Early View

Task force report

European Respiratory Society statement on frailty in adults with chronic lung disease


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European Respiratory Society statement on frailty in adults with chronic lung disease

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A world first European Respiratory Society Statement summarises the state of the science on understanding and managing frailty in adults with chronic respiratory disease.

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Abstract

Frailty is a complex, multidimensional syndrome characterised by a loss of physiological reserves that increases a person’s susceptibility to adverse health outcomes. Most knowledge regarding frailty originates from geriatric medicine, however, awareness of its importance as a treatable trait for people with chronic respiratory disease (including asthma, COPD and interstitial lung disease) is emerging. A clearer understanding of frailty and its impact in chronic respiratory disease is a pre-requisite to optimise clinical management in the future. This unmet need underpins the rationale for undertaking the present work.

This European Respiratory Society Statement synthesises current evidence and clinical insights from international experts and people affected by chronic respiratory conditions regarding frailty in adults with chronic respiratory disease. The scope includes coverage of frailty within international respiratory guidelines, prevalence and risk factors, review of clinical management options (including comprehensive geriatric care, rehabilitation, nutrition, pharmacological and psychological therapies), and identification of evidence gaps to inform future priority areas of research. Frailty is under-represented in international respiratory guidelines, despite being common and related to increased hospitalisation and mortality. Validated screening instruments can detect frailty to prompt comprehensive assessment and personalised clinical management. Clinical trials targeting people with chronic respiratory disease and frailty are needed.
Box 1: Summary of key statements

- Frailty is a multidimensional syndrome characterized by decreased physiological reserves and diminished resistance to stressors. This conceptual definition of frailty, defined first in geriatric medicine, is applicable for use in people with chronic respiratory disease.
- Frailty is under-represented in respiratory guidelines, which may contribute to limited recognition of its importance in some areas of current clinical respiratory care.
- Many validated instruments exist for screening and potentially detecting frailty. Such tools are rarely sufficient to inform high quality personalised clinical care without additional comprehensive evaluation.
- The presence and impact of frailty can change over time, suggesting a role for serial evaluations.
- Frailty is more common among people with respiratory diseases than the general population and prevalence estimates vary according to diagnosis and frailty definition.
- The increased vulnerability to endogenous (e.g. diseases) and exogenous (e.g. socio-cultural factors, environment) stressors associated with frailty increases risk of adverse outcomes including hospitalisation and mortality.
- Comprehensive geriatric assessment is an interdisciplinary process of care designed to identify and manage the biological, clinical, functional and social care needs of people with frailty. It may help identify individuals with health issues that persist despite optimal respiratory disease management that may require specialist input (e.g. from geriatric and/or palliative care services).
- Pulmonary rehabilitation interventions, even of a short duration, can mitigate many of the physical components that contribute to the development and consequences of frailty.
- Frailty status and co-morbidities may impact upon the pharmaceutical management of people with chronic lung disease. Specific agents exist that may target some well-defined disease subgroups.
- Nutritional management to optimise nutritional status (e.g. increased protein intake to increase muscle mass) may reduce the impact of frailty when offered, preferably in a multidisciplinary setting.
- The Task Force members do not consider the presence of frailty an appropriate reason to deny eligibility for 'gold standard' respiratory treatments, however specific studies examining this issue are lacking.
- People with respiratory disease and frailty report increased anxiety and depression symptoms. Existing models of rehabilitation and integrated care may improve psychological outcomes, however evidence is presently limited.
- People affected by frailty, patients and their caregivers, hold many varied concerns and uncertainties that can negatively impact their quality of life. Support (e.g. to ensure adequate health literacy) is essential to optimise active participation in shared decision-making.
- Clinical trials involving people with chronic respiratory disease who have frailty are required in order to address key issues raised by such individuals.
Introduction

Frailty is a treatable trait of relevance to people with various chronic respiratory diseases, especially those with severe chronic obstructive pulmonary disease (COPD) and/or lung transplantation. Frailty was acknowledged in 2016 by the European Innovation Partnership on Active and Healthy Ageing as an important factor that should be considered in the management of chronic respiratory diseases[1]. Despite this recognition, knowledge and evidence focused specifically on the intersection between frailty and chronic respiratory disease is only recently emerging (Figure 1). In response, the European Respiratory Society (ERS) approved the formation of a Task Force to develop the world’s first Statement synthesising evidence on the impact and management of frailty specifically in the context of chronic respiratory disease. The broad aims were to examine the coverage of frailty within international respiratory guidelines, the prevalence and risk factors for frailty, to review clinical management options (including comprehensive geriatric care, rehabilitation, nutrition, pharmacological and psychological therapies), and to identify evidence gaps and priority areas for future research.

Figure 1. Overview of database records related to chronic lung disease and frailty. Sources: PubMed terms ‘(chronic lung disease) and frailty’; PubVenn (access date April 2023), available at https://pubvenn.appspot.com/.

Procedure

In 2020, the Task Force was convened through voluntary nominations from ERS member candidates engaged in research or the clinical management of frailty. This group comprised clinicians and academics spanning nine countries and eight professions, possessing broad expertise across major disease groups, healthcare settings, and focus areas of clinical practice. Careful consideration was given to ensure balance of gender and career stages, and a patient representative was appointed with assistance from European Lung Foundation (ELF). The scope of work contained within the initial proposal to ERS was developed by the Task Force and approved by a delegation of societal leaders (scientific, cross-assembly panel).

- Frailty context and definition

Frailty is internationally and conceptually defined as “a multidimensional syndrome characterized by decreased [physiological] reserve[s] and diminished resistance to stressors”[2]. Frailty can manifest differently in each individual due to varying causes and contributors, but results in a common syndrome that is relevant across diagnoses that negatively impacts on dependency and/or premature death[2].

Many factors related to chronic respiratory disease contribute to the development of frailty (Figure 2). Frailty can also exacerbate the functional decline commonly observed in chronic respiratory disease (Figure 3). This underpins the rationale for developing a respiratory specific Statement on frailty. Frailty is a distinct concept from generalised ‘vulnerability’ (which anyone can exhibit at different times) and ‘disability’[3] (difficulty or dependency to carry out essential activities for independent living)[4]. While different dimensions of frailty are commonly described in existing literature (e.g. ‘physical frailty’[2], ‘cognitive frailty’, ‘social frailty’) [5], these can all be encapsulated under the more broad ‘umbrella’ concept of frailty. For the purposes of
advancing our knowledge, reducing unnecessary confusion, and for operational
definition purposes (i.e. to conduct a reproducible systematic search of the
literature), the Task Force consensus agreement was that frailty in the context of
chronic respiratory disease should be defined in accordance with the internationally
accepted definition previously described[2]. Any studies examining frailty within this
more broad ‘umbrella’ concept (which includes the more specific dimensions) were
therefore eligible for inclusion.

Figure 2. Summary of the complex interplay between factors that can contribute to the development of frailty in people with chronic respiratory disease.

*Social determinants of health external to the individual potentially contribute to the development of frailty and, once present, can mediate the impact of frailty and frailty severity on health outcomes in adults with chronic respiratory disease. While such factors are not represented in the figure, the Task Force acknowledge them as relevant.

Figure 3. Hypothetical trajectory models of function in people with chronic respiratory disease who have (red) and do not have (blue) frailty. Each drop in function (moving from left to right) occurs in response to a stressor event such as an acute respiratory exacerbation. Frailty is associated (figure insert) with declines of a greater impact and duration, poorer recovery and increased frequency over time compared to people without frailty, however the impact over time may vary.

Figure adapted with permission of the American Thoracic Society. Copyright © 2022 American Thoracic Society. All rights reserved. Cite: Singer J, Lederer D, Baldwin M (2016). Frailty in Pulmonary and Critical Care Medicine. Annals ATS; 13(8), 1394-1404. Annals of the American Thoracic Society is an official journal of the American Thoracic Society. Readers are encouraged to read the entire article for the correct context at https://www.atsjournals.org/doi/10.1513/AnnalsATS.201512-833FR. The authors, editors, and The American Thoracic Society are not responsible for errors or omissions in adaptations.

- Chronic respiratory disease definition

For the purpose of this Statement, ‘chronic respiratory disease’ refers to any
respiratory disease associated with a long-term presence that is not transient in
nature. This includes severe asthma, COPD, bronchiectasis, environmental/occupational lung disorders, adult cystic fibrosis, interstitial lung
disease (ILD), lung transplantation and pulmonary hypertension.

- Key review methodology

This statement is based on synthesis of evidence identified through systematic
database searches, clinical insights, and engagement with people affected by
chronic respiratory disease. Full details regarding the processes used to identify
relevant literature are available in the online supplement and summarised below.

A medical librarian performed searches of Medline (Ovid), EMBASE (Ovid),
Cochrane Library and CINAHL (EBSCO) from inception to April 5th 2022. Search
terms included frail* and a comprehensive list of respiratory disease search terms,
based on standardised Cochrane Airways strategies. A separate search strategy
tailored to identify clinical practice guidelines from 2016 onwards was executed in
Medline (Ovid), CINAHL (EBSCO) and TRIP databases. After combining results and
de-duplication, all records were screened on title and abstract by two independent
team members using Covidence software. All records coded as ‘maybe’ and ‘include’ were retrieved in full text and assessed for eligibility by two independent assessors. Additional papers were also sourced among Task Force members via handsearching relevant websites (e.g. international respiratory societies, organisations and agencies). This handsearching (only) was updated near the time of report publication. All empirical studies describing frailty in adults (aged ≥18 years) with chronic respiratory disease were eligible for inclusion. Theses, abstracts, commentaries, opinion pieces and case studies were not included as were studies published in languages other than the six spoken by the multinational ERS Task Force.

Small working groups (1-3 Task Force members per group) extracted and synthesised relevant findings from included studies relative to specific Statement aims (aligned with members’ areas of expertise). No original meta analyses were planned a priori to address review aims. Regular communication via an online collaborative working platform and quarterly teleconferences were implemented to facilitate ongoing communication, member checking of progress and verification of final outcomes. Key messages were drafted for each section and discussed by the Task Force. A final list was distributed for voting among the Task Force to derive consensus metrics (percentage agreement). Results are in the online supplement.

We developed a survey for people affected by chronic respiratory disease, in collaboration with patient representatives from ELF, to help inform content for the Statement and identify topics of inquiry needing future attention. The survey (online supplement) was translated into nine languages and distributed electronically via ELF. An interview was also conducted and posted in an ELF member newsletter and social media to help raise awareness of the initiative. Responses from the consumer survey were translated by members of the multinational Task Force, coded according to major and minor response themes and structured according to a simple content analysis framework. Findings were represented via a) a summary visual synopsis; b) detailed coding tree structure; and c) table of supportive quotes mapped to survey themes. An infographic was created to highlight key findings using simple language, and our patient representative produced a reflective piece as a supportive statement of reflexivity for the work. Further details regarding the survey development and analysis is available in the online supplement.
Statement

Frailty in international guidelines on chronic respiratory diseases

Detailed guidance for the clinical management of frailty already exists in the field of geriatric medicine[6, 7]. None, however, are designed to address the specific needs of people affected by chronic respiratory disease. Where acknowledged in respiratory guidelines, frailty was typically recognised (superficially) as a consequence or contributor to poor health outcomes (e.g. increased morbidity, mortality and poorer prognosis).

In COPD, frailty has been notably absent from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) international guidelines up to 2022[8], however the recent 2023 report update[9] now includes brief acknowledgement that frailty can be defined, that its prevalence is greater in people with compared to without COPD, and that it may help identify people at risk of poor outcomes. In the United Kingdom, the updated National Institute for Health and Care Excellence (NICE) COPD guideline mentions frailty amongst a list of factors that could be used to assist with prognostication for people with stable disease[10]. Australia and New Zealand's COPD guidelines ('the COPD-X Plan')[11] were one of the only sources that devoted significant attention to issues related to frailty. In addition to acknowledging frailty as a factor that may challenge the use of some inhaler devices, an entire section involving seven paragraphs is included (Section 07.4 – Frailty in COPD). This section outlines succinctly how frailty can be defined, how it may contribute to poor health outcomes, its increased prevalence in COPD, the importance of exercise, nutrition, smoking cessation and reducing readmission risk as part of good clinical management, and acknowledges the impact of frailty upon patients, carers and health and social services. No specific practice recommendations regarding frailty were made, however.

In asthma, frailty was not mentioned in the Global Initiative for Asthma (GINA) international guidelines[12]. The American Thoracic Society guidelines on the management of asthma in the elderly acknowledges the potential challenges of performing spirometry in people affected by frailty and advocates for the role of geriatric care in these individuals. More generalised information from the elderly is acknowledged as conferring potential relevance for people with frailty such as consideration of inhaler device selection in light of limitations of inspiratory flow, coordination and/or hand dexterity[13].

Frailty appears to have a more established presence in the area of lung transplantation. It is strongly emphasised as an important part of multifaceted assessments for heart and lung transplantation candidate selection[14] and a recent International Society for Heart and Lung Transplantation international consensus document for selection of lung transplant candidates states frailty assessment should be considered part of a comprehensive transplant evaluation in recognition of its negative impact upon waitlist and post-transplant mortality[15].
Assessment methods

Although numerous measures of frailty are available, they generally fall into one of two categories. The first are based upon physical frailty phenotype, developed by Fried and colleagues (referred to as the Frailty Phenotype [FP]). The FP quantifies five conceptual domains: wasting, slowness, weakness, low activity, and exhaustion and defines frailty as having deficits in at least three of those[16]. The second model conceptualizes frailty as an accumulation of deficits and is most commonly operationalized using the Frailty Index – a mathematical model that calculates a ratio based on the number of deficits present (e.g. clinical symptoms, laboratory findings, disabilities, and comorbidities) relative to the total number of items assessed[17].

Although measures of physical frailty and cumulative deficits are operationally different, both satisfy measures of content, construct, and predictive validity in community-dwelling older adults. Such measures are increasingly being applied to adults with chronic respiratory disease (Figure 1). Broadly speaking, the Task Force consider factors such as the needs or goals of a specific clinical setting or study as relevant when determining choice of frailty measure. For example, when a screening tool is desired for use in primary care, a version of the Frailty Index (original version contains 70 items, however shorter versions are available[18]) is used by Task Force members due to its relative simplicity to implement within electronic medical record systems[19]. Alternatively, in preventive or treatment environments, a physical frailty measure such as the FP or Short Physical Performance Battery (SPPB)[20, 21] may offer advantages due to a) the smaller number of items needing to change to affect frailty status; b) their basis on physical attributes which are often responsive to rehabilitative treatments, assuming an absence of instrument ceiling effects (in contrast to accumulated deficits frailty models that are based on the presence of comorbidities); and/or c) their ability to help identify candidates for rehabilitation interventions.

A summary of commonly used physical and cumulative deficit frailty measures, with an emphasis on those that been applied in chronic respiratory disease populations, is presented in Table 1. Other comprehensive lists are described elsewhere[22, 23]. Conceptually, operational measures of frailty domains should a) quantify vulnerability to stressors and b) be discriminative within the population of interest and c) be validated and consistent with ensuing treatments. Although the rapidly emerging biomedical literature examining frailty in chronic respiratory disease supports frailty as a valid and novel contributor to poor outcomes, refinements to existing measures may still be required. For example, the “low activity” domain of the original FP uses the Minnesota Leisure Time Activity Scale[24] which reports time expended in demanding leisure activities such as swimming, tennis, and racquetball, which may be less relevant to adults with severe chronic respiratory disease.

It is recognized that measurements of frailty will evolve, and biomarkers and anthropomorphic measures (such as sarcopenia) that reflect the underlying pathobiology of frailty could further improve measurement validity[2, 25-31]. The incorporation of frailty assessments in clinical practice to identify individuals at heightened risk for poor outcomes or detect indications for additional interventions (for example) is underpinned by modest evidence of clinimetric properties of available frailty measures. These properties include face, construct, and predictive
validity. Scant data exists regarding reliability. Although derived from observational studies, it does appear that physical frailty is dynamic and responsive to interventions[32-34]. Considering the limitations of any single frailty instrument (Table 1), as well as the dynamic nature of frailty and the lack of direct evidence to suggest otherwise, the Task Force does not use frailty assessments as a sole measure to determine eligibility for standard best practice care including lung transplantation.
Table 1. Commonly used instruments to evaluate frailty in adults with chronic respiratory disease*.

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Domains Assessed</th>
<th>Method of Frailty Domain Assessment</th>
<th>Score range</th>
<th>Frailty cutoffs**</th>
<th>Time to complete</th>
<th>Need for specialised equipment?</th>
<th>Need for specialised personnel?</th>
<th>Expected to respond to intervention?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fried Frailty Phenotype (FP)[16, 35]</td>
<td>Nutritional status, physical activity, mobility, strength, and energy</td>
<td>Physical tests for gait and grip strength; self-report assessment of weight loss, exhaustion, and low activity</td>
<td>Range: 0 - 5</td>
<td>Dichotomous: Frail: ≥3, Not frail 0-2</td>
<td>10 – 15 minutes</td>
<td>Yes.</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Short Physical Performance Battery (SPPB)[21]</td>
<td>Physical activity, mobility, strength, and energy</td>
<td>Physical tests of balance (tandem, semi-tandem, side-by-side), gait speed, and strength (sit to stand five times)</td>
<td>Range: 0 - 12</td>
<td>Dichotomous (various cutpoints proposed in the literature): Frail: ≤ 7; or ≤ 9; or ≤ 10</td>
<td>5 – 10 minutes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Clinical Frailty Scale[36]</td>
<td>Nutritional status, physical activity, mobility, strength, energy, cognition, mood, and social relations or social support</td>
<td>Interview-based assessment and physician assigned score of 1 (robust health) to 7 (complete functional dependence on others)</td>
<td>Range: 0 - 7</td>
<td>Various definitions. Categorical: Not frail: 0-3, Apparently Vulnerable: 4, Mildly Frail: 5, Severely Frail: 6-7, Dichotomous Frail: ≥ 5</td>
<td>&lt; 3 minutes</td>
<td>No</td>
<td>Yes. Clinical judgement</td>
<td>Yes</td>
</tr>
<tr>
<td>Frailty Index[18, 37]</td>
<td>Distinct diseases and their consequences including nutritional status, physical activity, mobility, strength, energy, cognition, mood, and social relations or social support</td>
<td>Chart review or survey that enumerates the number of diseases, their clinical and laboratory manifestations and consequences, and risk factors.</td>
<td>Range: Varies widely depending on specific measure but includes at least 30 items for a valid Frailty Index[37].</td>
<td>A cut point ≥ 0.25 is generally used to define frailty</td>
<td>20-40 minutes</td>
<td>No, but does require access to full medical record</td>
<td>Yes. Personnel must be able to navigate a medical chart to identify diseases and relevant laboratory investigations</td>
<td>Possibly</td>
</tr>
<tr>
<td>Frailty Scale</td>
<td>Domains</td>
<td>Self-report</td>
<td>Range</td>
<td>Categorical:</td>
<td>Time</td>
<td>Yes/No</td>
<td>Comments</td>
<td></td>
</tr>
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</tr>
<tr>
<td>Edmonton Frail Scale[38]</td>
<td>Cognition, general health, functioning, social support, medication use, nutrition, mood continence, physical performance</td>
<td>Self-report for 8 domains; physical performance: “Timed Get up and Go”[39], cognitive performance “Clock test”[40]</td>
<td>0 - 17</td>
<td>Categorical: Severe Frailty: ≥12; Moderate frailty 10-11; Mild frailty 8-9; Apparent vulnerability: 6-7; Not frail: ≤ 5</td>
<td>10-15 minutes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>FRAIL Scale[41]</td>
<td>Fatigue, resistance, ambulation, illness, loss of weight</td>
<td>Self-report</td>
<td>0 - 5</td>
<td>Categorical: Frail: ≥3; Pre-frail 1-2; Robust: 0</td>
<td>3-5 minutes</td>
<td>No</td>
<td>No</td>
<td>Possibly</td>
</tr>
<tr>
<td>Kihon Checklist[42, 43]</td>
<td>Instrumental, social activities of daily living, physical strength, nutritional status, oral function, cognitive status, depression risk</td>
<td>Self-report (25 items): 7 categories: instrumental (3 items), social activities of daily living (4 items), physical strength (5 items), nutritional status (2 items), oral function (3 items), cognitive status (3 items), and depression risk (5 items)</td>
<td>0 (no frailty) - 25 (severe frailty)</td>
<td>Robust (0-3), pre-frail (4-7), frail (8-25)</td>
<td>5-10 minutes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Risk factors for the development of frailty in chronic respiratory disease

The putative mechanisms causing frailty are multiple, reflecting the complexity of the aging process[44]. These mechanisms, along with physical inactivity, malnutrition, and age-related diseases (e.g. osteoporosis, hypertension) either individually or in combination, result in physiologic perturbations including chronic inflammation, immune senescence, endocrine dysregulation, and muscle dysfunction and sarcopenia[31]. There is likely a bidirectional interplay between frailty and chronic disease; frailty impacts chronic disease, and chronic disease increases the risk for frailty. Further, the biological hallmarks of some chronic respiratory diseases mirror the underlying mechanisms associated with frailty (e.g. chronic systemic inflammation). Patients with chronic respiratory disease appear susceptible to frailty, perhaps due to the strong relationship that exists between the development of frailty, the lifestyle of individuals and their socioeconomic context[45]. Behaviours such as poor diet, smoking, physical inactivity as well as the impact of comorbidities (often multimorbidity) may impose detrimental effects to a person's aging trajectory. Furthermore, the debilitating symptoms of chronic respiratory disease, which include not only respiratory symptoms, but also fatigue, anxiety, depression and sleep disturbances, may increase the risk for developing frailty. These symptoms are thought to share similar bio-behavioural mechanisms that lead to frailty – they are associated with inflammation, may impact food-related activities (e.g. grocery shopping, cooking), diet and/or appetite and physical activity levels, resulting in malnutrition and sarcopenia. Thus, associations between some biomarkers and clinical constructs underpinning frailty and adverse outcomes are well known but, notably, not consistent across disease types that have distinct underlying pathophysiological processes.

A summary of factors contributing to the development of frailty in chronic respiratory disease is presented in Figure 2. Within this model, there remains considerable potential for complex interplay between factors. For example, pre-disposing risk factors related to genes of detoxification enzymes may diminish resistance to other additional contributing factors such as smoke exposure. Accurate identification of aetiological factors for developing frailty in individuals can therefore be challenging, and sometimes impossible. However, an understanding of causal risk factors for frailty is important to inform tailored interventions to prevent or reverse frailty. Ideally, prevention of frailty should follow a life-course approach, starting early in life and trying to correct all reversible risk conditions affecting the organism’s capacities and functions[46]. The literature on frailty specific to chronic respiratory disease is still in its infancy, with existing studies largely limited to patients with COPD and ILD, or those on lung transplant waiting lists (many of which have COPD and/or ILD). When identifying risk factors for frailty, most studies have been based on retrospective analyses where, at best, an association might be established.

Hospitalised respiratory patients present a particular challenge when considering risk factors for frailty as features associated with the nature and severity of the acute illness are likely to be significant contributors, and may overshadow the influence of any pre-hospital risk factors. For example, exacerbations of COPD lead to acute changes in biological factors (such as systemic inflammation, body composition, sarcopenia), symptoms (dyspnoea, anxiety, depression), medications and
oxygenation. All of these factors have been postulated as potential risk factors for the development of frailty in respiratory disease[47].
Prevalence of frailty in people with chronic respiratory disease

Estimates of the prevalence of frailty in adults with chronic respiratory disease have been evaluated in studies with various clinical contexts. Differences between instruments used to assess frailty make accurate comparisons challenging, even between studies involving similar participants. While some similarities are apparent in terms of an increased prevalence of frailty in chronic respiratory disease compared to people without chronic respiratory disease, differences in individual pathologies means it is valuable to assess its presence on a disease-specific basis. An overview of key studies contributing to current knowledge of frailty prevalence in these patient groups is presented in Table 2.

Studies involving people with COPD[48], lung transplantation candidates/recipients[49], ILD[50] and asthma[51] reveal frailty occurs commonly (prevalence estimates ranging up to 58%). Prevalence was observed to be highest when severe airflow limitation, dyspnoea and frequent exacerbations were present. Very few studies examine the longitudinal association between respiratory disease and frailty. Future research will inevitably contribute to refining knowledge of frailty prevalence estimates in specific respiratory diseases, however significant scope remains to examine how these change over time.
Table 2. Prevalence estimates for frailty among relevant studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Country</th>
<th>Sample size</th>
<th>Disease</th>
<th>Frailty assessment method</th>
<th>Prevalence estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marengoni et al 2018[48]</td>
<td>Systematic review of cross-sectional and longitudinal studies</td>
<td>Various</td>
<td>27 studies involving 60,278 individuals</td>
<td>COPD: 19 studies involving community-dwelling persons, 8 involving hospitalized or outpatient samples</td>
<td>Seven different instruments</td>
<td>Pooled prevalence 20% (95% CI 15% to 24%); range 9% to 64%</td>
</tr>
<tr>
<td>Chin et al 2020[52]</td>
<td>Observational cohort</td>
<td>Canada</td>
<td>50 hospitalized patients</td>
<td>COPD exacerbation; mean age 71-76 across groups</td>
<td>Clinical Frailty Scale</td>
<td>58% mild / moderate / severe frailty</td>
</tr>
<tr>
<td>Dias et al 2020[53]</td>
<td>Cross-sectional cohort</td>
<td>Brazil</td>
<td>153 community-dwelling patients</td>
<td>COPD; mean age 67-70 across groups; mean FEV1 44-61.5%pred</td>
<td>FRAIL scale</td>
<td>50.3%</td>
</tr>
<tr>
<td>Ter Beek et al 2020[54]</td>
<td>Cross-sectional analysis of observational longitudinal cohort</td>
<td>Netherlands</td>
<td>57 patients commencing pulmonary rehabilitation</td>
<td>COPD; mean age 61.2 years; mean FEV1 36.1%pred</td>
<td>FP[16] and EFIP[55]</td>
<td>28% via FP; 83% via EFIP</td>
</tr>
<tr>
<td>Gephine et al 2021[56]</td>
<td>Observational cohort</td>
<td>Canada</td>
<td>44 patients commencing home-based rehabilitation</td>
<td>COPD with chronic respiratory failure; mean age 66 years; mean FEV1 33%pred</td>
<td>FP[16]</td>
<td>43%</td>
</tr>
<tr>
<td>Naval et al 2021[57]</td>
<td>Cross-sectional cohort</td>
<td>Spain</td>
<td>127 patients</td>
<td>COPD; mean age 66.5 years; COPD; mean age 68.3 years; mean FEV1 94.5%pred</td>
<td>FP[16]</td>
<td>24%</td>
</tr>
<tr>
<td>Lee et al 2022[58]</td>
<td>Prospective longitudinal population-based observational cohort</td>
<td>Singapore</td>
<td>1162 community-dwelling adults</td>
<td></td>
<td>Modified version of FP: detailed description available in publication</td>
<td>6.8%</td>
</tr>
<tr>
<td>Montgomery et al 2019[49]</td>
<td>Systematic review</td>
<td>Various</td>
<td>10 studies involving 2388 patients</td>
<td>Lung transplant candidates / recipients</td>
<td>Five different instruments</td>
<td>0-58%</td>
</tr>
<tr>
<td>Wilson et al 2016[59]</td>
<td>Retrospective cohort</td>
<td>USA</td>
<td>102 patients</td>
<td>Lung transplant recipients; mean age 57 years</td>
<td>Frailty Index[36]</td>
<td>45%</td>
</tr>
<tr>
<td>Varughese et al 2021[60]</td>
<td>Retrospective cohort</td>
<td>Canada</td>
<td>258 patients</td>
<td>Lung transplant recipients; mean age 52.8 years</td>
<td>Frailty Index[36]</td>
<td>Mean (SD) score 0.28 (0.09)</td>
</tr>
<tr>
<td>Güler et al 2020[50]</td>
<td>Review</td>
<td>Various</td>
<td>9 studies involving 1490 patients</td>
<td>Various ILDs including some listed / underwent lung transplantation</td>
<td>Four different instruments</td>
<td>12.55%</td>
</tr>
<tr>
<td>Study</td>
<td>Study Design</td>
<td>Location</td>
<td>Sample Size</td>
<td>Diagnosis</td>
<td>Characteristics</td>
<td>Frailty Index Method</td>
</tr>
<tr>
<td>-------------------------------------------</td>
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<td>----------------------------------</td>
<td>----------------------------------</td>
<td>---------------------------------------</td>
</tr>
<tr>
<td>Milne et al 2016[61]</td>
<td>Prospective cohort</td>
<td>USA</td>
<td>129 patients</td>
<td>Fibrotic ILD; mean age 69 years; mean FEV$<em>{1}$ 75.9% pred; mean DL$</em>{CO}$ 48.6% pred</td>
<td>Frailty Index (cut-off score &gt;0.21)[36]</td>
<td>50%</td>
</tr>
<tr>
<td>Farooqi et al 2021[62]</td>
<td>Prospective cohort</td>
<td>Canada</td>
<td>463 patients</td>
<td>Fibrotic ILD; mean age 68 years; mean FEV$<em>{1}$ 78% pred; mean DL$</em>{CO}$ 52% pred</td>
<td>Modified FP[16] criteria</td>
<td>26%</td>
</tr>
<tr>
<td>Kusunose et al 2021[63]</td>
<td>Cross-sectional observational cohort</td>
<td>Japan</td>
<td>69 patients</td>
<td>Asthma; mean age 69.4 years</td>
<td>Kihon Checklist[42, 43]</td>
<td>14.5%</td>
</tr>
<tr>
<td>Landrè et al 2020[51]</td>
<td>Cross-sectional cohort</td>
<td>France</td>
<td>12,345 community dwelling adults</td>
<td>Asthma (self-reported); mean age 69.8 years</td>
<td>Adapted (self-reported) version of FP[16]</td>
<td>13%</td>
</tr>
</tbody>
</table>

Abbreviations: COPD = chronic obstructive pulmonary disease; DL$_{CO}$ = diffusion capacity of carbon monoxide; EFIP = Evaluative frailty index for physical activity; FP = Frailty phenotype; ILD = interstitial lung disease; pred = predicted; USA = United States of America.
Clinical impact of frailty in chronic respiratory disease

Frailty is clinically relevant as both an exposure (the ‘upstream’ contributor to subsequent events) and an outcome (i.e. the ‘downstream’ consequence of events) in respiratory disease. For example, in a large longitudinal population study (n=3471) participants with frailty at baseline had greater odds of developing respiratory impairment (compared to those without frailty)[64], meanwhile participants with respiratory impairment at baseline had greater odds of developing frailty at 3-year follow-up (compared to those without respiratory impairment). A short synopsis describing the different impacts of frailty in specific contexts is presented below:

- **COPD**

Frailty in COPD has been associated with accelerated disease progression and increased symptom severity [47, 51, 52, 65-75], use of medications and symptom burden[47, 76-78]. Particularly in more severe stages of COPD, frailty has negative impacts on mobility and daily functioning[79]. It increases the risk of acute exacerbations of COPD [52, 73, 79-82] and may relate to higher levels of C-reactive protein which is, in turn, associated with increased exacerbations, poorer lung function and mortality[83, 84]. Moreover, COPD exacerbations in people with frailty carry an increased (6.3-fold) risk of requiring mechanical ventilation compared to people without frailty[80], and the presence of frailty during COPD exacerbations has been suggested to associate with increased risk of readmission and/or mortality[85]. People with COPD and frailty have a higher rate (adjusted hazard ratio 1.6; 95%CI 1.1 to 2.5) and longer-duration of hospitalizations (+8 days; 95%CI 4.4 to 11.6), and worse quality of life (adjusted hazard ratio 1.4; 95%CI 0.97 to 2.0) compared to people without frailty[86].

The worse health status and lower quality of life[76, 79, 86, 87] may be attributable to numerous factors, including a higher burden of respiratory symptoms, resultant functional decline, and increased risk of isolation and poor mental health[50, 67, 70, 76, 79, 86]. This can be further complicated if associated cognitive impairment is present[88]. People with COPD and frailty demonstrate lower physical activity levels than those without frailty[32, 51, 72, 73, 75, 77, 89-92]. Furthermore, people with COPD who engage in lower physical activity have increased exacerbations, dyspnoea, and depression[61, 75, 79, 87, 93, 94]. Frailty is also associated with sarcopenia, fatigue, and risk of falls in people with COPD [95-97]. Even after lung transplantation in very severe COPD, frailty negatively affects quality of life as well as mortality[98].

Qualitative research[99] shows psychological losses of confidence, hope and purpose, and correlational work suggests a relationship between higher frailty and lower levels of illness acceptance in older people with COPD[100]. Perhaps related to this, people with respiratory disease and frailty tend to report increased anxiety and depression symptoms compared to those without frailty[32, 56, 57, 101]. There are growing reports of associations between frailty and depression[57, 102]. Frailty may also compound existing issues relating to social isolation and loneliness that exist in chronic respiratory disease[103]. Participants describe feeling isolated from others, and experience diminishing social connections alongside reduced mobility in their community. Considering social isolation and loneliness are associated with
development of frailty[104] and increased risk of hospital admissions[105-107], addressing this aspect may have important implications for outcomes in this group.

People with frailty and COPD demonstrate higher mortality rates than those with frailty who do not have COPD[64, 65, 74, 108-110]. One study in older people found both COPD and a frailty score were predictive of long-term (12-year) mortality. Each unit increase in frailty (range 1-7 points) increased the risk of long-term mortality among those with COPD (HR=1.34; 95% CI=1.02-1.81; p<0.05)[108]. One explanation is that frailty is indicative of multiple comorbidities (e.g., COPD, cancer, connective tissue disease and diabetes) that significantly increase mortality risk[32, 50, 81, 111]. Nonetheless, in a large population-based cohort study, frail COPD participants had a four-fold higher mortality risk than non-frail COPD participants (hazard ratio 4.03, 95%CI 1.22 to 13.30, p = .022), even after accounting for disease severity (FEV₁% predicted) and differences in number of comorbidities[71].

- **ILD**

Frailty in ILD is considered an independent risk factor for hospital admissions and mortality, including pre and post lung transplantation[50]. Observational studies in ILD have shown frailty is associated with dyspnoea severity, reduced muscle mass, a two-fold increase in hospitalization, prolonged hospital stay, reduced quality of life, and mortality in people with ILD[61, 112, 113]. A systematic review on frailty impact in chronic respiratory disease concluded that frailty negatively affects quality of life and increases the risk of mortality in patients with idiopathic pulmonary fibrosis/ILD[114]. Large prospective cohort studies reinforce frailty as being independently associated with an increased risk of mortality in ILD[62], including inpatient mortality in hospitalized patients[115]. The heterogeneity of conditions that exists within the ILD umbrella contributes a certain extent to the research gap as studies involving pulmonary fibrosis, for example, may not be generalizable to other interstitial lung diseases.

- **Lung transplantation**

Frailty has emerged as a novel risk factor for poor outcomes before and after lung transplantation. In a multicenter, prospective cohort study, investigators found pre-transplant frailty was prevalent (28% via FP) and independently associated with both disability and waitlist mortality (adjusted hazard ratio 3.0 [95%CI 1.8 to 5.1] and 1.38 [95%CI 1.01 to 1.9] per standard deviation worsening in SPPB and FP frailty, respectively)[116]. Further, a single-point worsening in pre-operative SPPB or FP, even among patients without clinical frailty levels, is associated with a 20-50% increased mortality risk (adjusted hazard ratio 1.2 [95%CI 1.1 to 1.3] and 1.5 [95%CI 1.2 to 1.6] for SPPB and FP, respectively). This underscores the increased risk of untoward outcomes even among individuals with preclinical, incipient levels of frailty that may fall below conventional clinical thresholds[116]. Pre-transplant frailty has also been shown to associate with worse exercise capacity, health-related quality of life, re-hospitalization and increased mortality following lung transplantation[101, 117-120].

The acute and predictable physiologic stress induced by lung transplantation has demonstrated the dynamic, complex nature of physical frailty. First, pre-operative
physical frailty resolves in most patients within 6-months following transplant[33, 34]. Second, new physical frailty commonly emerges after transplant and, when it does, is associated with rehospitalization, poorer health-related quality of life, and death[98, 117] Lastly, frailty – either before or after transplant – is reversible through targeted exercise and nutrition interventions (refer rehabilitation and nutritional management sections) [84, 121].

Concurrent to studies evaluating the associations between frailty and clinical outcomes, efforts have examined the relevance of putative mechanisms that cause physical frailty in the lung transplant population. Lung transplant candidates appear to have higher serum markers of systemic and innate inflammation (interleukin-6 and tumor necrosis factor receptor-1; wasting (lower levels of leptin and albumin); anaemia; and evidence of neurohormonal dysfunction by lower insulin like growth factor-1[116]. Advanced measures of body composition show that preoperative adiposity and sarcopenia are strongly associated with risk of physical frailty[122-124]. Pre-operative frailty status, acute kidney injury and longer stays in the intensive care unit are risk factors for the development of frailty in the peri-operative period[117]. Later, the development of sarcopenia, obesity, malnutrition, and chronic kidney disease all preceded the development of frailty up to three-years after transplant[98]. Taken as a whole, these findings highlight frailty is common and associated with poor outcomes before and after transplant. They also suggest that: i) at least a component of pre-operative physical frailty is attributable to end-stage lung disease; ii) peri- and post-operative events can induce frailty after transplant; and iii) targeted interventions proven in non-transplant populations can reverse frailty in advanced lung disease and transplant patients. Disentangling “lung disease-attributable” frailty that would be expected to resolve with transplant from “systemic” frailty that confers markedly risk for poor outcomes before and after transplant is a major focus of current investigations.
Comprehensive geriatric assessment for managing frailty in chronic respiratory disease

The ‘gold standard’ approach to diagnosing and managing frailty is Comprehensive Geriatric Assessment (CGA) [125]. The process (Figure 4), developed in geriatric medicine, begins with a multidimensional comprehensive assessment of the person’s medical, psychological, functional, and social needs and problems, as well as their values, priorities and goals[126, 127]. Findings from the assessment and problem list then inform the development of a personalised care plan, delivered by a multidisciplinary team. Care plans commonly involve management strategies to address reversible causes, including medication review to prevent/manage polypharmacy, nutritional support, cognitive assessment, and physical activity or exercise training[7, 128]. Delivery and outcomes of the care plan are regularly reviewed, typically by the team conducting the CGA or by the patient’s primary care provider, in order to 1) monitor outcomes of the care plan, and 2) update the plan according to changes in the individual’s health.

Figure 4. Overview of Comprehensive Geriatric Assessment. Reproduced without change with permission from the British Geriatrics Society from [https://www.bgs.org.uk/cgatoolkit].

CGA is the cornerstone of several models of care that have been developed for frail patients (e.g. orthogeriatrics for providing care to frail older persons with hip fractures[129], or oncogeriatrics for frail patients with cancer[130]). Recommendations have also been recently developed to provide the principles of geriatric care and CGA to people who are frail who are living in the community[131]. This model of care might have particular applicability for patients with chronic respiratory disease, irrespective of the setting where they are evaluated. In fact, respiratory care is already characterized by the multidisciplinarity nested in the CGA methodology. One cohort study of inpatient respiratory rehabilitation has demonstrated improved disease-specific health-status and reduced exacerbations following a CGA-directed approach[82], which incorporated additional expertise from geriatric and palliative care colleagues. However, beyond this, studies evaluating CGA models of care within a respiratory context are limited.
Role of pharmaceutical agents in managing frailty

Early detection of frailty in people with chronic respiratory disease is essential to facilitate timely initiation of pharmacological agents aiming to increase resilience or prevent further functional decline and/or mortality. In the context of frailty, reducing polypharmacy[132] and deprescribing potentially harmful agents, particularly in vulnerable elderly individuals[133], are important priorities to prevent aggravation of frailty. Several key principles exist that guide the pharmaceutical management of people affected by frailty, as described by the Optimizing Geriatric Pharmacotherapy through Pharmacoepidemiology Network[134]. These include:

1. Perform medication reconciliation and maintain an up-to-date medication list;
2. Assess and plan based on the individual's capacity to self-manage medications. This may include additional evaluation of access, proper device use, ability to manage medications, capacity to maintain adherence, absence of socioeconomic barriers, and/or the presence/absence of carer support.
3. Ensure appropriate prescribing and deprescribing;
4. Simplify medication regimens when appropriate to reduce unnecessary burden;
5. Be alert to the contribution of medications to geriatric syndromes;
6. Regularly review medication regimens to align with changing goals of care; and
7. Facilitate multidisciplinary communication among patients, caregivers, and healthcare teams.

Frailty might also change the management of other chronic conditions in individuals due to its impact for example on pharmacokinetics and pharmacodynamics[134, 135]. In persons with respiratory impairment, sufficient coverage with inhaler therapies that are low-dose and have fewer side effects is important to reduce risks of side effects (e.g. avoiding frequent oral courses of corticosteroids). Additionally, inhaler devices must be carefully selected to match the functional abilities of frail patients. An example summary of such considerations for older patients who have asthma has been previously published[13].

Several pharmaceutical agents to prevent further clinical deterioration in patients with frailty have been investigated. Their mode of action is mainly anabolic or anti-inflammatory and data on long-term outcomes including mortality is scarce. While scores on comprehensive frailty indices did not improve when investigated in clinical trials, anabolic drugs such as testosterone or teriparatide, recombinant human chorionic gonadotropin and capromorelin, anti-inflammatory piroxicam and vitamin D analog alfacalcidol, did show improvement in subdomains of physical performance, muscle strength or body composition[136]. Bone mineral density is another outcome which tended to improve by hormonal therapy in clinical trials[137]. Other agents may have particular benefit in frail individuals with certain co-morbidities such as ghrelin in case of cachectic COPD, metformin in case of diabetes mellitus or angiotensin converting enzyme (ACE) inhibitors in case of hypertension[138]. While polypharmacy is common in patients with COPD[139, 140], evidence-based medications can be, by contrast, under-prescribed in people who are frail. [141]. Examples include osteoporosis treatment such as calcium and vitamin D supplementation, ACE inhibitors for chronic heart failure or ischemic heart disease,
and β-blockers for stable systolic heart failure [141]. However, the impact of potential adverse drug reactions or interactions, the potential risk-benefit ratio and time to benefit needs to be evaluated in frail older people and this should be in line with the therapeutic intent, patient preferences, and dose optimization [134]. Still, some existing drugs affect multiple pathways involved in frailty including apoptosis, proteolysis, muscle proliferation and inflammation e.g. existing antirheumatic agents modulate both the glucocorticoid receptor and ACE involved targets [142]. Other novel anabolic agents such as selective androgen receptor modulators (SARMs) [143] and ghrelin mimetics are still under investigation to tackle muscle and bone loss [138]. Since ghrelin increases appetite and body weight, promotes growth hormone secretion and reduces inflammation (e.g. Interleukin-1β, Interleukin-6, and Tumor Necrosis Factor-α) [138], interventions with this or analogues deserve further investigation. ACE-inhibitors, vitamin D analogues and allopurinol for its antioxidant properties are potentially interesting agents for specific COPD phenotypes as well, but have been investigated only in small, short-term, and non-tailored randomized clinical trials so far [144].

In summary, while various pharmaceutical agents target potentially important biological frailty pathways, more research is needed to make recommendations for clinical practice [77]. In general, several tools have been developed to assist clinicians with (de)prescribing in frail older people [145-148].
Rehabilitation interventions for frailty in people with chronic respiratory disease

-During stable disease

Exercise-based pulmonary rehabilitation programs can improve exercise performance, muscle strength, and symptoms of dyspnœa and fatigue in patients with chronic respiratory diseases, which are key determinants of frailty[149]. Self-management and multidisciplinary education components of pulmonary rehabilitation may further improve independence and reduce frailty[149]. A summary of key findings related to the role of pulmonary rehabilitation in the management of frailty is presented below. A more comprehensive report has been recently published[150].

In a United Kingdom cohort of patients referred for pulmonary rehabilitation (n=816), comprising aerobic and resistance exercise training and multidisciplinary education, the benefits in terms of breathlessness, exercise performance and health status were most pronounced in the frail subgroup. Over 60% of these frail patients no longer met Fried FP criteria at program end, demonstrating that physical frailty is reversible[32]. Similar findings were obtained in smaller cohorts of patients with chronic respiratory diseases, with improved gait speed and reductions in the prevalence of frailty post-rehabilitation[151, 152]. A further cohort study found an enhanced response to rehabilitation in terms of exercise performance among frail patients (based on the Prisma 7 questionnaire and timed up and go test) compared to non-frail patients. A more pronounced decline during the six months after the program was also observed, highlighting the need for adequate follow-up[153]. Furthermore, among 47 patients with COPD and chronic respiratory failure in Canada – all on long-term oxygen therapy or non-invasive ventilation – an 8 week home rehabilitation program enhanced health-related quality of life, fatigue, anxiety and depression only in the frail patients (Fried criteria[16]), while exercise and functional performance improved in both groups[154].

While patients with frailty may gain most benefit from pulmonary rehabilitation, they also have increased odds for program non-completion[32], highlighting a ‘frailty rehabilitation paradox’. Engagement with pulmonary rehabilitation may be especially challenging in the context of frailty. Patients have described loss across different areas of life, from mobility and usual activities, to loss of relationships and community engagement[99]. For many patients pulmonary rehabilitation represents an opportunity to actively improve their health, despite the physical and mental demands it entails. Interestingly, almost all patients completed the home-based rehabilitation study[154] and the use of mobile or telehealth to optimize program adherence is worthy of further study.

Based on the available evidence, Brighton and colleagues reflected on how exercise-based approaches may be better attuned to frailty in COPD[155]. Five key principles were identified: building trusting relationships, creating a shared understanding of priorities, individualizing content to match priorities, having capacity to address multidimensional losses; and having flexibility in service delivery. These align well to prior reflections that individual tailoring is crucial when dealing with multimorbid and frail patients, including a patient- and family-goal oriented approach[156].
During acute respiratory exacerbations

Inpatient respiratory admissions predispose to profound levels of physical inactivity and muscle weakness secondary to disuse atrophy. These factors, in conjunction with high levels of breathlessness and fatigue, can increase the risk of frailty. The short nature of hospital admissions means redressing many of these deficits, and indeed reversing frailty, via rehabilitation strategies can be challenging.

Limited data suggests that clinically meaningful benefit may be possible and that early rehabilitation after an acute hospitalisation appears important to reduce the risk of readmission and to optimise functional recovery. Torres-Sanchez et al. randomised 58 older Spanish inpatients (mean age >75 years) with acute exacerbation of COPD (AECOPD) and frailty (assessed via a Brief Frailty Index) to usual care with or without rehabilitation involving seated pedal exercises from day 2 until discharge[73]. Quadriceps strength, single leg balance time, number of sit-to-stand repetitions and daily physical activity levels improved in the intervention group, while no change or deterioration was observed with usual care. This suggests outcomes such as these are responsive to simple intervention over a relatively short duration. The impact on frailty status was not evaluated. A cohort study investigated a geriatric rehabilitation service in the Netherlands for older patients hospitalised for AECOPD, of which many were likely to have met frailty criteria[82]. The 6-week inpatient multidisciplinary rehabilitation service demonstrated significant and clinically meaningful improvements in disease-specific health-status and fewer exacerbations in the intervention group (n=78) compared to the control group comprising patients who declined the service (n=80) at 3-month follow-up.

Before and/or after lung transplantation

Studies have demonstrated that frailty is amenable to change in transplant candidates and recipients. In a retrospective study, 62/150 patients listed for transplantation underwent combined exercise training (90min, 3x/week)[157]. SPPB scores increased most markedly in those who were frail on enrolment, alongside improvements in muscle strength and exercise capacity. Similarly, trends towards improvements in SPPB and FP scores were observed among lung transplant candidates who participated in a pilot home mobile health intervention over 8 weeks[84].

Post-transplant, Courtwright and colleagues followed a cohort of transplant recipients referred to either an inpatient facility (n=26) or outpatient rehabilitation (n=83)[117]. Among those directed to outpatient rehabilitation, frail patients showed substantial improvements in SPPB scores over 6 weeks (median +6 points) such that 30/35 were no longer frail at discharge. The mobile health intervention studied by Singer et al[84] was also piloted in 18 patients post-transplantation, who reported it was easy to use and enhanced their motivation to engage in rehabilitation[121]. Improvements in frailty by SPPB score, physical activity and disability were found over 8 weeks. Controlled trials involving larger samples remain indicated to confirm these findings.
The precise nature of the relationship between nutrition and frailty has been difficult to establish as compromised nutritional status may be an aetiological factor and/or consequence of frailty. Additionally, established associations between malnutrition, sarcopenia and/or (sarcopenic) obesity, and the onset or development of frailty adds complexity to identifying the exact dynamics that exist between these constructs[98, 158-160]. Data on the prevalence of coexisting nutrition diagnoses in people with frailty as a subcategory of a chronic respiratory disease population are scarce. Furthermore, interpretation of prevalence data is complicated due to the lack of consistency and resultant high variability in evaluation methods. This is compounded further by the heterogeneity of chronic respiratory diseases and differences related to health care settings and contexts (e.g. community-dwelling vs hospital vs rehabilitation). Thus, in spite of limited availability of data, in some subgroups of a frail chronic respiratory disease population 17 to 49% have found to be malnourished[54, 161], whereas in the general chronic respiratory disease population the prevalence is established to be 17 to 30%[162, 163].

In assisting people living with chronic respiratory disease who are frail, dietitians will assess the presence of coexisting nutritional diagnoses that possibly underlie or contribute to frailty[164]. This is important as development of individualised nutritional care plans, as per any other behavioural considerations (e.g. physical activity, smoking cessation), should be underpinned by comprehensive evaluation of the cause(s) of frailty. Further, several nutritional diagnoses may present with similar clinical features due to mutual involvement in reductions of muscle mass (i.e. changes in body composition) and strength (Table 3). An important strategy to improving muscle mass is ensuring sufficient essential amino acids in ones diet[165, 166]. Resistance training stimulates increases in muscle mass, inhibits muscle breakdown, and stimulates muscle sensitivity to dietary proteins[167, 168]. The effect of resistance training on muscle mass is enhanced by adequate protein and energy intake, to ensure the protein required to enhance muscle development is not used as a source of energy[169-171].

Nutritional screening and assessment, commenced as early as possible, can help identify nutritional diagnoses such as malnutrition or sarcopenic obesity, which commonly coexist in adults with chronic respiratory disease[54, 172]. Differentiating between nutrition diagnoses is crucial to inform individualised nutritional management plans in accordance with (inter)national guidelines[173, 174]. While the specific aims of such plans can differ widely between patients and different chronic respiratory diseases, common principles among this patient group include[175, 176]:

- Maintaining or improving nutritional status;
- Maintaining or improving muscle mass;
- Weight loss with conservation of muscle mass;
- Nutrition education (including partners/carers), with a focus on food literacy and food insecurity;
- Improvement to self-efficacy and body-image; and
- Acquisition of self-management skills regarding nutrition.

The role of factors outside of nutrition may also require addressing in order to improve nutritional care outcomes. For example, reducing undesirable symptoms
such as nausea, fatigue or pain, or improving support in response to cognitive or psychosocial barriers may affect one’s ability to optimise protein/energy intake and therefore enhance the role for good nutritional management to help manage (or even prevent) frailty[54]. As with other areas, this reinforces the importance of nutrition management forming part of a multidisciplinary holistic care strategy to optimise outcomes for people affected by frailty.

Although there is emerging evidence on multidisciplinary interventions including nutritional intervention targeting frailty in generalised older populations, a research gap exists regarding the application of such approaches to a chronic respiratory disease population. Very few studies to date have yielded limited evidence to inform practice[84, 153, 154, 177, 178]. This may be partly attributed to nutritional intervention studies typically targeting contributing or underlying nutrition diagnoses (e.g. malnutrition, sarcopenia) rather than the construct of frailty directly. This notwithstanding, data from multidisciplinary pulmonary rehabilitation programs that include nutritional management have shown promise to improve frailty status.[154, 178] Systematic reviews of studies that evaluate multidisciplinary interventions including nutritional management in frail older populations have also shown similar effects[158, 179].

Table 3. Common nutrition diagnoses in chronic respiratory disease.

<table>
<thead>
<tr>
<th>Nutrition diagnoses</th>
<th>Description</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malnutrition</td>
<td>&quot;A state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat-free mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease&quot;[172]</td>
<td>GLIM criteria[180]: Diagnosis requires at least one phenotypic and one etiologic criterion. Severity is determined based on phenotypic criterion. Phenotypic: weight loss, BMI, reduced muscle mass. Etiologic: reduced food intake or assimilation, disease burden/inflammatory condition.</td>
</tr>
<tr>
<td>Cachexia</td>
<td>Cachexia or ‘pulmonary cachexia’ is considered a subcategory of malnutrition with inflammation in chronic disease[172]: ‘a complex metabolic syndrome associated with underlying illness and characterized by loss of muscle with or without loss of fat mass’[181]</td>
<td>No specific criteria are available. However, patients with cachexia meet the GLIM criteria[180] for malnutrition related to chronic disease with inflammation.</td>
</tr>
<tr>
<td>Sarcopenia</td>
<td>‘A progressive and generalised skeletal muscle disorder that involves the accelerated loss of muscle mass and function’[182]</td>
<td>EWGSOP 2 criteria[182] Muscle strength Muscle quantity/quality Severity is determined based on physical performance</td>
</tr>
<tr>
<td>Overweight</td>
<td>‘Excessive fat accumulation that may impair health’[183]</td>
<td>BMI (≥ 25 and &lt; 30 kg/m²) [183]</td>
</tr>
<tr>
<td>------------</td>
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</tr>
<tr>
<td>Obesity</td>
<td>‘A pathologically increased fat mass, which is associated with an increased health risk’[184]</td>
<td>BMI (≥ 30 kg/m²) [183]</td>
</tr>
</tbody>
</table>

Table adapted with permission from European Respiratory Society monograph on Pulmonary Rehabilitation 2021, chapter 6[175].

Abbreviations: BMI = Body Mass Index; EWGSOP 2 = European Working Group on Sarcopenia in Older People 2018; GLIM = Global Leadership Initiative on Malnutrition.
Psychological and social support for people with frailty who have chronic respiratory disease

Current evidence around addressing psychological aspects of living with respiratory disease and frailty reflects the role of established approaches like pulmonary rehabilitation. People with respiratory disease and frailty attending pulmonary rehabilitation have been shown to experience reductions in anxiety and depression symptoms alongside physical improvements, and these reductions tend to be greater than in people without frailty[32, 154]. This work echoes existing evidence supporting the role of pulmonary rehabilitation in reducing anxiety and depression symptoms in people with COPD[185], but shows a particular benefit for those living with frailty.

Alongside this, studies of new integrated models of care suggest benefits in terms of psychological outcomes for people with respiratory disease and frailty. A randomised controlled trial of a community-based integrated care model including 155 people with COPD and frailty (comprising supported self-management, individualised care plans, access to a call centre and coordination between levels of care)[70] found reduced anxiety and depression symptoms at 12-months. The success of this approach was attributed in part to appropriate assessment and stratification based on needs, and shared care agreements across specialist and primary care services. In addition, a prospective cohort study of an inpatient integrated palliative rehabilitation program in 100 people with chronic respiratory disease (majority with frailty) found that the intervention was associated with increased pharmacological treatment of anxiety and depression[186]. Although subsequent impact on patient-reported psychological symptoms was not measured, this approach illustrates how a structured comorbidity schema for screening and monitoring common co-existing conditions (including anxiety and depression) could increase offers of appropriate treatment. This finding aligns with existing recommendations around routine assessment for psychological comorbidities in people with chronic respiratory disease[8].

For individuals with more complex psychological needs, specialist support and provision of effective pharmacological and psychological interventions for anxiety and depression may be required[187]. However, given known hesitancies around proactively seeking additional support within people with respiratory disease and frailty[99], and inequities in receipt of existing interventions[116], further research is required to understand optimal processes for identifying and managing the psychological needs of people with both respiratory disease and frailty. For example, given that holistic services for chronic breathlessness that integrate palliative and respiratory care have shown comparable impacts to pulmonary rehabilitation in terms of reducing distress and depression[188], exploration of the role of these services in the context of frailty has been suggested[81]. Moreover, as existing evidence is mostly from populations with COPD, broadening the evidence-base around psychological health and support in people with frailty and other chronic respiratory diseases will be important.
Issues related to frailty in chronic respiratory disease: the voice of patients and carers

A short online survey was developed and distributed with the aim of identifying issues perceived to be important to people affected by chronic respiratory disease and frailty (including family members and/or carers). A full copy is provided in the online supplement. Responses were received from 335 individuals spanning 16 countries (59% from The Netherlands; 65% female), mostly from people who identified as someone living with a chronic respiratory disease (Figure 5).

Figure 5. Summary of consumer survey responses according to group (top left), age range (top right) and country (bottom).

Several issues and strategies for potential improvement were identified by patients and caregivers (Figure 6).

- **Key issues**

These included misconceptions about chronic respiratory diseases and frailty, as well as reports of a lack of support, lack of education/public awareness, and lack of research regarding frailty. Patients highlighted a need for information about self-management, therapy options and suggested better communication and cooperation were needed at all levels of healthcare.

Respondents felt there was a misperception among the general population that frailty only affected older people. This may contribute towards less support being directed to younger individuals with chronic respiratory disease in need, particularly regarding psychological support to manage anxieties, fears and social isolation. Daily limitations were also noted to impact upon broader activities such as travel and socialisation. A lack of education was also perceived to exist across multiple areas including ways to optimise quality of life, the role for adjuvant therapies such as respiratory exercises, the importance of fostering positive attitudes and a healthy environment, use of medications (including management of side-effects), management of breathlessness and the role of nutrition. Importantly, basic knowledge regarding the impact of frailty on everyday life and ways to optimise independence as an active contributor within their living environment was felt to be lacking.

Many participants expressed they felt their needs were not being addressed by healthcare professionals. They felt judged on their physical appearance, that their care was inadequate, and they did not feel they were actively engaged in shared decision-making. This was highlighted via examples of late/untimely referrals to pulmonary rehabilitation and specialists.

Participants proposed that improvements could be made for those with frailty as a vulnerable subgroup requiring more specialised input. Increased engagement and communication with general practitioners was desired, seemingly due to a perception that they function more effectively as health navigators or supervisors to assist with common questions.
Participants also expressed a desire for increased inclusion in clinical pharmaceutical trials and faster flow of information about new research and medications. Suggestions for future research directions included the role for natural supplements, effective drugs, therapies to target abnormal genes and DNA, and further evaluation of the economic impact of frailty.

Public awareness was voiced strongly as need improvement, primarily to facilitate greater awareness and acceptance of the issues faced by people affected by chronic respiratory disease and frailty in their social and working environments. Potential avenues for this included social networks, and organisation of preventive activities in educational institutions, increased consumer participation in civil co-operative activities and enhanced support from local communities.

While greater support was advocated across virtually all areas, specific issues felt in greatest need included improved knowledge of access to community services, provision of financial support and ‘safety nets’ to affected individuals in need (including a role for improved health insurance reimbursements for multiple appointments), and improved service provision in the home, and to access different healthcare settings.

Figure 6. Summary of key issues and areas for improvement identified by survey participants regarding frailty in chronic respiratory disease. Additional information is provided in the online supplement.

Many domains identified by consumers were addressed in this Statement, however other issues require attention at all levels. One highlighted example was the role for increased patient support groups and advocacy to address patients’ interests and influence local healthcare policy. Future enquiry should identify the best ways to enhance respiratory-specific healthcare professional communication and training to better address the needs of people with chronic respiratory disease who are affected by frailty. The relevance of key messages from this ERS Statement to consumers is highlighted through a written reflection by our patient representative team member (SP; Box 2) and accompanying patient-facing infographic (online supplement).
Box 2. Patient reflection on European Respiratory Society Statement

“When I was asked by ELF to take part to a Clinical Research Collaboration on Frailty in Chronic Lung Conditions, I immediately went back in my mind to the very long years of my illness when I very often had to face dark moments made even more difficult by my frailty state.

Later, in my role as a patient representative, I realised how frailty can affect the course of illness, even to the point of preventing access to a transplant list - the only alternative to death in particular cases.

To me, the state of frailty is both a pathological condition and a psychological one. The results of both, however, are considerably greater than either of the two factors alone. This ERS Statement is particularly apt in the case of chronic lung disease for several reasons.

First of all, every chronic disease puts a strain on a patient's strength as they face the decay of their vital functions year after year. Chronicity almost always correlates with progression.

In my opinion, breathing (or rather, the lack of breathing), leads to situations of true panic that can only be managed with a great deal of mental strength. This very often becomes exhausting, creating situations that are difficult to manage. The more you panic the more your hunger for air increases, and you literally feel your heart burst in the effort to compensate for breathing.

I totally agree with the key points of this ERS Statement. Frailty accompanies every patient along their journey with chronic lung disease. Detecting frailty should lead to a comprehensive assessment and an appropriate care plan. Frailty must be kept under control and must not be assessed for the purpose of excluding someone from receiving 'gold standard' therapies or surgical interventions such as organ transplantation.

My final point is that we should go beyond current practice where the patient is followed by a series of clinicians. Clinicians must collaborate with each other and with the patient in order to have a ‘complete’ understanding of the impact of their work. In my case, I needed clinicians to better understand the psychological impact of their individual actions.

Once this gap has been bridged, we can finally have a truly holistic healthcare team that works together to address patient needs.”

- Stefano Pavanello
**Implications for future improvements regarding frailty in chronic respiratory disease**

While the number and quality of studies addressing frailty in adult chronic respiratory disease is slowly increasing, we are not yet at a point where clinical decision making is informed by a large volume of robust evidence. This poses a significant barrier to the practice of true ‘evidence-based medicine’: both via exclusion of people who are frail from clinical trials[189] and a lack of frailty assessment prohibiting the applicability of evidence from studies to people with frailty.

Greater knowledge is necessary to understand: issues specific to frailty and its proximity to chronic disease and disability; specific aetiological mechanisms contributing to precision medicine models of healthcare; the timing and roles played by pharmacological and non-pharmacological interventions; and even increased awareness of mechanisms or pathways that may be struggling to address frailty in the pursuit of new treatment paradigms. While useful ‘point of care’ resources (e.g. https://www.cgakit.com/frailty) exist in geriatric medicine, the lack of respiratory-specific knowledge means caution must be exerted before such information is extrapolated into clinical respiratory care.

Future investment can help address several modifiable issues raised in this Statement. Key opportunities identified by the Task Force include:

1. Careful consideration of research project eligibility criteria to ensure a) people who are frail are not excluded from clinical trials and b) people who are frail are specifically targeted for inclusion in clinical trials;
2. Improve public messaging and awareness of frailty as a prevalent and important risk factor for disability, poorer quality of life and mortality (distinct from the lung disease itself). This includes improved systems to measure and monitor frailty in order to detect inequalities in healthcare access;
3. Further define and validate frailty measures and associated cut-points for people with chronic respiratory disease;
4. Ensure measures of frailty are included in comprehensive studies, both as an exposure and outcome, to facilitate improved knowledge of determinants and preventive health strategies;
5. Creation of funded, collaborative research partnerships to address issues such as frailty, which have broad cross-cutting potential spanning multiple diseases (e.g. between respiratory care and geriatric medicine and/or palliative care);
6. Studies of frailty should include outcomes beyond its physical dimensions (i.e. acknowledging psychological and social impacts) in line with its multidimensional definition, and be informed by meaningful consumer engagement to optimise acceptability and alignment to priority issues;
7. Optimising integration of existing healthcare services towards more multidisciplinary, personalised care.
Acknowledgements: We thank Elizabeth Stovold and Josh Cheyne for their information specialist support to run the database search strategies; We thank Courtney Coleman and Kathleen Skinner from ELF for their assistance to coordinate our consumer survey. We thank Rainer Gloeckl and William Poncin for their assistance to translate material for our consumer survey.

Financial support: This study was supported via Task Force funding provided by the ERS.
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65. Attwell L, Vassallo M. Response to Pulmonary Rehabilitation in Older People with Physical Frailty, Sarcopenia and Chronic Lung Disease. Geriatrics (Basel) 2017; 2(1).


Choi M, Kim H, Bae J. Does the combination of resistance training and a nutritional intervention have a synergic effect on muscle mass, strength, and physical function in older adults? A systematic review and meta-analysis. BMC Geriatrics 2021; 21(1).


Yohannes AM, Kaplan A, Hanania NA. Anxiety and Depression in Chronic Obstructive Pulmonary Disease: Recognition and Management. Cleveland Clinic Journal of Medicine 2018; 85(2 suppl 1): S11-S18.


Public awareness for:
- Education
- Public health campaigns
- Social media

Communication about:
- Therapies
- Side-effects
- Research
- Specialists & GPs

Deficits regarding:
- Overall support
- Financial assistance
- Understanding
- General information

Improvements needed in:
- Community support
- Personalised approach
- Shared decision-making
- Pain management
Online supplement:

Consensus voting outcomes for key messages
After drafting and discussion of each of the 14 Statement key messages, a final list was circulated among Task Force members for final voting. All participants were required to complete this survey and indicate their agreement with the wording by voting a decision of ‘agree’, ‘disagree’ or ‘abstain’. Results of voting yielded 14 / 14 (100%) agreement for each of the 14 key messages.

Creation of Venn diagram (manuscript figure 1)
This figure was created at https://www.pubvenn.appspot.com entering the terms ‘chronic lung disease AND frailty AND geriatrics’.

The resultant term mapping used to create the figure is listed below:

Database searches (additional information)
Electronic database searches were executed by an expert respiratory medicine librarian working with the Task Force co-chairs. Search terms included frail* and a comprehensive list of search terms related to respiratory diseases, based on standardised Cochrane Airways strategies (detailed in the tables below).

Main database searches:

Medline (Ovid) (1946 to May 2022)

1 exp lung diseases, obstructive/
2 (asthma$ or wheez$).tw.
3 ((chronic$ or obstruct$) adj3 (pulmonary or lung$ or airway$ or airflow$ or bronch$ or respirat$)).tw.
4 (COPD or AECOPD or AECB).ti,ab.
5 emphysema$.tw.
6 exp Bronchiectasis/
7 bronchiect$.tw.
8 kartagener$.tw.
9 (ciliary adj3 dyskinesia).tw.
10 (bronchial$ adj3 dilat$).tw.
11 bronchoect$.tw.
12 exp Lung Diseases, Interstitial/
13 exp Pulmonary Fibrosis/
14 ((pulmonary$ or lung$ or alveoli$) adj3 (fibros$ or fibrot$)).tw.
15 (interstitial$ adj3 (lung$ or disease$ or pneumon$)).tw.
16 ((pulmonary$ or lung$) adj3 (sarcoid$ or granulom$)).tw.
17 pneumoconiosis.tw.
18 silicosis.tw.
19 byssinosis.tw.
20 berylliosis.tw.
21 asbestosis.tw.
22 siderosis.tw.
23 anthracosis.tw.
24 ((environment$ or occupat$ or exposure$) adj3 (lung$ or pulmonary$ or respiratory$ or airway$)).tw.
25 exp Hypertension, Pulmonary/
26 Pulmonary Heart Disease/
27 (pulmonary adj3 hypertens$).tw.
28 Cystic Fibrosis/
29 (cystic$ adj3 fibros$).tw.
30 exp Lung Transplantation/
31 (lung$ adj2 (transplant$ or graft$)).tw.
32 Lung Diseases/
33 ((lung$ or respiratory$ or pulmonary$) adj3 disease$).tw.
34 or/1-33
35 Frailty/
36 Frail elderly/
37 frail$.tw.
38 (fragil$ adj3 (adult$ or elderly or geriatric or patient$ or person)).ti,ab.
39 or/35-38
40 34 and 39

**Cochrane CENTRAL database (inception to May 2022)**

#1 MeSH descriptor: [Lung Diseases, Obstructive] explode all trees
#2 asthma* or wheez*
#3 ((chronic* or obstruct*) Near/3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*))
#4 (COPD or AECOPD or AECB):ti,ab
#5 emphysema*
#6 MeSH descriptor: [Bronchiectasis] explode all trees
#7 bronchiect*
#8 kartagener*
#9 ciliary Near/3 dyskinesia
#10 bronchial* Near/3 dilat*
#11 bronchoect*
#12 MeSH descriptor: [Lung Diseases, Interstitial] explode all trees
#13 MeSH descriptor: [Pulmonary Fibrosis] explode all trees
#14 ((pulmonary* or lung* or alveoli*) Near/3 (fibros* or fibrot*))
#15 (interstitial* Near/3 (lung* or disease* or pneumon*))
#16 ((pulmonary* or lung*) Near/3 (sarcoid* or granulom*))
pneumoconiosis
silicosis
berylliosis
asbestosis
siderosis
anthracosis
((environment* or occupat* or exposure*) Near/3 (lung* or pulmonary* or respiratory* or airway*))
MeSH descriptor: [Hypertension, Pulmonary] explode all trees
pulmonary Near/3 hypertens*
MeSH descriptor: [Cystic Fibrosis] explode all trees
cystic* Near/3 fibros*
MeSH descriptor: [Lung Transplantation] explode all trees
lung* Near/2 (transplant* or graft*)
MeSH descriptor: [Lung Diseases] this term only
(lung* or respiratory* or pulmonary*) Near/3 disease*
(OR #1-#31)
MeSH descriptor: [Frail] this term only
MeSH descriptor: [Frail Elderly] this term only
Frail*
((fragil*) Near/3 (adult* or elderly or geriatric or patient* or person))
(OR #33-#36)
#32 AND #37
NCT*:au
ISRCTN*:au
ChiCTR*:au
EUCTR*:au
JPRN-UMIN*:au
ACTRN*:au
(OR #39-#44)
#38 NOT #45

EMBASE (Ovid) database (1974 to May 2022)
exp asthma/
(asthma$ or wheez$).tw.
chronic obstructive lung disease/
obstructive airway disease/
exp lung emphysema/
((chronic$ or obstruct$) adj3 (pulmonary or lung$ or airway$ or airflow$ or bronch$ or respirat$)).tw.
(COPD or AECOPD or AECB).ti,ab.
emphysema$.tw.
exp Bronchiectasis/
bronchiect$.tw.
kartagener$.tw.
(ciliary adj3 dyskinesia).tw.
(bronchial$ adj3 dilat$).tw.
bronchoect$.tw.
exp interstitial lung disease/
exp lung fibrosis/
((pulmonary$ or lung$ or alveoli$) adj3 (fibros$ or fibrot$)).tw.
(interstitial$ adj3 (lung$ or disease$ or pneumon$)).tw.
((pulmonary$ or lung$) adj3 (sarcoid$ or granulom$)).tw.
pneumoconiosis.tw.
silicosis.tw.
byssinosis.tw.
beryllosis.tw.
asbestosis.tw.
siderosis.tw.
anthracosis.tw.
((environment$ or occupat$ or exposure$) adj3 (lung$ or pulmonary$ or respiratory$ or airway$)).tw.
exp pulmonary hypertension/
(pulmonary adj3 hypertens$).tw.
cystic fibrosis/
cystic$ adj3 fibros$.tw.
exp lung transplantation/
(lung$ adj2 (transplant$ or graft$)).tw.
lung disease/
((lung$ or respiratory$ or pulmonary$) adj3 disease$).tw.
or/1-35
frail$.ti,ab.
(fragil$ adj3 (adult$ or elderly or geriatric or patient$ or person)).ti,ab.
37 or 38
36 and 39
conference abstract.pt.
40 not 41

CINAHL (EBSCO) database (1937 to May 2022)
S1 (MH "Lung Diseases, Obstructive")
S2 TI (asthma* OR wheez*) OR AB (asthma* OR wheez*)
S3 TI ((chronic* or obstruct*) N3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*)) OR AB ((chronic* or obstruct*) N3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*))
S4 TI (COPD or AECOPD or AECB) OR AB (COPD or AECOPD or AECB)
S5 TI emphysema OR AB emphysema
S6 (MH "Bronchiectasis")
S7 TI bronchiect* OR AB bronchiect*
S8 TI kartagener* OR AB kartagener*
S9 TI (ciliary N3 dyskinesia) OR AB (ciliary N3 dyskinesia)
S10 TI (bronchial* N3 dilat*) OR (bronchial* N3 dilat*)
S11 TI bronchoect* OR AB bronchoect*
S12  (MH "Lung Diseases, Interstitial")
S13  (MH "Pulmonary Fibrosis")
S14  TI ((pulmonary* or lung* or alveoli*) N3 (fibros* or fibrot*)) OR AB ((pulmonary* or lung* or alveoli*) N3 (fibros* or fibrot*))
S15  TI (interstitial* N3 (lung* or disease* or pneumon*)) OR AB (interstitial* N3 (lung* or disease* or pneumon*))
S16  TI ((pulmonary* or lung*) N3 (sarcoid* or granulom*)) OR AB ((pulmonary* or lung*) N3 (sarcoid* or granulom*))
S17  TI pneumoconiosis OR AB pneumoconiosis
S18  TI silicosis OR AB silicosis
S19  TI byssinosis OR AB byssinosis
S20  TI berylliosis OR AB berylliosis
S21  TI asbestosis OR AB asbestosis
S22  TI siderosis OR AB siderosis
S23  TI anthracosis OR AB anthracosis
S24  TI ((environment* or occupat* or exposure*) N3 (lung* or pulmonary* or respiratory* or airway*)) OR AB ((environment* or occupat* or exposure*) N3 (lung* or pulmonary* or respiratory* or airway*))
S25  (MH "Hypertension, Pulmonary")
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S27  TI (pulmonary N3 hypertens*) OR AB (pulmonary N3 hypertens*)
S28  (MH "Cystic Fibrosis")
S29  TI (cystic* N3 fibros*) OR AB (cystic* N3 fibros*)
S30  (MH "Lung Transplantation")
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S32  (MH "Lung Diseases")
S33  TI ((lung* or respiratory* or pulmonary*) N3 disease*) OR AB ((lung* or respiratory* or pulmonary*) N3 disease*)
S34  S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33
S35  (MH "Frailty Syndrome")
S36  (MH "Frail Elderly")
S37  TI Frail* OR AB Frail*
S38  TI (fragil* N3 (adult* or elderly or geriatric or patient* or person)) OR AB (fragil* N3 (adult* or elderly or geriatric or patient* or person))
S39  S35 OR S36 OR S37 OR S38
S40  S34 AND S39
S41  S34 AND S39
Search strategies for clinical practice guidelines:

**Medline (Ovid) (2016 to 2022)**

1. exp lung diseases, obstructive/
2. (asthma$ or wheez$).tw.
3. ((chronic$ or obstruct$) adj3 (pulmonary or lung$ or airway$ or airflow$ or bronch$ or respirat$)).tw.
4. (COPD or AECOPD or AECB).ti,ab.
5. emphysema$.tw.
6. exp Bronchiectasis/
7. bronchiect$.tw.
8. kartagener$.tw.
10. (bronchial$ adj3 dilat$).tw.
11. bronchoect$.tw.
12. exp Lung Diseases, Interstitial/
13. exp Pulmonary Fibrosis/
14. ((pulmonary$ or lung$ or alveoli$) adj3 (fibros$ or fibrot$)).tw.
15. (interstitial$ adj3 (lung$ or disease$ or pneumon$)).tw.
16. ((pulmonary$ or lung$) adj3 (sarcoid$ or granulom$)).tw.
17. pneumoconiosis.tw.
18. silicosis.tw.
19. byssinosis.tw.
20. berylliosis.tw.
21. asbestosis.tw.
22. siderosis.tw.
23. anthracosis.tw.
24. ((environment$ or occupat$ or exposure$) adj3 (lung$ or pulmonary$ or respiratory$ or airway$)).tw.
25. exp Hypertension, Pulmonary/
26. Pulmonary Heart Disease/
27. (pulmonary adj3 hypertens$).tw.
28. Cystic Fibrosis/
29. (cystic$ adj3 fibros$).tw.
30. exp Lung Transplantation/
31. (lung$ adj2 (transplant$ or graft$)).tw.
32. Lung Diseases/
33. ((lung$ or respiratory$ or pulmonary$) adj3 disease$).tw.
34. or/1-33
35. (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt.
36. 34 and 35
37. limit 36 to yr="2016 - 2022"
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### CINAHL (EBSCO) database

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| S2  | TI (asthma* OR wheez*) OR AB (asthma* OR wheez*)                        |
| S3  | TI ((chronic* or obstruct*) N3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*)) OR AB ((chronic* or obstruct*) N3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*)) |
| S4  | TI (COPD or AECOPD or AECB) OR AB (COPD or AECOPD or AECB)              |
| S5  | TI emphysema OR AB emphysema                                            |
| S6  | (MH "Bronchiectasis")                                                  |
| S7  | TI bronchiect* OR AB bronchiect*                                        |
| S8  | TI kartagener* OR AB kartagener*                                       |
| S9  | TI (ciliary N3 dyskinesia) OR AB (ciliary N3 dyskinesia)                |
| S10 | TI (bronchial* N3 dilat*) OR (bronchial* N3 dilat*)                     |
| S11 | TI bronchoect* OR AB bronchoect*                                       |
| S12 | (MH "Lung Diseases, Interstitial+")                                    |
| S13 | (MH "Pulmonary Fibrosis+”)                                             |
| S14 | TI ((pulmonary* or lung* or alveoli*) N3 (fibros* or fibrot*)) OR AB ((pulmonary* or lung* or alveoli*) N3 (fibros* or fibrot*)) |
| S15 | TI (interstitial* N3 (lung* or disease* or pneumon*)) OR AB (interstitial* N3 (lung* or disease* or pneumon*)) |
| S16 | TI ((pulmonary* or lung*) N3 (sarcoid* or granulom*)) OR AB ((pulmonary* or lung*) N3 (sarcoid* or granulom*)) |
| S17 | TI pneumoconiosis OR AB pneumoconiosis                                   |
| S18 | TI silicosis OR AB silicosis                                            |
| S19 | TI byssinosis OR AB byssinosis                                          |
| S20 | TI berylliosis OR AB berylliosis                                        |
| S21 | TI asbestosis OR AB asbestosis                                          |
| S22 | TI siderosis OR AB siderosis                                           |
| S23 | TI anthracosis OR AB anthracosis                                       |
| S24 | TI ((environment* or occupat* or exposure*) N3 (lung* or pulmonary* or respiratory* or airway*)) OR AB ((environment* or occupat* or exposure*) N3 (lung* or pulmonary* or respiratory* or airway*)) |
| S25 | (MH “Hypertension, Pulmonary+”)                                       |
| S26 | (MH “Pulmonary Heart Disease”)                                         |
| S27 | TI (pulmonary N3 hypertens*) OR AB (pulmonary N3 hypertens*)            |
| S28 | (MH “Cystic Fibrosis”)                                                 |
| S29 | TI (cystic* N3 fibros*) OR AB (cystic* N3 fibros*)                     |
| S30 | (MH “Lung Transplantation+”)                                           |
| S31 | TI (lung* N2 (transplant* or graft*)) OR AB (lung* N2 (transplant* or graft*)) |
List of hand searched web resources (searches updated as of May 2023):

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<td>• <a href="https://palliaweb.nl/richtlijnen-palliatieve-zorg/richtlijn/copd">https://palliaweb.nl/richtlijnen-palliatieve-zorg/richtlijn/copd</a></td>
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<td>Federation of medical specialists-Diagnostics and treatment of COPD in hospital:</td>
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<td>• <a href="https://richtlijnendatabase.nl/richtlijn/behandeling_copd-">https://richtlijnendatabase.nl/richtlijn/behandeling_copd-</a></td>
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<td>Federation of medical specialists-Diagnostics and treatment of severe asthma:</td>
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<td>• <a href="https://richtlijnendatabase.nl/richtlijn/diagnostiek_en_behandeling_van_ernstig_">https://richtlijnendatabase.nl/richtlijn/diagnostiek_en_behandeling_van_ernstig_</a></td>
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<td>• astma/startpagina_-_ernstig_astma.html</td>
</tr>
<tr>
<td>Greece</td>
<td>EPE (Greek Respiratory Society)</td>
<td>• <a href="https://hts.org.gr/372">https://hts.org.gr/372</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td>University of Crete primary care guidelines:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• <a href="http://www.greekphcguidelines.gr">http://www.greekphcguidelines.gr</a></td>
</tr>
<tr>
<td>Italy</td>
<td>Italian Respiratory Society</td>
<td>• <a href="https://www.sipirs.it/cms/">https://www.sipirs.it/cms/</a></td>
</tr>
<tr>
<td>Belgium</td>
<td>Belgian Respiratory Society</td>
<td>• <a href="https://www.belgianrespiratorysociety.be/nl">https://www.belgianrespiratorysociety.be/nl</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Belgian GP COPD and asthma management guideline:</td>
</tr>
</tbody>
</table>
PRISMA flow diagram for the main database search:

- Electronic database searches (n = 2840)
  - Medline (n = 1041)
  - Cochrane Library (n = 116)
  - EMBASE (n = 1456)
  - CINAHL plus (n = 227)

Records after de-duplication (n = 1799)

Title and abstract screening (n = 1799)

Hand searching (n = 26) → Excluded (n = 1640)

Eligible for full text review (n = 185)

Full text exclusions
- Did not address ERS Statement objectives (n=94)

Included studies (n = 91)
PRISMA flow diagram for the clinical practice guideline search:

Electronic database searches (n = 1321)
- Medline (n = 459)
- CINAHL plus (n = 435)
- TRIP Pro (n = 427)

Records after de-duplication (n = 1261)

Title and abstract screening (n = 1261)

Hand searched websites (n = 15) → Excluded (n = 1066)

Full text review (n = 210)

Full text exclusions
- Did not adequately address frailty (n=205)

Included studies (n = 5)
**Consumer survey**

A consumer survey was conducted with the objective to help inform content for the Statement and identify topics of inquiry needing future attention. First, a small number of trigger questions, worded without scientific jargon, was developed following discussion among Task Force members. Questions were then refined and a draft version piloted with our consumer representative as well as a COPD patient advisory group of European Lung Foundation (ELF). Following minor amendments, a final version was confirmed comprising a simple structure involving 2-3 open ended questions and multiple-choice responses to characterise participant demographics (e.g. age group, gender, country). The surveys were translated into nine languages via the broad multinational representation of our Task Force and professional contacts and uploaded into SurveyMonkey for electronic distribution via ELF. An interview was also conducted with ELF and posted in their monthly consumer newsletter and social media pages to help raise awareness of the initiative. A copy of the English language version of the final survey is supplied below. Ethics approval was deemed unnecessary for this phase of the project.

The focus of the cross-sectional survey and associated outreach activities was to find people living with chronic lung disease who may be affected by frailty and/or their carers. We used a convenience single-stage sampling approach involving online distribution of the anonymous survey internationally with no pre-defined target sample size. It was distributed to members of the ELF consumer network and promoted by members of the Task Force among their direct professional and consumer networks in their respective countries (including our patient representative who is President of the Lung Transplant Patients Union – Padova, Italy). Direct contact with consumer/patient agencies or other societies to facilitate survey completion was not formally undertaken by ourselves or any project partner organisation (to the best of our knowledge), however the snowballing nature of recruitment means we cannot verify all lines of communication that may have been engaged to some extent.

Survey analysis was conducted by summarising characteristics of participants using basic descriptive statistics in Microsoft Excel. No adjustments were made for missing data and no clarification of responses were possible considering the anonymous nature of the survey. No sensitivity or subgroup analyses were planned *a priori* or conducted *post-hoc*. Analysis of open-ended responses was performed via a content analysis framework. Briefly, responses underwent initial coding to identify major themes which were reduced to the minimum number of unique subthemes that represented participant sentiments. Findings were organised into two major categories: ‘deficits’ and ‘needs’, and seven major themes containing various sub-themes. Detailed results of the survey and are presented in the table and figure below.

The survey findings offers descriptive insights regarding the views of patients and their carers regarding issues of frailty in the context of chronic respiratory disease. Some findings were limited due to insufficient or ambiguous text responses or responses that did not relate to the question(s) being asked. It is also very challenging to determine a response rate relative to our target audience, however it is likely to be very low which may affect the external validity of its findings more broadly.
Survey response quotes to the trigger question: "What issues around frailty are important to you?"

<table>
<thead>
<tr>
<th>Theme / subtheme</th>
<th>Participant</th>
<th>Quotes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Public awareness</td>
<td>P216</td>
<td>The attitude of others. E.g. People with even a slight cold are not welcome in my neighbourhood, because I can as a result a serious infection. Some believe that nonsense</td>
</tr>
<tr>
<td></td>
<td>P218</td>
<td>Enlarge awareness among others in the area so that there will be more understanding by accepting your own vulnerability and not shame because you don’t see it on the outside</td>
</tr>
<tr>
<td>Social media</td>
<td>P110</td>
<td>Information and dissemination of information (media) Inclusiveness of patients with regard to research of medicines or medicine</td>
</tr>
<tr>
<td>Community support</td>
<td>P30</td>
<td>How to maintain sufferers as long as physically and mentally capable of working and life in their community. Promotion of health and prevention of chronic pulmonary diseases at earlier age</td>
</tr>
<tr>
<td></td>
<td>P2</td>
<td>Loss of social contacts, the unpredictability of the disease and limited support options</td>
</tr>
<tr>
<td></td>
<td>P22</td>
<td>The hardest thing is to accept that you cannot do what you used to do and to accept help.</td>
</tr>
<tr>
<td>Pain management</td>
<td>P30</td>
<td>How to maintain sufferers as long as physically and mentally capable of working and life in their community. Promotion of health and prevention of chronic pulmonary diseases at earlier age</td>
</tr>
<tr>
<td></td>
<td>P74</td>
<td>Not able to easily carry out routine activities. Coating with chronic pain. The consequences of taking massive drug doses</td>
</tr>
<tr>
<td></td>
<td>P78</td>
<td>Joint / muscle and respiratory pain that do not allow me to carry out a normal life</td>
</tr>
<tr>
<td>Therapies</td>
<td>P70</td>
<td>Fragility for me is to be forced to live attached to oxygen for every movement</td>
</tr>
<tr>
<td></td>
<td>P57</td>
<td>Handling access and treatment options</td>
</tr>
<tr>
<td>Side-effects</td>
<td>P316</td>
<td>Feeling isolated, overload and ever increasing list of medication and having to cope with side effects, lack of information on self-help, difficulty to exercise, lack of pain relief, lack of information on improving my quality of life</td>
</tr>
<tr>
<td>Specialist and GP's</td>
<td>P105</td>
<td>Medical control by general practitioner or specialist. Proper guidance through physical therapist</td>
</tr>
<tr>
<td></td>
<td>P17</td>
<td>More awareness in general practitioners about rare lung disease</td>
</tr>
<tr>
<td></td>
<td>P136</td>
<td>Accessibility of the first line aid (general practitioner)</td>
</tr>
<tr>
<td>Overall support</td>
<td>P12</td>
<td>I do not dare to travel. I am not afraid to die but I hope to get support/help when my time has come.</td>
</tr>
<tr>
<td></td>
<td>P104</td>
<td>Support, both psychological and social and not just medical</td>
</tr>
<tr>
<td></td>
<td>P301</td>
<td>Being able to contact support team if concerned</td>
</tr>
<tr>
<td>Financial assistance</td>
<td>P42</td>
<td>Better supply refer to the participation. Example: By taxi or patient transport to a meeting with friends or family, to cultural events, etc. Life consists not only from medical appointments, physiotherapy and e.g. dialysis centres. A complex for private paths / transports should be possible.</td>
</tr>
<tr>
<td></td>
<td>P129</td>
<td>Financial vulnerability by stacking of healthcare costs (care policies are becoming increasingly expensive, while care package is undressed: less physiotherapy, more personal drug contributions, etc.); financial vulnerability by structural purchasing power loss of disability (no inflation correction in the event of disability benefits, constantly increasing fixed loads)</td>
</tr>
<tr>
<td>Topic</td>
<td>Page</td>
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<td>-------------------------------</td>
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<tr>
<td>Lack of understanding</td>
<td>P66</td>
<td></td>
</tr>
<tr>
<td>Difficulty to carry out daily activities and even walking to fast gait. Fatigue, poor appetite, depression</td>
<td></td>
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<tr>
<td>Pulmonary disease is somewhat 'invisible' so I experience a lack of understanding/sympathy</td>
<td>P14</td>
<td></td>
</tr>
<tr>
<td>More understanding of vulnerability by healthcare staff, especially in hospitals. That you have more questions and worry if you are sick or when it's not going well. Be taken seriously because you know your body well through your illness and the changes notice</td>
<td>P264</td>
<td></td>
</tr>
<tr>
<td>Sometimes I am very tired, for example. Not everyone in my area (working environment) understands that</td>
<td>P148</td>
<td></td>
</tr>
<tr>
<td>General information</td>
<td>P91</td>
<td></td>
</tr>
<tr>
<td>Information, Info about new medication, contact moments of fellow sufferers, explanation use medication, exercise programs, nutrition information</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Which people with pulmonary diseases are more likely to develop fragility? How do fragility affect people with pulmonary diseases?</td>
<td>P41</td>
<td></td>
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<tr>
<td>Need for</td>
<td>P13</td>
<td></td>
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<tr>
<td>Older people with breathing problems should be more empowered with self-monitoring devices</td>
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<tr>
<td>Focus on unambiguous and adequate education/communication.</td>
<td>P21</td>
<td></td>
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<tr>
<td>To increase awareness of frailty in people with lung diseases</td>
<td>P28</td>
<td></td>
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<tr>
<td>I think it is necessary to further investigate the influence of fragility in people with lung disease on the family: Family dynamics, emotional relations, socio-economic impact</td>
<td>P34</td>
<td></td>
</tr>
<tr>
<td>Improvement needed</td>
<td>P72</td>
<td></td>
</tr>
<tr>
<td>Facilitate access to care</td>
<td></td>
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<tr>
<td>The speed in being able to perform checks and visits, availability and courtesy of the doctors</td>
<td>P86</td>
<td></td>
</tr>
<tr>
<td>Make sure diagnosis is accurate. Make appointments easy to get</td>
<td>P325</td>
<td></td>
</tr>
<tr>
<td>Fear of infections</td>
<td>P3</td>
<td></td>
</tr>
<tr>
<td>How can we protect ourself against bacteria and viruses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>How to prevent infections when being frail because of pulmonary disease</td>
<td>P26</td>
<td></td>
</tr>
<tr>
<td>I feel very fragile. Even with a simple cold, I'm afraid of worsening my condition. We need total support and information. We need to accept, face, disease, but at the same time don't feel sick</td>
<td>P75</td>
<td></td>
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<tr>
<td>Fear</td>
<td>P9</td>
<td></td>
</tr>
<tr>
<td>Learning to deal with panic and fear, especially in the initial phase.</td>
<td></td>
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<tr>
<td>Fatigue</td>
<td>P68</td>
<td></td>
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<tr>
<td>Loneliness, anxiety, fear for the future</td>
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<tr>
<td>Permanent physical fatigue</td>
<td>P73</td>
<td></td>
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<tr>
<td>Fail to complete the daily tasks due to fatigue</td>
<td>P76</td>
<td></td>
</tr>
<tr>
<td>Isolation</td>
<td>P7</td>
<td></td>
</tr>
<tr>
<td>Still count in and for society. Mobility, movement freedom</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No more belong to society</td>
<td>P93</td>
<td></td>
</tr>
<tr>
<td>Social isolation because too many people still ignore what it means to live with chronic lung disease. Secondary care, in my case, is absolutely brilliant. But there is no primary care/community follow up.</td>
<td>P330</td>
<td></td>
</tr>
</tbody>
</table>
Coding tree of open-ended responses
Dear participant,

We would like to understand your experience of living with frailty and a chronic lung disease such as chronic obstructive pulmonary disease, asthma, bronchiectasis or pulmonary fibrosis. Patients, relatives and carers of people with chronic lung diseases are invited to participate. By providing your insights, you will help identify ways to improve awareness and management of frailty in respiratory healthcare, and help shape future research to overcome challenges associated with these issues.

This survey is part of work by the European Lung Foundation and the European Respiratory Society Frailty Task Force which aims to improve our understanding of the impact of frailty on the lives of people affected by chronic lung diseases.

Frailty has been described as a state of vulnerability where people become more affected than expected following small declines in their health, for example after a mild infection. Having frailty may also make it harder to recover or ‘bounce back’ afterwards. People with frailty may walk at a slower speed, or experience greater difficulties completing day-to-day tasks than people without frailty. Frailty is more common in people with multiple health problems and those of older age.

If you or someone you care for have been affected by chronic lung disease and frailty, we would really like to hear from you. By completing this short survey, you will be able to tell us about the issues of greatest importance to you to ensure our work focuses on the needs of people most impacted by frailty.

All suggestions will be considered and some may be voted on at a later date – for example if we need to reduce a long list of topics down to a shorter priority selection. All survey responses will remain confidential (not shared with anyone outside the research team), and you will not be required to provide personal details (unless you wish to leave an email address for future contact). The survey is expected to take approximately 5 minutes to complete and will close on June 30th, 2021.

If you have any questions, please don’t hesitate to contact a member of the team.

Thank you very much for helping.
We plan to work on a range of issues relevant to frailty in people with chronic lung diseases. The following list of topics will already be covered by our team of healthcare professionals, researchers and patient representatives:

- How well is frailty currently included in lung health guidelines?
- Which people with lung disease are likely to develop frailty?
- How does frailty impact people with lung disease?
- How can we best support people with frailty and lung disease? This will include treatments such as medications, exercise, nutritional support and psychological/social support.
- What future research do we need to do in this area?
- How can we increase awareness of frailty in people with lung disease?

We would now like you to think about how frailty has affected you or someone you know with chronic lung disease.

Q1: What issues related to frailty are important to you? We will add new topics to our work plan based on feedback from patients and carers.

Please type into the free text box below in your preferred language.

Q2: Do you have any other comments you would like to share with our team about this project?

Please type into the free text box below in your preferred language.

Q3: Are you completing this questionnaire as:
- An individual with a chronic lung disease
- A family member/carer of someone with a chronic lung disease
- A staff/volunteer representative of a patient organisation
- Other (please provide details) [free text box option]

Q4: Are you:
- Male
- Female
- Other
- Prefer not to say

Q5: What age are you?
- Under 18
Q6: In what country do you live?
[Drop down list of countries]

Q7: Further information (optional)
If you would like to be informed of the progress of this work or have an interest in being contacted for future research regarding frailty in people with chronic lung disease, please type your email into the box below:

[free text box]

Thank you for taking the time to help us with this work.
Frailty is when a person has difficulty overcoming even small changes in their health. People with frailty often find it harder to ‘bounce back’ from illness or injury.

People with chronic lung conditions are twice as likely to develop frailty.

This infographic shows what we know so far about frailty in adults with chronic lung disease. It was prepared by an expert Task Force of the European Respiratory Society and is not intended as a general recommendation.

<table>
<thead>
<tr>
<th>What is known about frailty in adults with chronic lung disease?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frailty impact</strong></td>
</tr>
<tr>
<td>Frailty increases risk of poor health &amp; adverse events (e.g. hospital admission)</td>
</tr>
<tr>
<td><strong>Identifying frailty</strong></td>
</tr>
<tr>
<td>Validated, standardized tools exist to assess frailty which can help with accurate monitoring</td>
</tr>
<tr>
<td><strong>Acting on frailty</strong></td>
</tr>
<tr>
<td>The identification of frailty can be used to direct best practice care</td>
</tr>
<tr>
<td><strong>Exercise</strong></td>
</tr>
<tr>
<td>Exercise can address some of the physical parts of frailty</td>
</tr>
</tbody>
</table>

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