COPD-Lower Respiratory Tract Infection Visual Analogue Score (cLRTI-VAS) validation in stable and exacerbated patients with COPD

Introduction:

- Chronic obstructive pulmonary disease (COPD) is the fourth-leading cause of mortality worldwide and an important cause of morbidity. 1 COPD is a common preventable and treatable disease that is characterised by persistent respiratory symptoms and airflow limitation and chronic low-grade local and systemic inflammation .
- Clinical measures such as forced expiratory volume 1 s (FEV1) or oxygen saturation correlate only moderately with functional capacity of patients with COPD.
- The main determinants of a patient's healthrelated quality of life (HRQL) appear to be the degree of dyspnoea, fatigue, muscle wasting, sleep and mood disturbances.
- Measurement of these symptoms and signs is very useful in monitoring patients with COPD. It is a strong predictor of future disease outcome and potentially modifies treatment management

- Time consuming, and less suitable fobedside usage.

- An alternative for this problem would be a Visual Analogue Score (VAS). VAS has been used in many settings
- VAS is known to be used at the bedside.11 Additionally, VAS can also be used for the quantification of respiratory symptoms such as dyspnea, cough and sputum volume in COPD
- To date, no questionnaire measuring symptoms has been properly validated in acute exacerbations of COPD (AECOPD). The incentive for the development of a practical health status instrument, the COPD-Lower Respiratory Tract Infection-VAS (c-LRTI-VAS) arose from routine clinical management of COPD. In daily practice, clinicians require a simple questionnaire designed to provide practitioners with standardised, reliable and valid information for assessing symptoms in AECOPD.

- The LRTI-VAS was used before to quantify symptoms in AECOPD but was not validated before.
- However, it was recently validated in non-CF bronchiectasis and since then adopted by the European Bronchiectasis Registry. On all occasions, the LRTI-VAS was generally well accepted by patients, and showed a high response rate. The aim of this study was to validate the c-LRTI-VAS for assessment of symptoms in patients with COPD in stable condition and during an AECOPD.

MATERIAL AND METHODS:

Study population:

From November 2011 to November 2014, clinically stable patients with COPD visiting the outpatient clinic of the Department of Pulmonary Medicine of the Medical Centre Alkmaar, a large teaching hospital, were asked to participate by the primary investigator. A stable situation was defined as not having had an AECOPD defined by Global Initiative for Chronic Obstructive Lung Disease (GOLD) <1month before study entry, no recent change in COPD associated medication <1month before study entry. Also, immunocompromised patients or patients with respiratory disease other than COPD were excluded from participation.

Data from patients with an AECOPD were available from a randomised clinical trial performed between July 2011 and February 2015. The study population consisted of patients diagnosed with COPD stages I–IV as defined by the GOLD, and a minimum smoking history of 10 pack years.1 All patients provided written informed consent in both patients groups. All patients provided their written informed consent.

- Development of the c-LRTI-VAS:
- The initial specifications for the c-LRTI-VAS identified that the questionnaire should only contain the symptoms that physicians consider to be the most important for estimating the clinical status of the airways. Therefore, item generation was performed based on Anthonisen criteria with the addition of the symptom: Fatigue was added as being one of the most prominent symptoms in COPD.
- A VAS scale was chosen to meet the specification of simplicity. The c-LRTI-VAS is short (four items) and easy to complete . It takes patients approximately 1min to complete the questionnaire, and assistance is generally not required. Patients were instructed

COPD-Lower Respiratory Tract Infection Visual Analogue Score (c-LRTI-VAS)

Name/ date of birth:

THIS QUESTIONNAIRE DEALS WITH THE COMPLAINTS YOU EXPERIENCED DURING THE LAST DAYS. PLEASE PUT A CROSS AT THE FOLLOWING LINES.

1. Shortness of breath

2. TIREDNESS

3. COUGH

4. COLOUR OF SPUTUM?

Figure 1 c-LRTI-VAS.

- Patients were instructed to recall their experiences during the last day. They respond to each question using a VAS scale. The scale ranges from 1 to 10, the subjects being unaware of the numbers. Higher scores indicate more severe symptoms. Four symptom domains are scored: shortness of breath, tiredness, cough and sputum colour. Separate scores are calculated for each symptom and a total score is provided, consisting of the addition of all symptom scores.

Other questionnaires

- Clinical COPD Questionnaire (CCQ) is defined as a disease-specific questionnaire that consists of 10 items. The items are divided into three different domains (functional state, symptoms and mental state) which can be scored separately. Added together they provide a total score, representing the impairment of quality of life. The CCQ requires about 4min to complete
- St George Respiratory Questionnaire (SGRQ) is defined as a condition specific HRQL measure that consists of 76 items. These items are partitioned into three sections (symptoms, activity, impact), which are scored separately and can be added together to provide a total score, ranging from 0% to 100%. Zero indicates no impairment of quality of life. The SGRQ requires about 10min to complete

Study visits:

- All participants with stable COPD visited our outpatient clinic on two separate occasions 30 days apart. On both occasions, participants were asked to complete the LRTI-VAS, the CCQ and SGRQ. In addition, spirometry was measured. In case of participants with AECOPD, the first study visit was scheduled within 24 hours after the admission for AECOPD and 30 days after patients visited our outpatient clinic. On both occasions, patients were asked to complete the c-LRTI-VAS, CCQ and SGRQ. In addition, arterial oxygen saturation was measured using a fingertip pulse oximeter (Beurer Y23/003700, Ulm, Germany)

Sputum colour analysis:

- Sputum samples were collected on the first day after admission and 1month after admission. At the laboratory for microbiology, sputum colour was assessed with a previously validated five-point sputum colour chart
- This data were used to assess the correlation between reported sputum colour compared with objectified sputum colour.

Validity of the c-LRTI-VAS

Patients with clinical stable COPD and patients with an AECOPD completed the c-LRTI-VAS, the CCQ and the SGRQ on two separate occasions. In addition, in patients with stable COPD spirometry was performed as well as pulse oxygen saturation measurement on both occasions. Correlation of c-LRTI-VAS, CCQ and SGRQ, FEV1 , forced vital capacity (FVC) and oxygen saturation was calculated in order to test validity

Patients were excluded if they had an exacerbation, an increase of respiratory symptoms due to heart failure or upper respiratory infection or a change in smoking status. An exacerbation was defined as an acute event characterised by worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and one that leads to a change in medication.

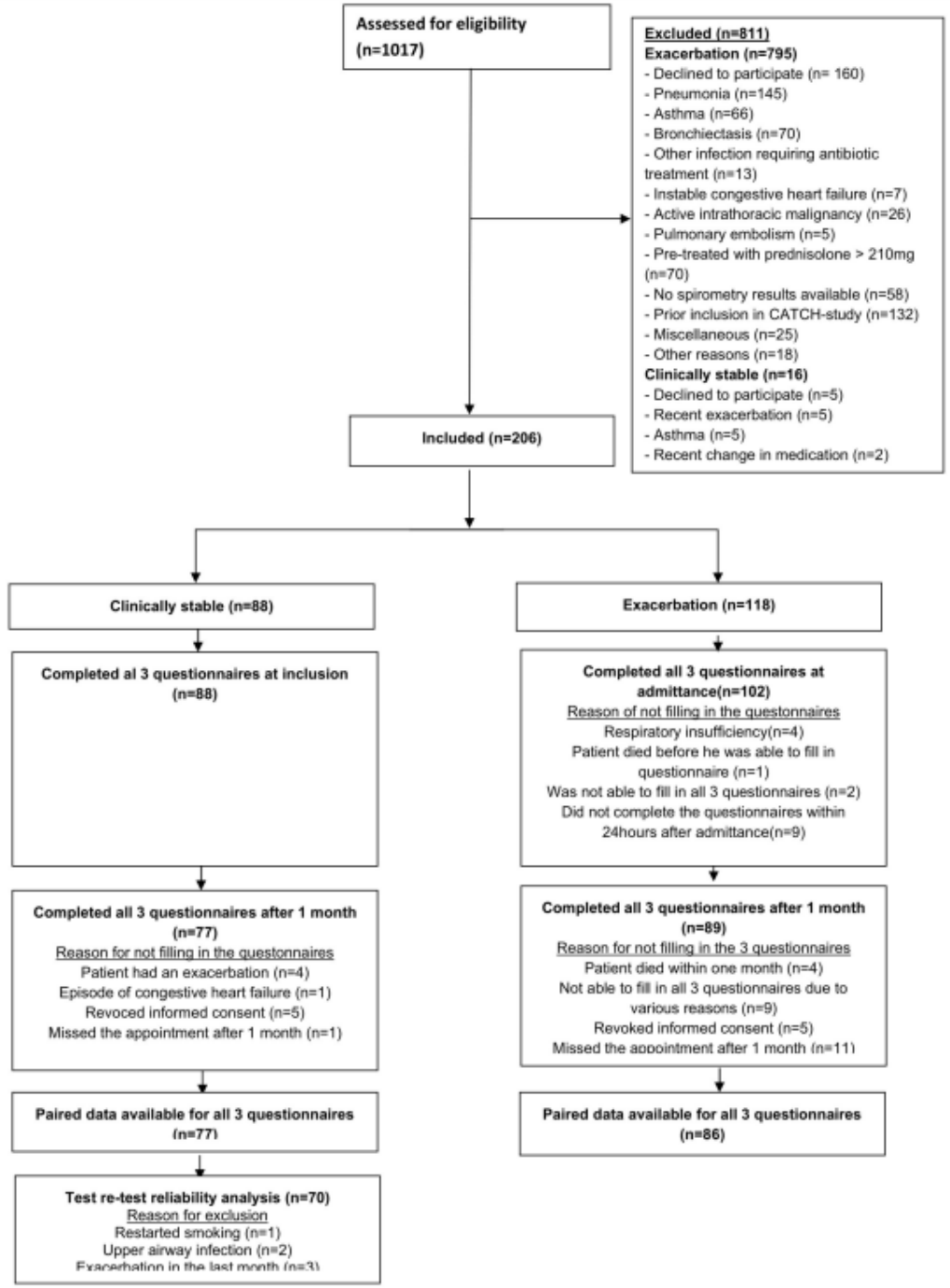

Figure 2 Trial profile.

Table 1 Baseline characteristics

	AECOPD (n=102)	Clinically stable (n=88)
Gender male (%)	44 (43.1)	56 (63.6)
Age, years	68.8 (10.4)	69 (12.5)
Current smoking n (%)	32 (31.4)	20 (23.5)
Pack-years	38.3 (18.4)	37.8 (15.1)
FEV1 % pred	46.8 (16.9)	54.2 (16.6)
FVC % pred	84.1 (21.7)	91.5 (16.5)
FEV1/FVC %	41.1 (12.4)	44.3 (11.6)
GOLD classification		
Stage I n (%)	7 (6.9)	7 (8.0)
Stage II n (%)	35 (34.3)	42 (47.7)
Stage III n (%)	45 (44.1)	37 (42.0)
Stage IV n (%)	15 (14.7)	2 (2.3)
number of exacerbations last year median (IQR)	1 (1–2)	0 (0–1)

RESULTS

Two hundred and six patients were included; 88 of whom were clinically stable and 102 that had an exacerbation (figure 2). Patients characteristics are shown in table 1. Eighty-six patients in the exacerbation group and 77 in the stable group completed all 3 questionnaires on two occasions.

Median c-LRTI-VAS score during stable state was 11 (IQR 7–16) and during AECOPD, the mean was 23.2 (SD 6.2). Median CCQ score during the stable state was 2.25 (IQR 1.50–2.75), and during AECOPD, 3.88 (IQR 3.00–4.50). Mean SGRQ score during stable state was 44.1 (SD 21.2), and during AECOPD it was 63.5 (SD17.1)

Test–retest reliability

- Seventy-seven patients with stable COPD completed all three questionnaires on day 1 and day 30. Six patients

were excluded due to various reasons . Mean difference of the c-LRTI-VAS was 0.143 (SD 5.42) (p=0.826) . The ICC was 0.667 (95%CI 0.733 to 0.892,p<0.001) for the total c-LRTI-VAS score. The ICC of the SGRQ was 0.953 (95%CI 0.924 to 0.970,p<0.001). The ICC of the CCQ was 0.871 (95%CI 0.793 to 0.919,p<0.001).

The relation between c-LRTI-VAS score on T=0and T=30 is shown in the Bland and Altman plots (figure 4). No systematic errors can be seen as the mean difference was 0.143 with an upper limit of agreement of 10.775 and a lower limit of agreement of −10.480.

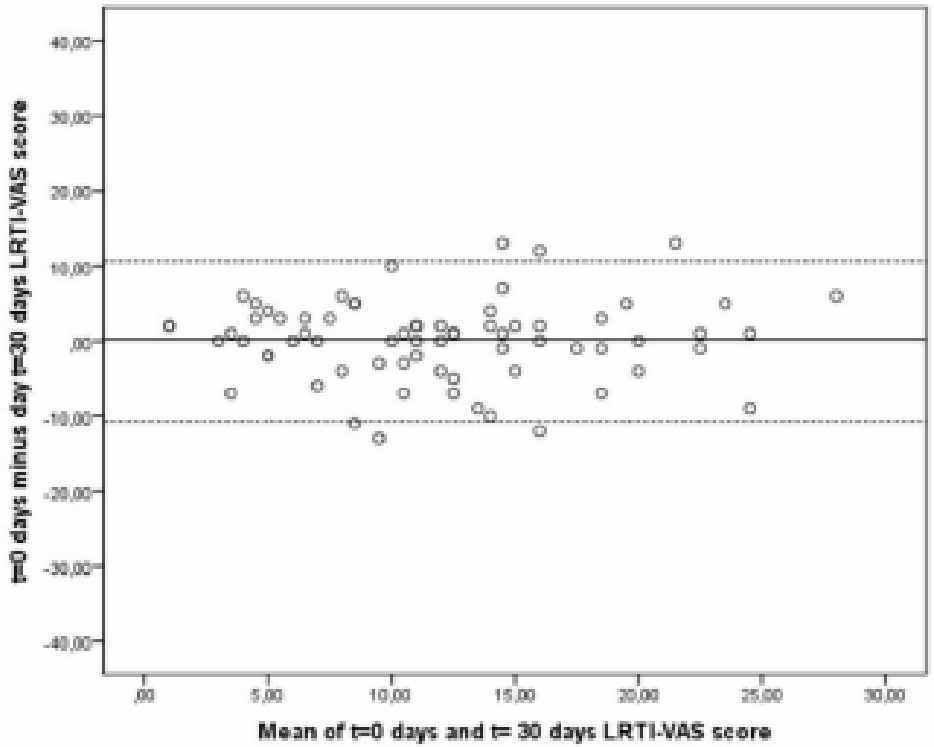

Figure 4 Bland-Altman plot c-LRTI-VAS. COPD-lower respiratory tract infections-Visual Analogue Score.

Internal consistency

- For the validation of internal consistency of the c-LRTI-VAS, both datasets of the AECOPD as well as the stable situation were merged (n=190). alpha for the internal consistency for the 4 domains was 0.755, indicating a good consistency.
- Internal consistency increased when the item sputum purulence was deleted from the questionnaire to 0.803. Cronbach's alpha for the internal consistency during AECOPD (n=102) for the four domains was 0.533. Internal consistency increased further when sputum purulence was deleted to 0.642.
- alpha for the internal consistency during the stable state (n=89) for the four domains was 0.623 Internal consistency increased further when the item sputum purulence was deleted from the questionnaire to 0.676. Internal consistency of SGRQ was 0.818 and of the CCQ 0.783

- Responsiveness Eighty-six patients completed the c-LRTI-VAS, CCQ and SGRQ at admission and 1month later. Mean difference of the c-LRTI-VAS was 8.14 SD 9.13 (95%CI 6.16 to 10.12 p=<0.001). Responsiveness for individual GOLD stages was shown

Table 2 Responsiveness of c-LRTI-VAS according to GOLD stages

	c-LRTI-VAS T=0	c-LRTI-VAS t=30	Difference	P value
GOLD I (n=6)	22.5 (22.0–24.0)	9.5 (2.5–23.0)	–13.0 (-19.5;–1.0)	0.075
GOLD II (n=32)	23.5 (19.5–26.5)	16.0 (5.5–24.5)	–7.5 (-14.0;–2.0)	<0.001
GOLD III (n=35)	24.0 (19.0–27.0)	17.5 (7.0–26.0)	–6.5 (-12.0;–1.0)	0.001
GOLD IV (n=13)	24.0 (21.0–27.5)	16.0 (5.0–27.5)	–8.0 (-16;0.0)	0.013

All data are represented as median (IQR).
c-LRTI-VAS, COPD-lower respiratory tract infections-Visual Analogue Score; GOLD, Global initiative for chronic Obstructive Lung Disease.

Prins HJ, *et al*. *BMJ Open Resp Res* 2021;**8**:e000761. doi:10.1136/bmjresp-2020-000761

DISCUSSION

- This study shows that the c-LRTI-VAS questionnaire is valid, reliable and promises to be responsive to changes in patients with COPD. The VAS instrument has been around for a long time and initially mainly used for the quantification of pain. It has been shown to be reliable and is widely used.
- The VAS in COPD has mainly been used for quantification of dyspnoea, but has also been validated for the quantification of quality of life in COPD.

- Currently many HRQL questionnaires are available such as the SGRQ, CCQ and COPD assessment test. All are comprehensive and do contain a domain of symptoms, but are not exclusively designed for measurements of symptoms.8 9 Although such an instrument was developed in the form of the EXACT-pro, this questionnaire still has the shortcoming that it is less suitable for illiterate or poorly educated patients compared with a VAS instrument

- It was, therefore, thought that there is a need for a less extensive and time consuming questionnaire for patient-reported outcome in clinical settings that solely focusses on the most reported symptoms in COPD and that is suitable for poorly educated or illiterate patients. The items were generated based on the Anthonisen criteria and fatigue as being one of the most prominent features in COPD.

- The strength of our study is that patients with all GOLDclasses were included. An other strength is that the c-LRTI-VAS was validated for patients with stable COPD, as well as with AECOPD.
- Potential weaknesses were the high number of patients that were lost to follow-up. This potentially might have influenced our results. Another potential weakness is the generalisability of our results as this trial was performed in a hospital setting with patient admitted to hospital as well ambulant patients. It remains to be seen whether the LRTI-VAS is a useful tool in general practices.

Conclusion

- The LRTI-VAS showed proper repeatability and responsiveness, moderate to high correlation with other validated questionnaires and a moderate internal consistency that was lowered by sputum purulence. The c-LRTI-VAS, therefore, meets all the criteria to be used in monitoring disease and can be used in clinical practice.