sources of tuberculosis may preferentially transmit infection to people close to their own age.[15] As the average age of cases has increased, sources may have become less likely to infect children in whom the risk of infection was measured.[15]

The contact rate is defined in this paper as the average number of infections generated by an infectious case. After 1980, the ARTI was no longer measured, and was therefore estimated from the model using the incidence of infectious cases (Ti) and the contact rate (incidence × contact rate = ARTI). The contact rate among the Dutch population was fixed to a value of 8 for the period 1980–2030. The ARTI estimated for year t was used to calculate new infections in the year t+1. Population data (and projections of population data) for 5-year age groups and each fifth calendar year (1970, 1975, 1980, . . . 2030) were obtained from Statistics Netherlands for the years 1997 to 2015.[16]

Immigrant scenarios

We considered a basic model for a hypothetical closed Dutch population ignoring immigration completely, and four immigrant scenarios. The immigrant scenarios were distinguished by their assumed contact rate between immigrants and the Dutch population, and by different projections (middle, upper) of the immigrant population in The Netherlands.[17] The scenarios were defined as follows:

Immigrant scenario 1: contact rate for immigrants with the Dutch population = 1; middle variant of projection of immigrants in The Netherlands
Immigrant scenario 2: contact rate (non-Dutch→Dutch) = 1; upper variant of projection of immigrants
Immigrant scenario 3: contact rate (non-Dutch→Dutch) = 4; middle variant of projection of immigrants
Immigrant scenario 4: contact rate (non-Dutch→Dutch) = 4; upper variant of projection of immigrants

The number of first generation immigrants living in The Netherlands was 1 345 000 in 1998, and according to the middle and upper variant was projected to increase regularly until 2030 to 1 890 000 and 2 252 000, respectively.[17] Only projections for first generation immigrants were used for the scenarios. The total numbers of immigrants, and not age-specific figures, were used in the scenarios.

Annual incidence in the indigenous Dutch population as a result of transmission from foreign sources was calculated as follows. For the years 1998–2030, the number of foreign infectious tuberculosis cases was estimated from the projected total number of immigrants in The Netherlands in a given year times an incidence rate of infectious tuberculosis among immigrants of 30/100 000. The latter estimate was based on observed data from 1997, when 579 out of 1 818 000 immigrants were diagnosed with infectious tuberculosis. For the years 1980–1997, the numbers of foreign infectious tuberculosis cases were known from notifications. For the years 1970–1979, only total numbers of new tuberculosis cases were available. In 1980, 12% of all tuberculosis cases were foreign infectious cases. For the years 1970–1979, it was assumed that the same 12% applied.

The number of foreign infectious cases times the contact rate (1 or 4) yielded the additional number of newly infected individuals in the indigenous Dutch population. Of those who were newly infected, it is assumed that 14% would develop primary tuberculosis (Table 1). These cases were added to the number of cases calculated from the basic model. The prevalence of tuberculosis infection in 2030 was estimated by adding all newly infected individuals in the indigenous Dutch population due to a foreign source over the period 1990 to 2030 to the prevalence of infection in the year 2030 as estimated by the basic model.

RESULTS

In the basic model which excludes the impact of immigration, the incidence rate of tuberculosis (all forms) in The Netherlands continues to decline from 3.3/100 000 in 1997 to 0.5/100 000 in 2030 (Figure 2). In 2030, 37% of all incident cases among the Dutch (cases resulting from a foreign source excluded) are due to reactivation of remote infection: this percentage increases strongly with age.

In both immigrant scenarios with an assumed contact rate of 1, the incidence of new cases (all forms) among the Dutch continues to decline until 2030 to a rate of 1.2–1.3/100 000. In the immigrant scenarios with contact rate of 4, the incidence rate of new tuberculosis cases stabilises after 2010 at a rate of 3.3–3.6/100 000 (Figure 2). For the period 1990–1997, the immigrant models with a contact rate of 4 did not fit the observed data very well (Table 2).

According to all four immigrant scenarios, tuberculosis elimination as a public health problem in the Dutch population will have been achieved by the year 2030, if elimination is defined as an infection prevalence of less than 1% which continues to decline (Table 3). According to that definition, elimination of tuberculosis in the Dutch population will be achieved for the first time in 2027 if the scenario with the lowest impact of immigration is used (scenario 1), and in 2028 according to scenario 4. However, the incidence of smear-positive tuberculosis, which is projected to be 1.4 per million in the basic scenario, varies from 3.8 to 11.8 per million in the four immigrant scenarios. Therefore, in none of the scenarios will the incidence of smear-positive tuberculosis be less than 1 per million, although the basic scenario comes close.

The proportion of Dutch cases resulting from transmission from a foreign source case is expected to become very substantial over time. In 1990, 5% of all new cases of tuberculosis among the Dutch population were the result of a foreign source according to immigrant scenario 1. This percentage increases to 12% by the year 2000, 22% by the year 2010, 41% by the year 2020 and 60% by the year 2030.

In 1997, 59% of all new tuberculosis cases in The Netherlands occurred among the immigrant population. If the incidence rate of tuberculosis among immigrants remains at 30/100 000, according to the middle variant of immigrant projection, there will be approximately 1150 foreign tuberculosis cases in The

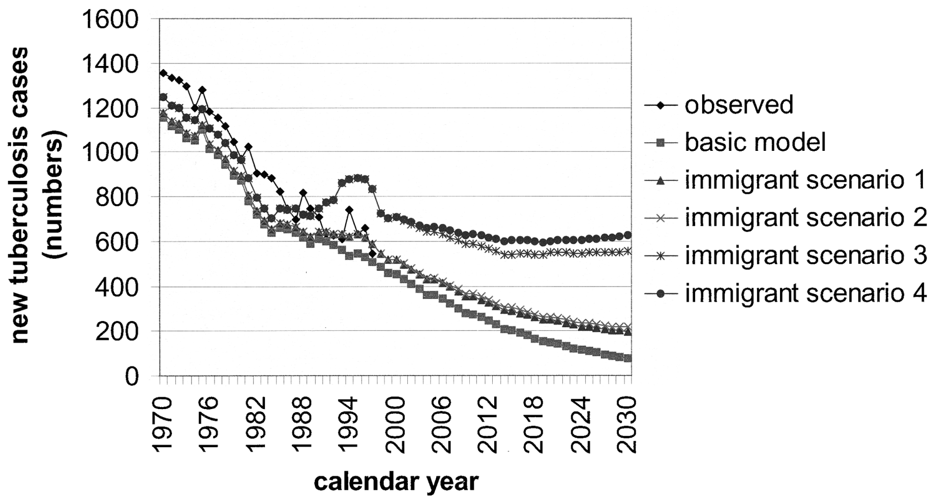

Figure 2 Annual trend of new tuberculosis cases in The Netherlands 1970–2030. Observed cases (1970–1997), estimations from the basic model without cases in the Dutch population derived from a foreign source (1970–2030), and estimations based on immigrant scenarios as defined in the Methods section.

Table 2 Observed tuberculosis cases among the Dutch and non-Dutch and model estimations of the number of cases among the Dutch, 1970–1997

Year	Observed Dutch cases	Observed non-Dutch cases	Dutch cases in immigrant scenarios with contact rate = 1	Dutch cases in immigrant scenarios with contact rate = 4
1970	1357	639	1187	1287
1971	1334	628	1146	1245
1972	1322	623	1133	1230
1973	1293	609	1092	1188
1974	1195	563	1077	1165
1975	1279	603	1128	1223
1976	1181	556	1039	1126
1977	1154	544	1010	1096
1978	1113	525	970	1053
1979	1043	491	916	993
1980	968	461	893	964
1981	1021	464	805	881
1982	903	387	736	792
1983	859	359	691	748
1984	884	284	653	704
1985	823	342	680	744
1986	747	306	674	740
1987	699	367	663	744
1988	818	345	640	720
1989	748	432	619	711
1990	710	523	643	744
1991	608	599	643	773
1992	624	708	632	782
1993	608	787	634	858
1994	739	871	619	878
1995	630	856	629	883
1996	661	800	616	874
1997	546	776	589	833

Netherlands in 2030. The models estimate 198 to 625 cases among the indigenous Dutch population, depending on the contact rate used. Thus, the percentage of all new tuberculosis cases being non-Dutch is expected to be 63%–80% in 2030.

DISCUSSION

Using a simple life-table model, we estimate that tuberculosis will be eliminated as a public health problem in the Dutch population by the year 2030, in terms of infection prevalence. However, tuberculosis will not be eliminated as a public health problem in terms of the incidence of smear-positive tuberculosis, as based on all of the immigrant scenarios explored this incidence will remain above 1 per million. By 2030 we expect not only that most tuberculosis cases will be observed among non-Dutch individuals, but also that at least 60% of tuberculosis among the Dutch will be attributable to infection from a non-Dutch source case. This suggests that tuberculosis control will need to further shift its attention to immigrants.

For this prediction several assumptions were made. First, most parameter values were taken as published by Dye et al.[9] Second, the ARTI after 1980 depends crucially on the assumed contact rates. In general, there is substantial uncertainty about the value of contact rates, as they are not directly measurable. They should be derived indirectly, e.g., from the ratio of the number of infectious patients to new infections (as measured by the ARTI). Before 1970, when tuberculin surveys were still being carried out, the ARTI was included in the model as estimated from tuberculin surveys.[12,13] It was subsequently calculated from the calculated number of cases and presumed contact rates, presumed on the basis of extrapolation. Thus, for instance, a further reduction of the contact rate might lead to a somewhat more rapid reduction in the tuberculosis problem. However, an

Table 3 Model estimates for the incidence of tuberculosis cases (all forms), incidence rate of smear-positive cases and prevalence of tuberculosis infection among the Dutch in the year 2030

Model	New cases *n*	Smear-positive cases (per million)	Prevalence of infection (%)
Basic model (Dutch population only)	79	1.4	0.82
Immigrant scenario 1*	198	3.8	0.85
Immigrant scenario 2†	215	4.1	0.86
Immigrant scenario 3‡	556	10.5	0.92
Immigrant scenario 4§	625	11.8	0.93

* Contact rate for immigrants with the Dutch population = 1; middle variant of projection of immigrants in The Netherlands by Statistics Netherlands.
† Contact rate = 1; upper variant of projection of immigrants.
‡ Contact rate = 4; middle variant of projection of immigrants.
§ Contact rate = 4; upper variant of projection of immigrants.

increasing contact rate between non-Dutch and Dutch individuals might lead to slower tuberculosis elimination among the Dutch.

For the period 1970–1990, the basic model and immigration scenarios assuming a low contact rate of 1 between immigrants and the Dutch underestimated the observed number of cases, while the immigrant scenarios assuming a high contact rate fitted well. For the period 1990–1997, the latter models overestimated tuberculosis incidence, while the former models fitted well. There may be various explanations for this. First, model parameters as presented by Dye et al.[9] might not provide the best fit for the Dutch situation. Second, the composition of immigrant groups has changed, from predominantly long term immigrants from Turkey and Morocco, to many recent immigrants among asylum seekers from countries such as Somalia and Yugoslavia. It seems likely that the contact rate would indeed be lower for such recent immigrants, in part because these are screened at arrival and are not yet integrated into Dutch society. Third, the definition of foreigners is not identical in the population statistics (based on country of birth), and the tuberculosis register (based on citizenship). In the immigrant scenarios we excluded second-generation immigrants from the analyses in order to correct at least partly for the effect of naturalisation, as most second-generation immigrants probably have Dutch nationality.

A very important limitation of the projections from 1998 onwards is uncertainty regarding the number of tuberculosis cases among immigrants. Even if the scenarios of the number of immigrants were correct, tuberculosis incidence is still uncertain, as it depends strongly on the country of origin of immigrants, their age distribution and their duration of stay in The Netherlands.[6,18–20] For instance, as tuberculosis incidence is highest in the first few years after arrival in The Netherlands and the average number of immigrant arrivals per year is projected to be stable, the incidence of tuberculosis among immigrants might not increase over time, despite increasing population numbers. If this were the case, we may have somewhat overestimated the impact of immigrants on tuberculosis among the Dutch.

A recent study estimated that 17% of the tuberculosis cases in the period 1993–1995 among the Dutch were attributable to active transmission from non-Dutch source cases.[6] This percentage is comparable to the percentages of Dutch cases stemming from a foreign source for those years found in the immigrant scenarios with a contact rate of 1 (14%). Despite this agreement, we realise that our scenarios are but crude estimates of the impact of immigration on tuberculosis epidemiology and based on highly uncertain information. Unfortunately, solid data on the contact rate between immigrants and the Dutch population and on differences between first- and second-generation immigrants are not available.

At present, tuberculosis control in The Netherlands is implemented by approximately 40 public health services, each covering an average of 40 patients per year. Further concentration of services has been proposed, to maintain a smaller number of centres with sufficient experience and expertise. The projections presented in this paper suggest that over the next few decades the total numbers of patients may not change dramatically, but that the shift from Dutch to immigrant patients observed over the past few decades may continue. The debate on concentration of services should take these projections into account.

In conclusion, using prevalence of infection rather than incidence of smear-positive tuberculosis as a yardstick, tuberculosis will probably be eliminated from the indigenous Dutch population by 2030. By then, the majority of new tuberculosis cases among the Dutch will result from infection by a foreign source case. However, as these projections are affected by many uncertainties, they will need to be revised when further information on immigration and tuberculosis incidence becomes available.

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RÉSUMÉ

OBJECTIF : Déterminer dans quelle mesure l'élimination de la tuberculose dans la population néerlandaise peut être atteinte en l'an 2030 si l'on prend en compte l'impact de l'immigration.

MÉTHODES : L'incidence de la tuberculose (toutes formes) pendant la période de 1970 à 2030 a été estimée en utilisant un modèle de tables de survie pour la population néerlandaise sans impact de l'immigration. L'influence de l'immigration sur l'incidence de la tuberculose parmi les Hollandais a été modélisée en utilisant quatre scénarios d'immigration qui se distinguent l'un de l'autre par le taux de contact supposé entre immigrants et la population néerlandaise et selon différentes hypothèses (moyenne et supérieure) de la dimension future de la population immigrante aux Pays-Bas.

RÉSULTATS : La projection de l'incidence d'une tuberculose à bacilloscopie positive parmi la population néerlandaise est de 1,4 par million dans le scénario excluant l'influence des cas immigrés et va de 3,8 à 11,8 par million dans les quatre scénarios d'immigration. Dans tous les scénarios d'immigration, la prévalence de l'infection tuberculeuse va continuer à diminuer et à descendre en dessous d'1% d'ici l'année 2030. On s'attend à ce qu'au moins 60% des cas de tuberculose chez les Hollandais pendant l'année 2030 soient le résultat de la transmission provenant d'un cas de source étrangère.

CONCLUSION : Si l'on utilise une prévalence de l'infection tuberculeuse inférieure à 1% comme critère d'élimination, la tuberculose sera probablement éliminée dans la population autochtone d'ici 2030. Toutefois, l'incidence de la tuberculose à bacilloscopie positive sera probablement supérieure à 1 par million et la majorité des nouveaux cas de tuberculose parmi les Hollandais pourra être attribuée à une infection récente provenant d'un cas d'origine étrangère.

RESUMEN

OBJETIVO : Determinar si la eliminación de la tuberculosis en la población holandesa podría obtenerse de aquí al año 2030, teniendo en cuenta el impacto de la inmigración.

MÉTODO : Se estimó la incidencia de la tuberculosis (todas las formas) durante el período 1970 a 2030, utilizando un modelo de tablas de vida para la población holandesa, sin el impacto de la inmigración. Se modelizó la influencia de la inmigración sobre la incidencia de la tuberculosis, utilizando cuatro escenarios de inmigración, que se distinguen por el supuesto grado de contacto entre los inmigrantes y la población holandesa y por las diferentes proyecciones (intermedia y superior) de la futura dimensión de la población inmigrante en Holanda.

RESULTADOS : La proyección de la tasa de incidencia de tuberculosis con baciloscopia positiva en la población holandesa es de 1,4 por un millón de habitantes en el escenario que excluye la influencia de los casos en los inmigrantes y es de 3,8 a 11,8 por millón en los cuatro escenarios de inmigración. En todos los escenarios de inmigración, la prevalencia de la infección tuberculosa seguirá disminuyendo y será de menos de 1% da aquí al año 2030. Se puede prever que por lo menos el 60% de los casos de tuberculosis en los holandeses en el año 2030 será el resultado de la transmisión a partir de un caso de fuente extranjera.

CONCLUSIÓN : Utilizando una prevalencia de la infección tuberculosa de menos de 1% como criterio de eliminación, la tuberculosis será probablemente eliminada de la población holandesa autóctona, da aquí al año 2030. Sin embargo, se puede prever que la incidencia de la tuberculosis con baciloscopia positiva permanecerá superior a un caso por millón y que la mayoría de los nuevos casos de tuberculosis en los holandeses podrán ser atribuidos a una infección reciente proveniente de un caso de origen extranjero.