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Bronchiectasis in indigenous and non-indigenous residents of Australia and New Zealand

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ABSTRACT

Background and objective: **Bronchiectasis not associated with cystic fibrosis is an increasingly recognized chronic lung disease. In Oceania, indigenous populations experience a disproportionately high burden of disease. We aimed to describe the natural history of bronchiectasis and identify risk factors associated with premature mortality within a cohort of Aboriginal Australians, New Zealand Māori and Pacific Islanders, and non-indigenous Australians and New Zealanders.**

Methods: **This was a retrospective cohort study of bronchiectasis patients aged >15 years at three hospitals: Alice Springs Hospital and Monash Medical Centre in Australia, and Middlemore Hospital in New Zealand. Data included demographics, ethnicity, sputum microbiology, radiology, spirometry, hospitalization and survival over 5 years of follow-up.**

Results: **Aboriginal Australians were significantly younger and died at a significantly younger age than other groups. Age- and sex-adjusted all-cause mortality was higher for Aboriginal Australians (hazard ratio (HR): 3.9), and respiratory-related mortality was higher for both Aboriginal Australians (HR: 4.3) and Māori and Pacific Islander people (HR: 1.7). Hospitalization was common: Aboriginal Australians had 2.9 admissions/person-year and 16.9 days in hospital/person-year. Despite Aboriginal Australians having poorer prognosis, calculation of the FACED score suggested milder disease in this group. Sputum microbiology varied with *Aspergillus fumigatus* more often isolated from non-indigenous patients. Airflow obstruction was common (66.9%) but not invariable.**

Conclusions: **Bronchiectasis is not one disease. It has a significant impact on healthcare utilization and survival. Differences between populations are likely to relate to differing aetiologies and understanding the drivers of bronchiectasis in disadvantaged populations will be key.**

SUMMARY AT A GLANCE

This study compares the nature and outcomes associated with bronchiectasis in adult indigenous and non-indigenous populations in Australia and New Zealand. It highlights the disproportionate impact of bronchiectasis in terms of premature mortality and healthcare utilization for indigenous populations, particularly Aboriginal Australians.

Key words: bronchiectasis, hospitalization, premature mortality, Oceania, survival analysis.

Abbreviations: AR-DRG, Australian Refined Diagnosis Related Groups; ASH, Alice Springs Hospital; CF, cystic fibrosis; cHRCT, chest HRCT; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; HR, hazard ratio; IQR, interquartile range; IRR, incidence rate ratio; MAC, *Mycobacterium avian* complex; MH, Middlemore Hospital; MMC, Monash Medical Centre; MRSA, methicillin-resistant *Staphylococcus aureus*; nmMRSA, non-multiresistant MRSA; NTM, non-tuberculous mycobacteria.

INTRODUCTION

Bronchiectasis is a chronic respiratory condition characterized by irreversible airway dilation, usually demonstrated on chest high-resolution computed tomography (cHRCT).[1,2] Whilst often associated with cystic fibrosis (CF), bronchiectasis that is unrelated to CF is increasingly recognized and often presents, and is first diagnosed, in adulthood.[1]

European studies have highlighted significant morbidity and mortality associated with bronchiectasis. They reported a median age of patients of 59–68 years and 5-year mortality of 12–20%.[3–5] There is evidence to suggest a younger age profile for bronchiectasis in less affluent countries with patients in western India[6] having a mean age of 43 years and mortality of 8% over 2 years and those in Nepal a mean age of 48 years.[7]

In Australia, Aboriginal people living in the remote regions experience a disproportionately high burden of disease associated with significant morbidity and

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premature mortality.[8,9] Aboriginal Australian children have one of the highest reported rates of bronchiectasis in the world.[10] Similarly, studies from New Zealand have reported that the incidence of bronchiectasis in Pacific Islander and Māori children is far greater than in children of 'European' descent.[11–13] Despite this, there is little information regarding the nature of bronchiectasis in indigenous peoples residing in high-income countries.[8–13] This study aimed to describe the natural history of adult non-CF bronchiectasis and identify risk factors associated with premature mortality within a cohort of indigenous and non-indigenous Australians and New Zealanders.

METHODS

This was a retrospective cohort study of adult non-CF bronchiectasis patients undertaken in accordance with the Strengthening the Reporting of Observational studies in Epidemiology Statement for reports of cohort studies.[14] Participants were from three hospitals: Alice Springs Hospital (ASH) and Monash Medical Centre (MMC) in Australia, and Middlemore Hospital (MH) in New Zealand. ASH is located in remote central Australia, an area with a significant Aboriginal Australian population. MMC and MH are both urban tertiary teaching hospitals. MMC is located in Melbourne, Australia, and provides care to a predominantly non-indigenous population while MH is in Auckland, New Zealand, and provides care to significant Māori and Pacific Islander populations.[15]

Patients aged 15 years and older with a discharge diagnosis of bronchiectasis (International Statistical Classification of Diseases and Related Health Problems 10th Revision code J47[16]) over 5 years from 2004 to 2008 were first identified. Inclusion criteria were then applied through review of medical records: clinician diagnosis of non-CF bronchiectasis at least 5 years prior to the date of data collection and bronchiectasis confirmed on cHRCT. Individuals known to have CF were excluded. Participants were retrospectively followed from 2009 to 2013.

Data were collected from: paper and electronic medical records; pathology, radiology, lung function and hospital separation databases; and jurisdictional death registries. The earliest results during the period of review were collected. Hospitalization data were restricted to respiratory-related admissions including exacerbations of bronchiectasis, COPD or asthma, pneumonia and respiratory failure. FACED scores were calculated based on percentage predicted forced expiratory volume in 1 s (FEV_1), age, presence of *Pseudomonas aeruginosa* on sputum microbiology and radiological extent (data relating to dyspnoea were not consistently recorded).[5]

Standard univariate and bivariate statistical techniques were utilized to describe the cohort and compare groups. Survival was graphically represented with Kaplan–Meier curves. Differences in survival between groups were assessed using the log-rank test. Forward stepwise multivariate Cox proportional hazard modelling was used to identify variables independently associated with mortality. Analyses were interpreted as significant if $P < 0.05$ and all statistical tests were two-sided. Data analysis was performed using Stata 14 (StataCorp, College Station, TX, USA).

The study was approved by the Central Australian, James Cook University, Monash Health and New Zealand Health and Disability Human Research Ethics Committees.

RESULTS

Enrolment encompassed 406 adults: 85 Aboriginal Australians; 79 non-indigenous Australians; 72 Māori; 85 Pacific Islanders; and 85 non-indigenous New Zealanders. Māori and Pacific Islander subjects were combined for all analyses given the similarity in age, sex distribution, disease and outcomes. Non-indigenous Australian and New Zealand subjects were combined for survival analysis to facilitate presentation of results.

Demographics and FACED scores are presented in Table 1. Aboriginal Australians were younger ($P < 0.001$) and non-indigenous New Zealanders older ($P < 0.001$). Non-indigenous New Zealanders were more likely to be female ($P \leq 0.022$) and were less likely to have ever smoked ($P \leq 0.008$) compared with other groups. All Aboriginal Australian participants resided in a remote or very remote location compared with only 2.5% of non-indigenous Australian participants. In New Zealand, the median deprivation index (ranging from 1 to 10, where 10 represents the most deprived) for Māori/Pacific Islanders was 10 (interquartile range (IQR): 9–10) while that of non-indigenous individuals was 6 (IQR: 3–9) ($P < 0.001$).[17] Aboriginal Australians had significantly lower FACED scores and categorization than both New Zealand groups ($P < 0.004$). Aboriginal Australians were more likely to have bronchiectasis classified as mild in comparison with other groups ($P < 0.022$).

There was no difference in unadjusted all-cause mortality at 5 years between groups (Table 1, Fig. 1). However, death occurred at a significantly younger age for Aboriginal Australians ($P < 0.001$) with median age of death for this group being at least 20 years earlier than for other groups. Respiratory-related mortality for Aboriginal Australians was significantly greater compared with non-indigenous Australians ($P = 0.026$) and New Zealanders ($P = 0.004$) but not significantly different from Māori/Pacific Islanders (Table 1, Fig. 2). Compared with non-indigenous people, unadjusted respiratory-related mortality in Aboriginal Australians was more than double (hazard ratio (HR): 2.3, 95% CI: 1.3–3.9). A similar significant difference in unadjusted respiratory-related mortality was not observed in Māori/Pacific Islanders. Aboriginal Australians died at a significantly younger age when analysis was restricted to respiratory-related causes ($P < 0.001$).

Routine bacterial and mycobacterial sputum culture results are summarized in Table 2. Aboriginal Australians were more likely to have sputum microbiology performed compared with other groups ($P < 0.016$). Common respiratory pathogens (defined as only ever having *Streptococcus pneumoniae, Haemophilus influenzae* or *Moraxella catarrhalis* isolated)

Table 1 Demographical characteristics, FACED scoring and 5-year mortality

	Aboriginal Australian (n = 85)	Non-indigenous Australian (n = 79)	Māori or Pacific Islander (n = 157)	Non-indigenous New Zealander (n = 85)	P-value
Age, mean years (SD)	43.7 (12.3)	59.4 (17.5)	58.2 (15.2)	68.7 (12.2)	<0.001
Sex, % female (95% CI)	42.4 (31.7–53.6)	50.6 (39.1–62.1)	52.2 (44.1–60.3)	68.2 (57.2–77.9)	0.007
Ever smoked, % (95% CI)	67.5 (55.9–77.8)	52.8 (40.7–64.7)	61.8 (53.7–69.4)	31.8 (22.1–42.8)	<0.001
FACED score					
Median score (IQR)	1 (0–2)	2 (0–3)	2 (1–3)	2 (1–3)	0.007
Severity % (95% CI)					
Mild	75.3 (64.7–84.0)	64.6 (53.0–75.0)	56.7 (48.6–64.6)	58.8 (47.6–69.4)	0.005
Moderate	24.7 (16.0–35.3)	27.8 (18.3–39.1)	40.8 (33.0–48.9)	34.1 (24.2–45.2)	
Severe	0 (0–4.2)	7.6 (2.8–15.8)	2.5 (0.7–6.4)	7.1 (2.6–14.7)	
Five-year mortality					
All-cause, n (%, 95% CI)	36 (42.4, 31.7–53.6)	23 (29.1, 19.4–40.4)	53 (33.8, 26.4–41.7)	26 (30.6, 21.0–41.5)	0.269
Age at death, median years (IQR)	50.1 (41.8–54.6)	72.3 (63.4–77.3)	70.8 (60.4–76.6)	75.1 (70.0–84.9)	<0.001
Respiratory-related, n (%, 95% CI)	28 (32.9, 23.1–44.0)	14 (17.7, 10.0–27.9)	37 (23.6, 17.2–31.0)	12 (14.1, 7.51–23.4)	0.019
Age at death, median years (IQR)	48.8 (36.4–52.9)	69.6 (64.2–75.1)	69.1 (58.3–75.4)	75.2 (70.1–87.4)	<0.001

IQR, interquartile range.

were more often observed in Aboriginal Australians (P < 0.001) and Māori/Pacific Islanders (P < 0.001) compared with their non-indigenous counterparts. Non-multiresistant methicillin-resistant *Staphylococcus aureus* (nmMRSA) was more often isolated in Aboriginal Australians compared with all other groups (P = 0.001–0.049). *Klebsiella* species were also more likely in Aboriginal Australians compared with non-indigenous Australians (P = 0.004), whereas non-indigenous patients were more likely to have these species than Māori/Pacific Islanders in New Zealand (P = 0.022). *Aspergillus fumigatus* was more often seen in non-indigenous Australians (P < 0.001) and New Zealanders (P = 0.027). There were no significant differences in the isolation of *P. aeruginosa*, methicillin-susceptible *S. aureus* and MRSA between groups.

Aboriginal Australians were more likely to have mycobacterial culture performed compared with other groups (P < 0.001). Mycobacterial cultures were no different in regard to positive cultures for *Mycobacterium avium* complex (MAC). However, Aboriginal Australians were more likely to have a positive mycobacterial culture for other (non-MAC) non-tuberculous mycobacteria (NTM) compared with Māori/Pacific Islanders (P = 0.003).

Spirometry and cHRCT results are summarized in Table 3. Non-indigenous Australians had fewer lobes affected than both groups of New Zealand patients (P < 0.001 and P = 0.018) but with no significant difference when compared with Aboriginal Australians. Percentage predicted FEV_1 and forced vital capacity (FVC) were significantly lower in Aboriginal Australians

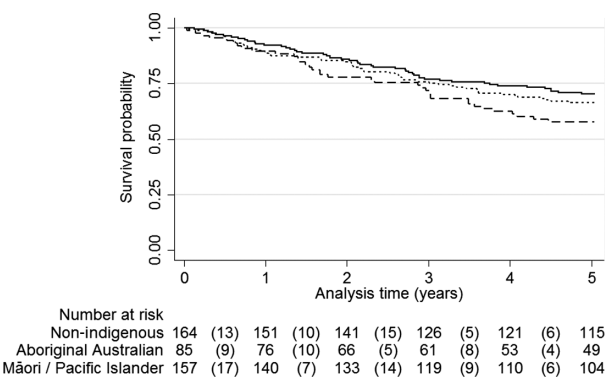

Figure 1 Kaplan–Meier survival curve: unadjusted all-cause mortality stratified by ethnicity (log-rank: P = 0.141). ——, Non-indigenous; ------, Aboriginal Australian; ·····, Māori/Pacific Islander.

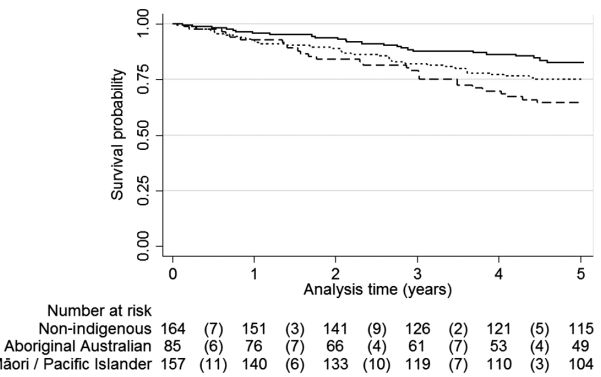

Figure 2 Kaplan–Meier survival curve: unadjusted respiratory-related mortality stratified by ethnicity (log-rank: P = 0.009) (hazard ratio compared with non-indigenous: Aboriginal Australian: 2.3 (95% CI: 1.3–3.9, P = 0.003) and Māori/Pacific Islander: not significant). ——, Non-indigenous; ------, Aboriginal Australian; ·····, Māori/Pacific Islander.

Table 2 Sputum microbiology

	Aboriginal Australian % (95% CI)	Non-indigenous Australian % (95% CI)	Māori or Pacific Islander % (95% CI)	Non-indigenous New Zealander % (95% CI)	*P*-value
Routine bacterial					
Available	89.4 (80.9–95.0)	64.6 (52.9–75.0)	66.2 (58.3–73.6)	75.3 (64.7–84.0)	<0.001
Positive if available					
S. pneumoniae, *H. influenza* or *M. catarrhalis* only	35.5 (24.9–47.3)	5.9 (1.2–16.2)	49.0 (39.1–59.0)	28.1 (17.6–40.8)	<0.001
P. aeruginosa	32.9 (22.5–44.6)	41.2 (27.6–55.8)	27.9 (19.5–37.5)	43.8 (31.4–56.7)	0.140
Methicillin-susceptible *S. aureus*	9.2 (3.8–18.1)	9.8 (3.3–21.4)	2.9 (0.6–8.2)	10.9 (4.5–21.2)	0.170
Non-multiresistant MRSA	13.2 (6.5–22.9)	2.0 (0.1–10.5)	0.0 (0–3.5)	0.0 (0.0–5.6)	<0.001
MRSA	1.3 (0.0–7.1)	0.0 (0.0–7.0)	1.0 (0.0–5.2)	0.0 (0.0–5.6)	1.000
Klebsiella species	18.4 (10.5–28.9)	2.0 (0.1–10.5)	2.9 (0.6–8.2)	12.5 (5.6–23.2)	<0.001
A. fumigatus	4.0 (0.8–11.1)	25.5 (14.3–39.6)	9.6 (4.7–17.0)	21.9 (12.5–34.0)	0.001
Mycobacteria					
Available	84.7 (75.3–91.6)	34.2 (23.9–45.7)	29.9 (22.9–37.8)	30.6 (21.0–41.5)	<0.001
Positive if available					
MAC	4.2 (0.9–11.7)	7.4 (0.9–24.3)	0.0 (0–7.5)	0.0 (0–13.2)	0.166
Non-MAC mycobacteria	15.3 (7.9–25.7)	7.4 (0.9–24.3)	0.0 (0–7.5)	5.4 (1.0–26.0)	0.018

MAC, *Mycobacterium avium* complex; MRSA, methicillin-resistant *Staphylococcus aureus.*

compared with all other groups ($P < 0.001$). Māori/Pacific Islanders had significantly lower percentage predicted FEV_1 and FVC than their non-indigenous counterparts ($P = 0.004$ and 0.025, respectively).

There were marked differences in healthcare utilization between Aboriginal Australians and other groups (Table 4). Aboriginal patients were more likely to be admitted to hospital ($P \leq 0.041$), more likely to require more than five admissions ($P < 0.001$) and, during admission, more likely to require intensive care ($P < 0.001$) and ventilation ($P < 0.001$) than any other group. Overall intensive care and ventilation use was greater in Australia (31.7% (95% CI: 24.7–39.4) and 35.4% (28.1–43.2), respectively) as compared with New Zealand (2.9% (1.2–5.9) and 5.8% (3.2–9.5)) ($P < 0.001$ for both comparisons). Aboriginal Australians had a higher incidence of admission (incidence rate ratio (IRR): 4.15, 95% CI: 3.59–4.83) and longer total days in hospital (IRR: 2.64, 95% CI: 2.51–2.78) than non-indigenous Australians. No such differences were observed between Māori/Pacific Islanders and non-indigenous New Zealanders.

Factors independently predicting all-cause mortality included being Aboriginal Australian (HR: 3.9, 95% CI: 2.3–6.7), female sex (HR: 0.7, 95% CI: 0.5–0.9) and increasing age (HR: 1.1/year, 95% CI: 1.0–1.1). Factors independently predicting respiratory-related mortality included being Aboriginal Australian (HR: 4.3, 95% CI: 2.3–8.2) or Māori/Pacific Islander (1.7, 1.1–3.0), female sex (0.6, 0.4–0.9) and increasing age (1.0/year, 1.0–1.1). Sputum organisms, cHRCT findings, lung function and healthcare utilization were not independently associated with all-cause or respiratory-related mortality. Kaplan-Meier survival curves for all-cause and respiratory-related survival adjusted for age and sex are presented in Supplementary Figures S1 and S2 respectively.

In multivariate modelling, the absolute FACED score was associated with all-cause and respiratory-related

Table 3 HRCT and lung function results

	Aboriginal Australian	Non-indigenous Australian	Māori or Pacific Islander	Non-indigenous New Zealander	*P*-value
HRCT					
Number of lobes with bronchiectasis (median, IQR)	3 (2–4)	2 (2–4)	4 (2–5)	3 (2–6)	<0.001
Bilateral bronchiectasis (%, 95% CI)	76.9 (66.2–85.0)	80.0 (69.3–87.6)	86.0 (79.6–90.6)	76.5 (66.2–84.3)	0.508
Spirometry					
Result available (%, 95% CI)	54.4 (42.8–65.7)	36.5 (26.3–47.6)	45.9 (37.9–54.0)	45.9 (35.0–57.0)	0.148
FEV_1 % predicted (median, IQR)	30 (20–37)	48 (39–81)	42 (31–56)	61 (42–68)	<0.001
FVC % predicted (median, IQR)	41 (32–48)	65 (48–93)	57 (49–69)	70 (52–85)	<0.001
FEV_1/FVC ratio (%) (median, IQR)	60 (45–71)	63 (52–78)	62 (54–70)	66 (52–75)	0.292
FEV_1/FVC < 70% (%, 95% CI)	74.1 (53.7–88.9)	62.8 (46.7–77.0)	72.2 (60.4–82.1)	56.4 (39.6–72.2)	0.283

FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; IQR, interquartile range.

Table 4 Five-year healthcare utilization

	Aboriginal Australian % (95% CI)	Non-indigenous Australian % (95% CI)	Māori or Pacific Islander % (95% CI)	Non-indigenous New Zealander % (95% CI)	*P*-value
Any admission	80.0 (69.9–87.9)	65.8 (54.3–76.1)	63.1 (55.0–70.6)	64.7 (53.6–74.8)	0.049
≥5 Admissions	47.1 (36.1–58.2)	17.7 (10.1–27.9)	23.6 (17.2–31.0)	20.0 (12.1–30.1)	<0.001
Required critical care	44.7 (33.9–55.9)	17.7 (10.1–27.9)	3.2 (1.0–7.3)	2.4 (0.3–8.2)	<0.001
Ventilation (any)	50.6 (39.5–61.6)	19.0 (11.0–29.4)	7.6 (4.0–13.0)	2.4 (0.3–8.2)	<0.001
Non-invasive ventilation	37.6 (27.4–48.8)	17.7 (10.1–27.9)	5.7 (2.7–10.6)	1.2 (0.0–6.4)	<0.001
Invasive ventilation	8.2 (3.4–16.2)	5.1 (1.4–12.5)	0.0 (0.0–2.3)	0.0 (0.0–4.2)	0.417
Incidence rate					
Hospital admissions (no./person-year)	2.9 (2.7–3.1)	0.7 (0.6–0.8)	0.7 (0.6–0.8)	0.7 (0.6–0.8)	—
Length of stay (days/person-year)	16.9 (16.4–17.3)	6.4 (6.1–6.7)	4.1 (4.0–4.3)	3.97 (3.8–4.2)	—

mortalities (HR: 1.16, 1.04–1.29 and HR: 1.25, 1.09–1.43, respectively) and this association persisted when controlling for ethnicity (1.18, 1.05–1.32 and 1.29, 1.12–1.49). Furthermore, in regression modelling, the FACED score was also significantly associated with the number of hospital admissions ($P = 0.002$) and total length of stay in hospital ($P < 0.001$). These associations again persisted when controlling for ethnicity ($P < 0.001$).

DISCUSSION

We report, for the first time, data to describe bronchiectasis and its outcome in adult indigenous and non-indigenous populations in Australia and New Zealand. Aboriginal Australians were significantly younger with an age profile more comparable to that reported in low- and middle-income countries including India and Nepal[6,7] than in Europe.[3–5] This younger age suggests that different factors, or similar factors acting at an earlier age, drive disease development in this population. It is likely that Aboriginal Australians' well-described social and environmental disadvantages, compounded by remoteness, are important. Although a range of risk factors may be associated with such health determinants, it is probable that repeated respiratory infections in childhood and, particularly in Central Australia, the impact of a higher prevalence of human T-cell lymphotropic virus type 1 infection on host immune response to such infections are both important.[18]

Unadjusted all-cause mortality was substantial with 34% of patients dying within 5 years. This is higher than European studies that demonstrated a 5-year mortality of between 12% and 20%.[3–5] While there was no significant difference in unadjusted all-cause mortality between groups, Aboriginal Australians died at a younger age, a fact that is also likely to explain the younger age of Aboriginal Australians in this study. Furthermore, 42% of Aboriginal Australian participants died during 5 years of follow-up, more than double rates reported from European studies. In relation to unadjusted respiratory-related survival, Aboriginal Australians were more than twice as likely to die compared with other groups in our study and again at a significantly younger age.

While unadjusted all-cause mortality did not differ between subgroups, when adjusted for age and sex, there was significantly greater mortality in Aboriginal Australians who were nearly four times more likely to die over the 5-year period of follow-up compared with non-indigenous groups. A similar increased risk for adjusted respiratory-related mortality was seen in Aboriginal Australians with a smaller significant increased risk in Māori and Pacific Islanders.

Results of FACED scores demonstrated that Aboriginal Australians had milder assessed disease that did not translate to a better prognosis. Caution must therefore be exercised when extrapolating prognostic scores based on European cohorts to other populations. An important determinant of less severe FACED categorization seen in Aboriginal Australians was their younger age. Given the socio-economic and health disadvantages faced by indigenous Australians and their earlier onset of bronchiectasis, it may be argued that the age stratification used in the FACED score should be recalibrated for this ethnic group. Nonetheless, our finding of an independent association between FACED and survival and hospital admission suggests that these factors remain important when assessing disease severity in disparate populations.

Sputum microbiology highlights important differences between groups. Aboriginal Australian and Māori/Pacific Islander subjects were more likely to have sputum microbiology restricted to the three common respiratory bacteria: *S. pneumoniae, H. influenzae* and *M. catarrhalis.* Such information can be key in informing empiric guidelines for population-specific management of exacerbations. It may also suggest that environmental and social disadvantages may influence the dynamics of sputum microbiology. The over-representation of nmMRSA and *Klebsiella* species in Aboriginal Australians is likely to reflect the greater burden of these bacteria in this population more generally.[19,20]

While the more frequent isolation of *A. fumigatus* in non-indigenous patients may suggest that this fungus is a more important factor in non-indigenous disease, it may also be a commensal that is less likely to be supplanted by the common respiratory bacteria more

frequently seen in indigenous patients. An alternative explanation is that this may indicate a greater contribution of allergic bronchopulmonary aspergillosis[21] in non-indigenous patients. The limited and inconsistent investigation of secondary causes of bronchiectasis in our study restricts the ability to determine the significance of this finding and provides a persuasive case for more consistent investigation for secondary causes in patients with bronchiectasis. A recent review of studies investigating secondary causes in patients with bronchiectasis found that such causes were identified in 18–95% of patients. While the veracity of attributing bronchiectasis to conditions such as COPD or past infections may be debated, it was noted that such diagnoses nonetheless altered management in 18% of patients.[22]

Overall sputum mycobacterial cultures were available in less than one-third of patients. Aboriginal Australians were more likely to have these performed which may reflect the greater burden of pulmonary tuberculosis in this setting.[23] When performed, the results indicated a low level of NTM with a higher proportion of non-MAC mycobacteria seen in Aboriginal Australians. This was consistent with previous studies that found NTM isolated in 8–12% of patients and MAC in 4%.[24,25]

Radiology and spirometry findings showed little difference between groups except with an indication of less extensive disease based on cHRCT in non-indigenous Australians. This may in part relate to selection bias with such patients being more likely to access cHRCT and gain a radiological diagnosis in this urban setting. Spirometry results were available in less than half of the participants suggesting clinicians may not value these greatly. When available, they highlighted that airflow obstruction was common but not universal. The lower percentage predicted values of FEV_1 and FVC seen in Aboriginal Australians did not take into account of any correction for ethnicity but we have previously argued that such correction may relate to social and environmental disadvantages rather than ethnicity *per se*.[26]

Healthcare utilization including hospitalization and critical care admission demonstrated the significant burden that bronchiectasis places on hospitals. While admission was substantial for all patients, it was notably high for Aboriginal Australians. Given the compounding effects of remoteness, disadvantage and premature mortality, such higher levels may point to difficulties in ensuring community-based treatment of exacerbations. The difference in critical care use in Australia compared with New Zealand is likely to indicate differences in clinical practice with a lower threshold for ventilatory support and critical care support in Australia.

In Australia and New Zealand, case-mix funding models based on Australian Refined Diagnosis Related Groups (AR-DRG) are utilized in determining health service resourcing.[27] While there are two specific codes available for CF, there is currently no specific disease category for bronchiectasis.[27] This is likely to be a disadvantage for healthcare services that care for populations with a greater burden of bronchiectasis. Greater recognition and understanding of the actual cost of bronchiectasis related to healthcare utilization and particularly hospitalization will be aided by the planned future implementation of a specific funding-linked AR-DRG for this condition. This will also provide a persuasive rationale in advocating for initiatives to prevent disease and exacerbations and to encourage community-based management.

A number of limitations arise from the retrospective nature of this study. A key consideration is the use of clinical reports of cHRCT to define cases of bronchiectasis, a case definition that is likely to differ by site and reporting radiologist. In addition, sputum and other investigations were not available for all patients and the impact of such missing data on selection bias should be appreciated. Other factors associated with outcomes including co-morbidities were not recorded and these may have been important contributors to differences in healthcare utilization and survival. Finally, study groups were recruited in different hospitals and countries potentially representing a source of bias. Nonetheless, the similarities in healthcare delivery in Australia and New Zealand and resources available for investigation and management of patients at the hospitals involved in this study enable meaningful and valid comparison between groups such that differences observed between groups are unlikely to be explained by healthcare site alone.

Despite such limitations, it is clear from this study that bronchiectasis is not one disease. The earlier onset of severe disease and premature mortality seen in Aboriginal Australians and, to a lesser extent, Māori and Pacific Islander peoples, highlight the importance of social and environmental disadvantages as drivers of respiratory disease in general and bronchiectasis specifically.[28] There is a need to move beyond observational studies such as this. Prospective studies focusing on the mechanisms underlying primordial and primary prevention and perinatal and environmental exposures in early life, particularly in disadvantaged and vulnerable populations, should be a focus for future research.

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Supplementary Information

Additional supplementary information can be accessed via the *html* version of this article at the publisher's website.

Figure S1 Kaplan–Meier survival curve: age- and sex-adjusted all-cause mortality stratified by ethnicity.
Figure S2 Kaplan–Meier survival curve: age- and sex-adjusted respiratory-related mortality stratified by ethnicity.

