CHEST

Adult Patients With Bronchiectasis
A First Look at the US Bronchiectasis Research Registry

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OBJECTIVES: We sought to describe the characteristics of adult patients with bronchiectasis enrolled in the US Bronchiectasis Research Registry (BRR).

METHODS: The BRR is a database of patients with non-cystic-fibrosis bronchiectasis (NCFB) enrolled at 13 sites in the United States. Baseline demographic, spirometric, imaging, microbiological, and therapeutic data were entered into a central Internet-based database. Patients were subsequently analyzed by the presence of NTM.

RESULTS: We enrolled 1,826 patients between 2008 and 2014. Patients were predominantly women (79%), white (89%), and never smokers (60%), with a mean age of 64 ± 14 years. Sixty-three percent of the patients had a history of NTM disease or NTM isolated at baseline evaluation for entry into the BRR. Patients with NTM were older, predominantly women, and had bronchiectasis diagnosed at a later age than those without NTM. Gastroesophageal reflux disease (GERD) was more common in those with NTM, whereas asthma, primary immunodeficiency, and primary ciliary dyskinesia were more common in those without NTM. Fifty-one percent of patients had spirometric evidence of airflow obstruction. Patients with NTM were more likely to have diffusely dilated airways and tree-in-bud abnormalities. *Pseudomonas* and *Staphylococcus aureus* isolates were cultured less commonly in patients with NTM. Bronchial hygiene measures were used more often in those with NTM, whereas antibiotics used for exacerbations, rotating oral antibiotics, steroid use, and inhaled bronchodilators were more commonly used in those without NTM.

CONCLUSIONS: Adult patients with bronchiectasis enrolled in the US BRR are described, with differences noted in demographic, radiographic, microbiological, and treatment variables based on stratification of the presence of NTM. CHEST 2017; 151(5):982-992

KEY WORDS: airways; bronchiectasis; nontuberculous mycobacteria; *Pseudomonas*; registry

FOR EDITORIAL COMMENT SEE PAGE 953

ABBREVIATIONS: AFB = acid-fast bacillus; BRR = Bronchiectasis Research Registry; CF = cystic fibrosis; DCC = data coordinating center; GERD = gastroesophageal reflux; LUL = left upper lobe; NCFB = non-cystic-fibrosis bronchiectasis; NTM = nontuberculous mycobacteria; PEP = positive expiratory pressure; RML = right middle lobe; RUL = right upper lobe

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Bronchiectasis is a chronic lung disease characterized by dilatation of airways, with injury to the bronchial walls due to recurrent infection and inflammation. It is typically distinguished by whether or not the patient has underlying cystic fibrosis (CF). Adult non-CF bronchiectasis (NCFB) is heterogeneous and has numerous causes.[1-5] Idiopathic bronchiectasis and infection-related bronchiectasis represent the majority of adult cases of NCFB in most series.[4-8] The prevalence of NCFB appears to be increasing in the United States. Seitz et al[9] analyzed a 5% sample of Medicare Part B beneficiaries and reported that from 2000 to 2007, the prevalence increased 8.74% annually. In addition, the prevalence of NCFB increases substantially with aging.[10] Furthermore, NCFB imposes a significant financial burden on patients and the US health-care system, with annual costs approximating $630 million.[10]

Despite the significant morbidity of NCFB and significant financial burden, there are limited data regarding the characteristics of patients with NCFB in the United States. To better define the characteristics of patients with NCFB and provide a resource for clinical trials and other research, the Bronchiectasis Research Registry (BRR) was established within the COPD Foundation in 2008. The registry includes 13 sites across the country where patients are enrolled through a centralized database. As such, the BRR is not a tool to generate population-based prevalence data. To our knowledge, this is the first report describing the US BRR cohort.

Methods

The BRR is a centralized database of patients with bronchiectasis identified at 13 clinical sites throughout the United States (e-Appendix 1). Adult patients with a physician-established diagnosis of bronchiectasis were eligible for inclusion. The institutional review board of each participating site approved the study, as did an administrative institutional review board for the data collecting center (DCC). After providing informed consent, medical records were queried by a study coordinator or principal investigator using standardized recording forms. For purposes of this report, NCFB is heretofore labeled as bronchiectasis. The exclusion of patients with primary CF was established based on clinical history, previous sweat chloride test results, genetic testing results, or a combination, at the time of enrollment. Exacerbations were recorded based on historical information. Data were entered through a centralized Internet-based entry system at the University of North Carolina. Study coordinators received training from the DCC. Quality control occurred in real time, as the data management system incorporated expected range checks. The BRR is sponsored by the COPD Foundation.

Spirometry

Spirometric results measured closest to the time of enrollment were abstracted from patient records. Spirometric results were considered normal when the FEV_1/FVC was $\geq$ 0.70 and the FVC and FEV_1 were $>$ 80% of predicted. Airflow obstruction was defined as FEV_1/FVC $<$ 0.70 and was defined as mild, moderate, severe, and very severe obstruction with a FEV_1 of $\geq$ 80% predicted, $\geq$ 50% and $<$ 80%, $\geq$ 30% and $<$ 50%, and $<$ 30% of predicted, respectively.[11] Patients in whom the FEV_1/FVC was $>$ 0.70 and the FVC was $<$ 80% were labeled as having restriction. A bronchodilator response was considered present when the FEV_1 or FVC improved $\geq$ 12% after bronchodilator use.

Chest Imaging

Chest CT scans were read by principal investigators or site radiologists.

Microbiological Evaluation

A maximum of three respiratory culture results for bacteria, fungi, and mycobacteria (total of a maximum of nine culture results) were abstracted between the 2 years prior to and 90 days after enrollment, which was defined as the baseline period. We recorded positive culture results during the baseline period, and we subsequently stratified these results based on patients' nontuberculous mycobacteria (NTM) status. For the purposes of this analysis, we defined patients with NTM as those with either a reported history of pulmonary NTM disease prior to enrollment or those with one or more NTM isolates in respiratory specimen cultures within the baseline period, or both.

Treatment

Treatment information was abstracted across several domains, including the use of antibiotics, corticosteroids, or bronchodilators; medication for acid suppression; mucus-active agents; and measures to enhance bronchial hygiene. Categories of antibiotic use included antibiotics for exacerbation only, any suppressive antibiotic, rotation of oral suppressive antibiotics, or inhaled suppressive antibiotics. Measures to improve bronchial hygiene were defined as any nonpharmacologic measure to improve bronchial hygiene.

Statistical Analysis

The analysis population consisted of patients enrolled in the BRR as of July 1, 2014. Demographic and physical characteristics, medical history, respiratory symptoms, imaging findings, spirometric

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findings, microbiological culture results, and therapies administered were summarized for all participants, with subsequent stratification based on NTM status, as already described. χ^2 tests for categorical data and *t* tests for continuous data were used to compare patients with NTM and those without NTM for the subset of variables for which clinically meaningful relationships were hypothesized. These comparisons were considered exploratory, and no adjustment for potential confounding variables or multiple comparisons were made.

Results

Demographic and Baseline Characteristics

A total of 1,941 patients were enrolled in the BRR as of July 1, 2014. One hundred fifteen patients were subsequently excluded from analysis due to withdrawal of consent (19 patients), diagnosis of NTM without bronchiectasis (11 patients), missing identification of sex (24 patients), or missing NTM status (61 patients). The evaluable 1,826 patients with bronchiectasis enrolled between 2008 and 2014 were then categorized based on NTM status. Baseline information at the time of enrollment is detailed in Table 1. The study population was predominantly composed of women (79%) and non-Hispanic white patients (89%). The mean age was 64 ± 14 years, with a diagnosis of bronchiectasis in most patients (77%) occurring between the ages of 50 and 79 years. Forty-seven percent had commercial insurance coverage and 47% had Medicare or Medicaid. Sixty percent were never smokers and 68% had a prior history of pneumonia. Three percent had primary ciliary dyskinesia, 3% had pectus excavatum, and 1% had HIV infection.

As also shown in Table 1, 63% (1,158 of 1,826) had coexistent NTM. Patients with NTM compared with patients without NTM were older, diagnosed with bronchiectasis at a later age, predominantly women, and had a lower BMI. Gastroesophageal reflux disease (GERD) was present more frequently in those with NTM, whereas asthma, primary ciliary dyskinesia, and immunodeficiency were more common in those without NTM.

Exacerbations were reported at baseline in 64% of patients within the preceding 2 years. Patients with NTM had fewer exacerbations (2.7 ± 2.3) during the prior 2 years than did those without NTM (3.4 ± 3.3; $P < .01$) (Table 1).

Table 2 summarizes respiratory symptoms. The most common symptoms included cough (73%) that was productive (53%), dyspnea (64%), and fatigue (50%). Fatigue and hemoptysis were more common in those with NTM, whereas cough was more common in those without NTM. Sweat chloride testing and CF nasal potential difference measurements were performed in 12% and 1.9% of patients, respectively; the results were abnormal in 9% and 11%, respectively (data not shown).

Spirometry

Eighty-five percent of patients had spirometric results reported. No significant difference was observed between patients with NTM and patients without NTM (Table 3). Twenty-six percent had normal spirometric results. Fifty-one percent of patients had obstruction. Three-quarters of patients with obstruction (76%) fell into the mild to moderate category. Twenty percent of patients had suggestive restrictive impairment. Only 5% of patients had a response to aerosol bronchodilators.

Chest CT

CT scans were available for analysis from 1,553 patients (85%). The right middle lobe (RML) (69%) was the most commonly involved lobe, whereas the upper division of the left upper lobe (LUL) (44%) was the least commonly involved. RML, lingular, right upper lobe (RUL), and LUL airway dilation was more common in those with NTM (Fig 1). A single lobe was involved in only 11% of patients and occurred more commonly in those without NTM (Table 4). Sixty percent of patients had tree-in-bud infiltrates, with involvement of all lobes including a higher percentage of tree-in bud infiltrates in patients with NTM. Mucoid impaction within the RML, lingula, and RUL was more common in patients with NTM (data not shown). In general, patients with NTM were more likely to have dilated airways, thickened walls, or mucoid impaction within the upper lobes, lingula, and middle lobes.

Microbiological Evaluation

Of 1,826 evaluable patients, 1,645 (90%) had at least one type of culture performed during the baseline period. This included 1,314 patients (72%) with one or more acid-fast bacillus (AFB) cultures, 1,406 (77%) with one or more bacterial cultures, and 1,087 patients (60%) with one or more fungal cultures performed. For patients with AFB cultures, 484 (37%) isolated *Mycobacterium avium* complex, 130 (10%) isolated *M. abscessus/chelonae*, and 90 (8%) isolated other mycobacterial or *Nocardia* species (Table 5). Of those with bacterial cultures, 470 (33%) isolated *Pseudomonas* species and 170 (12%) isolated

TABLE 1] Demographics and Clinical Characteristics of Patients With Bronchiectasis[a]

Characteristic	Data Available (No.)	Overall (N = 1,826)	NTM (n = 1,158)	No NTM (n = 668)	*P* Value[b]
Sex, No. (%)	1,826				
Female		1,439 (79)	964 (83)	475 (71)	< .01
Age, mean ± SD, y	1,823	64 ± 14	66 ± 12	61 ± 17	< .01
Age at diagnosis, mean ± SD, y	1,456	57 ± 17	59 ± 15	53 ± 19	< .01
Race/ethnicity, No. (%)	1,709				
Non-Hispanic white		1,514 (89)	1,003 (91)	511 (85)	< .01
Non-Hispanic black		34 (2)	7 (1)	27 (4)	
Hispanic		73 (4)	41 (4)	32 (5)	
Asian		60 (4)	41 (4)	19 (3)	
Other		28 (2)	16 (1)	12 (2)	
Primary insurance, No. (%)	1,684				
Commercial		794 (47)	504 (48)	290 (46)	< .01
Medicaid and other state programs		49 (3)	24 (2)	25 (4)	
Medicare		749 (44)	485 (46)	264 (42)	
No insurance		18 (1)	9 (1)	9 (1)	
Other (including Tricare)		74 (4)	29 (3)	45 (7)	
BMI, mean ± SD, kg/m^2	1,812	23.2 ± 5.7	22.5 ± 5.5	24.3 ± 5.8	< .01
q1, q3,		19.9, 25.1	19.7, 24.3	20.3, 26.8	
Smoking, No. (%)	1,815				
Never		1,094 (60)	686 (60)	408 (61)	.74
Former		693 (38)	447 (39)	246 (37)	
Current		28 (2)	18 (2)	10 (2)	
Chest wall deformity, No. (%)	1,731				
None		1,657 (96)	1,038 (96)	619 (96)	.02
Pectus excavatum		56 (3)	39 (4)	17 (3)	
Other		18 (1)	6 (1)	12 (2)	
Otitis or rhinosinusitis, No. (%)	1,562				
Yes		388 (25)	222 (23)	166 (29)	< .01
Comorbidities, No. (%)					
History of pneumonia	1,745	1,187 (68)	758 (69)	429 (67)	.45
COPD	1,778	350 (20)	217 (19)	133 (20)	.60
Asthma	1,783	515 (29)	298 (26)	217 (33)	< .01
GERD	1,789	841 (47)	577 (51)	264 (40)	< .01
Rheumatologic disease	1,775	142 (8)	87 (8)	55 (8)	.60
Chronic ulcerative colitis or Crohn's disease	1,795	47 (3)	26 (2)	21 (3)	.25
Primary immunodeficiency	1,776	89 (5)	44 (4)	45 (7)	< .01
Primary ciliary dyskinesia	1,791	52 (3)	20 (2)	32 (5)	< .01
Prior tuberculosis, No. (%)	1,781				
Yes		70 (4)	50 (4)	20 (3)	.14

(Continued)

TABLE 1] *(Continued)*

Characteristic	Data Available (No.)	Overall (N = 1,826)	NTM (n = 1,158)	No NTM (n = 668)	*P* Value[b]
History of pulmonary exacerbation in the past 2 y, No. (%)	1,754	1,124 (64)	687 (62)	437 (68)	.01
No. of pulmonary exacerbations in the past 2 y, No. (%)	992	3.0 ± 2.8	2.7 ± 2.3	3.4 ± 3.3	< .01

GERD = gastroesophageal reflux disease; NTM = nontuberculous mycobacteria.
[a]Percentages and other descriptive statistics calculated after excluding participants with missing data from the column total. Less than 1% of participants had missing data for all items except the following: age at diagnosis (30%), race/ethnicity (6%), primary insurance (8%), chest wall deformity (5%), history of pneumonia (4%), otitis or rhinosinusitis (14%), respiratory distress at birth (17%), COPD (3%), asthma (2%), GERD (2%), rheumatologic disease (3%), chronic ulcerative colitis or Crohn's disease (2%), primary immunodeficiency (3%), primary ciliary dyskinesia (2%), and prior tuberculosis (2%).
[b]*P* values for categorical variables are from χ^2 tests, and from *t* tests for continuous variables comparing patients with NTM vs patients without NTM.

S. aureus. A variety of other bacterial pathogens were reported. Among those with fungal cultures, *Aspergillus* species were most commonly isolated.

Although isolation of *Pseudomonas* species was common among the entire cohort, it was significantly less common among patients with NTM (n = 270 [30%]) vs patients without NTM (n = 200 [40%; $P < .01$]. Similarly, *S. aureus* was also less common among patients with NTM, occurring in 92 patients with NTM (10%) and 78 patients without NTM (15%), respectively ($P < .01$). No significant difference in *Aspergillus* isolation was identified between NTM (n = 159 [21%]) and non-NTM groups (n = 52 [16%]; $P = .08$).

Treatment

Therapies for bronchiectasis were reported in 1,826 patients (Table 6). Forty-one percent (727 of 1,764) of patients reported antibiotic use for exacerbations only. Any suppressive antibiotic use was noted in 694 of 1,775 patients (39%), with aerosol antibiotics reported in 178 of 1,759 (10%). Compared with patients without NTM, patients with NTM used antibiotics for exacerbations only less often (36% vs 51%; $P < .01$) but used any suppressive antibiotic (43% vs 32%; $P < .01$) more often. There was no difference in aerosol antibiotic use. Seven percent of patients (125 of 1,771) used rotating oral antibiotics, and this was less common in those with NTM (6% vs 9%; $P < .01$).

Inhaled steroids were used almost three times more commonly than were oral steroids (39% vs 13%). Inhaled bronchodilators were used in 61% of patients. Inhaled vs oral steroids were used less commonly in those with NTM compared with those without NTM (35% vs 45%; $P < .01$, and 10% vs 19%; $P < .01$,

TABLE 2] Symptoms in Patients With Bronchiectasis by NTM Status[a]

Symptom	Data Available (No.)	Overall (N = 1,826)	NTM (n = 1,158)	No NTM (n = 668)	*P* Value[b]
Fatigue, No. (%)	1,770				
Yes		886 (50)	591 (53)	295 (46)	< .01
Daily bouts of coughing, No. (%)	1,804				
Yes, any		1,314 (73)	825 (72)	489 (74)	.32
Daily productive cough, No. (%)	1,788				
Yes, productive cough		951 (53)	568 (50)	383 (59)	< .01
Hemoptysis, No. (%)	175				
Yes		409 (23)	283 (25)	126 (19)	< .01
Dyspnea, No. (%)	1,442				
No, not at rest or when active		663 (46)	420 (46)	243 (46)	.98
Yes, only when active		779 (54)	493 (54)	286 (54)	

See Table 1 legend for expansion of abbreviations.
[a]Percentages and other descriptive statistics calculated after excluding participants with missing data from the column total. Less than 1% of participants had missing data for all items except the following: undue fatigue (3%), daily bouts of coughing (1%), daily productive cough (2%), hemoptysis (3%), and dyspnea (21%).
[b]*P* values for categorical variables are from χ^2 tests and from *t* tests for continuous variables comparing patients with NTM vs patients without NTM.

TABLE 3] Spirometric Test Results for Patients With Bronchiectasis

Results	Data Available (No.)	Overall (N = 1,826)	NTM (n = 1,158)	No NTM (n = 668)	*P* Value[a]
Prebronchodilator findings, No. (%)[b]	1,552				
$FEV_1/FVC \geq 0.70$, $FVC \geq 0.80$, and $FEV_1 \geq 0.80$ (normal)		399 (26)	252 (26)	147 (26)	
$FEV_1/FVC \geq 0.70$, $FVC \geq 0.80$, and $FEV_1 < 0.80$ (nearly normal)		363 (23)	229 (23)	134 (24)	
Any obstruction		790 (51)	502 (51)	208 (51)	.86
Mild or moderate obstruction		555 (36)	366 (37)	189 (33)	.11
Severe or very severe obstruction		235 (15)	136 (14)	99 (17)	.06
Restriction		317 (20)	200 (20)	117 (21)	.92
Postbronchodilator findings, No. (%)[c]	963				
FVC or FEV_1 improved ≥ 12%		47 (5)	33 (5)	14 (4)	

See Table 1 legend for expansion of abbreviations.
[a]*P* values for categorical variables are from χ^2 tests and from *t* tests for continuous variables comparing patients with NTM and patients without NTM.
[b]Includes participants with prebronchodilator FEV_1, FVC, and FEV_1/FVC measurements. Any obstruction is defined as $FEV_1/FVC < .70$. Mild or moderate obstruction combines the mild and moderate groups defined in text. Severe or very severe obstruction combines the severe and very severe groups defined in text. Restricted is defined as $FEV_1/FVC \geq 0.70$ and $FVC < 0.80$.
[c]Includes only participants with both prebronchodilator and postbronchodilator FEV_1 and FVC measurements.

respectively), as was the use of inhaled bronchodilators (56% vs 70%; $P < .01$). Medication for acid suppression was used in slightly greater than one-third of patients (37%); 86% of such substances were proton pump inhibitors (data not shown). No difference in the use of medication for acid suppression was reported in those with and those without NTM. Mucus-active agents were used in 24% of patients and included hypertonic saline in 76% of those using mucus-active agents (data not shown). These agents were used slightly more commonly in those without NTM.

Nonpharmacologic measures to improve bronchial hygiene were used in 56% of patients, including 48% of patients (825 of 1,719) using a flutter or positive expiratory pressure (PEP) valve. The overall use of chest percussion/postural drainage and high-frequency chest oscillation was similar at 16% and 15%, respectively. Those with NTM were more likely to use bronchial hygiene, chest percussion, or a flutter or PEP valve compared with those without NTM (59% vs 50%; $P < .01$; 19% vs 12%; $P < .01$; or 52% vs 40%; $P < .01$, respectively).

Discussion

This first report from the BRR describes the largest US cohort of patients with bronchiectasis to date. The registry has prospectively enrolled > 1,900 patients with NFCB, 1,826 of whom were evaluable. Most are

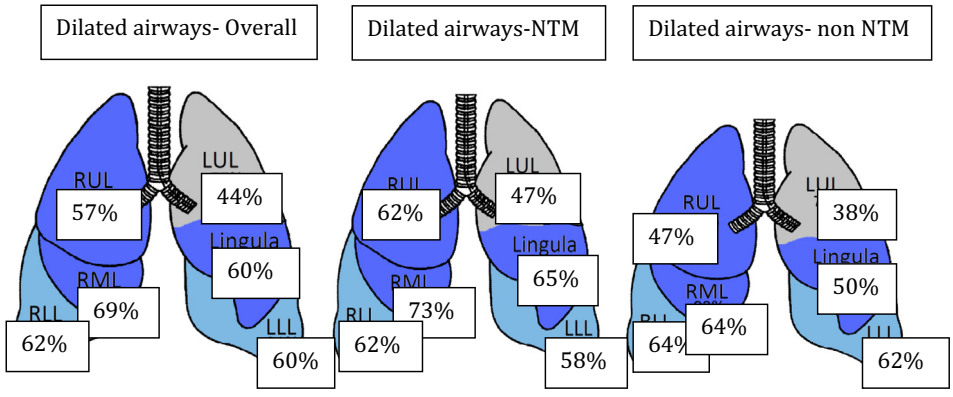

Figure 1 – *All lobes were involved; the RML (69%) was involved most and the upper division of the LUL (44%) was involved least. Except for the lower lobes, the other lobes were involved to a greater extent in NTM than in subjects without NTM. LUL =left upper lobe; NTM = nontuberculous mycobacteria; RLL = right lower lobe; RML = right middle lobe; RUL = right upper lobe.*

TABLE 4] Chest CT Imaging Findings in Patents With Bronchiectasis

Chest CT Finding	Data Available (No.)	Overall (N = 1,826)	NTM (n = 1,158)	No NTM (n = 668)	*P* Value[a]
Dilated airways, No. (%)					
None indicated[b]	1,553	105 (7)	72 (7)	33 (6)	.18
Left upper lobe (upper division)	1,390	607 (44)	413 (47)	194 (38)	< .01
Lingula	1,392	832 (60)	573 (65)	259 (50)	< .01
Left lower lobe	1,389	830 (60)	510 (58)	320 (62)	.13
Right upper lobe	1,392	787 (57)	544 (62)	243 (47)	< .01
Right middle lobe	1,398	969 (69)	639 (73)	330 (64)	< .01
Right lower lobe	1,388	867 (62)	536 (62)	331 (64)	.36
Only 1 of the above sites	1,419	152 (11)	82 (9)	70 (13)	< .01
2-3 of the above sites	1,419	479 (34)	276 (31)	203 (39)	
> 3 of the above sites	1,419	683 (48)	464 (52)	219 (42)	
Tree-in-bud infiltrates, No. (%)					
None indicated	1,542	610 (40)	315 (32)	295 (52)	< .01
Left upper lobe (upper division)	1,465	366 (25)	279 (30)	87 (16)	< .01
Lingula	1,467	528 (36)	394 (43)	134 (24)	< .01
Left lower lobe	1,472	556 (38)	388 (42)	168 (31)	< .01
Right upper lobe	1,474	520 (35)	397 (43)	123 (22)	< .01
Right middle lobe	1,464	581 (40)	419 (46)	162 (30)	< .01
Right lower lobe	1,472	611 (42)	426 (46)	185 (34)	< .01
Only 1 of the above sites	1,491	119 (8)	78 (8)	41 (7)	< .01
2-3 of the above sites	1,491	331 (22)	222 (24)	109 (20)	
> 3 of the above sites	1,491	431 (29)	324 (35)	107 (19)	
Any dilated airways, thickened airway walls, or mucoid impaction, No. (%)					
None indicated	1,577	40 (3)	26 (3)	14 (2)	.77
Left upper lobe (upper division)	1,380	713 (52)	482 (56)	231 (45)	< .01
Lingula	1,380	926 (67)	634 (73)	292 (58)	< .01
Left lower lobe	1,399	965 (69)	585 (67)	380 (73)	.02
Right upper lobe	1,393	899 (65)	613 (70)	286 (55)	< .01
Right middle lobe	1,397	1,062 (76)	698 (79)	364 (71)	< .01
Right lower lobe	1,396	1,004 (72)	618 (70)	386 (74)	.12
Only 1 of the above sites	1,470	135 (9)	84 (9)	51 (9)	< .01
2-3 of the above sites	1,470	491 (33)	280 (30)	211 (39)	
> 3 of the above sites	1,470	804 (55)	537 (58)	267 (49)	

See Table 1 legend for expansion of abbreviations.
[a]*P* values for categorical variables are from χ^2 tests and from *t* tests for continuous variables comparing patients with NTM vs patients without NTM.
[b]Participant met the inclusion criteria for bronchiectasis, but site with dilated airways not identified.

non-Hispanic white women and lifelong nonsmokers. In this cohort, a large proportion of the patients had a history of NTM disease or had NTM isolated at their baseline evaluation. Although we identified important differences in patients with and those without NTM, it should be recognized that this registry was developed as a bronchiectasis registry. As such, NTM lung-disease-specific data domains appropriate for a specific NTM lung disease registry were not collected. Nonetheless, our findings are in agreement with published data reporting that most patients with idiopathic bronchiectasis are female nonsmokers.[4-8] In addition, we report that those with NTM and bronchiectasis are more likely to be women, are less likely to have *Pseudomonas* isolated in sputum, and are older at the time of diagnosis than those without NTM.

TABLE 5] Microbiological Results for Patients With Bronchiectasis

Microbiological Result	Data Available (No.)	Overall (N = 1,826)	NTM (n = 1,158)	No NTM (n = 668)	*P* Value[a]
Bacterial culture findings, No. (%)					
No growth in any culture	1,406	93 (7)	68 (8)	25 (5)	.06
Oropharyngeal flora	1,406	1,037 (74)	669 (74)	368 (73)	.57
Haemophilus influenzae	1,406	116 (8)	72 (8)	44 (9)	.64
Streptococcus pneumoniae	1,406	49 (3)	26 (3)	23 (5)	.10
Staphylococcus aureus[b]	1,406	170 (12)	92 (10)	78 (15)	< .01
Pseudomonas aeruginosa[c]	1,406	470 (33)	270 (30)	200 (40)	< .01
Stenotrophomonas maltophilia	1,406	76 (5)	54 (6)	22 (4)	.19
Klebsiella pneumoniae	1,406	35 (2)	24 (3)	11 (2)	.58
Moraxella catarrhalis	1,406	20 (1)	9 (1)	11 (2)	.10
Achromobacter	1,406	15 (1)	9 (1)	6 (1)	.79
Alcaligenes	1,406	13 (1)	5 (1)	8 (2)	.08
Serratia marcescens	1,406	30 (2)	25 (3)	5 (1)	.03
Burkholderia species	1,406	5 (0)	3 (0)	2 (0)	1.00
Mycobacterial smear/culture					
AFB smear positive	1,314	319 (24)	302 (33)	17 (4)	< .01
Growth in any culture	1,314	657 (50)	653 (71)	4 (1)	< .01
Mycobacterium avium complex	1,314	484 (37)	484 (52)	0	
Mycobacterium abscessus/chelonae[d]	1,314	130 (10)	130 (14)	0	
Mycobacterium kansasii	1,314	8 (1)	8 (1)	0	
Mycobacterium gordonae	1,314	37 (3)	37 (4)	0	
Other mycobacterial species	1,314	36 (3)	36 (4)	0	
Nocardia	1,314	9 (1)	8 (1)	1 (0)	
Fungal culture findings, No. (%)					
No growth in any culture	1,087	534 (49)	364 (48)	170 (53)	.10
Aspergillus species[e]	1,087	211 (19)	159 (21)	52 (16)	.08
Scedosporium apiospermum[f]	1,087	34 (3)	28 (4)	6 (2)	.18
Other fungal species	1,087	392 (36)	284 (37)	108 (34)	.28
Summary of lower respiratory culture findings, No. (%)	1,645				
No growth in any culture		136 (8)	85 (8)	51 (9)	
Multiple pathogens isolated		1,050 (64)	736 (67)	314 (58)	

AFB = acid-fast bacillus; MRSA = methicillin-resistant *Staphylococcus aureus*. See Table 1 legend for expansion of other abbreviations.
[a]*P* values for categorical variables are from Fisher's exact tests when counts are < 10 and from χ^2 tests otherwise, comparing patients with NTM vs patients without NTM.
[b]Includes 30 reported as methicillin sensitive, 58 as methicillin resistant, and 3 coded as "MRSA" from open-ended responses.
[c]Includes 52 reported as none mucoid, 174 as at least 1 mucoid, and 17 coded as *"Pseudomonas"* from open-ended responses.
[d]Includes 4 reported in open-ended findings that were coded as *Mycobacterium chelonae* and 9 reported as *Mycobacterium massiliense*.
[e]Includes 56 responses to open-ended findings that were coded as *Aspergillus* not otherwise speciated.
[f]Includes 6 responses to open-ended findings that were coded as *Scedosporium* not otherwise speciated.

In agreement with previous studies, we also describe a broad spectrum of comorbidities associated with bronchiectasis.[1-3,7,8] Patients with asthma, primary immunodeficiency, and primary ciliary dyskinesia were less likely to have NTM, whereas those with GERD were more likely to have NTM. Prior investigations have demonstrated coexistent NTM lung disease and GERD.[12,13]

In this study, more than one-half of the subjects had evidence of airflow obstruction. Interestingly, one-fifth of the patients also had suggestion of restriction on spirometry. Worse lung function in bronchiectasis is associated with more involvement of bronchiectasis on CT scans, the presence of P*seudomonas* species,[14-18] and the presence of COPD.[19] Response to bronchodilator

TABLE 6] Therapies Reported for Patients With Bronchiectasis[a]

Therapy	Data Available (No.)	Overall (N = 1,826)	NTM (n = 1,158)	No NTM (n = 668)	*P* Value[b] NTM vs No NTM
Antibiotic use, No. (%)					
Antibiotics for acute exacerbations only	1,764	727 (41)	402 (36)	325 (50)	< .01
Any suppressive antibiotic	1,775	694 (39)	491 (43)	203 (32)	< .01
Rotating oral suppressive antibiotics	1,771	125 (7)	64 (6)	61 (9)	< .01
Inhaled suppressive antibiotics	1,759	178 (10)	113 (10)	65 (10)	.98
Use of other therapies, No. (%)					
Inhaled steroid	1,794	696 (39)	403 (35)	293 (45)	< .01
Any oral steroid	1,789	237 (13)	112 (10)	125 (19)	< .01
Inhaled bronchodilator	1,798	1,098 (61)	638 (56)	460 (70)	< .01
Medication for gastric acid suppression	1,786	667 (37)	432 (38)	235 (36)	.43
Mucus-active agent	1,784	424 (24)	252 (22)	172 (26)	.04
Measures to improve bronchial hygiene, No. (%)					
Yes	1,730	965 (56)	642 (59)	323 (50)	< .01
Chest percussion/postural drainage	1,711	279 (16)	200 (19)	79 (12)	< .01
Flutter or positive expiratory pressure valve	1,719	825 (48)	568 (52)	257 (40)	< .01
High-frequency chest oscillation	1,716	252 (15)	142 (13)	110 (17)	.02

See Table 1 legend for expansion of abbreviation.

[a]Percentages and other descriptive statistics calculated after excluding participants with missing data from the column total. Less than 1% of participants had missing data for all items except the following: antibiotics for acute exacerbations only (3%), any suppressive antibiotic (3%), rotating oral suppressive antibiotics (3%), aerosol suppressive antibiotics (4%), inhaled steroid (2%), any oral steroid (2%), inhaled bronchodilator (2%), medication for gastric acid suppression (2%), mucolytic agent (2%), measure to improve bronchial hygiene (5%), chest percussion/postdrainage (6%), uses flutter or Acapella valve (6%), uses high frequency chest oscillation (6%).

[b]*P* value is from χ^2 test comparing patients with NTM vs patients without NTM.

use was documented in 5% of subjects, which is lower than has been reported previously.[20]

There appeared to be no difference in spirometric results between those with NTM and those without in this cohort of patients, a finding that has not been well described previously.

This cohort includes descriptive high-resolution CT imaging findings in those with and those without NTM. Both diseases involve multiple lobes, although NTM-associated bronchiectasis involves upper lobe and middle lobe distribution more than non-NTM bronchiectasis does, as has been noted by others.[21-24]

Treatments for bronchiectasis varied widely within both groups of patients. Antibiotic use was common and nearly evenly split between antibiotics used for acute exacerbations only and suppressive antibiotics. Antibiotics for acute exacerbations only were more commonly used for those without NTM, and suppressive antibiotics were used more frequently in those with NTM. Designation of antibiotics used for NTM vs bronchiectasis was not specified. A relatively small percentage of patients with bronchiectasis used aerosol antibiotics, likely reflecting the lack of positive clinical trials in this population and the period of enrollment. Moreover, current practice patterns in the participating centers reflect the lack of data to support rotating oral antibiotics, which is similar to recommendations in published guidelines.[25]

Even though there is a paucity of data to support its use, bronchodilator use was noted in more than one-half of patients with bronchiectasis and was more commonly used in those without NTM. Given the central role of mucociliary clearance and bronchial hygiene in the management of bronchiectasis, it is surprising that slightly more than one-half of patients used some measure to improve bronchial hygiene; the majority used a flutter or PEP valve. Consistent use of bronchial hygiene is in alignment with published literature and was used more often by those with NTM than by those without NTM.[2,4,25,26]

There are several limitations to our study. Because this study describes a cohort of patients enrolled from tertiary referral institutions with interest in NTM lung disease, the demographic information described is potentially biased, including overrepresentation of patients with NTM. Moreover, there was a predominance of geographic groupings of participating sites in the eastern United States. The presence or absence of coexistent illnesses was based on history. It is difficult to ascertain if GERD or coexistent obstructive lung disease, or both, was truly present in conjunction with bronchiectasis or had been ascribed based on compatible symptoms or spirometric findings, or both.

In conclusion, the BRR has enrolled 1,826 evaluable patients with bronchiectasis from 13 sites across the United States. Despite baseline characteristics of the study population sharing phenotypic similarities, this study notes significant differences in patient groups with and without the presence of NTM.

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Additional information: The e-Appendix can be found in the Supplemental Materials section of the online article.

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