

CONTENT VALIDATION OF THE RESPIRATORY SYMPTOMS SUBSCALE (RSS) OF THE QUALITY OF LIFE QUESTIONNAIRE-BRONCHIECTASIS (QoL-B) IN NON-CYSTIC FIBROSIS BRONCHIECTASIS (NON-CF BE)



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BACKGROUND

- Non-cystic fibrosis bronchiectasis (non-CF BE) is a chronic, progressive respiratory disorder characterised by persistent cough, excessive sputum production, and frequent chest infections^(1,2)
- Evidence suggests that high symptom burden reduces quality of life in patients with non-CF BE^(3,4)
- The Quality of Life-Bronchiectasis (QoL-B) is the first disease-specific patient-reported outcome measure, validated to assess health related quality of life in bronchiectasis. It has 37 items across eight sub-scales: Respiratory Symptoms, Physical, Role, Emotional Functioning, Social Functioning, Vitality, Health Perceptions, and Treatment Burden^(5,6)

OBJECTIVE

- To evaluate whether the content of QoL-B Respiratory Symptoms Subscale (RSS) (items 29-37) relates to the symptom experience of patients included in a dose-finding study for tobramycin inhalation powder in non-CF BE, iBEST-1 (NCT02712983)

METHODS

- iBEST-1 was a randomised, blinded, parallel group, multi-centre dose-finding study, to assess the efficacy, safety, and tolerability of different doses of tobramycin inhalation powder in patients with non-CF BE and pulmonary *P. aeruginosa* infection⁷
- Patients ≥18 years old with clinical diagnosis of non-CF BE confirmed radiologically by computerized tomography scan, a history of exacerbations requiring systemic antibiotic administration and who had one positive culture for *P. aeruginosa* in sputum in the last 12 months and a *P. aeruginosa*-positive culture at screening were included in the study⁷
- To evaluate the content validity of the QoL-B RSS in the context of the iBEST-1 trial, exit interviews were conducted with a subset of patients completing the study in the United Kingdom

Interview procedure

- To participate in the telephone exit interviews, patients were required to have completed the final study visit in the iBEST-1 trial, have sufficient level of hearing and spoken English-language ability, and were able to read a paper questionnaire. Patients also had to agree in the informed consent form
- Qualitative, semi-structured telephone interviews (up to 1 hour in length) were conducted with a subsample of patients who satisfied the above criteria at four clinical trial sites in the United Kingdom
- Patients were asked to describe the disease symptoms they experienced, and their feedback was collected on understandability, meaning, relevance of the items and response options contained within QoL-B RSS. Interviews were audio-recorded and transcripts were produced

RESULTS

- Out of the 18 patients who consented to participate in the exit interviews, five were screen failures and thus were not randomized, four were randomized but withdrew from the trial prematurely, and two completed the trial but withdrew their consent to take part in the exit interview. Hence, this study included seven exit interviews that were conducted between September 2017 and May 2018
- Patients reported having bronchiectasis for 4 to 60 years (mean, 36.3 years). The baseline characteristics of the sample are presented in **Table 1**

Table 1. Exit Interview Sample Characteristics

Baseline Characteristics	Exit Interview Sample (N = 7)
Age, years: Mean (SD), Range	62.1 (13.1), 40–72
Sex, n (%): Male, Female	3 (42.9), 4 (57.1)
Race, n (%):Caucasian, Asian	6 (85.7), 1 (14.3)
Body mass index, kg/m²: Mean (SD), Range	25.8 (4.9), 19.7–32.3
FEV ₁ , % predicted: Mean (SD), Range	66.0 (24.9), 27.6–99.5
Bronchiectasis Severity Index score: Mean (SD), Range	9.6 (3.6), 4.0–14.0
QoL-B RSS score: Mean (SD), Range	58.2 (12.0), 40.7–77.8

FEV₁ = forced expiratory volume in 1 second; QoL-B = Quality of Life Questionnaire–Bronchiectasis; RSS = Respiratory Symptoms Subscale; SD = standard deviation

Symptoms experienced

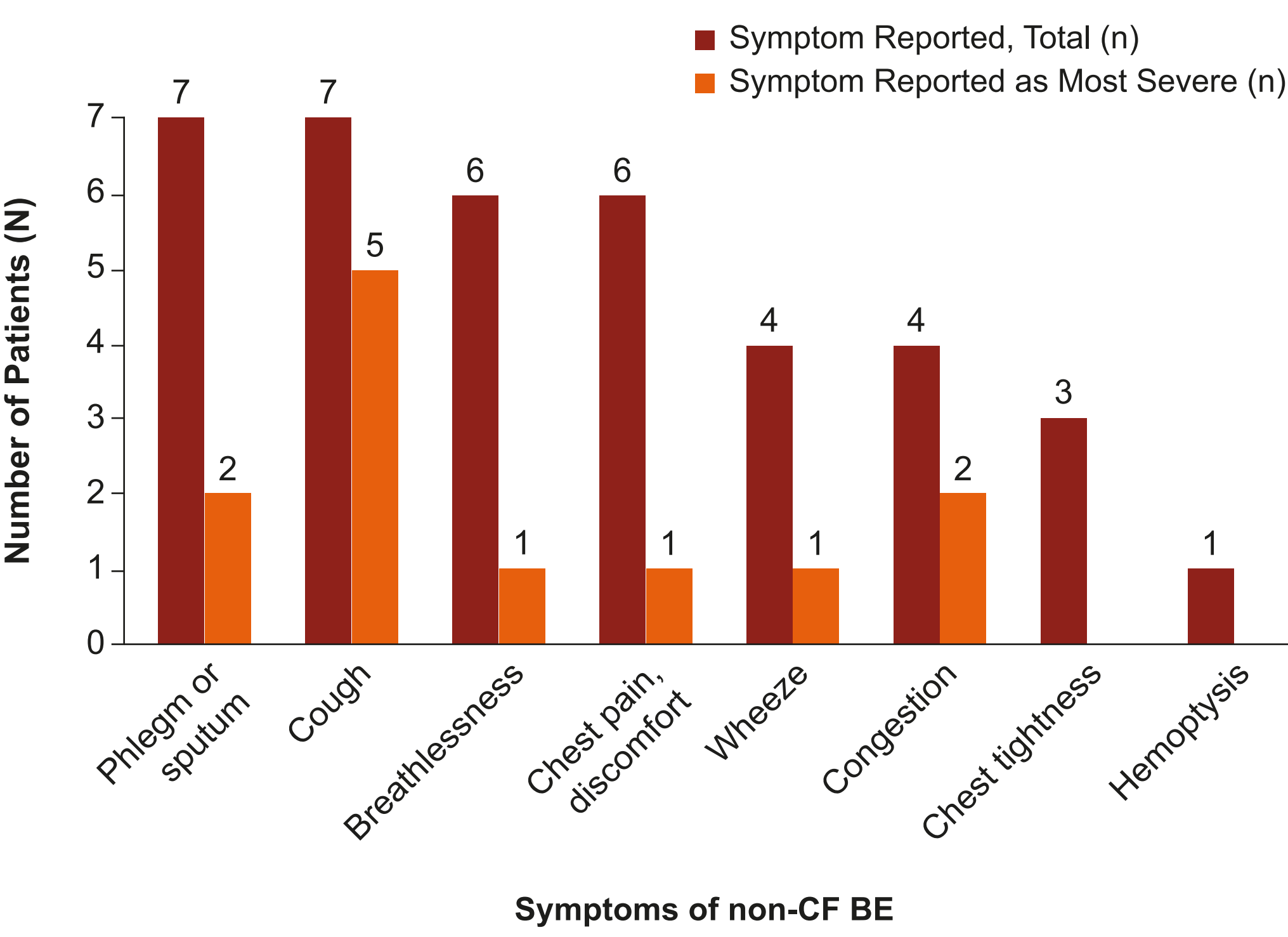
- Figure 1** presents all the respiratory symptoms experienced by the patients in the exit interviews, along with their verbatims

Figure 1. Patient verbatims describing their symptoms

Phlegm/sputum – “I suppose on a day-to-day basis, I cough up sputum. It varies, it depends on whether I’m unwell or not, but I cough every day”
Cough – “It sometimes wakes me up at night coughing, and until I move what’s making me cough, I can’t get to sleep again”
Breathlessness – “Yes, it makes me get out of breath when I’m coughing”
Chest pain/discomfort – “I do get pains in my like lower rib cage. But then that usually signifies an infection...So that’s not every day or every month, it’s just literally when I’m brewing something... It is a sharp pain, so on the intake of breath”
Wheeze – “So it’s [the wheeze and the cough] there constantly. And I think acting a certain way. When I sit next to someone, they’re like, “Oh my God, are you okay you’re breathing really heavily”
Congestion – “...my lungs get congested, so I have to produce, cough up sputum on a regular basis during the course of the day”
Chest tightness – “I guess I wouldn’t call it congestion, I think it was congestion of not being able to cough up properly, like things being stuck, which I wouldn’t say I feel like. I feel a tightness more than any congestion. I would experience a tightness only if I was getting an infection but not on a normal basis.”
Hemoptysis – “Hemoptysis, so I do cough up blood as well”

- The most frequently reported symptoms were excess phlegm and cough, followed by breathlessness, chest pain or discomfort, congestion, and wheeze (**Figure 2**). Cough was reported as the most severe symptom, followed by excess phlegm and congestion.

Figure 2. Frequency and severity of symptoms as reported by the patients



Feedback on understandability of items of the QOL-B RSS

- Overall, the items were easily and consistently understood and were considered self-explanatory by the patients. The patients interpreted all items as intended (**Figure 3**)
- Of the nine items in the RSS, most issues were identified with the congestion item. While some patients made a clear distinction between congestion and chest tightness, others conflated the two concepts

Figure 3. Patient verbatims reflecting their understandability of QoL- RSS items

Item 29 >>	Chest congestion –“Congestion/fullness is inability to breathe normally without any sort of wheezing and, um, just basically difficulty in getting your lungs to work”
Item 30 >>	Coughing during the day – “I thought it was perfectly clear. Have you been coughing”
Item 31 >>	Cough up sputum – “Whether I do have sputum to cough up...It is just asking me literally whether I actually get rid of it or not”
Item 32 >>	Color of sputum – “I presume going through the range of colors and consistency of it presumably will be marking the severity of the infection that you’ve got”
Item 33 >>	Shortness of breath on activity –“It’s, have I experienced shortness of breath when I’m doing day-to-day activities”
Item 34 >>	Wheezing – “It’s whether in your daily life you’re making that noise of where you can hear air moving in and out of your lungs. It’s like a crackling noise...”
Item 35 >>	Chest pain – “Whether I have pains in my chest area”
Item 36 >>	Shortness of breath on talking – “So if I’ve struggled to talk and breathe at the same time basically”
Item 37 >>	Woken up during night due to coughing – “Whether I have a disturbed night’s sleep because of my bronchiectasis”

Feedback on relevance of items of the QOL-B RSS

- Overall, patients generally found the items of the RSS to be highly relevant to their experiences of non-CF BE. Even when patients did not experience a specific symptom, they generally understood it to be relevant to other people with the condition

Item 32 (Color of sputum)

- This item was considered quite relevant and important to patients
- While only four patients reported that they experienced the full spectrum all colors of sputum listed in the response options, all patients understood the meaning and significance of the different colors
- Three patients reported experiencing a color not listed in the response options; but only one of these patients expressed any uncertainty in responding to the question
- Patients were able to relate the changes in sputum color to changes in symptoms, with darker colors corresponding to a deterioration in other symptoms as indicated below:
“Invariably, there’s always another symptom that comes with it. If it goes to dark green, you invariably find that your cough is worse or there’s something else with your chest and you just don’t feel right.”

Feedback on relevance of response options

- Overall, the response scales were considered distinct, appropriate, easy to use, and allowed the patients to indicate the full range of severity or frequency levels of the changes experienced (**Figure 4**)

Change in symptoms and meaningful change

- Six patients confirmed that their respiratory symptoms had changed over the course of the trial; only one patient reported that the symptoms had not changed in any way. Patients reported that any change would be positive and noticeable but for a change on the RSS to be considered as meaningful, an improvement of at least 1-point would need to occur in several respiratory symptoms

Figure 4. Patient verbatims indicating relevance of response options used for the QoL-B RSS items

QOL-B Section II. Respiratory Symptoms					
Indicate how have you been feeling during the <u>past week</u> :					
Item	A A lot moderate A little Not amount at all				Verbatims
29. Have you felt congestion (fullness) in your chest?	●	●	●	●	“...I guess if I am producing sputum in a pot, which I tend to do on a daily basis so I can check it, and it is the amount that I would put in that pot during the course of a day [that] would determine if I put a moderate amount or a little amount. And if it was about half full, I would say moderate; if it was a quarter full, I'd say a little. If it was full up, I'd say a lot.”
30. Have you been coughing during the day?	●	●	●	●	
31. Have you had to cough up sputum?	●	●	●	●	
32. Has your sputum been mostly:	Clear Clear to yellow Yellowish-green Brownish-dark Green with traces of blood Don't know				“I presume going through the range of colors and consistency of it presumably will be marking the severity of the infection that you've got” “It can be clear to yellow when I'm well. And it can go also to yellowish-green. It can vary between...Those two can apply to me at any time. Gets green with infection” “Clear is excellent, brownish-dark would be the most severe; green with traces of blood suggests that coughed so much that you've broken an artery or a vein in your throat”
How often during the <u>past week</u> :					
Item	Always	Often	Sometimes	Never	Verbatims
33. Have you had shortness of breath when being more active, such as when doing housework or gardening?	●	●	●	●	“you've got a clear difference in between them, haven't you” “It gives you enough to be getting on with. The more options you get, the harder it is to answer because you're sort of looking at things and you're just trying to work out which category you're actually going to fall into. But these are distinct enough that you can basically sort of, you know, choose one out of four. That's not too bad at all.”
34. Have you had wheezing?	●	●	●	●	
35. Have you had chest pain?	●	●	●	●	
36. Have you had shortness of breath when talking?	●	●	●	●	
37. Have you woken up during the night because you were coughing?	●	●	●	●	

Source: Adapted from Quittner et al 2015⁵

Missing items

- Six patients were asked whether any symptoms were missing from the RSS. Four patients indicated that there was nothing missing from the subscale, one patient highlighted chest tightness as a key symptom that was missing, and another patient highlighted sore throat, nasal mucous, eye symptoms, and headaches as missing items

CONCLUSIONS

- This qualitative study suggests that the QoL-B RSS was well accepted, easily comprehended, and was considered highly relevant to patients’ experiences of non-CF BE. Patients also found the response scales for the items in the RSS appropriate, distinct, and capable of describing their symptoms at their least and most severe
- Although based on only seven interviews, these results provide support for the content validity of the QoL-B RSS, including the importance and relevance of the item assessing sputum color.
- Confirmation of these initial findings through additional interviews would help support the robustness of the evidence

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