Original Research

Low Incidence of High Frequency Chest Wall Oscillation in Bronchiectasis Registry Data Despite Indications and Reimbursement

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***Running Head*: Low HFCWO Use in Bronchiectasis Registry**

Keywords: high frequency chest wall oscillation; bronchiectasis; CMS criteria; nontuberculous mycobacteria; Bronchiectasis and Nontuberculous Mycobacteria Research Registry

***Abbreviations*:** ABPA=allergic bronchopulmonary aspergillosis; ACT=Airway Clearance Technique; ATS=American Thoracic Society; BE=bronchiectasis; BMI=body mass index; BRR=Bronchiectasis and Nontuberculous Mycobacteria Research Registry; CMS=Centers for Medicare and Medicaid Services; COPD=chronic obstructive pulmonary disease; ESCMID=European Society of Clinical Microbiology and Infectious Diseases, FEV1=forced expiratory volume in 1 second; FVC=forced vital capacity; GERD=gastroesophageal reflux disease; IDSA=Infectious Disease Society of American; HFCWO=high frequency chest wall oscillation; mBSI=modified bronchiectasis severity index; NTM=nontuberculous mycobacteria; PCD=primary ciliary dyskinesia

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This article has an online supplement.

ABSTRACT

Background: Airway clearance techniques (ACTs) are required in international bronchiectasis (BE) management guidelines, and high frequency chest wall oscillation (HFCWO) is the only ACT with a Centers for Medicare and Medicaid Services (CMS) reimbursement guideline.

Objective: Compare patient demographics and clinical characteristics between BE patients using HFCWO to BE patients not using HFCWO.

Methods: Bronchiectasis and Nontuberculous Mycobacteria Research Registry (BRR) (2008-2025) data were retrospectively analyzed. Patients were grouped by baseline HFCWO use and non-users were further stratified by selected CMS eligibility criteria (productive cough or more than two exacerbations per year) and subsequent HFCWO utilization.

Results: Of 5,673 patients (median age 69 years), 518 used HFCWO and 5,155 did not. HFCWO users had higher rates of asthma (31.7 vs. 25.3%, P=0.002), gastroesophageal reflux disease (48.5 vs. 41.9%, P=0.004), primary ciliary dyskinesia (5.8 vs. 2.1%, P<0.001), allergic bronchopulmonary aspergillosis (3.3 vs. 1.7%, P=0.013) and nontuberculous mycobacteria (20.1 vs. 15.7%, P=0.011). Symptoms more common in HFCWO users included dyspnea (72.1 vs. 38.5%), fatigue (61.5 vs. 46.8%), cough (90.9 vs. 76.6%,), and hemoptysis (27.1 vs 19.8%) (all P<0.001). Median modified bronchiectasis severity index (mBSI) score was higher in HFCWO users (8 vs. 7, P<0.001), and HFCWO users more frequently received antibiotics, bronchodilators, hypertonic saline, inhaled and oral corticosteroids, indicating greater disease burden. Notably, 58% (2,703/4,679) of non-HFCWO users appeared to meet selected CMS symptom/exacerbation criteria and their characteristics resembled HFCWO users.

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Conclusion: These findings suggest areas to explore to standardize BE management and motivate clearer treatment guidelines to optimize patient health outcomes.

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INTRODUCTION

Bronchiectasis (BE) is a chronic lung disease characterized by irreversible, permanent, pulmonary dilatation of the bronchi and is typically associated with ineffective mucociliary clearance, eventually leading to mucus stasis, bacterial colonization, inflammation, and recurrent lung infections.[1] BE disease pathogenesis has been described as a "vicious vortex" involving mucociliary insufficiency, chronic airway inflammation, and bacterial colonization.[2] Clinically significant BE is often characterized by at least two of the following: cough most days of the week, sputum production most days of the week and a history of exacerbations[3] defined as periods of acute respiratory symptoms.

A comprehensive treatment approach is recommended to target the vicious vortex. Standard pharmacological BE treatments include mucolytics and antibiotics. Airway clearance techniques (ACTs) are a mainstay feature of guideline-based BE management, including, but not limited to, positive expiratory pressure, manual techniques and high frequency chest wall oscillation (HFCWO).[4,5] International BE guidelines advocate a tailored airway clearance regimen for each BE patient[4,6,7] and more research to better understand BE-patient clinical support.

HFCWO works by rapidly cycling an inflatable vest to compress and release the chest wall to create a potential shearing force within the airways to loosen and thin mucous, improve airway clearance and enhance bronchial drainage. One study[8] reported effective 20- to 30-minute HFCWO treatments with short compression periods at different frequencies separated by coughing. HFCWO benefits in BE patients were reported to include stabilized lung function, reduced exacerbations requiring hospitalization, reduced antibiotic use, reduced dyspnea and cough, and improved health and quality of life scores compared to pharmacological therapy alone.[9-11] HFCWO is the only ACT in the United States with BE-specific, Centers for Medicare

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and Medicaid Services (CMS) HFCWO reimbursement guidance requiring: a) diagnosis of BE confirmed by CT scan, b) having tried and failed another method of ACT, and c) a daily productive cough for at least 6 months or more than two pulmonary exacerbations requiring antibiotics within 12 months (https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?LCDId=33785). Unfortunately, HFCWO and other ACT methods have few studies clearly demonstrating efficacy.[5]

The BRR is a centralized database collecting patient data from multiple clinical institutions across the United States. A previous BRR analysis from 2008 and 2021[13] reported 9.3% (371/4,000) BE patients in the BRR were documented HFCWO users at baseline and 54.8% (149/272) had severe Modified Bronchiectasis Severity Index (mBSI) scores, 81.4% (285/350) experienced an exacerbation in the last 12 months (defined as a deterioration in three or more of the following key symptoms for at least 48 hours−cough, sputum volume and/or consistency, sputum purulence, breathlessness and/or exercise tolerance, fatigue and/or malaise, hemoptysis−and the clinician determines a change in BE treatment is required), 32.4% (112/346) were hospitalized at least once due to pulmonary illness in the prior two years and those with more severe disease were more likely to continue ACT with HFCWO including 75 BE patients confirmed as continuing use at 1-year follow-up.

This study was designed to expand and build upon these prior findings by evaluating the following aims: differences in demographics and clinical characteristics between BE patients with and without HFCWO devices (Aim 1); differences between patients with no HFCWO device at baseline who appeared to meet or did not meet selected CMS symptom/exacerbation criteria for HFCWO use (Aim 2); and differences between patients with no HFCWO device at baseline who received HFCWO or not over time (Aim 3).

METHODS

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Study Design

This retrospective, cross-sectional and longitudinal clinical data analysis evaluated BRR data collected between 2008 and 2025 from adult BE patients at baseline, defined as two-years prior to enrollment, and annually thereafter (**Figure 1**).

Standardized data collection included demographics, past medical history, respiratory symptoms, and concomitant medication and therapies.[14] The data coordinating center and each participating site received institutional review board approval and written informed consent was obtained from all BRR participants at participating institutions.

Study-Aim-Specific Methods

For Aim 1: Patients were grouped by those who did and did not use HFCWO therapy to improve bronchial hygiene during the baseline period. Associations were evaluated, including the following baseline demographics and clinical characteristics: age, sex, race and co-existing conditions including asthma, chronic obstructive pulmonary disease (COPD), gastroesophageal reflux disease (GERD), primary ciliary dyskinesia (PCD), rheumatologic disease, allergic bronchopulmonary aspergillosis (ABPA) and NTM. Concomitant NTM infection was defined based on the American Thoracic Society (ATS), Infectious Disease Society of America (IDSA), European Society of Clinical Microbiology and Infectious Diseases (ESCMID), and European Respiratory Society guidelines for culture positivity and active treatment. Additional associations were evaluated for body mass index (BMI, continuous), pre-bronchodilator spirometry including forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1) absolute and percent predicted,

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exacerbation and hospitalization history, mBSI,[15,16] bacterial culture isolation, defined as at least one positive culture during the baseline period and respiratory symptoms, including presence of dyspnea, fatigue, cough, sputum volume among those with a productive cough and hemoptysis. Associations with concomitant treatments and therapies were also evaluated including chronic-suppression antibiotic use (yes/no), inhaled bronchodilator use (yes/no), hypertonic saline use (yes/no), ACT use (yes/no), and inhaled and/or oral corticosteroid use (yes/no).

For Aim 2: Aim 1 patients with no HFCWO use at baseline were stratified into groups who did and did not meet selected CMS symptom/exacerbation criteria for HFCWO prescriptions. The selected CMS symptom/exacerbation criteria were defined as patients who reported a daily productive cough (defined as a usually productive cough among those experiencing regular bouts of coughing in the two years prior to enrollment) during the baseline period or who experienced more than two exacerbations per year during the baseline period. Associations with baseline demographics and clinical characteristics were the same as previously described for Aim 1.

For Aim 3: Aim 1 patients with no HFCWO use at baseline and with at least one year of follow-up over a three-year period were evaluated for incident HFCWO therapy. These patients were grouped by those with and without incident HFCWO therapy during follow-up and evaluated for key clinical outcomes at follow-up, including lung function (FEV1 absolute and %predicted), reported exacerbations, treatment for exacerbations, pulmonary-related hospitalizations, and antibiotics for chronic suppression.

Statistical Analysis

For all three aims, differences between groups were compared using Wilcoxon-Mann-Whitney and independent two-sample t-tests for continuous variables and chi-square tests for categorical variables. All measures of association were evaluated using a significance level of 0.05, and no

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corrections for multiplicity were made. SAS version 9.4 (SAS Institute, Cary, NC, United States) was used for all analyses.

RESULTS

Aim 1

Cross-sectional BRR data were evaluated from 5,673 adult patients who were 80% female and had a 69-year-old median age (**Table 1**).

At baseline, HFCWO therapy was prescribed in 9.1% (518/5,673) of BRR BE patients and these patients had greater proportions of common co-morbidities with more severe disease characteristics than patients not prescribed HFCWO therapy. Compared to patients without prescribed HFCWO, BE patients prescribed HFCWO had increased incidence of asthma, gastroesophageal reflux disease (GERD), primary ciliary dyskinesia (PCD), allergic bronchopulmonary aspergillosis (ABPA), and nontuberculous mycobacteria (NTM) (**Figure 2**).

The cohort using prescribed HFCWO had more severe symptoms of disease with higher rates of dyspnea presence, fatigue, cough, hemoptysis, and positive cultures for *Pseudomonas aeruginosa* (**Figure 3**).

In addition, patients prescribed HFCWO at baseline were more likely to receive antibiotics, inhaled bronchodilators, hypertonic saline, inhaled corticosteroids and oral corticosteroids (**Figure 4**).

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In the two years before entry into the BRR, patients with HFCWO were more likely to experience exacerbations (67.5% vs. 54.9%, *P*<0.001), were more often hospitalized for pulmonary-related causes (27.0% vs. 18.4%, *P*<0.001), and had higher median mBSI scores (8 vs. 7, *P*<0.001) than patients without HFCWO (**SUPPLEMENT 1**). Once enrolled in the BRR, 82.4% (427/518) were still using HFCWO while 12.9% (67/518) had stopped, and 4.6% (24/518) were unknown.

AIM 2

Most (58%, 2,703/4,679) patients without HFCWO prescriptions at baseline appeared to meet selected CMS symptom/exacerbation criteria for HFCWO therapy and these patients were more likely to have severe disease, similar to those receiving HFCWO at baseline (**SUPPLEMENT 2**). Specifically, patients without HFCWO prescriptions at baseline who appeared to meet selected CMS symptom/exacerbation criteria had higher rates of asthma (28.0% vs. 21.3%, *P*<0.001), COPD (18.4% vs. 13.5%, *P*<0.001) and PCD (2.4% vs. 0.5%, *P*<0.001) than those who did not meet selected CMS symptom/exacerbation criteria.

BE patients without HFCWO prescriptions at baseline who appeared to meet selected CMS symptom/exacerbation criteria were more likely to be treated for acute exacerbation (47.1% vs. 27.1%, *P*<0.001), have pulmonary-related hospitalization (21.2% vs. 12.9%, *P*<0.001), experience dyspnea (45.7% vs. 31.3%, *P*<0.001), fatigue (52.4% vs. 38.7%, *P*<0.001), hemoptysis (24.5% vs. 13.3%, *P*<0.001), one or more positive cultures for *Pseudomonas aeruginosa* (27% vs. 13.2%, *P*<0.001) and a higher mBSI score (7 vs. 6, *P*<0.001) (**SUPPLEMENT 2**). Additionally, patients without HFCWO prescriptions at baseline who potentially met selected CMS symptom/exacerbation criteria for HFCWO prescription had greater use of antibiotics, bronchodilators, hypertonic saline, inhaled corticosteroids and oral corticosteroids (**Figure 5**).

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For all BE patients with appropriate baseline and follow-up data available in the BRR within 3 years of baseline, HFCWO was prescribed to 12.9% (220/1,709) without HFCWO prescriptions at baseline, including 14.0% (149/1,064) who appeared to meet selected CMS symptom/exacerbation criteria and 11.0% (71/645) who did not meet selected CMS symptom/exacerbation criteria (P=0.073).

Aim 3

BE patients prescribed HFCWO during the follow-up within three years of baseline tended to be more unstable with higher rates of exacerbations (47.8% vs. 28.1%, *P*<0.001), hospitalizations (20.5% vs. 10.8%, *P*<0.001), and antibiotic users (27.6% vs. 9.3%, *P*<0.001) (**SUPPLEMENT 3**).

DISCUSSION

In the present study, HFCWO was used as a test case to understand ACT devices used in BE patient treatments. Only 9% (518 of 5,673) of BE patients in the BRR were using HFCWO at baseline, even though 58% of patients not prescribed HFCWO at baseline appeared to meet selected CMS symptom/exacerbation criteria for HFCWO prescriptions and had more severe disease signs and symptoms than those who did not meet these selected CMS symptoms/exacerbation criteria for HFCWO prescription. BE patients prescribed HFCWO and those who appeared to meet selected CMS symptom/exacerbation criteria for HFCWO prescription were more likely to receive antibiotics, inhaled bronchodilators, hypertonic saline, inhaled corticosteroids, and oral corticosteroids; all signs of higher-burdened disease.

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Recent evidence suggested HFCWO may be an effective ACT to reduce hospital stays, antibiotic uses, radiology exams, hospitalizations, exacerbations, symptoms, outpatient visits, and laboratory services[16] and HFCWO use presented few safety concerns.[17,18] More research, clear practice guidelines and provider education may be helpful to increase opportunities to improve BE patient symptoms. These symptom improvements may slow patient decline as worse respiratory symptoms are independently associated with exacerbation risk and BE disease progression.

We acknowledge the absence of well-defined practice guidelines for HFCWO prescriptions based on consistent and long-term data. One systematic review[19] evaluated seven, small, low-quality studies using ACTs including HFCWO in 105 adults and children with BE and reported no significant difference in the number of exacerbations at 12 weeks (low-quality evidence); however, HFCWO treatment for 15 days significantly improved quality of life for both disease-specific and cough-related measures, reduced symptoms of breathlessness and cough and improved sputum production as well as FEV1 compared to no treatment without any reported adverse events or any other safety concerns. Efforts are ongoing among regulatory agencies and health organizations to identify specific patients most likely to benefit from HFCWO therapy.[20]

Limitations of this study included the retrospective nature of this evaluation, lack of a randomized control arm, inability to quantify standard BE treatment failures as required for CMS qualification, and the potential selection bias where only a portion of all BE patients were perhaps selectively enrolled in the BRR database. Additionally, HFCWO utilization research using the BRR database was limited for several reasons. A given patient may not have started HFCWO use until the sixth or seventh year after their baseline enrollment and patient follow up data varied greatly. This study analyzed 518 HFCWO users at their baseline visit, and 247 who started HFCWO use within 3 years after their baseline visit, and captured 76% (765/1,003) of all HFCWO users in the BRR;

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however, the BRR included 238 additional patients who used HFCWO but were not included in this analysis. Also, HFCWO re-use data may be confounded because insurance companies typically require a five-year wait period and an entirely new qualification before a patient can restart reimbursed HFCWO use. Of the 5,962 BE patients included in this analysis with data available in the BRR database, 17% (1,003/5,962) reported ever having HFCWO therapy. This 17% overall HFCWO use was nearly double the 9% (518 of 5,673) of BE patients who were using HFCWO at baseline for this study and may be a useful benchmark to assess HFCWO use changes over time.

This study was also limited because sites enrolling patients into the BRR were all academic medical centers with principal investigators who were leading experts in the field, creating financial and logistical barriers where perhaps only a subset of all BE patients could afford to receive this level of care. These medical centers may have better access and higher HFCWO utilization than the national average, which could suggest HFCWO prescribing practices were likely even lower across the United States than reported here. Another limitation potentially biasing the number of patients who met selected CMS symptom/exacerbation prescribing criteria but did not receive HFCWO could be patients who were offered but refused HFCWO treatment. Finally, utilization calculations were unable to distinguish between non-HFCWO patients receiving inadequate airway clearance and those receiving other ACT modalities, such as Positive Expiratory Pressure, manual techniques or other airway clearance strategies.

Relative sample sizes were small with the baseline HFCWO patient group (Aim 1) making up less than 10% (9.1%; 518/5,673) and the follow-up group data (Aim 3) only a little more than a third (36.6%; 1,885/5,155). HFCWO status was unknown for more than half of BRR patients (54.8%; 3,270/5,962), and the selected CMS symptom/exacerbation criteria status was unknown for nearly

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10% (9.2%; 476/5,155). In addition, symptom data collection, including daily productive cough, was subject to patient reporting accuracy and did not include details to determine if daily cough symptoms were experienced continuously for six months, as stipulated in the CMS criteria. Finally, no quality of life data were considered. Given the exploratory and hypothesis-generating nature of this analysis, we did not adjust for multiple comparisons, which increases our type I error rate and the possibility of chance findings.

Future research should evaluate outcomes for BE patients who met criteria to be started on HFCWO and were started on this, compared to patients who appeared to meet selected CMS symptom/exacerbation criteria for HFCWO prescriptions but were never started. Future ACT research studies should be done in larger BE patient populations and sub-groups over a longer term and should include independent datasets, quality of life measures, physician prescribing practices, BE treatment failures, barriers to access, real-world uses, adverse event rates (especially related to concomitant cardiac implantable electronic device uses), improved cough symptom measures over time, and longer-term health economic data. These new studies might even evaluate prospective, randomized, controlled, comparative data with patient-use decisions documenting why patients or their physicians might refuse to use or prescribe HFCWO, respectively.

CONCLUSIONS

In this cross-sectional, retrospective BRR analysis, BE patients prescribed HFCWO at baseline had more severe disease than BE patients not prescribed HFCWO therapy at baseline. Surprisingly, most BE patients in the BRR without an HFCWO prescription at baseline appeared to meet selected CMS symptom/exacerbation criteria for HFCWO prescription and had similar baseline characteristics to patients already on HFCWO. These findings indicate that a clinically more severe BE patient population was offered HFCWO selectively, and our preliminary longitudinal analysis

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indicate only a small proportion (~13%) of BE patients were prescribed HFCWO over time, whether they appeared to meet selected CMS symptom/exacerbation criteria or not. These descriptive and hypothesis-generating results raise the question whether standardized BE management and clearer treatment guidelines may be helpful to drive better and more equitable patient health outcomes. Further, identifying BE patients receiving no adequate airway clearance, adding ACT and HFCWO adoption tracking to measure the percentage of baseline non-users who later initiated therapy, and including HFCWO utilization across the entire BRR, could provide valuable context for further research into overall ACT and HFCWO use in the future to support effective BE management.

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Declaration of Competing Interest

AEB is a Bronchiectasis and Nontuberculous Mycobacteria Research Registry employee. RC declares no relevant conflict of interest. CJR reports advisory board service for Insmed. France Foundation, clinical trials for Insmed, Vertex, Verona, Mannkind and grants from CFF. GMS received grants from Vertex, BiomX, AstraZeneca, Insmed, Electromed, Splisense, NIH, COPD Foundation, and CFF.

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Table 1. Baseline Demographics

Variable	Results (n=5673)
Age, median [interquartile range], *n=5,634*	69 [61-76]
Female, n (%), *n=5,663*	4,510 (79.6)
Race and ethnicity, n (%), *n=5,275*	
non-Hispanic White	4,591 (87.0)
non-Hispanic Black	156 (3.0)
Hispanic	175 (3.3)
Asian	231 (4.4)
Other	122 (2.3)

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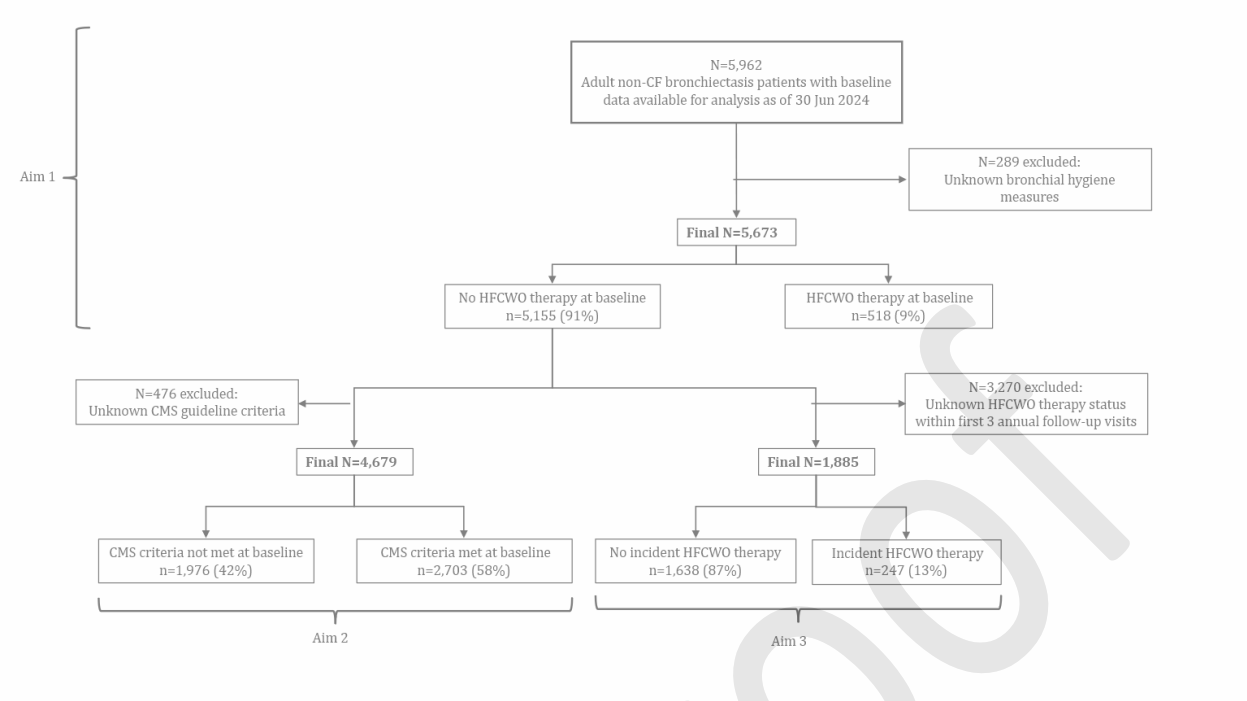

Figure 1. BRR Study Flow Diagram

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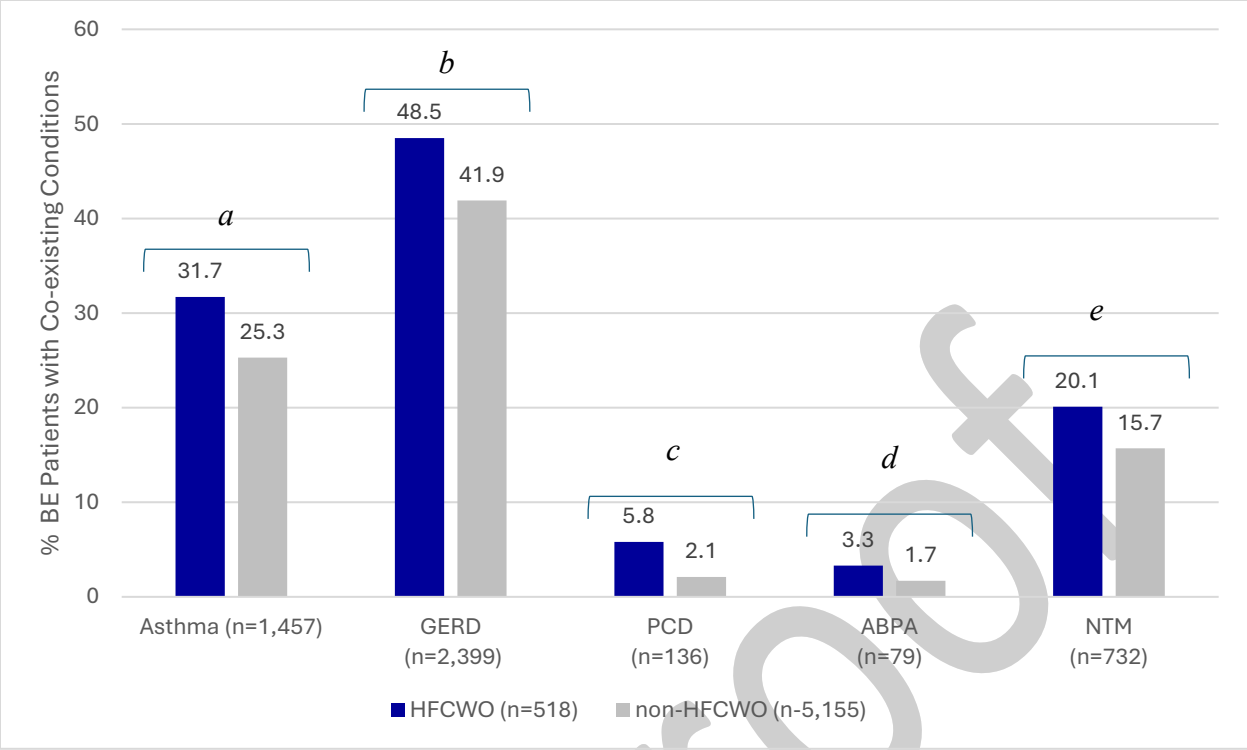

Figure 2. Co-existing conditions in BE patients with and without HFCWO therapy (%)

[a]P=0.002, [b]P=0.004, [c]P<0.001, [d]P=0.013, [e]P=0.011

Abbreviations: ABPA=Allergic Bronchopulmonary Aspergillosis; BE=bronchiectasis; GERD=gastroesophageal reflux disease; HFCWO=high frequency chest wall oscillation; NTM=nontuberculous mycobacteria; PCD=primary ciliary dyskinesia

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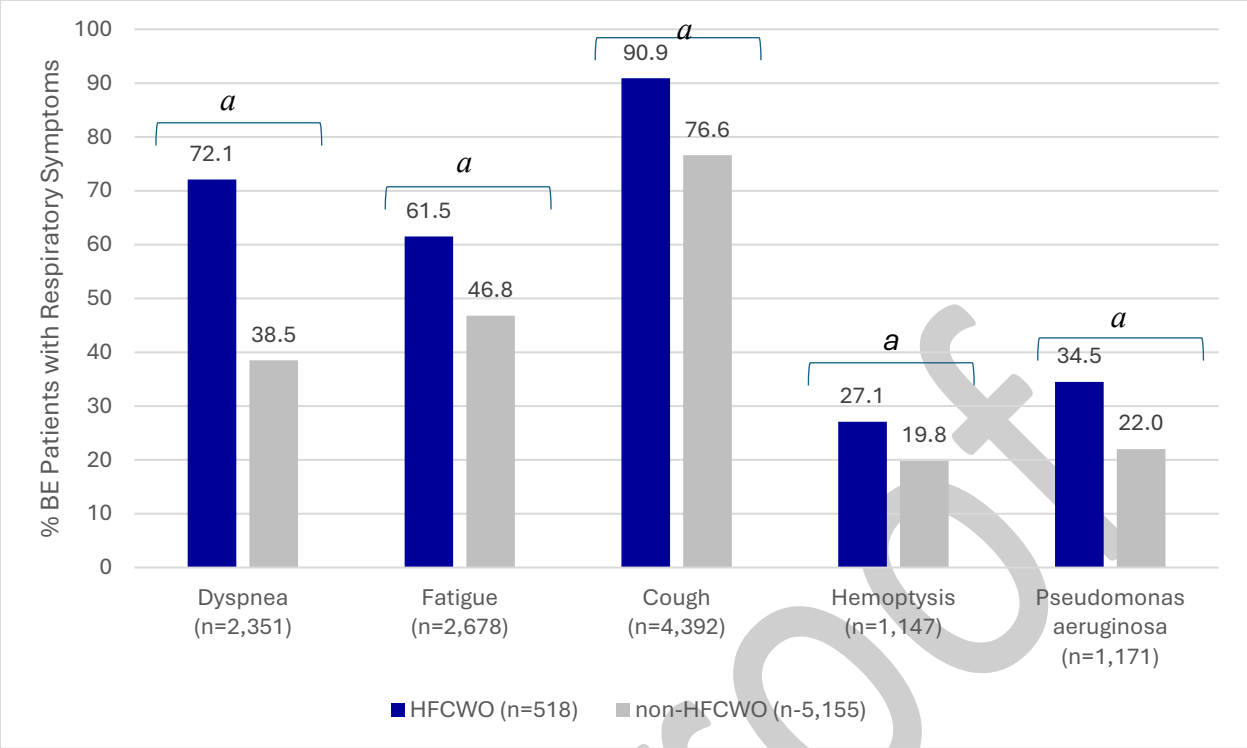

Figure 3. Respiratory symptoms in BE patients with and without HFCWO therapy (%)

[a]*P<0.001*

Abbreviations: BE=bronchiectasis; HFCWO=high frequency chest wall oscillation

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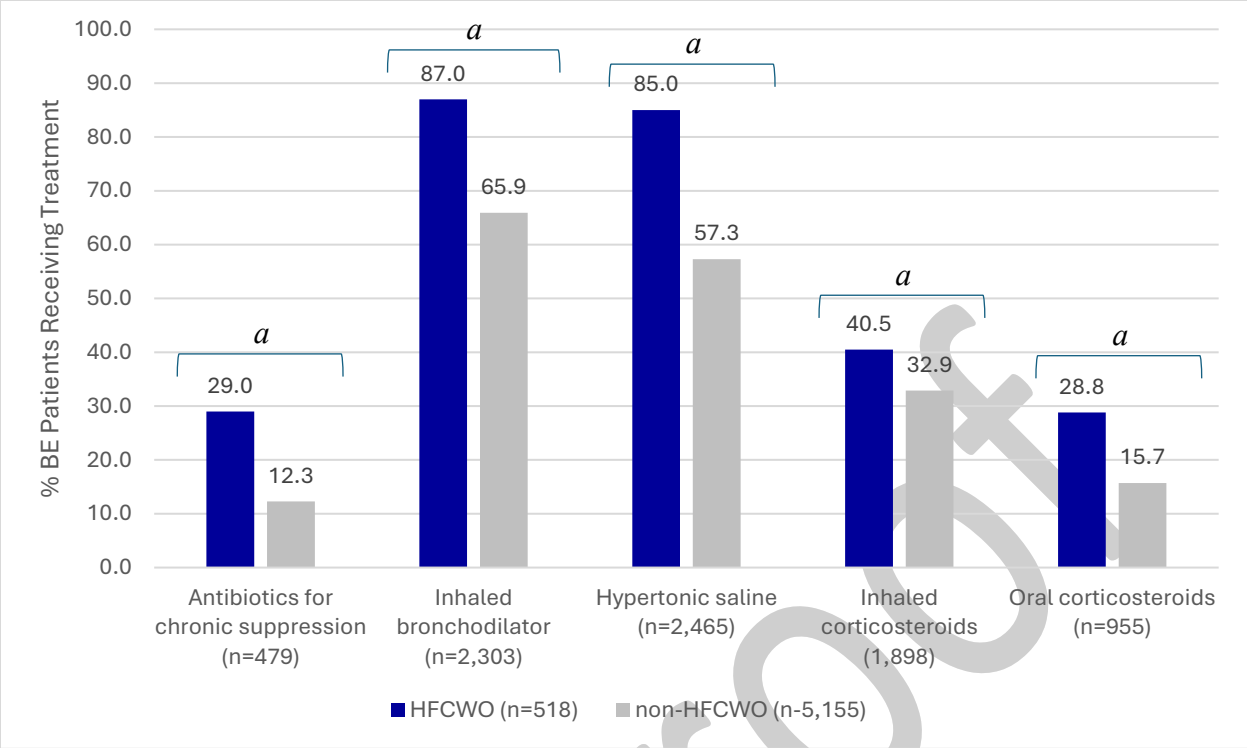

Figure 4. Treatments in BE patients with and without HFCWO therapy (%)

[a]*P<0.001*

Abbreviations: BE=bronchiectasis; HFCWO=high-frequency chest wall oscillation

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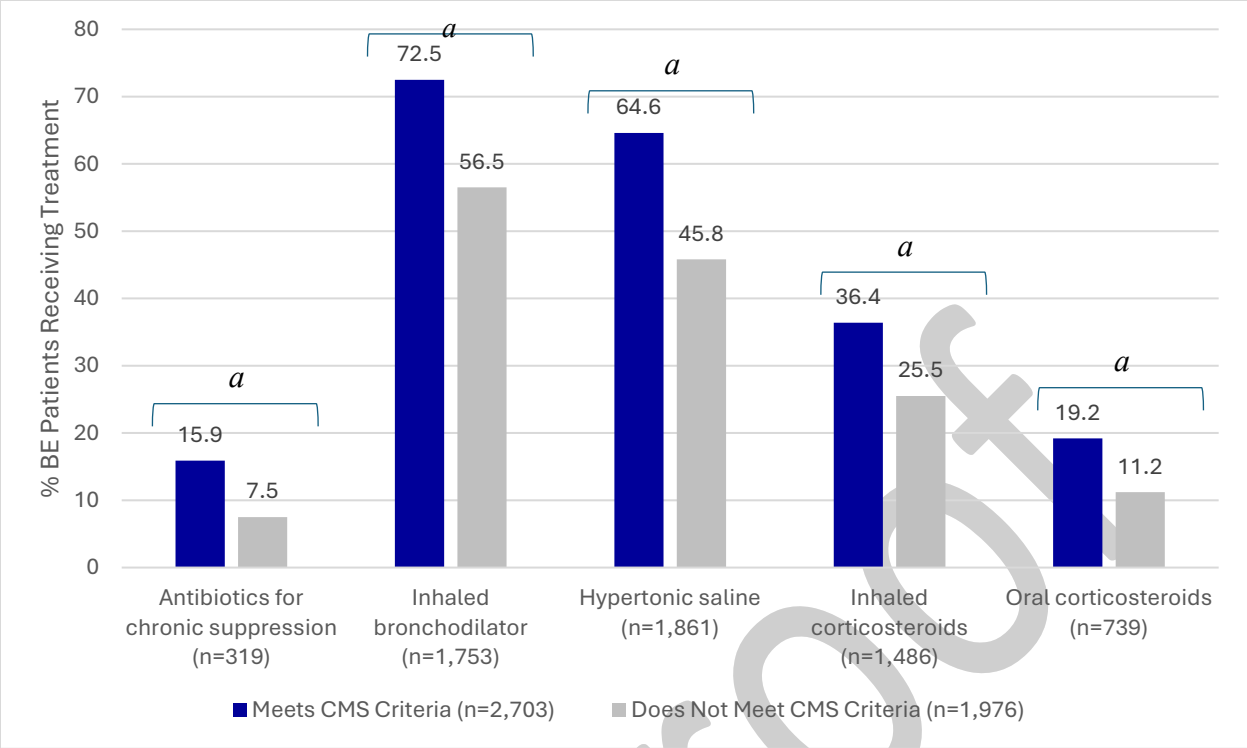

Figure 5. Treatments in BE patients meeting selected CMS symptom/exacerbation criteria vs. not (%)

[a]*P<0.001.*

Abbreviations: BE=bronchiectasis; CMS= Centers for Medicare and Medicaid Services

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Online Supplement

Supplement 1: Clinical characteristics of bronchiectasis patients with and without HFCWO therapy among patients enrolled in the U.S. Bronchiectasis and NTM Research Registry (Aim 1)

	Overall (n=5,673)	non-HFCWO therapy (n=5,155)	HFCWO therapy (n=518)	p-value*
Demographics				
Age, median [IQR]	5,634	69 [61-76]	69 [61-76]	68 [58-75]
Female, n (%)	5,663	4,510 (79.6)	4,086 (79.4)	424 (82.0)
Race and ethnicity, n (%)	5,275			
non-Hispanic White		4,591 (87.0)	4,153 (87.0)	438 (87.1)
non-Hispanic Black		156 (3.0)	138 (2.9)	18 (3.6)
Hispanic		175 (3.3)	162 (3.4)	13 (2.6)
Asian		231 (4.4)	204 (4.3)	27 (5.4)
Other		122 (2.3)	115 (2.4)	7 (1.4)
Co-existing conditions				
Asthma, n (%) *available n = 5,626*	1,457 (25.9)	1,293 (25.3)	164 (31.7)	0.002
COPD, n (%) *available n=5,625*	922 (16.4)	834 (16.3)	88 (17.0)	0.700
Meets ROSE criteria, n (%)	297 (5.2)	261 (5.1)	36 (6.9)	0.066
GERD, n (%) *available n=5,646*	2,399 (42.5)	2,148 (41.9)	251 (48.5)	0.004
PCD, n (%) *available n=5,634*	136 (2.4)	106 (2.1)	30 (5.8)	<0.001
Rheumatologic disease, n (%) *available n=5,615*	472 (8.4)	425 (8.3)	47 (9.1)	0.566
ABPA, n (%) *available n=4,183*	79 (1.9)	62 (1.7)	17 (3.3)	0.013
NTM†, n (%) *available n=4,515*	732 (16.2)	628 (15.7)	104 (20.1)	0.011
Clinical Characteristics				
BMI, median [IQR] *available n=5,208*	22.1 [19.8-25.2]	22.2 [19.8-25.2]	21.5 [19.5-24.7]	0.016
Pre-bronchodilator spirometry, mean (±SD)				
FVC (L) *available n=4,718*	2.7 (0.9)	2.7 (0.9)	2.6 (0.9)	0.004
FVC %predicted *available n=4,721*	84.0 (20.3)	84.2 (20.1)	81.7 (21.6)	0.016
FEV1 (L) *available n=4,749*	1.9 (0.7)	1.9 (0.7)	1.8 (0.7)	<0.001
FEV1 %predicted *available n=4,736*	74.7 (22.4)	75.2 (22.2)	69.5 (24.1)	<0.001
≥1 exacerbation in the 2 years prior to enrollment, n (%) *available n=5,526*	3,097 (56.0)	2,753 (54.9)	344 (67.5)	<0.001
Treated for acute exacerbations, n (%) *available n=1,614*	1,260 (78.1)	982 (77.1)	278 (81.5)	0.082

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	Overall (n=5,673)	non-HFCWO therapy (n=5,155)	HFCWO therapy (n=518)	p-value*
Demographics				
Age, median [IQR]	5,634	69 [61-76]	69 [61-76]	68 [58-75]
Female, n (%)	5,663	4,510 (79.6)	4,086 (79.4)	424 (82.0)
Race and ethnicity, n (%)	5,275			
non-Hispanic White		4,591 (87.0)	4,153 (87.0)	438 (87.1)
non-Hispanic Black		156 (3.0)	138 (2.9)	18 (3.6)
Hispanic		175 (3.3)	162 (3.4)	13 (2.6)
Asian		231 (4.4)	204 (4.3)	27 (5.4)
Other		122 (2.3)	115 (2.4)	7 (1.4)
≥1 pulmonary related hospitalization in the 2 years prior to enrollment, n (%) *available n=5,566*	1,066 (19.2)	928 (18.4)	138 (27.0)	<0.001
mBSI score, median [IQR] *available n=3,079*	7 [4-10]	7 [4-10]	8 [5-11]	<0.001
Microbiology (≥1 positive culture)				
Haemophilus influenzae, n (%) available n=5,037	322 (6.4)	294 (6.5)	28 (5.6)	0.432
Staphylococcus aureus, n (%) available n=5,037	444 (8.8)	388 (8.6)	56 (11.2)	0.051
Pseudomonas aeruginosa, n (%) available n=5,037	1,171 (23.2)	998 (22.0)	173 (34.5)	<0.001
Respiratory Symptoms				
Dyspnea, n (%) *available n =5,662*	2,351 (41.5)	1,979 (38.5)	372 (72.1)	<0.001
Fatigue, n (%) *available n=5,561*	2,678 (48.2)	2,365 (46.8)	313 (61.5)	<0.001
Cough, n (%) *available n=5,637*	4,392 (77.9)	3,924 (76.6)	468 (90.9)	<0.001
Sputum volume, n (%) available n=1,169	718 (61.4)	604 (65.6)	114 (46.0)	
<15mL	289 (24.7)	210 (22.8)	79 (31.9)	
15-45 mL	162 (13.9)	107 (11.6)	55 (22.2)	
>45 mL	718 (61.4)	604 (65.6)	114 (46.0)	
Hemoptysis, n (%) *available n=,5598*	1,147 (20.5)	1,008 (19.8)	139 (27.1)	<0.001
Treatment and Therapies				
Received antibiotics for chronic suppression, n (%) *available n=3,206*	479 (14.9)	331 (12.3)	148 (29.0)	<0.001
Inhaled bronchodilator, n (%) *available n=3,330*	2,303 (69.2)	1,854 (65.9)	449 (87.0)	<0.001
Hypertonic saline, n (%) *available n=4,051*	2,465 (60.8)	2,027 (57.3)	438 (85.0)	<0.001
Inhaled corticosteroids, n (%) *available n=5,656*	1,898 (33.6)	1,688 (32.9)	210 (40.5)	<0.001
Oral corticosteroids, n (%) *available n=5,651*	955 (16.9)	806 (15.7)	149 (28.8)	<0.001

Abbreviations: ABPA=Allergic Bronchopulmonary Aspergillosis, BMI=body mass index, COPD=chronic obstructive pulmonary disease, FEV1=forced expiratory volume in 1 second, FVC=forced vital capacity, GERD=gastroesophageal reflux disease, HFCWO=high-frequency chest wall oscillation, IQR=interquartile range, mBSI=modified Bronchiectasis Severity Index, NTM=nontuberculous mycobacteria, PCD=primary ciliary dyskinesia, SD=standard deviation

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**Wilcoxon-Mann-Whitney test, independent two-sample t-test, chi-square test*
†Defined as those meeting ATS/IDSA/ESCMID/ERS guideline criteria for culture positivity and actively being treated

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Supplement 2: Demographics and clinical characteristics of bronchiectasis patients without HFCWO therapy among patients enrolled in the U.S. Bronchiectasis and NTM Research Registry, stratified by those who do and do not meet selected CMS symptom/exacerbation criteriacriteria† for HFCWO therapy (Aim 2)

	Overall (n=4,679)	Does not meet criteria (n=1,976)	Meets criteria (n=2,703)	p-value*
Demographics				
Age, median [IQR] available n=4,653	69.0 [61.0-76.0]	70.0 [62.0-77.0]	69.0 [60.0-76.0]	<0.001
Female, n (%) available n=4,672	3,700 (79.2)	1,622 (82.1)	2,078 (77.1)	<0.001
Race and ethnicity, n (%) available n=4,340				0.556
non-Hispanic White	3,782 (87.1)	1,586 (87.1)	2,196 (87.1)	
non-Hispanic Black	133 (3.1)	51 (2.8)	82 (3.3)	
Hispanic	150 (3.5)	64 (3.5)	86 (3.4)	
Asian	186 (4.3)	86 (4.7)	100 (4.0)	
Other	89 (2.1)	33 (1.8)	56 (2.2)	
Co-existing conditions				
Asthma, n (%) available n = 4,641	1,169 (25.2)	416 (21.3)	753 (28.0)	<0.001
COPD, n (%) available n=4,644	758 (16.3)	264 (13.5)	494 (18.4)	<0.001
Meets ROSE criteria, n (%)	242 (5.2)	54 (2.7)	188 (7.0)	<0.001
GERD, n (%) available n=4,659	1,954 (41.9)	792 (40.2)	1,162 (43.2)	0.045
PCD, n (%) available n=4,646	74 (1.6)	10 (0.5)	64 (2.4)	<0.001
Rheumatologic disease, n (%) available n=4,633	393 (8.5)	189 (9.7)	204 (7.6)	0.011
ABPA, n (%) available n=3,365	60 (1.8)	17 (1.2)	43 (2.2)	0.030
NTM‡, n (%) available n=3,666	580 (15.8)	245 (15.7)	335 (15.9)	0.891
Clinical Characteristics				
BMI, median [IQR] available n=4,283	22.1 [19.8-25.2]	22.1 [19.8-25.1]	22.2 [19.7-25.3]	0.740
Pre-bronchodilator spirometry, mean (±SD)				
FVC (L) available n=3,880	2.7 (0.9)	2.8 (0.8)	2.7 (0.9)	0.041
FVC %predicted available n=3,887	84.5 (20.2)	86.5 (19.2)	83.2 (20.7)	<0.001
FEV1 (L) available n=3,907	1.9 (0.7)	1.9 (0.7)	1.9 (0.7)	<0.001
FEV1 %predicted available n=3,901	75.5 (22.1)	78.7 (20.7)	73.5 (22.8)	<0.001
Annualized exacerbation rate	0.7	0.3	0.9	<0.001
Treated for acute exacerbations, n (%) available n=2,574	996 (38.7)	292 (27.1)	704 (47.1)	<0.001
≥1 pulmonary related hospitalization in the 2 years prior to enrollment, n (%) available n=4,648	822 (17.7)	253 (12.9)	569 (21.2)	<0.001
mBSI score, median [IQR] available n=2,548	7.0 [4.0-9.5]	6.0 [4.0-8.0]	7.0 [5.0-10.0]	<0.001
Microbiology (≥1 positive culture)				
Haemophilus influenzae, n (%)	270 (6.6)	90 (5.6)	180 (7.2)	0.042

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	Overall (n=4,679)	Does not meet criteria (n=1,976)	Meets criteria (n=2,703)	p-value*
available n=4,110				
Staphylococcus aureus, n (%) available n=4,110	343 (8.3)	105 (6.5)	238 (9.5)	<0.001
Pseudomonas aeruginosa, n (%) available n=4,110	886 (21.6)	212 (13.2)	674 (27.0)	<0.001
Respiratory Symptoms				
Dyspnea, n (%) available n=4,679	1,853 (39.6)	618 (31.3)	1,235 (45.7)	<0.001
Cough, n (%) available n=4,673	3,537 (75.7)	911 (46.1)	2,626 (97.3)	<0.001
Fatigue, n (%) available n=4,616	2,151 (46.6)	754 (38.7)	1,397 (52.4)	<0.001
Hemoptysis, n (%) available n=4,635	916 (19.8)	259 (13.3)	657 (24.5)	<0.001
Treatment and Therapies				
Received antibiotics for chronic suppression, n (%) available n=2,574	319 (12.4)	81 (7.5)	238 (15.9)	<0.001
Inhaled bronchodilator, n (%) available n=2,660	1,753 (65.9)	622 (56.5)	1,131 (72.5)	<0.001
Hypertonic saline, n (%) available n=3,262	1,861 (57.1)	598 (45.8)	1,263 (64.6)	<0.001
Inhaled corticosteroids, n (%) available n=4,672	1,486 (31.8)	503 (25.5)	983 (36.4)	<0.001
Oral corticosteroids, n (%) available n=4,668	739 (15.8)	221 (11.2)	518 (19.2)	<0.001
Received HFCWO at follow-up¶, n (%) available n=1,709	220 (12.9)	71 (11.0)	149 (14.0)	0.073

Abbreviations: ABPA = Allergic Bronchopulmonary Aspergillosis, BMI = body mass index, CMS = Centers for Medicare & Medicaid Services, COPD = chronic obstructive pulmonary disease, FEV1 = forced expiratory volume in 1 second, FVC = forced vital capacity, GERD = gastroesophageal reflux disease, HFCWO = high-frequency chest wall oscillation, IQR = interquartile range, mBSI = modified Bronchiectasis Severity Index, NTM = nontuberculous mycobacteria, PCD = primary ciliary dyskinesia, ROSE = radiology, obstruction, symptoms, and exposure, SD = standard deviation

*Wilcoxon-Mann-Whitney test, independent two-sample t-test, chi-square test

†Defined as those with a usually productive cough during the 2 years prior to enrollment and >2 exacerbations per year

‡Defined as those meeting ATS/IDSA/ESCMID/ERS guideline criteria for culture positivity and actively being treated

¶Defined as ≥1 follow-up visit in a 3 year period

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Supplement 3: Clinical characteristics of patients with and without incident HFCWO therapy within the first 3 annual follow-up visits among patients with no HFCWO therapy at baseline (Aim 3)

		Overall	non-HFCWO	Incident HFCWO	p-value
	N	**1,709**	**1,489**	**220**	
Annual follow-up years since baseline, mean (SD)	1,709	1.4 (0.7)	1.3 (0.6)	1.6 (0.8)	<0.001
Meets selected CMS criteria, n (%)	1,709	1,064 (62.3)	915 (61.5)	149 (67.7)	0.073
Baseline Demographics					
Age, median [IQR]	1,702	69.0 [62.0-76.0]	69.0 [62.0-76.0]	68.0 [62.0-76.0]	0.674
Female, n (%)	1,706	1421 (83.3)	1241 (83.5)	180 (81.8)	0.529
Baseline Microbiology (≥1 positive culture)					
Haemophilus influenzae, n (%)	1,592	105 (6.6)	91 (6.6)	14 (6.7)	0.949
Staphylococcus aureus, n (%)	1,592	129 (8.1)	110 (8.0)	19 (9.1)	0.574
Pseudomonas aeruginosa, n (%)	1,592	366 (23.0)	304 (22.0)	62 (29.7)	0.014
Baseline Respiratory Symptoms					
Dyspnea, n (%)	1,709	737 (43.1)	626 (42.0)	111 (50.5)	0.019
Fatigue, n (%)	1,689	817 (48.4)	710 (48.2)	107 (49.8)	0.661
Cough, n (%)	1,709	1,347 (78.8)	1,158 (77.8)	189 (85.9)	0.006
Sputum volume, n (%)	379				0.099
<15 mL		229 (60.4)	202 (61.2)	27 (55.1)	
15-45 mL		95 (25.1)	85 (25.8)	10 (20.4)	
>45 mL		55 (14.5)	43 (13.0)	12 (24.5)	
Hemoptysis, n (%)	1701	387 (22.8)	334 (22.5)	53 (24.2)	0.584
Baseline Treatment					
Received antibiotics for chronic suppression, n (%)	523	157 (30.0)	98 (24.6)	59 (47.2)	<0.001
Inhaled bronchodilator, n (%)	1,115	719 (64.5)	593 (62.8)	126 (73.7)	0.006
Hypertonic saline, n (%)	1,334	792 (59.4)	649 (57.9)	143 (66.8)	0.015
Airway clearance, n (%)	1,709	1,240 (72.6)	1,080 (72.5)	160 (72.7)	0.952
Inhaled corticosteroids, n (%)	1,706	526 (30.8)	459 (30.9)	67 (30.5)	0.897
Oral corticosteroids, n (%)	1,706	270 (15.8)	231 (15.5)	39 (17.7)	0.408
Follow-up clinical characteristics					
FEV1 (L), median [IQR]	737	1.8 [1.4-2.2]	1.9 [1.5-2.2]	1.7 [1.3-2.3]	0.082
FEV1 %predicted, mean (SD)	732	79.0 (21.2)	80.3 (20.4)	73.3 (23.7)	0.002
≥1 exacerbation reported during the visit window, n (%)	1,399	434 (31.0)	336 (28.1)	98 (47.8)	<0.001
Treated for acute exacerbation, n (%)	1,263	402 (31.8)	312 (29.7)	90 (42.1)	<0.001
≥1 pulmonary related hospitalization reported during the visit window, n (%)	1,690	204 (12.1)	159 (10.8)	45 (20.5)	<0.001
Received antibiotics for chronic suppression, n (%)	1,263	157 (12.4)	98 (9.3)	59 (27.6)	<0.001

Abbreviations: FEV1=forced expiratory volume in 1 second, HFCWO=high-frequency chest wall oscillation, SD=standard deviation

**Wilcoxon-Mann-Whitney test, independent two-sample t-test, chi-square test*

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