Science for Communities

TUBERCULOSIS IN NEW ZEALAND ANNUAL REPORT 2015

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Disclaimer

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SUMMARY

This report describes the epidemiology of tuberculosis in New Zealand for 2015 as well as trends during the past 5–10 years.

Tuberculosis disease (TB) is a notifiable condition in New Zealand. The TB notification rate has been relatively stable since 2007 apart from a small decrease recorded in 2013. The 2015 TB notification rate was 6.4 per 100,000 population (294 cases). The majority of TB notifications were for new disease, with relapse/reactivation cases made up a small number of the notifications. A high proportion of TB cases (88.8%) were laboratory confirmed. The highest notification rates in 2015 were recorded for Auckland, followed by Counties Manukau, and Capital & Coast DHBs.

Between 2011 and 2015, there were demographic differences among new TB case rates. Rates were higher in males than females, especially those aged 15–39 years. Over the past 5 years, the Asian ethnic group has consistently experienced the highest notification rates. Although the absolute number of MELAA cases remains relatively low, the next highest rates were recorded in the Middle Eastern/Latin American/African (MELAA) ethnic group up until 2015 when the rate in this group was surpassed by the rate in the Pacific peoples ethnic group. As in previous years (2006–2015), higher rates of TB occurred in socioeconomically deprived areas.

Not being born in New Zealand and current or recent residence with a person not born in New Zealand have consistently been dominant risk factors.

The pattern of disease detection for new TB cases has been consistent over the past 5 years, with more than two thirds of TB cases diagnosed when they presented with symptoms to a health practitioner. Around 8% of cases were identified through immigrant/refugee screening.

Pulmonary disease was more common among new TB cases born in New Zealand than in cases born overseas. One case of miliary TB in a child aged <5 years was reported in 2015 and only three cases have been reported in this age group in the last 5 years. There were no cases of tuberculous meningitis reported in this age group over the last 5 years.

Most (96.2%) new TB cases in 2015 were reported to have received appropriate treatment. For pulmonary cases where the time between the onset of symptoms and start of treatment could be calculated, 34.5% of cases started treatment within 1 month of the onset of illness and 37.3% started treatment between 1 and 3 months.

One of the new TB cases notified in 2015 was co-infected with HIV.

Two outbreaks of *Mycobacterium tuberculosis* with seven associated cases were reported in 2015.

Two (0.8%) of the culture-positive TB cases reported in 2015 were multidrug-resistant TB (MDR-TB, defined as resistance to at least isoniazid and rifampicin). Both these MDR-TB cases were born overseas. Resistance to all antimicrobials was higher, although not significantly so, among isolates from cases born overseas than among isolates from New Zealand-born cases.

Between 2006 and 2015, there has been a significant trend of decreasing pyrazinamide resistance, but no significant changes in resistance to isoniazid, rifampicin, ethambutol or streptomycin. Over the same 10 years, an average of 1.2% of culture-positive TB cases were MDR-TB.

Over a third of the *M. tuberculosis* isolates that underwent molecular typing between 2011 and 2015 had results that matched other typed isolates, that is, were non-unique and could be assigned to a cluster. Most clusters contained fewer than five cases. Three new clusters were identified in 2015 with two cases each.

INTRODUCTION

Globally, tuberculosis disease (TB) is one of the most common causes of death from a communicable disease. TB had almost disappeared from the world's public health agenda in the 1960s, but returned in the early 1990s following the HIV/AIDS pandemic, and was sustained by a subsequent increase in drug resistance. Infection is usually curable with a combination of specific antibiotics, but this relies upon full compliance with treatment. TB is more prevalent in, but not confined to, low-income countries.

The World Health Organization's (WHO) estimated global TB incidence rate for 2015 was 142 per 100,000 population. WHO estimates also show a reduction in TB incidence of 2% per year between 2000 and 2013, and a reduction in mortality rates of 3.3% per year for the same period [1]. This means that the 2015 Millennium Development Goal of halting and reversing TB incidence has been achieved globally [2]. However, WHO reports that "the TB epidemic is larger than previously estimated, reflecting new surveillance and survey data from India". It was estimated there were 10.4 million newly incident TB cases worldwide in 2015 and TB deaths remained one of the top 10 causes of death. People living with HIV accounted for 1.2 million (11%) of new TB cases in 2015 and 60% of all new TB cases occurred in six countries, India, Indonesia, China, Nigeria, Pakistan and South Africa [1]. WHO notes that global progress in TB control and elimination requires major advances in TB prevention and care in these countries. Other components of the "End TB Strategy" includes preventive treatment (LTBI treatment) of persons at high risk, such as those living with HIV newly enrolled in HIV care and children aged <5 years who are household contacts of a TB case [1, 2].

In New Zealand in 2015, TB was notifiable under the Tuberculosis Act 1948. The 2014 notification rate was 6.7 per 100,000, similar to the average rates recorded since 2007. Notification rates decreased during the 1980s, then ranged between 8.5 and 11.6 per 100,000 from 1990 to 2003, followed by a further decrease between 2003 and 2007 to 6.7 per 100,000 [3]. Although rates have been relatively stable since 2007, TB is one of a number of infectious diseases (including acute rheumatic fever, meningococcal disease and skin infections), that play a major role in ethnic and socioeconomic inequalities in New Zealand [4].

In this report we describe the epidemiology of TB in New Zealand for 2015 and detailed trends during the past 5–10 years. The report includes the distribution of TB disease notifications geographically, by age and sex, among specific ethnic groups and across protective and risk factors where information is available. We describe clinical outcomes based on hospitalisation and death data from the Ministry of Health's National Minimum Dataset and the National Mortality Collection. TB drug susceptibility and molecular typing data is also summarised.

The primary audience of this report is the New Zealand Ministry of Health and TB practitioners, including Medical Officers of Health, respiratory and infectious disease physicians, clinical microbiologists and medical laboratory scientists.

METHODS

DATA SOURCES

Tuberculosis disease (TB) notification data recorded on EpiSurv, the national notifiable diseases database, is used in this report. Data provided by the mycobacteriology laboratories at Auckland City Hospital, Waikato Hospital, Wellington SCL and Canterbury Health Laboratories on the species identification, antimicrobial susceptibility and molecular types of *Mycobacterium tuberculosis* complex isolates from cases of TB is also included. In addition, Ministry of Health data on hospitalisations and deaths due to tuberculosis is presented.

Notifications

In 2015, clinicians were required to notify all cases of active TB to their local Medical Officer of Health under the Tuberculosis Act 1948. However, cases diagnosed with latent tuberculosis infection (LTBI) or with old inactive tuberculosis disease were not notifiable under the Tuberculosis Act 1948[i]. Only cases of active tuberculosis disease (referred to as TB) are presented in this report.

TB notification data is entered into EpiSurv by staff at each public health unit (PHU) via a secure web-based portal. This near real-time data is collated and analysed by ESR on behalf of the Ministry of Health. Notification data includes information such as the type of TB, case demography, clinical details, laboratory results, risk factors and case management details.

TB cases are recorded in EpiSurv as one of the following:

Tuberculosis disease – new case: active TB in a person who has never been treated for TB before, or has active disease from a new genotype.

Tuberculosis disease – relapse or reactivation: active TB in a person whose tuberculosis has been non-infectious or quiescent following full, partial or no treatment.

The case classification for TB, as defined by the Ministry of Health's Communicable Disease Control Manual in 2012 [5], is provided below.

Under investigation:	A suspected case that has been notified, but information is not yet available to classify it as probable, confirmed or not a case.
Probable:	Presumptive (without laboratory confirmation). There is no laboratory confirmation but: there are symptoms or signs compatible with active tuberculosis, such as compatible radiology or clinical evidence of current disease; and full anti-tuberculosis treatment has been started by a clinician.
Confirmed:	A clinically compatible illness that is laboratory confirmed. Laboratory confirmation requires at least one of the following: positive culture for *Mycobacterium tuberculosis* complex; positive microscopic examination for acid-fast bacilli when a culture has not been or cannot be obtained; demonstration of *M. tuberculosis* complex nucleic acid directly from specimens histology strongly suggestive of tuberculosis when there is a strong clinical probability.
Not a case:	A case that has been investigated and subsequently found not to meet the case definition.

[i] Cases of latent TB infection or with old inactive TB may be entered onto EpiSurv with patient consent for case management purposes.

Hospitalisations

Hospital discharge data for TB (*ICD-10* AM codes A15−A19 and P37.0) was extracted from the Ministry of Health's National Minimum Dataset (NMDS) (see www.health.govt.nz for more information). Hospitalisation numbers from the NMDS may differ from EpiSurv, since the NMDS data can include multiple hospital discharges for the same individual and discharges that relate to cases notified in previous years. In addition, the criteria for TB notification differ from that required for diagnostic coding.

Deaths

Mortality data for TB was extracted from the National Mortality Collection, which records a classification for the underlying cause of each death registered in New Zealand. Mortality data is available only up to 2013 due to the time taken to complete coronial inquiries. In the Mortality Collection, deaths due to TB are assigned to the year in which the person died, while in EpiSurv, deaths are assigned to the year of initial disease notification. For this reason, the number of deaths per year may differ.

Co-infections

Data for TB/HIV co-infection cases was provided by the AIDS Epidemiology Group at the University of Otago.

Speciation and drug susceptibility

First-line drug susceptibility testing (DST) is undertaken by the mycobacteriology laboratories at Auckland City Hospital (LabPlus), Waikato Hospital, Wellington SCL and Canterbury Health Laboratories. Susceptibility to isoniazid (at concentrations of 0.1 and 0.4 mg/L), rifampicin, ethambutol, pyrazinamide and streptomycin is routinely tested. In addition, first-line DST at Wellington SCL includes fluoroquinolone (ofloxacin) susceptibility testing. Multidrug-resistant TB (MDR-TB) isolates (ie, isolates resistant to at least isoniazid and rifampicin) are tested at LabPlus for susceptibility to second-line antituberculous agents, including ethionamide, moxifloxacin, amikacin, capreomycin, *p*-aminosalicylic acid and linezolid.

The BACTEC® MGIT 960 method is used to test phenotypic drug susceptibility. Pyrazinamide DST can be performed by either the BACTEC® MGIT 960 method or the Wayne's pyrazinamidase assay.

Molecular methods are used to aid the detection of drug resistance in certain cases. For example:

- Isolates with high-level isoniazid resistance are screened for rifampicin resistance using the Cepheid GeneXpert® system. Rifampicin resistance detected in the GeneXpert system or in phenotypic susceptibility tests is further investigated by sequencing the *rpoB* gene.
- The *pncA* gene is sequenced in all MDR-TB isolates, regardless of their phenotypic susceptibility to pyrazinamide, and in all other isolates that are resistant to pyrazinamide in phenotypic susceptibility tests.
- For cases in which mixed cultures (eg, *M. tuberculosis* mixed with a rapid-growing *Mycobacterium* species) are suspected, the Hain Lifescience GenoType® line probe, Mycobacterium CM, may be used to identify *Mycobacterium* species in clinical specimens or cultures. The presence of two or more *Mycobacterium* species will delay phenotypic DST, as pure cultures are needed before DST can be performed.
- For cases where there is a high index of clinical suspicion for MDR-TB, Hain Lifescience GenoType® line probes, MTBDR*plus* and MTBDR*sl,* may be used directly on smear-positive clinical specimens and on cultures before DST results are available. These assays detect the

presence of mutations in the *inhA*, *katG*, *rpoB*, *embB*, *gyrA* and *rrs* genes that are associated with resistance to low-level isoniazid, high-level isoniazid, rifampicin, ethambutol, fluoroquinolone and aminoglycosides, respectively. As these assays only target the common mutations associated with resistance, results need to be reported in conjunction with the phenotypic DST results.

- In addition to these commercial assays, in-house PCR (polymerase chain reaction) assays are used to detect mutations in the *rpoB* gene, within and outside the 81 bp mutation hotspot, and in the *katG* gene. These assays are useful tools to confirm phenotypic rifampicin and high-level isoniazid resistance where no mutations in the *rpoB* gene or *katG* gene are detected by the GeneXpert® or Hain Lifescience GenoType® line probe assays.

Susceptibility testing and species identification results are sent to ESR and integrated with the TB notifications recorded on EpiSurv.

Molecular typing

The national TB molecular typing database is maintained by LabPlus, which carries out all human TB molecular typing in New Zealand. Since October 2011, typing of TB isolates has been undertaken by mycobacterial interspersed repetitive units (MIRU) analysis alone. Primary typing includes analysis at 12 loci (MIRU 12). Secondary typing at a further 12 loci (MIRU 24) is performed when an isolate has the same MIRU 12 as a previously typed isolate. Between October 2009 and October 2011, primary typing was by MIRU and secondary typing was by restriction fragment length polymorphism (RFLP). Prior to October 2009, RFLP was the primary typing method and MIRU was only performed where isolates had ≤5 bands on RFLP.

A TB isolate is defined as having a unique molecular type if either the MIRU 12 alone or the MIRU 12 + MIRU 24 combination does not match that of any other isolate in the national database. At least one isolate from each of the known MIRU/RFLP or RFLP-based clusters has been MIRU 12- and MIRU 24-typed so that new isolates can be matched to these existing clusters. The TB molecular typing data from LabPlus is routinely reported to ESR and periodically integrated with the TB notifications recorded in EpiSurv.

ANALYTICAL METHODS

The analytical methods used in this report are outlined below.

Dates

In this report, data is presented by the date the case was notified rather than by the date of onset of illness and focuses on cases of TB notified in 2015 and trends since 2006 or 2011, depending on the availability of data. Due to the length of time taken to complete TB treatment, information regarding the use of directly observed treatment (DOT) and treatment outcomes is presented for cases reported in 2014 rather than 2015.

Notification data presented in this report is based on information recorded in EpiSurv as at 21 September 2016. Changes made to EpiSurv data by PHU staff after this date will not be reflected in this report. Consequently, future data analysis may produce revised results.

Case status for notifications

All notifications of TB recorded in EpiSurv that meet the case classification criteria are included for analysis in this report, although their status may not be final. Any subsequent changes in the status of a case will be reflected in future surveillance reports.

Population rate calculations

Population data used to determine all disease rates, except that used to determine disease rates for ethnic groups and country of birth, has been derived from the 2015 mid-year population estimates published by Statistics New Zealand.

The denominator data used to determine ethnic-specific disease rates for 2011–2015 is based on the proportion of people in each ethnic group from the usually resident 2013 census population applied to the corresponding mid-year population estimates.

The denominator used to determine rates in the New Zealand-born children between 2006–2015 is based on the proportion of people born in New Zealand from the usually resident 2006 (for 2005 to 2009) and 2013 (for 2011 to 2015) census population applied to the corresponding mid-year population estimates.

Population data used to determine disease rates for each country of birth is derived from the 2013 census usually resident population count by birthplace.

In this report, disease rates are written as cases per 100,000 population where they first appear in a section and subsequently as cases per 100,000.

Disease rates are not presented in the tables in this report if there were fewer than five notified cases in a category. Calculating population rates from fewer than five cases may produce unstable rates, especially in smaller populations.

Percentages

Percentages are calculated with the denominator as the total number of cases for which information was recorded, unless otherwise specified.

Categorisation

Countries of birth were grouped into regions according to the Statistics New Zealand standard.

Ethnic groups presented are based on a prioritised classification of ethnicity, with the Māori ethnic group at the top of the hierarchy, followed by Pacific peoples, Asian, Middle Eastern/Latin American/African (MELAA) and European or Other ethnic groups. More information about ethnicity classification is available on the Ministry of Health website:

http://www.health.govt.nz/publication/ethnicity-data-protocols-health-and-disability-sector.

Socioeconomic deprivation is based on the 2013 New Zealand Deprivation Index (NZDep13). The index, which measures relative socioeconomic deprivation, is derived from a weighted combination of nine variables from the 2013 census, with each reflecting a different aspect of material and social deprivation. The deprivation score is calculated for each geographical meshblock in New Zealand [6]. Quintiles of NZDep13, ranging from 1 (least deprived) to 5 (most deprived), are presented in this report. Approximately equal numbers of people reside in areas associated with each of the five deprivation levels.

Drug susceptibility

Drug susceptibility data is only available for cases of TB that were culture positive. An isolate is considered resistant if either the phenotypic susceptibility testing indicates such resistance or the molecular testing detects a mutation associated with resistance.

The Chi-square test or Fisher's exact test, as appropriate, were used to determine the significance of any observed differences. The Cochran-Armitage trend test was used to calculate the significance of time trends. An associated *p*-value of ≤0.05 was used to assess whether a difference or trend was significant.

Molecular typing

Analysis of molecular typing data was only undertaken for culture-positive TB cases infected with *M*. *tuberculosis*. A case was categorised as having a non-unique molecular type if the combination of their MIRU 12 and MIRU 24 typing results matched at least one other case in the national database. If there was no matching strain type in the national database, the case was considered to have a unique strain.

QUALITY OF SURVEILLANCE DATA

The level of completeness of data recorded in EpiSurv for key TB surveillance variables from 2011 to 2015 is shown in Table 1.

For most variables the level of completeness was more or less stable over the 5 year period, but there were two notable exceptions. The completeness of the extra-pulmonary involvement variable improved to 99% or above following changes to this section of the case report form during 2012. Completion of risk factor information for the variables exposure in a healthcare setting and current or recent residence in an institution has gradually improved over the 5 years (80% to 92% and 82% to 95%, respectively).

Variables with consistently high levels of data completeness (≥95%) were the demographic variables (age, sex, ethnicity and geocoding accuracy), basis of discovery, pulmonary disease and the risk factor relating to being not born in New Zealand. The completeness of data associated with the treatment variables was also high (≥97%) across the 4 years analysed (2011–2014).

The date of onset of illness variable had the lowest levels of completeness, ranging from 60% to 78%. However, this is partly explained by the nature of the disease as some cases are asymptomatic.

Table 1. Percentage of data completeness for tuberculosis notifications (new case) by variable and year, 2011–2015

Variable	2011	2012	2013	2014	2015
Basis of diagnosis					
Basis of discovery	97	100	97	94	100
Laboratory confirmation	89	97	98	100	100
Demographic details					
Age	100	100	100	100	100
Sex	100	100	100	100	100
Ethnicity	97	99	99	98	100
Geocoding accuracy [a]	95	96	95	97	98
Clinical course and outcomes					
Onset date	61	60	71	72	78
Hospitalisation status	99	99	99	99	99
Survival status	100	98	98	99	100
Protective and risk factors					
BCG vaccination [b]	100	100	100	100	100
Has immunosuppressive illness	94	95	92	97	98
On immunosuppressive medication	94	95	93	97	98
Contact with confirmed case of tuberculosis	79	82	82	87	85
Case born outside New Zealand	100	100	100	100	100
Date of arrival [c]	74	89	78	80	88
Current/recent residence with person not born in New Zealand	91	91	90	92	90
Exposure in a healthcare setting	80	84	87	92	89
Current/recent residence in an institution	82	87	89	95	91
Clinical characteristics					
Pulmonary disease	97	100	100	99	99
Extra-pulmonary involvement	87	99	100	100	98
Treatment [d]					
Date treatment started	97	100	100	100	99
Treatment outcome [e]	100	99	100	99	-
Use of directly observed therapy (DOT) [d]	100	100	98	100	-

[a] Geocoding accuracy is based on exact and nearest match to LINZ addresses.

[b] Cases in the <5 years age group only.

[c] Cases born outside New Zealand only.

[d] Cases reported as having received treatment only.

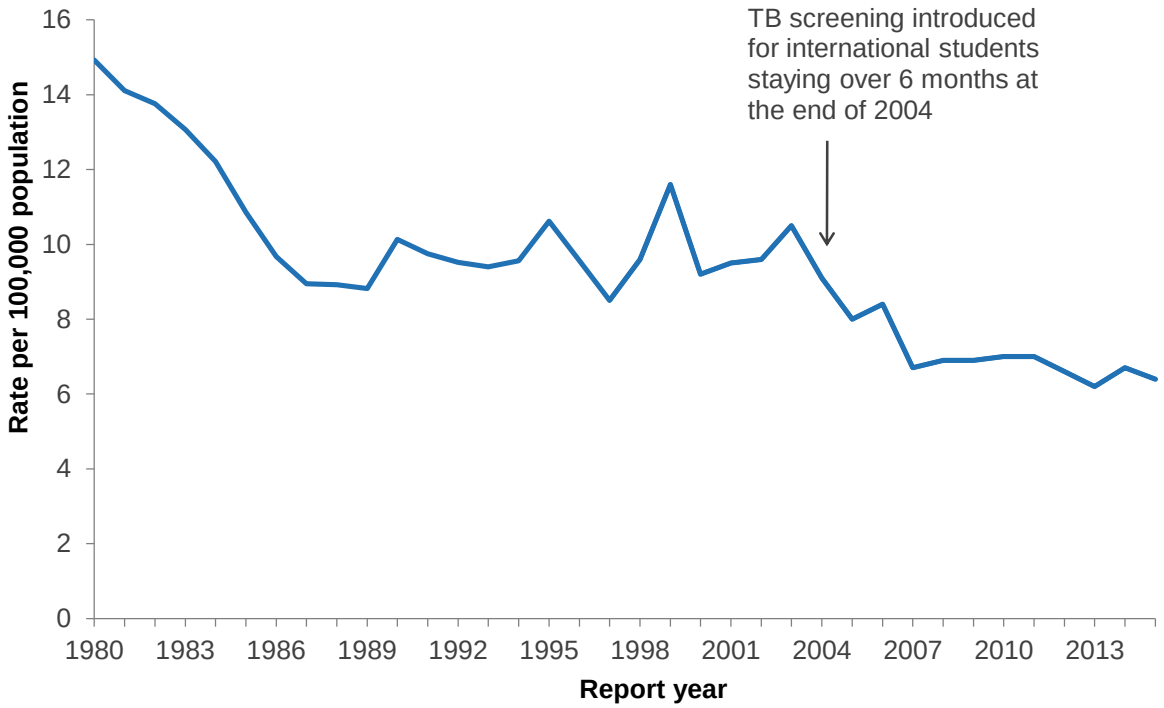
[e] Data is only reported for 2011−2014 due to length of time taken for TB treatment to be completed.

NOTIFICATIONS

There were 294 cases of TB disease notified in 2015, including 286 (97.3%) new cases. The 2015 TB disease notification rate was 6.4 per 100,000 population, a slight decrease from the rate recorded in 2014 (6.7 per 100,000). A high proportion of TB cases (88.8%, 261/294) were laboratory confirmed.

Trends in TB disease rates since 1980 are shown in Figure 1. The TB disease notification rate in 2015 was the second lowest observed since 1980. The lowest rate was in 2013 (6.2 per 100,000). From 1980 to 1989 the rate decreased from 14.9 to 8.8 per 100,000; between 1990 and 2003 the rate remained between 8.5 and 11.6 per 100,000; there was a decrease between 2003 and 2007 to 6.7 per 100,000; followed by relatively stable rates over the last 9 years. On average, the TB notification rate declined by 1.6% per year between 1980 and 2015.

Figure 1. Tuberculosis disease notification rates by year, 1980−2015



Note: Census population data was used as the denominator to calculate rates before 1991 and the Statistics New Zealand mid-year population estimates were used from 1991 onwards.

TUBERCULOSIS DISEASE – NEW CASE

This section presents data for notifications of "tuberculosis disease – new case" only. These notifications will be referred to as new TB cases.

There were 286 new TB cases notified in 2015, giving a notification rate of 6.2 per 100,000 population. This is similar to the 2014 rate of 6.4 per 100,000 (289 new TB cases). Between 2011 and 2015, the notification rate showed a slight decrease from 6.8 to 6.2 per 100,000 (Table 12).

Basis of discovery and diagnosis

Information on the way TB was discovered was recorded for all 286 new TB cases. The majority (80%, 242/286) were diagnosed when the symptomatic case presented to a health practitioner (Table 2).

Between 2011 and 2015, the proportion of cases discovered by each method ranged from 71−85% for symptomatic case presented to health practitioner, 4−12% for immigrant/refugee screening, 4−9% for contact follow-up, and 2−11% for other means of discovery.

Table 2. Tuberculosis (new case) notification by basis of discovery, 2015

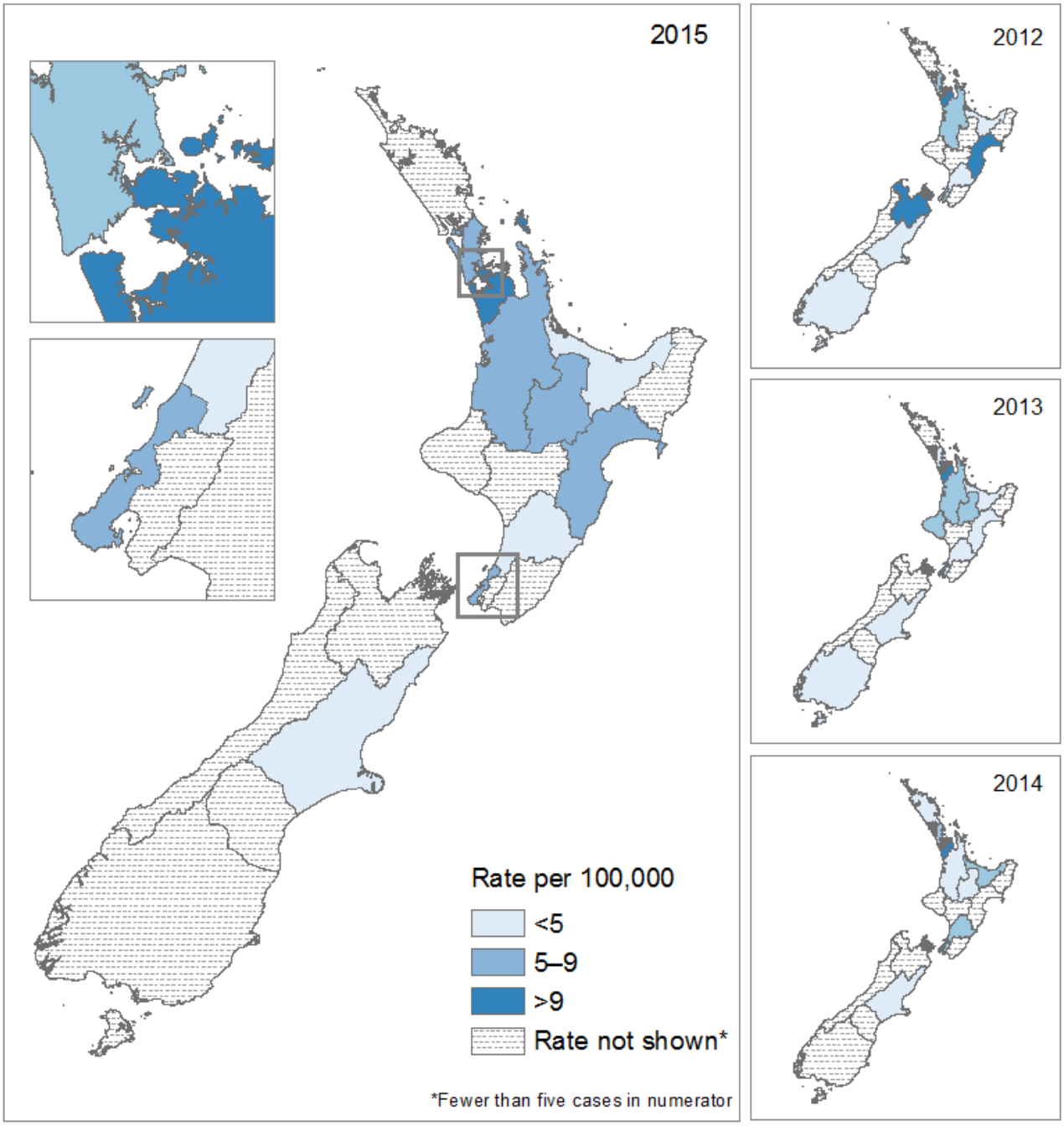
Basis of discovery	Cases	%
Symptomatic case presented to health practitioner	242	84.6
Immigrant/refugee screening	20	7.0
Contact follow-up	17	5.9
Other	7	2.4
Total	**286**	**100.0**

In 2015, 88.8% (254/286) new TB cases were laboratory confirmed. Among the 254 laboratory-confirmed cases, 93.7% (238 cases) were confirmed by isolation of *M. tuberculosis* (91.7%, 233 cases), *M. orygis* (1.2%, 3 cases), *M. bovis* (0.4%, 1 case) and *M. tuberculosis* complex (0.4%, 1 case) from a clinical specimen. A further 16 cases were confirmed by the following methods; 2.0% (5 cases) by demonstration of acid-fast bacilli in a clinical specimen, 2.0% (5 cases) by demonstration of *M. tuberculosis* nucleic acid directly from specimens and 2.4% (6 cases) by histology strongly suggestive of TB.

Notifications by District Health Board

New TB case notification rates by district health board (DHB) for 2012 to 2015 are shown in Figure 2. The highest notification rates in 2015 were recorded for Auckland (12.7 per 100,000, 62 cases), followed by Counties Manukau (12.3 per 100,000, 64 cases) and Capital & Coast (7.0 per 100,000, 21 cases) DHBs (Table 12).

Figure 2. Tuberculosis (new case) notification rates by district health board and year, 2012–2015



Notifications by age and sex

Table 3 shows that TB notification rates were higher among adults than children (<15 years). This trend is consistent over the last 5 years (Table 12). The highest notification rate for new TB cases in 2015 was the 15–39 years age group (9.5 per 100,000, 145 cases), followed by the ≥60 years (6.7 per 100,000, 62 cases) and the 40–59 years (5.7 per 100,000, 70 cases) age groups (Table 3).

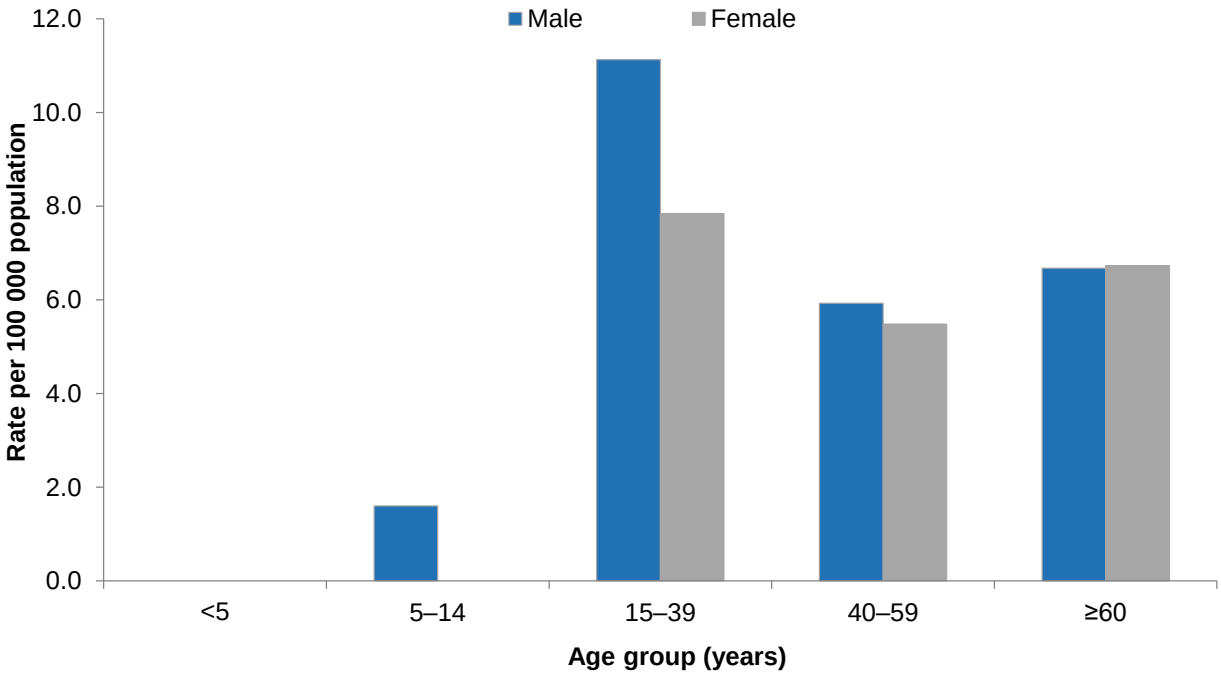
Table 3. Numbers and rates of tuberculosis notifications (new case) by age group and sex, 2015

Age group (years)	Male		Female		Total	
	Cases	Rate[a]	Cases	Rate[a]	Cases	Rate[a]
<5	1	-	2	-	3	-
5–14	5	1.6	1	-	6	1.0
15–39	85	11.1	60	7.8	145	9.5
40–59	35	5.9	35	5.5	70	5.7
≥60	29	6.7	33	6.7	62	6.7
Total	**155**	**6.9**	**131**	**5.6**	**286**	**6.2**

[a] Rate per 100,000 based on 2015 mid-year population estimates; not shown for counts less than five cases.

The notification rate for males (6.9 per 100,000, 155 cases) was higher than the rate for females (5.6 per 100,000, 131 cases) (Figure 3). This has remained a consistent trend over the last 5 years (Table 12). The 15–39 years age group had the highest rate for both males (11.1 per 100,000) and females (7.8 per 100,000) (Figure 3, Table 3).

Figure 3. Notification rates of tuberculosis (new case) by age group and sex, 2015

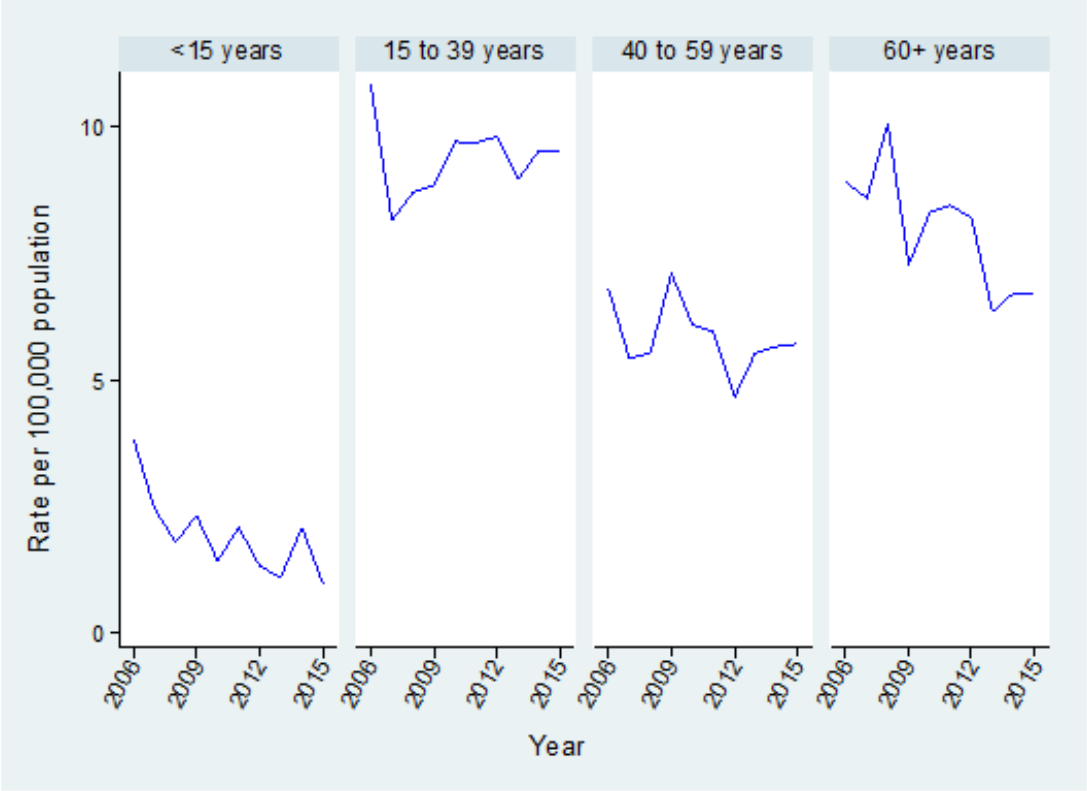


Note: Rates not calculated for males and females <5 years and females aged 5–14 years as numbers are too small.

Over the past 10 years (2006–2015), the average annual notification rate was highest in the 15–39 years age group (9.2 per 100,000), followed by the ≥60 years (7.9 per 100,000), 40–59 years (5.9 per 100,000) and the <15 years (2.0 per 100,000) age groups.

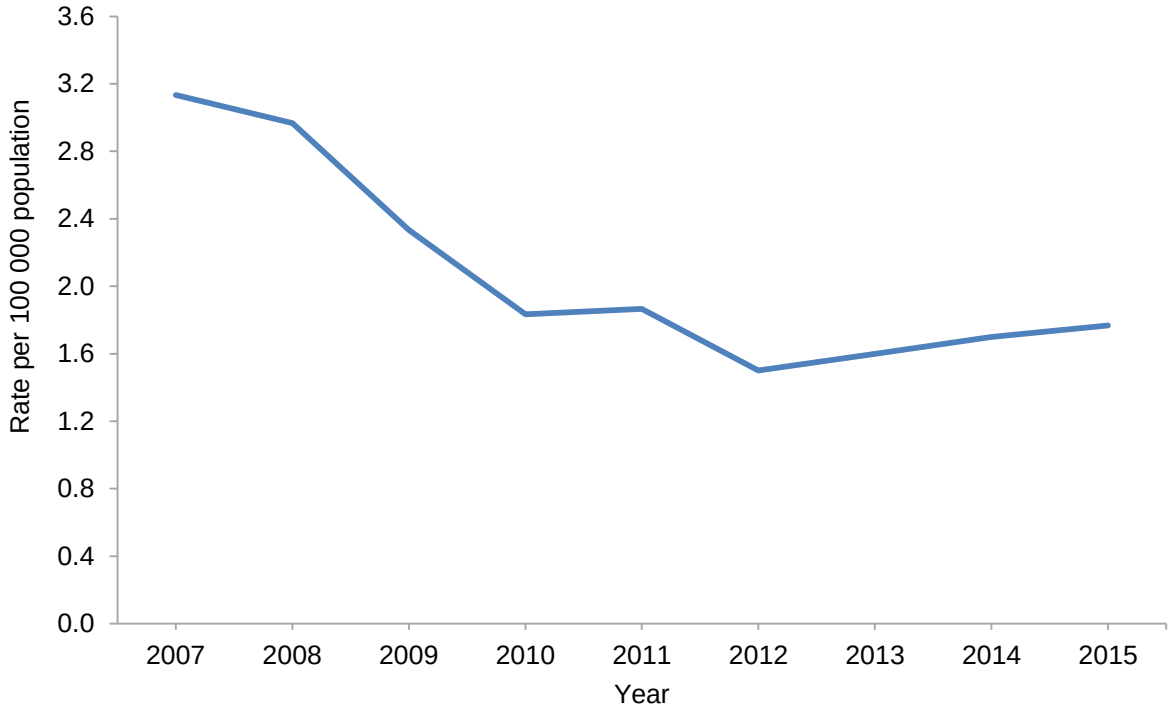
During this time (2006–2015), there was an overall decreasing trend in the notification rate for all age groups (Figure 4). The decrease was mainly observed in those aged <15 years (down 74.3% from 3.8 to 1.0 per 100,000), ≥60 years (down 24.5% from 8.9 to 6.7 per 100,000) and 40–59 years (down 16.0% from 6.8 to 5.7 per 100,000). However, in the 15–39 years age group, despite the overall decreasing trend (down 12.1% from 10.8 to 9.5 per 100,000) for this time period, the rate increased from 2007 to 2010 and since then has remained relatively stable.

Figure 4. Tuberculosis (new case) notification rates by age group and year, 2006–2015



In 2015, the rate of TB (new cases) in New Zealand-born children aged less than 15 years, an indirect indicator of recent transmission within the country, was 1.3 per 100,000 (8 cases). This was lower than the 2014 rate of 2.4 per 100,000 (15 cases). The low numbers (7–26 cases a year from 2004 to 2015) mean that the trend is better assessed by calculating a 3-year moving average annual rate. The 3-year moving average annual rate in 2007 was 3.1 per 100,000, following this it decreased to1.5 per 100,000 in 2012 and then increased slightly to 1.8 per 100,000 in 2015 (Figure 5).

Figure 5. Three-year moving average annual rate of tuberculosis (new case) in New Zealand-born children (<15 years old), 2007–2015

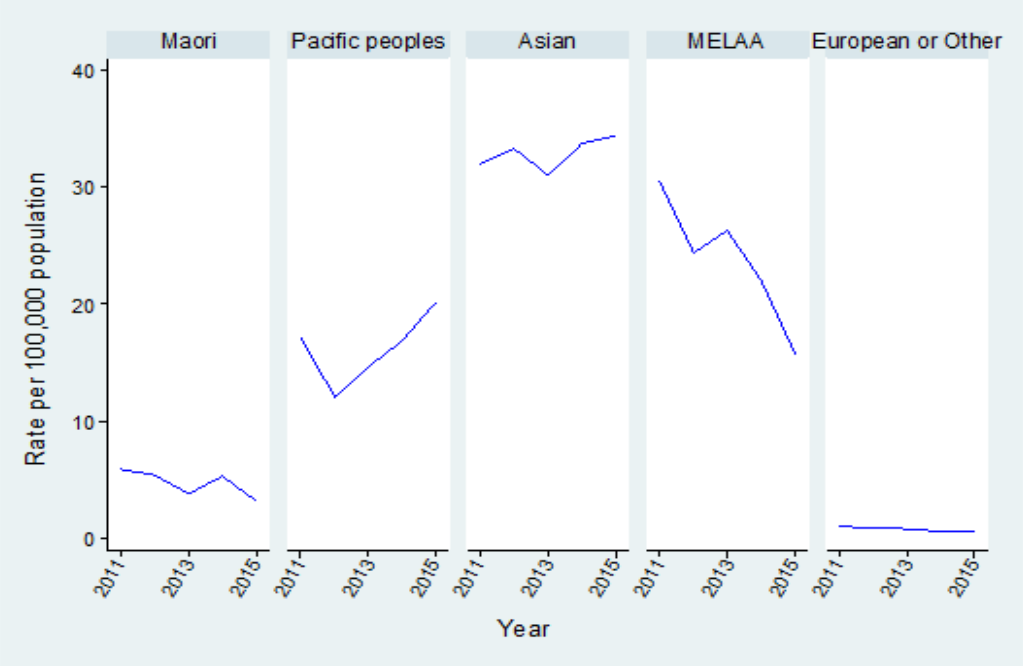


Ethnicity

Ethnicity was recorded for 99.7% (285/286) of the new TB cases notified in 2015. The Asian ethnic group had the highest notification rate (34.4 per 100,000, 181 cases), followed by Pacific peoples (20.2 per 100,000, 57 cases), MELAA (15.7 per 100,000, 8 cases), Māori (3.2 per 100,000, 22 cases) and European or Other (0.6 per 100,000, 17 cases) ethnic groups (Table 12). For the new TB cases born in New Zealand, 44.9% (22/49) were in the Māori ethnic group, 24.5% (12/49) in the Pacific peoples and 22.4% (11/49) in the European or Other ethnic groups. A further 8.2% (4/49) were in the Asian ethnic group.

Between 2011 and 2015 the Asian and MELAA ethnic groups had the highest rates apart from in 2015 where Pacific peoples had the second highest rate (Figure 6). However, the trend data for MELAA rates should be interpreted with caution as the number of cases each year were low (8–15 cases annually).

Figure 6. Tuberculosis (new case) notification rates by ethnic group and year, 2011–2015



MELAA: Middle Eastern/Latin American/African.

Hospitalisations

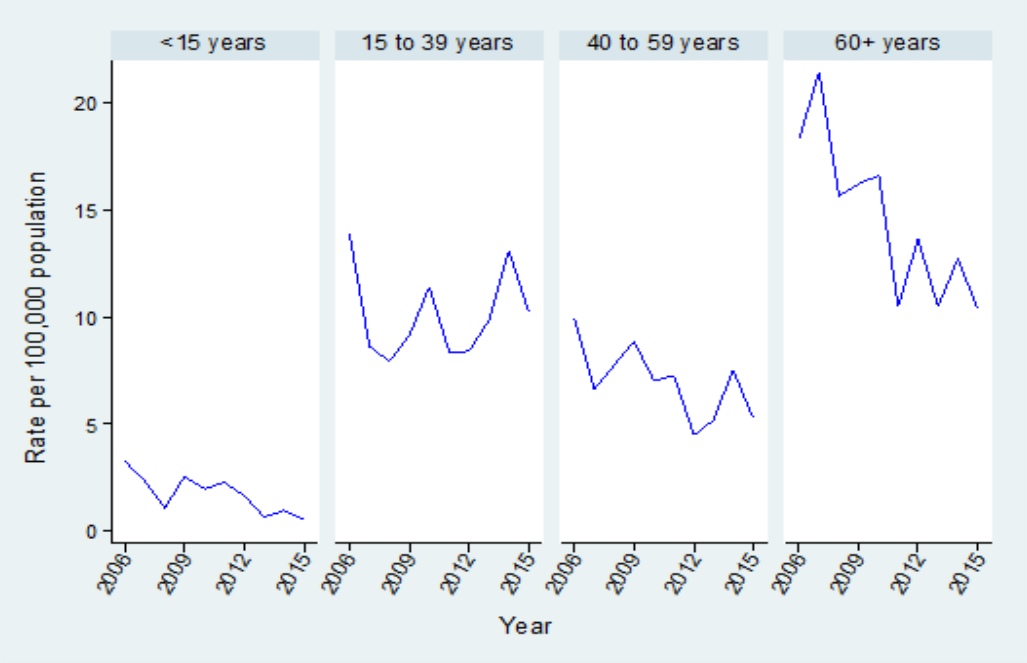
Hospitalisation status was complete for 99.3% (284/286) new TB cases notified to EpiSurv in 2015, of which 60.6% (172/284) were hospitalised. Over half of the cases in ≥60 years (68.9%), 40–59 years (60.0%) and 15–39 years (59.7%) were hospitalised (Table 4).

Table 4. Hospitalisation by age group, 2015

Age group (years)	Hospitalised		
	Yes	No	%
<5	1	2	33.3
5–14	1	5	16.7
15–39	86	58	59.7
40–59	42	28	60.0
≥60	42	19	68.9

Data from the Ministry of Health's National Minimum Dataset (NMDS) shows a decreasing trend in the TB hospitalisation rates for the <15 years and ≥60 years in the past 10 years (Figure 7). The trend was similar to the notification rates (Figure 4).

Figure 7. Hospitalisation rates for tuberculosis by age group and year, 2006–2015



Source: National Minimum Dataset, Ministry of Health.

Deaths

There were five deaths (where TB was the primary cause of death) among the 286 new TB cases notified in 2015. The cases were aged ≥60 years (4 cases) and 40–59 years (1 case) age groups. In the last 10 years (2006−2015), 44 deaths were reported among the notified new TB cases, giving a mortality rate of 1.5%. The majority (97.7%, 43/44) of deaths were in cases aged ≥20 years with one death reported in a child aged <5 years in 2014.

Between 2006 and 2013 TB was recorded in the Ministry of Health's Mortality Collections dataset as the underlying cause of death in 58 cases. During this period 4–11 deaths were recorded each year, all of whom were aged ≥20 years. The majority of cases (93.1%, 54 cases) were aged ≥50 years.

Protective factors

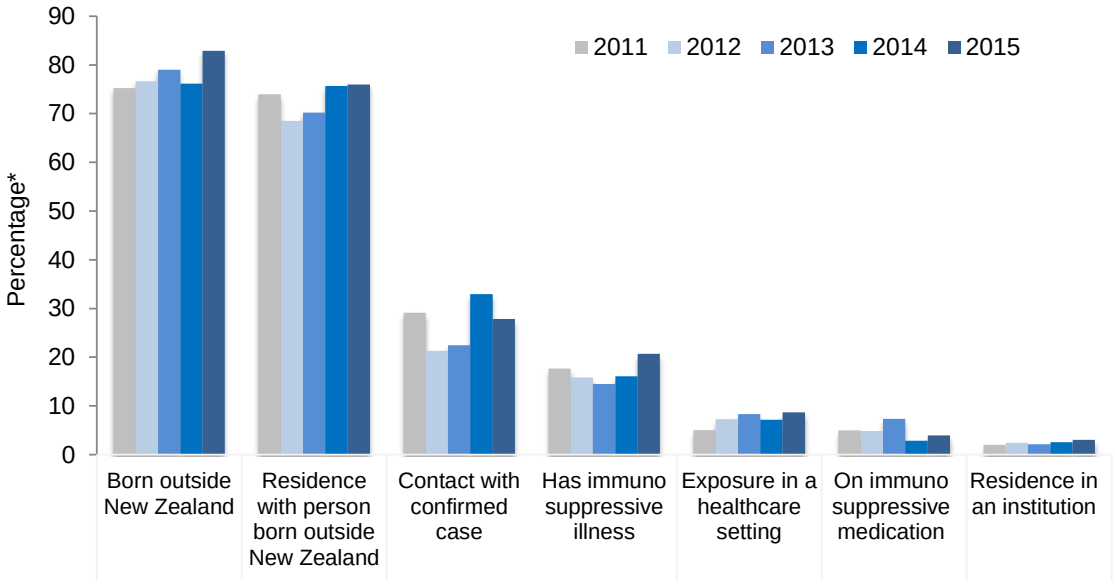
Immunisation of neonates with the Bacillus Calmette-Guérin (BCG) vaccine was introduced in New Zealand in 1976. As New Zealand is a low endemicity country, vaccination is recommended to neonates at increased risk of exposure to TB and is primarily given to protect young children from developing severe disease, particularly miliary TB and tuberculous meningitis. However, there has been an ongoing global shortage of BCG vaccine since 2015 which has led to postponement of vaccination clinics. [7]

In 2015, three cases of TB in the <5 years, all cases were born in New Zealand. Two of the cases had pulmonary disease and one had miliary TB. None of the cases were reported to have received BCG vaccine. There was insufficient information provided to know whether these children were eligible for the high risk vaccination programme.

Risk factors

The percentage of cases with available information for the various risk factors ranged from 79.0% to 100% over the last 5 years. In 2015, the most common risk factors reported by new TB cases were being not born in New Zealand (82.9%) and current/recent residence with person(s) not born in New Zealand (76.0%) (Table 5, Figure 8).

Figure 8. Percentage of tuberculosis (new case) notifications reporting exposure to risk factors by year, 2011–2015



*Number of cases with the factor divided by the total number of cases for which the response is known, for the year.

Table 5. Risk factors reported for tuberculosis (new case) notifications, 2015

Risk factor	Cases[a]	Total[b]	%
Born outside New Zealand	237	286	82.9
Current/recent residence with person born outside New Zealand	196	258	76.0
Contact with confirmed case	68	244	27.9
Has immunosuppressive illness	58	280	20.7
Exposure in a healthcare setting	22	254	8.7
On immunosuppressive medication	11	280	3.9
Current/recent residence in an institution	8	261	3.1

[a] Number of cases with 'yes' recorded for the risk factor.

[b] Number of cases for which information was recorded for the risk factor.

*Cases can have multiple risk factors.

Cases born in the Southern and Central Asia region had the highest notification rate in 2015 (125.2 per 100,000, 108 cases), followed by the South-East Asia (45.6 per 100,000, 40 cases) and Pacific Island (33.7 per 100,000, 51 cases) regions (Table 6).

More than 90% (99/108) of the cases born in the Southern and Central Asia region were born in India. The most commonly reported country of birth for cases born in South-East Asia was the Philippines (50.0%, 20/40).

Table 6. Tuberculosis notifications (new case) by region of birth, 2015

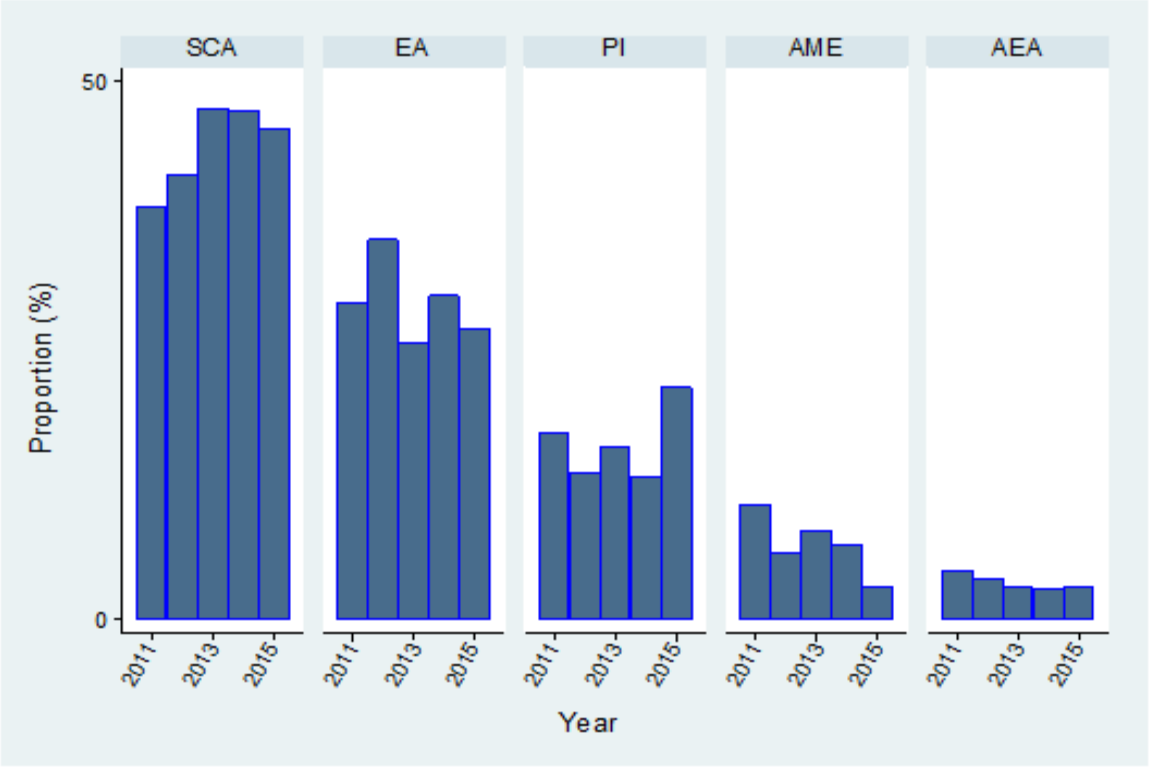
Region of birth	Cases	Rate[a]
Born in New Zealand	**49**	**1.6**
Born outside New Zealand	**237**	**18.7**
Australia	0	-
Pacific Islands	51	33.7
North Africa and the Middle East	0	-
Sub-Saharan Africa	7	9.7
North-East Asia	24	16.9
South-East Asia	40	45.6
Southern and Central Asia	108	125.2
Europe	5	0.8
The Americas	2	4.5
Total	**286**	

[a] Rate per 100,000 population. Population data used for the denominator was derived from the 2013 census usually resident population count by birthplace, published by Statistics New Zealand.

Among new TB cases who were not born in New Zealand, there was an increase between 2011 and 2015 in the proportion of cases born in the Southern and Central Asia region (from 38.2% to 45.6%) and in the Pacific Islands (from 13.2% in 2014 to 21.5%) (Figure 9).

The trend is decreasing for those born in other regions.

Figure 9. Percentage of tuberculosis (new case) notifications born outside New Zealand by birth region and year, 2011−2015



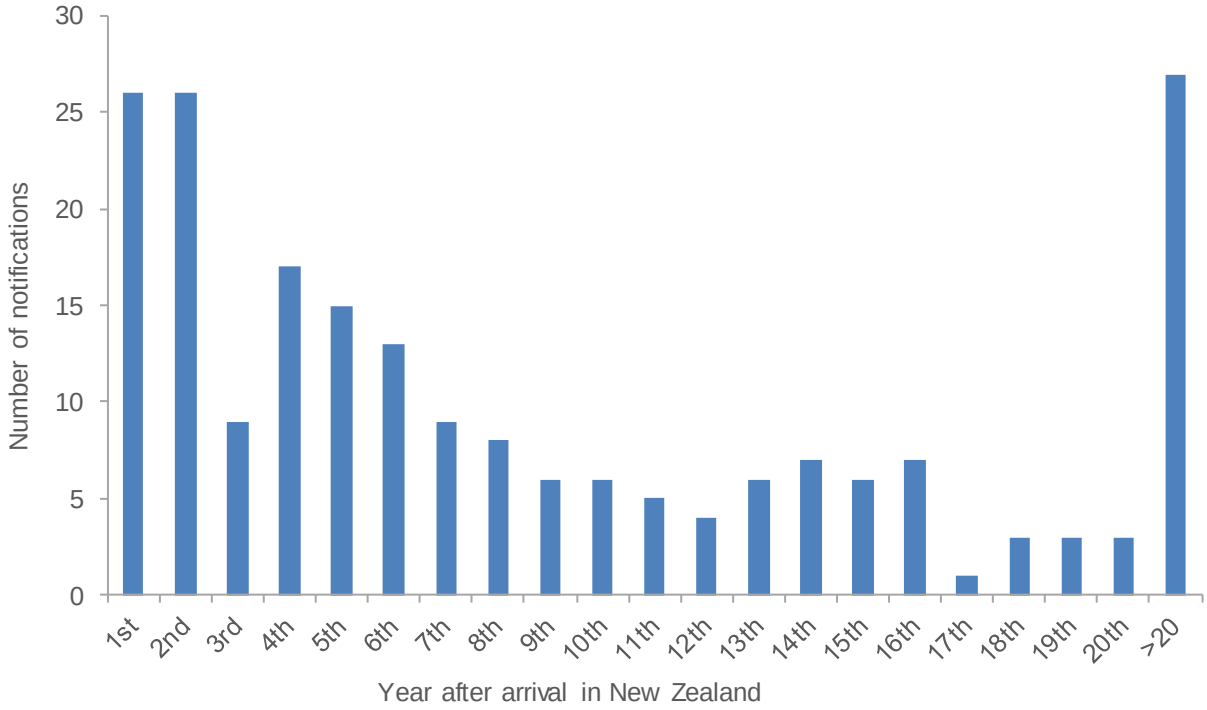
SCA – Southern and Central Asia
EA – East Asia (includes North-East and South-East Asia).
PI – Pacific Islands
AME – Africa and the Middle East
AEA – Australia, Europe and the Americas
* Number of cases born in a region divided by the total number of cases born outside New Zealand, and for which the country of birth is known, for the year.

Years since arrival in New Zealand

The date of arrival in New Zealand was recorded for 87.3% (207/237) new TB cases in 2015 who were not born in New Zealand. Of these, the time between the date of arrival in New Zealand and the TB notification date ranged from 0 to 57 years (mean 9.5 years and median 5 years). TB notification occurred in the first year of arrival in New Zealand for 12.6% (26/207) of cases not born in New Zealand, for 44.9% of cases within the first 5 years after arrival in New Zealand and for 51.2% within the first 6 years after arrival (Figure 10).

Between 2011 and 2015, the annual median time between arrival in New Zealand and the date of TB notification remained stable at 4 years. The annual mean time ranged between 7.2 and 9.5 years.

Figure 10. Tuberculosis new cases born outside New Zealand, notifications by year after arrival, 2015



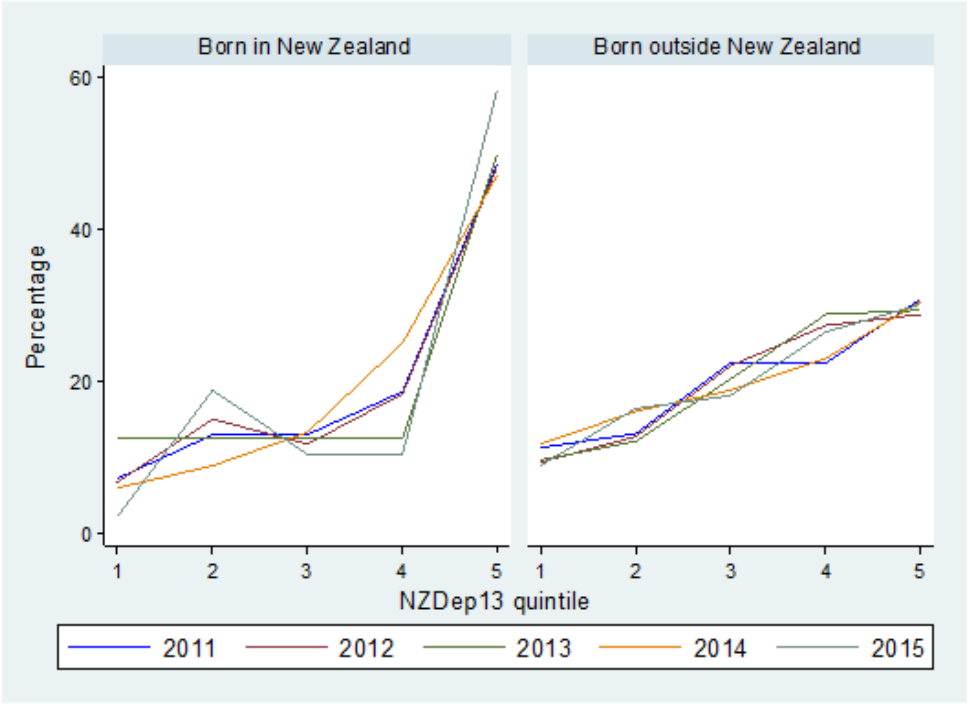
Note: The date of arrival was not recorded for 29 cases.

Socioeconomic deprivation

In 2015, 95.8% (274/286) of new TB cases could be assigned a 2013 New Zealand Socioeconomic Deprivation Index (NZDep13) score. Of the 274 cases, 161 (58.8%) resided in the most deprived areas (NZDep13 quintile 4 or 5).

Figure 11 shows the relationship between deprivation quintile and percentage of new TB cases in the last 5 years (2011–2015) by birth place (New Zealand/non-New Zealand). Of the 1350 cases with available information between 2011 and 2015, 294 (21.7%) cases were born in New Zealand. Higher numbers of new TB cases were observed among those from more socioeconomically deprived areas. This trend was observed each year and was most notable for cases born in New Zealand living in areas of highest deprivation (quintile 5).

Figure 11. Percentage of tuberculosis (new case) notifications by birth place (New Zealand/non-New Zealand), 2013 New Zealand Index of Deprivation and year, 2011−2015



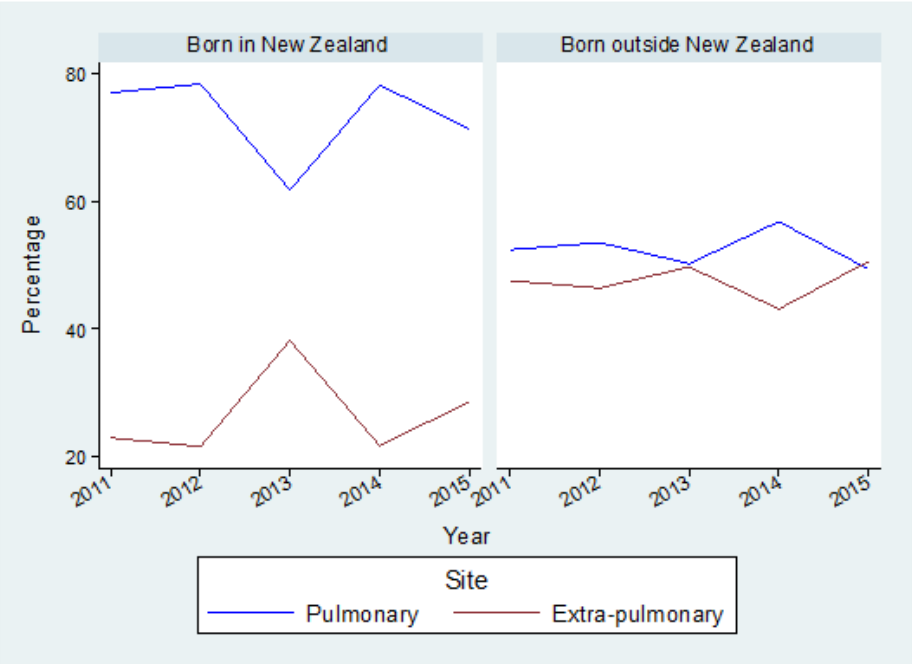
Site of infection

In 2015, 53.1% (152/286) of new TB cases had pulmonary disease, including 50 cases who also had extra-pulmonary involvement. A further 46.9% (134 cases) had only extra-pulmonary involvement.

Between 2011 and 2015, there were marked differences in the clinical characteristics of cases born in New Zealand compared with cases not born in New Zealand. Among cases born in New Zealand, 74.4% (232/312) were reported with pulmonary disease, increasing from 61.8% in 2013 to 71.4% in 2015, while 42.5% (133/313) were reported with solely extra-pulmonary disease.

In contrast, new TB cases not born in New Zealand had less pulmonary disease and more extra-pulmonary disease than those born in New Zealand, with the percentage being fairly stable at about 49–57% between 2011 and 2015 (Figure 12).

Figure 12. Comparison of pulmonary versus solely extra-pulmonary involvement for tuberculosis (new case) notifications by birth place (New Zealand/non-New Zealand) and year, 2011−2015



Note: Cases of pulmonary disease presented in this graph include cases with both pulmonary disease and extra-pulmonary involvement.

Of the 152 new TB cases in 2015 with pulmonary disease, 144 had available information on whether acid-fast bacilli were demonstrated in a direct smear of a clinical specimen. Of these, 55.6% (80/144) were smear positive, with sputum reported as the specimen site for 68.8% (55/80) of these cases.

Of the 184 cases with extra-pulmonary involvement in 2015, 46.7% (86/184) had lymph node (excluding abdominal) recorded as a site of infection (Table 13). Ten cases of central nervous system TB were reported in 2015, all aged ≥20 years. Four of these cases were reported as having tuberculous meningitis. Nine cases of miliary TB were reported, including one case aged <5 years and eight cases aged ≥15 years. All nine cases of miliary TB had information on whether they had an underlying immunosuppressive illness, three cases were reported as having underlying immunosuppressive illness (bone marrow transplant, diabetes, and sarcoidosis).

Between 2011 and 2015, the most common site of infection recorded for cases with extra-pulmonary involvement was lymph node (excluding abdominal) (44.5%), followed by pleural (15.9%) and intra-abdominal (excluding renal) (12.2%). There were 32 cases of central nervous system TB and 36 cases of miliary TB. There were three miliary TB cases aged <5 years; one an infant aged <1 year,

one aged 1 year, and another aged 3 years of whom none had received the BCG vaccine. There were no cases of tuberculous meningitis in the <5 years age group. Table 13 gives a breakdown of the new TB cases with extra-pulmonary involvement by site of infection and year.

HIV status

In 2015, 99.0% (283/286) of cases had information on whether an HIV test was done. Of these, 83.4% (236/283) were tested for HIV. In 2015, one new TB case was co-infected with HIV compared with two being co-infected with HIV in 2014.

Receipt of treatment

In 2015, 96.2% (275 /286) of new TB cases were reported to have received treatment. The interval between the onset of symptoms and start of treatment could be calculated for 78.5% (216/275). Of these, 49 (22.6%) started treatment within one month of the onset of symptoms and 122 (56.5%) started treatment between 1 and 3 months. The median interval to the start of treatment was 72 days from the onset of symptoms.

A treatment delay for patients with pulmonary TB represents a risk to public health from disease transmission. In 2015, 97.4% (148/152) of the 152 new TB cases with pulmonary disease, were reported to have received appropriate treatment. The interval between the onset of symptoms and the start of treatment could be calculated for 74.3% (110/148) of these cases. Among these, 41 (37.3%) started treatment within 1 month of the onset of symptoms and 38 (34.5%) started treatment between 1 and 3 months. The median interval to the start of treatment was 42 days from the onset of symptoms.

Treatment outcomes for cases notified in 2014

Due to the length of time taken for the treatment of TB to be completed, the data presented in this section is for the 289 new TB cases notified in 2014. Of these, 97.6% (282/289) were reported to have received appropriate treatment for TB.

The majority of these cases (88.3%, 249/282 cases) completed treatment to the satisfaction of the prescribing doctor. Of the 249 new TB cases who completed treatment to the satisfaction of the prescribing doctor, 53.4% (133/249) received directly observed therapy (DOT) during the intensive phase of their treatment. The proportion of cases who received DOT during the intensive phase of their treatment was higher in those not born in New Zealand (66.1%) than those born in New Zealand (33.8%). For cases with pulmonary disease, the proportion who received DOT intensive phase of their treatment was higher in cases not born in New Zealand (63.0%) than those born in New Zealand (37.0%).

Treatment for the remaining 11.7% (33/282) of cases ended earlier than planned for the following reasons: case transferred to overseas medical care (4.6%, 13 cases), case died (2.5%, 7 cases), case went overseas (1.4%, 4 cases), treatment was stopped because of adverse effects (1.1%, 3 cases), case refused to complete treatment (0.7%, 2 cases), and treatment stopped due to pregnancy (0.4%, 1 case). The remaining three cases (1.0%) were still on treatment at the time of data extraction.

No treatment was received by 2.4% (7/289) of cases. Of these, four cases were not treated because they died before treatment was initiated and/or the diagnosis was a post-mortem finding, three cases had treatment reported as inappropriate (two cases were not treated as further investigation showed there was no evidence of active TB, and one case where a decision was made not to attempt TB treatment due to multiple failed appointments and concerns about compliance).

TUBERCULOSIS DISEASE – RELAPSES OR REACTIVATIONS

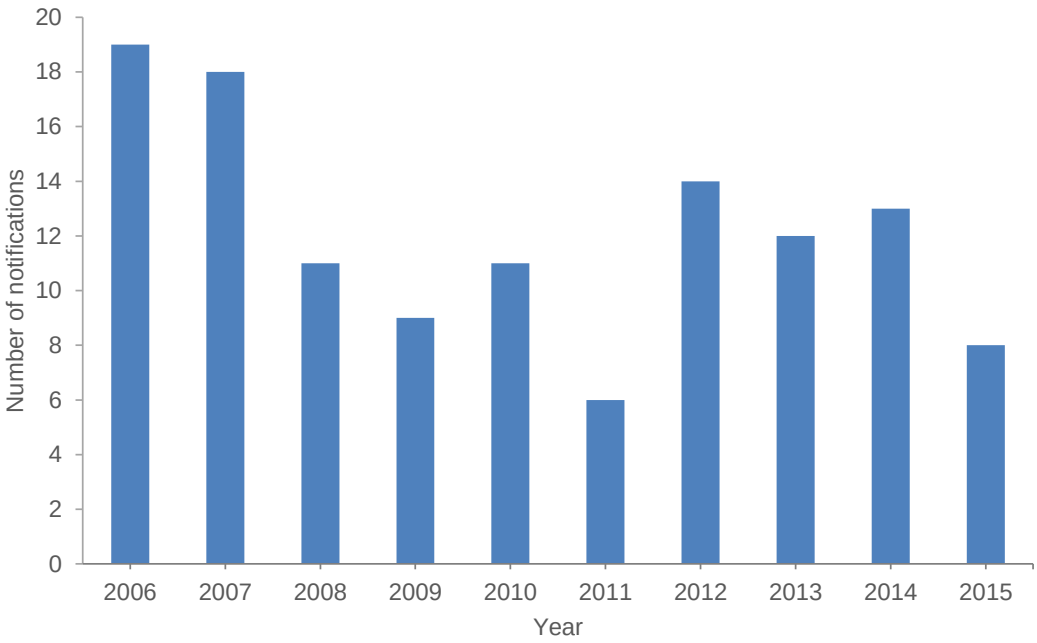
In 2015, eight TB relapse/reactivation cases were notified. This category of disease could also include cases of re-infection. The number of TB relapse/reactivation cases has remained low over the last 10 years (2006–2015) ranging from 6–19 cases a year (Figure 13).

In 2015, the TB relapse/reactivation cases were reported from the following five DHBs: Counties Manukau (3 cases), Waitemata (2 cases), Northland, Bay of Plenty and Canterbury (1 case each). The cases were aged in the 15–39 years (3 cases) and ≥60 years (5 cases) age groups. Relapse/reactivation cases were reported in the following ethnic groups: Asian (4 cases), Māori (3 cases), and European or Other (1 case).

Information about the place of birth, place of original diagnosis and whether the case had been previously treated for TB was recorded for seven of the relapse/reactivation cases. Three cases were both born and originally diagnosed with TB in New Zealand. Of the four cases born overseas, two were originally diagnosed in New Zealand and two were diagnosed overseas. Five of the cases had been previously treated for TB. Of the five cases originally diagnosed in New Zealand, two had previously received treatment for 12 and 13 months, respectively, for smear positive pulmonary TB. During this treatment one of these cases was reported to have received DOT during the intensive phase of treatment but the other case did not receive DOT. The duration of treatment was unknown for the remaining three cases originally diagnosed in New Zealand but all were now aged ≥60 years and their previous diagnoses had been decades ago. The two cases diagnosed overseas had previously received treatment for 3 and 9 months, respectively.

Hospitalisation status was recorded for all eight relapse/reactivation cases and four (50.0%) were hospitalised. One death was reported among reactivation cases. The case was of Māori ethnicity in the ≥60 years age group.

Figure 13. Tuberculosis (relapse/reactivation) notifications by year, 2006−2015



OUTBREAKS

In 2015, two TB outbreaks were reported:

- Auckland DHB (5 cases), the exposure occurred in a private home and a tertiary educational institute.
- Counties Manukau DHB (2 cases), the exposure occurred in a private home.

CULTURE CONFIRMATION, SPECIATION AND DRUG SUSCEPTIBILITY

Data presented in this section was collected from the four mycobacteriology laboratories in New Zealand.

CULTURE CONFIRMATION AND SPECIATION

In 2015, 238 new TB cases were culture positive. The mycobacterial species identified were *M. tuberculosis* (233 cases), *M. orygis* (3 cases), *M. bovis* (1 case), and the remaining isolate was only identified as *M. tuberculosis* complex. 88.2% (134/152) of the new TB cases with pulmonary disease were culture positive, comprising 133 cases identified as *M. tuberculosis* and one case as *M. bovis.*

Of the eight TB relapse/reactivation cases notified in 2015, six were culture positive and the isolates were identified as *M. tuberculosis* (5 cases) or *M. tuberculosis* complex (1 case).

Fewer than five cases of culture-positive TB due to *M. bovis* were reported each year between 2011 and 2015.

DRUG SUSCEPTIBILITY

Antimicrobial susceptibility data for the isolates from 243 (238 new cases and 5 relapses/reactivations) of the total 244 culture-positive TB cases in 2015 was available. The proportion of isolates resistant to the five antimicrobials routinely tested is shown in Table 7.

In addition to the five antimicrobials routinely tested, 50 isolates were tested for susceptibility to either moxifloxacin or ofloxacin. All 50 isolates were susceptible to the fluoroquinolone tested. A further isolate was tested for susceptibility to both moxifloxacin and ofloxacin and had discordant results: ofloxacin resistant but moxifloxacin susceptible.

Table 7. Resistance to each antimicrobial, by mycobacterial species, 2015

Antimicrobial	Resistant[a]							
	M. tuberculosis *n* = 238		*M. orygis* *n* = 3		*M. bovis* *n* = 1		All isolates *n* = 243[c]	
	No.	%	No.	%	No.	%	No.	%
Isoniazid (0.1 mg/L)	11	4.6	0	-	0	-	12	4.9
Isoniazid (0.4 mg/L)[b]	8	3.4	0	-	0	-	8	3.3
Rifampicin	2	0.8	0	-	0	-	2	0.8
Ethambutol	1	0.4	0	-	0	-	1	0.4
Pyrazinamide	0	-	0	-	1[d]	100	2	0.8
Streptomycin	16	6.7	0	-	0	-	16	6.6

[a] Includes resistance alone or in combination with other antimicrobials.

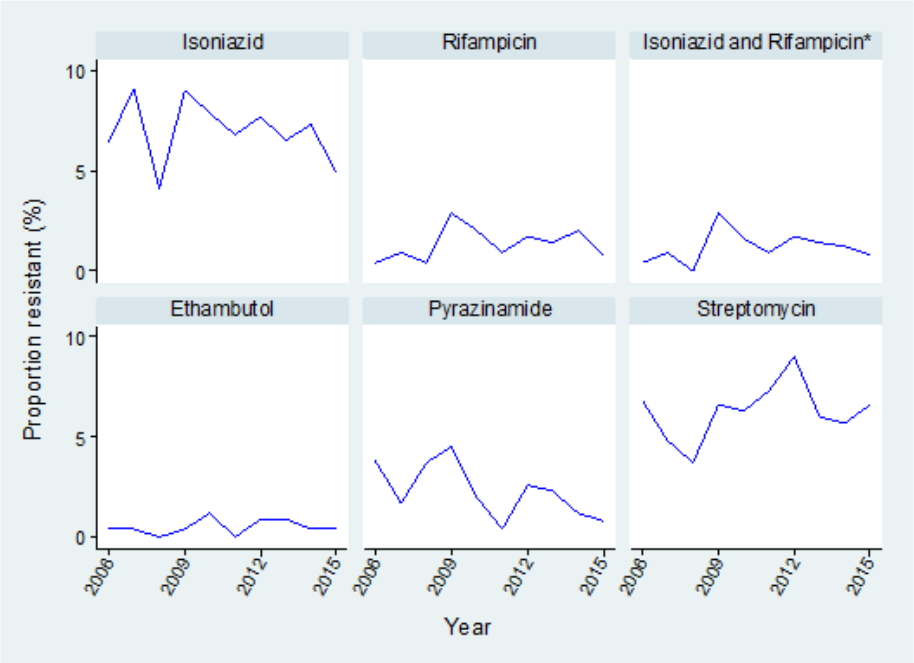
[b] All isolates resistant to isoniazid at the standard breakpoint concentration of 0.1 mg/L were also tested at the higher concentration of 0.4 mg/L.

[c] This total of 243 isolates includes data for one isolate identified only as *M. tuberculosis* complex which was resistant to isoniazid at 0.1 mg/L only and pyrazinamide.

[d] *M. bovis* is intrinsically resistant to pyrazinamide.

In the 10 years from 2006 to 2015, there has been a significant trend (*p* 0.009) of decreasing pyrazinamide resistance, but no significant changes in resistance to isoniazid, rifampicin, ethambutol or streptomycin have been observed (Figure 14).

Figure 14. Antimicrobial resistance among tuberculosis isolates by antimicrobial and year, 2006−2015



*Isoniazid and rifampicin resistant isolates are defined as multidrug-resistant tuberculosis (MDR-TB).

In 2015, 89.7% (218/243) of the isolates were fully susceptible to all five routinely tested antimicrobials. There were two (0.8%) cases of multidrug-resistant tuberculosis (MDR-TB, defined as resistance to at least isoniazid and rifampicin) (Table 8).

During the last 10 years (2006–2015) there have been a total of 28 cases of MDR-TB – an average annual rate of 1.2% among culture-positive TB cases. MDR-TB isolates are tested for susceptibility to an extended range of antibiotics to detect extensively drug-resistant tuberculosis (XDR-TB, defined as MDR-TB with additional resistance to any fluoroquinolone and at least one of the following second-line injectable drugs: amikacin, capreomycin or kanamycin). Only one case (in 2010) of XDR-TB has been identified in New Zealand.

Table 8. Distribution of antimicrobial resistance patterns among tuberculosis isolates, 2015

	Resistance pattern[a]	% (No.) of isolates with each pattern	
Fully susceptible		**89.7**	**(218)**
Resistant to 1 agent		**8.2**	**(20)**
	S	4.9	(12)
	H	2.9	(7)
	Z[b]	0.4	(1)
Resistant to 2 agents		**1.2**	**(3)**
	HS	0.8	(2)
	HZ	0.4	(1)
Resistant to 3 agents		**0.4**	**(1)**
	HRS[c]	0.4	(1)
Resistant to 4 agents		**0.4**	**(1)**
	HRES[c]	0.4	(1)

[a] H, isoniazid resistance at the standard concentration of 0.1 mg/L; R, rifampicin; E, ethambutol; Z, pyrazinamide; S, streptomycin.

[b] The isolate with this resistance pattern was the one *M. bovis* isolate.

[c] MDR-TB, multidrug-resistant tuberculosis, that is, resistant to at least isoniazid and rifampicin.

Table 9 compares antimicrobial resistance among isolates from cases born in New Zealand and cases born overseas. Resistance to all antimicrobials was higher, although not significantly so, among isolates from cases born overseas than among isolates from New Zealand-born cases.

Both MDR-TB cases identified in 2015 were born overseas. All but two of the 28 MDR-TB cases that have occurred in the last 10 years were born overseas and assumed to have acquired MDR-TB overseas. The majority (23, 88.5%) of the 26 MDR-TB cases assumed to have acquired MDR-TB overseas were born in an Asian country.

Table 9. Antimicrobial resistance among isolates from tuberculosis cases by place of birth, 2015

	Born in New Zealand (*n* = 36)		Born overseas (*n* = 207)		*p*-value[a]
	No.	%	No.	%	
Fully susceptible					
	35	97.2	183	88.4	0.141
Resistant to:[b]					
Isoniazid[c]	1	2.8	11	5.3	1.000
Rifampicin	0	-	2	1.0	1.000
Ethambutol	0	-	1	0.5	1.000
Pyrazinamide	0	-	2	1.0	1.000
Streptomycin	0	-	16	7.7	0.139
MDR-TB[d]					
	0	-	2	1.0	1.000

[a] Rates compared by the Chi-square test or Fisher's Exact test, as appropriate.

[b] Includes resistance alone or in combination with other antimicrobials.

[c] Isoniazid resistance at the standard concentration of 0.1 mg/L.

[d] Multidrug-resistant tuberculosis, that is, resistant to at least isoniazid and rifampicin.

Isoniazid and streptomycin resistance was most frequent among isolates from cases of Asian ethnicity (Table 10). One of the two MDR-TB cases was of Asian ethnicity and the other belonged to the Pacific peoples ethnic group.

Table 10. Antimicrobial resistance among isolates from tuberculosis cases by ethnic group, 2015

	Māori[a] (*n* = 18)		Pacific peoples (*n* = 54)		Asian (*n* = 153)		MELAA (*n* = 8)		European or Other (*n* = 9)		Unknown (*n* = 1)	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Fully susceptible												
	17	94.4	49	90.7	136	88.9	6	75.0	9	100	1	100
Resistant to:[b]												
Isoniazid[c]	1	5.6	1	1.9	9	5.9	1	12.5	0	-	0	-
Rifampicin	0	-	1	1.9	1	0.7	0	-	0	-	0	-
Ethambutol	0	-	0	-	1	0.7	0	-	0	-	0	-
Pyrazinamide	0	-	1	1.9	0	-	1	12.5	0	-	0	-
Streptomycin	0	-	4	7.4	11	7.2	1	12.5	0	-	0	-
MDR-TB[d]												
	0	-	1	1.9	1	0.7	0	-	0	-	0	-

[a] Ethnic groups were prioritised in the following order: Māori, Pacific peoples, Asian, Middle Eastern/Latin American/African (MELAA), European or Other ethnicity (including New Zealander).

[b] Includes resistance alone or in combination with other antimicrobials.

[c] Isoniazid resistance at the standard concentration of 0.1 mg/L.

[d] Multidrug-resistant tuberculosis, that is, resistant to at least isoniazid and rifampicin.

In 2015, 2.5% (6/244) of the culture-positive cases were reported to be TB relapses/reactivations. This category of disease could also include cases of re-infection. Because the number of cases notified as TB relapses/reactivations in any one year is small, the following analysis of drug resistance among relapses/reactivations is for the 5 years from 2011 to 2015. During this period, 3.5% (41/1172) of the culture-positive cases were reported to be relapses/reactivations. Information about previous treatment was recorded for 33 of the 41 relapses/reactivations cases and 32 were recorded as having received previous anti-tuberculosis drug treatment.

Antimicrobial resistance among new cases of TB, cases reported to be relapses/reactivations and cases who were reported to have been previously treated, is shown in Table 11. Compared with isolates from new cases, isolates from previously treated cases were significantly more resistant to isoniazid and rifampicin, and consequently also more likely to be MDR-TB.

Table 11. Antimicrobial resistance among isolates from tuberculosis cases (new cases, relapses/reactivations and previously treated cases), 2011–2015

	New cases (*n* = 1131)	Relapse/reactivation cases			
		All (*n* = 41)		Previously treated[a] (*n* = 32)	
	%	%	*p*-value[b]	%	*p*-value[b]
Fully susceptible					
	88.0	82.9	0.332	84.4	0.579
Resistant to:[c]					
Isoniazid[d]	6.4	14.6	0.050	15.6	0.055
Rifampicin	1.0	12.2	<0.001	12.5	<0.001
Ethambutol	0.5	0.0	1.000	0.0	1.000
Pyrazinamide	1.4	2.4	0.456	3.1	0.380
Streptomycin	6.8	9.8	0.522	9.4	0.479
MDR-TB[e]					
	0.8	12.2	<0.001	12.5	<0.001

[a] Information on previous treatment was reported for only 33 of the 41 relapse/reactivation cases, 32 of whom were recorded as being treated.

[b] Rate compared with that among new cases by the Chi-square test or Fisher's Exact test, as appropriate.

[c] Includes resistance alone or in combination with other antimicrobials.

[d] Isoniazid resistance at the standard concentration of 0.1 mg/L.

[e] Multidrug-resistant tuberculosis, that is, resistant to at least isoniazid and rifampicin.

MOLECULAR TYPING

TB molecular typing results were available for the 238 culture-positive new TB cases in 2015. The mycobacterial species identified were *M. tuberculosis* (233 cases), *M. orygis* (3 cases), and *M. bovis* (1 case). The remaining isolate was only identified as *M. tuberculosis* complex. Among the 238 new TB cases, 96 (40.3%) had non-unique molecular types and were in 41 separate molecular clusters. Three new clusters were identified in 2015 with two cases each. The remaining 142 cases (59.7%) had a unique strain type.

In the last 5 years (2011–2015), 1,131 new TB cases had TB molecular typing results, of which 439 (38.8%) had non-unique molecular types and were in 169 separate molecular clusters.

The median cluster size, based on cases in the last 5 years, was two cases (range 1-38)[ii] and 91.1% (154/169) of clusters had fewer than five cases. The remaining 15 clusters were distributed into the following cluster sizes: 5−9 cases (9), 10−19 cases (4) and 20 or more cases (2).

Figure 15 to Figure 20 show the proportion of non-unique molecular types in new TB cases for subgroups within selected variables between 2011 and 2015 compared with the mean proportion for each variable. Table 14 shows a detailed breakdown of non-unique and unique molecular types for new TB cases by age group, sex, ethnic group, DHB, region of birth, NZDep2013 quintiles and clinical manifestation.

There was a high proportion of cases with non-unique molecular types in cases aged <15 years (81.0%), but a lower proportion across all other age groups apart from the 40–59 years age group (40.6%) where the proportion was just above the mean. Proportions were similar to the mean in both sexes.

Pacific peoples (80.1%) and Māori (74.1%) ethnic groups also had a high proportion of cases with non-unique molecular types whereas the proportion was much lower in the MELAA (12.8%), Asian (24.3%) and European or Other (32.5%) ethnic groups.

Figure 15. Percentage of new tuberculosis cases that were non-unique molecular types by age group and sex

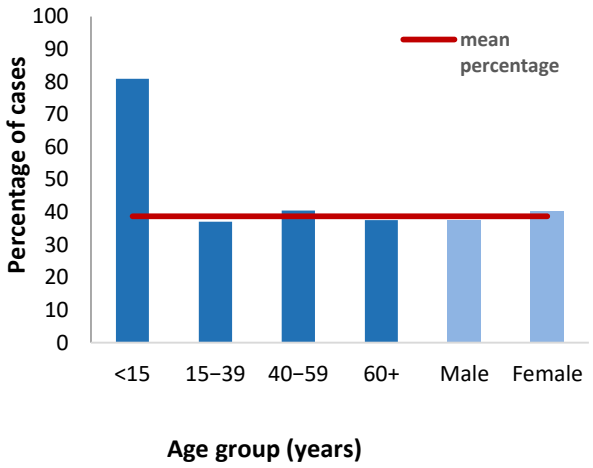
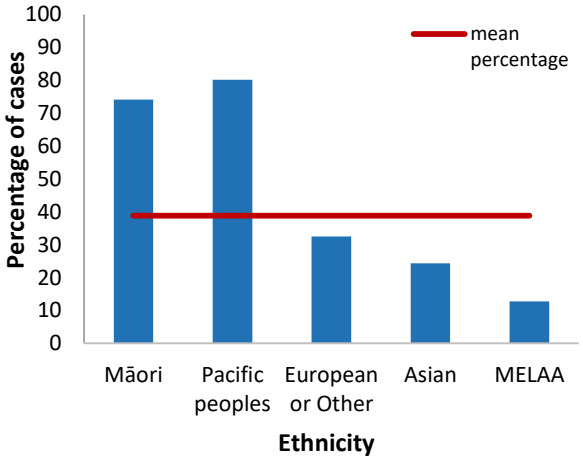


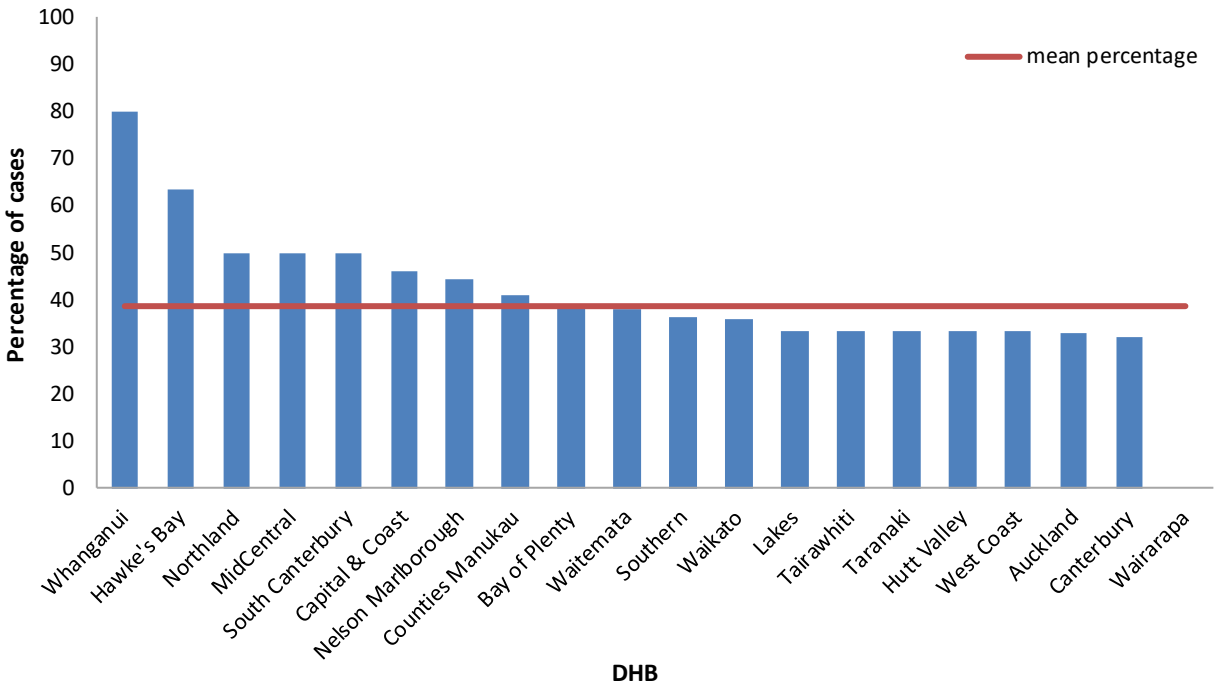
Figure 16. Percentage of new tuberculosis cases that were non-unique molecular types by ethnic group



[ii] A cluster can contain just one case when the other cases within that cluster were either not notified on EpiSurv or were notified prior to the last 5 years.

Whanganui (80.0%) and Hawke's Bay (63.6%) DHBs had the highest proportions of cases with non-unique molecular types, whereas, Canterbury (32.1%) and Auckland (33.1%) DHBs had the lowest proportions (Figure 17).

Figure 17. Percentage of new tuberculosis cases that were non-unique molecular types by DHB



Cases born in the Pacific Islands (72.1%) and New Zealand (61.4%) had a higher proportion of non-unique molecular types than the mean, whereas for other foreign-born cases the proportion was well below the mean (Figure 18).

There was a high proportion of cases with non-unique molecular types residing in NZDep13 quintile 5 (more socioeconomically deprived) areas (48.1%) (Figure 19).

Figure 18. Percentage of new tuberculosis cases that were non-unique molecular types by region of birth

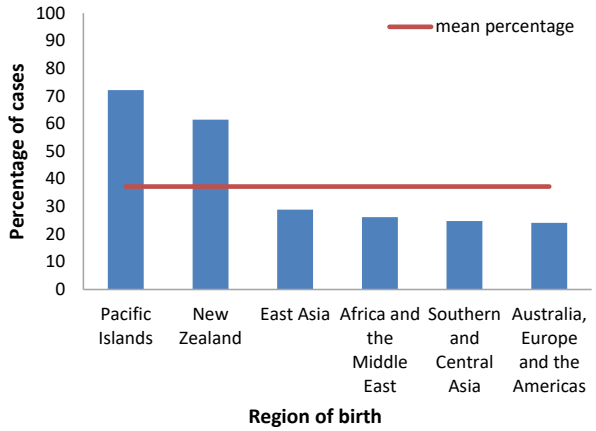
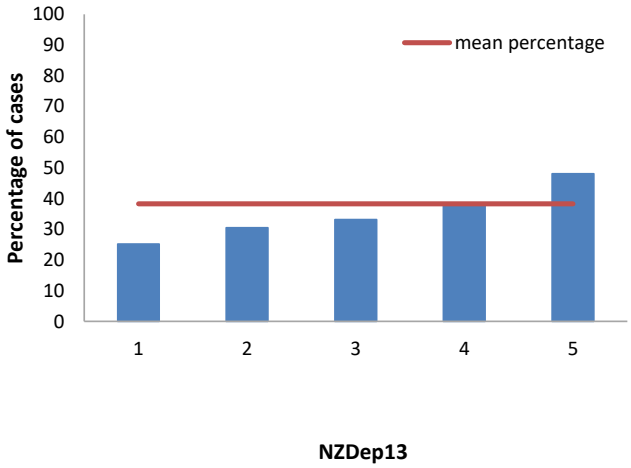
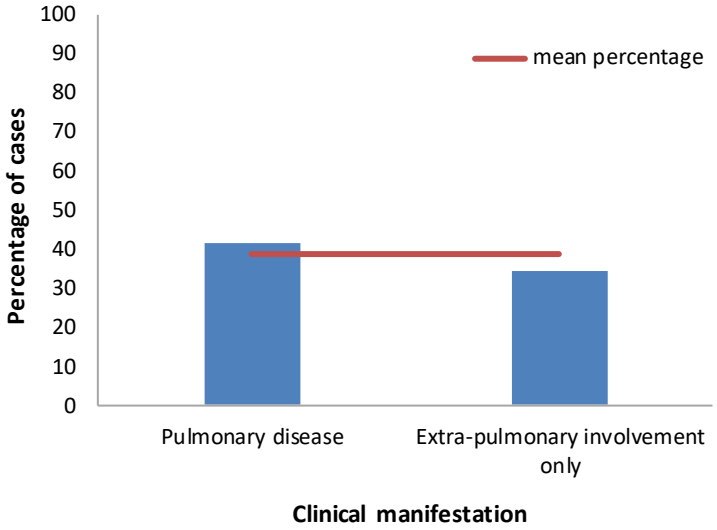


Figure 19. Percentage of new tuberculosis cases that were non-unique molecular types by deprivation index



New TB cases with pulmonary disease (41.6%) had a higher proportion of non-unique molecular types compared with cases that had extra-pulmonary involvement only (Figure 20).

Figure 20. Percentage of new tuberculosis cases that were non-unique molecular types by clinical manifestation



DISCUSSION

The incidence of TB in New Zealand (6.4 per 100,000 population in 2015) has remained fairly stable over the past 7 years. This rate is higher than the 2015 incidences reported in Australia (5.3 per 100,000), the United States (3.0 per 100,000) and Canada (4.6 per 100,000) [8-10], but lower than the 2015 incidence recorded in the United Kingdom (10.5 per 100,000) [11].

PLACE OF RESIDENCE AND ETHNICITY

The overall incidence rate masks substantial differences in the rates of TB in different areas of the country and between population subgroups.

Geographically Auckland, Counties Manukau, Capital & Coast, Lakes and Waitemata DHBs all had incidence rates above the national rate. Apart from Lakes DHB, these DHBs have large urban populations and the higher incidence may reflect the ethnic makeup of these communities, settlement patterns of migrants from high endemicity countries and housing issues such as overcrowding. This is similar to the distribution of cases noted in the United Kingdom where TB is concentrated in large urban areas. In 2015, 58.8% of TB cases resided in the most deprived areas of New Zealand (Quintiles 4 and 5), a slightly lower proportion than the 70% of cases residing in the 40% most deprived areas in the England in 2014 [12].

Among cases born in New Zealand the highest proportion of new TB cases were in the Māori ethnic group (44.9%), a decrease from the proportion of 51.5% reported in 2014. The incidence in the Māori ethnic group (3.2 per 100,000) was over five times higher than the incidence in the European or Other ethnic group (0.6 per 100,000), although this was lower than the incidence reported for Pacific peoples (20.2 per 100,000) and for people born overseas (18.7 per 100,000). In comparison, the 2014 incidence rate for Australian-born indigenous people (5.8 per 100,000) was six times higher than the rate for Australian-born non-indigenous people (0.9 per 100,000), but is still much lower than the rate in overseas-born people (19.1 per 100,000) [13]. In Canada the 2015 incidence rate for Canadian-born people was much higher among indigenous people (17.1 per 100,000 population) compared with non-indigenous people (0.6 per 100,000) and the indigenous rate was also higher than the rate in people born overseas (14.8 per 100,000)[10]. The pattern is somewhat different in the United States where the 2015 incidence rate is higher in indigenous people (6.1 per 100,000) compared with those of European ethnicity (0.6 per 100,000) but lower than the rate in people born overseas (15.1 per 100,000) [9].

COUNTRY OF BIRTH

During the past 5 years, 75–83% of TB cases notified were born outside of New Zealand, an increase from earlier periods (61.3% for 1995–1999 and 67.7% for 2000–2004) [14]. A similar pattern has been seen in Australia where the proportion of cases born outside the country was reported to have increased over 10 years, reaching a high of 90% in 2010 and was reported as 86% in 2014 [13]. The proportion of cases born outside New Zealand in 2015 (82.9%) is higher than that reported in England (72.5% in 2015), Canada (71% in 2015) and the United States (66.4% in 2015) [8, 9, 11].

Although the proportion of cases born overseas has been increasing in New Zealand, the incidence rate in people born overseas in 2015 was 18.7 per 100,000 which is lower than the rates reported for 1995–1999 (31.7 per 100,000) and 2000–2004 (32.3 per 100,000). This decrease may be due to changes in immigration screening practices, such as the introduction of screening for international students staying over 6 months at the end of 2004, as well as the impact of interventions to improve the control of TB transmission both within New Zealand and overseas. Although this rate is higher than the 15.1 per 100,000 reported for foreign-born people in the United States in 2015, the US

foreign-born rate excludes several high endemicity territories and countries such as the Federated States of Micronesia, Guam, the Northern Marianas and Palau [9].

Of the cases born outside New Zealand, the majority were born in South and Central Asia, followed by South East Asia, all high TB burden areas. The most frequently reported countries of birth, India, followed by the Philippines, are similar to the most common countries of birth for TB cases reported in 2014 by Australia (India, Vietnam, Philippines, China and Myanmar) [13]. However, this differs from the countries of birth most commonly reported for cases notified in England (India, Pakistan, Bangladesh and Somalia) [11]. This difference reflects differing immigration patterns but all the countries listed underscore the high risk of being born in country with high endemicity.

The time since arrival in New Zealand and notification date was recorded for 87.3% of new TB cases born overseas and showed a similar pattern to that seen in Australia but a higher proportion of cases were diagnosed within six years of arrival compared with the United Kingdom. Approximately 13% of cases born overseas were notified within the first year after arrival, approximately 45% within 5 years of arrival, and 51% within 6 years of arrival. Australia recorded this information for 97% of those born overseas in 2014 and reported that 43% of these cases were notified in the first 4 years after arrival [13]. In 2015, time from arrival until diagnosis was known for 94.3% of non-UK-born cases notified in England with 15.2% diagnosed within 2 years and 37.6% within 6 years of arrival [11].

CLINICAL PRESENTATION AND TREATMENT

Pulmonary disease was reported in 53.1% of new TB cases in 2015, a decrease from 61.9% of new TB cases in 2014. This is similar to the proportion reported in England (53.4% in 2014) but a lower proportion than most recently reported in Canada (66% in 2015), and Australia (63% in 2014 [8, 11, 13].

Of the three cases of TB in the <5 years age group in 2015, all cases were born in New Zealand. Two of the cases had pulmonary disease and one had miliary TB. None of the cases were reported to have received BCG vaccine and there was insufficient information provided to know whether these children were eligible for the high risk vaccination programme. Collection of information about eligibility in future years would be useful to assess whether high-risk children aged <5 years diagnosed with TB had missed out on vaccination.

Nearly all the TB cases notified in 2015 were “new disease” (97.3%), meaning there was no history of prior treatment. This is a slightly higher proportion than that reported from Australia (95%, 2014), England (93.3%, 2015) and Canada (92%, 2015) [8, 11, 13]. Information about previous disease was recorded for seven of the eight relapse/reactivation cases, five were diagnosed and treated in New Zealand, two for 12 and 13 months respectively for smear positive pulmonary disease. It is of concern that only one of these cases was reported to have received DOT and this only during the intensive stage of treatment. The other three cases treated in New Zealand were aged over 60 years and details on previous diagnoses and treatment were not available. The two cases previously diagnosed overseas reported they were treated for 3 and 6 months respectively. From the data available it is unclear whether these cases were genuine relapse or reinfection. However, it is of concern that isolates from previously treated cases over the past 5 years were significantly more resistant to isoniazid and rifampicin. This underscores the importance of ensuring adequate treatment is completed for all cases diagnosed in New Zealand, as well as early identification of relapse cases to prevent transmission of resistant organisms.

For cases notified in 2014, 88.2% were reported to have completed treatment, a similar proportion to Canada (85% of cases reported in 2014) and the United Kingdom (84.5% of drug sensitive cases reported in 2014 had completed treatment within 12 months) [8, 11]. These percentages are all lower than the 96% reported by Australia for cases diagnosed in 2013 [13]. However, the Australian percentage is not directly comparable as it is based only on cases considered "assessable", meaning that cases that had transferred out of Australia, died of other causes or were still under treatment were excluded from the analysis.

The proportion of cases notified in New Zealand in 2014 reported to have not completed treatment because they died (2.5%) is lower than the 8% of cases reported in 2014 in Canada that died before or during treatment and also lower than the 5.5% recorded in England for cases notified in 2014. However, the English outcomes only refer to drug-sensitive cases and therefore may not be directly comparable. Similarly, although the New Zealand rate is higher than the 1% mortality rate reported by Australia for cases diagnosed in 2013, this rate only refers to deaths due to TB in the cases considered to have assessable outcomes. There were another 3.3% of total cases in Australia that were reported to have died from other causes. All three countries have previously reported problems with the quality of the follow-up data with about 5% of cases lost to follow up for a similar variety of reasons [8, 11, 13].

DRUG SUSCEPTIBILITIES AND MDR-TB

Over the last 10 years (2006–2015), there has been a significant trend of decreasing pyrazinamide resistance, but no significant changes in resistance to isoniazid, rifampicin, ethambutol or streptomycin. However, the apparent decrease in pyrazinamide resistance may be due to changes in the laboratory methods used to detect pyrazinamide resistance rather than a real change in the prevalence of resistance (*Roberts Sally, Personal communication, 2014*).

The proportion of cases (both new disease and relapses/reactivations) with MDR-TB in 2015 (0.8%) was similar to the average proportion for the past 10 years (1.2%). This rate of MDR-TB is similar to that reported in the United States (1.1% for 2015) and England (1.3% for 2015), but lower than the 1.7% reported in Australia in 2014 [9, 11, 13]

Over the past 10 years, 92.8% (26/28) of MDR-TB cases were both born overseas, the majority in Asian countries, and assumed to have acquired their resistant organisms overseas. In England a high proportion (90.6%) of MDR-TB cases in 2015 were also reported to be born overseas, and the most common countries of birth for these cases were Lithuania and India [11]. For the United States, the proportion of MDR-TB cases that occurred in foreign-born persons has increased from 25% (103 of 407) in 1993 to 86.3% (63 of 73) in 2015 [9]. There was a similar pattern reported from Australia in 2014 with the majority of the MDR-TB cases reported as being born overseas [13].

From 2011–2015, 12.5% of New Zealand relapse/reactivation cases that had previously been treated for TB had MDR-TB, a much higher proportion than the 0.8% for cases with "new disease". This is higher than the 4.8% of MDR-TB in previously treated cases reported from the United Kingdom in 2015 [11].

TRANSMISSION AND CONTROL

Several indicators are used by Public Health England (PHE) to assess transmission in low endemicity countries such as the United Kingdom and New Zealand. For recent transmission the indicator used is the rate of TB in children <15 years of age born within the country [11]. The 2015 rate of TB in New Zealand-born children in the <15 years age group was 1.3 per 100,000, lower than the 2015 rate reported in England of 1.8 per 100,000 in children born in the United Kingdom but both are higher than the rate in non-indigenous Australian-born children <15 years of age in 2014 which was 0.8 per

100,000, but similar to the 2014 rate for indigenous Australian-born children (1.7 per 100,000) [11, 13]. However, as the rates recorded in New Zealand are based on low case numbers they tend to be quite unstable and three year moving average annual rate gives a better indication of trends in local transmission. This decreased from a rate of 3.1 per 100,000 calculated for 2007 and has been fairly stable since 2012 at about 1.7 per 100,000.

For ongoing transmission within a community, the indicator now used by PHE is to identify clustered cases (with indistinguishable MIRU-VNTR strain types) as these may reflect cases that are part of the same chain of transmission. However, it is also recognised that these may also reflect common endemic strains circulating either within the country or in overseas countries where cases acquired their infection. The proportion of cases in clusters, the number of new clusters formed each year and the number of cases within each cluster are all considered useful when assessing the frequency of recent transmission [11]. Between 2011 and 2015, 38.8% of strain typed TB cases in New Zealand were part of a cluster (91% of these clusters had fewer than five cases, median cluster size was two cases). This is lower than the 58.4% of strain-typed TB cases in England that were part of a cluster between 2010 and 2015 (75.1% of these clusters having fewer than five cases, median cluster size three cases) [11]. This suggests there may be a lower rate of community transmission of TB within New Zealand compared with England. However, it is pertinent that cases born in New Zealand or the Pacific Islands are more likely to be part of a cluster compared with the regions from where all other cases were born overseas.

These indicators suggest decreasing or low transmission of TB infection within New Zealand and support the premise that most cases of TB diagnosed in New Zealand result from infection acquired overseas. However, the proportion of cases born within New Zealand or the Pacific region that are part of a cluster indicates that there is a higher risk of transmission within the country from cases that were born in New Zealand or the Pacific. This suggests that as well as continuing with current strategies of early detection and treatment of TB disease and contact follow up to decrease the incidence of TB in New Zealand, consideration could also be given to identifying high risk groups for LTBI screening and treatment, as suggested in the WHO framework to eliminate TB in low incidence countries [15].

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APPENDIX

Table 12. Numbers and rates of tuberculosis (new case) notifications by age group, sex, ethnic group, district health board and year, 2011–2015

Category	2011		2012		2013		2014		2015	
	Cases	Rate[a]	Cases	Rate[a]	Cases	Rate[a]	Cases	Rate[a]	Cases	Rate[a]
Age group (years)										
<5	8	2.5	4	-	5	1.6	12	3.9	3	-
5–14	11	1.9	8	1.3	5	0.8	7	1.2	6	1.0
15–39	141	9.7	142	9.8	130	9.0	141	9.5	145	9.5
40–59	71	5.9	56	4.6	67	5.5	69	5.6	70	5.7
≥60	69	8.4	69	8.2	55	6.3	60	6.7	62	6.7
Sex										
Male	152	7.1	147	6.8	139	6.4	169	7.6	155	6.9
Female	148	6.6	132	5.9	123	5.4	120	5.2	131	5.6
Ethnic group[b]										
Māori	39	5.9	36	5.4	25	3.8	36	5.3	22	3.2
Pacific	47	17.2	33	12.1	40	14.6	47	16.9	57	20.2
Asian	161	32.0	168	33.3	157	31.0	173	33.7	181	34.4
MELAA	15	30.5	12	24.4	13	26.3	11	22.0	8	15.7
European or Other	30	1.0	26	0.9	24	0.8	17	0.6	17	0.6
Unknown	8	-	4	-	3	-	5	-	1	-
District Health Board										
Northland	6	3.7	3	-	1	-	7	4.2	2	-
Waitemata	33	6.1	40	7.3	21	3.8	36	6.4	38	6.6
Auckland	78	17.3	53	11.6	53	11.5	69	14.6	62	12.7
Counties Manukau	51	10.5	45	9.2	54	10.9	48	9.4	64	12.3
Waikato	18	4.8	22	5.9	23	6.1	17	4.4	24	6.1
Lakes	2	-	2	-	6	5.8	5	4.8	7	6.7
Bay of Plenty	14	6.6	9	4.2	10	4.7	11	5.1	6	2.7
Tairawhiti	3	-	2	-	2	-	1	-	1	-
Taranaki	1	-	4	-	6	5.3	3	-	2	-
Hawke's Bay	17	10.8	19	12.0	6	3.8	4	-	9	5.6
Whanganui	1	-	1	-	1	-	1	-	3	-
MidCentral	11	6.6	6	3.6	6	3.6	11	6.5	7	4.1
Hutt Valley	9	6.3	10	7.0	6	4.2	12	8.4	4	-
Capital & Coast	36	12.4	22	7.5	34	11.6	33	11.1	21	7.0
Wairarapa	0	-	0	-	2	-	1	-	0	-
Nelson	4	-	14	9.9	4	-	2	-	3	-
West Coast	0	-	1	-	1	-	1	-	1	-
Canterbury	12	2.4	17	3.4	21	4.2	24	4.7	26	4.9
South	0	-	1	-	0	-	1	-	0	-
Southern	4	-	8	2.6	5	1.6	2	-	6	1.9
Total	**300**	**6.8**	**279**	**6.3**	**262**	**5.9**	**289**	**6.4**	**286**	**6.2**

[a] Rate is expressed as cases per 100,000 population. Rates are not presented if there are fewer than five cases.

[b] Population data used to determine the rates for ethnic groups is based on the proportion of people in each ethnic group from the estimated resident 2013 census population applied to the mid-year population estimates. Ethnicity is prioritised and grouped in the following order: Māori, Pacific peoples, Asian, Middle Eastern/Latin American/African (MELAA) and European or Other (including New Zealander).

Table 13. Site of infection for tuberculosis (new case) notifications with extra-pulmonary involvement by year, 2011–2015

Site of infection	2011		2012		2013		2014		2015	
	Cases[b]	%	Cases[b]	%	Cases[b]	%	Cases[b]	%	Cases[b]	%
Lymph node (excl. abdominal)	67	45.6	55	35.9	76	45.0	82	49.4	86	46.7
Pleural	18	12.2	30	19.6	25	14.8	24	14.5	34	18.5
Intra-abdominal (excl. renal)	27	18.4	18	11.8	17	10.1	18	10.8	18	9.8
Bone/joint	16	10.9	14	9.2	15	8.9	24	14.5	12	6.5
Renal/genitourinary tract	5	3.4	15	9.8	10	5.9	5	3.0	15	8.2
Soft tissue/skin	8	5.4	10	6.5	8	4.7	5	3.0	16	8.7
Miliary tuberculosis	3	2.0	5	3.3	9	5.3	10	6.0	9	4.9
Central nervous system TB (CNS TB)[C]	7	4.8	1	0.7	6	3.6	8	4.8	10	5.4
Other	10	6.8	15	9.8	19	11.2	17	10.2	14	7.6
Total[a]	**147**	**100**	**153**	**100**	**169**	**100**	**166**	**100**	**184**	**100**

[a] Note: Total number of new tuberculosis cases reported with extra-pulmonary involvement, including cases with pulmonary disease.
[b] Some cases had more than one site of infection recorded.
[C] Includes meningitis

Table 14. Numbers and percentages of non-unique and unique strain of tuberculosis (new case) notifications for selected variables, 2011−2015

Variable[a]	Non-unique		Unique	
	Cases	%[b]	Cases	%[b]
Age group (years)	**439**	**38.8**	**692**	**61.2**
<15	17	81.0	4	19.0
15−39	218	37.1	369	62.9
40−59	103	40.6	151	59.4
≥60	101	37.5	168	62.5
Sex	**439**	**38.8**	**692**	**61.2**
Male	231	37.5	385	62.5
Female	208	40.4	307	59.6
Ethnic group	**432**	**38.8**	**682**	**61.2**
Māori	83	74.1	29	25.9
Pacific peoples	149	80.1	37	19.9
Asian	167	24.3	519	75.7
Middle Eastern/Latin American/African	6	12.8	41	87.2
European or Other	27	32.5	56	67.5
District Health Board	**439**	**38.8**	**692**	**61.2**
Northland	8	50.0	8	50.0
Waitemata	53	38.1	86	61.9
Auckland	88	33.1	178	66.9
Counties Manukau	92	41.1	132	58.9
Waikato	27	36.0	48	64.0
Lakes	6	33.3	12	66.7
Bay of Plenty	15	38.5	24	61.5
Tairawhiti	2	33.3	4	66.7
Taranaki	4	33.3	8	66.7
Hawke's Bay	21	63.6	12	36.4
Whanganui	4	80.0	1	20.0
MidCentral	17	50.0	17	50.0
Hutt Valley	11	33.3	22	66.7
Capital & Coast	47	46.1	55	53.9
Wairarapa	0	0.0	3	100.0
Nelson Marlborough	8	44.4	10	55.6
West Coast	1	33.3	2	66.7
Canterbury	26	32.1	55	67.9
South Canterbury	1	50.0	1	50.0
Southern	8	36.4	14	63.6
Region of birth	**439**	**38.8**	**691**	**61.2**
New Zealand	137	61.4	86	38.6
Southern and Central Asia	142	24.8	431	75.2
East Asia	26	28.9	64	71.1
Pacific Islands	111	72.1	43	27.9
Africa and the Middle East	16	26.2	45	73.8
Australia, Europe and the Americas	7	24.1	22	75.9
NZ Deprivation Index (NZDep13) quintile	**417**	**38.3**	**672**	**61.7**
1	27	25.2	80	74.8
2	43	30.5	98	69.5
3	68	33.2	137	66.8
4	104	38.2	168	61.8
5	175	48.1	189	51.9
Clinical manifestation	**439**	**38.8**	**692**	**61.2**
Pulmonary disease	291	41.6	409	58.4
Extra-pulmonary involvement only	148	34.3	283	65.7

[a] The total provided for each variable is the number of cases for which the information is recorded.

[b] Percentage of the total number of cases in each sub-category.

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