The Content Validity of the St. George's Respiratory Questionnaire – COPD (SGRQ-C) in Patients with Alpha-1 Antitrypsin Deficiency

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Introduction

- Alpha-1 antitrypsin deficiency-associated lung disease (AATD-LD) is a rare genetic cause of chronic airflow limitation due to a severe 'loss of function' deficiency of the alpha-1 antitrypsin (AAT) protein.
  - It is estimated that 1% to 3% of the chronic obstructive pulmonary disease (COPD) population has AATD, though it remains underdiagnosed.[1]
- Dyspnea is a key symptom of AATD and occurs at rest or with exertion and can cause severe activity limitations.
- The St. George's Respiratory Questionnaire for COPD (SGRQ-C)[2] is a well-known and established clinical outcome assessment (COA) for assessing health-related quality of life across a range of chronic respiratory conditions.
- To date, there is limited research on patients' direct experiences of this disease, and no COA measures have been developed or validated specifically for this population.
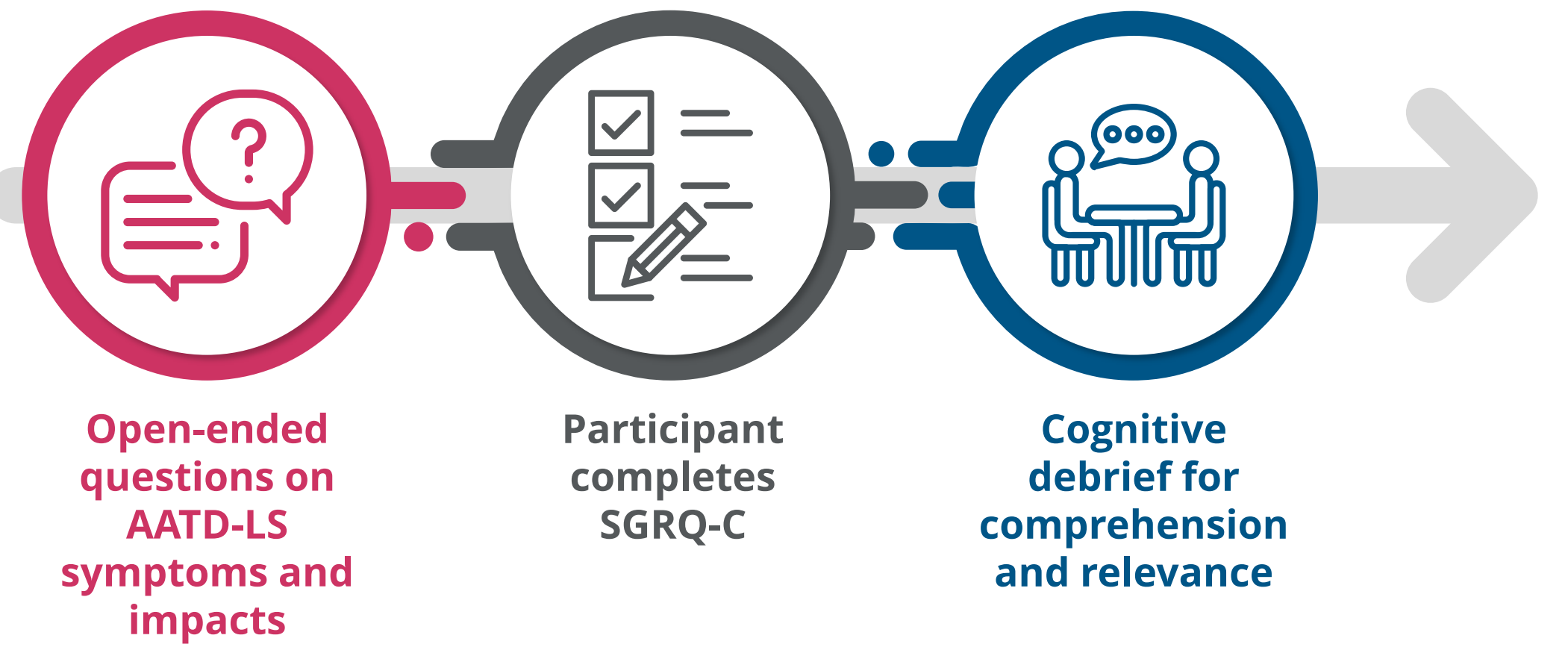
Objectives

- The objectives of this study were to identify important symptoms and impacts that patients with AATD-LD experience and evaluate the content validity of the SGRQ-C.

Methods

Study Design

- This was an observational, cross-sectional, qualitative, hybrid concept elicitation, and cognitive interview study involving one-on-one telephone interviews with adults with AATD-LD in the US (**Figure 1**).
- Three US clinical sites identified study participants through reviews of medical records and clinical databases.
- Adult participants (18 to 80 years old) were eligible for the study if they had a confirmed diagnosis of AATD PiZZ, null, or other rare phenotype/genotype; lung disease related to AATD by CT scan; forced expiratory vital capacity (FEV$_1$) percent predicted ≥30% and ≤80% or FEV$_1$/forced vital capacity (FVC) <0.7; non-smoker for at least 12 months; and on stable COPD medications for at least 6 weeks.

Figure 1. Interview Components (Approximately 90 minutes)

- Open-ended questions on AATD-LS symptoms and impacts
- Participant completes SGRQ-C
- Cognitive debrief for comprehension and relevance

Abbreviations: AATD-LD = alpha-1 antitrypsin deficiency lung disease; SGRQ-C = St George's Respiratory Questionnaire for COPD

Analysis

- Interview transcripts were coded and analyzed using content analysis in ATLAS.ti version 22.0.
- Sociodemographic and clinical characteristics, along with data from the SGRQ-C, were analyzed using descriptive statistics (e.g., mean, SD, and frequency).

Methods (cont.)

Measures

- Participants completed a sociodemographic form.
- Clinical sites completed a brief clinical form on AATD-LD, COPD, and emphysema diagnosis, AATD phenotype/genotype, comorbidities, treatment, and exacerbation history.
- The SGRQ-C was developed as a COPD-specific measure of the original SGRQ. The 40-item measure comprises three domains (Symptom, Activity, and Impact) and a total score. Items use dichotomous response options or a Likert-type scale. Domain and total scores range from 0 (minimal impairment) to 100 (worsening impairment).[2]
- Chronic Airways Assessment Test (CAAT) is an eight-item measure to assess disease severity, using items to evaluate symptoms and function impacts. The total score ranges from 0 to 40, with higher scores indicating worse health status.[3]

Results

Sociodemographic and Clinical Characteristics

- Fifteen participants were recruited (n=8 female), with a mean (SD) age of 62.2 (8.8) years. All were White and non-Hispanic (**Table 1**), consistent with the disease population.
- The average (mean (SD)) duration of AATD-LD diagnosis was 14.9 (11.4) years.
- Two-thirds of participants (67%) were on augmentation therapy, and all participants (100%) were on inhaled medication for COPD.

Table 1. Sociodemographic and Clinical Characteristics

Sociodemographic Characteristics	Total (N=15)
Age, years, Mean (SD), Median [Min–Max]	62.2 (8.8), 66.0 [45.0–72.0]
Sex assigned at birth, n (%)	
Male	7 (46.7%)
Female	8 (53.3%)
Ethnicity, n (%)	
Not Hispanic or Latino	15 (100%)
Racial background, n (%)	
White	15 (100%)
Highest level of education, n (%)	
Secondary/high school	3 (20.0%)
Some college/university	4 (26.7%)
College/university degree (BA, BS)	7 (46.7%)
Postgraduate degree (MA, PhD)	1 (6.7%)
Time Since AATD-LD diagnosis (years)	
Mean (SD)	14.9 (11.4)
Median [Range]	16.8 [2.9–49.2]
Time Since COPD/emphysema diagnosis (years)	
Mean (SD)	10.8 (7.5)
Median [Range]	8.1 [0.9–22.4]
Number of moderate/severe AECOPD episode(s) in past 12 months, n (%)	
None	7 (46.7%)
1	2 (13.3%)
2	4 (26.7%)
> 2	2 (13.3%)

Abbreviations: AATD-LD = alpha-1 antitrypsin deficiency lung disease; AECOPD = acute exacerbation of COPD; COPD = chronic obstructive pulmonary disease

Results (cont.)

CAAT and SGRQ Descriptives

- The mean (SD) CAAT total score was 12.6 (5.8). Almost half the sample (46.7%) were medium severity, followed by low severity (40.0%).
- The mean (SD) SGRQ total score was 41.3 (16.2), with a symptom score of 52.0 (16.9) and an activity score of 58.5 (23.8).

Concept Elicitation

- Participants reported a broad range of symptoms and impacts, with shortness of breath (dyspnea) and cough being the most common (**Figure 2**).
  - All participants (n=15) reported shortness of breath, which was endorsed by most (n=11) as being the most relevant and important symptom.

Figure 2. Most Common Participant-reported AATD-LD Symptoms
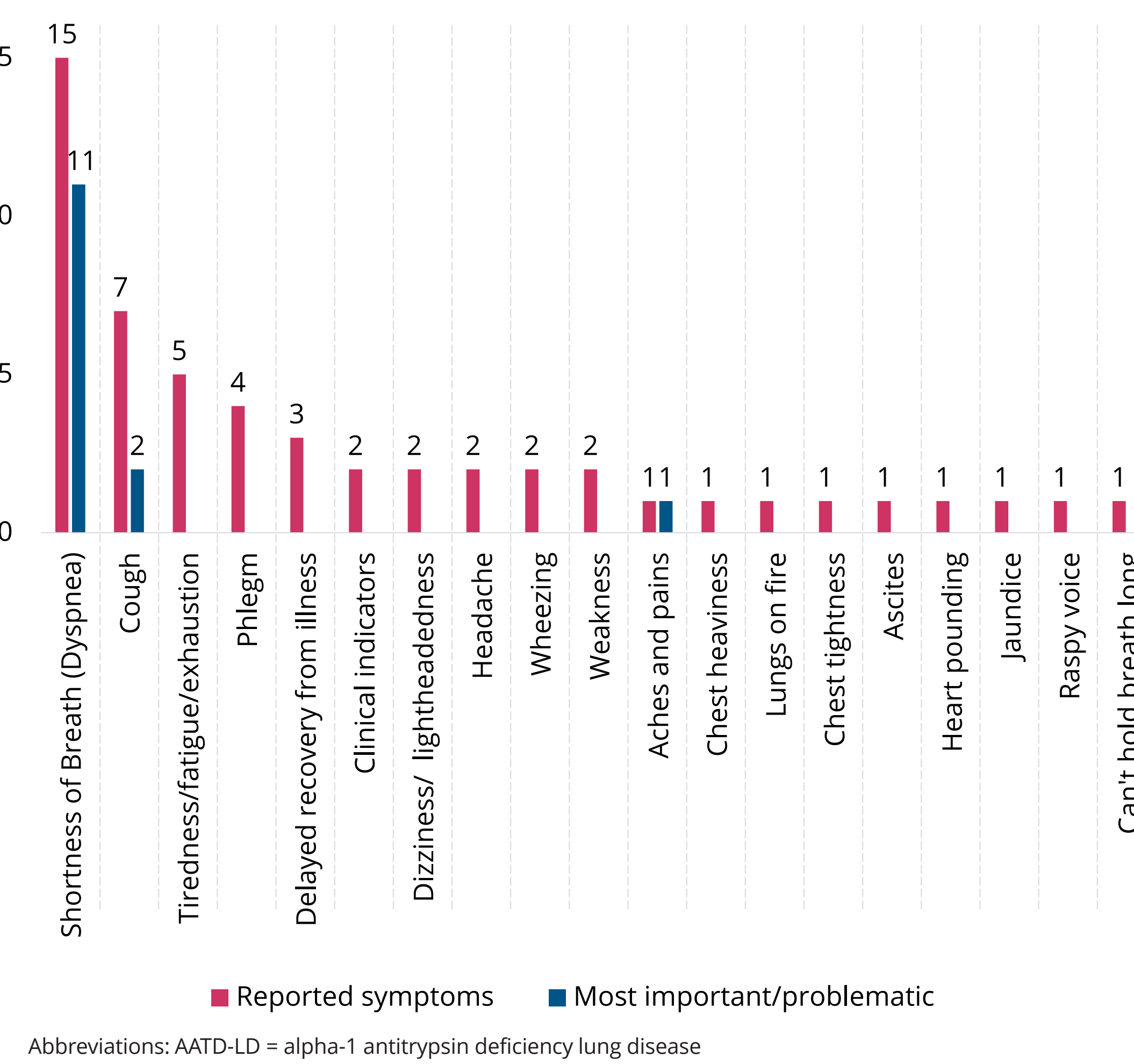
Abbreviations: AATD-LD = alpha-1 antitrypsin deficiency lung disease

- All participants (n=15) reported experiencing some activity limitation due to AATD-LD, with physical activity limitations considered most important by eight participants (**Figure 3**).
  - The participants also mentioned other activity limitations including difficulty with walking, exercise, housework, and daily activities.

Figure 3. Most Common Participant-reported AATD-LD Impacts
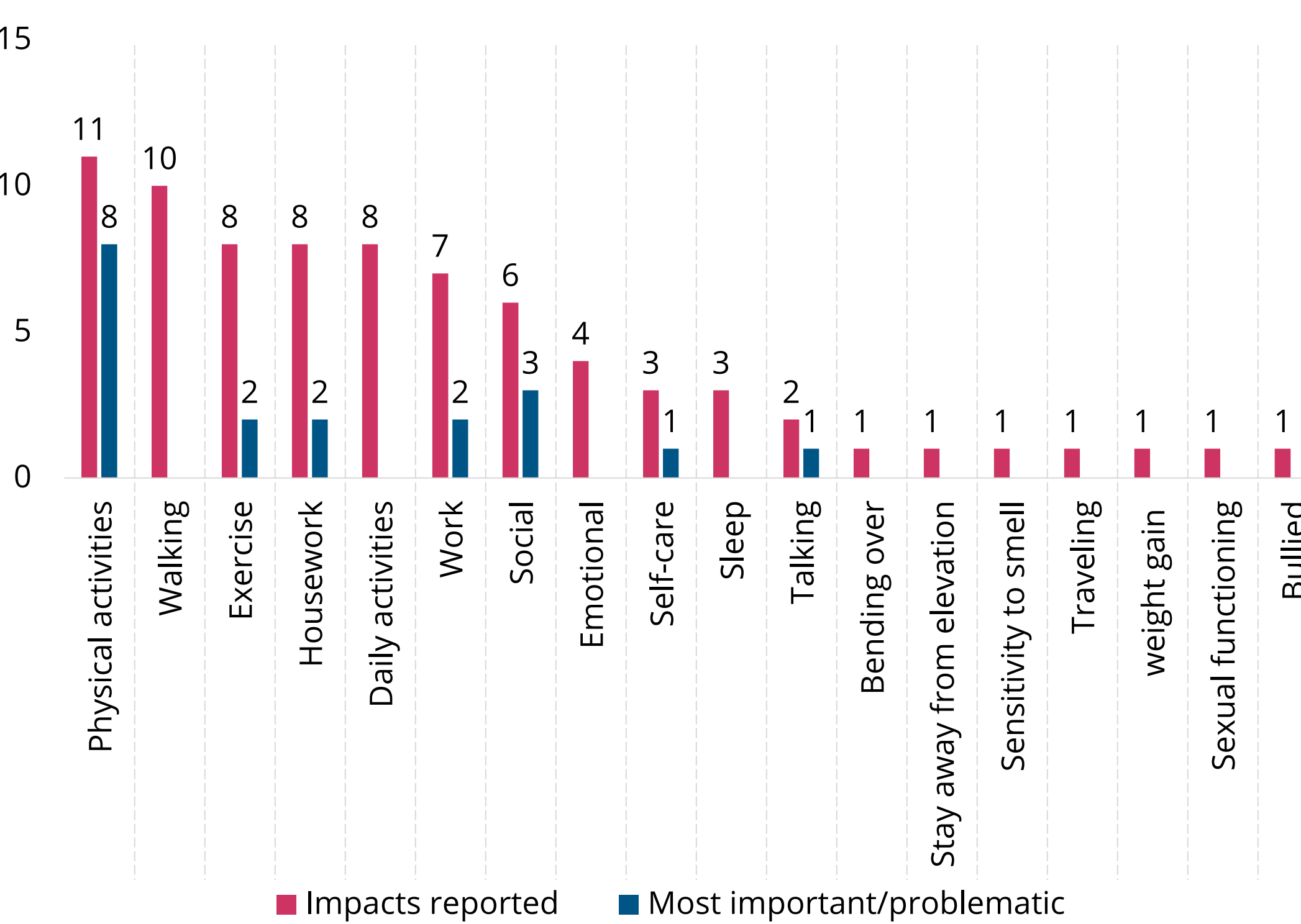
Abbreviations: AATD-LD = alpha-1 antitrypsin deficiency lung disease

Content Validity of the SGRQ-C

- Overall, the SGRQ-C was well-understood by participants with AATD, included all relevant concepts, and the participants were able to respond to and complete the SGRQ-C.
- There were minor issues identified in the SGRQ-C, including a few items that were not as relevant to participants, minor issues with response options to a few questions, and a few comments about item wording for select items.
  - For item 4 ("I have attacks of wheezing"), one participant (6.7%) was unfamiliar with the term wheezing.
  - For item 5 ("how many attacks of chest trouble did you have during the last year?"), one participant (6.7%) was unsure how to interpret the word "attack;" another (6.7%) participant was unclear on the meaning of "chest trouble."
  - For item 8 ("how would you describe your chest condition"), one participant (6.7%) did not know how to define "chest condition."
  - For item 10f ("I get exhausted easily"), one participant (6.7%) did not know how to define "exhausted."
  - Another participant (6.7%) reported item 13b ("I cannot go out for entertainment or recreation") was too vague and was uncertain of the meaning of the item.
- Despite these minor and infrequent issues, all participants were able to respond to the questions.

Limitations

- The sample of participants with AATD-LD included participants with a broad range of severity (based on their CAAT and SGRQ-C scores), however the sample was slightly skewed toward more mild or moderate symptoms.

Conclusions

- The SGRQ-C is a very well-established COA measure that is familiar to clinicians and commonly used in respiratory indications.
- Overall, the SGRQ-C was well-understood by individuals with AATD-LD, included all relevant concepts, and the participants were able to easily respond to and complete the SGRQ-C.
- The SGRQ-C is a fit-for-purpose, content valid measure for patients with AATD-LD and is suitable for use as a COA endpoint in its current form.

References
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3. Tomaszewski EL, et al. *Respir Res*. 2023;24(1):106.

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