
















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

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Shareable abstract (@ERSpublications)

A world first, this European Respiratory Society statement summarises the state of the science on understanding and managing frailty in adults with chronic respiratory disease <https://bit.ly/436PgDq>

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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 prerequisite 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 underrepresented 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.

Introduction

Frailty is a treatable trait of relevance to people with various chronic respiratory diseases, especially those with severe 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

BOX 1 Summary of key statements

- Frailty is a multidimensional syndrome characterised 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 underrepresented 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 comorbidities 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.

specifically on the intersection between frailty and chronic respiratory disease is only lately 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 of and risk factors for frailty; to review clinical management options (including comprehensive geriatric care, rehabilitation, nutrition,

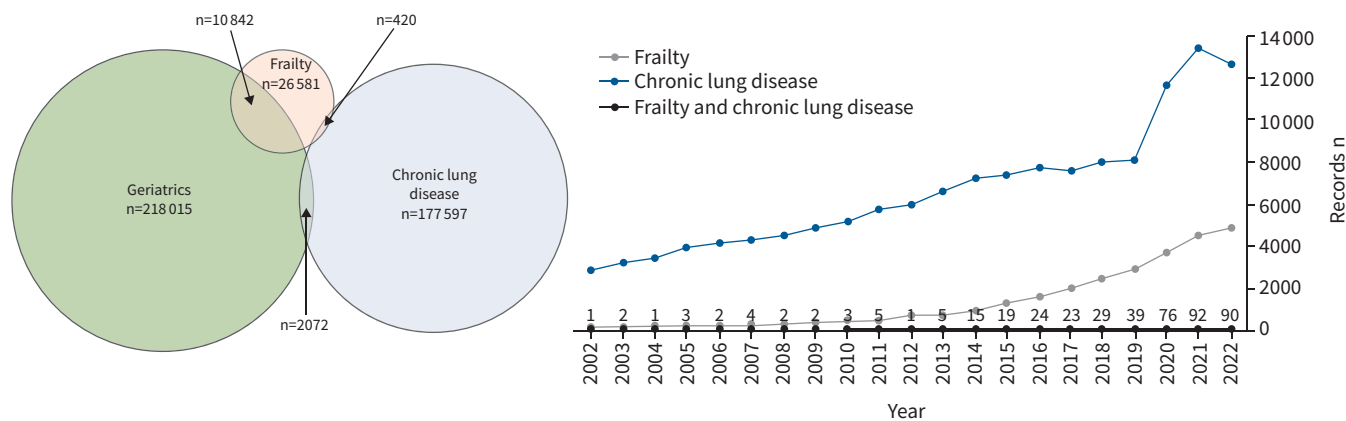


FIGURE 1 Overview of database records related to chronic lung disease and frailty. Sources: PubMed terms “(chronic lung disease) and frailty”; PubVenn, available at <https://pubvenn.appspot.com/>, accessed April 2023.

pharmacological and psychological therapies); and to identify evidence gaps and priority areas for future research.

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 genders and career stages, and a patient representative was appointed with assistance from the European Lung Foundation (ELF). The scope of work contained within the initial proposal to the 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” [4] (difficulty or dependency to carry out essential activities for independent living) [5]. While different dimensions of frailty are commonly described in existing literature (*e.g.* “physical frailty” [2], “cognitive frailty”, “social frailty”) [6], these can all be encapsulated under the broader “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 described previously [2]. Any studies examining frailty within this more broad umbrella concept (which includes the more specific dimensions) were therefore eligible for inclusion.

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 supplementary material and summarised herein.

A medical librarian performed searches of MEDLINE (Ovid), Embase (Ovid), Cochrane Library and CINAHL (EBSCO) from inception to 5 April 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, CINAHL 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 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; nor were studies published in languages other than the six spoken by the multinational ERS task force.

Small working groups (between one and three 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

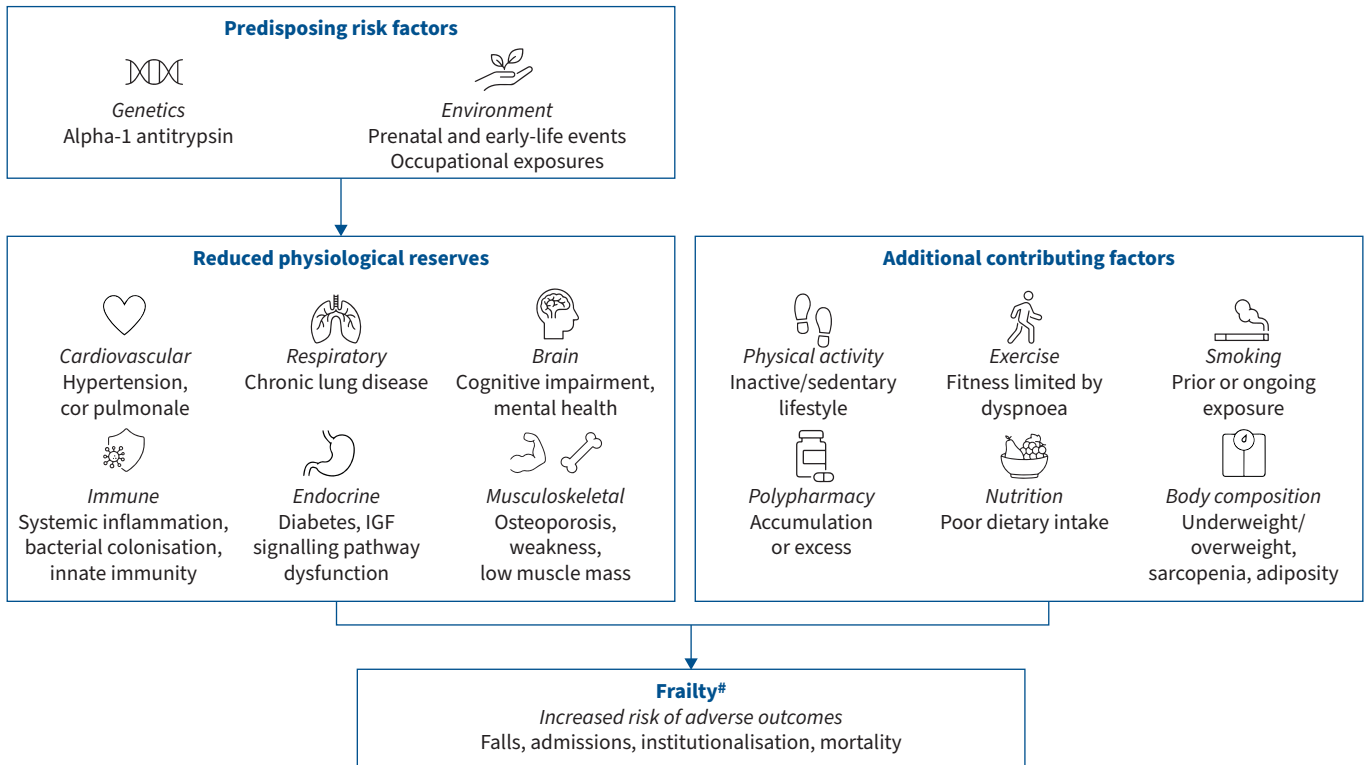


FIGURE 2 Summary of the complex interplay between factors that can contribute to the development of frailty in people with chronic respiratory disease. IGF: insulin-like growth factor. #: social determinants of health external to the individual potentially contribute to the development of frailty, and, 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 acknowledges them as relevant.

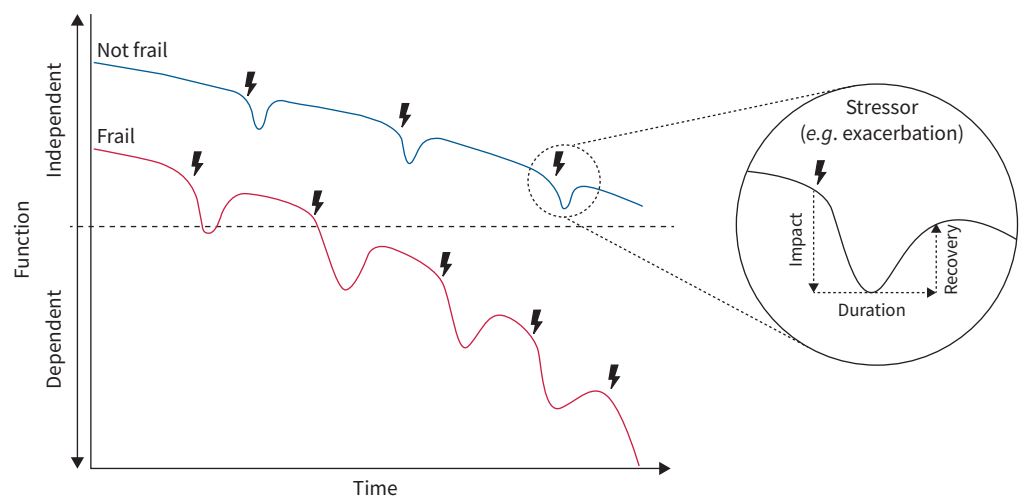


FIGURE 3 Hypothetical trajectory models of function in people with chronic respiratory disease who have and do not have frailty. Each drop in function (moving from left to right) occurs in response to a stressor event such as an acute respiratory exacerbation. Frailty is associated (inset) with declines 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. Reproduced and modified from [3] with permission.

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 members to derive consensus metrics (percentage agreement). Results are presented in the supplementary material.

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 (supplementary material) was translated into nine languages and distributed electronically *via* ELF. In addition, an interview was 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* 1) a summary visual synopsis; 2) detailed coding tree structure; and 3) 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 supplementary material.

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 [7, 8]. However, none 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 international guidelines up to 2022 [9]; however, the recent 2023 report update [10] 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 COPD guideline mentions frailty among a list of factors that could be used to assist with prognostication for people with stable disease [11]. Australia and New Zealand's COPD guidelines document ("the COPD-X Plan") [12] was 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 of 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. However, no specific practice recommendations regarding frailty were made.

In asthma, frailty was not mentioned in the Global Initiative for Asthma international guidelines [13]. 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 [14].

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 [15] and a recent International Society for Heart and Lung Transplantation international consensus document for selection of lung transplant candidates states that frailty assessment should be considered part of a comprehensive transplant evaluation in recognition of its negative impact upon waitlist and post-transplant mortality [16].

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 co-workers (referred to as the frailty phenotype). The frailty phenotype quantifies five conceptual domains: wasting, slowness, weakness, low activity and exhaustion and defines frailty as having deficits in at least three of those [17]. The second model conceptualises frailty as an accumulation of deficits and is most commonly operationalised 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 [18].

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 considers 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 [19]) is used by task force members due to its relative simplicity to implement within electronic medical record systems [20]. Alternatively, in preventive or treatment environments, a physical frailty measure such as the frailty phenotype or Short Physical Performance Battery (SPPB) [21, 22] may offer advantages due to 1) the smaller number of items needing to change to affect frailty status; 2) 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 3) 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 [32, 33]. Conceptually, operational measures of frailty domains should 1) quantify vulnerability to stressors and 2) be discriminative within the population of interest and 3) 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 frailty phenotype uses the Minnesota Leisure Time Activity Scale [34] 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 recognised 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, 35–41]. 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 exist regarding reliability. Although derived from observational studies, it does appear that physical frailty is dynamic and responsive to interventions [42–44]. 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.

Risk factors for the development of frailty in chronic respiratory disease

The putative mechanisms causing frailty are multiple, reflecting the complexity of the ageing process [45]. These mechanisms, along with physical inactivity, malnutrition, and age-related diseases (*e.g.* osteoporosis, hypertension) either individually or in combination, result in physiological perturbations including chronic inflammation, immune senescence, endocrine dysregulation and muscle dysfunction and sarcopenia [41]. There is probably a bidirectional interplay between frailty and chronic disease; frailty impacts chronic disease, and chronic disease increases the risk of frailty. Furthermore, 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 [46]. Behaviours such as poor diet, smoking and physical inactivity, as well as the impact of comorbidities (often multimorbidity) may impose detrimental effects to a person’s ageing 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 of 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.

TABLE 1 Commonly used instruments to evaluate frailty in adults with chronic respiratory disease[#]

	Domains assessed	Method of frailty domain assessment	Score range	Frailty cutpoints [¶]	Time to complete	Need for specialised equipment?	Need for specialised personnel?	Expected to respond to intervention?
Fried frailty phenotype [17, 23]	Nutritional status, physical activity, mobility, strength and energy	Physical tests for gait and grip strength; self-report assessment of weight loss, exhaustion and low activity	Range: 0–5	Dichotomous*: frail ≥ 3 , not frail 0–2 Not frail 0, pre-fail 1–2, frail ≥ 3	10–15 min	Yes	No	Yes
Short Physical Performance Battery [22]	Physical activity, mobility, strength and energy	Physical tests of balance (tandem, semi-tandem, side-by-side), gait speed and strength (sit-to-stand five times)	Range: 0–12	Dichotomous* (various cutpoints proposed in the literature): frail ≤ 7 or ≤ 9 or ≤ 10 Categorical (various cutpoints proposed in the literature): not frail 12, pre-fail 10–11, frail ≤ 9 or not frail 11–12, pre-fail 8–10, frail ≤ 7	5–10 min	No	No	Yes
Clinical Frailty Scale [24]	Nutritional status, physical activity, mobility, strength, energy, cognition, mood and social relations or social support	Interview-based assessment and physician-assigned score of 1 (robust health) to 7 (complete functional dependence on others)	Range: 0–7	Various definitions Categorical: not frail 0–3, apparently vulnerable 4, mildly frail 5, severely frail 6–7 Dichotomous*: frail: ≥ 5	<3 min	No	Yes Clinical judgement	Yes
Frailty index [19, 25]	Distinct diseases and their consequences including nutritional status, physical activity, mobility, strength, energy, cognition, mood and social relations or social support	Chart review or survey that enumerates the number of diseases, their clinical and laboratory manifestations and consequences, and risk factors	Range: varies widely depending on specific measure, but includes ≥ 30 items for a valid frailty index [25] Continuous or categorical	A cutpoint ≥ 0.25 is generally used to define frailty	20–40 min	No, but does require access to full medical record	Yes Personnel must be able to navigate a medical chart to identify diseases and relevant laboratory investigations	Possibly

Continued

TABLE 1 Continued

	Domains assessed	Method of frailty domain assessment	Score range	Frailty cutpoints [¶]	Time to complete	Need for specialised equipment?	Need for specialised personnel?	Expected to respond to intervention?
Edmonton Frail Scale [26]	Cognition, general health, functioning, social support, medication use, nutrition, mood continence, physical performance	Self-report for 8 domains; physical performance: “timed get-up-and-go” [30], cognitive performance “clock test” [31]	Range: 0–17	Categorical: severe frailty ≥ 12 , moderate frailty 10–11, mild frailty 8–9, apparent vulnerability 6–7, not frail ≤ 5	10–15 min	Yes	No	Yes
FRAIL scale [27]	Fatigue, resistance, ambulation, illness, loss of weight	Self-report	Range: 0–5	Categorical: frail ≥ 3 , pre-frail 1–2, robust 0	3–5 min	No	No	Possibly
Kihon checklist [28, 29]	Instrumental, social activities of daily living, physical strength, nutritional status, oral function, cognitive status, depression risk	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)	Range: 0 (no frailty) to 25 (severe frailty)	Robust (0–3), pre-frail (4–7), frail (8–25)	5–10 min	No	No	Yes

FRAIL: fatigue, resistance, ambulation, illnesses and loss of weight. [#]: instruments in this table vary widely, including measures of physical frailty (e.g. frailty phenotype, Short Physical Performance Battery), clinician-based judgements (e.g. Clinical Frailty Scale), cumulative deficit measures (e.g. frailty index) and measures that consider factors external to the patient such as social support (e.g. Edmonton Frailty Scale). Different measures and cutpoints used to define frailty will influence a measure’s relative sensitivity and specificity. More detailed discussion of the importance of such factors is provided in the Assessment methods section; [¶]: for most instruments used, various cutpoints and scales have been used to define frailty; [†]: defining frailty using a dichotomous cutpoint presumes frailty to be an “all-or-nothing” state.

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, predisposing 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 [47]. 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 whom 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 [48].

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 [49], lung transplantation candidates/recipients [56], ILD [59] and asthma [63] reveal that 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.

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) [65]; 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 follows.

COPD

Frailty in COPD has been associated with accelerated disease progression and increased symptom severity [48, 50, 63, 66–76], use of medications and symptom burden [48, 77–79]. Particularly in more severe stages of COPD, frailty has negative impacts on mobility and daily functioning [80]. It increases the risk of acute exacerbations of COPD (AECOPD) [50, 74, 80–83] and may relate to higher levels of C-reactive protein, which is, in turn, associated with increased exacerbations, poorer lung function and mortality [84, 85]. Moreover, COPD exacerbations in people with frailty carry an increased (6.3-fold) risk of requiring mechanical ventilation compared to people without frailty [81], and the presence of frailty during COPD exacerbations has been suggested to associate with increased risk of readmission and/or mortality [86]. People with COPD and frailty have a higher rate (adjusted hazard ratio 1.6, 95% CI 1.1–2.5) and longer duration of hospitalisations (+8 days, 95% CI 4.4–11.6 days) and worse quality of life (adjusted hazard ratio 1.4, 95% CI 0.97–2.0) compared to people without frailty [87].

The worse health status and lower quality of life [77, 80, 87, 88] 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 [59, 68, 71, 77, 80, 87]. This can be further complicated if associated

TABLE 2 Prevalence estimates for frailty among relevant studies

First author, year [reference]	Study design	Country	Sample size	Disease	Frailty assessment method	Prevalence estimate
MARENGONI, 2018 [49]	Systematic review of cross-sectional and longitudinal studies	Various	27 studies involving 60 278 individuals	COPD: 19 studies involving community-dwelling persons; 8 involving hospitalised or outpatient samples	Seven different instruments	Pooled prevalence 20%, 95% CI 15–24%; range 9–64%
CHIN, 2020 [50]	Observational cohort	Canada	50 hospitalised patients	COPD exacerbation; mean age 71–76 years across groups	Clinical Frailty Scale	58% mild/moderate/severe frailty
DIAS, 2020 [51]	Cross-sectional cohort	Brazil	153 community-dwelling patients	COPD; mean age 67–70 years across groups; mean FEV ₁ 44–61.5% pred	FRAIL scale	50.3%
TER BEEK, 2020 [52]	Cross-sectional analysis of observational longitudinal cohort	The Netherlands	57 patients commencing pulmonary rehabilitation	COPD; mean age 61.2 years; mean FEV ₁ 36.1% pred	FP [17] and EFIP [64]	28% <i>via</i> FP 83% <i>via</i> EFIP
GEAPHINE, 2021 [53]	Observational cohort	Canada	44 patients commencing home-based rehabilitation	COPD with chronic respiratory failure; mean age 66 years; mean FEV ₁ 33% pred	FP [17]	43%
NAVAL, 2021 [54]	Cross-sectional cohort	Spain	127 patients	COPD; mean age 66.5 years;	FP [17]	24%
LEE, 2022 [55]	Prospective longitudinal population-based observational cohort	Singapore	1162 community-dwelling adults	COPD; mean age 68.3 years; mean FEV ₁ 94.5% pred	Modified version of FP (detailed description available in publication)	6.8%
MONTGOMERY, 2020 [56]	Systematic review	Various	10 studies involving 2388 patients	Lung transplant candidates/recipients	Five different instruments	0–58%
WILSON, 2016 [57]	Retrospective cohort	USA	102 patients	Lung transplant recipients; mean age 57 years	Frailty index [24]	45%
VARUGHESE, 2021 [58]	Retrospective cohort	Canada	258 patients	Lung transplant recipients; mean age 52.8 years	Frailty index [24]	Mean±SD score 0.28±0.09
GULER, 2020 [59]	Review	Various	9 studies involving 1490 patients	Various ILDs including some listed for/underwent lung transplantation	Four different instruments	12–55%
MILNE, 2017 [60]	Prospective cohort	USA	129 patients attending a specialised clinic	Fibrotic ILD; mean age 69 years; mean FEV ₁ 75.9% pred; mean D _{LCO} 48.6% pred	Frailty index (cut-off score >0.21) [24]	50%
FAROOQI, 2021 [61]	Prospective cohort	Canada	463 patients	Fibrotic ILD; mean age 68 years; mean FEV ₁ 78% pred; mean D _{LCO} 52% pred	Modified FP [17] criteria	26%
KUSUNOSE, 2021 [62]	Cross-sectional observational cohort	Japan	69 patients	Asthma; mean age 69.4 years	Kihon checklist [28, 29]	14.5%
LANDRÉ, 2020 [63]	Cross-sectional cohort	France	12 345 community-dwelling adults	Asthma (self-reported); mean age 69.8 years	Adapted (self-reported) version of FP [17]	13%

FEV₁: forced expiratory volume in 1 s; FRAIL: fatigue, resistance, ambulation, illnesses and loss of weight; FP: frailty phenotype; EFIP: Evaluative Frailty Index for Physical Activity; ILD: interstitial lung disease; D_{LCO}: diffusion capacity of the lung for carbon monoxide.

cognitive impairment is present [89]. People with COPD and frailty demonstrate lower physical activity levels than those without frailty [42, 63, 73, 74, 76, 78, 90–93]. Furthermore, people with COPD who engage in lower physical activity have increased exacerbations, dyspnoea and depression [60, 76, 80, 88, 94, 95]. Frailty is also associated with sarcopenia, fatigue and risk of falls in people with COPD [96–98]. Even after lung transplantation in very severe COPD, frailty negatively affects quality of life as well as mortality [99].

Qualitative research [100] 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 [101]. Perhaps related to this, people with respiratory disease and frailty tend to report increased anxiety and depression symptoms compared to those without frailty [42, 53, 54, 102]. There are growing reports of associations between frailty and depression [54, 103]. Frailty may also compound existing issues relating to social isolation and loneliness that exist in chronic respiratory disease [104]. 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 [105] and increased risk of hospital admissions [106–108], 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 [3, 65, 66, 75, 109, 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 (hazard ratio 1.34, 95% CI 1.02–1.81; $p < 0.05$) [109]. One explanation is that frailty is indicative of multiple comorbidities (*e.g.* COPD, cancer, connective tissue disease and diabetes) that significantly increase mortality risk [42, 59, 82, 111]. Nonetheless, in a large population-based cohort study, frail COPD participants had a four-fold higher mortality risk than nonfrail COPD participants (hazard ratio 4.03, 95% CI 1.22–13.30; $p = 0.022$), even after accounting for disease severity (forced expiratory volume in 1 s % predicted) and differences in number of comorbidities [72].

Interstitial lung disease

Frailty in ILD is considered an independent risk factor for hospital admissions and mortality, including pre- and post-lung transplantation [59]. Observational studies in ILD have shown frailty is associated with dyspnoea severity, reduced muscle mass, a two-fold increase in hospitalisation, prolonged hospital stay, reduced quality of life, and mortality in people with ILD [60, 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 [61], including inpatient mortality in hospitalised 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 generalisable 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 multicentre, prospective cohort study, investigators found that pre-transplant frailty was prevalent (28% *via* frailty phenotype) and independently associated with both disability and waitlist mortality (adjusted hazard ratio 3.0 (95% CI 1.8–5.1) and 1.38 (95% CI 1.01–1.9) per standard deviation worsening in SPPB and frailty phenotype, respectively) [116]. Furthermore, a single-point worsening in pre-operative SPPB or frailty phenotype, even among patients without clinical frailty levels, is associated with a 20–50% increased mortality risk (adjusted hazard ratio 1.2 (95% CI 1.1–1.3) and 1.5 (95% CI 1.2–1.6) for SPPB and frailty phenotype, respectively). This underscores the increased risk of untoward outcomes even among individuals with pre-clinical, 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, rehospitalisation and increased mortality following lung transplantation [102, 117–120].

The acute and predictable physiological 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 [43, 44]. Second, new physical frailty commonly emerges after transplant and, when it does, is associated with rehospitalisation, poorer health-related quality of life, and death [99, 117]. Lastly, frailty (either before or after transplant) is reversible through targeted exercise and nutrition interventions (refer to the sections on rehabilitation and nutritional management) [85, 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 tumour 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 pre-operative 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 3 years after transplant [99]. Taken as a whole, these findings highlight that frailty is common and associated with poor outcomes before and after transplant. They also suggest that 1) at least a component of pre-operative physical frailty is attributable to end-stage lung disease; 2) peri- and post-operative events can induce frailty after transplant; and 3) targeted interventions proven in nontransplant 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 the 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 [127, 128]. 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

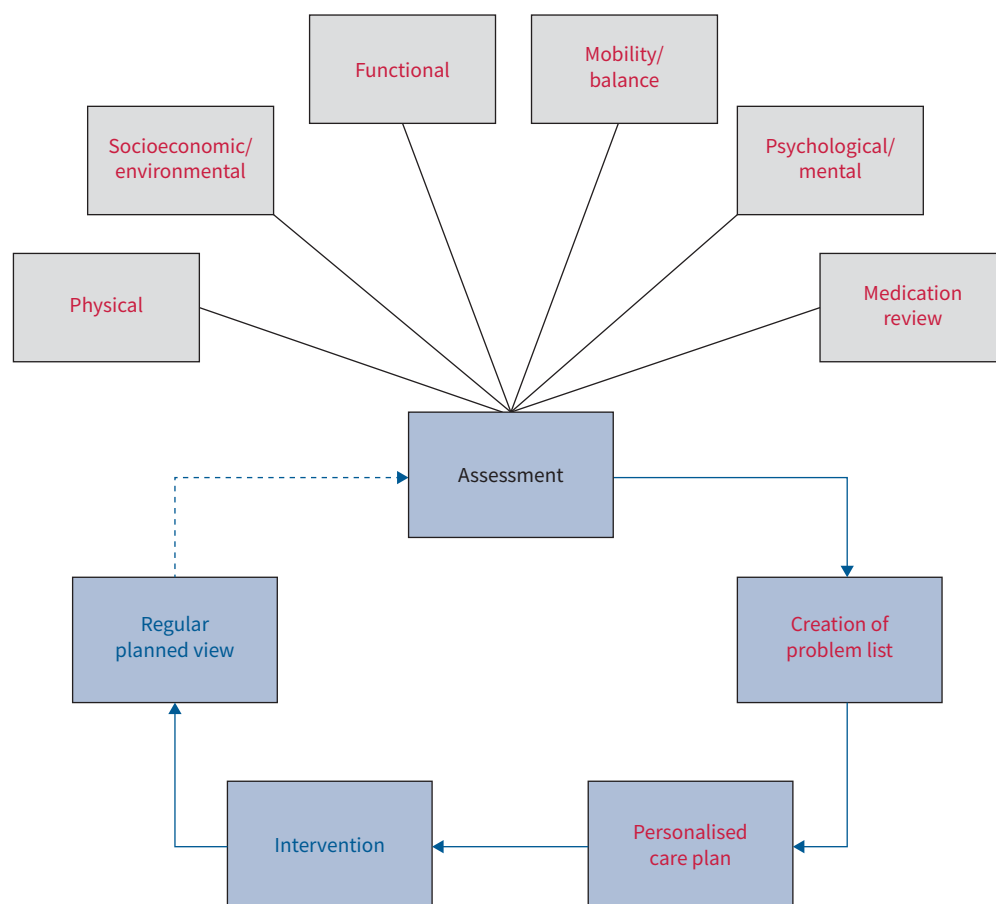


FIGURE 4 Overview of Comprehensive Geriatric Assessment. Reproduced from [126] with permission.

activity or exercise training [8, 129]. 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.

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 [130], or oncogeriatrics for frail patients with cancer [131]). In addition, recommendations have been developed recently to provide the principles of geriatric care and CGA to people who are frail who are living in the community [132]. This model of care might have particular applicability for patients with chronic respiratory disease, irrespective of the setting in which they are evaluated. In fact, respiratory care is already characterised by the multidisciplinary nature 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 [83], 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 [133] and de-prescribing potentially harmful agents, particularly in vulnerable elderly individuals [134], 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 [135]. 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 de-prescribing.
- 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.
- 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 [135, 136]. 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 published previously [14].

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 are 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 the vitamin D analogue alfacalcidol, did show improvement in subdomains of physical performance, muscle strength or body composition [137]. Bone mineral density is another outcome which tended to improve by hormonal therapy in clinical trials [138]. Other agents may have particular benefit in frail individuals with certain comorbidities, such as ghrelin in case of cachectic COPD, metformin in case of diabetes mellitus or angiotensin-converting enzyme (ACE) inhibitors in case of hypertension [139]. While polypharmacy is common in patients with COPD [140, 141], by contrast, evidence-based medications can be underprescribed in people who are frail [142]. Examples include osteoporosis treatment such as calcium and vitamin D supplementation, ACE inhibitors for chronic heart failure or ischaemic heart disease and β -blockers for stable systolic heart failure [142]. 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 optimisation [136]. 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 [143]. Other novel anabolic agents such as selective androgen receptor modulators [144], and ghrelin mimetics are still under investigation to tackle muscle and bone loss [139].

Since ghrelin increases appetite and body weight, promotes growth hormone secretion and reduces inflammation (*e.g.* interleukin-1 β , interleukin-6 and tumour necrosis factor- α) [139], 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 nontailored randomised clinical trials so far [145].

In summary, while various pharmaceutical agents target potentially important biological frailty pathways, more research is needed to make recommendations for clinical practice [78]. In general, several tools have been developed to assist clinicians with (de-)prescribing in frail older people [146–149].

Rehabilitation interventions for frailty in people with chronic respiratory disease

During stable disease

Exercise-based pulmonary rehabilitation programmes can improve exercise performance, muscle strength and symptoms of dyspnoea and fatigue in patients with chronic respiratory diseases, which are key determinants of frailty [150]. Self-management and multidisciplinary education components of pulmonary rehabilitation may further improve independence and reduce frailty [150]. A summary of key findings related to the role of pulmonary rehabilitation in the management of frailty is presented in this section. A more comprehensive report has been published recently [151].

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. >60% of these frail patients no longer met Fried frailty phenotype criteria at programme end, demonstrating that physical frailty is reversible [42]. 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 [152, 153]. 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 nonfrail patients. A more pronounced decline during the 6 months after the programme was also observed, highlighting the need for adequate follow-up [154]. Furthermore, among 47 patients with COPD and chronic respiratory failure in Canada, all on long-term oxygen therapy or noninvasive ventilation, an 8-week home rehabilitation programme enhanced health-related quality of life, fatigue, anxiety and depression only in the frail patients (Fried criteria [17]), while exercise and functional performance improved in both groups [155].

While patients with frailty may gain most benefit from pulmonary rehabilitation, they also have increased odds for programme noncompletion [42], 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 [100]. 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 [155] and the use of mobile or telehealth to optimise programme adherence is worthy of further study.

Based on the available evidence, BRIGHTON *et al.* [156] reflected on how exercise-based approaches may be better attuned to frailty in COPD. Five key principles were identified: building trusting relationships; creating a shared understanding of priorities; individualising 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 [157].

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 that redressing many of these deficits, and indeed reversing frailty *via* rehabilitation strategies can be challenging.

Limited data suggest 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-SÁNCHEZ *et al.* [74] randomised 58 older Spanish inpatients (mean age >75 years) with 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. 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 that 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 whom many were likely to have met frailty criteria [83]. 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 out of 150 patients listed for transplantation underwent combined exercise training (90 min, three times per week) [158]. 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 frailty phenotype scores were observed among lung transplant candidates who participated in a pilot home mobile health intervention over 8 weeks [85].

Post-transplant, COURTWRIGHT *et al.* [117] followed a cohort of transplant recipients referred to either an inpatient facility (n=26) or outpatient rehabilitation (n=83). Among those directed to outpatient rehabilitation, frail patients showed substantial improvements in SPPB scores over 6 weeks (median +6 points), such that 30 out of 35 were no longer frail at discharge. The mobile health intervention studied by SINGER *et al.* [85] was also piloted in 18 patients post-transplantation, who reported that 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.

Nutritional management of frailty in chronic respiratory disease

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 [99, 159–161]. 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 healthcare settings and contexts (*e.g.* community-dwelling *versus* hospital *versus* rehabilitation). Thus, in spite of limited availability of data, in some subgroups of a frail chronic respiratory disease population, 17–49% have been found to be malnourished [52, 162], whereas in the general chronic respiratory disease population the prevalence is established to be 17–30% [163, 164].

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 [165]. 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. Furthermore, 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 improve muscle mass is ensuring sufficient essential amino acids in the diet [173, 174]. Resistance training stimulates increases in muscle mass, inhibits muscle breakdown and stimulates muscle sensitivity to dietary proteins [175, 176]. 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 [177–179].

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 [52, 166]. Differentiating between nutrition diagnoses is crucial to inform individualised nutritional management plans in accordance with (inter)national guidelines [180, 181]. While the specific aims of such plans can differ widely between patients and different chronic respiratory diseases, common principles among this patient group include [172, 182]:

- maintaining or improving nutritional status;
- maintaining or improving muscle mass;

TABLE 3 Common nutrition diagnoses in chronic respiratory disease

	Description	Criteria
Malnutrition	“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” [166]	GLIM criteria [167]: diagnosis requires at least one phenotypic and one aetiological criterion. Severity is determined based on phenotypic criterion Phenotypic: weight loss, BMI, reduced muscle mass Aetiological: reduced food intake or assimilation, disease burden/inflammatory condition
Cachexia	Cachexia or “pulmonary cachexia” is considered a subcategory of malnutrition with inflammation in chronic disease [166]: “a complex metabolic syndrome associated with underlying illness and characterised by loss of muscle with or without loss of fat mass” [168]	No specific criteria are available. However, patients with cachexia meet the GLIM criteria [167] for malnutrition related to chronic disease with inflammation
Sarcopenia	“A progressive and generalised skeletal muscle disorder that involves the accelerated loss of muscle mass and function” [169]	EWGSOP 2 criteria [169] Muscle strength Muscle quantity/quality Severity is determined based on physical performance
Overweight	“Excessive fat accumulation that may impair health” [170]	BMI (≥ 25 and < 30 kg·m ⁻²) [170]
Obesity	“A pathologically increased fat mass, which is associated with an increased health risk” [171]	BMI (≥ 30 kg·m ⁻²) [170]

GLIM: Global Leadership Initiative on Malnutrition; BMI: body mass index; EWGSOP 2: European Working Group on Sarcopenia in Older People 2018. Reproduced with permission [172].

- 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 an individual’s ability to optimise protein/energy intake and therefore enhance the role for good nutritional management to help manage (or even prevent) frailty [52]. 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. The very few studies to date have yielded limited evidence to inform practice [85, 154, 155, 183, 184]. 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 programmes that include nutritional management have shown promise to improve frailty status [155, 184]. Systematic reviews of studies that evaluate multidisciplinary interventions including nutritional management in frail older populations have shown similar effects [159, 185].

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 [42, 155]. This work echoes existing evidence supporting the role of pulmonary rehabilitation in reducing anxiety and depression symptoms in people with COPD [186], 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) [71] 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 programme in 100 people with chronic respiratory disease (majority with frailty) found that the intervention was associated with increased pharmacological treatment of anxiety and depression [187]. Although subsequent impact on patient-reported psychological symptoms was not measured, this approach illustrates how a structured comorbidity schema for screening and monitoring common coexisting 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 [9].

For individuals with more complex psychological needs, specialist support and provision of effective pharmacological and psychological interventions for anxiety and depression may be required [188]. However, given known hesitations around proactively seeking additional support within people with respiratory disease and frailty [100], 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 [189], exploration of the role of these services in the context of frailty has been suggested [82]. 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 supplementary material. 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).

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.

Additionally, participants 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

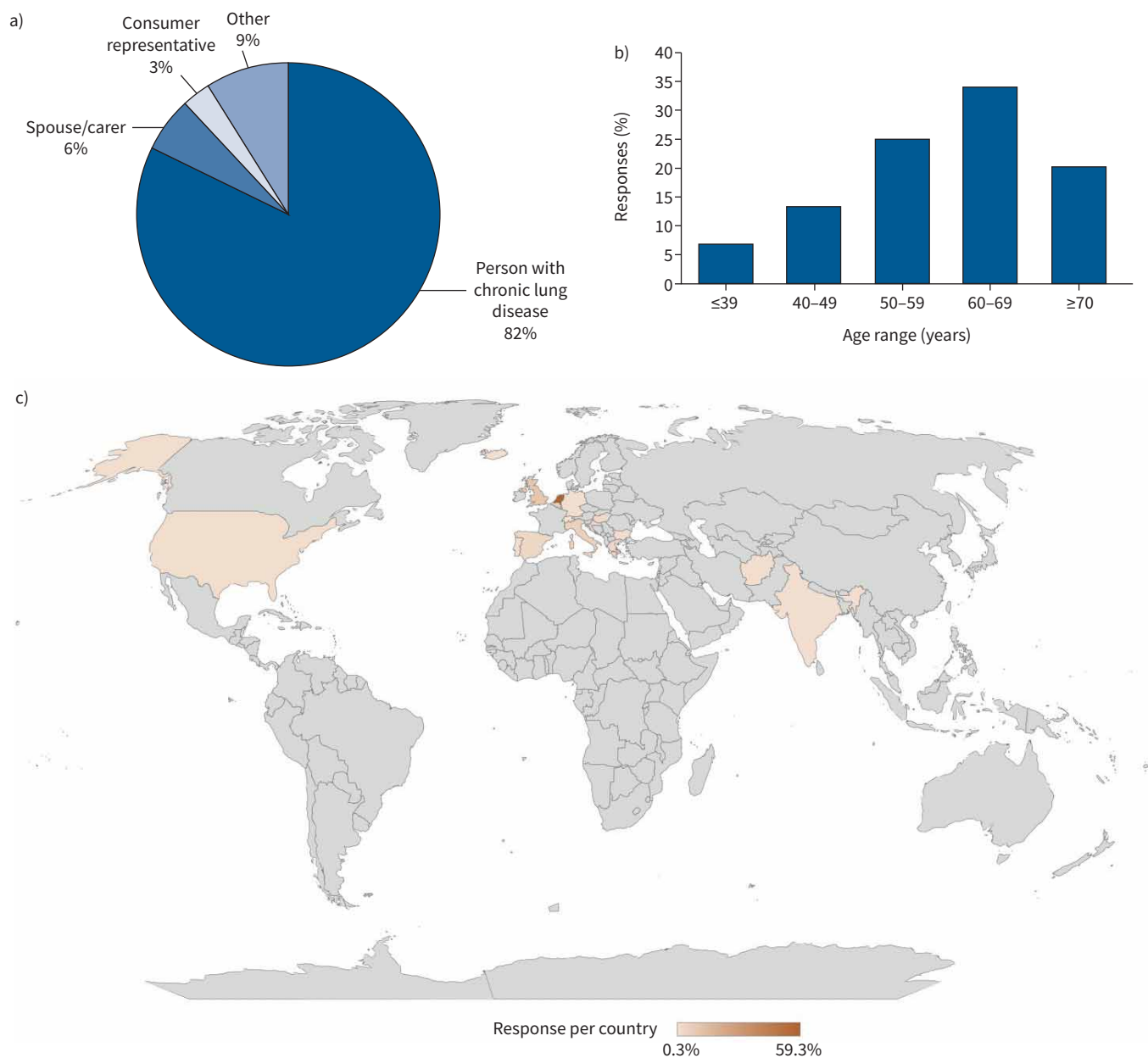


FIGURE 5 Summary of consumer survey responses according to a) group, b) age range and c) country.

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 needing 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 cooperative 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), improved service provision in the home and to access different healthcare settings.

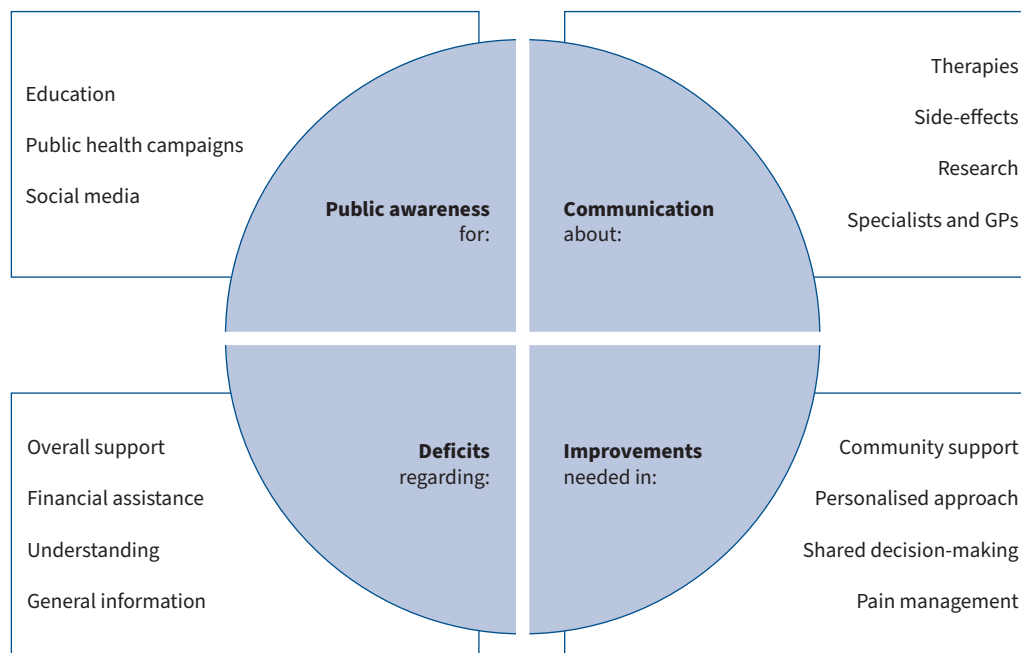


FIGURE 6 Summary of key issues and areas for improvement identified by survey participants regarding frailty in chronic respiratory disease. Additional information is provided in the supplementary material.

Many domains identified by consumers have been 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 the key messages from this ERS statement to consumers is highlighted through a written

BOX 2 Patient reflection on European Respiratory Society statement

When I was asked by ELF to take part in 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

reflection by our patient representative team member (S. Pavanello; box 2) and accompanying patient-facing infographic (supplementary material).

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 [190] 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 nonpharmacological 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.* www.cgakit.com/frailty) exist in geriatric medicine, the lack of respiratory-specific knowledge means that 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 that people who are frail are not excluded from clinical trials; and 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.

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