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Spinou, Arietta; Hererro-Cortina, Beatriz; Aliberti, Stefano; Goeminne, Pieter C.; Polverino, Eva; Dimakou, Katerina

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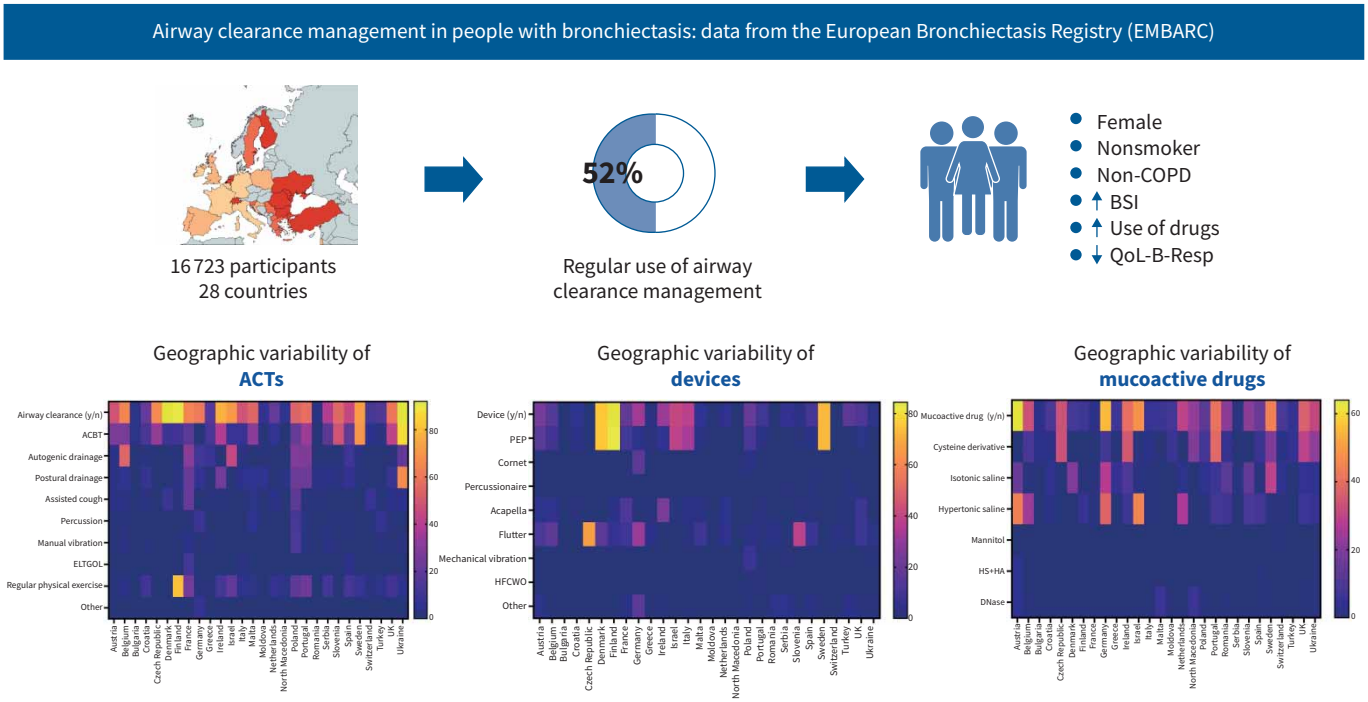

GRAPHICAL ABSTRACT Summary of the study. EMBARC: European Multicentre Bronchiectasis Audit and Research Collaboration; BSI: bronchiectasis severity index; QoL-B-Resp: Quality of Life Questionnaire–Bronchiectasis Respiratory symptoms; ACT: airway clearance technique; y/n: yes/no; ACBT: active cycle of breathing technique; ELTGOL: slow expiration with glottis opened in lateral position; PEP: positive expiratory pressure; HFCWO: high-frequency chest wall oscillation; HS+HA: hypertonic saline and hyaluronic acid.

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[1]Population Health Sciences, Faculty of Life Sciences and Medicine, King's College London, London, UK. [2]King's Centre for Lung Health, King's College London, London, UK. [3]Universidad San Jorge, Zaragoza, Spain. [4]Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain. [5]Instituto de Investigación Sanitaria (IIS) de Aragón, Zaragoza, Spain. [6]IRCCS Humanitas Research Hospital, Respiratory Unit, Milan, Italy. [7]Department of Biomedical Sciences, Humanitas University, Milan, Italy. [8]Department of Respiratory Disease, AZ Nikolaas, Sint-Niklaas, Belgium. [9]Pneumology Department, Hospital Universitari Vall d'Hebron, Vall d'Hebron Institut de Recerca (VHIR), Vall d'Hebron Barcelona Hospital Campus, CIBERES, Barcelona, Spain. [10]5th Respiratory Department and Bronchiectasis Unit, "SOTIRIA" General Hospital of Chest Diseases Medical Practice, Athens, Greece. [11]Cambridge Centre for Lung Infection, Royal Papworth Hospital and University of Cambridge, Cambridge, UK. [12]Royal Brompton and Harefield Hospitals and National Heart and Lung Institute, Imperial College London, London, UK. [13]Population and Health Science Institute, Newcastle University and NIHR Biomedical Research Centre for Ageing, Freeman Hospital, Newcastle, UK. [14]Department of Pulmonology, Dr Trueta University Hospital, Girona Biomedical Research Institute (IDIBGI), University of Girona, Girona, Spain. [15]Department of Respiratory Medicine and French Cystic Fibrosis National Reference Center, Hôpital Cochin, AP-HP, Paris, France. [16]Université Paris Cité, Inserm U1016, Institut Cochin, Paris, France. [17]Department of Respiratory Medicine, Galway University Hospital, Galway, Ireland. [18]Department of Pulmonary Medicine, University Hospital Essen – Ruhrlandklinik, Adult Cystic Fibrosis Center, University of Duisburg-Essen, Essen, Germany. [19]University Medical Centre Ljubljana, Department of Pulmonary Diseases and Allergy, Ljubljana, Slovenia. [20]Medical Faculty, University of Ljubljana, Ljubljana, Slovenia. [21]University Clinic of Respiratory and Allergic Diseases Golnik, Golnik, Slovenia. [22]Chronic Bronchial Infection Unit, Pneumology Service, Ramón y Cajal Hospital, Alcalá de Henares University, Madrid, Spain. [23]Servicio de Neumología, Instituto Clínico de Respiratorio, IDIBAPS, Hospital Clínic, University of Barcelona, Barcelona, Spain. [24]CIBER de Enfermedades Respiratorias, ISCIII, Madrid, Spain. [25]Department of Pneumology, Faculty of Medicine, University of Freiburg, Freiburg, Germany. [26]Clinic of Respiratory Medicine and Pulmonary Cell Research, University of Basel, Basel, Switzerland. [27]Heart and Lung Center, Helsinki University Hospital and University of Helsinki, Helsinki, Finland. [28]Department of Respiratory Medicine and Allergy, Karolinska University Hospital, Stockholm, Sweden. [29]Division of Lung and Airway Research, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden. [30]Royal Infirmary of Edinburgh, Department of Respiratory Medicine, Edinburgh, UK. [31]Leeds Teaching Hospitals NHS Trust, Leeds, UK. [32]Division of Molecular and Clinical Medicine, University of Dundee, Ninewells Hospital and Medical School, Dundee, UK. [33]Liverpool University Hospitals Foundation NHS Trust, Liverpool, UK. [34]Pneumology Department, Hospital Universitario y Politécnico La Fe–Instituto de Investigación Sanitaria La Fe, Valencia, Spain. [35]Istanbul University – Cerrahpasa, Cerrahpasa Medical Faculty, Department of Pulmonology Diseases, Istanbul, Turkey. [36]Faculty of Medicine Novi Sad, University of Novi Sad, Novi Sad, Serbia. [37]Institute for Pulmonary Diseases, University of Novi Sad, Sremska Kamenica, Serbia. [38]Department of Epidemiology, National Tuberculosis and Lung Diseases Research Institute, Warsaw, Poland. [39]Pulmonology Department, Centro Hospitalar Universitário S. João, Porto, Portugal. [40]Faculty of Medicine, University of Porto, Porto, Portugal. [41]Department of Pulmonology Hospital Clinic of Barcelona, Spain University of Barcelona, CIBERES, IDIBAPS, ICREA Barcelona, Barcelona, Spain. [42]Department of Respiratory Diseases, University Hospitals Leuven, Leuven, Belgium. [43]Department of Respiratory Medicine and Infectious Diseases, Hannover Medical School, Hannover, Germany. [44]Biomedical Research in End-Stage and Obstructive Lung Disease Hannover, German Center for Lung Research, Hannover, Germany. [45]European Reference Network on Rare and Complex Respiratory Diseases, Frankfurt, Germany. [46]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy. [47]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy. [48]University of Zagreb School of Medicine and University Hospital Centre Zagreb, Zagreb, Croatia. [49]Clinic for Pulmonary Diseases, University Hospital Centre Zagreb, Zagreb, Croatia. [50]Pulmonology Institute and CF Center, Carmel Medical Center, Haifa, Israel. [51]The Technion, Israel Institute of Technology, The B. Rappaport Faculty of Medicine, Haifa, Israel. [52]Department of Pulmonary Diseases, Northwest Clinics, Alkmaar, The Netherlands. [53]Faculty of Medicine, Health and Life Sciences, Queen's University, Belfast, UK. [54]A. Spinou and B. Herrero-Cortina contributed equally to this paper.

Corresponding author: James D. Chalmers (j.chalmers@dundee.ac.uk)

Shareable abstract (@ERSpublications)
Only around a half of patients with bronchiectasis in Europe perform regular airway clearance. Techniques and use of airway clearance management is heterogeneous, suggesting the need for clearer guidelines and stronger evidence. https://bit.ly/3v2CFGy

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Abstract

Background International guidelines recommend airway clearance management as one of the important pillars of bronchiectasis treatment. However, the extent to which airway clearance is used for people with bronchiectasis in Europe is unclear. The aim of the study was to identify the use of airway clearance management in patients with bronchiectasis across different countries and factors influencing airway clearance use.

Methods This was a prospective observational study using data from the European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) Registry between January 2015 and April 2022. Prespecified options for airway clearance management were recorded, including airway clearance techniques, devices and use of mucoactive drugs.

Results 16 723 people with bronchiectasis from 28 countries were included in the study. The mean age was 67 years (interquartile range 57–74 years, range 18–100 years) and 61% were female. 72% of the participants reported daily sputum expectoration and 52% (95% CI 51–53%) of all participants reported using regular airway clearance management. Active cycle of breathing technique was used by 28% of the participants and airway clearance devices by 16% of participants. The frequency of airway clearance management and techniques used varied significantly between different countries. Participants who used airway clearance management had greater disease severity and worse symptoms, including a higher daily sputum volume, compared to those who did not use it regularly. Mucoactive drugs were also more likely to be used in participants with more severe disease. Access to specialist respiratory physiotherapy was low throughout Europe, but particularly low in Eastern Europe.

Conclusions Only a half of people with bronchiectasis in Europe use airway clearance management. Use of and access to devices, mucoactive drugs and specialist chest physiotherapy appears to be limited in many European countries.

Introduction

Impaired mucociliary clearance is one of the defining features of the clinical syndrome of bronchiectasis [1, 2]. The most frequent symptoms that impact upon patients' quality of life are cough and sputum production, commonly characterised by secretions with high viscoelasticity [3–5]. Chronic inflammation and infection in bronchiectasis result in excess mucus production through hyperplasia and metaplasia of goblets cells, reduced hydration of the airway surface liquid and impaired cilia beating [3, 6, 7]. Failure of mucociliary transport leads to progressive lung damage, bacterial infection and an increased risk of exacerbations [8].

Improving clearance of mucus from the airways is therefore recognised by international and national guidelines for bronchiectasis as a central component of management [9–11]. Airway clearance is, however, not supported by high-quality evidence [5, 12, 13]. The European Respiratory Society (ERS) guidelines in 2017 recommended using airway clearance management in symptomatic adult patients as a weak recommendation with a low quality of evidence due to a paucity of randomised studies [9]. The limited research into airway clearance techniques (ACTs), as well as the heterogeneity in the patient population, leads to diverse practice [5]. Access to healthcare is variable across Europe and worldwide, and therefore access to specialist respiratory physiotherapists and airway clearance management is also variable between different countries and within countries [5, 14, 15].

To date there have been no large studies describing the use of airway clearance management, including ACTs, devices and mucoactive drug treatments, in people with bronchiectasis in Europe. The objective of this study was to describe the proportion of people using regular airway clearance management; to describe the most commonly used techniques, devices and mucoactive drugs; and to evaluate the characteristics of patients receiving these treatments using the large prospective European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) registry.

Methods

The EMBARC registry is a prospective observational study of patients with clinically and computed tomography-confirmed bronchiectasis conducted across 28 countries in Europe and Israel [16]. The study

was approved by the ethics committee in the host country (UK) and by institutional review boards or ethics committees in all countries in which the study is conducted. A detailed protocol of the study has been previously published and baseline characteristics reported in detail [15, 16].

Data collection

Patient enrolment commenced in January 2015 and recruitment is open-ended and ongoing. For the present analysis, patients enrolled up to April 2022 were included. Patient data were collected annually using a standardised case report form. Comprehensive clinical data incorporating demographics, comorbidities, medications, aetiological testing, microbiology, radiology, lung function and disease history were recorded. Aetiology was recorded by the attending physician/medical team and the aetiology in the opinion of the investigator is reported. Data on aetiological testing supporting the investigator decision is recorded. Data on clinically indicated sputum samples, sent during clinical stability and exacerbation, were collected and patients classified according to whether they had isolated specific bacteria in any sample in the previous 12 months. Data on microbiology and frequency of exacerbations were collected for 12 months prior to date of consent into the EMBARC registry. Radiological severity was evaluated in the patients' most recent computed tomography scan using the modified Reiff score, as previously described [17]. Disease severity was evaluated using the bronchiectasis severity index (BSI) [18]. Data on medication use at the time of enrolment and during follow-up were collected through patient history and clinical records. Exacerbations were defined as use of antibiotics for acute respiratory symptoms and were recorded from a combination of patient history, hospital and prescription records [19]. Breathlessness was evaluated using the modified Medical Research Council dyspnoea scale. Symptoms were evaluated using the Quality of Life Questionnaire–Bronchiectasis (QoL-B) version 3.1 using validated translations into native languages [20, 21].

Airway clearance management

To standardise data collection, a number of airway clearance management options were prespecified within the electronic EMBARC case report form (CRF). The CRF included the question, "does the patient practice regular chest physiotherapy". For participants replying yes, a series of additional options were provided. Regular chest physiotherapy could include manual ACT, devices or both. The list of options was developed by the EMBARC steering committee and a specialist working group, including physiotherapists with special interest in bronchiectasis and/or cystic fibrosis. For self-administered and manual ACTs, the options were active cycle of breathing technique (ACBT), autogenic drainage, postural drainage, assisted cough, manual vibration, manual percussion, slow expiration with glottis opened in lateral position (ELTGOL), regular exercise, other and none. It is acknowledged that exercise is not strictly an ACT [22], but based on patient feedback that this is widely used to aid airway clearance, it was included in the CRF. Data are presented with and without regular exercise as an ACT.

The ERS bronchiectasis guidelines and national guidelines recommend regular ACT for all patients with bronchiectasis, including those with regular expectoration and those with difficulty expectorating who do not expectorate daily. Therefore, the primary analysis used all participants as the denominator. We also report the proportion using ACT when limited only to those with daily expectoration of sputum.

For airway clearance devices the options were positive expiratory pressure (PEP) device, Flutter, Acapella, Cornet, mechanical vibration, intrapulmonary percussive ventilation, high-frequency chest wall oscillation (HFCWO), other and none.

For mucoactive drugs the options were nebulised normal saline, nebulised hypertonic saline, nebulised hypertonic saline with the addition of hyaluronic acid, inhaled mannitol, inhaled Dornase alfa (recombinant human deoxyribonuclease), N-acetylcysteine/carbocistine (oral mucoactive drugs), other and none.

The CRF recorded data on "regular use" of these ACTs, devices and mucoactive treatments to differentiate from situations where these interventions may be used only during exacerbations or otherwise intermittently. To meet the registry's definition of regular use, the CRF required that participants use the technique/device/drug most days while clinically stable. The CRF did not record data on frequency or duration of ACT use.

Participants who did not practice airway clearance management were requested to provide the reasons for this and the options provided were non-adherence due to lack of time, non-adherence due to lack of motivation or perception of benefit, doctor or other healthcare professional indicated that it was not needed, and physical inability to perform ACT.

At 12 months follow-up and annually thereafter, the data collection tool included a question asking if the patient had seen a specialist respiratory physiotherapist in the previous 12 months. This was designed to account for new patients, so that patients have had at least 1 year before it is reasonable to expect they have seen a physiotherapist. At follow-up, data were again collected on the use of ACTs, devices and mucoactive drugs.

Statistical analysis

Summary data are presented as median with interquartile range (IQR). Comparisons between two groups used the Mann–Whitney U test. To identify if the differences in practice between countries were independent of disease severity and other clinical variables, we performed logistic regression analysis. Airway clearance management was used as the dependent variable and country as the independent variable, with the model adjusted for multiple confounders known from the literature as being associated with severity, prognosis or practice [18, 23–25]. Results are expressed as adjusted odds ratios with 95% CIs. The UK was used as the reference country for analysis as the country with the largest group of patients in the registry [15]. All analyses used SPSS version 27 (IBM, Chicago, IL, USA) or GraphPad Prism version 9 (GraphPad Software, La Jolla, CA, USA).

Results

Population

Data were collected from 16 963 patients. 240 patients were excluded due to missing or incomplete data on ACT use. Therefore, the analysis included 16 723 adults with bronchiectasis from 28 countries. The overall demographics, patient characteristics and countries contributing to the EMBARC registry population have been previously described [15]. The flow of patients through the study is shown in figure 1.

The median (IQR) age of participants was 67 years (57–74 years) and 10 182 participants (60.9%) were female. The cohort was evenly distributed into participants with mild (n=4857, 29.0%), moderate (n=5968, 35.7%) and severe (n=5898, 35.3%) bronchiectasis according to the BSI (figure 1). Most patients reported daily expectoration of sputum (n=11 971, 71.6%). Median (IQR) daily sputum volume was 6 mL (0–20 mL) across the whole population, including patients without daily expectoration.

Use of airway clearance management

8739 participants (52.2%, 95% CI 51–53%) reported using regular airway clearance management at baseline. Rates by region varied from 58.9% of patients in the UK to 33.0% in Central and Eastern Europe (table 1). In 570 participants (3.4%), the only method of airway clearance management reported was regular exercise. Excluding these patients, 8169 (48.8%) reported regular airway clearance management. Table 1 shows the baseline characteristics of participants who did and did not use airway clearance

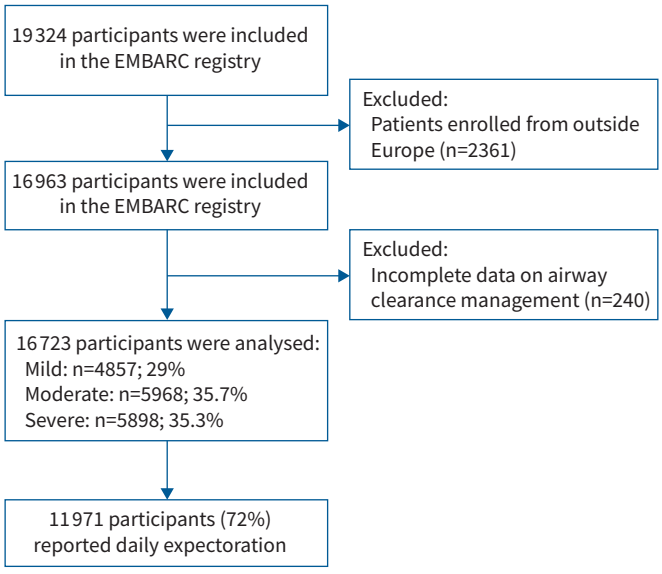

FIGURE 1 Flow chart of participants in the study. EMBARC: European Multicentre Bronchiectasis Audit and Research Collaboration.

TABLE 1 Demographics, clinical characteristics and differences between patients who use airway clearance management *versus* those who do not use airway clearance management

Variables	Regular airway clearance management	No regular airway clearance management	p-value
Participants (n)	8739	7984	
Demographics			
Age (years)	67 (58–74)	67 (57–74)	0.74
Female	5513 (63.1)	4669 (58.5)	<0.0001
BMI ($kg \cdot m^{-2}$)	24.7 (21.6–28.6)	25.1 (21.9–28.7)	<0.0001
Never-smoker	4952 (56.7)	4001 (50.1)	
Ex-smoker	3454 (39.5)	3237 (40.5)	
Current smoker	333 (3.8)	746 (9.3)	<0.0001
Comorbidities			
Cardiovascular disorders	2711 (31.0)	2752 (34.5)	<0.0001
Stroke	315 (3.6)	273 (3.4)	0.52
Diabetes	845 (9.7)	863 (10.8)	0.015
Liver disease	46 (0.5)	49 (0.6)	0.45
Chronic renal failure	341 (3.9)	317 (4.0)	0.82
COPD	2072 (23.7)	2201 (27.6)	<0.0001
Asthma	3002 (34.4)	2207 (27.6)	<0.0001
Osteoporosis	1263 (14.5)	947 (11.9)	<0.0001
Depression	1298 (14.9)	1066 (13.4)	0.0054
Solid tumour	950 (10.9)	893 (11.2)	0.52
Aetiology			
Idiopathic	3416 (39.1)	3009 (37.7)	
Post-infective	1862 (21.3)	1728 (21.6)	
COPD	573 (6.6)	776 (9.7)	
Asthma	592 (6.8)	546 (6.8)	
Tuberculosis	302 (3.5)	523 (6.6)	
Immunodeficiency	364 (4.2)	330 (4.1)	
ABPA	285 (3.3)	179 (2.2)	
Rheumatoid arthritis	250 (2.9)	202 (2.5)	
Other	1095 (12.5)	691 (8.7)	<0.0001
Clinical status			
FEV_1 (L)	1.73 (1.24–2.31)	1.84 (1.24–2.31)	<0.0001
FEV_1 (% predicted)	75.1 (54.4–95.2)	78.6 (57.7–98.1)	<0.0001
FVC (L)	2.61 (2.03–3.30)	2.68 (2.05–3.40)	0.55
FVC (% predicted)	90.9 (73.3–107.2)	91.7 (73.7–107.8)	0.38
Reiff score	4 (2–6)	3 (2–6)	<0.0001
Sputum volume ($mL \cdot day^{-1}$)	10 (2–25)	5 (0–15)	<0.0001
QoL-B-Resp score	59.3 (40.7–74.1)[¶]	66.7 (45.8–81.5)[+]	<0.0001
Does not produce daily sputum	1767 (20.2)	2985 (37.4)	<0.0001
mMRC score			
0	2165 (24.8)	2214 (27.7)	
1	2940 (33.6)	2531 (31.7)	
2	1923 (22.0)	1659 (20.8)	
3	1125 (12.9)	1043 (13.1)	
4	507 (5.8)	383 (4.8)	
Missing	79 (0.9)	154 (1.9)	<0.0001
Treatment			
Long-term macrolide treatment	1878 (21.5)	975 (12.2)	<0.0001
Other long-term non-macrolide oral antibiotics treatment	496 (5.7)	298 (3.7)	<0.0001
Inhaled/nebulised antibiotic treatment	958 (11.0)	343 (4.3)	<0.0001
Inhaled corticosteroids	4927 (56.4)	3660 (45.8)	<0.0001
Region[#]			
UK	4807 (55.0)	3356 (42.0)	
Western and Northern Europe	1830 (20.9)	1374 (17.2)	
Southern Europe	1752 (20.0)	2543 (31.9)	
Central and Eastern Europe	350 (4.0)	711 (8.9)	<0.0001

Data are presented as median (interquartile range) or n (%), unless otherwise indicated. BMI: body mass index; ABPA: allergic bronchopulmonary aspergillosis; QoL-B-Resp: Quality of Life Questionnaire–Bronchiectasis Respiratory symptoms; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; mMRC: modified Medical Research Council. [#]: data show the proportion of patients using and not using airway clearance management; [¶]: n=6354 patients with available baseline data; [+]: n=4798 patients with available baseline data.

management at baseline. Participants performing airway clearance were more likely to be female, nonsmokers and without co-existing COPD. Participants who used airway clearance management had more severe bronchiectasis, reflected by worse lung function and higher radiological severity using the Reiff score, as well as a higher proportion presenting with daily sputum production and a higher daily sputum volume. Consistent with the greater disease severity, participants who used airway clearance management were more likely to receive macrolides, oral antibiotics, inhaled antibiotics and inhaled corticosteroids (table 1). The results were similar when considering participants who expectorated on a daily basis, with 6387 participants (53.4%) performing regular airway clearance. Subsequent analyses are performed on the overall population.

Participants who used airway clearance management *versus* those who did not use it had a higher median (IQR) BSI score (7 points (5–11 points) *versus* 6 points (4–10 points), p<0.0001), were more frequently infected with *Pseudomonas aeruginosa* (22.7% *versus* 13.2%, p<0.0001) and had more frequent exacerbations (⩾3 exacerbations) in the past year (44.5% *versus* 32.3%, p<0.0001). Participants receiving airway clearance management also had worse median (IQR) score on the respiratory domain of QoL-B (59.3 points (40.7–74.1 points) *versus* 66.7 points (45.8–81.5 points), p<0.0001). Disease severity is shown in supplementary table S1. Supplementary table S2 shows that the types of ACTs and devices used were similar across the majority of different bronchiectasis aetiologies.

A reason for not performing airway clearance was recorded in 4361 participants (55% of those not using regular airway clearance management). The most common reason in 3115 participants (71.4%) was "clinician decision that it was not needed", while 839 participants (19.2%) reported lack of motivation, 240 participants (5.5%) were physically unable to perform airway clearance management and just 167 participants (3.8%) reported the lack of time as the main reason. Characteristics of these participants are shown in supplementary table S3. Participants physically unable to perform airway clearance management were markedly older and had higher disease severity and a higher frequency of comorbidities, including COPD and cardiovascular disease, than other participants. Participants who were judged to not require airway clearance management by their clinician had slightly milder disease than the other groups. However, 58.3% of the patients in this group reported daily sputum production, 11.4% were receiving long-term macrolide treatment and 3.2% were receiving inhaled antibiotics.

Airway clearance management showed marked geographic variability

The most frequently used ACTs were ACBT (n=4751, 28.4%), regular exercise (n=1550, 9.3%), postural drainage (n=1332, 8.0%), autogenic drainage (n=1081, 6.5%) and assisted cough (n=577, 3.5%). Patients were able to report using more than one method of airway clearance management. There was marked geographical variability in the use of specific techniques as shown in figure 2 and in supplementary table S4.

The highest use of airway clearance management was in Ukraine (92.0%), Denmark (91.7%), Finland (89.6%) and Sweden (72.0%). The lowest use of airway clearance management was in Central and Eastern European countries, particularly in Bulgaria (2.9%), Romania (3.1%), Moldova (6.7%), Switzerland (11.8%) and Turkey (14.9%).

Remarkable differences were also observed in the use of specific ACTs. The highest use of ACBT was reported in Ukraine, UK, Sweden, Slovenia, Ireland and Portugal. In contrast, ACBT was used by only 8.1% of the participants in Italy and 8.0% of the participants in Israel; these countries had relatively high use of airway clearance management but a preference for other techniques. Autogenic drainage was particularly favoured in Belgium and Israel, and postural drainage was most popular in Ukraine, Poland, Portugal, Ireland and France. Percussion and manual vibrations were infrequently used. Participants in Finland were largely using exercise for airway clearance. ELTGOL was almost exclusively used in Belgium, Spain, Italy and France (figure 2).

Airway clearance devices and mucoactive drugs

Among those receiving airway clearance management, airway clearance devices were used by 2748 participants (16.4%). Similar to ACTs, there was substantial variation between countries as shown in figure 3. Denmark, Finland and Sweden showed the highest use of airway clearance devices, followed by Israel, Italy and Germany. Full details are shown in supplementary table S5.

Mucoactive drugs were used by 4680 participants (28.0%). The most commonly used were carbocisteine/n-acetylcysteine, which were used by 2907 participants (17.4%), and hypertonic saline, which was used by 1454 participants (8.7%). Other mucoactive drugs were less commonly used. Figure 4 shows the geographical variation in the use of mucoactive drugs, illustrating that Austria, Germany, Ireland, Israel,

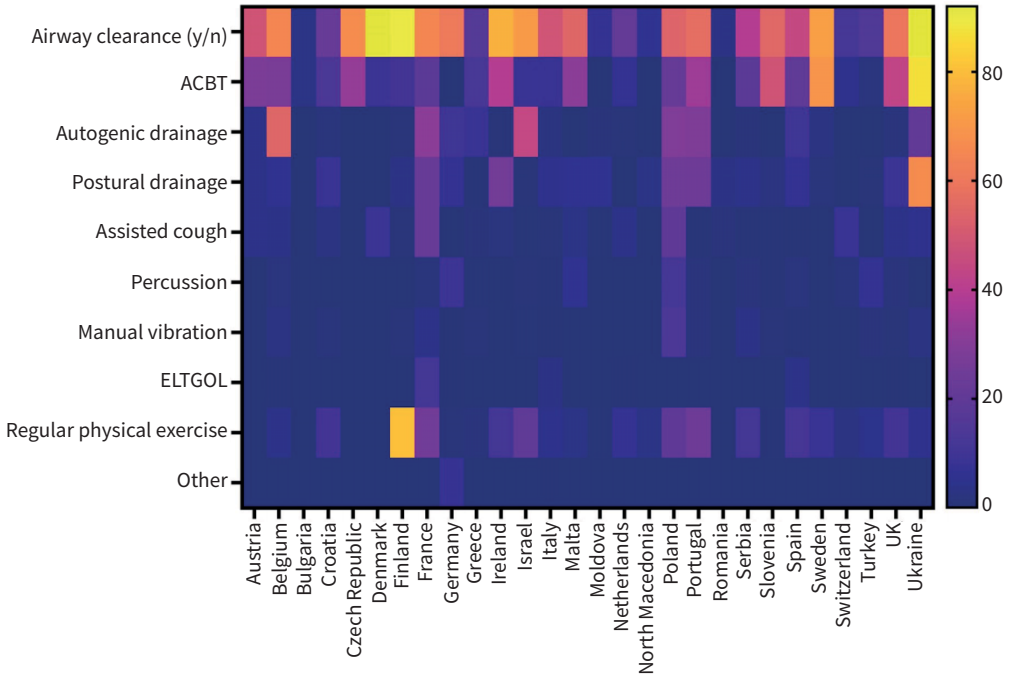

FIGURE 2 Heatmap illustrating differences in airway clearance techniques (ACTs) between different countries. Heat colour represents the percentage of patients who reported using each ACT. y/n: yes/no; ACBT: active cycle of breathing technique; ELTGOL: slow expiration with glottis opened in lateral posture.

Portugal and Sweden had among the highest use. Portugal, UK and Ireland had the highest use of cysteine derivatives (carbocisteine/N-acetylcysteine), while hypertonic saline was more commonly used in other countries. Supplementary table S6 shows full details of the differences between countries.

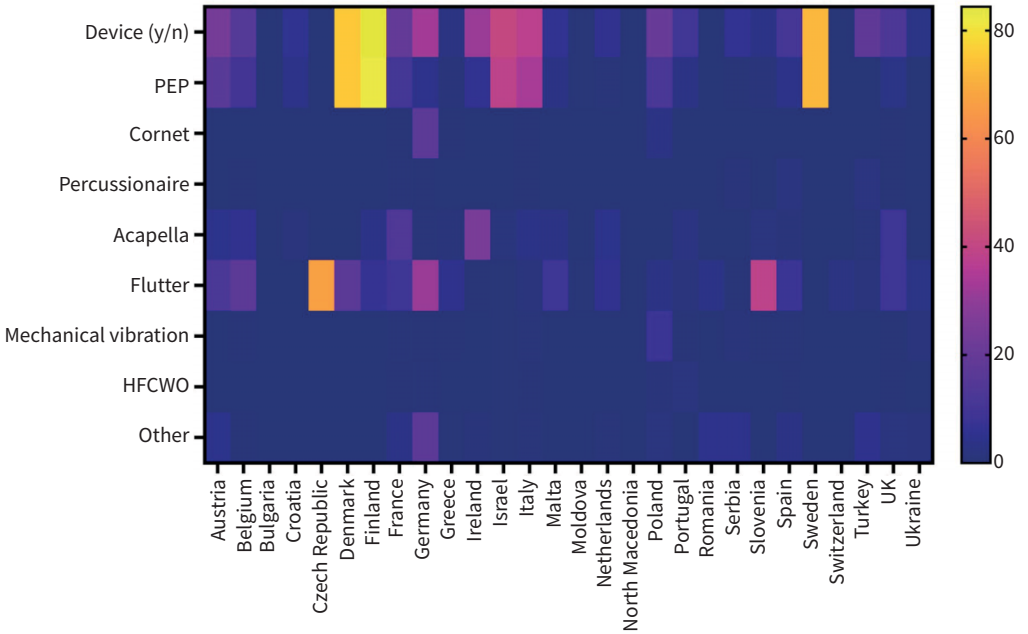

FIGURE 3 Heatmap illustrating the differences in airway clearance device use between different countries. Heat colour represents the percentage of patients who reported using each airway clearance device. y/n: yes/no; PEP: positive expiratory pressure; HFCWO: high-frequency chest wall oscillation.

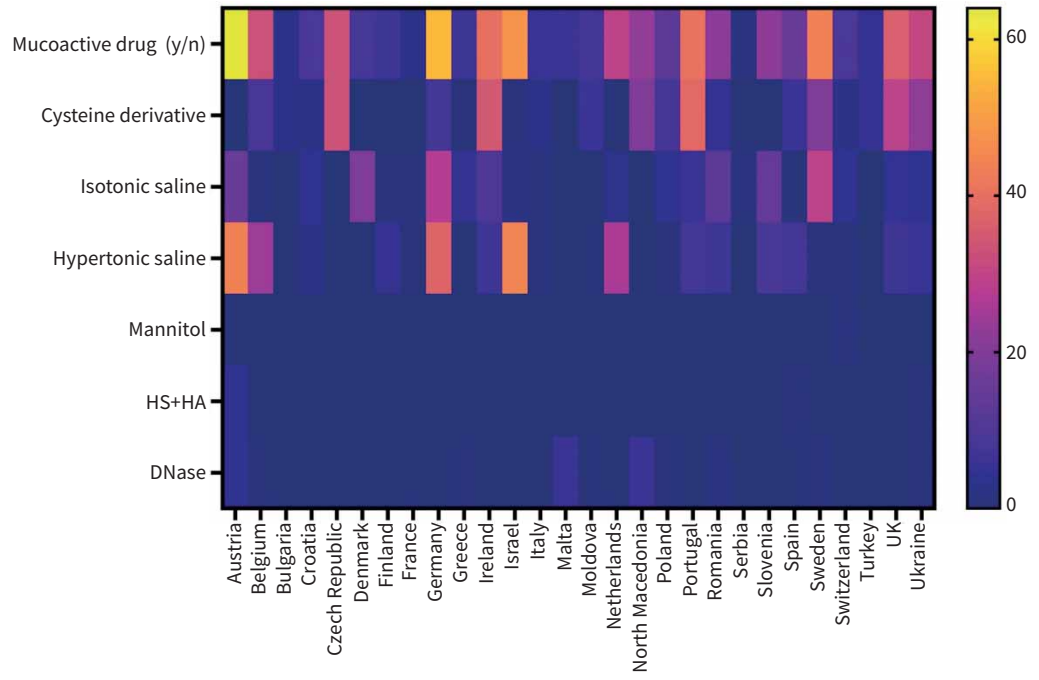

FIGURE 4 Heatmap illustrating differences in mucoactive drug use between different countries. Heat colour represents percentage of patients who reported using each mucoactive drug treatment. y/n: yes/no; HS+HA: hypertonic saline and hyaluronic acid; DNase: deoxyribonuclease.

Combination treatments

Of 8739 participants (52.2%) reporting using regular airway clearance management at baseline, 3285 participants (37.5% of those using any airway clearance management) used a single airway clearance modality, 2956 (33.8%) used two modalities, 1582 (18.1%) used three modalities and 916 (10.5%) used four or more (maximum 12 per person). ACTs were most frequently combined with devices; 1889 participants (21.6%) used one or more ACT with one or more device. 2826 participants (32.3%) used ACT plus one or more mucoactive drug. 786 participants (9.0%) used ACTs, devices and mucoactive drugs. The most common combinations were ACBT plus cysteine derivatives (n=1316, 15.1%), ABCT plus Flutter (n=661, 7.6%), ABT plus Acapella (n=541, 6.2%), ACBT plus hypertonic saline (n=488, 5.6%) and ACBT plus PEP (n=400, 4.6%).

Adjustment for severity and clinical characteristics

The above differences between countries may reflect genuine differences in clinical practice but could also reflect differences in patient characteristics between different countries, such as enrolment of patients with more severe disease, with different aetiologies or with comorbid conditions. To account for this, we performed a logistic regression analysis adjusting for multiple confounders. This confirmed statistically significant differences between countries, using the largest enrolling country (the UK) as a reference (figure 5).

Supplementary tables S7–S9 show the logistic regression models for ACTs, devices and mucoactive drugs, respectively. In addition to the geographical variation, these models show that multiple markers of severity including lung function, radiology, infection with *P. aeruginosa* and use of oral and inhaled antibiotics were associated with airway clearance management, confirming that airway clearance is more frequently used in patients with more severe disease.

Out of 10 817 follow-up visits at 12 months, 2455 participants (22.7%) had seen a specialist respiratory physiotherapist. The countries with the highest proportion of participants seen by respiratory physiotherapy were Belgium (45.7%), Ireland (37.5%), Italy (37.4%) and France (30.2%). The countries with the lowest proportion were Romania (0%), Bulgaria (0%) and Moldova (3.0%). The distribution of countries is shown in figure 6, and overall shows low access to respiratory physiotherapy in Central and Eastern Europe with higher levels of access in Northern and Western Europe as well as Southern Europe.

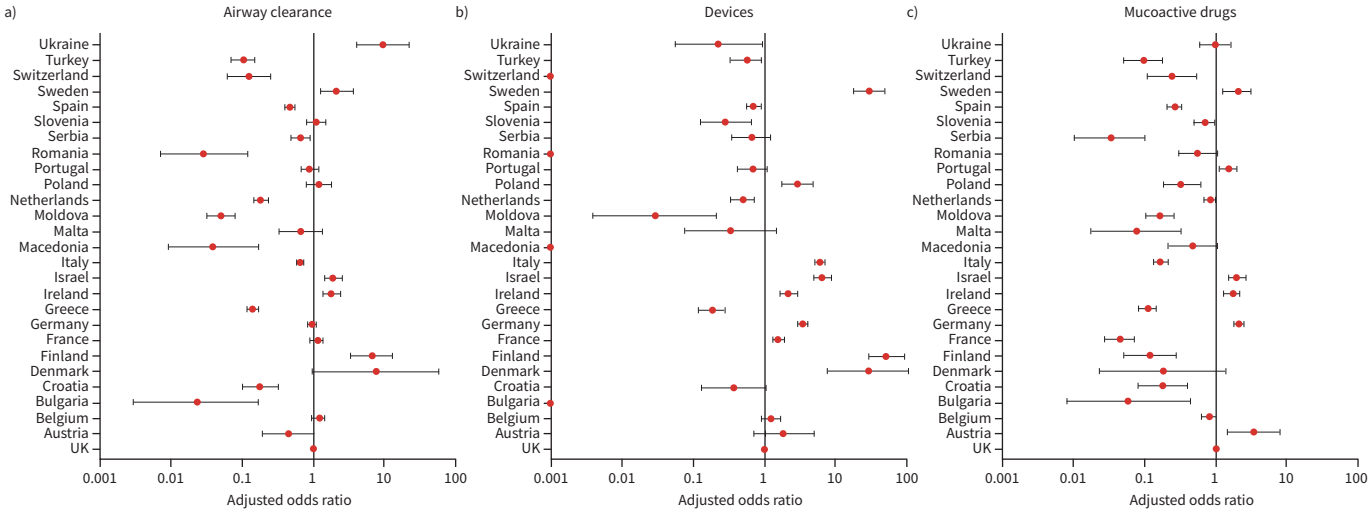

FIGURE 5 Forest plot showing the adjusted odds ratios and 95% confidence intervals for the relationship between country and the use of different airway clearance management modalities. Logistic regression models were adjusted for age, sex, exacerbation frequency, infection status, cardiovascular disease, neoplastic disease, diabetes, forced expiratory volume in 1 s, asthma, COPD, smoking history, aetiology, radiological severity, inhaled antibiotic use, macrolide use and inhaled corticosteroid use.

Discussion

This study represents the largest and most detailed description on the use of airway clearance management in bronchiectasis to date. Using the EMBARC registry, which has prospectively collected data from across European bronchiectasis centres, we show that nearly a half of European people with bronchiectasis do not

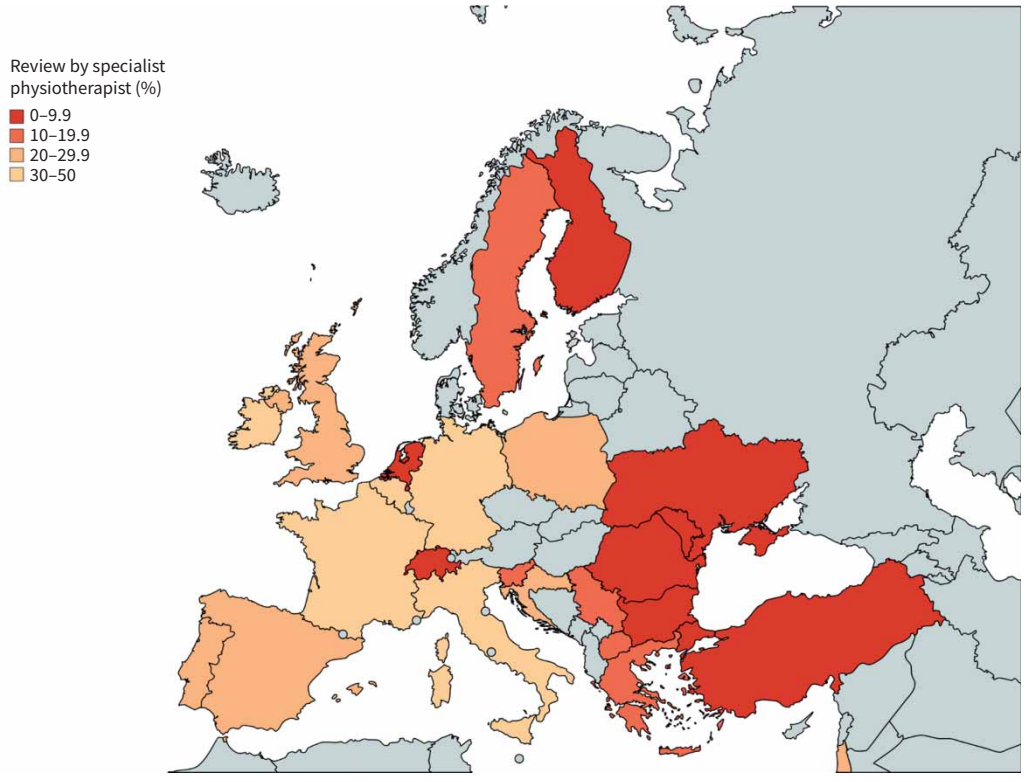

FIGURE 6 Access to specialist respiratory physiotherapy for airway clearance management across Europe. n=10 817 patients with a minimum of 12 months observation included. Created with mapchart.net.

regularly practice airway clearance management. The proportion performing airway clearance was similar when analysis was limited to patients reporting daily sputum expectoration. This is despite recommendations from all the major bronchiectasis guidelines to teach airway clearance management to people with bronchiectasis and for patients to practice these techniques regularly. Although our data show that people with more severe bronchiectasis are more likely to receive airway clearance management, we found that large numbers of people with severe bronchiectasis, including people chronically infected with *P. aeruginosa* and people receiving long-term antibiotic treatments, are not regularly practicing airway clearance management.

Most guidelines recommend that airway clearance is best implemented by specialist respiratory physiotherapy, but we show that after at least 1 year of follow-up less than a quarter of people with bronchiectasis had received training from a respiratory physiotherapist. This suggests widespread lack of implementation of airway clearance management as an intervention for people with bronchiectasis.

There is a lack of high-quality evidence for the benefits of airway clearance management in bronchiectasis but available trial data show substantial benefits. For example, a 12-month trial by Muñoz *et al*. [26] found a significant reduction in exacerbations and there is a marked improvement in quality of life in patients with productive cough when ELTGOL technique is used twice daily [27]. Increased use of airway clearance management, particularly in people with severe bronchiectasis, could potentially reduce the burden of disease seen in Europe [23, 28]. Barriers to implementation of airway clearance management include the lack of access to specialist physiotherapists, lack of access to airway clearance devices and mucoactive drugs, lack of knowledge and experience among healthcare professionals and lack of motivation from patients [29–31]. Nevertheless, the ERS guidelines for bronchiectasis were only able to make a weak recommendation for ACTs in bronchiectasis owing to the low quality of evidence. This low quality of evidence and lack of large-scale randomised trials demonstrating benefit may be one of the key reasons for the inconsistent uptake observed in our study [9, 11].

The large sample size of the EMBARC registry allowed us to explore differences between countries in terms of the use of airway clearance management. We observed marked differences, with higher use of ACTs in Northern European and some Western European countries in particular, and low use in many Eastern European countries. Interestingly, however, even within Western and Southern European countries we observed great differences in the use of interventions such as ACBT, autogenic drainage and the use of airway clearance devices. The scale of these differences suggests that the lack of evidence in this field leads to decisions based on local preference and clinical experience rather than evidence, given that differences between countries persisted even after adjustment for patient characteristics and disease severity. Our data are similar to those reported in a study of 905 patients by Basavaraj *et al.* [32], who found that 59% of US patients used ACTs at baseline. Although it had a small sample size, the US study found that 44% of patients used PEP devices and 10% used HFCWO at baseline, in contrast to our European data where only 16% used devices and HFCWO was not used in most European countries, and the country with the highest use only had a frequency of 1.9%. These data emphasise global variation in practice, likely reflecting differences in reimbursement practices as well as lack of availability of specialist chest physiotherapists in many countries [24, 32]. It should be noted that, while we had a large sample size overall, the numbers in individual countries varied. Some estimates for countries where low number of patients were enrolled may not be fully representative.

Our data should serve as a call to action on two fronts: first, to improve the global uptake of airway clearance management in bronchiectasis, with the goal of reducing exacerbations, potentially avoidable antibiotic exposures and improving symptom burden and quality of life; and second, to generate additional evidence to determine which ACTs and devices are most effective for specific patient groups and to strengthen the guidelines on which healthcare professionals and healthcare commissioners rely [11, 33]. Airway clearance management in bronchiectasis has been described as a neglected aspect of a neglected disease and our data support calls for further research [11]. The lack of evidence in this field extends to mucoactive drug treatments, such as hypertonic saline, for which large-scale trials are also lacking.

Limitations of our analysis should be acknowledged. We prespecified several ACTs and devices, which may bias responses towards these. Participation in the registry is voluntary and so the patients enrolled may not be representative of the countries described here. No data were collected in the registry on the dose or frequency of airway clearance management and associated treatments. We also did not collect data on the professionals who taught airway clearance to patients and their professional background and experience. Terminology in airway clearance management across Europe is not standardised and this may confound data on the use of specific techniques. We are unable to capture data regarding patient adherence in the

registry. Most importantly, the poor evidence base for ACT in bronchiectasis means that while our data show a generally low uptake of ACT compared to guideline recommendations, it is not possible to definitively state which patient subgroups would benefit most from manual ACT, devices or mucoactive treatments. In some cases, ACT may provide little benefit, while in others it may be highly beneficial. Bronchiectasis is a heterogeneous disease and mucus properties are highly heterogeneous between individuals. It is important that future studies generate a more robust evidence base for ACT in addition to identifying appropriate precision medicine approaches [3, 24, 33–35].

In summary, our data show that airway clearance management is underused in people with bronchiectasis in Europe. It is also reserved for patients with severe disease, suggesting a reactive rather than proactive approach to preventing disease progression. The choice of ACT, airway clearance device and mucoactive drug is determined primarily through local practice rather than evidence. Thus, efforts to increase the use and standardisation of airway clearance management in Europe are needed.

Ethics statement: The study was approved by the ethics committee in the host country (UK) and by institutional review boards or ethics committees in all countries and regions in which the study was conducted.

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