Tuberculosis in New South Wales

Surveillance Report 2018

NSW GOVERNMENT

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Contents

Summary

- There were 508 tuberculosis (TB) cases notified in New South Wales (NSW) in 2018, 6% lower than the number of cases notified in 2017.
- Notification rate was 6.4 cases per 100,000 population per year.
- Overseas born TB cases accounted for 93% of cases. The most frequently reported countries of birth were India, Vietnam and Nepal.
- Of the 35 Australian born cases, three (9%) identified as Aboriginal or Torres Strait Islander people.
- Notification rates were highest in Western Sydney and Sydney Local Health Districts.
- The most frequently reported risk factors were being born, or past residence (≥3mths), in a high risk country for TB, known contact with TB, or having an immunosuppressive health condition or being on immunosuppressive therapy.
- 79% of cases were laboratory confirmed by culture or polymerase chain reaction (PCR), with 21% of cases receiving a clinical diagnosis only.
- Of those cases with laboratory confirmation, 10 cases were classified as having multi-drug resistant TB (MDR-TB) and no cases had extensively drug resistant TB (XDR-TB). This represents 3% of laboratory confirmed cases and is consistent with previous years.

	2018	**Change since 2017**
Tuberculosis cases (number)	508	↓ 6% (n=542)
Tuberculosis notification rate	6.4 per 100,000	↓ 8% (6.9 per 100,000)
Australian born non-Indigenous cases (number)	32	↓ 29% (n=45)
Australian born non-Indigenous rate	0.6 per 100,000	↓ 30% (0.8 per 100,000)
Australian born Aboriginal cases (number)	3	↓ 40% (n=5)
Australian born Aboriginal notification rate	1.2 per 100,000	↓ 41% (2.0 per 100,000)
MDR-TB cases	10	↑ 20% (n=8)
% cases tested for HIV at diagnosis	90%	↑ 1% (89%)

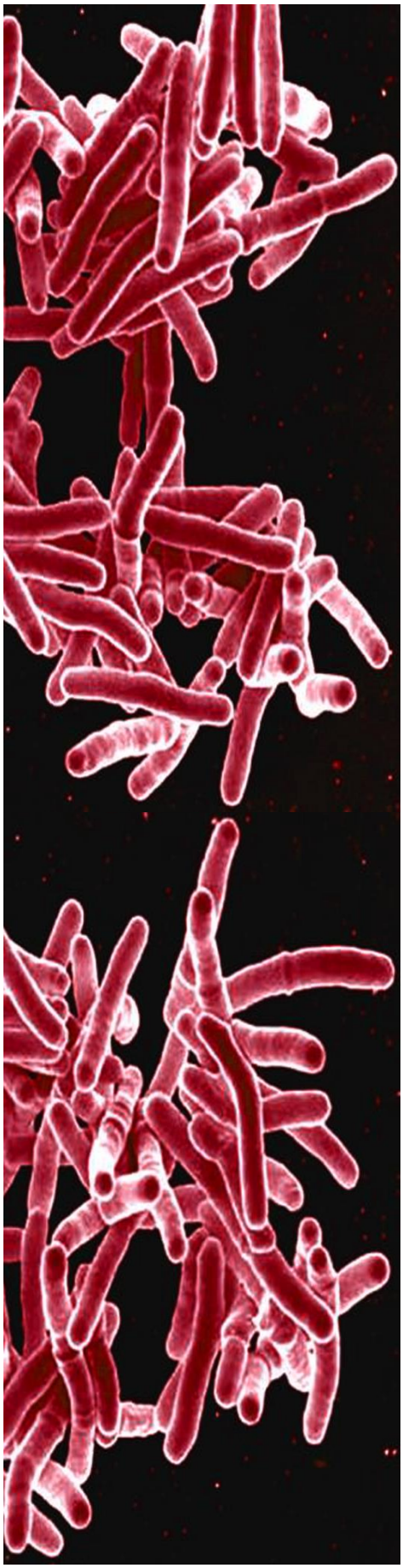


Image: CDC PHIL #18139: Scanning Electron Microscopy image of Mycobacterium Tuberculosis Credit: National Institute of Allergy and Infectious Diseases (NIAID)

Introduction

Tuberculosis (TB) is a bacterial disease caused by infection with *Mycobacterium tuberculosis.* Globally TB remains a disease of public health significance with the World Health Organization (WHO) estimating 10 million new cases in 2017, and an estimated 1.3 million deaths [1]. Drug resistant TB is an increasing threat globally, with over 550,000 cases of rifampicin resistant TB estimated worldwide in 2017, of which 82%, 451,000 cases, had multi drug resistant TB (MDR-TB) [1]. Almost half of these cases were reported from three countries – India, China, and the Russian Federation [1].

Australia continues to have a low incidence of TB, with the Commonwealth Department of Health reporting a rate of 5.8 cases per 100,000 population in 2018 [2]. In 2014, the proportion of TB cases with HIV/TB co-infection in Australia was reported at 2% [3]. Mortality from TB in Australia is very low with 1% of cases reported to have died from TB in 2014 [2].

Australia, and NSW, is committed to working towards the 'End TB Strategy' target of a 20% reduction in TB incidence by 2020, compared with 2015 [4]. The NSW TB Program, through a network of dedicated TB services across the state, continue to focus on active case finding, early diagnosis, and effective treatment of cases and contacts to minimise local transmission of TB in NSW.

Surveillance of TB in NSW is conducted under the NSW *Public Health Act 2010*.

The purpose of this report is to describe the epidemiology of TB in NSW in 2018.

Methods

Data were extracted from the Notifiable Conditions Information Management System (NCIMS) on 10 July 2019 for all confirmed cases of TB notified from 1 January 1999 to 31 December 2018. Population data including NSW mid-year population estimates, estimated populations by country of birth and population estimates by local health district (LHD) were obtained from the Australian Bureau of Statistics (ABS) via the Secure Analytics for Population Health Research and Intelligence System.

For whole genome sequencing, high quality DNA of *M. tuberculosis* was extracted from positive cultures by the NSW Mycobacterium Reference Laboratory. Library are prepared by the Microbial Genomics Reference Laboratory as per manufacture procedure for Nextera XT DNA preparation kit (Illumina). Sequencing was performed in NextSeq500 with 2 x 150 bp paired-end chemistry. Sequence data was trimmed with Trimmomatic and lineage determined using Mykrobe Predictor TB. Drug resistance was determined by SNP calling using Snippy with inhouse scripts and CRyPTIC database for mutations associated with drug resistance. Cluster detection was determined by SNP difference through Reddog pipeline. Cases were considered cluster if there was less than 12 SNPs differences between cases. Only cases from 2018 or earlier were included in the analysis.

Statistical analyses

Notification data were analysed using descriptive and analytic methods. Overseas born cases were categorised into regions of birth using ABS standards. Notification rates per 100,000 population per year were calculated for the whole of NSW using select fields from demographic, clinical, risk factor and contact management data categories. Notification rates for TB by LHD of residence were calculated and mapped using R (R core team, Vienna, Austria, 2018). Data were analysed using SAS® Enterprise Guide® (version 4.3, SAS Institute, Cary, NC, USA). The chi squared test was used for sample sizes of 5 or greater and fisher's exact test for samples sizes of less than 5. Significance was tested at the 0.05 level.

Definitions

Laboratory confirmed TB is isolation of *Mycobacterium tuberculosis* complex (*M. tuberculosis, M. bovis*, or *M. africanum*, excluding *M. bovis var* BCG) by culture or detection of *M. tuberculosis* complex by nucleic acid testing except where this is likely to be due to previously treated or inactive disease.

Clinically diagnosed TB is when a clinician experienced in TB makes a clinical diagnosis of TB disease[4] without a culture or PCR result. Other laboratory suggestive evidence such as smear results for acid fast bacilli or histology may be taken into account. Cases of latent TB infection are not included.

Pulmonary TB is disease affecting the lung, excluding the pleura.

Extrapulmonary TB is disease affecting any other region of the body, including the pleura.

SNP Single nucleotide polymorphisms

High risk countries are those with an annual TB incidence of 40 cases per 100,000 population per year or more in 2018, as per estimates in WHO Global Tuberculosis Report 2018 at the time the data were collected [2].

MDR-TB are cases with isolates that demonstrate resistance to at least isoniazid and rifampicin [5].

Extensively drug-resistant TB (XDR-TB) are cases in which isolates demonstrated resistance to isoniazid and rifampicin, as well as additional resistance to any fluoroquinolone, and to at least one injectable second-line drug (capreomycin, kanamycin or amikacin) [5].

Permanent resident is a person who holds a permanent visa (or has become an Australian citizen) and is usually resident in Australia.

Overseas student is a person studying or seeking study, training, or skills development in Australia.

Visitor is a person entering Australia temporarily for tourism, to visit family and friends, to undergo pre-arranged medical treatment or for business related purposes.

Refugee / humanitarian is a person in humanitarian need overseas or a person already in Australia who arrived on a temporary visa or in an unauthorised manner, claiming Australia's protection.

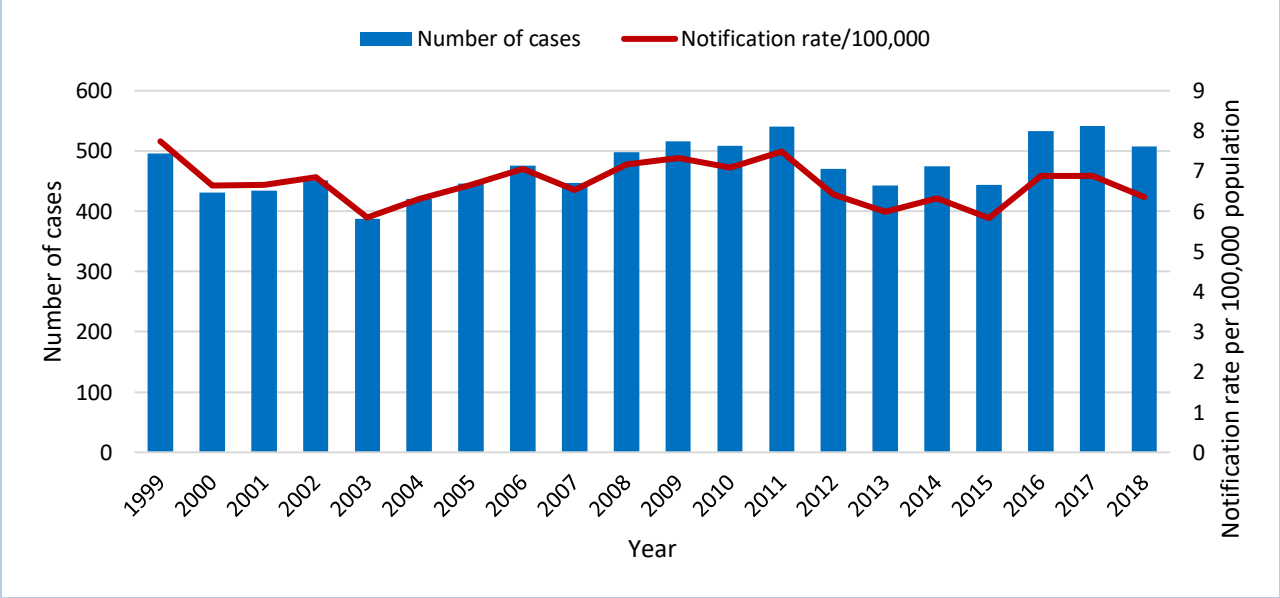
Unauthorized person is an unlawful non-citizen.

Section 1: Demographics

There were 508 notified cases of TB in 2018 in NSW (Figure 1). These cases comprised 35% of the total notified cases in Australia in 2018 (1,438 cases) [3]. It is unclear why case notifications fluctuate from year to year, underlying factors may include immigration and TB screening patterns. The number of notifications received in 2018 was 6% lower than the number notified in 2017. However, 2017, along with 2011, had the equal highest number of cases notified in a year in the past 20 years (Figure 1).

The annual notification rate of TB in 2018 in NSW was 6.4 cases per 100,000 population per year. The 2018 rate has decreased slightly compared to 2017. The highest rate of the past 20 years was in 1999 (7.7 cases per 100,000) with another peak in 2011 (7.5 cases per 100,000) (Figure 1).

Figure 1: Number and rate of TB disease notifications, NSW, 1999-2018



2018

508
Number of cases notified

6.4
Rate per 100,000 population

Demographics

Of the 508 cases of TB notified in 2018, 52% of cases were male (n=266). The median age among males was 41 years (range 2 months-92 years); while the median age among females was 35 years (range 9 months-91 years). The median age overall was 37 years (range 2 months-92 years).

Nearly half the cases notified were aged between 20 and 39 years (n=246) with a peak in the number of notifications in the 25-29 year age group (n=76, rate=13 cases per 100,000) and the rate of notifications in the 20-24 year age group (n=66, rate=14 cases per 100,000). A second peak in the rate of notifications was observed in those aged 60-64 years (n=46, rate=10 cases per 100,000). There were seven cases notified in children aged less than five years (1%) (Figures 2 and 3).

Age and Sex

Sex

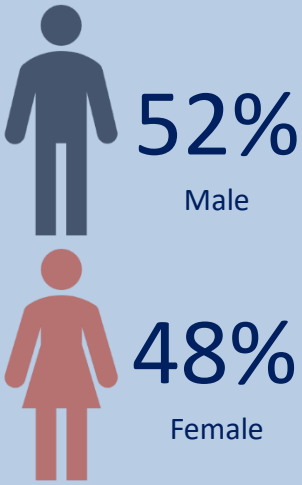
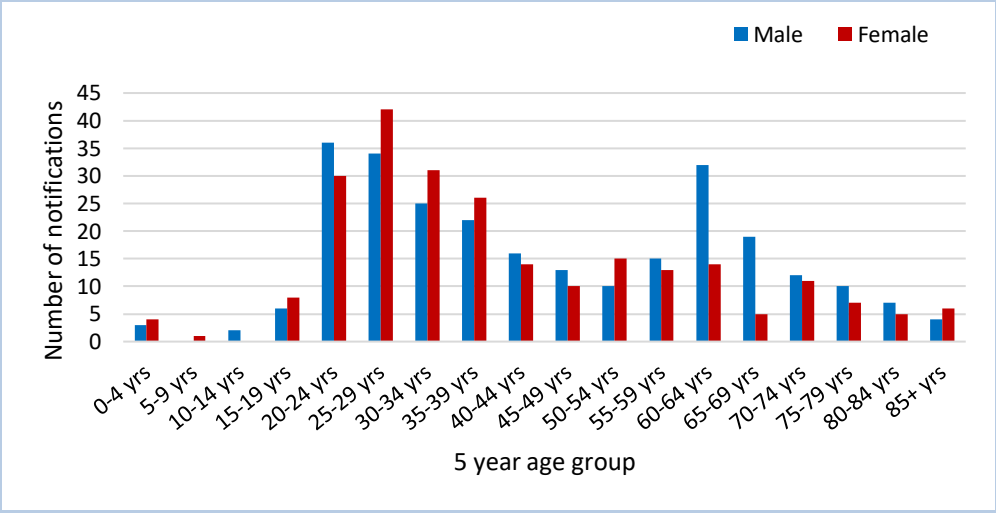


Figure 2: Number of TB notifications by age group and sex, NSW, 2018



Age Overall

Range: 2 months-92 years
Median: 37 years

Age by Sex

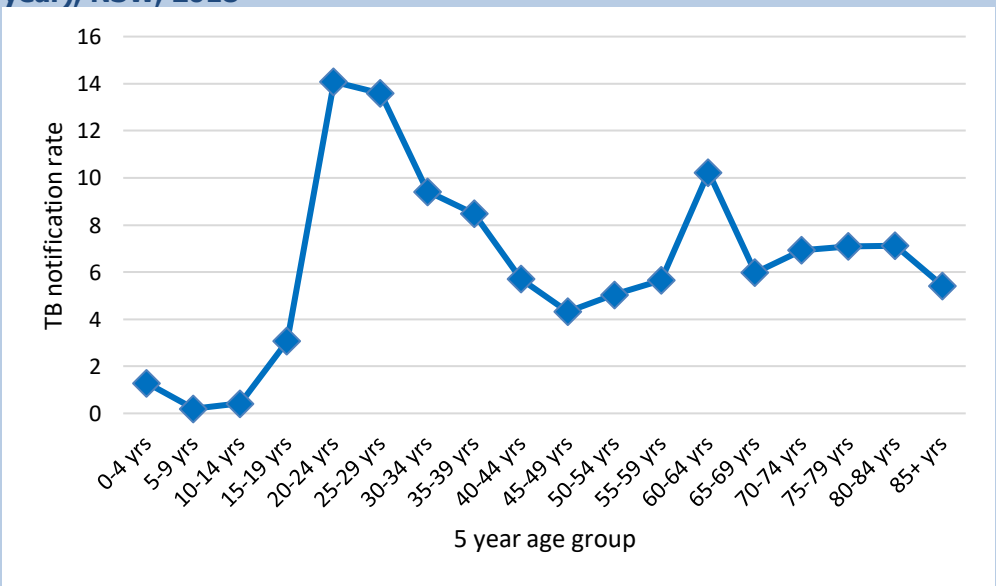
Male

Range: 2 months-92 years
Median: 41 years

Female

Range: 9 months-91 years
Median: 35 years

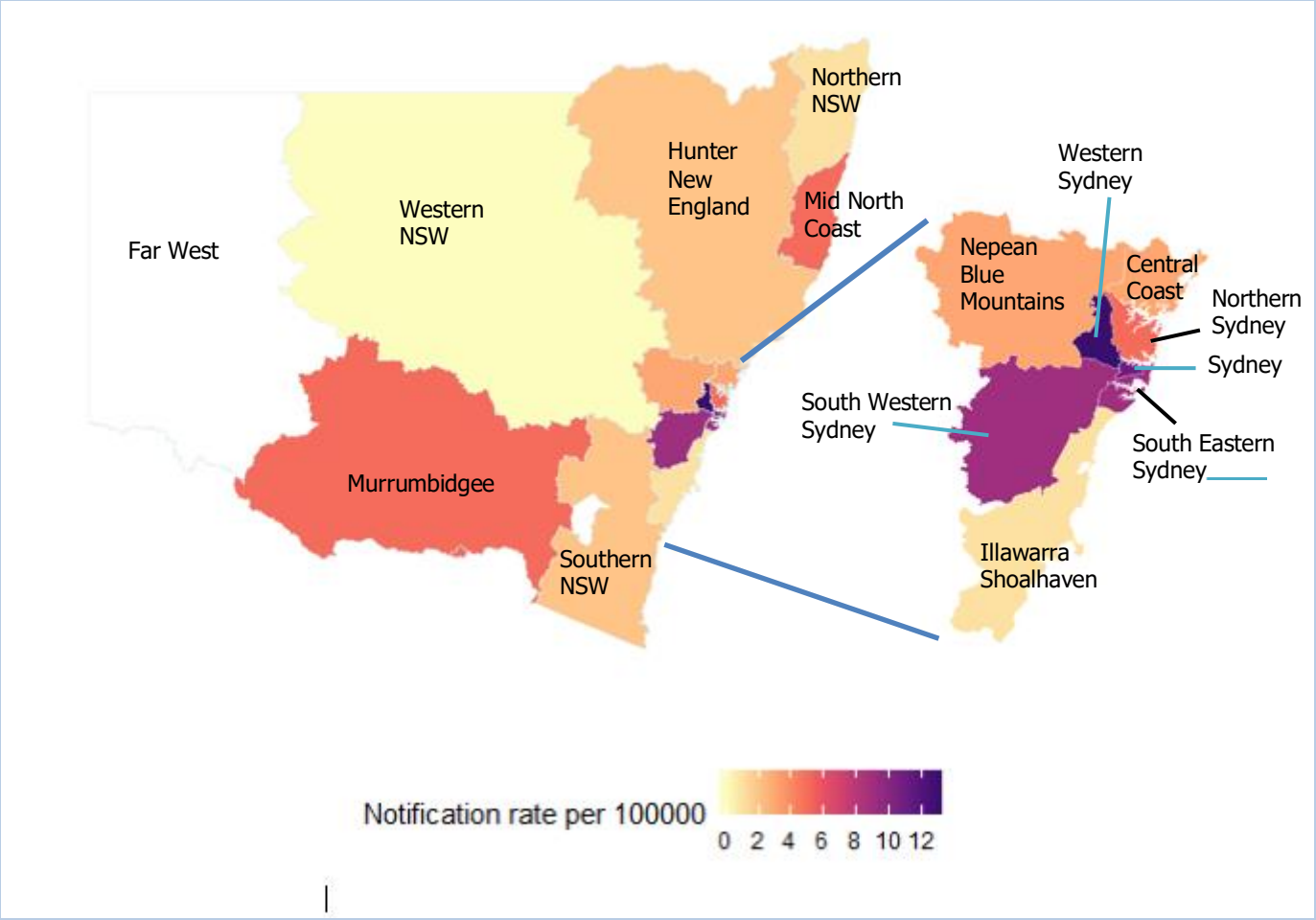
Figure 3: Age specific TB notification rate (per 100,000 population per year), NSW, 2018



Place of residence

Western Sydney Local Health District (LHD) had the highest notification rate, with 12.9 cases per 100,000 population (n=129), followed by Sydney LHD with 11.4 cases per 100,000 population (n=76) (Figure 4). Nepean Blue Mountains LHD had the highest rate among LHDs in outer Sydney at 3.3 cases per 100,000 population (n=13), followed by Central Coast with 2.6 cases per 100.000 population per year (n=9). Of LHDs comprising regional NSW, Murrumbidgee LHD had the highest rate at 5.1 cases per 100,000 (n=15) followed by Mid North Coast LHD at 4.5 cases per 100,000 (n=10). For data on individual LHDs see Table 1.

Figure 4: Age and sex standardised rate of notified TB cases per 100,000 population per year by Local Health District of residence, NSW, 2018



10.5

Rate per 100,000, Metropolitan Sydney
(Sydney, South Western Sydney, Western Sydney, Northern Sydney and South Eastern Sydney LHDs)

2.0

Rate per 100,000, Outer Sydney
(Illawarra Shoalhaven, Central Coast and Nepean Blue Mountains LHDs)

1.8

Rate per 100,000, Regional NSW
(Far West, Western NSW, Northern NSW, Mid North Coast, Hunter New England, Southern NSW and Murrumbidgee LHDs)

Table 1: Age and sex standardised rate of notified TB cases per 100,000 population per year by Local Health District of residence, NSW, 2018

Local Health District	Number	Rate
Western Sydney	129	12.86
Sydney	76	11.36
South Eastern Sydney	86	9.14
South Western Sydney	92	9.02
Murrumbidgee	15	5.07
Northern Sydney	45	4.86
Mid North Coast	10	4.45
Nepean Blue Mountains	13	3.33
Central Coast	9	2.58
Southern NSW	4	1.84
Hunter New England	17	1.81
Illawarra Shoalhaven	5	1.21
Northern NSW	3	0.97
Western NSW	1	0.36
Far West	0	0

*Excludes 3 Justice Health cases

Country of Birth

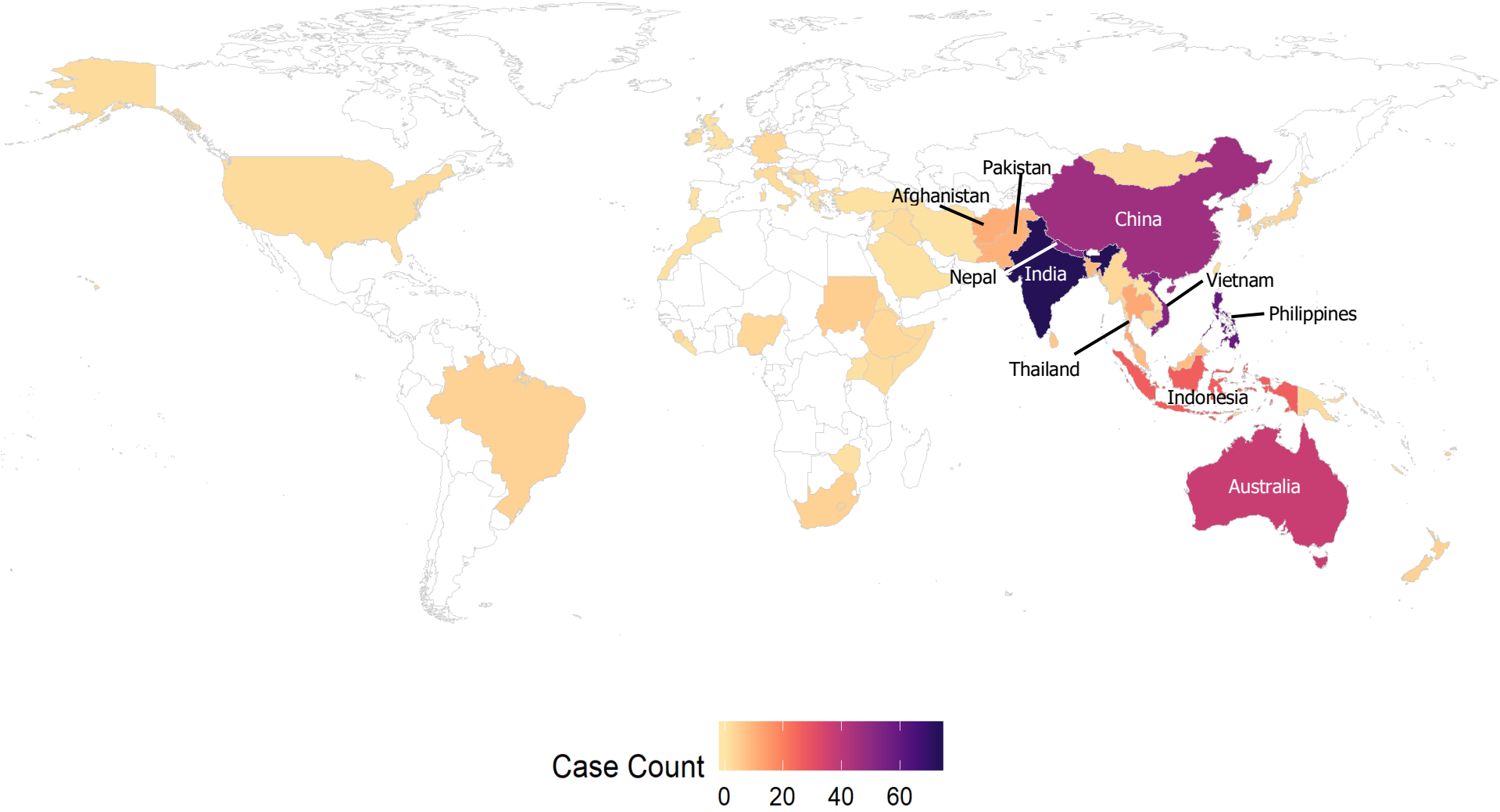
In 2018, 93% (n=473) of cases were born overseas. Of these, 92% (n=433) were born in a high risk country (HRC) for TB. There were 60 individual countries of birth reported among NSW TB cases (Figure 5), with the most commonly reported countries of birth being India (14% of all cases, n=73), Philippines (12%, n=59), and Nepal (10%, n=53) (Table 2).

Of cases born in a HRC, 44% (n=192) were born in a country within the WHO South East Asian region, and a further 42% (n=184) were born in a country within the WHO Western Pacific region. The Eastern Mediterranean region accounted for 7% (n=31), African region 5% (n=22), American region 1% (n=0), and European region 0% (n=0).

Table 2: Countries of birth of TB cases, NSW, 2018

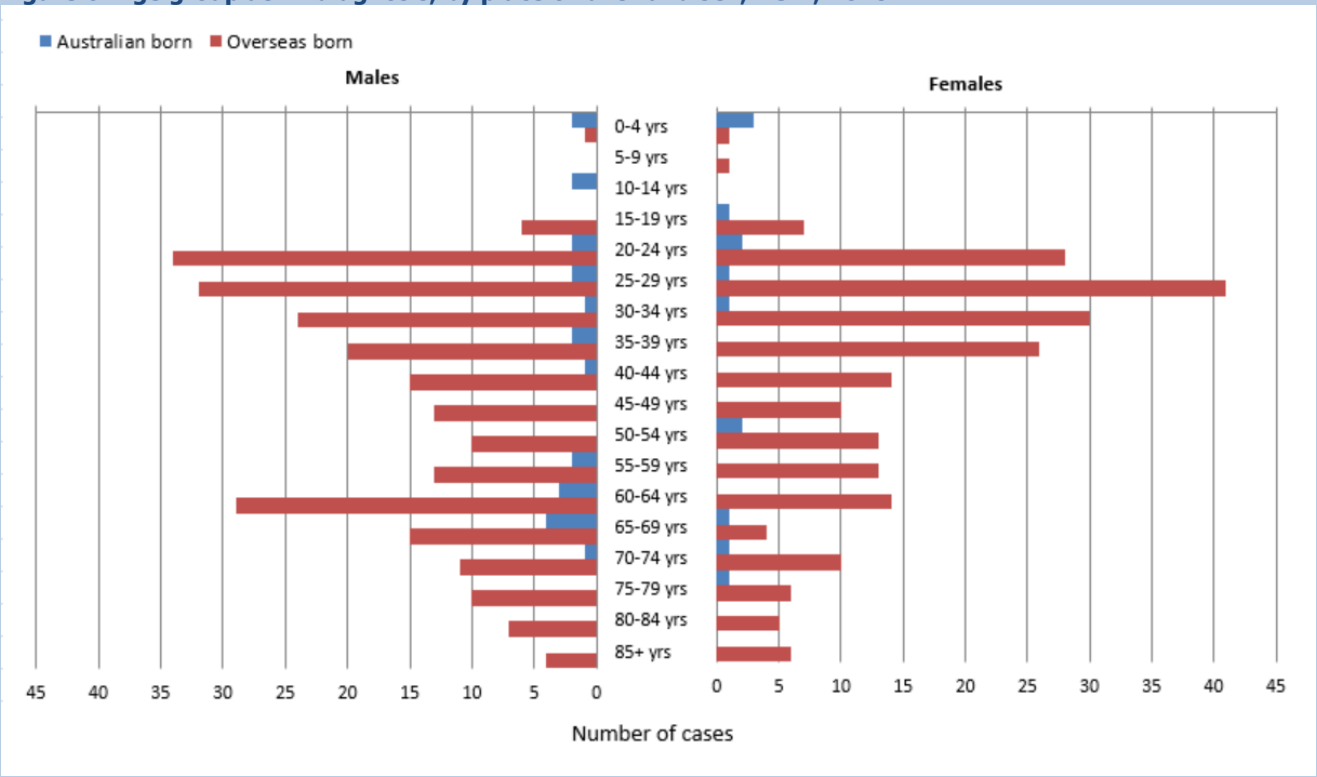
Country of birth	Number of cases	Proportion of cases
India	73	14%
Philippines	59	12%
Nepal	53	10%
Vietnam	52	10%
China	46	9%
Australia	35	7%
Indonesia	26	5%
Thailand	12	2%
Afghanistan	11	2%
Bangladesh	10	2%
Pakistan	10	2%
Other	121	24%
Total	**508**	**100%**

Figure 5. Number of TB cases by country of birth, NSW, 2018



The median age of Australian born cases is generally higher than the median age of overseas born cases. Males tended to be older at diagnosis compared to females. This is consistent with previous years. In 2018, the median age at diagnosis for Australian born cases was 48 years; 40 years for females (range 3 months-88 years) and 54 years for males (range 8 months-97 years). For overseas born cases, the median age at TB diagnosis was 36 years; 34 years for females (range 2 months-92 years), and 40 years for males (range 3-97 years). Over 50% of overseas born cases were aged between 20 and 39 years at diagnosis (Figure 6).

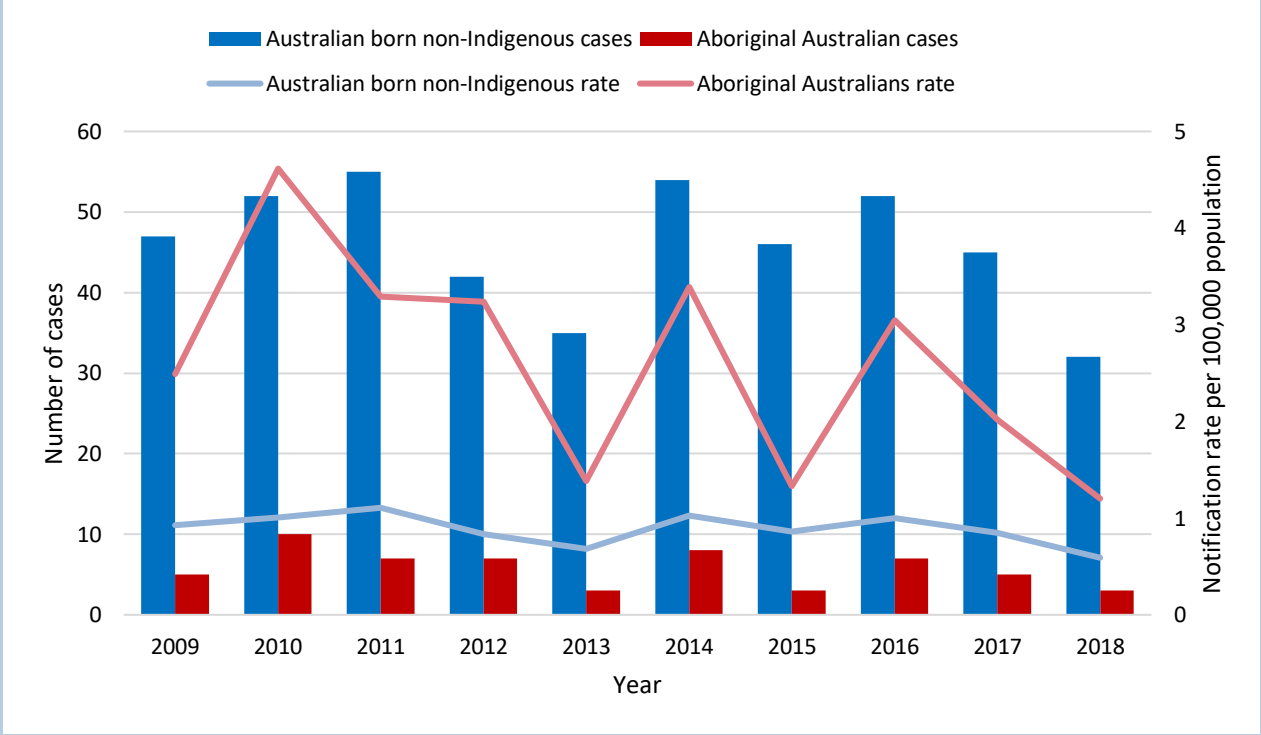
Figure 6: Age group at TB diagnosis, by place of birth and sex, NSW, 2018



Australian born cases

Of the 35 Australian born cases in 2018, 9% (n=3) identified as Aboriginal (Figure 7). The number of TB cases who identify as Aboriginal fluctuates from year to year and the number notified in 2018 is less than the average number notified per year (n=6) since 2009. The average rate of TB among Indigenous Australians over the past 10 years is almost three times higher than that among non-Indigenous Australian born cases (relative rate = 2.9, 95% confidence interval 2.2 to 3.7, p<0.0001). Over the 10 years to 2018, the rate in Aboriginal and Torres Strait Islander Australians and non-Indigenous Australians in NSW has decreased, though these decreases were not found to be statistically significant (p>0.05).

Figure 7: Number and rate of notified TB in Australian born cases by Indigenous status, NSW, 2009-2018



Overseas born cases

Of the 473 overseas born cases in 2018, those born in a HRC for TB (n=433) had a shorter median length of stay in Australia prior to diagnosis of TB (6 years, range 0-57 years) when compared to the other overseas born cases (n=40) (23 years, range 1-74 years) (Figure 8).

Over half of the overseas born cases were permanent residents at the time of diagnosis (n=259, 55%), 22% (n=102) were overseas students, 9% (n=44) were visitors, 3% (n=13) were refugees, 1% (n=4) were unauthorised persons, 8% (n=38) were on other types of visas, and 3% (n=13) had an unknown or missing Australian status (Table 3).

Some Australian visas require the applicant to undergo a medical examination prior to the visa being granted. These include all permanent visa applicants and some temporary visa applicants depending on how long they intend to stay

in Australia, if they intend to work or study, and their country of origin. If the medical examination shows that the visa applicant might be at increased risk of developing active TB, offshore applicants are placed on a TB Health Undertaking (TBU) and onshore applicants are placed on an Onshore Deferral. Both are required to be followed up by the health authorities in Australia. Of the 433 NSW TB cases born in HRCs, 18% (n=79) were on a TBU or Onshore Deferral at the time of diagnosis, a further 5% (n=22) had previously been on a TBU or onshore deferral, 69% (n=299) had never been on a TBU or onshore deferral and for 8% (n=33) the TBU status was unknown.

Length of Stay in Australia

18%

Proportion of NSW TB cases, born in a HRC, currently on a TB Health Undertaking or Onshore Deferral at diagnosis with TB

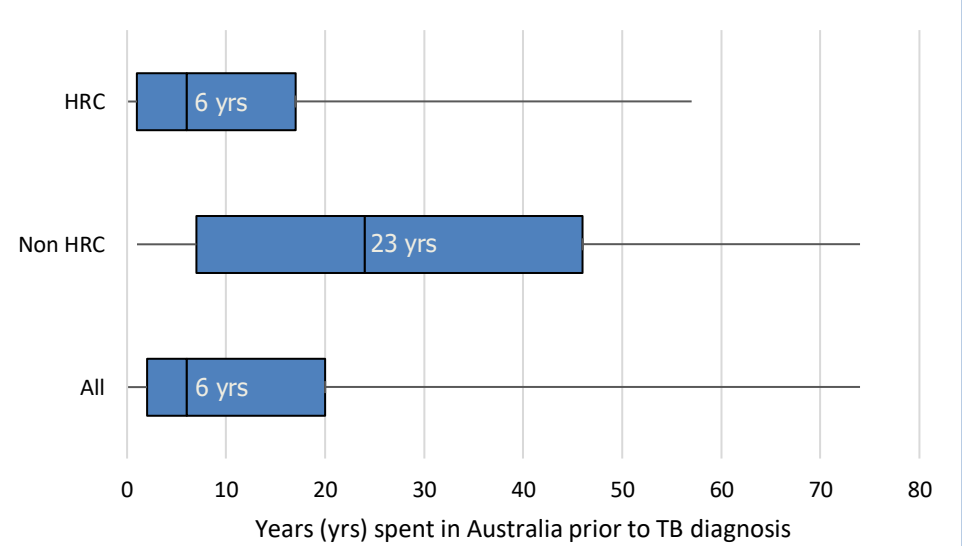
5%

Proportion of NSW TB cases, born in a HRC, who have previously been on a TB Health Undertaking or Onshore Deferral

69%

Proportion of NSW TB cases, born in a HRC, who have never been on a TB Health Undertaking or Onshore Deferral

Figure 8: Median years spent in Australia prior to TB diagnosis, among overseas born cases, by country of birth risk category, NSW, 2018



HRC = High risk country (TB incidence >40 cases per 100,000 population)

Table 3: Residency status of overseas born TB cases at diagnosis, NSW, 2018

Residency status	Number of cases	Percentage
Permanent resident	259	55%
Overseas student	102	22%
Visitor	44	9%
Refugee / humanitarian entrant	13	3%
Unauthorised person	4	1%
Other	38	8%
Unknown/ missing status	13	3%
Total	**473**	**100%**

Risk Factors

The most commonly reported risk factor for all notified cases in 2018 was being born overseas in a HRC for TB (86%, n=435). Past residence for three months or more in a HRC that was not the person's country of birth (16%, n=82) and being either a household member or having other close contact with another person with TB (14%, n=72) were the next highest reported risk factors. Health conditions causing immunosuppression, or being on immunosuppressive therapy was reported by 13% (n=64) of cases.

There was variation in reported risk factors between Australian born and overseas born cases. In Australian born cases, the most frequently reported risk factor was past residence in a HRC (more than 3 months) (26%, n=9), followed by having a household or close contact with TB (23%, n=8). For overseas born cases, 92% (n=435) were born in a HRC. Other reported risk factors can be found in Table 4.

Table 4: Reported risk factors for TB* among notified case, by place of birth, NSW, 2018

	All cases		Australian born		Overseas born	
	N	%	N	%	N	%
Total	**508**	**100%**	**35**	**100%**	**473**	**100%**
Born in a HRC	435	86%	n/a	n/a	435^	92%
Past residence (≥3 months) in a HRC	82	16%	9	26%	73	15%
Household member or close contact with TB	72	14%	8	23%	64	14%
Immunosuppressive health condition/therapy	64	13%	6	17%	58	12%
Previously diagnosed with TB	35	7%	2	9%	33	7%
CXR suggestive of old untreated TB	27	5%	1	3%	26	5%
Ever employed in healthcare	24	5%	4	11%	20	4%
Australian born child of parent(s) born in HRC	7	1%	7	20%	n/a	n/a
Ever resided in a correctional facility	5	1%	2	6%	3	1%
Ever homeless/residing in a shelter	2	<1%	0	0%	2	<1%
Ever employed in an institution	2	<1%	0	0%	2	<1%
Other	12	2%	0	0%	12	3%
Not able to be determined	16	3%	6	17%	10	2%

*Multiple risk factors can be recorded
^Born in a HRC is recorded as well as country of birth, as some countries may have been high incidence when the person was born but are no longer considered HRC

Australian born cases

1st ≥3 months spent in a high risk country

2nd Household member or close contact with TB

3rd Australian born child of parent(s) born in HRC

Overseas born cases

1st Born in a high risk country

2nd ≥3 months spent in a high risk country (other than country of birth)

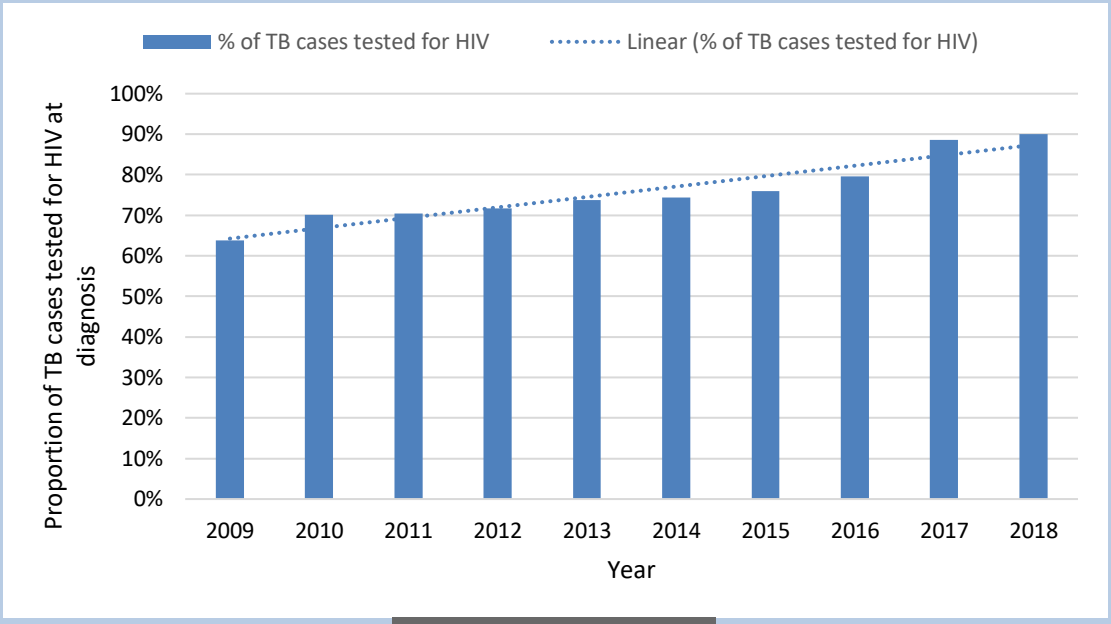
3rd Household member or close contact with TB

HIV Testing

Over the 10 year period to 2018, there has been a 26% increase in the proportion of TB cases tested for HIV at the time of TB diagnosis, from 64% in 2009 to 90% in 2018 (Figure 9). Of cases tested in 2018, 2% (n=8) were co-infected with HIV and TB.

Of the eight TB cases who were HIV positive in 2018, 63% (n=5) were male, 100% (n=8) were overseas born. More than half (63%, n=5) were newly diagnosed with HIV around the same time as TB, two had been previously diagnosed with HIV unrelated to their TB diagnosis (25%) and one was unknown (13%).

Figure 9: Proportion of TB cases tested for HIV at TB diagnosis, NSW, 2009 - 2018



90%

Proportion of NSW TB cases tested for HIV at diagnosis, 2018

8

Number of NSW TB cases co-infected with HIV, 2018

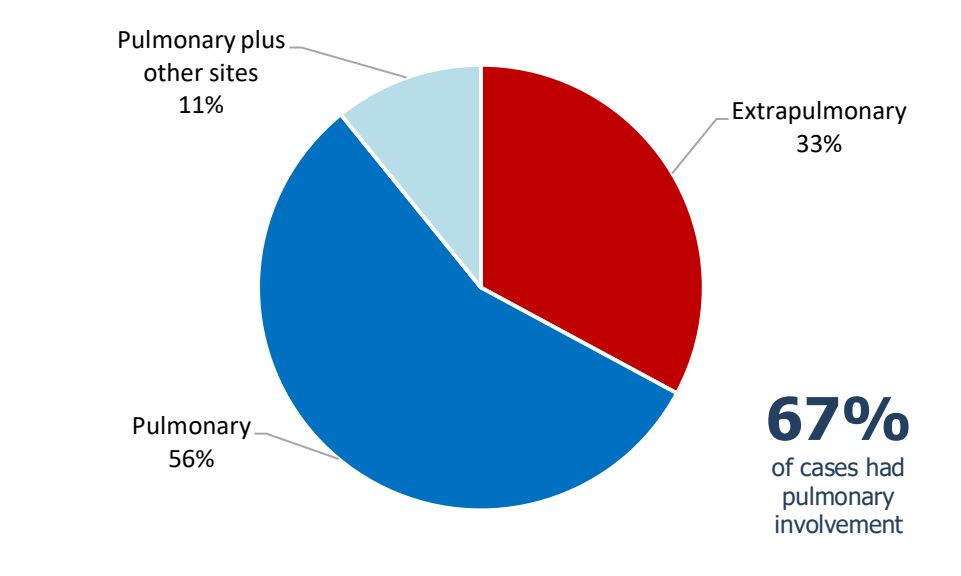
100%

Target for TB cases tested for HIV at diagnosis

Site of Infection

In 2018, pulmonary only disease accounted for 56% (n=286) of cases. A further 11% (n=55) of cases had pulmonary disease plus other sites and 33% (n=167) had extrapulmonary TB only (Figure 10). Of extrapulmonary sites reported, lymph node was the most common (n = 70, 42% of cases with extrapulmonary involvement), followed by infection of the pleura (n=25, 15%) and infection of the eye or eye appendages (n=15, 9%) (Table 5).

Figure 10: Site of disease for NSW TB cases, 2018



56%
Pulmonary only

33%
Extrapulmonary only

11%
Pulmonary plus other sites

Table 5: Extrapulmonary sites* of infection for NSW TB cases with extrapulmonary involvement, 2018

Site	Number of cases	Percentage
Lymph node	70	42%
Pleura	25	15%
Eye	15	9%
Gastrointestinal tract	11	7%
Brain/central nervous system/meninges, dural sinus, choroid plexus	11	7%
Genitourinary tract	8	5%
Skin	5	3%
Pericardium	5	3%
Bone	4	2%
Disseminated disease	4	2%
Joints (synovial fluid)	3	1%
Other	18	11%

*Multiple sites can be recorded

Clinical Presentation and Treatment

Of the 508 cases notified in 2018, 94% (n=475) were new diagnoses of TB; while 6% (n=33) of cases were classified as a relapse, following treatment either in Australia (2%, n=9) or overseas (5%, n=24) (Table 7). Cases classified as relapse may also include re-infection.

The median time from first health presentation to treatment for Australian born cases was 26 days, and 28 days for overseas born cases. Cases with pulmonary involvement were commenced on treatment sooner (27 days) than those cases with extrapulmonary disease only (33 days).

Almost all cases were commenced on antimicrobial treatment in NSW following diagnosis (98%, n=497). Twenty-three per cent of cases (n=115) that commenced on treatment did so within 7 days of their first health presentation, with 42% (n=209) commencing within 21 days of first health presentation.

Of the eleven cases (2%) who were not commenced on antimicrobial treatment in NSW, six (55%) had died prior to their TB diagnosis, and five (45%) had returned overseas and their diagnosis referred to the relevant country.

Table 7: Disease classification*, NSW TB cases 2018

Disease classification	Number of cases	Percentage
New	475	94%
Recurrence following full treatment only in Australia	6	1%
Recurrence following partial treatment only in Australia	3	1%
Recurrence following full treatment overseas	16	3%
Recurrence following partial treatment overseas	8	2%
Total	**508**	**100%**

*Recurrence may include cases who have relapsed or have been reinfected

98%

Proportion of cases commenced on antimicrobial therapy

28 days

Median time to treatment from first health presentation

6 days

Difference in median time to treatment between pulmonary and extrapulmonary cases

Section 3: Laboratory

Laboratory Testing

Of the 508 TB cases in 2018, 79% (n=401) of diagnoses were laboratory confirmed; 73% (n=373) were cultured, and an additional 6% laboratory diagnosed by molecular methods (polymerase chain reaction (PCR)) only (n=28). Clinical diagnoses were made in the remaining 21% (n=107) of cases (Figure 11). Laboratory confirmation was more commonly obtained for pulmonary involvement (84%, n=286), compared to those with extrapulmonary disease only (69%, n=167). A greater proportion of laboratory confirmation by PCR only occurred in extrapulmonary cases (15%, n=17), compared to PCR only confirmation of pulmonary cases (4%, n=11). For the ten year period to 2018, there has been a significant increase (p=0.006) in the proportion of cases confirmed using PCR only, while a significant decrease (p=0.02) in the number of cases with clinical diagnosis has been seen over the same period (Figure 12). The majority of cases notified in NSW in 2018 (71%, n=361) were tested for TB as part of an investigation of clinical symptoms.

71%

Proportion of TB cases identified via investigation of symptomatic disease

16%

Proportion of NSW TB cases identified via immigration, occupational or other health screening

1%

Proportion of NSW TB cases identified via contact investigation

Figure 11: Method of diagnosis of TB, laboratory vs. clinical, NSW, 2018

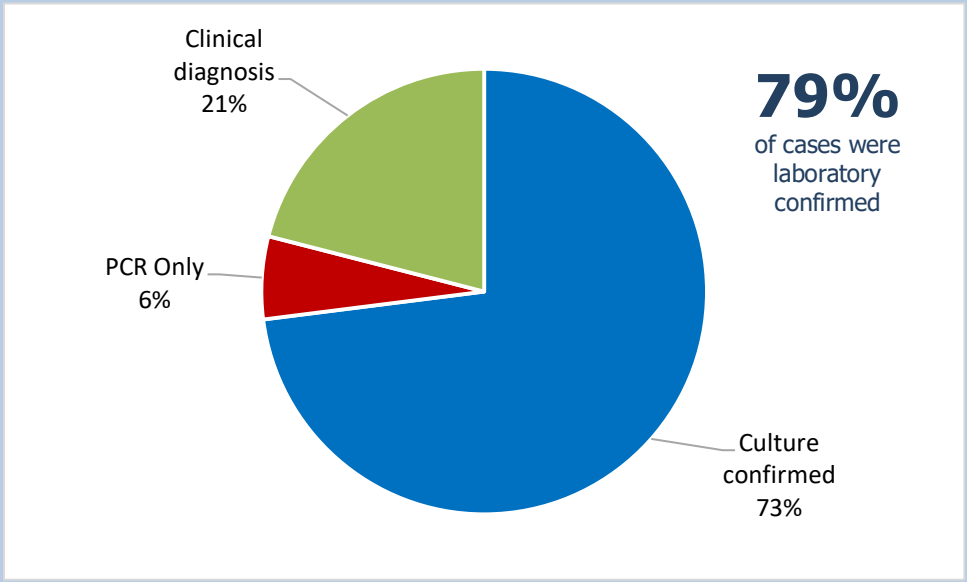
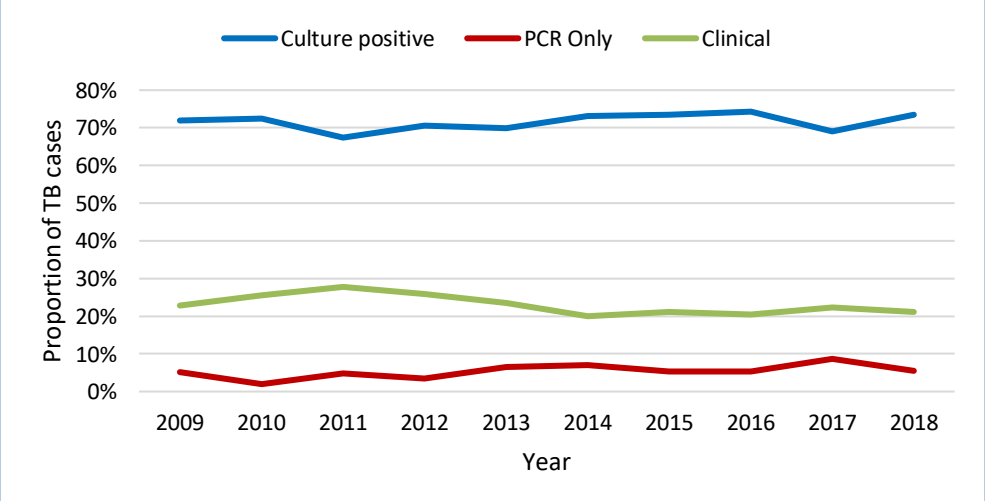


Figure 12: Method of laboratory confirmation of diagnosis of TB cases, NSW, 2009-2018



2%

Decrease in diagnoses made on clinical grounds only since 2009

1%

Increase in diagnoses confirmed by PCR only since 2009

1%

Increase of diagnoses confirmed by culture since 2009

Drug susceptibility testing (DST)

Of the 366 culture positive TB cases in NSW in 2018, 99% (n=363) had drug susceptibility results reported. Of these, 88% (n=318) were fully susceptible to first line TB drugs, 10% (n=35) were resistant to one or more first line TB drug, and 3% (n=10) were classified as MDR-TB (Figure 13). These proportions have not significantly changed over the last 10 years (Table 6).

Of the ten cases classified as MDR-TB, 80% (n=8) were new cases and 20% (n=2) were relapses following treatment overseas. There were three MDR-TB cases in individuals born in Australia, one case identified as an Aboriginal person. The country of birth for the overseas born cases were Vietnam (n=3), China (n=1), Thailand (n=1), Mongolia (n=1), and Nepal (n=1).

88%

Proportion of culture positive cases (with DST) fully susceptible to first line TB drugs, 2018

9%

Proportion of culture positive cases with any kind of mono-resistance to a first line TB drug, 2018

3%

Proportion of culture positive cases which were MDR-TB, 2018

Figure 13: Drug Susceptibility of culture confirmed cases, NSW, 2009-2018

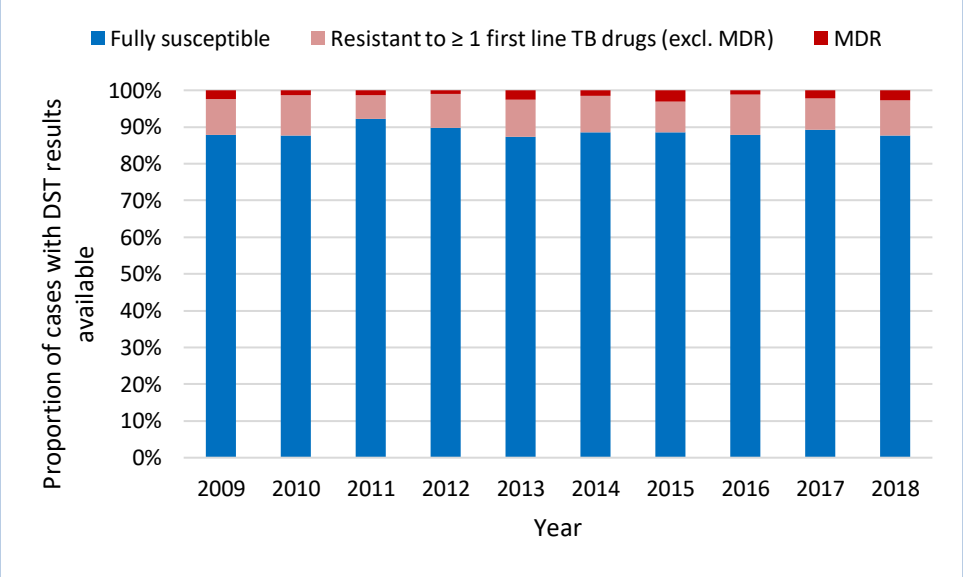


Table 6: Drug susceptibilities of culture confirmed TB cases with DST results available, NSW, 2009 - 2018

Drug Susceptibility		2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Fully susceptible		325 (88%)	328 (88%)	334 (92%)	288 (90%)	271 (87%)	307 (88%)	284 (88%)	321 (88%)	335 (89%)	318 (88%)
Ethambutol	Mono-resistance	0	0	0	1 (<1%)	0	2 (1%)	0	0	0	0
Isoniazid		34 (9%)	34 (9%)	21 (6%)	26 (8%)	23 (7%)	26 (7%)	22 (7%)	36 (10%)	26 (7%)	28 (8%)
Pyrazinamide		2 (1%)	3 (1%)	2 (1%)	2 (1%)	5 (2%)	4 (1%)	1 (<1%)	3 (1%)	6 (2%)	3 (1%)
Rifampicin		0	2 (1%)	0	0	1 (<1%)	0	2 (1%)	0	0	3 (1%)
Resistant to ≥2 first line drugs (but not MDR)		0	2 (1%)	0	1 (<1%)	2 (1%)	3 (1%)	2 (1%)	1 (<1%)	0	1 (<1%)
MDR*		9 (2%)	4 (1%)	5 (1%)	3 (1%)	8 (3%)	5 (1%)	10 (3%)	4 (1%)	8 (2%)	10 (3%)
XDR**		0	1 (<1%)	0	0	0	0	1 (<1%)	0	0	0

* Multi Drug Resistant: Resistance to at least Isoniazid AND Rifampicin
** Extensively Drug Resistant: Resistance to Isoniazid AND Rifampicin, AND any fluoroquinolone AND at least 1 injectable TB drug

Cluster analysis

In 2018, 364 (98%) of culture positive cases had whole genome sequencing (WGS) performed on one or more isolates. Of these, 33 (9%) were found to be part of a cluster with another TB case notified in NSW from 2018 or earlier. The remaining 331 (91%) were not linked to any other NSW case prior to 2018 at the time of analysis.

Of the 33 clustered cases, 20 (61%) were male, the median age was 31 years (range 19-79 years) and 82% (n=27) lived in a metropolitan LHD (Sydney, Western Sydney, Northern Sydney, South Eastern Sydney, or South Western Sydney). Cases with pulmonary involvement accounted for 88% (n=29), with 64% (n=16) with a positive smear on a respiratory specimen, and 12% (n=4) had extrapulmonary disease only.

Of the 331 non-clustered cases, 170 (51%) were male, the median age was 37 years (range 2 months-92 years) and 86% (n=284) lived in a metropolitan LHD. Cases with pulmonary involvement accounted for 73% (n=242), with 37% (n=84) with a positive smear on a respiratory specimen, and 28% (n=89) had extrapulmonary disease only.

The top countries of birth for clustered cases were Nepal (n=9, 27%), Australia (n=6, 18%), the Philippines (n=3, 9%) and Vietnam (n=3, 9%). For non-clustered cases the top countries of birth were India (n=49, 15%), Vietnam (n=37, 11%), China (n=37, 11%) and the Philippines (n=36, 11%).

There was no difference found between clustered and non-clustered cases in regard to gender, Indigenous status, or residence in a metropolitan or regional/rural LHD (Table 8). Pulmonary cases were 2.22 times more likely to be clustered by WGS then extrapulmonary cases, but this association was not found to be statistically significant (CI 0.87 to 5.65, p=0.09). There was a significant difference, among pulmonary cases, between respiratory smear positive and smear negative cases; smear positive cases were 1.75 times more likely to be clustered by WGS than smear negative case (CI 1.02 to 2.97, p=0.01).

Cases born in either Australia (RR 1.17, CI 1.00 to 1.38; p=0.0008) or Nepal (RR 1.23, CI 1.00 to 1.51; p=0.003) had a higher risk of being clustered then cases born in other countries. Cases born in India (RR 0.85, CI 0.81 to 0.89; p=0.001) were less likely to be clustered then cases born in other countries. There was no significant difference found for cases born in other countries analysed (China, the Philippines, Vietnam, Indonesia, Thailand, Afghanistan, Pakistan, and Bangladesh) (Table 9).

Table 8: Whole genome sequenced cases, 2018

		Clustered		Not clustered		Relative risk
		N	%	N	%	
Cases	Total number of cases	**33**	**100%**	**331**	**100%**	**-**
Age	Median age (age range)	33 years (19-79 years)		37 years (2 months -92 years)		-
Gender	Male	20	61%	170	51%	RR = 1.23 (CI 0.80 to 1.91) p = 0.31
	Female	13	39%	161	49%	
Indigenous status	Aboriginal	1	3%	1	<1%	RR = 0.10 (CI 0.01 to 1.56) p = 0.17
	Not Aboriginal	34	97%	330	99%	
Place of residence	Metropolitan Sydney[#]	27	82%	284	86%	RR = 0.78 (CI 0.36 to 1.69) p = 0.54
	Rural or regional NSW[#]	6	18%	47	14%	
Site of infection	Pulmonary involvement	29	88%	242	73%	RR = 2.22 (0.87 to 5.65) p =0.09
	Extrapulmonary only	4	12%	89	28%	
Respiratory smear positive*	Smear positive	16	64%	84	37%	RR = 1.75 (CI 1.03 to 2.97) p =0.01
	Smear negative	9	36%	142	63%	

#Metropolitan Sydney LHDs –Sydney LHD, Western Sydney LHD, Northern Sydney LHD, South Eastern Sydney LHD, South Western Sydney LHD

#Regional or rural LHDs – Nepean Blue Mountains LHD, Central Coast LHD, Illawarra Shoalhaven LHD, Hunter New England LHD, Mid North Coast LHD, Northern NSW LHD, Western NSW LHD, Far West LHD, Murrumbidgee LHD, Southern NSW LHD.

*Pulmonary cases only with smear results available

Table 9: Countries of birth of whole genome sequenced cases, 2018

	Clustered		Not clustered		Relative risk
	N	%	N	%	
Total number of cases	**33**	**100%**	**331**	**100%**	
India	0	0%	49	15%	RR = 0.85 (CI 0.81 to 0.89) p = 0.001
Philippines	3	9%	36	11%	RR = 0.98 (CI 0.87 to 1.10) p = 1.00
Nepal	9	27%	32	10%	RR = 1.23 (CI 1.00 to 1.51) p = 0.003
Vietnam	3	9%	37	11%	RR = 0.97 (CI 0.87 to 1.09) p = 1.00
China	1	3%	37	11%	RR = 0.91 (CI 0.85 to 0.98) p = 0.15
Australia	6	18%	14	4%	RR = 1.17 (CI 1.00 to 1.38) p = 0.0008
Indonesia	1	3%	23	7%	RR = 0.96 (CI 0.90 to 1.03) p = 0.71
Thailand	1	3%	9	3%	RR = 1.00 (CI 0.94 to 1.07) p = 1.00
Afghanistan	0	0%	9	3%	RR = 0.97 (CI 0.96 to 0.99) p = 1.00
Bangladesh	0	0%	6	2%	RR = 0.98 (CI 0.97 to 0.99) p = 1.00
Pakistan	0	0%	5	2%	RR = 0.98 (CI 0.97 to 1.00) p = 1.00

*RR = Relative Risk, CI = Confidence Interval

The 33 clustered cases were in 24 different clusters ranging in time from 2014 to 2018. Eleven clusters (46%) were confined to transmission of infection within the household or among known casual contacts. These clusters tended to contain a small number of cases. There were five clusters (21%) resulting from household transmission plus casual contact and/ or community transmission. These clusters were larger in the number of cases and investigations into the epidemiological links are ongoing. Two clusters (8%) involved community transmission only. There were four (17%) clusters where the epidemiological links were unknown at the time of reporting. There was one new cases added to the North Coast cluster (cluster 14-0003), this has been described elsewhere [6, 7] and one new case from a cluster from the early 2000's, this case was considered to be a relapse and not a result of ongoing transmission (Table 10).

These classifications are subject to change as new cases are added to the clusters. There were two clusters identified in 2018 that were attributed to laboratory cross contamination. These clusters were excluded from further analysis.

Table 10: Whole genome clusters with 2018 cases*

Cluster name	Year cluster detected	Number of 2018 cases	Year of first case	Total number of cases	SNP differences	Epidemiological links#	Epidemiological links description#
14-0002	2014	1	2011	7	0 - 8	B, C, D	Household & community
14-0003	2007	1	2000	42	0 - 7	B, C, D	Household, casual & community
16-0003	2016	1	2016	4	0 - 2	A	Household
16-0006	2016	1	2013	10	0	B, C, D	Household & community
16-0007	2019	1	2015	3	1 - 3	B, C	Household & casual
17-0007	2017	1	2016	3	0	B, C	Casual & community
17-0009	2017	1	2015	11	0 - 2	B, C, D	Household & community
17-0013	2017	1	2016	2	0	A	Household
18-0001	2018	3	2013	7	0 - 9	B, C, D	Household, casual & community
18-0002	2018	1	2017	2	0	A	Household
18-0003	2018	1	2017	2	0	A	Household
18-0004	2018	1	2016	2	0	A	Household
18-0005	2018	1	2016	2	0	C	Community
18-0006	2018	1	2012	6	0 - 6	C, D	Community
18-0007	2018	1	2017	2	2	D	Unknown
18-0008	2018	1	2017	2	0	A	Household
18-0009	2018	2	2018	2	0	A	Casual
18-0011	2018	2	2018	2	1	A	Household
18-0012	2018	1	2017	2	2	A	Household
18-0013	2018	2	2018	2	4	D	Unknown
18-0014	2018	1	2016	2	5	A	Household
18-0015	2018	3	2018	3	0	D	Unknown
18-0016	2018	3	2018	3	0	D	Unknown

*Exclude clinically diagnosed cases or cases without WGS links. Excludes cluster MTB-14-0001 as 2018 case was a relapse and not a result of ongoing transmission

#Epidemiological links	#Epidemiological links description
A. Confirmed epidemiological links all cases; B. Confirmed epidemiological links some cases; C. Plausible community transmission (when the index case was infectious it is plausible that they could have transmitted their infection to another member, or members, of the cluster in a place where both cases were known to have been); D. Unable to be determined.	Household contacts – Cases who live together in the same house. Casual contacts – Cases who either know each other socially or have come into contact with each other in other casual situations such as in a public place, workplace, or educational facility. Community contacts – Cases with no known social or casual links but transmission is plausible based on based on the infectious period of the index case and travel to a common place Unknown – epidemiological links are unknown

Section 4: Outcomes

Clinical Outcomes

Clinical outcomes are reported for cases diagnosed in the previous year (for non MDR-TB cases) or two years previously (for MDR-TB cases) to allow time for treatment completion. Clinical outcomes for non MDR-TB cases from 2017 and MDR-TB cases from 2016 are recorded in Table 8. Of the non-MDR 2017 cases 89% (n=477) completed treatment, consisting of 7% (n=37) who were considered cured (culture positive prior to treatment and culture negative after completion of treatment) and 93% (n=442) who completed treatment (without demonstration of cure). There were no TB-related deaths reported. Thirteen cases (2%) defaulted before completion of treatment; the remainder had either transferred overseas, died of a non-TB related cause, were continuing on treatment at the time of analysis, or outcome was unknown.

Of those cases in 2017 where the outcome was known (excluding continues on treatment, transferred overseas, died unrelated or unknown if related to TB and outcome unknown), 96% of cases successfully completed treatment.

Of the four cases classified as MDR-TB in 2016, 100% completed treatment.

96%

Proportion of cases with a successful outcome in 2017

100%

Proportion of successfully treated MDR-TB cases in 2016

Table 8: Clinical outcomes of non MDR-TB cases diagnosed in 2017 and MDR-TB cases diagnosed in 2016*

		Year of diagnosis	
		2017 Non MDR cases	**2016 MDR-TB**
Total cases		**534**	**4**
Alive	Completed treatment	442 (83%)	4 (100%)
	Cured	35 (7%)	-
	Defaulted	13 (2%)	-
	Continues on treatment	1 (<1%)	-
	Transferred overseas	15 (3%)	-
	Treatment failure	1 (<1%)	-
	Outcome unknown	0 (0%)	-
Died	Cause related to TB	0 (0%)	-
	Unrelated to TB	22 (4%)	-
	Unknown if related to TB	4 (1%)	-
Outcome unknown		1 (<1%)	-

*Outcome data are reported for the year prior for non MDR cases and 2 years prior for MDR cases to allow time for treatment completion

Contact Investigations

Of the 508 TB notifications received in 2018, 95% (n= 482) had contact information completed in NCIMS at the time of analysis. A total of 2,914 contacts had been identified and of these, 60% (n=1,752) were recorded to have completed screening. Of the 1,752 contacts screened, 1% (n=11) were found to have TB disease, 3% (n=52) had a tuberculin skin test (TST) or interferon gamma release assay (IGRA) conversion (indicating likely acquisition of tuberculosis infection from the case patient), and 19% (n=334) had a positive TST result on initial screening (indicating likely tuberculosis infection earlier in their life). Of those with a positive TST 94% (n=315) had a risk factor for TB other than recent exposure to the infectious case (such as having been born in, or spent greater than three months in a TB high risk country). There were 112 (6%) contacts commenced on preventative treatment.

The median number of contacts per case was two (range 0-315), and 5% (n=26) of contact investigations involved more than 20 contacts.

95%	2,914	60%
Proportion of NSW TB cases, 2018, with contact information recorded	**Total contacts identified 2018**	**Proportion of identified contacts completing screening, 2018**

There were 116 sputum or respiratory smear positive cases notified in 2018, these cases are generally considered to be more infectious than smear negative cases. Over 96% of smear positive cases (n=111) had contact information available identifying 1602 contacts. Of these contacts, 936 (58%) were recorded as having completed screening where 3 (<1%) were found to have active TB disease, 40 (2%) had TST conversion, and 177 (11%) had a positive TST result on initial screening. There were 64 (4%) contacts commenced on preventative treatment.

Section 5: Discussion

Following a decline in the 2012-2015 period, TB notifications in NSW increased in 2016 and 2017 and decreased slightly in 2018; consistent with national trends [2]. The notification rate of TB in NSW also decreased slightly compared with 2017 and was consistent with rates seen in the previous ten-year period from 2002 to 2011. The majority of TB cases in NSW continue to occur in persons born overseas, particularly among those born in countries with a high incidence of TB. The burden of TB disease in NSW is concentrated in local health districts with large populations of migrants from countries in the South-East Asian and Western Pacific regions; reflective of both the global epidemiology of TB, and current trends in migration patterns. The rate of TB in NSW remains low by global comparison [2].

The proportion of Australian born cases of TB remained steady at just under 10%. The notification rate in the Australian born non-Indigenous population has remained relatively steady for more than a decade and has decreased over the last three years. The rate in Australian born Aboriginal and Torres Strait Islander people in NSW is on average 3.5 times higher than in non-Indigenous Australian born people over the past 10 years. This has also decreased over the last three years to 1.2 cases per 100,000 in 2018, the lowest rate in the last 10 years.

Risk factors reported among NSW TB cases in 2018 were similar to those reported in previous years in NSW and nationally. Birth or previous residence longer than three months in a TB high risk country remain the most commonly reported risk factors.

Drug resistance, including multi-drug resistance and mono-resistance to isoniazid and rifampicin, continues to pose a challenge to the control and management of TB, both globally and within NSW. There has been no statistically significant change to the proportions of drug resistant cases as a group or to individual drugs over a 10 year period in NSW. Monitoring and review of NSW TB cases identified as drug resistant continues to be a priority of the NSW TB Program.

The proportion of NSW TB cases tested for HIV at the time of diagnosis continues to increase, with 90% tested in 2018. The prevalence of HIV among NSW TB cases remains low, with one per cent of cases tested found to have HIV.

Routine WGS of all culture positive TB isolates has been occurring in NSW since October 2016. All pulmonary isolates from between January 2013 and October 2016 are also in the process of being sequenced. Over time, as the number of sequenced cases increases more WGS clusters are likely to be identified.

Many of the clusters with 2018 cases are still under investigation. Results so far has found that clustered cases are more likely to have infectious pulmonary disease than not clustered cases. Additionally, cases born in Australia or Nepal are more likely be to part of a cluster then those born in any of the other top 10 countries of birth for 2018. Interestingly, none of the 2018 clustered cases were born in India, the number one country of birth for all TB cases. Analysis of WGS clusters identified so far is indicating that there may be more local transmission of TB than previously thought.

Ninety six per cent of non MDR-TB cases in 2017 successfully completed treatment (excluding continues on treatment, transferred overseas died unrelated or unknown if related to TB and outcome unknown). Mortality among NSW TB cases remained stable (5%), there were no cases reported to have died due to TB in 2017. NSW continued to see low rates of treatment default (2%) and treatment failure (<1%), among TB cases in 2017. One case

diagnosed in 2017 was reported as still being on treatment; this is because of extended treatment due to extensive disease. All four MDR-TB cases in 2016 successfully completed treatment.

Despite the low incidence, TB control in Australia remains an ongoing challenge. TB control cannot be viewed in the context of one country alone, and the global epidemiology of this disease has significant impact on control measures in low incidence countries, due to increasing international travel to and migration from high incidence countries. This is particularly true for Australia as 62% of incident TB cases globally in 2017 occurred in the Western Pacific, and South East Asian regions [1]

Conclusion:

Whilst the number of TB cases in NSW decreased in 2018 when compared to 2017, it was still one of the highest number of cases reported over the past 20 years. It is important to remember that although the number of cases and notification rate in NSW and Australia remain low compared to global incidence, the control and elimination of TB in an individual country must be considered in the context of the global epidemiology of TB. Increasing rates of travel and migration from high burden countries remains one of the ongoing challenges to TB elimination in Australia.

The WHO END TB strategy calls for a 20% reduction in incident cases of TB by 2020 compared to 2015. The NSW TB Program, along with the network of around the state remains dedicated to managing and preventing TB within our borders, through timely and appropriate identification and management of cases, and their contacts.

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