

## Original Article

# THE EPIDEMIOLOGY OF TUBERCULOSIS IN THE AUSTRALIA CAPITAL TERRITORY, 2006-2015

Belinda Jones, Vanessa Johnston, Ranil Appuhamy, Marlena Kaczmarek, Mark Hurwitz

## Abstract

### Aim

To review the epidemiology of tuberculosis (TB) in the Australian Capital Territory (ACT) over a 10 year period.

Methods: A retrospective analysis of the ACT TB notification data from 1 January 2006 to 31 December 2015 was conducted.

### Results

Over the 10 year study period there were 171 TB notifications in the ACT, with an increasing trend in the number of notifications over time. The median age of cases was 36 years (range 14 to 91 years) and 53.8% of cases were male. Most TB cases (84.2%) were born overseas. Among Australian-born cases the most common risk factor for acquiring TB was close/household contact with a known case of TB (30.8%). The most common risk factor in the overseas-born population was past travel or residence in a high-risk country (86.9%). Of all the TB cases notified, 82.4% successfully completed treatment.

### Conclusion

There was an increasing trend in the number of TB notifications in the ACT over the study period. The highest rate of TB notifications remained in the overseas-born population; with other studies suggesting this is commonly due to reactivation of latent tuberculosis infection (LTBI). As Australia starts working towards TB elimination, options for the screening and management of LTBI, especially in high risk populations, need to be explored.

### Introduction

Despite a significant decline in the incidence of tuberculosis (TB) over the past few decades, it remains a significant cause of morbidity and mortality worldwide.<sup>1</sup> The World Health Organization (WHO) estimated that globally there were 10.4 million cases of TB in 2015.<sup>1</sup> Between 2006 and 2015, the rate of TB notifications in Australia has remained fairly stable; in 2015 this was 5.3 per 100,000 population per year;<sup>2</sup> corresponding to

1,244 individual notifications.<sup>3</sup> While Australia experiences low rates of TB, importation of cases associated with migration and overseas visitors remains an important source of new cases, highlighting the necessity for ongoing screening and control measures. Of further concern is the rise in the number of cases of multi-drug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) in some of Australia's close neighbours, such as Papua New Guinea, Vietnam and the Philippines, and the potential public health implications associated with this.<sup>4,5</sup>

The Australian Capital Territory (ACT) is a relatively small jurisdiction with an estimated population of just over 390,000 in 2015.<sup>6</sup> Data from the 2011 census reported only 1.5% of the ACT population were Aboriginal or Torres Strait Islander, and 36% of the ACT population were born overseas.<sup>6</sup> In the ACT, TB is a notifiable condition under the *Public Health Act 1997*, with notifications made to the ACT Health Protection Service. Information on risk factors, treatment and treatment outcomes is collected and sent to the Commonwealth National Notifiable Disease Surveillance System (NNDSS). Clinical management of pulmonary TB is provided by the Department of Respiratory and Sleep Medicine at the Canberra Hospital, whilst extrapulmonary TB is managed by the Infectious Diseases Department. The Department of Respiratory and Sleep Medicine is also responsible for TB screening for health care workers, provision of LTBI treatment and contact tracing.

The aim of this study was to review the epidemiology of TB cases notified in the ACT over the 10 year period between 2006 and 2015.

### Materials and method

Data for all TB cases notified to the ACT Health Protection Service between 1 January 2006 and 31 December 2015 were reviewed. Case inclusion was based on notification receipt date. The Communicable Disease Network of Australia case definition was used to classify cases of TB, which requires either laboratory confirmation through

isolation of *Mycobacterium tuberculosis* or detection through nucleic acid, or a clinically consistent picture as assessed by a clinician experienced in the diagnosis of TB.<sup>7</sup>

Data were obtained from the ACT Notifiable Disease Management System database and associated enhanced data spreadsheets. This included: demographics, year of arrival to Australia (if applicable), notification date, diagnostic testing results, site(s) of infection, risk factors for TB, HIV status, resistance profile, case classification and outcome.

Annual rates of TB were calculated using the mid-year ACT population estimate for each year, taken from the Australian Bureau of Statistics Estimated Resident Population, States and Territories.<sup>8</sup> Age group rates were calculated using 2010 mid-year estimated ACT resident population data.<sup>9</sup>

When reviewing the country of birth or travel history of cases, high-incidence countries were those with an annual incidence of more than 40 TB cases per 100,000 population as estimated in the World Health Organization Tuberculosis Report 2016.<sup>1</sup>

Negative binomial regression analysis was used to determine the trends in the number and rate of TB notifications over the 10-year study period. The data were analysed using Microsoft Excel® (2007) and SPSS® (Grad Pack v23.0 for Mac). STATA 14® was used for the trend analysis.

## Results

### Rates of TB

The ACT received 171 notifications of TB between 1 January 2006 and 31 December 2015, with a range of 10 to 30 notifications per year (Figure 1). Over the 10-year review period there was a single cluster of TB involving 10 cases with the same whole genome sequence, 8 of whom had an epidemiological link.

Between 2006 and 2015 the rate of TB notifications in the ACT ranged from 2.8 per 100,000 ACT population per year to 7.8 per 100,000 ACT population per year. In 2009 and 2014, the ACT notification rate was higher (6.5 and 7.8 per 100,000 ACT population per year, respectively) than the national average (6.0 and 5.7 per 100,000 national population per year, respectively).

Analysis of the trend in TB notifications over the 10 year period showed a significant increase in the number of cases ( $p = 0.05$ ). An upward trend in notification rate was also seen, although this was not statistically significant ( $p = 0.15$ ).

### Socio-demographic characteristics of TB notifications

Of the TB notifications, 53.8% ( $n=92$ ) were male. The median age of cases was 36 years (range 14 to 91 years) (Figure 2). The majority of cases (84.2%) were overseas-born (Figure 3). Of these, 127 (87.6%) cases were born in a high-incidence country. The most common countries of birth were India, Vietnam and China. The majority of the overseas-born population (68.1%) were Australian residents (citizens or permanent visa holders), and the remainder were overseas students (15.3%), visitors (12.5%), 5 cases (3.9%) were classified as 'other', and one case (0.8%) was a refugee (Figure 4). Only a small number of overseas-born cases (7.6%,  $n = 11$ ) were diagnosed through a TB health undertaking. One case occurred in a person of unknown country of birth. Of these cases, 15.2% ( $n=26$ ) were in Australian-born individuals, none of whom identified as being of Aboriginal or Torres Strait Islander origin.

Of the TB cases in people born in a high-incidence country, the median time between arrival in Australia and diagnosis of TB was 4 years (range of <1 year to 66 years) (Figure 5). A high proportion of the notifications occurred within the first 3 years of arrival in Australia (47.2%).

### Clinical characteristics

#### Site of infection

Nearly half of the TB notifications (49.7%) between 2006 and 2015 were for pulmonary-only disease (Table 1), 40.4% were extrapulmonary, and 9.9% were both pulmonary and extrapulmonary disease. Sites of extrapulmonary infection included lymph node (44.2%), pleura (14%), bone (8.1%), peritoneal (8.1%), genitourinary (7.0%), and meningeal (2.3%). Disseminated TB disease occurred in 4.7% of cases.

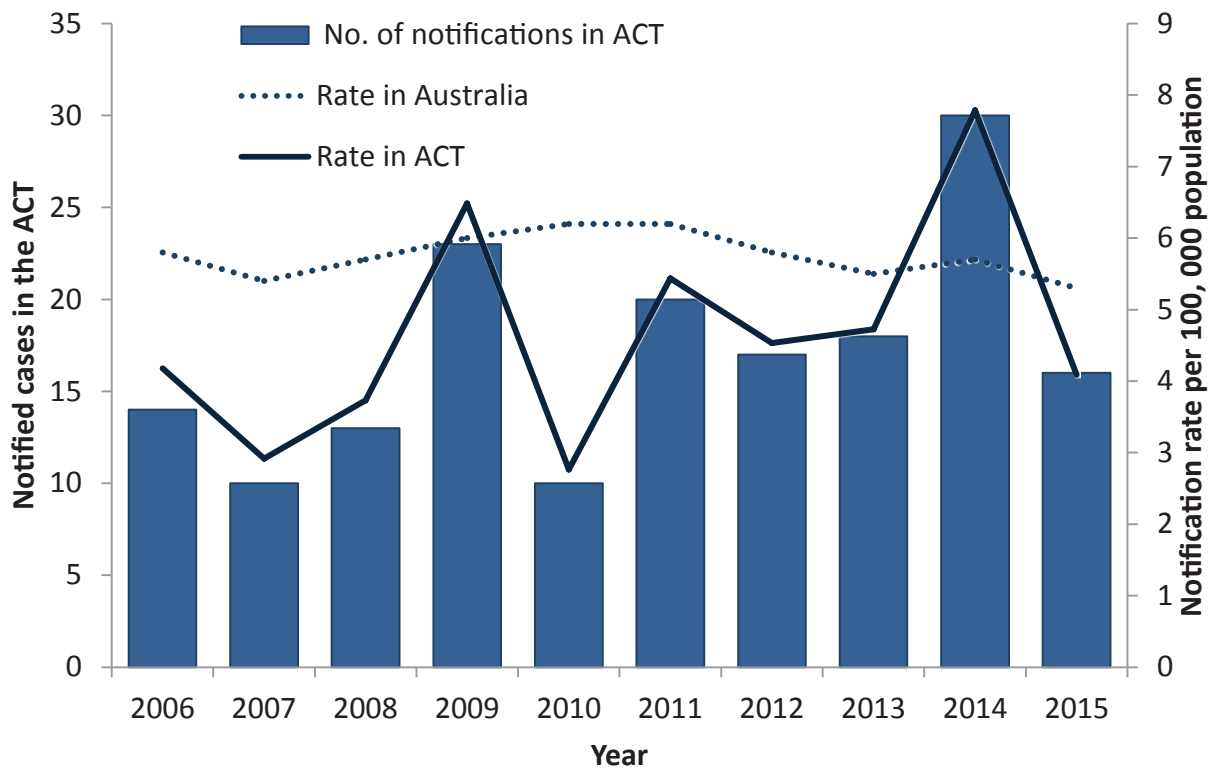
#### Case classification

The majority of TB notifications (91.2%,  $n=156$ ) were classified as new cases (Table 1). Eleven cases (6.4%) were classified as relapse (relapse of previously treated disease or a new episode of TB caused by re-infection) following treatment in Australia or overseas. The relapse rate was 0.8 per 100,000 population per year in 2012 and 0.5 per 100,000 population per year in 2013.

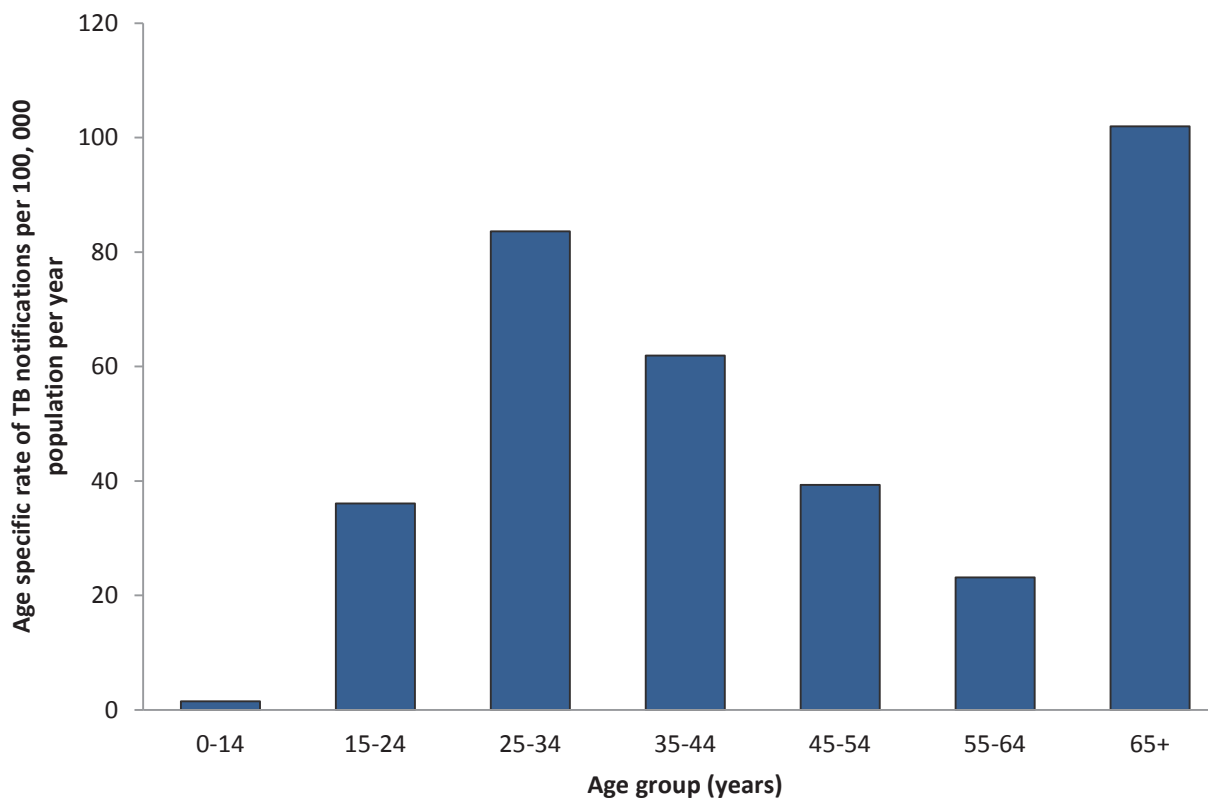
#### Laboratory confirmation

Approximately one third (35.3%) of pulmonary or pulmonary plus extrapulmonary cases were sputum smear positive on microscopy. The majority of

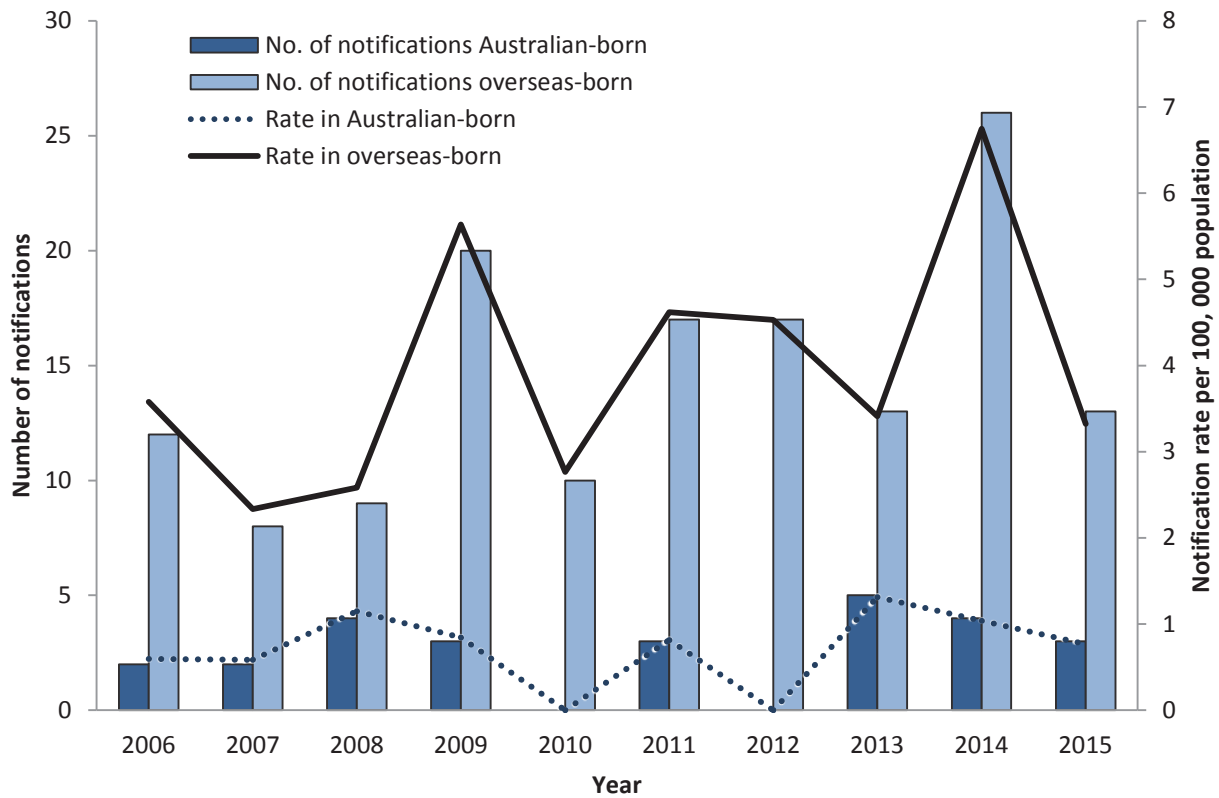
**Figure 1: Number of TB notifications in the ACT and rates of TB notifications per 100,000 population per year in the ACT and Australia, by year, 1 January 2006 to 31 December 2015.**



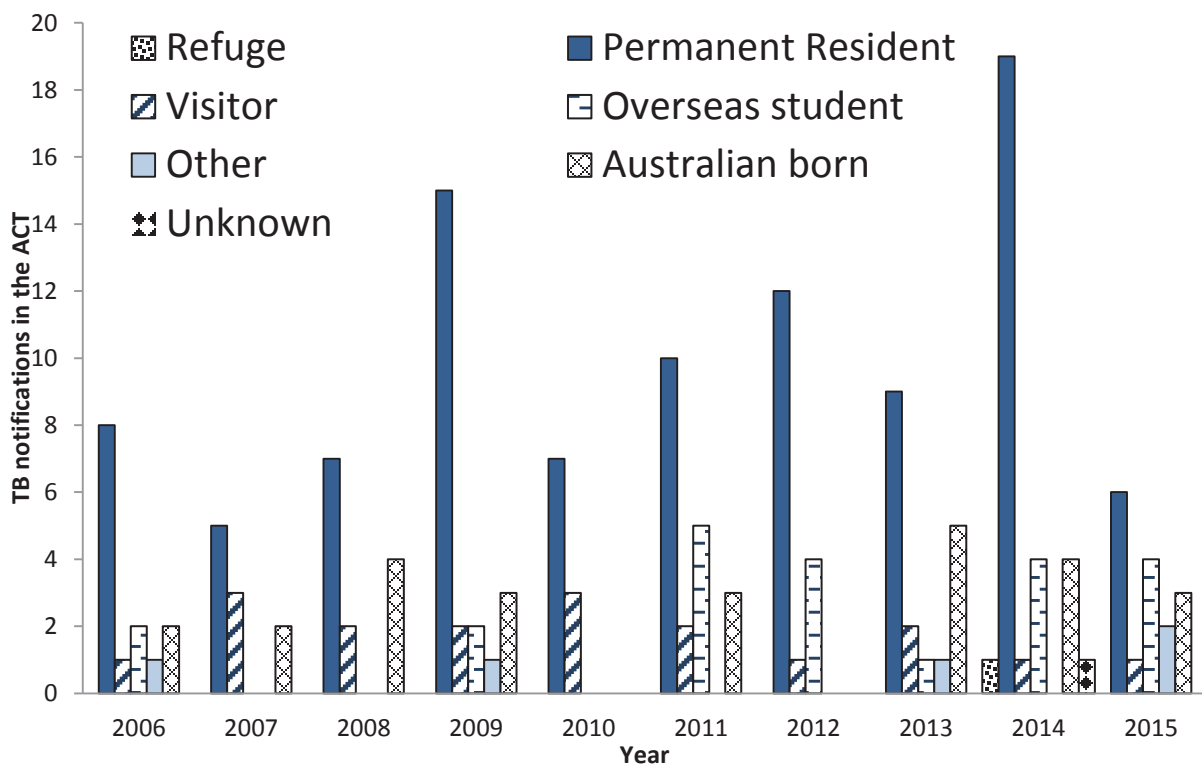
**Figure 2: Age specific rate of TB notifications, ACT, 1 January 2006 to 31 December 2015.**



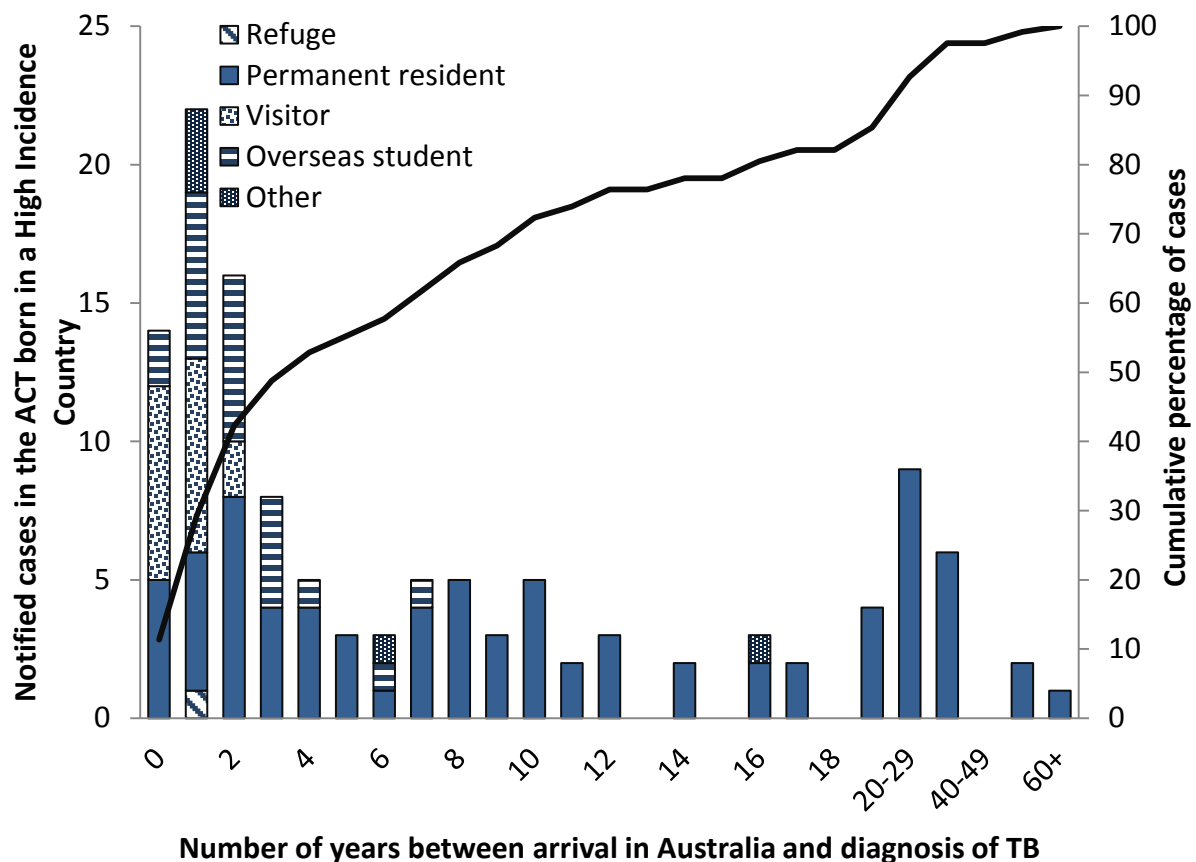
**Figure 3: Number and rates per 100,000 ACT population per year of TB notifications in Australian-born versus overseas-born cases, by year, ACT, 1 January 2006 to 31 December 2015.**



**Figure 4: Number of TB notifications by residency status, ACT, 1 January 2006 to 31 December 2015**



**Figure 5: Number of years between arrival in Australia and diagnosis of TB for cases born in a high incidence country\*, by number of cases and residency status, and cumulative percentage, ACT 1 January 2006 to 31 December 2015**



\*High-incidence countries were those with an annual incidence of more than 40 TB cases per 100,000 population as estimated in the World Health Organization Tuberculosis Report 2016.<sup>1</sup>

TB cases (78.3%) were either pulmonary sputum culture or other-specimen culture positive. Only 3 cases were diagnosed by PCR only and 12 cases were confirmed by histology only. Twenty-two cases were diagnosed on clinical grounds only (i.e. negative for TB on culture, microscopy, nucleic acid testing and/or histology); of these, 13 cases were diagnosed with pulmonary TB.

#### HIV co-infection

Over the 10 year period, the majority of cases (74.3%, n=127) tested as HIV negative and only 5 cases (2.9%) were identified as having HIV co-infection (Table 1). Four of the 5 TB-HIV co-infected cases were born overseas, and four cases were male. Twenty-three percent of TB notifications (n=39) were not tested or had unknown HIV testing history.

#### Resistance

There were 23 cases of TB with resistance to one or more anti-tuberculous drugs. Of these, the majority (n=16, 69.6%) had resistance to one drug, most commonly isoniazid. Three cases fit the classifica-

tion of MDR-TB, defined as resistance to at least isoniazid and rifampicin.<sup>10</sup> There were no cases of XDR-TB.

#### Risk factors

The most common TB risk factor in the Australian-born population was having a household or close contact with TB (30.8%, n= 8) followed by past travel and/or residence in a high-risk country (19.2%, n= 5) (Table 2). In the overseas-born population the most common risk factor was past travel or residence in a high-risk country (86.9%). Prior to 2013, data collected regarding past travel or residence in a high-risk country may have included the country of birth, however following agreement from the National TB Advisory Committee, future recording of this data field was to only include travel and residence in high risk country excluding country of birth.<sup>11</sup>

#### Treatment and outcomes

Most TB cases notified between 2006 and 2015 completed treatment (82.5%), with a small proportion (2.9%) still undergoing treatment at the

**Table 1: Clinical characteristics of TB cases, ACT, 1 January 2006 to 31 December 2015.**

		Number (n)	Percentage (%)
<b>Site of infection</b>	Pulmonary only	85	49.7
	Pulmonary plus other sites	17	9.9
	Extra pulmonary only	69	40.4
<b>Extra pulmonary site *</b>	Pleural	12	14.0
	Lymph node	38	44.2
	Genitourinary	6	7.0
	Meningeal	2	2.3
	Bone/joint	6	7.0
	Disseminated TB	4	4.7
	Peritoneal including other GI sites	7	8.1
	Other	12	14.0
<b>Case classification</b>	New case	156	91.2
	Relapse following treatment overseas	7	4.1
	Relapse following treatment in Australia	4	2.3
	Unknown	4	2.3
<b>Laboratory confirmation †</b>	Sputum culture positive	74	43.2
	Other culture positive	83	48.5
	PCR	93	54.4
	Histology	64	37.4
	Nil	22	12.9
<b>HIV</b>	Negative	127	74.3
	Positive	5	2.9
	Not tested/unknown testing history	39	22.8
<b>Resistance</b>	Fully Sensitive	112	65.5
	Resistance $\geq 1$ drug (not meeting criteria for multi-drug resistant TB)	13	7.6
	Multi-drug resistant TB	3	1.8
	Unable to test sensitivity (culture negative)	43	25.1

\* Categories are not mutually exclusive, one case had more than one extrapulmonary site.

† Categories are not mutually exclusive, some cases had more than one method of laboratory confirmation

time of the review. Of those who completed treatment, only one case had interrupted treatment. Among sputum smear and culture positive cases (n=34), 11 (32.3%) met the criteria of being cured (defined as a smear positive, culture positive case who completes treatment and is documented to be culture negative on two separate occasions, one of which is in their last month of treatment). A small proportion of cases (14.6%, n=21) fell under another treatment outcome category: one case died as a result of TB, 11 died from other causes, and 9 had their care transferred to another health facility. Only two cases had an unknown treatment outcome.

## Discussion

Between 2006 and 2015 the ACT experienced low annual TB notifications, ranging from 10 to 30 notifications per year. Over this period, the rate

of TB has generally remained lower than national rates, with the exception of in 2009 and 2014 where the notification rates were higher. The reason behind the high notification rates in these two years is unclear as these cases were not linked to clusters or outbreaks, and screening practices have remained largely unchanged. Of note, in 2009 and 2014 there were a higher number of TB cases in overseas-born permanent residents (figure 4).

Analysis of the trend in the number of TB notifications in the ACT over the 10 year period revealed a statistically significant increase, although the observed upward trend in the notification rate was not statistically significant. This reflects that while the number of TB cases notified has generally increased over the past 10 years, increasing population growth has kept the rate fairly stable. This is consistent with national increases in the number of notifications seen over the same time period.<sup>2</sup>

**Table 2: Risk factors for TB cases, ACT, 1 January 2006 to 31 December 2015. ‡**

	Australian-born		Overseas-born		Total	
	Number (n)	Percentage (%)	Number (n)	Percentage (%)	Number (n)	Percentage (%)
Household or close contact	8	30.8	15	10.3	23	13.5
Ever resided in a correctional facility	0	0	2	1.4	2	1.2
Ever resided in an aged care facility	1	3.8	0	0	1	0.6
Ever employed in an institution	1	3.8	4	2.8	5	2.9
Previous employment in health industry						
Australia	3	11.5	8	5.5	11	6.4
Overseas	0	0	8	5.5	8	4.7
Current employment in health industry (past 12 months)						
Australia	1	3.8	8	5.5	9	5.3
Overseas	1	3.8	3	2.1	4	2.3
Ever homeless	0	0	4	2.8	4	2.3
Past travel to or residence in a high-risk country (> 3 months)	5	19.2	126	86.9	131	76.6
Chest X-ray suggestive of old untreated TB	1	3.8	26	17.9	27	15.8
Currently on immunosuppressive treatment	2	7.7	4	2.8	6	3.5
None of the above risk factors	7	26.9	1	0.7	8	4.7
Not assessed	1	3.8	2	1.4	3	1.8

‡ Risk factor categories are not mutually exclusive, some cases had more than one risk factor

While the overall number of TB notifications in the ACT remains small, there are significant resource implications even with small increases in cases. Appropriate ongoing resourcing of TB services is particularly important as the proportion of the ACT population born overseas is projected to increase in the future.<sup>12, 13</sup>

Most of the notifications over the study period occurred in the overseas-born population, consistent with observations from other jurisdictions in Australia, where the proportion of overseas-born TB cases ranged from 55 to 100% of notifications in 2013.<sup>11</sup> In the ACT, overseas-born cases were primarily from high-incidence countries, with a median interval between arrival in Australia and TB diagnosis of 4 years. The majority (67.6%), of overseas-born cases were permanent residents with the second most common group being overseas students (15.2%).

These findings are consistent with national data from 2012 and 2013 which also found the highest proportion of cases amongst these two groups.<sup>11</sup>

Findings from other epidemiological studies in low-incidence countries suggest most cases of TB are due to reactivation of LTBI, rather than people arriving with active disease or as a result of local transmission.<sup>14-17</sup>

An increased rate of reactivation in migrants from high-incidence countries may be due to a number of factors making this population more susceptible such as acquiring LTBI just prior to migrating, stress, low socioeconomic status, underlying medical conditions or household crowding.<sup>14, 17</sup> Re-exposure to TB when travelling back to their country of birth may also be another important consideration.<sup>14</sup>

The most common risk factors for TB in the overseas-born population were travel or residence in a high-incidence country (86.9%) and previous chest x-ray findings suggestive of old untreated TB (17.9%). What this points to is the need for sustained efforts to target screening for TB infection among new migrant arrivals. Migrants, refugees and long-term visitors to Australia undergo pre-

migration screening for active disease, with any cases identified required to undergo treatment prior to entering Australia, thereby minimising the risk of spreading TB within Australia.<sup>18</sup> Expanding efforts to systematic screening and treatment of LTBI among overseas-born populations, particularly new permanent residents, in Australia is a potentially cost-effective method to further reduce the rates of TB.<sup>14, 19, 20</sup>

Currently, LTBI cases are not reported at a national level, and while screening for LTBI is recommended in some high risk groups such as refugees,<sup>18,21</sup> there are no national guidelines for LTBI screening. The National TB Advisory Council is currently developing a National Position Statement for the management of LTBI, which would facilitate a coordinated national approach.<sup>22</sup> Identification of higher risk populations such as new permanent residents from high-incidence countries could allow for more tailored screening approaches, although care would need to be taken to prevent stigmatising groups who are already potentially marginalised.<sup>23</sup>

The most common risk factor for TB amongst Australia-born cases was having a household or close contact with TB (30.8%), highlighting the importance of contact tracing and screening efforts. This is slightly higher than the 2012 and 2013 national data, which reported 26% and 22% of Australian-born cases as having household or close contact with TB as a risk factor, respectively.<sup>11</sup>

The low rates of other high risk groups for LTBI reactivation, such as people living with human immunodeficiency virus (HIV) or those with immunosuppression, observed over the study period suggest that these are not drivers for the persistence of TB in the ACT. However, 23% of TB notifications were not tested for HIV or had unknown testing history. Ideally, all patients with TB should be tested for co-infection with HIV. This is because TB is more common in patients with HIV and the treatment of tuberculosis can be more complex (e.g. the potential for undesirable drug interactions).<sup>24</sup> Indigenous Australians are another high risk group for TB;<sup>11, 25</sup> however none of the cases of TB notified in the ACT were reported as being Aboriginal or Torres Strait Islander Peoples. This may reflect the relatively small Indigenous population living in the ACT compared with other states, or inaccurate identification and/or recording of Aboriginal or Torres Strait status.<sup>26</sup>

Treatment failure and disease relapse are of particular concern, as they can lead to the development of drug-resistant TB and can counter

efforts to reduce TB rates.<sup>27</sup> Global data estimates that 3.3% of new TB diagnoses are multi-drug-resistant.<sup>(1)</sup> In this study, the number of cases with MDR-TB was low (1.8%). Of note, all cases of MDR-TB were people born in high-incidence countries, and all were new cases that had not previously been treated for TB. Over 90% of cases in the ACT were newly diagnosed, however there were a small number of cases of relapse after treatment in either Australia (n=4) or overseas (n=7). Compared to the national relapse rate of 0.2 per 100,000 population per year in 2012 and 2013, the ACT had higher rates of 0.8 and 0.5 per 100,000 population per year, respectively.<sup>11</sup>

Without the use of molecular techniques, it was not possible to determine whether relapse was due to treatment failure or re-infection. Previous studies suggest that recurrent tuberculosis in high-income countries with low rates of tuberculosis is most commonly due to relapse of infection with the same strain.<sup>28</sup> Although the overall number of relapse cases is small, over a third of cases were in individuals treated in Australia, which is of concern as relapse in this context is one indicator of TB control. This highlights an area of potential future focus for the ACT and every effort should be made to reduce the relapse rate by identifying high-risk groups for consideration of a longer treatment course (e.g. patients with extensive cavitations on chest X-ray) and to differentiate true relapse from re-infection where possible, using molecular techniques.<sup>28</sup>

A significant number of TB cases were negative on all diagnostic testing, (12.9%, n = 22), with a diagnosis made on clinical grounds only. Lack of diagnostic confirmation has implications for resistance testing and treatment. Over half (59%, n =13) of these cases were pulmonary only, suggesting that improved methods of induced sputum collection may help improve diagnostic testing results in these cases.

The use of TB notification data, which is compiled from mandatory reporting of all TB diagnoses in the ACT under the *Public Health Act 1997*, reduces the likelihood that any TB cases will be missed during our study period. Although notifications cannot capture TB cases that remain undiagnosed, this is presumed to be low in Australia due to the availability of free TB services to anyone in the country.<sup>29,30</sup> This study was conducted using existing notification data without a review of medical charts. Although the data quality and completion of some fields was inconsistent over the study period, this is unlikely to have made an impact on the overall findings. The relatively small number of TB notifications in the ACT reflects the size of this jurisdiction. While this limits the statistical

power for analysing trends, it was still possible to compare ACT rates with national TB notification rates.

## Conclusion

The number of TB notifications in the ACT has remained relatively low over the past 10 years although it appears to be increasing. The majority of TB notifications are in the overseas-born population. This highlights a potential group that can be identified for more targeted screening and intervention programs to work towards eliminating TB in Australia. Managing an increasing number of TB cases in the ACT, as well as screening for and treating LTBI in high-risk groups, has significant resource implications. Future national and jurisdictional plans to address the goal of TB elimination will need to take this into account.

## Authors and affiliations

Dr Belinda J. Jones (Corresponding author), Former Public Health Medicine Registrar, Health Protection Service, Population Health Protection and Prevention, ACT Health, Canberra ACT.

Address: HNE Population Health, Locked Bag 10, Wallsend NSW 2287.

Email: [Belinda.Jones1@hnehealth.nsw.gov.au](mailto:Belinda.Jones1@hnehealth.nsw.gov.au) Ph: (02) 4924 6353

Dr Vanessa Johnston, Public Health Physician, Office of the Chief Health Officer, Population Health Protection and Prevention, ACT Health, Canberra ACT.

Dr Ranil D. Appuhamy, Public Health Physician, Office of the Chief Health Officer, Population Health Protection and Prevention, ACT Health, Canberra ACT.

Dr Marlena C. Kaczmarek, Epidemiologist & Surveillance Coordinator, Communicable Disease Control Section, Health Protection Service, Population Health Protection and Prevention, ACT Health, Canberra ACT.

Associate Professor Mark Hurwitz, Respiratory Physician, Department of Respiratory and Sleep Medicine, ACT Health, Canberra ACT.

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