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Australian adults with bronchiectasis: The first report from the Australian Bronchiectasis Registry

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ABSTRACT

Background: /objective: There are no large, multi-centre studies of Australians with bronchiectasis. The Australian Bronchiectasis Registry (ABR) was established in 2015 to create a longitudinal research platform. We aimed to describe the baseline characteristics of adult ABR participants and assess the impact of disease severity and exacerbation phenotype on quality of life (QoL).

Methods: The ABR is a centralised database of patients with radiologically confirmed bronchiectasis unrelated to cystic fibrosis. We analysed the baseline data of adult patients (≥18 years).

Results: From March 2016–August 2018, 799 adults were enrolled from 14 Australian sites. Baseline data were available for 589 adults predominantly from six tertiary centres (420 female, median age 71 years (interquartile range 64–77), 14% with chronic *Pseudomonas aeruginosa* infection). Most patients had moderate or severe disease based on the Bronchiectasis Severity Index (BSI) (84%) and FACED (59%) composite scores. Using Global Lung function Initiative-2012 reference equations, the majority of patients (48%) had normal spirometry; only 34% had airflow obstruction ($FEV_1/FVC < LLN$). Disease severity scores (BSI and FACED) were negatively correlated with QoL-Bronchiectasis domain scores (r_s between −0.09 and −0.58). The frequent exacerbator phenotype (≥3 in the preceding year) was identified in 23%; this group had lower scores in all QoL-B domains ($p \leq 0.001$) and more hospitalisations ($p < 0.001$) than those with < 3 exacerbations.

Conclusions: The largest cohort of Australian adults with bronchiectasis has been described. Using contemporary criteria, most patients with bronchiectasis did not have airflow obstruction. The frequent exacerbation trait connotes poorer QoL and greater health-care utilisation.

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List of abbreviations

ABPA	Allergic Bronchopulmonary Aspergillosis
ABR	Australian Bronchiectasis Registry
BMI	Body Mass Index (kg/m^2)
BSI	Bronchiectasis Severity Index
COPD	Chronic Obstructive Airways Disease
CT-chest	Computed Tomography scan of the chest
FACED	FEV_1, Age, Colonisation, Extension, Dyspnoea
FEV_1	Forced Expiratory Volume in 1 s
FEV_1%pred	Forced Expiratory Volume in 1 s as a percent of predicted (per Global Lung function Initiative-2012 reference equations)
FVC	Forced Vital Capacity
FVC%pred	Forced Vital Capacity as a percent of predicted (per Global Lung function Initiative-2012 reference equations)
GLI	Global Lung function Initiative
GORD	Gastro-oesophageal Reflux Disease
IQR	Interquartile range
LLN	Lower Limit of Normal defined by the Global Lung function Initiative-2012 reference equations
MABSC	*M. abscessus* complex
MCID	Minimal Clinically Important Difference
mMRC	modified Medical Research Council dyspnoea scale
n	number of participants
NTM	Nontuberculous mycobacteria
PCD	Primary Ciliary Dyskinesia
QoL	Quality of Life
QoL-B	Quality of Life Questionnaire-Bronchiectasis
TB	Tuberculosis

1. Introduction

Bronchiectasis, a chronic lung disease defined radiologically by abnormal bronchial dilatation, is characterised clinically by chronic cough, sputum production and recurrent pulmonary exacerbations [1]. Patients with bronchiectasis are markedly heterogeneous with a diverse disease aetiology [2].

The reported prevalence of bronchiectasis is increasing worldwide [3–5]. Recent United Kingdom data estimates a prevalence of 566/100,000 women and 485/100,000 men [4], although significant geographic diversity exists [6]. Females, the elderly [3–5] and indigenous populations [7] are more commonly affected; notably, Indigenous children in Australia's Northern Territory have the highest reported disease prevalence of 1470/100,000 children [8]. Nevertheless, no large multi-centre study has been conducted to examine the prevalence or characteristics of bronchiectasis in an Australian setting.

The Australian Bronchiectasis Registry (ABR) is a nationwide collaboration established in 2015 with the aims of evaluating the clinical phenotypes of Australians with bronchiectasis and providing a platform for ongoing collaborative research. Documenting the varying characteristics of bronchiectasis among cohorts, countries and settings is important for patient management and for planning the delivery of health service [6]. Furthermore, in a heterogeneous condition for which licensed therapies are non-existent and recent clinical trials have not met their primary endpoints, defining targetable phenotypes is important to ensure trials meet their endpoints and to progress towards precision management for patients [9–12]. We report the baseline characteristics of the ABR adult cohort, and assess the influence of disease severity and exacerbation phenotype on patient quality of life (QoL) and health-care utilisation.

2. Methods

2.1. The Australian Bronchiectasis Registry

The ABR is a secure online database of Australian adults and children with bronchiectasis. Sites recruiting to the ABR are predominantly tertiary centres located across Australia. Eligible patients are those with a physician diagnosis of bronchiectasis with abnormal bronchial dilatation demonstrated on computed tomography chest scan (CT-chest) [13]. Patients with known cystic fibrosis are excluded. National ethical approval was obtained (Protocol No X16-0382, Project no HREC/15/CRGH/225), with local research governance approval subsequently granted at investigating sites. Further information is available in Appendix S1.

2.2. Data collection and definitions

At enrolment, participants' baseline data were collected from the patient and by searching all available hospital and outpatient records, including electronic medical records. Baseline data were collected at times of clinical stability.

The likely aetiology of bronchiectasis was determined by the treating physician and obtained from patient records.

Spirometry results measured closest to the date of enrolment were collected. Global Lung function Initiative (GLI)-2012 reference equations were used to determine the upper/lower limits of normal (LLN) and percent of predicted forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) based on age, sex, height and ethnicity [14]. Airflow obstruction was defined as FEV_1/FVC < lower limit of normal (LLN), normal spirometry as FEV_1, FVC, and FEV_1/FVC > LLN, and restrictive pattern spirometry as FEV_1/FVC > LLN and FVC < LLN [15].

Details of CT chest performed closest to the date of enrolment were extracted from radiology reports, including the location of bronchiectasis and presence of cystic dilatation.

Airway culture results were obtained for the period two years prior to, and three months after enrolment. Chronic infection was pragmatically defined as two or more positive cultures for the same organism during this period [16].

Pulmonary exacerbations, defined by the treating physician, in the year preceding enrolment, were obtained from the patient and/or records.

The Quality of Life Questionnaire-Bronchiectasis (QoL-B) [17] was completed by participants at enrolment.

Bronchiectasis severity was quantified as "mild", "moderate" or "severe" using validated, disease-specific composite scales – the Bronchiectasis Severity Index (BSI) [18] and the FACED (FEV_1, Age, Colonisation, Extension, Dyspnoea) [19] score.

2.3. Statistical analysis

Patients < 18yrs and those lacking the results of both CT-chest and spirometry were excluded (Fig. 1).

Data are not normally distributed; results are presented as median and interquartile range (IQR). Descriptive statistics were used to characterise the demographics and disease features of the cohort.

Analysis of patient characteristics by spirometric pattern (normal, obstructed, restricted) was performed using a Kruskal-Wallis (for continuous or ordinal dependent variables) or Chi-square test (for categorical dependent variables) to compare independent groups. The relationship between FEV_1/FVC and disease severity (BSI and FACED scores) was assessed using Spearman's correlation (r_s).

Sub-group analysis of patient characteristics by cultured organism

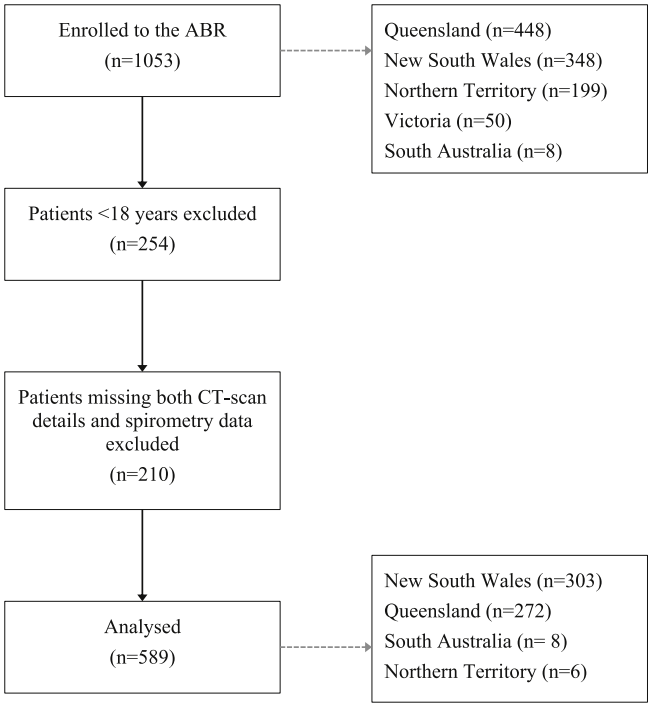

Fig. 1. *Consort Diagram.*

(*P. aeruginosa*, *H. influenzae,* nil organisms*)* was performed using a Kruskal-Wallis or Chi-square test. For this microbiological analysis, patients without airway culture results, those who cultured both *H. influenzae* and *P. aeruginosa*, and those with nontuberculous mycobacteria were excluded.

Cohen's kappa coefficient (κ) was used to measure agreement between BSI and FACED-determined severity categories (mild, moderate, severe). The relationship between severity scores - BSI score (0-26) and FACED score (0–7) - and QoL-B domain scores (0–100) were explored with scatterplots. Subsequently, Spearman's correlation was performed between the BSI/FACED scores and QoL-B domain scores.

The characteristics of patients with frequent (≥3 exacerbations in the preceding year) (10) versus non-frequent exacerbations were compared using a Mann-Whitney (for continuous or ordinal dependent variables) or Chi-square test (for categorical variables). Data were analysed in StataSE Version 15.1.621.

3. Results

Between March 2016 and August 2018, 14 sites across the Australian mainland recruited a total of 1053 patients to the ABR: 799 (76%) adults (42 Indigenous) and 254 (24%) paediatric participants (130 Indigenous). Of these, 589 adults, predominantly from six centres across the states of New South Wales (303 patients) and Queensland (272 patients) met the inclusion criteria for this study (Fig. 1). The demographics and clinical characteristics of the cohort are presented in Tables 1 and 2. Patients were predominantly Caucasian (86%) and female (71%), with a median age of 71 years (IQR 64–77). Physician-reported disease aetiology (Fig. 2) was mostly idiopathic (32.5%) or post-infective (28%).

3.1. Spirometry

Airflow obstruction was present in 168 (34%) patients using the lower-limit of normal definition (FEV_1/FVC < LLN) (15) versus 50% of the population when defined by the Global initiative for Chronic Obstructive Lung Disease criteria of $FEV_1/FVC < 0.7$ (20). Restrictive pattern spirometry was observed in 72 (15%) patients.

The spirometric ratio (FEV_1/FVC) was negatively correlated with bronchiectasis severity, measured by the FACED score ($r_s = -0.43$, $p < 0.001$) and the BSI score ($r_s = -0.34$, $p < 0.001$). Airflow obstruction was the predominant pattern in patients with severe disease; present in 40% of patients with BSI-severe disease and 60% of those with FACED-severe disease. Nevertheless, 36% of those with BSI-severe disease and 19% of those with FACED-severe disease had normal spirometry (Fig. 3).

Table 3 displays patient characteristics and QoL stratified by spirometric pattern. Compared to patients with normal spirometry, those with restrictive patterns and those with obstruction had more lobes involved, more exacerbations, were more likely to have been hospitalised in the preceding year, and had lower QoL-B scores ($p < 0.05$ for all comparisons).

3.2. Microbiology

Standard airway culture results were available for 345 (59%) patients. *P. aeruginosa* was the most commonly isolated organism (at least once in 35% of patients; 14% had chronic infection). *H. influenzae* was the second most common bacterium isolated (at least once in 17% of patients; 4% had chronic infection). *S. aureus* was cultured in 17 (5%) patients, was methicillin-sensitive in 16, and was chronic in 4 patients. No other single microorganism was isolated in ≥5% of the tested cohort.

Results of mycobacterial testing were available in 169 (29%) patients. Of these, 40 patients (24%) had one or more positive results, which were predominantly *M. intracellulare* (23/40) and *M. avium* (11/40). *M. abscessus* complex (MABSC) was found in 6/40 patients and was chronic in 4/40.

Of the 356 (60%) patients for whom any culture (standard and/or mycobacterial) was available, 117 (33%) had no microorganisms isolated. More than one organism was found in 49 (14%) patients in either the same or subsequent samples, however only four patients cultured both *H. influenzae* and *P. aeruginosa*.

Patients with *P. aeruginosa* were older, with lower FEV_1%pred, more frequent exacerbations and more hospitalisations than those with *H. influenzae* or no organisms cultured on testing. Patients with no organisms cultured had significantly higher FEV_1%pred and FEV_1/FVC, and fewer lobes affected than those with either *P. aeruginosa* or *H. influenzae.* Notably, QoL-B domain scores were similar across groups, with the exception of lower scores in the Treatment Burden domain in patients with *P. aeruginosa* ($p < 0.05$ for all stated comparisons, Table S1).

Table 1
Demographics of adult registry participants.

	Result	n
Age, years	71 (64–77)	589
Gender		589
Female	420 (71%)	
Male	169 (29%)	
Ethnicity		450
Caucasian	386 (86%)	
Asian	48 (11%)	
Indigenous	1 (0.2%)	
Other	15 (3%)	
Body Mass Index, kg/m^2	25 (22–29)	499
Smoking Status		581
Never	451 (78%)	
Former	123 (21%)	
Current	7 (1%)	

Values are median (interquartile range) or proportions.
n – number of participants for whom variable data was available.

Table 2
Baseline characteristics of the Australian adult bronchiectasis cohort.

	Result		n
Spirometric Indices			
FEV_1 %pred	75 (57–91)		499
FVC %pred	84 (71–97)		498
Normal Spirometry[a]	239 (48%)		498
Airflow Obstruction			509
FEV_1/FVC < LLN	168 (34%)		498
FEV_1/FVC < 0.7	252 (50%)		
Restrictive Pattern[b]	72 (15%)		
Radiology			563
Number of lobes affected	3 (2–5)		
Cystic bronchiectasis	81 (14%)		
Microbiology			
Airway culture available			345
AFB culture available			169
	Ever	**Chronic^**	
P. aeruginosa	119 (35%)	49 (14%)	345
H. influenzae	60 (17%)	15 (4%)	345
Nontuberculous mycobacteria	40 (24%)	15 (9%)	169
Exacerbations in the last 12 months			
Total	1 (0–2)		557
Number of respiratory hospitalisations	0 (0–1)		580
Respiratory hospitalisation (Y)	166 (29%)		580
Symptoms			
mMRC	1 (0–2)		570
Limited exercise tolerance (mMRC > 0)	393 (69%)		570
Daily cough with sputum	416 (71%)		589
Disease severity scores			
BSI	10 (6–13)		290
FACED	3 (2–4)		310
QoL-B Scores [c]			
Respiratory Symptoms	67 (48–78)		414
Physical Functioning	83 (67–100)		414
Vitality	56 (33–67)		414
Role Functioning	73 (47–87)		414
Health Perceptions	60 (27–87)		414
Emotional Functioning	83 (67–100)		414
Social Functioning	58 (42–83)		414
Treatment Burden	78 (56–89)		414

Values are median (interquartile range) or proportions.
n - number of participants for whom variable data was available; FEV1 %pred – forced expiratory volume in 1 s, percent of predicted (GLI-2012); FVC – forced viral capacity; LLN - lower limit of normal (per GLI-2012); AFB – acid-fast bacillus; mMRC - modified Medical Research Council dyspnoea scale; BSI – Bronchiectasis Severity Index; FACED - FEV_1, Age, Colonisation, Extension, Dyspnoea; QoL-B – Quality of Life Questionnaire-Bronchiectasis.
[#] respiratory-related hospitalisations in the year preceding enrollment.
[a] FEV_1/FVC, FEV_1, FVC > LLN.
[b] FEV_1/FVC > LLN & FVC < LLN; ^ Defined as 2 + airway cultures positive for the same pathogen.
[c] Out of a total of 100 possible points for each domain.

3.3. Disease severity

Fig. 3 displays the disease severity of the cohort, as defined by the BSI (18) and FACED (19) score. According to BSI, 58% of our cohort has severe disease, whereas 17% have FACED-defined severe disease. Weak agreement was found between the FACED and BSI severity categories ($\kappa = 0.2$, SE 0.03, $p < 0.001$).

3.4. Quality of life

Most patients expectorated sputum every day (71%) and experienced limited effort tolerance (69%) (modified Medical Research Council dyspnoea scale score ≥1). In the 12 months preceding enrolment, 29% of patients had been hospitalised for bronchiectasis. QoL-B scores were impaired in all domains.

Negative linear associations between disease severity (BSI and FACED scores) and QoL (QoL-B domain scores) were seen on scatterplots. QoL and disease severity were most strongly correlated in the Physical (BSI $r_s = -0.47$, FACED $r_s = -0.58$) and Role Functioning domains (BSI $r_s = -0.42$, FACED $r_s = -0.44$) ($p < 0.001$ for all stated) – see Table S2.

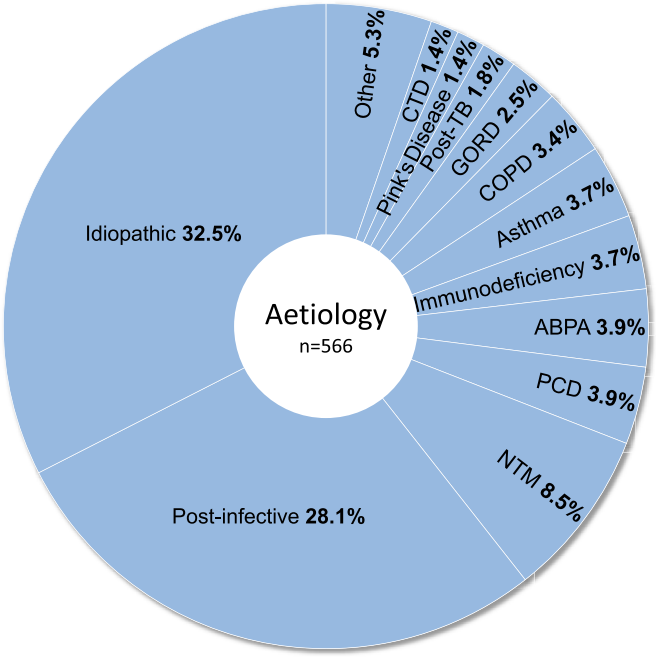

Fig. 2. *Physician-reported aetiology of bronchiectasis in the Australian adult cohort (n = 566).* NTM – nontuberculous mycobacteria; ABPA – allergic bronchopulmonary aspergillosis; PCD – primary ciliary dyskinesia; COPD – chronic obstructive lung disease; GORD – gastro-oesophageal reflux disease; TB- tuberculosis; CTD – connective tissue disease.

Table 4 displays the characteristics of disease according to exacerbation phenotype (10). Frequent exacerbators (≥3 in preceding year) had significantly lower QoL-B scores compared to those with < 3 exacerbations, with differences exceeding the MCID for each domain. Frequent exacerbators had more respiratory hospitalisations, lower FEV_1%pred, lower FEV_1/FVC, and were more likely to have chronic *P. aeruginosa* infection, produce sputum daily, and have limited exercise tolerance ($p < 0.05$ for all comparisons).

4. Discussion

In this report on the largest cohort (n = 589) of Australian adults with bronchiectasis, we describe important findings about bronchiectasis in the Australian context that have broader relevance.

Although traditionally classified as an obstructive airways disease, it is recognised that patients with bronchiectasis can exhibit normal, restrictive, or mixed spirometric pattern [1]. American and European registries report airflow obstruction in approximately 50% of each cohort [18,21] using the former diagnostic criteria of $FEV_1/FVC < 0.70$ [20]. Using this criterion, 50% of our cohort also had obstruction. In contrast, using the current definition [15] of abnormality (below the lower limit of normal as determined by GLI-2012 reference equations [14]), we showed that the largest proportion (48%) of our patients had normal spirometry. Airflow obstruction (FEV_1/FVC < LLN) was present in only one-third of patients. We found a moderate negative correlation between spirometric ratio and disease severity as measured by FACED and BSI. Nevertheless, a large proportion of those classified as having severe disease did not demonstrate obstruction (60% of BSI-severe, 40% of FACED-severe).

To our knowledge, this is the largest bronchiectasis study to examine spirometric pattern using the current LLN criteria. It demonstrates that even patients with "severe" bronchiectasis, as defined by

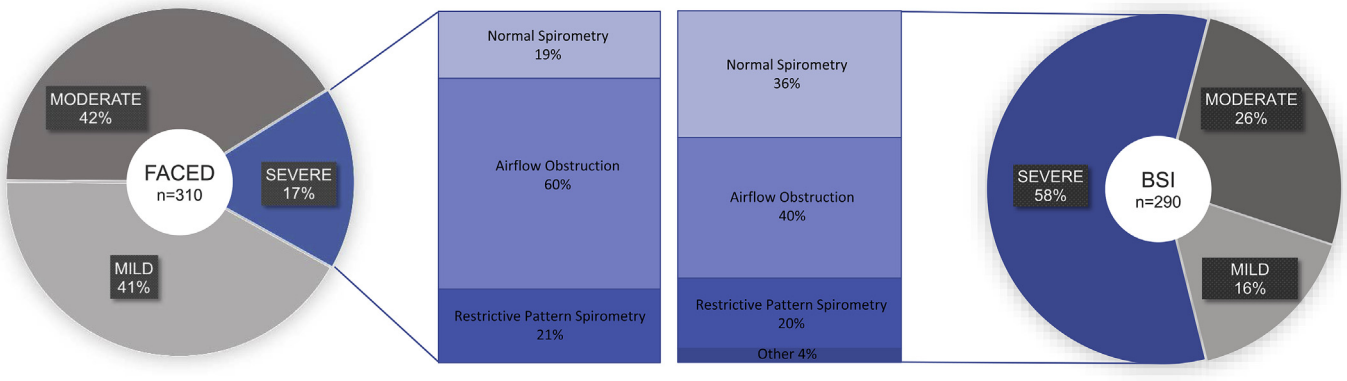

Fig. 3. *Severity of disease and spirometry.*
BSI; Bronchiectasis Severity Index; FACED; FEV_1, Age, Colonisation, Extension, Dyspnoea; n - number of participants for whom all included variables were available for score calculation.
Normal spirometry =
Forced Expiratory Volume in 1 s
(FEV_1), Forced Vital Capacity (FVC), and FEV_1/FVC all > lower limit of normal per GLI-2012.
Airflow Obstruction =
FEV_1/FVC < LLN.
Restrictive Pattern =
FEV_1/FVC > LLN & FVC < LLN.

Table 3
Analysis of baseline clinical characteristics and quality of life by spirometric pattern.

	Normal Spirometry	Airflow Obstruction	Restrictive Pattern	p-value
n = 489	239 (49%)	168 (34%)	72 (15%)	
Age (yrs)	71 (63–78)	69 (62–75)	72 (63–78)	0.05
Ever smoked (Y)	46 (19%)	47 (29%)	13 (18%)	0.06
Lobes affected	3 (2–4)	4 (2–6)	4 (2–6)	**0.02**[a]
P. aeruginosa[b] (Y)	39 (16%)	43 (26%)	26 (36%)	**0.001**[a]
BSI	8 (5–11)	12 (8–15)	11 (7–13)	< **0.001**[a]
FACED score	2 (1–4)	4 (3–5)	3 (2–4)	< **0.001**[a]
Respiratory hospitalisation[c]	44 (18%)	65 (39%)	27 (38%)	< **0.001**[a]
No. of Exacerbations[c]	1 (0–2)	2 (1–3)	2 (0–3)	**0.001**[a]
QoL-B Domains[d]				
Respiratory Symptoms	70 (58–82)	56 (41–70)	67 (41–78)	< **0.001**[a]
Physical Functioning	73 (40–93)	40 (13–73)	40 (17–73)	< **0.001**[a]
Vitality	56 (33–67)	44 (33–56)	44 (22–67)	**0.01**[a]
Role Perceptions	80 (60–93)	67 (33–83)	53 (27–87)	< **0.001**[a]
Health Perceptions	50 (33–67)	42 (25–58)	42 (22–58)	< **0.001**[a]
Emotional Functioning	83 (67–100)	83 (67–100)	67 (58–92)	**0.049**[a]
Social Functioning	67 (50–83)	57 (33–78)	66 (33–75)	**0.004**[a]
Treatment Burden	77 (67–100)	67 (57–89)	67 (44–89)	< **0.001**[a]

Results are presented as median (interquartile range) or proportions.
Normal spirometry = Forced Expiratory Volume in 1 s (FEV_1), Forced Vital Capacity (FVC), and FEV_1/FVC all > lower limit of normal per GLI-2012; Airflow Obstruction = FEV_1/FVC < LLN; Restrictive Pattern = FEV_1/FVC > LLN & FVC < LLN; n - number of participants for whom variable data was available; BSI - Bronchiectasis Severity Index; FACED - FEV_1, Age, Colonisation, Extension, Dyspnoea; QoL-B – Quality of Life Questionnaire-Bronchiectasis.

[a] Significant differences ($\alpha < 0.05$) between independent groups on Kruskal-Wallis (for continuous/ordinal variables) or Chi-square test (for categorical variables).

[b] Isolation of *P. aeruginosa* on ≥1 sample.

[c] Within the year preceding enrollment.

[d] Out of a total of 100 possible points for each domain.

validated composite scores that incorporate radiology and predict mortality [18,19], often do not meet the current diagnostic criterion for airflow obstruction and may have normal spirometry. We also showed that both obstructive and restrictive patterns are associated with poorer QoL and increased exacerbations and hospitalisations. As reporting of spirometry based on LLN per GLI becomes more widespread, it is important to recognise that normal results do not exclude clinically significant or even "severe" bronchiectasis and its attendant morbidity and mortality [18,19].

Most of the Australian cohort had moderate or severe bronchiectasis (84% according to the BSI, 59% according to the FACED score). The weak agreement between severity scores and the tendency for the BSI to assign patients a higher severity grade than FACED is consistent with recent literature [22]. While both scores predict mortality, BSI has also been shown to predict exacerbations and QoL (per St George Respiratory Questionnaire) [22]. In our cohort, weak to moderate negative correlations were seen between severity scores (BSI and FACED) and QoL-B domain scores; the strongest negative correlations were seen with the Physical and Role Functioning domains. These findings highlight the difficulty of comprehensively appreciating QoL with existing tools in a complex condition such as bronchiectasis [23,24], but also suggest that there are clinical factors impacting QoL which are not captured in severity scores. Additionally, local prospective studies are required to determine the validity of the Qol-B and the BSI and FACED severity scores in Australian patients, especially in Indigenous Australians. As an example, a recent study found that Aboriginal Australians with bronchiectasis had lower FACED scores (due to younger age and less *P. aeruginosa*) but higher 5-year respiratory-related mortality than non-indigenous patients, and suggested that recalibration of age scoring may be required for Indigenous patients [25].

Most patients within our cohort have a daily productive cough, making sputum collection feasible. However, only 29% had mycobacterial culture results available, of which 24% had NTM isolated and 9% had chronic NTM. These were predominantly *M. avium* and *M intracellulare*, however *M. abscessus* complex (MABSC) was cultured in 6 patients, and was chronic in 4 patients. NTM have long been recognised as a cause or complication of bronchiectasis, however the increasing prevalence of NTM in bronchiectasis patients is now appreciated [26]. Of particular concern are MABSC; multidrug-resistant NTM with the potential for person-to-person spread and a contraindication to lung transplant in many centres [27]. In patients with bronchiectasis, mycobacterial cultures are recommended at diagnosis, periodically for surveillance in stable spontaneously expectorating patients, during times of clinical or radiological deterioration, and prior to and during

Table 4
Characteristics of disease according to "Frequent Exacerbator" phenotype.

	< 3 exacerbations/year[a]	≥3 exacerbations/year[a]	Data Available	p-value
n	429 (77%)	128 (23%)	557	
Female	308 (72%)	92 (72%)	557	1.0
Age, yrs	71 (64–77)	71.5 (64–77)	557	0.9
BMI kg/m^2	25 (22–29)	26 (21–29)	471	0.7
FEV_1 %pred	78 (62–92)	67 (51–86)	471	< **0.001**[b]
FEV_1/FVC	0.72 (0.64–0.79)	0.66 (0.58–0.76)	482	**0.001**[b]
P. aeruginosa (ever)	73 (31%)	41 (42%)	329	0.06
P. aeruginosa (chronic)[c]	19 (8%)	28 (29%)	329	< **0.001**[b]
H. influenzae (ever)	47 (20%)	10 (10%)	329	0.03[b]
H. influenzae (chronic)[c]	10 (4%)	5 (5%)	329	0.7
Limited exercise tolerance	278 (66%)	101 (82%)	546	**0.002**[b]
Daily sputum	285 (67%)	105 (82%)	557	**0.001**[b]
No. of hospitalisations[d]	0 (0–0)	1(0–2)	557	< **0.001**[b]
QoL-B Domains[e]				
Respiratory Symptoms	70(52–78)	54(33–67)	393	< **0.001**[b]
Physical Functioning	67 (33–87)	33(10–67)	393	< **0.001**[b]
Vitality	56 (33–67)	44 (22–56)	393	**0.001**[b]
Role Functioning	80(53–93)	53(27–80)	393	< **0.001**[b]
Health Perception	50(33–67)	33 (22–50)	393	< **0.001**[b]
Emotional Functioning	83(67–100)	75(58–92)	393	**0.005**[b]
Social Functioning	67(42–83)	50(25–75)	393	< **0.001**[b]
Treatment Burden	78(67–100)	67(44–89)	393	**0.001**[b]

Values are median (interquartile range) or proportions.
n – number of participants; BMI – Body Mass Index; FEV1%pred – forced expiratory volume in 1 s, percent of predicted (per GLI-2012); FVC – forced vital capacity; QoL-B – Quality of Life Bronchiectasis.
[a] Refers to number of pulmonary exacerbations in the year preceding enrolment.
[b] Significant differences ($\alpha < 0.05$) between independent groups on Mann-Whitney (for continuous variables) or Chi-square test (for categorical variables).
[c] Defined as ≥2 airway cultures positive for the same pathogen.
[d] Respiratory-related hospitalisations in the year preceding enrolment.
[e] Out of a total of 100 possible points.

long-term macrolide therapy [26,28,29]. Therefore, these ABR data serve as a useful guide as to where simple tests should be utilised more frequently to improve diagnostic yield and optimise infection control and treatment.

Clinical phenotyping has been advocated as a strategy to minimise patient heterogeneity within bronchiectasis clinical trials and facilitate delivery of precision medicine [10,12,30,31]. The recently identified "frequent exacerbator" phenotype (≥3 exacerbations/year) is associated with an increased 5-year mortality [10], and in recent clinical trials frequent exacerbators experienced greater benefit from inhaled ciprofloxacin than non-frequent exacerbators [9]. In the present study, frequent exacerbators comprised 23% of the cohort, experienced more hospitalisations, higher symptom burden and poorer QoL, representing a group that may benefit from more intensive treatment and monitoring. Further, the higher prevalence of *P. aeruginosa* in frequent exacerbators in our study argues for surveillance and directed treatment of this organism [32].

This study has a number of limitations. The ABR currently recruits patients attending tertiary centres with an interest in bronchiectasis, and potentially selects patients with prominent symptoms, more severe disease, and/or a higher prevalence of NTM. Data completeness limits the number of participants who can be evaluated; consequently this analysis predominantly represents non-indigenous patients from six sites on the East Coast of Australia. Patients with missing variable data were removed from the denominator of each variable; this may introduce some bias into our estimates. Furthermore, at this early point in registry operations, only cress-sectional data are available. Presently, the registry does not have an electronic repository of CT images. The use of the term "physician-reported aetiology" throughout the paper reflects the characteristics of an observational registry, where the degree to which aetiology is investigated is physician-dependant and historical aetiological test results are not always available. "Exacerbations" are currently defined by the treating physician, due to the lack of a validated consensus definition of pulmonary exacerbations in non-cystic fibrosis bronchiectasis. The ABR plans to improve data collection and completeness and recruit from a broader range of health providers and sites in the future. Finally, this study aimed to describe the adult cohort comprehensively, however the ABR also recruits children. These paediatric data will be presented in time as the cohort increases.

The establishment of the ABR has allowed description of the characteristics of the largest cohort of Australian adults with bronchiectasis within 3 years of inception. These data reveal that many patients with bronchiectasis have normal spirometry, even in the presence of "severe" disease as defined by current composite severity scores. This study highlights the opportunity for improved sputum collection in Australian patients, particularly for mycobacterial testing. It demonstrates the negative influence of frequent exacerbations on QoL and health-care utilisation, and highlights a clinical phenotype that could be targeted in a treatable traits approach to bronchiectasis management. Longitudinal studies, including validation of widely used severity scores and the QoL-B questionnaire, are required in Australian patients with bronchiectasis.

5. Declarations of interest

None.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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Appendix A. Supplementary data

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