

Tuberculosis in New South Wales

Surveillance Report 2020



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Summary

- There were 625 tuberculosis (TB) cases notified in New South Wales (NSW) in 2020, 6% higher than the number of cases notified in 2019.
- Notification rate was 7.6 cases per 100,000 population per year. This is the highest notification rate in NSW in the past twenty-years.
- Overseas born TB cases accounted for 571 cases (92%). The most frequently reported countries of birth were India, Nepal and the Philippines.
- Migration changes to Australia due to COVID-19 pandemic related border closures and a subsequent decline in immigration referrals received by the NSW TB program did not have an immediate impact on TB numbers. This is in line with data suggesting a median time of 4 years from emigration to diagnosis.
- Of the 53 Australian born cases, six (11%) identified as Aboriginal or Torres Strait Islander people.
- The rate in Aboriginal and Torres Strait Islander people in NSW is on average 2.5 times higher than in non-Indigenous Australian born people over the past 10 years, this is lower than the national difference which is five to six times higher on average.
- Notification rates were highest in Western Sydney and Sydney Local Health Districts (LHDs).
- The most frequently reported risk factors were being born, or past residence (≥ 3 months), in a high-risk country for TB; known contact with TB; or having an immunosuppressive health condition or being on immunosuppressive therapy.
- 459 cases (73%) were laboratory confirmed by culture or polymerase chain reaction (PCR), with 166 cases (27%) receiving a clinical diagnosis only.
- Of those cases with laboratory confirmation, 7 cases were classified as having multi-drug resistant TB (MDR-TB), no cases had extensively drug resistant TB (XDR-TB). This represents 2% of culture confirmed cases and is consistent with previous years.
- Over the past ten years the proportion of cases detected through screening has significantly increased, demonstrating the impact of immigration and contact screening programmes on early detection of TB.
- The number of cases and notification rate in NSW and Australia remain low compared to global incidence, however, the control and elimination of TB in an individual country must be considered in the context of the global epidemiology of TB.

	2020	Change since 2019
TB cases (number)	625	↑ 6% (n=590)
TB notification rate	7.6 per 100,000	↑ 4% (7.3 per 100,000)
Australian born non-Indigenous cases (number)	47	↑ 5% (n=41)
Australian born non-Indigenous rate	0.8 per 100,000	↑ 14% (0.7 per 100,000)
Australian born Aboriginal cases (number)	6	↑ 200% (n=2)
Australian born Aboriginal notification rate	2.4 per 100,000	↑ 242% (0.7 per 100,000)
MDR-TB cases	7	↓ 36% (n=11)
% cases tested for HIV at diagnosis	92%	0% (92%)



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 5.8 million new cases in 2020, an 18% decline from 2019 with potential delayed diagnosis due to the global COVID-19 pandemic [1]. Drug resistant TB is an increasing threat globally, with over 157,000 cases of drug resistant TB (rifampicin-resistant, multi drug resistant [MDR-TB], pre-XDR, or XDR) worldwide in 2020, of which 16% had pre-XDR or XDR TB [1].

Australia continues to have a low incidence of TB, with the Commonwealth Department of Health reporting a rate of 6.3 cases per 100,000 population in 2020 [2]. In contrast with global trends, the incidence of TB reported in NSW in 2020 increased which is most likely attributable to immigration trends in preceding years. Mortality from TB in Australia is very low with 1% of cases reported to have died from TB in 2017 [3].

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 2020.

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

Methods

Data were extracted from the Notifiable Conditions Information Management System (NCIMS) on 17 November 2021 for all confirmed cases of TB notified from 1 January 2001 to 31 December 2020. 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 (SAPHaRI).

Phenotypic drug susceptibility testing was performed at the NSW Mycobacterium Reference Laboratory using the modified proportion method with the Bactec MGIT 960 system (Becton Dickinson), in liquid culture media. Isolates were tested at World Health Organization (WHO) defined critical concentrations for anti-mycobacterial agents. All isolates received phenotypic testing for isoniazid, rifampicin, pyrazinamide and ethambutol; second-line agents were tested for MDR-TB isolates, and upon clinician request. Select isolates also received testing for pyrazinamide susceptibility using Wayne's pyrazinamide assay. When phenotypic drug susceptibility was unavailable drug resistance was determined by SNP calling using Snippy with inhouse scripts and CRYPTIC database for mutations associated with drug resistance.

High quality DNA of *M. tuberculosis* was extracted from positive cultures for whole genome sequencing 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. Cluster detection was determined by SNP difference through Reddog pipeline. Cases were considered clustered if there was less than 12 SNPs difference between cases. Only cases notified in 2020 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 data categories. Notification rates for TB by LHD of residence, and country of birth, were calculated and mapped using R (R core team, Vienna, Austria, 2018). The TB notification rate by country of birth was calculated utilising the 2016 ABS Census Data with country of birth for NSW residents as a denominator. Data were analysed using SAS® Enterprise Guide® (version 8.3, SAS Institute, Cary, NC, USA). The chi squared test was used for cell 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

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.

Default is when a person did not commence treatment or ceased treatment early either by own choice or by the recommendation of the treating medical team.

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

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].

High risk countries are those with an annual TB incidence of 40 cases per 100,000 population per year or more in 2019 [2].

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.

Medical default is a person who ceased treatment early on the recommendation of the treating medical team.

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

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

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

Pre-extensively drug-resistant TB (pre-XDR-TB) are cases in which isolates demonstrated resistance to isoniazid and rifampicin, as well as additional resistance to any fluoroquinolone or at least one injectable second-line drug (capreomycin, kanamycin or amikacin) but not both [5].

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

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.

SNP Single nucleotide polymorphisms.

Unauthorized person is an unlawful non-citizen

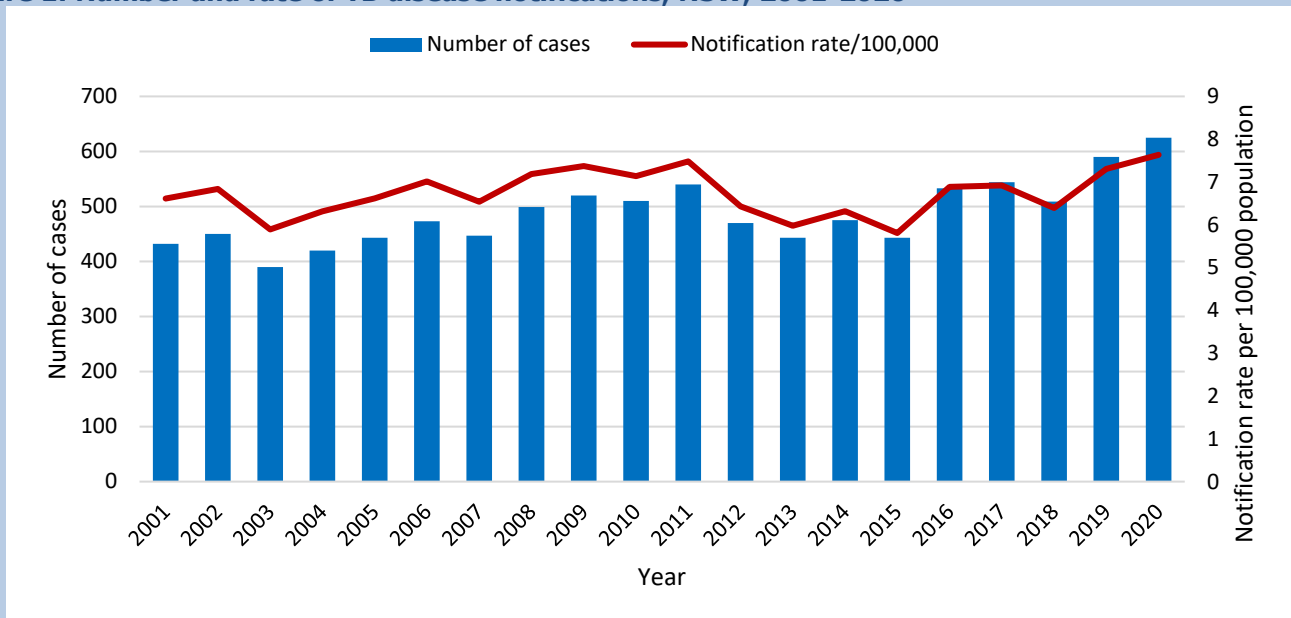
Visitor is a person entering Australia temporarily for tourism, to visit family and friends, to undergo pre-arranged medical treatment or for business related purposes.

Section 1: Demographics

There were 625 notified cases of TB in 2020 in NSW (Figure 1). These cases comprised 39% of the total notified cases in Australia in 2020 (1613 cases) [6]. 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 2020 was 6% higher than the number notified in 2019 (590 cases). The number was the highest number of cases notified in a year in the past 20 years (Figure 1).

The annual notification rate of TB in 2020 in NSW was 7.6 cases per 100,000 population per year. This is the highest notification rate of the past 20 years (Figure 1).

Figure 1: Number and rate of TB disease notifications, NSW, 2001-2020



2020

625

Number of cases notified

7.6

Rate per 100,000 population

Demographics

Of the 625 cases of TB notified in 2020, 56% of cases were male (n=348). The median age among males was 38 years (range 1-99 years); while the median age among females was 34 years (range 9 months-93 years). The median age overall was 36 years (range 9 months-99 years).

Over half of the cases notified were aged between 20 and 39 years (n=322) with a peak in the number of cases in the 25-29 year age group (n=102, rate=18.3 cases per 100,000). A second peak in the notification rate was observed in those aged 70-74 years (n=35, rate=9.9 cases per 100,000). There were three cases (<1%) in the 0-4 year age group (Figures 2 and 3).

Age and Sex

Sex

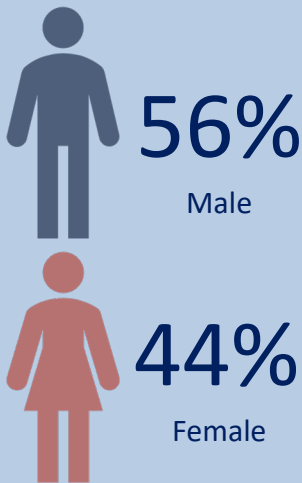
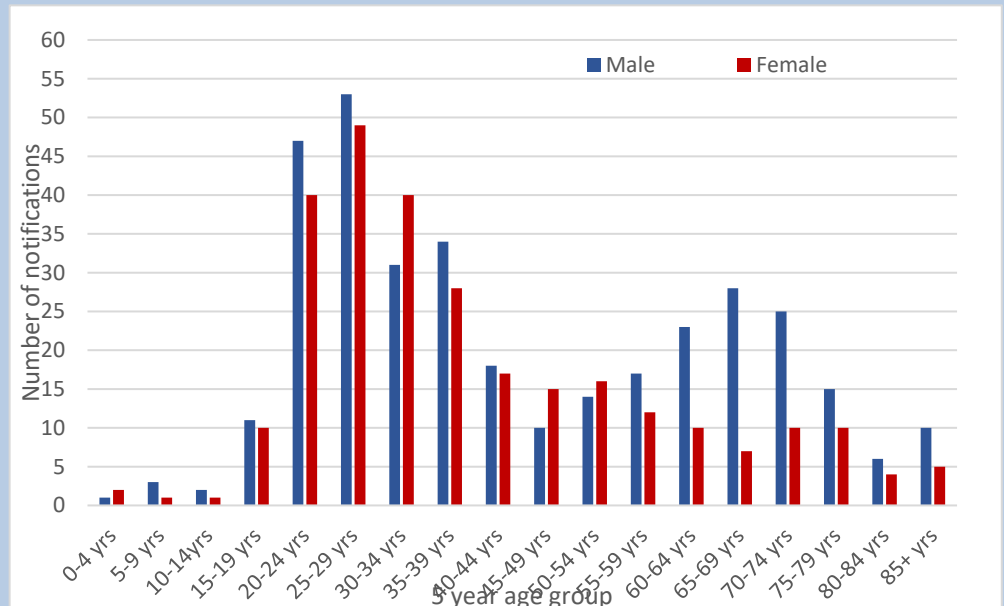


Figure 2: Number of TB notifications by age group and sex, NSW, 2020



Age Overall

Range: 11 months-99 years
Median: 36 years

Age by Sex

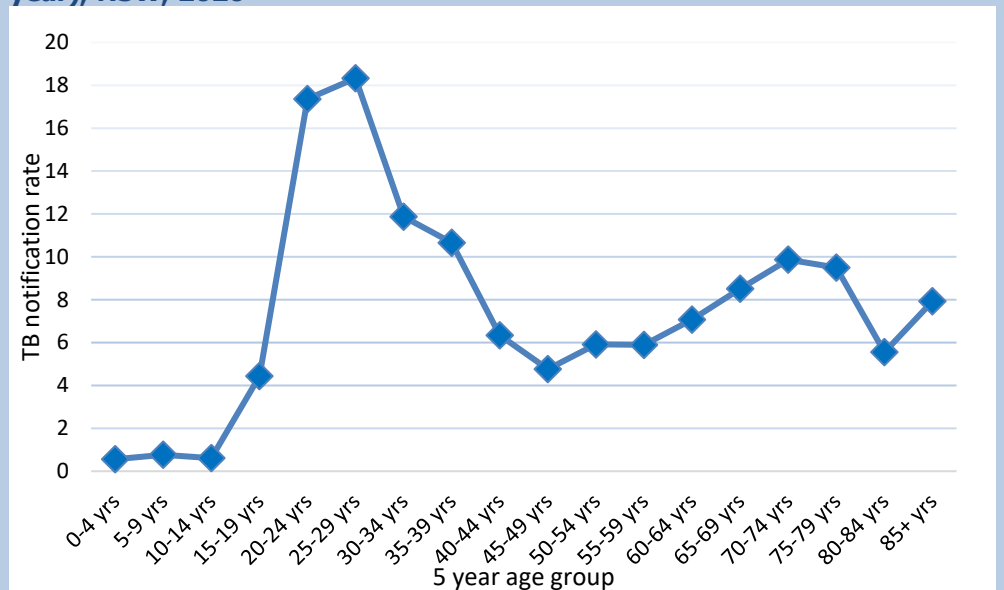
Male

Range: 1-99 years
Median: 38 years

Female

Range: 9 months-93 years
Median: 34 years

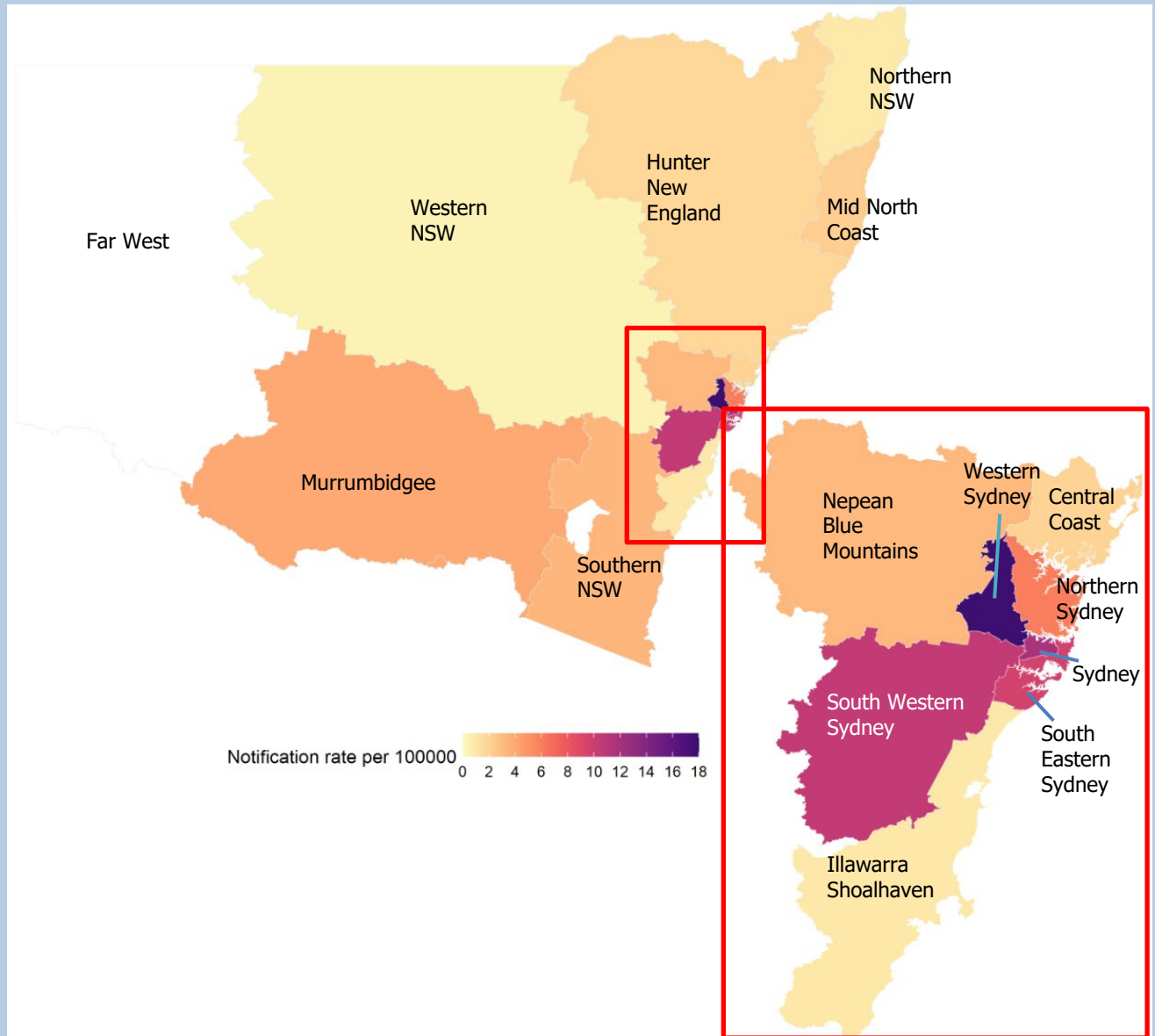
Figure 3: Age specific TB notification rate (per 100,000 population per year), NSW, 2020



Place of residence

Western Sydney LHD had the highest notification rate, with 18.1 cases per 100,000 population per year (n=192), followed by Sydney LHD with 12.3 cases per 100,000 population per year (n=98) (Figure 4). Of the LHDs in rural and regional NSW, Murrumbidgee LHD had the highest rate at 4.0 cases per 100,000 per year (n=11) along with Nepean Blue Mountains LHD with 3.6 cases per 100,000 population (n=14). 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, 2020



11.8

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

2.0

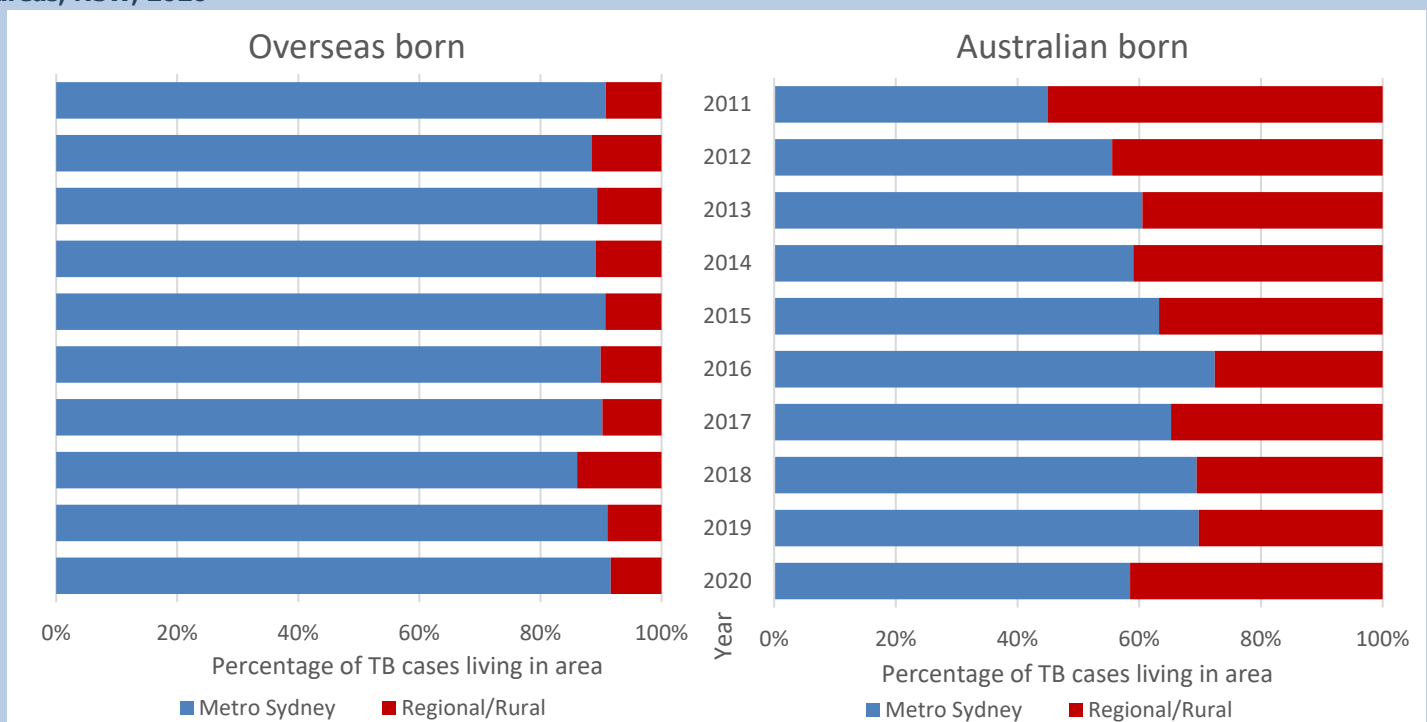
**Rate per 100,000,
Regional/Rural NSW**
(Illawarra Shoalhaven, Central Coast, Nepean Blue Mountains, Far
West, Western NSW, Northern NSW, Mid North Coast, Hunter New
England, Southern NSW and Murrumbidgee LHDs)

Table 1: Age and sex standardised rate of notified TB cases per 100,000 population per year by Local Health District of residence, NSW, 2020

Local Health District	Number	Rate (95% CI)
Western Sydney	192	18.1 (15.6-20.7)
Sydney	98	12.3 (9.8-14.7)
South Western Sydney	110	10.5 (8.5-12.5)
South Eastern Sydney	97	9.4 (7.4-11.1)
Northern Sydney	58	6.2 (4.6-7.8)
Murrumbidgee	11	4.0 (1.6-6.4)
Southern NSW	6	3.4 (0.6-6.2)
Nepean Blue Mountains	14	3.6 (1.7-5.6)
Mid North Coast	5	3.0 (0.3-5.7)
Central Coast	8	2.1 (0.5-3.6)
Hunter New England	17	1.8 (1.0-2.7)
Northern NSW	4	1.0 (0.0-2.0)
Illawarra Shoalhaven	4	0.9 (0.0-1.8)
Western NSW	1	0.5 (0.0-1.4)
Far West	0	0.0

Australian born cases are more likely to reside in regional or rural NSW when compared with overseas born cases. In 2020, 42% (n = 22) of Australian born cases resided in regional or regional NSW compared to 8% (n=48) of overseas born cases. For overseas born TB cases this trend has largely not changed over the past ten years while for Australian born TB cases the number of cases in metropolitan areas fluctuates year to year, the proportion of Australian born cases located in metropolitan areas in 2020 was less than average (Figure 5). Australian born cases in regional or rural NSW were more likely to be older (median 52 years) than Australian born cases in metropolitan areas (median 27 years). The median age for overseas born cases in regional/rural areas was 35 years, and 33 years for metropolitan areas.

Figure 5. Percentage of overseas born and Australian born cases diagnosed in metropolitan and regional/regional areas, NSW, 2020



Country of Birth

In 2020, 92% of cases (n=572) were born overseas. Of these, 96% (n=548) were born in a current high-risk country (HRC) for TB. There were 50 individual countries of birth reported among NSW TB cases (Figure 6), with the most reported countries of birth being India (20%, n=128), Nepal (14%, n = 87), Philippines (12%, n=76), and Vietnam (8%, n=49) (Table 2). The TB notification rate by country of birth was calculated utilising the 2016 ABS Census Data with country of birth for NSW residents as a denominator (Table 2 and Figure 7). Notification rates for the countries with the highest proportion of cases varied from 1.0 cases per 100,000 for Australian born cases to 252.4 per 100,000 for Nepalese born cases. There were three other countries of birth with notification rates greater than 150 per 100,000; however, each country had three or less TB notifications with high rates due to small population numbers (<2,000) in NSW. The total notification rate for all overseas born cases was 30.0 per 100,000 compared to 1.0 per 100,000 for Australian born cases (Table 2).

In 2020 there was a significant increase (p=0.01) in the number of TB cases notified with India as a country of birth and a significant decrease (p=<0.01) in the number of TB cases notified with China as a country of birth (Table 2).

Table 2: Countries of birth of TB cases, NSW, 2020

Country of birth	Number of cases	Change in cases since 2019	Notification rate per country of birth per 100,000 population
India	128 (20%)	↑ 40	83.2
Nepal	87 (14%)	↑ 16	252.4
Philippines	76 (12%)	↑ 4	80.8
Australia	53 (8%)	↑ 10	1.0
Vietnam	49 (8%)	↑ 5	52.7
China (excludes SARs and Taiwan)	45 (7%)	↓ 28	17.6
Indonesia	33 (5%)	↑ 2	96.9
Pakistan	16 (3%)	↑ 9	58.2
Malaysia	15 (2%)	↑ 13	42.9
Bangladesh	12 (2%)	↓ 3	44.1
Other countries	111 (18%)	↓ 33	10.2
Total overseas born	572 (92%)	↑ 25	30.0
Total	625 (100%)	↑ 35	7.6

Figure 6. Number of TB cases by country of birth, NSW, 2020

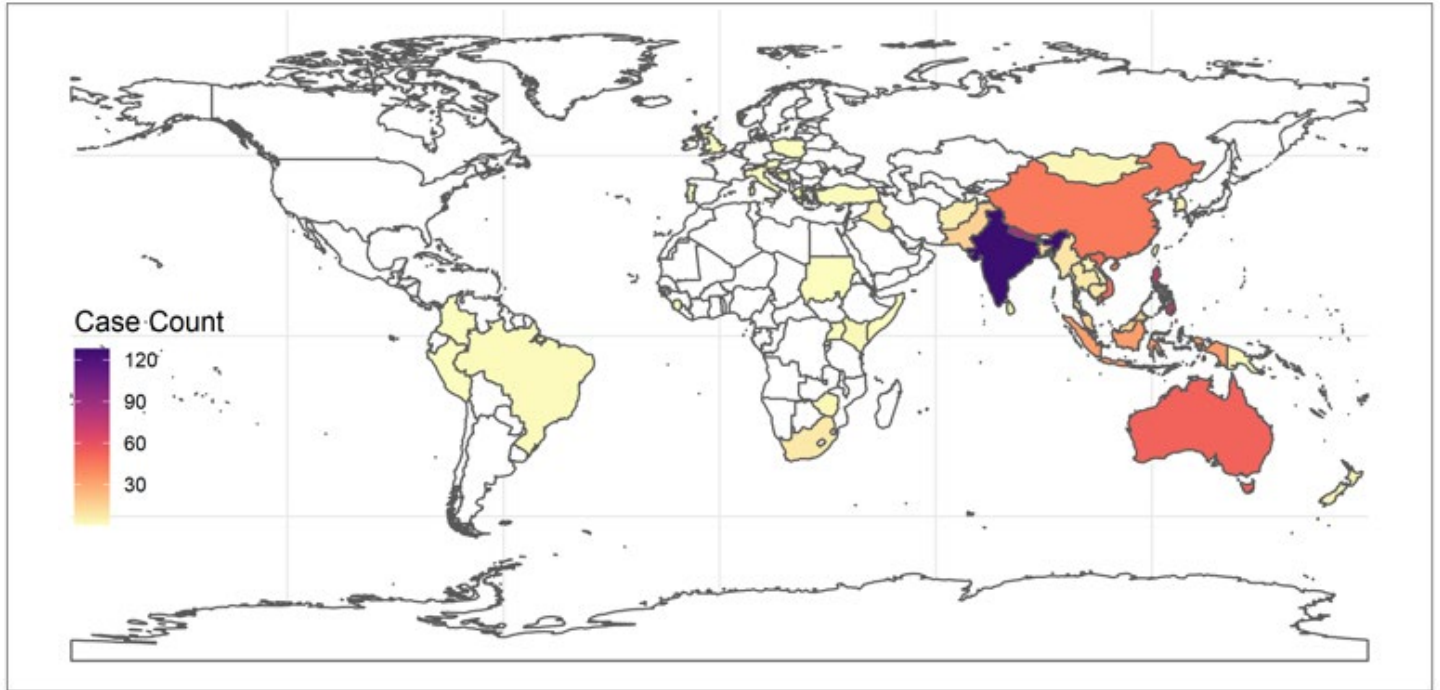
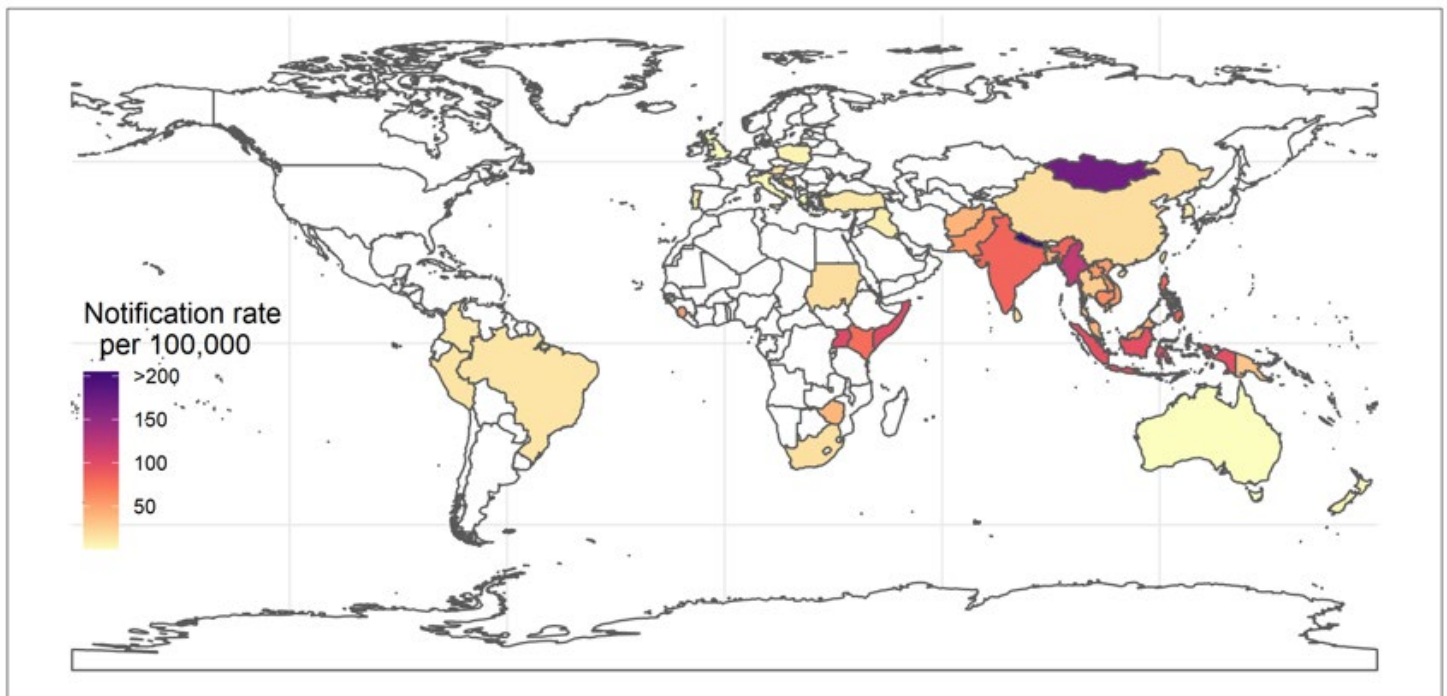


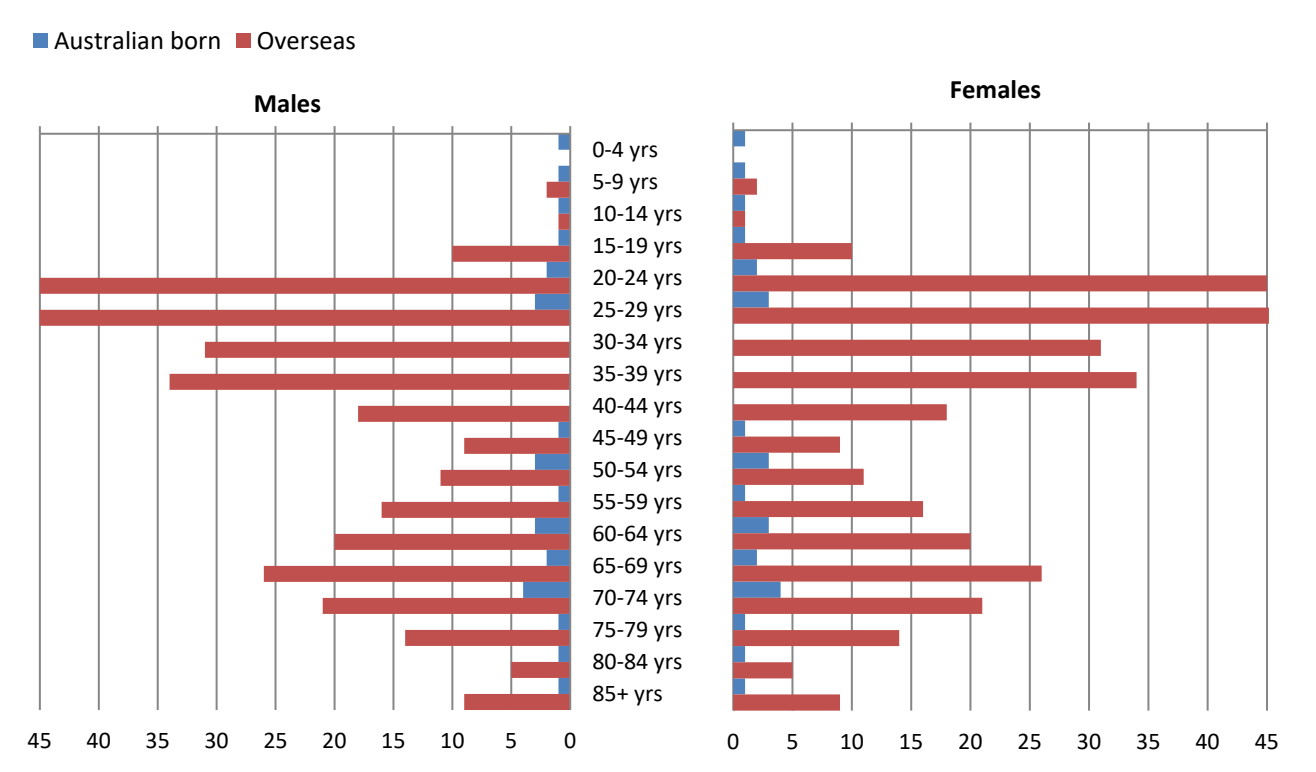
Figure 7. Notification rate of TB cases by country of birth*, NSW, 2020



*Notification rate by country of birth calculated utilising ABS 2016 Census Data for country of birth for residents of NSW

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 2020, the median age at diagnosis for Australian born cases was 46 years; 28 years for females (range 9 months-93 years) and 57 years for males (range 1-94 years). For overseas born cases, the median age at TB diagnosis was 36 years; 34 years for females (range 10-88 years), and 38 years for males (range 8-99 years). Over 50% of overseas born cases were aged between 20 and 39 years at diagnosis (Figure 8).

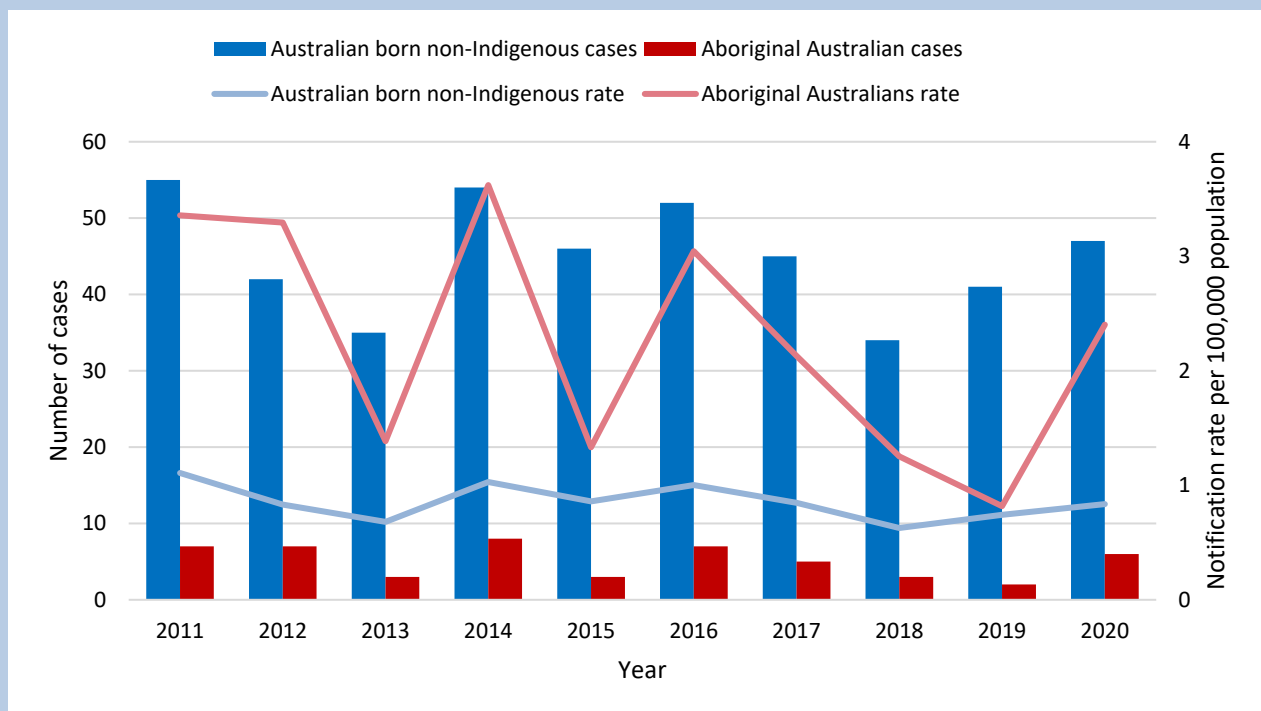
Figure 8: Age group at TB diagnosis, by place of birth and sex, NSW, 2020



Australian born cases

Of the 53 Australian born cases in 2020, six cases (11%) identified as Aboriginal people (Figure 9). The number of TB cases who identify as Aboriginal and Torres Strait Islander people fluctuates from year to year and the number notified in 2020 is more than the average number notified per year ($n=5$) since 2011. The average rate of TB among Aboriginal and Torres Strait Islander people over the past 10 years is over double that of non-Indigenous Australian born cases (RR 2.5, 95% CI 1.8-3.4, $p<0.0001$). In 2020, there remained a statistically significant difference between the rate of TB in Aboriginal and Torres Strait Islander people and non-Indigenous Australian born cases (RR 2.9, 95% CI 1.2-6.7, $p=0.01$).

Figure 9: Number and rate of notified TB in Australian born cases by Aboriginal and Torres Strait Islander status, NSW, 2011-2020



Overseas born cases

Of the 572 overseas born cases in 2020, those who had migrated from a current HRC (as of 2020) for TB (n=548) had a shorter median length of stay in Australia prior to diagnosis of TB (4 years, range 0-69 years) when compared to the other overseas born cases (n=24) (25 years, range 0-61 years) (Figure 10).

Over half of the overseas born cases were permanent residents at the time of diagnosis (n=310, 54%), 23% (n=131) were overseas students, 9% (n=51) were visitors, 1% (n=6) were refugees, <1% (n=1) were unauthorised persons, 12% (n=70) were on other types of visas, and 1% (n=3) had an unknown or missing visa status (Table 3).

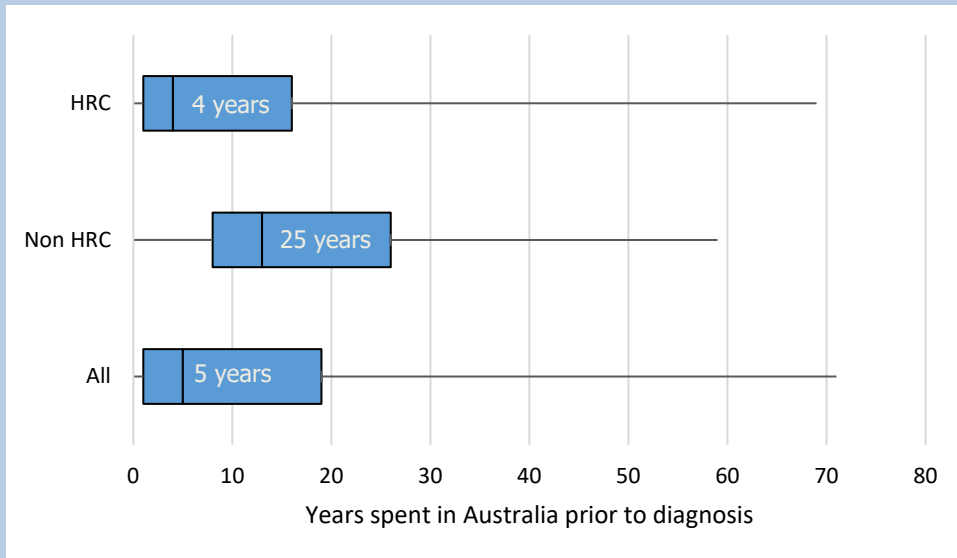
Some Australian visas require the applicant to undergo a medical examination prior to the visa being granted. These include all permanent visa applicants, and some temporary visa applicants depending on how long they intend to stay in Australia, if they intend to work or study, and their country of origin. If the medical examination shows that the visa applicant might be at increased risk of developing active TB, applicants screened overseas are placed on a TB Health Undertaking (TBU) and applicants that apply or re-apply in Australia are placed on an onshore deferral. Both are required to be followed up by TB services in Australia.

Immigration referrals to the NSW TB Program for patients to undergo screening required for a TBU decreased in 2020 (n=765) compared to the yearly average (n=1732). This is a direct result of reduced immigration to Australia due to border policy changes in response to COVID-19. The number of people referred to the TB program and placed on an onshore deferral in 2020 (n=706) slightly increased from the yearly average (n=651). Due to the COVID-19 pandemic, temporary visitors were allowed to apply for visa renewals, extensions, or a new visa in Australia instead of having to travel overseas. This likely accounts for the increase in these types of referrals.

Of the 572 TB cases born overseas, 18% (n=104) were on a TBU or onshore deferral at the time of diagnosis, a further 4% (n=24) had previously been on a TBU or an onshore deferral, 76% (n=435) had never been on a TBU or onshore deferral and for 2% (n=9) this was unknown (Figure 11). These numbers are consistent with the proportion of overseas born cases diagnosed on an immigration referral in 2019. The proportion of cases diagnosed while on an onshore deferral increased from 12% in 2019 to 14% in 2020 while the number of cases diagnosed while on a TBU decreased from 5% in 2019 to 4% in 2020.

Length of Stay in Australia

Figure 10: Median years spent in Australia prior to TB diagnosis among overseas born cases, by country of birth risk category, NSW, 2020

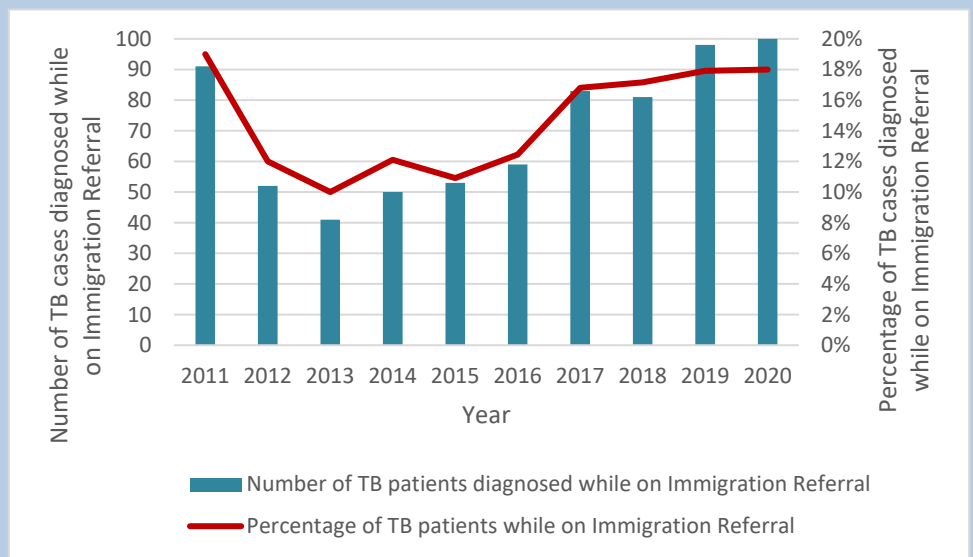


HRC = High risk country (TB incidence >40 cases per 100,000 population per year)

Table 3: Residency status of overseas born TB cases at diagnosis, NSW, 2020

Residency status	Number of cases	Percentage
Permanent resident	310	54%
Overseas student	131	23%
Visitor	51	9%
Refugee / humanitarian entrant	6	1%
Unauthorised person	1	<1%
Other	70	12%
Unknown/ missing status	3	1%
Total	572	100%

Figure 11: TB patients diagnosed while on immigration referral



18%

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

4%

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

Risk Factors

The most reported risk factor for all cases in 2020 was being born overseas in a HRC for TB (89%, n=557). Being 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 a HRC. Having either a household member or another close contact with TB (16%, n=101) and past residence for three months or more in a HRC (15%, n=94) were the next highest reported risk factors. Immunosuppression (due to health condition or medication) was reported by 11% (n=70) of all cases (Table 4). 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 having a household member or close contact with TB (32%, n=17) followed by past residence in a HRC (more than 3 months) (26%, n=14). For overseas born cases, 97% (n=557) 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, 2020

	All cases		Australian born		Overseas born	
	N	%	N	%	N	%
Total	625	100%	53	100%	572	100%
Born in a HRC [^]	557	(89%)	-	-	557	(97%)
Household member or close contact with TB	101	(16%)	17	(32%)	84	(15%)
Past residence (≥3 months) in a HRC	94	(15%)	11	(18%)	83	(15%)
Immunosuppressive health condition/therapy	70	(11%)	14	(26%)	56	(10%)
Previously diagnosed with TB	35	(6%)	2	(4%)	33	(6%)
Ever employed in healthcare	33	(5%)	6	(11%)	27	(5%)
CXR suggestive of old untreated TB	20	(3%)	0	(0%)	20	(3%)
Other	11	(2%)	6	(11%)	5	(1%)
Australian born child of parent(s) born in HRC	7	(1%)	7	(13%)	-	-
Ever resided in a correctional facility	2	(<1%)	2	(4%)	0	(0%)
Ever homeless/residing in a shelter	1	(<1%)	0	(0%)	1	(<1%)
Ever employed in an institution	1	(<1%)	1	(2%)	0	(0%)
Not able to be determined	11	(2%)	9	(17%)	2	(<1%)

*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

Household member or close contact with TB

2nd

Immunosuppressive health condition/therapy

3rd

≥3 months spent in a high risk country

Overseas born cases

1st

Born in a high risk country

2nd

Household member or close contact with TB

3rd

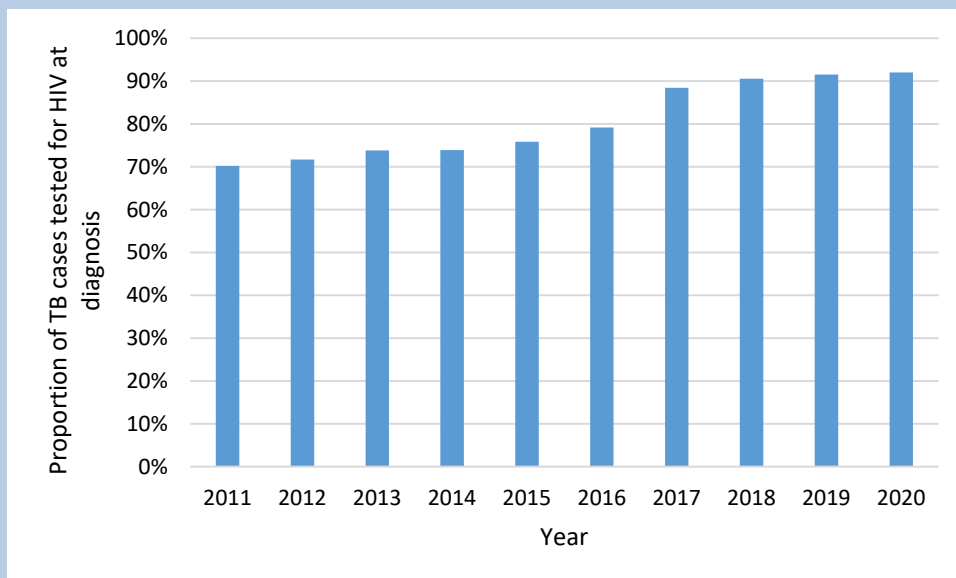
≥3 months spent in a high risk country

HIV Testing

Over the 10 year period to 2020, there has been a 22% increase in the proportion of TB cases tested for HIV at the time of TB diagnosis, from 70% in 2011 to 92% (n=578) in 2020 (Figure 9). Of cases tested in 2020, 1% (n=5) were co-infected with HIV and TB.

Of the five TB-HIV co-infected cases in 2020, 60% (n=3) were male and all were overseas born (n=5). Only one case (20%) was newly diagnosed with HIV around the same time as TB, four had been previously diagnosed with HIV (80%).

Figure 12: Proportion of TB cases tested for HIV at TB diagnosis, NSW, 2011 – 2020



92%

Proportion of NSW TB cases tested for HIV at diagnosis



5

Number of NSW TB cases co-infected with HIV

100%

Target for TB cases tested for HIV at diagnosis

Section 2: Clinical Presentation

Site of Infection

In 2020, 64% (n = 398) of all cases had pulmonary involvement. Fifty-five per cent of cases (n=344) had pulmonary disease only, a further 9% (n=54) had pulmonary disease plus other sites. Extrapulmonary TB only was reported for 36% (n=227) of cases (Figure 13). Of extrapulmonary sites reported, lymph node was the most common (n = 116, 45% of cases with extrapulmonary involvement), followed by infection of the pleura (n=35, 14%) and infection of the gastrointestinal tract (n=20, 8%) (Table 5).

Figure 13: Site of disease for NSW TB cases, 2020

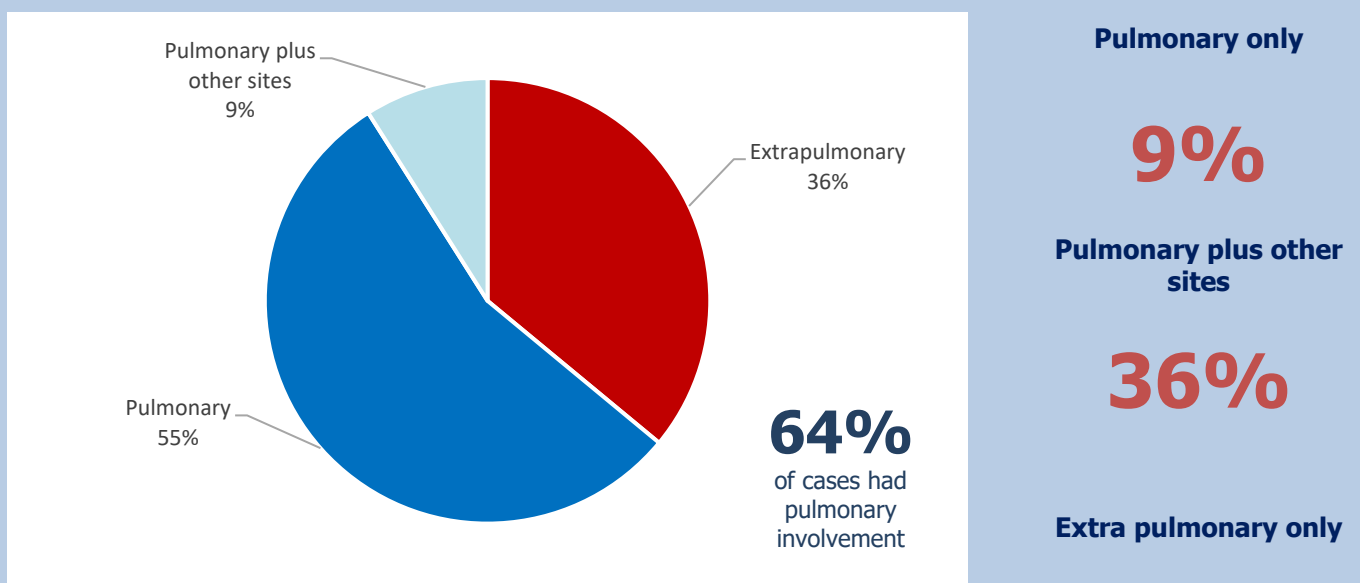


Table 5: Extrapulmonary sites* of infection for NSW TB cases with extrapulmonary involvement, 2020

Site	Number of cases	Percentage
Lymph node	141	50%
Pleura	42	15%
Eye	21	7%
Other	20	7%
Gastrointestinal tract	18	6%
Bone	12	4%
Brain/central nervous system/meninges, dural sinus, choroid plexus	10	4%
Disseminated disease	10	5%
Joints (synovial fluid)	10	4%
Genitourinary tract	9	3%
Spinal Cord	7	2%
Skin	5	2%

*Multiple sites can be recorded

Clinical Presentation and Treatment

Of the 625 cases notified in 2020, 95% (n=591) were new diagnoses of TB; while 5% (n=33) were classified as a TB recurrence, following treatment either in Australia (1%, n=7) or overseas (4%, n=26) (Table 6). TB recurrences may either be due to relapse or reinfection.

Most cases notified in NSW in 2020 (n=415, 66%) were tested for TB as part of an investigation of clinical symptoms. An additional 146 cases (23%) were tested for TB due to screening, while only 12 cases (2%) were identified via contact investigation. The proportion of cases detected while symptomatic has significantly decreased by 7% ($p < 0.0001$) over the past ten years, while the proportion of cases detected through screening has increased by 9% ($p < 0.0001$) (Figure 14).

The median time from first health contact to treatment for Australian born cases was 32 days (range 0 – 249 days), and 21 days (range 0 – 2957 days) for overseas born cases. Cases with pulmonary involvement were commenced on treatment sooner (19 days, range 0 – 2957 days) than those cases with extrapulmonary disease only (24 days, range 0 - 1439 days). Only two pulmonary cases in 2020, had a delay in diagnosis while symptomatic, a case who had a co-morbid diagnosis of melanoma and lung changes were thought to be related to the cancer diagnosis, and a case with abnormal CT changes incidentally detected who was not followed up.

Almost all cases were commenced on antimicrobial treatment in NSW following diagnosis (99%, n=616). Of the nine cases (1%) who were not commenced on antimicrobial treatment in NSW, six (67%) had died prior to their TB diagnosis, and three (33%) had returned overseas prior to commencing treatment.

Table 6: Disease classification*, NSW TB cases 2020

Disease classification	Number of cases	Percentage
New	591	95%
Recurrence following full treatment only in Australia	6	1%
Recurrence following partial treatment only in Australia	1	<1%
Recurrence following full treatment overseas	20	3%
Recurrence following partial treatment overseas	6	1%
Unknown	1	<1%
Total	625	100%

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

99%

21 days

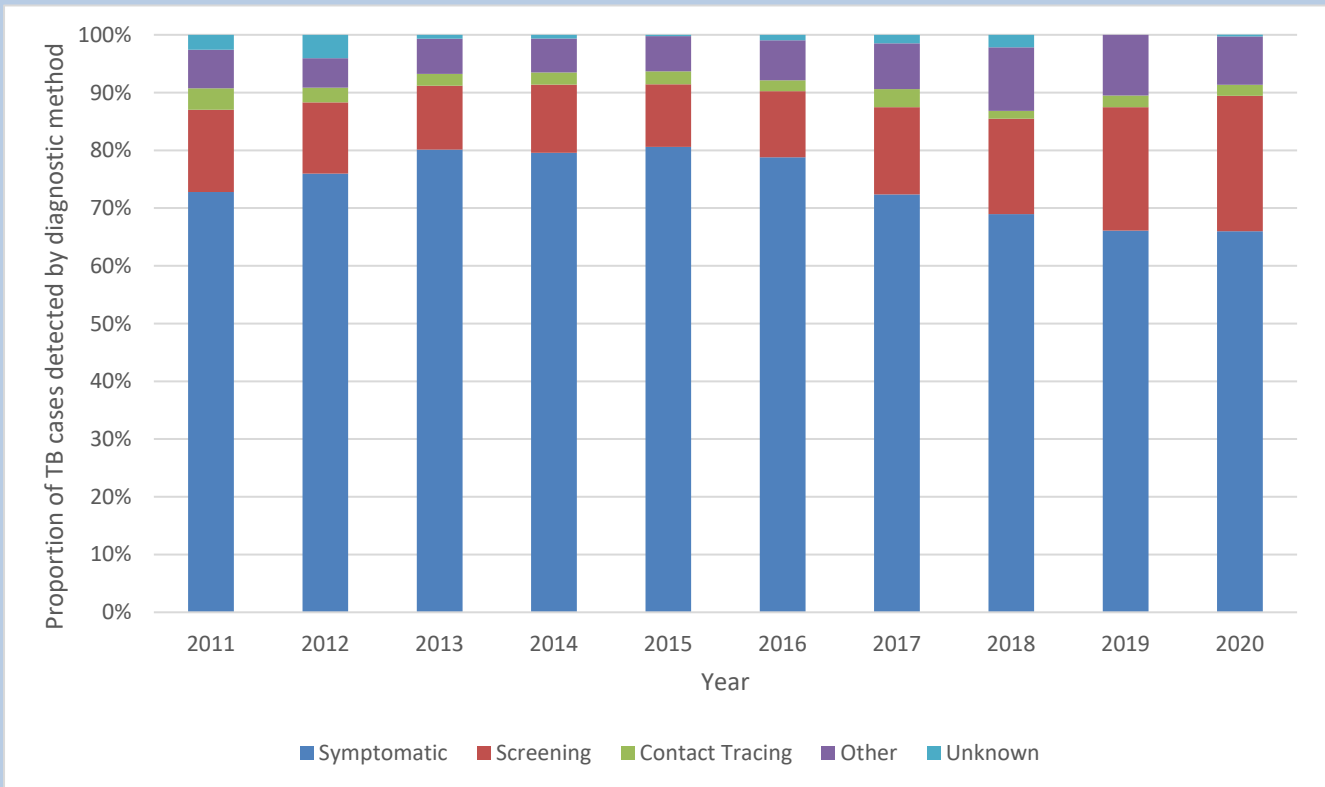
5 days

Proportion of cases commenced on antimicrobial therapy in NSW

Median time to treatment from first health presentation

Difference in median time to treatment between pulmonary and extrapulmonary cases

Figure 14: Proportion of TB cases identified through different detection methods, NSW 2020



66%

Proportion of TB cases identified via investigation of symptomatic disease

23%

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

9%

Increase in NSW TB cases detected through screening since 2011

Section 3: Laboratory

Laboratory Testing

Of the 625 TB cases in 2020, 73% of diagnoses (n=459) were laboratory confirmed; 65% (n=404) were cultured, and 9% diagnosed by polymerase chain reaction (PCR) only (n=55). The remaining 27% of cases (n=166) were diagnosed clinically (Figure 15). Laboratory confirmation was more commonly obtained for pulmonary involvement (78%, n=312), compared to those with extrapulmonary disease only (65%, n=147). A greater proportion of laboratory confirmation by PCR only occurred in extrapulmonary cases (11%, n=25), compared to PCR only confirmation of pulmonary cases (8%, n=30). For the ten-year period to 2020, there has been a significant increase ($p < 0.0001$) in the proportion of cases confirmed using PCR only (Figure 16).

Figure 15: Method of diagnosis of TB, laboratory vs. clinical, NSW, 2020

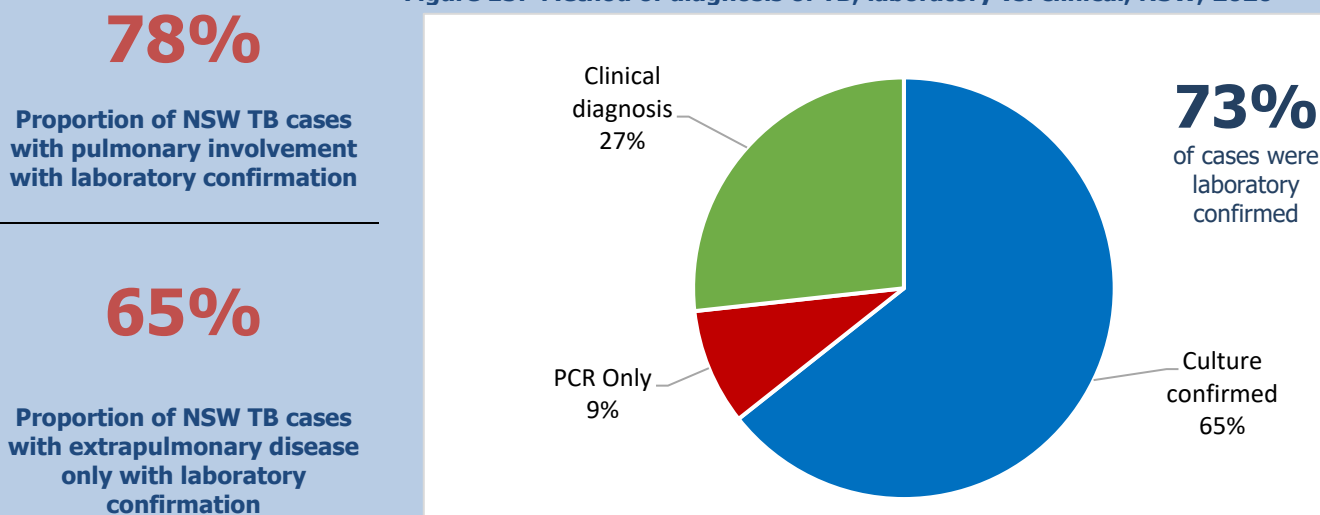
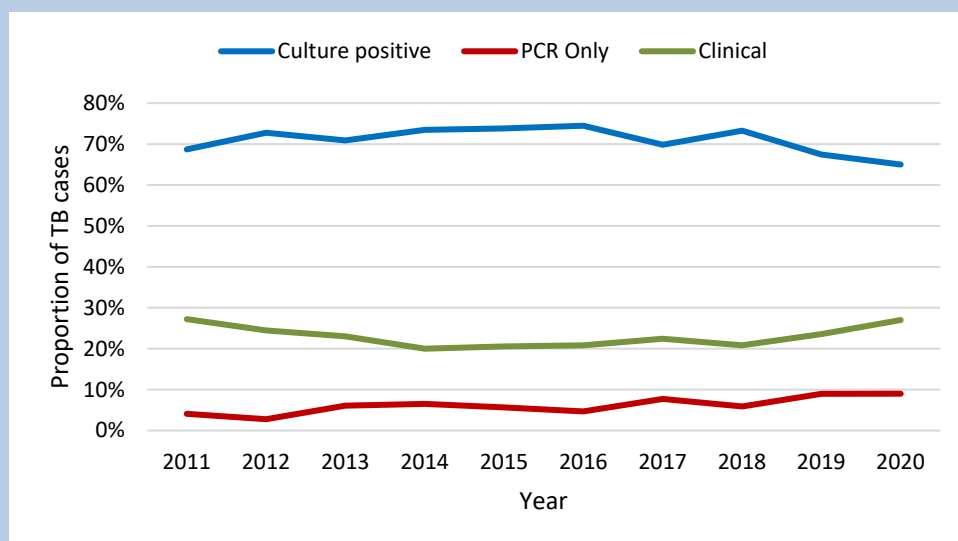


Figure 16: Method of laboratory confirmation of diagnosis of TB cases, NSW, 2011-2020



5%
Increase in diagnoses confirmed by PCR only since 2011

4%
Decrease of diagnoses confirmed by culture since 2011

Drug susceptibility testing (DST)

Of the 404 culture positive TB cases in NSW in 2020, 99% (n=401) had drug susceptibility results reported. Of these, 91% (n=363) were fully susceptible to first line TB drugs, 8% (n=31) were resistant to one or more first line TB drug, and 2% (n=7) were classified as MDR-TB or pre-XDR-TB (Figure 17). These proportions have not significantly changed over the last 10 years (Table 7). The three cases without DST were mixed infections with another mycobacterium which prevented DST from being performed. Of the seven cases classified as MDR-TB, 86% (n=6) were new cases and 14% (n=1) were relapses following treatment overseas. The countries of birth for the MDR-TB cases were Nepal (n=2), China (n=1), Vietnam (n=1), India (n=1), Malaysia (n=1), and Australia (n=1).

91%

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

8%

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

2%

Proportion of culture positive cases which were MDR-TB

Figure 17: Drug susceptibility of culture confirmed cases, NSW, 2011-2020

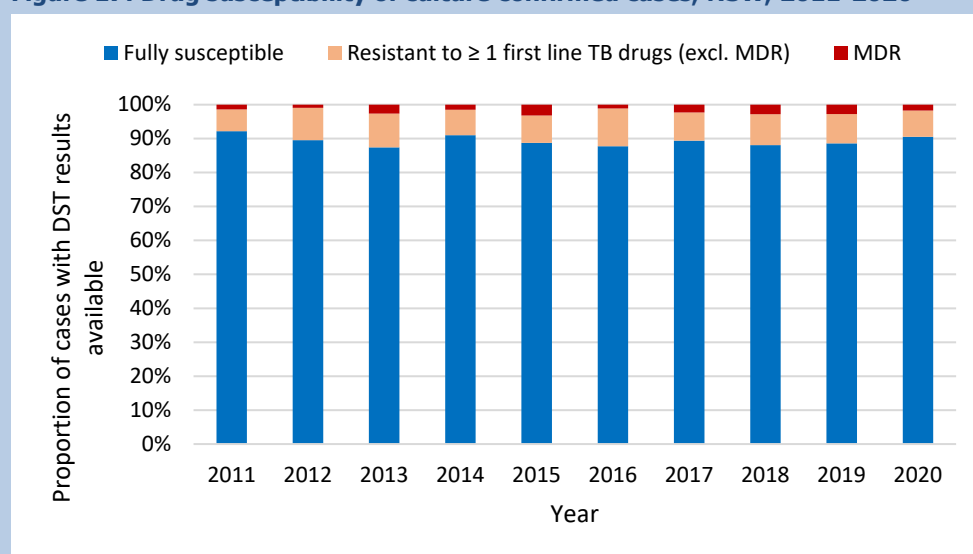


Table 7: Drug susceptibilities of culture confirmed TB cases with DST results available, NSW, 2011-2020

Drug Susceptibility	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Fully susceptible	311 (92%)	283 (90%)	264 (87%)	303 (89%)	276 (89%)	308 (88%)	312 (89%)	311 (88%)	350 (89%)	363 (91%)
Ethambutol	0 (0%)	1 (<1%)	0 (0%)	2 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (<1%)	0 (0%)
Isoniazid	21 (6%)	26 (8%)	23 (8%)	25 (7%)	20 (6%)	35 (10%)	24 (7%)	26 (7%)	28 (7%)	25 (6%)
Pyrazinamide	2 (1%)	2 (1%)	4 (1%)	3 (1%)	1 (<1%)	3 (1%)	5 (1%)	3 (1%)	3 (1%)	2 (<1%)
Rifampicin	0 (0%)	0 (0%)	1 (<1%)	0 (0%)	2 (1%)	0 (0%)	0 (0%)	2 (1%)	0 (0%)	3 (1%)
Resistant to ≥2 first line drugs (but not MDR)	0 (0%)	1 (<1%)	2 (1%)	3 (1%)	2 (1%)	1 (<1%)	0 (0%)	1 (<1%)	1 (<1%)	1 (<1%)
MDR*	5 (1%)	3 (1%)	7 (2%)	4 (1%)	9 (3%)	2 (1%)	8 (2%)	10 (3%)	10 (3%)	5 (1%)
Pre-XDR**	0 (0%)	0 (0%)	1 (<1%)	1 (<1%)	0 (0%)	2 (1%)	0 (0%)	0 (0%)	1 (<1%)	2 (<1%)
XDR***	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (<1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

* Multi Drug Resistant: Resistance to at least Isoniazid AND Rifampicin

**Pre-Extensively Drug Resistant: Resistance to Isoniazid AND Rifampicin, AND any fluoroquinolone OR at least one injectable drug

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

Cluster analysis

In 2020, 395 (98%) of culture positive cases had whole genome sequencing (WGS) performed on one or more isolates. Of these, 30 (8%) were found to be part of a cluster with another TB case notified in NSW from 2020 or earlier. The remaining 365 culture positive cases (92%) were not linked to any other NSW case in or prior to 2020 at the time of analysis.

Of the 30 clustered cases, 21 (70%) were male, the median age was 27 years (range 14-74 years) and 80% (n=24) lived in a metropolitan LHD. Cases with pulmonary involvement accounted for 90% (n=27), with 63% (n=15) with a positive smear on a respiratory specimen, and 10% (n=3) had extrapulmonary disease only.

Of the 365 non-clustered cases, 193 (53%) were male, the median age was 36 years (range 7 -96 years) and 89% (n=324) lived in a metropolitan LHD. Cases with pulmonary involvement accounted for 68% (n=248), with 38% (n=86) with a positive smear on a respiratory specimen, and 32% (n=117) had extrapulmonary disease only.

The top countries of birth for clustered cases were Australia (n=11, 35%) and Nepal (n=3, 10%). For non-clustered cases the top countries of birth were India (n=71, 20%), Nepal (n=50, 14%) and Philippines (n=47, 11%).

Cases with pulmonary involvement were more likely to be clustered than cases with only extrapulmonary involvement (RR 3.21, CI 1.08-9.48; p=0.01). There was no significant difference found regarding gender, Aboriginal and Torres Strait Islander status, residence in a metropolitan or regional/rural LHD, or respiratory smear status.

Cases born in Australia (RR 1.47, CI 1.12 to 1.93; p=<0.01) were more likely to be clustered than cases born in other countries. There was no significant difference found for cases born in other countries analysed (Table 9).

Table 8: Demographic and clinical analysis for whole genome sequenced cases, NSW, 2020

		Clustered		Not clustered		Relative risk
		N	%	N	%	
Cases	Total number of cases	30	100%	365	100%	-
Age	Median age (age range)	27 years (14-74 years)		36 years (7-96 years)		-
Gender	Male	21	70%	193	53%	RR = 1.57 (95% CI 0.90 – 2.74) p = 0.07
	Female	9	30%	172	47%	
Indigenous status (Australian born)	Aboriginal	3	10%	2	1%	RR = 1.11 (95% CI 0.98 – 1.25) p = <0.01
	Not Aboriginal	27	90%	363	99%	
Place of residence	Metropolitan Sydney [#]	24	80%	324	89%	RR = 1.10 (0.92 – 1.33) P = 0.15
	Rural or regional NSW [#]	6	20%	41	11%	
Site of infection	Pulmonary involvement	27	90%	248	68%	RR = 3.21 (95% CI 1.08 – 9.48) p = 0.01
	Extrapulmonary only	3	10%	117	32%	
Respiratory smear positive*	Smear positive	15	63%	86	38%	RR = 1.65 (95% CI 0.98 – 2.80) p = 0.02
	Smear negative	9	37%	140	62%	

[#]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 culture positive cases only with smear results available

Table 9: Countries of birth of whole genome sequenced cases, NSW, 2020

	Clustered		Not clustered		Relative risk
	N	%	N	%	
Total number of cases	30	100%	365	100%	
India	2	(7%)	71	(19%)	RR = 0.86 (95% CI 0.77 – 0.96) p = 0.09
Nepal	3	(10%)	53	(15%)	RR = 0.95 (95% CI 0.84 – 1.08) p = 0.78
Philippines	2	(7%)	47	(13%)	RR = 0.93 (95% CI 0.84 – 1.04) p = 0.56
China	1	(3%)	29	(8%)	RR = 0.95 (95% CI 0.89 – 1.02) p = 0.72
Vietnam	2	(7%)	27	(7%)	RR = 0.99 (95% CI 0.90 – 1.10) p = 1.00
Australia	11	(37%)	25	(7%)	RR = 1.47 (95% CI 1.12 – 1.93) p = <0.01
Indonesia	1	(3%)	21	(6%)	RR = 0.98 (0.91 – 1.05) p = 1.00
Malaysia	2	(7%)	10	(3%)	RR = 1.04 (95% CI 0.95 – 1.15) p = 0.23
Pakistan	0	(0%)	9	(2%)	RR = 0.98 (95% CI 0.96 – 0.99) p = 1.00
Myanmar	0	(0%)	8	(2%)	RR = 0.98 (95% CI 0.96 – 0.99) p = 1.00
Bangladesh	0	(0%)	7	(2%)	RR = 0.98 (95% CI 0.97 – 1.00) p = 1.00
South Africa	1	(3%)	5	(1%)	RR = 1.02 (95% CI 0.95 – 1.09) p = 0.38
Thailand	1	(3%)	5	(1%)	RR = 1.02 (95% CI 0.95 – 1.09) p = 0.38

*RR = Relative Risk, CI = Confidence Interval

The 30 clustered cases were in 20 different clusters ranging in time from first case of 2000 to 2020. There were seven clusters (35%) which had a total of five or more cases diagnosed in 2020 or earlier years. Two of these clusters, 18-0001 and 19-0015 accounted for 30% (n = 9) of clustered cases notified in 2020. There were eight clusters (40%) involving household transmission plus casual contact and/or community transmission. Three clusters (15%) involved community or casual transmission only. There were nine (45%) clusters where the epidemiological links were unknown at the time of reporting, these clustered tended to have a larger number of SNPs (>6) between cases.

There were five cases diagnosed in 2020 in cluster 19-0015 associated with a large metropolitan hospital from a highly infectious patient with extensive pulmonary disease. There has been over 1100 people screened for TB in relation to this cluster.

As of the end of 2020, cluster 18-0001 consisted of 16 cases with WGS available and four clinical cases without WGS. The origin of the cluster is 2012. The cluster began with a case from Ethiopia diagnosed in 2012. Transmission chains were unknown for many earlier cases but did occur among some household and other close contacts. Around 2018 the demographics of the cluster cases changed to consist of predominantly cases from the Pacific Islands. Transmission is occurring predominantly within households and other close contacts. Contact tracing is ongoing to attempt to halt transmission.

Table 10: Whole genome clusters with 2020 cases*

Cluster name	Year cluster detected	Number of 2020 cases	Year of first case	Total number of WGS cases	SNP differences	Epidemiological links#	Epidemiological links description^
14-0003	2007	1	2000	36	0 – 7	B, C, D	Household, casual & community
16-0006	2016	1	2013	13	0-1	B, C, D	Household & community
17-0008	2017	2	2017	7	0-12	B, D	Household & casual
17-0009	2017	1	2015	14	0 – 4	B, C, D	Household & community
18-0001	2018	4	2013	16	0 - 11	B, C, D	Household, casual & community
19-0004	2019	1	2010	9	0-12	B, C, D	Household, casual & community
19-0006	2019	1	2019	2	1-4	D	Unknown
19-0008	2019	1	2019	3	1	B, D	Household & casual
19-0009	2019	1	2017	3	3-10	D	Unknown
19-0014	2019	1	2016	3	0-9	D	Unknown
19-0015	2019	5	2019	7	0-1	B, D	Casual
20-0001	2020	1	2018	2	6	D	Unknown
20-0002	2020	1	2017	2	1	A	Casual
20-0003	2020	1	2019	2	9	D	Unknown
20-0004	2020	1	2019	2	10	D	Unknown
20-0005	2020	1	2019	2	10	D	Unknown
20-0007	2020	1	2019	2	1	D	Unknown
20-0008	2020	2	2020	2	1	A	Household
20-0009	2020	2	2020	2	0	C	Community
20-0010	2020	1	2017	2	7	D	Unknown

*Excludes clinically diagnosed cases or cases without WGS links.

#Epidemiological links	^Epidemiological links description
<ul style="list-style-type: none"> 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. 	<p>Household contacts – Cases who live together in the same house.</p> <p>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.</p> <p>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</p> <p>Unknown – epidemiological links are unknown</p>

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 2019 and MDR-TB cases from 2018 are recorded in Table 11. Of the non-MDR 2019 cases, 88% (n=507) completed treatment, consisting of 7% (n=34) who were considered cured (culture positive prior to treatment and culture negative after completion of treatment) and 93% (n=473) who completed treatment (without demonstration of cure). There were eight TB-related deaths reported. Nineteen cases (3%) defaulted before completion of treatment, of which five were medical defaults. The remaining 8% (n=44) had either transferred overseas, died of a non-TB related cause, or the cause of death was unknown.

Of those cases in 2019 where the outcome was known (excluding transferred overseas, died unrelated or unknown if related to TB and outcome unknown), 95% of cases successfully completed treatment.

Of the ten cases classified as MDR-TB in 2018, 100% (n=10) successfully completed treatment.

95%

Proportion of cases with a successful outcome in 2019

100%

Proportion of successfully treated MDR-TB cases in 2018

Table 11: Clinical outcomes of non MDR-TB cases diagnosed in 2019 and MDR-TB cases diagnosed in 2018*

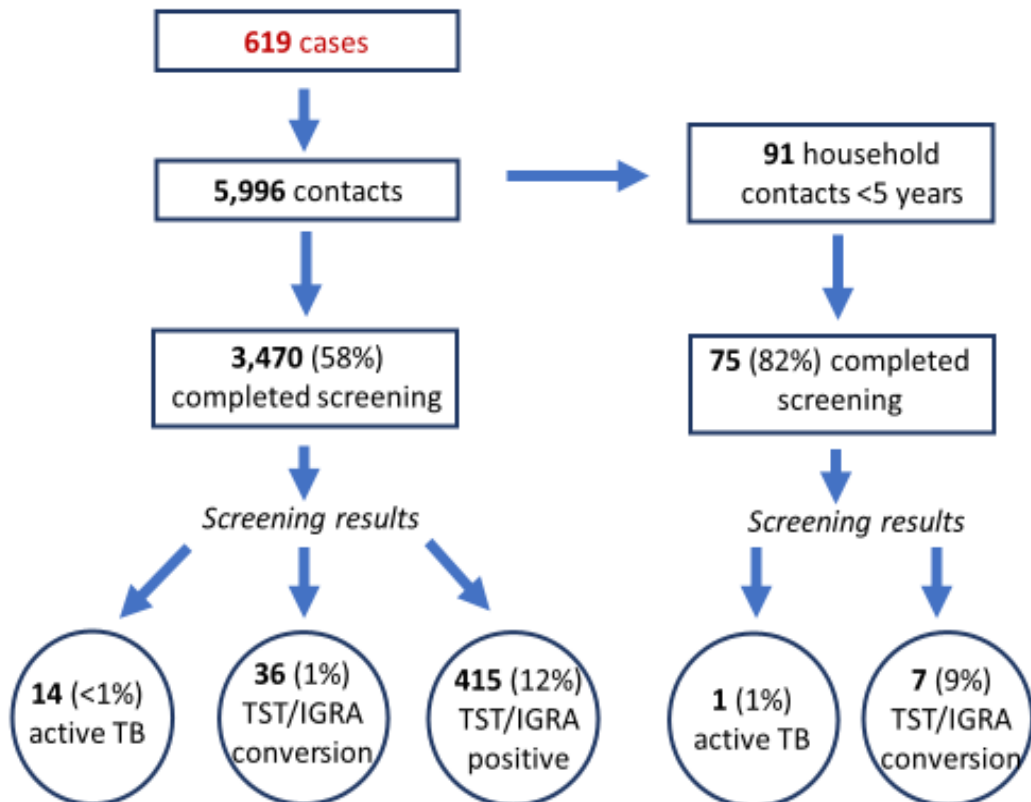
		Year of diagnosis	
		2019 Non MDR cases	2018 MDR-TB
Total cases		578 (100%)	10 (100%)
Alive	Completed treatment	507 (88%)	10 (100%)
	Defaulted	19 (3%)	-
	Transferred overseas	28 (5%)	-
	Treatment failure	0 (0%)	-
	Outcome unknown	0 (0%)	-
	Died	Cause related to TB	8 (1%)
	Unrelated to TB	15 (3%)	-
	Unknown if related to TB	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

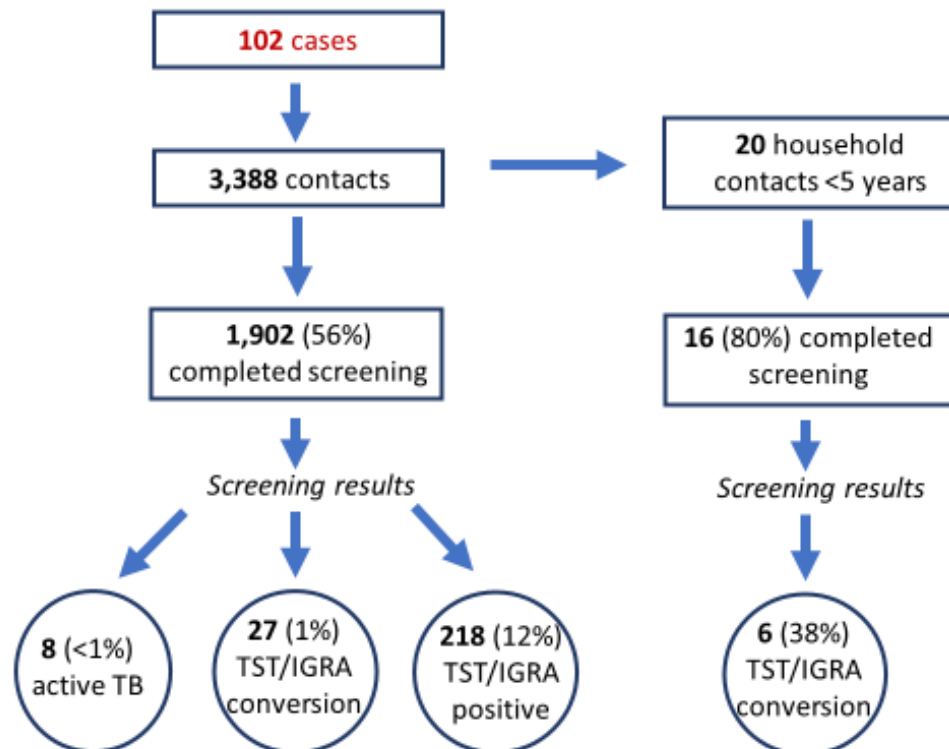
Of the 625 TB notifications received in 2020, 99% (n= 619) had contact information completed at the time of analysis. The median number of contacts per case was two (range 0-1080), and 7% (n=42) of contacts investigations involved more than 25 contacts. A total of 5,996 contacts had been identified, including 91 household contacts under the age of five years, and of these 58% (n=3,470) were recorded to have completed screening. Of the 3,470 contacts screened, less than 1% (n=14) were found to have active TB disease, 1% (n=36) had a tuberculin skin test (TST) or interferon gamma release assay (IGRA) conversion (indicating recent tuberculosis infection from the case patient), and 12% (n=415) had a positive TST or IGRA result on a single screen. Screening outcomes are shown in Figure 18.

Figure 18: Contact investigation outcomes from TB cases diagnosed in 2020, NSW



There were 103 sputum or respiratory smear positive cases notified in 2020, these cases are generally considered to be more infectious than smear negative cases. Over 99% of smear positive cases (n=102) had contact information available identifying 3388 contacts, including 20 household contacts under 5 years of age. Of these contacts, 1902 (56%) were recorded as having completed screening where 8 (<1%) were found to have active TB disease, 27 (1%) had TST or IGRA conversion, and 218 (12%) had a positive TST or IGRA result on initial screening. Screening outcomes are shown in Figure 19.

Figure 19: Contact investigation outcomes from TB pulmonary smear positive cases diagnosed in 2020, NSW



Section 5: Discussion

TB notifications increased in 2020, representing the highest number of TB cases in NSW over the past 20 years. TB cases in NSW continue to occur more frequently 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 LHDs 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 6% increase in TB notifications from 2019 to 2020 in NSW contrasts with the 18% decrease in global TB notifications reported by the WHO in 2020 [1].

The proportion of Australian born TB cases has decreased over the past ten years for both Aboriginal and Torres Strait Islander people as well as non-Indigenous Australians. The notification rate in the Australian born non-Indigenous population in NSW has remained relatively steady for more than a decade and has overall decreased over the last five years with some yearly fluctuation. The rate in Australian born Aboriginal and Torres Strait Islander people in NSW is on average 2.5 times higher than in non-Indigenous Australian born people over the past 10 years, this is lower than the national rate which is five to six times higher on average [3]. In 2020, the rate in Australian born Aboriginal and Torres Strait Islander people in NSW remained 2.8 times higher than in non-Indigenous Australian born people.

Over the past ten years the proportion of cases detected while symptomatic in NSW has significantly decreased, while the proportion of cases detected through screening has significantly increased, demonstrating the impact of immigration and contact screening programmes on earlier detection of TB.

Risk factors reported among NSW TB cases in 2020 were similar to those reported in previous years in NSW and nationally [3]. Birth in an HRC, or household member or close contact with another TB case are the most reported risk factors.

Drug resistant TB continue to pose a challenge to the control and management of TB, both globally and within NSW. There has been no 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. There were significant changes made in the management recommendations of multi-drug resistant TB by the WHO in 2019 which include standardised shorter MDR-TB regimens which at the time of report have not been used in NSW [7].

The proportion of NSW TB cases tested for HIV at the time of diagnosis continues to increase, with 92% tested in 2020. The prevalence of HIV among NSW TB cases remains low, with one per cent of cases tested found to have HIV.

Ninety-five per cent of non MDR-TB cases in 2019 successfully completed treatment (excluding cases, transferred overseas or died unrelated or unknown if related to TB). Mortality among NSW TB cases remained stable (5%), there were eight cases reported to have died due to TB in 2019. NSW continued to see low rates of treatment default (3%) and treatment failure (<1%), among TB cases in 2019. Of the ten MDR-TB cases in 2018, all successfully completed treatment.

Despite the low incidence, management and prevention of TB in Australia remains an ongoing challenge. TB 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. In 2019-2020 South and Central Asia was the most common region for migrants to Australia accounting for 120,441 arrivals followed by the Pacific with 91,703 arrivals [8]. These areas remain high incident TB areas [1]. In 2020, seven of the top ten countries of birth for overseas-born residents in Australia were classified as high-risk countries for TB by the WHO [8]. The significant increase in cases from India and significant decrease in cases from China in 2020 are most likely reflective of wider immigration patterns in Australia. From June 2019 to June 2020, the Indian born population in Australia increased by 56,300 people to 721,000 and is the second largest group of overseas-born people living in Australia behind England. Over the same period, the Chinese born population in Australia decreased by 17,300 people [8].

Overall, migration to Australia decreased in the June 2019-June 2020 period by 46,900 compared to the previous reporting year [8], due to changes in border policies implemented in March 2020 due to the COVID-19 pandemic which prevented non-Australian citizens or permanent residents from entering Australia during 2020., This resulted in a decline in the number of immigration referrals received by the NSW TB Program of individuals migrating to Australia and requiring screening. These decreases in immigration to Australia during 2020 did not lead to an immediate impact on TB numbers which is in line with data suggesting a median time of 4 years in Australia prior to TB diagnosis. The decreases in migration due to the COVID-19 pandemic, may however, contribute to a potential decrease in the TB burden in NSW in the future.

Conclusion:

The number of TB cases in NSW increased in 2020 and was 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, it remains to be seen what impact COVID-19 related migration changes will have on TB notification rates in the future.

Acknowledgements:

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