Frailty is a syndrome which leads to decreased strength, endurance, and physiological function resulting in increased vulnerability, dependence and/or risk of dying (1). Frailty is an evolving concept in clinical practice, as frail patients are predisposed...
to falls, hospitalization, and institutionalization (2). Additionally, the presence of frailty has been shown to substantially increase dying risk (2-4). The prevalence of frailty is extremely high in some population groups and further increases with age (5-8). Aging (patients aged ≥65 years) and chronic disease can promote deterioration and increase the risk for, and severity of, frailty (6,9).

Chronic obstructive pulmonary disease (COPD) is a disease that shares risk factors with frailty; namely aging, smoking, and dysregulated inflammation and endocrine function (10). Along with asthma, COPD is one of the two more common chronic respiratory diseases (11). In 2017, 572 million persons were affected by COPD worldwide (11). COPD is the most frequently studied chronic respiratory disease with regard to frailty (12). Marengoni et al. (13) showed that COPD increases the risk of frailty twofold (13).

Frailty is also common in elderly patients with idiopathic pulmonary fibrosis (IPF) (14-16). IPF is a progressive, chronic respiratory disease, which mainly affects older adults in whom it early leads to activity-limiting dyspnea and debilitating fatigue (16).

The goal of our study was to synthesize available research evidence about the burden of frailty in patients with COPD, IPF, and asthma, which related with quality of life, respiratory dysfunction, mortality and age association. Based on our goal, we hope that revisiting this field, we can better understand the impact of frailty on patients with chronic respiratory morbidity and the need for an interdisciplinary care approach.

Method

Search strategy

We conducted a systematic review based on recommendations by the Centre For Reviews And Dissemination (17), following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (18). We searched manually the PubMed electronic databases using combinations of the following medical subject heading (MeSH) terms and key words: (“idiopathic pulmonary fibrosis”[MeSH Terms] OR (“idiopathic”[All Fields] AND “pulmonary”[All Fields] AND “fibrosis”[All Fields]) OR “idiopathic pulmonary fibrosis”[All Fields]) AND (“frailty”[MeSH Terms] OR “frailty”[All Fields]); (“pulmonary disease, chronic obstructive”[MeSH Terms] OR (“pulmonary”[All Fields] AND “disease”[All Fields] AND “chronic”[All Fields] AND “obstructive”[All Fields]) OR “chronic obstructive pulmonary disease”[All Fields] OR “copd”[All Fields]) AND (“frailty”[MeSH Terms] OR “frailty”[All Fields]); (“asthma”[MeSH Terms] OR “asthma”[All Fields]) AND (“frailty”[MeSH Terms] OR “frailty”[All Fields]). We also applied additional filters, including peer reviewed articles in English, published between 2010 up to July 2020. To avoid any publication bias, we did not limit the type of publication (e.g. original research, review, or commentary). The same (medical subject) headings were applied to the Cochrane database. Studies that examined frailty in patients with COPD, IPF, and asthma were included. Articles without available full text online, studies reporting data with unclear associations, overlapping population groups or published in languages other than English were excluded.

Additionally, title/abstract and full-text screening was carried out by one author (AK) to determine inclusion based on the above criteria. A second author (EKS) cross-checked the list of the articles included and their content. Whenever there was a disagreement or uncertainty between the two authors, another author (KA) was consulted. When necessary, discussion among the three authors took place to reach a final decision. Last, the reference lists of all eligible studies were manually examined for any additional studies meeting inclusion criteria. The above strategy is depicted in the PRISMA(18) flow diagram Figure 1.

Quality appraisal

All selected articles were appraised for type of study and level of evidence according to the adapted Hierarchy of Evidence Rating System, as it is configured from Oregon Health and Science University (19). Hierarchy of Evidence Rating System is assigned to studies based on the methodological quality of their design, validity, and applicability (19,20). As in a previous study (21), this appraisal step allows for interpretation of the usefulness and transferability of the review findings to practice and policy. In addition, we used the GRADE guidelines according to Balshem et al. (22) to rate the quality of the body
of evidence. Table 1 presents the significance of the four GRADE levels of evidence: “high”, “moderate”, “low”, or “very low”.

Results

Thirty one were included in the final synthesis. The majority (n=13) were cohort studies; 10 prospective (3,6,7,15,24,26,28,38,40,44) and 3 retrospective (27,36,41), with evidence appraised at level IV. Eleven studies were appraised as level IV/cross-sectional study (8,10,29,30,31,32,34,35,37,41,42), one study was appraised as level V/ systematic review of descriptive statistics (13), one as level VI/ Quantitative descriptive study (33) and five studies as level VI/ Qualitative study (14,23,25,39,43). Study characteristics are provided in Table 2, subtopics, number of included studies, author(s), level of evidence, quality appraisal, methods and main findings.

Frailty and COPD

Twenty studies reported information on frailty in patients with COPD. In two of them cigarette smoking was identified as a major prevalence contributor between frailty and COPD (23,24). Furthermore, there was a study which reported a higher prevalence of frailty in COPD in males than in females, mostly due to higher smoking exposure and greater disease burden in males compared to females with COPD (23). In eight studies it was highlighted that frailty in COPD may particularly occur in elderly patients (6-8,13,25,26-28), and is strongly associated with dyspnea (30). Additionally, in two studies it was reported that frail patients with COPD have poorer quality of life than patients with COPD who are not frail (29,30). Frailty in COPD can also be mitigated through pulmonary rehabilitation (6-8,25,27), while patients with frailty and COPD showed lower levels of physical activity (31,32), and increased symptoms of anxiety and depression (6). In patients with COPD, frailty rose sharply after hospitalization, with a corresponding impact of exacerbations, in terms of patients’ physical status and disability (33). Patients with both COPD and frailty syndrome were at increased risk of death (34). It was also reported that frailty and COPD are expected to worsen patients’ quality of life (35,36). Finally, according to Park et al.(8) and Dias et al. (37), it was suggested that in patients with frailty and COPD there is a direct association between dyspnea and frailty (8,37).

Frailty and IPF

Five studies reported information on frailty in patients with IPF. Frailty was common in older patients with IPF (14,15), strongly associated with dyspnea (38) and linked to reduced pectoralis muscle mass (15). As a consequence, this combination has considerable impact on patients’ quality of life.

Table 1. Significance of the four quality levels*.

| Quality level | Definition                                                                 |
|---------------|---------------------------------------------------------------------------|
| High          | There is confidence that the true effect lies close to that of the estimate of the effect. |
| Moderate      | There is moderate confidence in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. |
| Low           | There is limited confidence in the effect estimate: The true effect may be substantially different from the estimate of the effect. |
| Very low      | There is very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect. |

*Based on the GRADE guidelines:3(Balshem et al,2011).
### Table 2. Data extraction and appraisal for studies evaluating association of COPD and frailty, IPF and frailty, asthma and frailty (n=31)

| Subtopics | Number of included studies | Author(s)/Year | Study design/ Level of Evidence** | Quality Appraisal** | Methods | Main findings |
|-----------|-----------------------------|----------------|-----------------------------------|---------------------|---------|---------------|
| COPD & Frailty | 20 | Ameen et al., 2012 [33] | Level V/ Quantitative study | High | Study including 820 patients with COPD entering pulmonary rehabilitation assessment | In patients with COPD, frailty rises sharply due to hospitalizations and the impact of exacerbations in patients' physical status and disability |
| | | Aryal et al., 2014 [23] | Level VI/ Qualitative study | High | [Frail patients with COPD also reported a poorer quality of life, suggesting that their health situation considerably impairs their everyday life] | Frailty prevalence was high and was correlated with higher Medical Research Council dyspnea scale and COPD Assessment Test scores. The CAT/MRC combination [(CAT/8)+MRC] ≥5.5 was highly associated with frailty, suggesting that an additional specific evaluation for the presence of frailty is indicated |
| | | Aryal et al., 2014 [23] | Level IV/Qualitative study | High | 148 consecutive patients who underwent transcatheter aortic valve implantation were enrolled and stratified by history of chronic obstructive pulmonary disease (COPD) | Frailty in COPD may be prevalent especially in the elderly patients |
| | | Chen et al., 2018 [35] | Level IV/Cross-sectional study | High | The study enrolled 489 patients with COPD and 799 subjects without COPD, selected in 1992 | Patients with both COPD and frailty syndrome are at increased risk of mortality |
| | | Galizia et al., 2011 [34] | Level IV/Cross-sectional study | High | A cross-sectional study. Subjects who visited a State Center for High-Cost Medicines to obtain free monthly COPD medicines were considered eligible | Frailty in COPD was also reported a poorer quality of life, suggesting that their health situation considerably impairs their everyday life |
| | | Ierodiakonou et al., 2019 [29] | Level IV/Cross-sectional study | High | 25 COPD patients enrolled from primary care in Greece between 2015 and 2016. Physicians used structured interventions to collect cross-sectional data, including demographics, medical history, symptoms and COPD Assessment Tool (CAT) or modified Medical Research Council Dyspnea scale (mMRC) score | Among adults with chronic obstructive pulmonary disease, frailty (modified from the Fried frailty phenotype) was associated with incident and longer-disease hospitalization, and with poor quality of life. |
| | | Kennedy et al., 2019 [36] | Level IV/ Cohort study | High | Data from the National Emphysema Treatment Trial (NETT) were retrospectively analyzed | Frail patients with COPD are at increased risk of mortality |
| | | Kojima et al., 2018 [24] | Level IV/ Cohort study | High | This study used data of 2,542 community-dwelling older people aged 65 years in England. Participants were classified as current smokers or non-smokers. | COPD was a disease caused by cigarette smoke, which contributes to high prevalence of frailty in patients |
| | | Kaniaki et al., 2019 [30] | Level IV/Cross-sectional study | High | This study included 201 older (aged ≥65 years) outpatients with COPD. | Frail patients with COPD also reported a poorer quality of life, suggesting that their health situation considerably impairs their everyday life. |
| | | Kusumoto et al., 2017 [32] | Level IV/Cross-sectional study | High | 24 consecutive patients recruited with clinically stable COPD, as defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD), between January 2013 and July 2016. | People with COPD and frailty have lower levels of physical activity |
| | | Lahousse et al., 2016 [27] | Level IV/ Cohort study | High | Patients are invited every 3–5 years to the research center in the city of Rotterdam for extensive follow-up examinations, including physical examination, electrocardiogram, echocardiography, blood sampling, and spirometry | Patients with both COPD and frailty syndrome are at increased risk of mortality |
| | | Lahousse et al., 2016 [27] Maddocks et al., 2016 [6] | Level IV/ Cohort study | High | Participants are invited every 3–5 years to the research center in the city of Rotterdam for extensive follow-up examinations, including physical examination, electrocardiogram, echocardiography, blood sampling, and spirometry | Frailty in COPD may be prevalent especially in the elderly patients |
| | | Lahousse et al., 2016 [27] Maddocks et al., 2016 [6] Marenzoni et al., 2019 [31] | Level IV/ Cohort study | High | Participants were recruited to this prospective cohort study from respiratory outpatient and pulmonary rehabilitation clinics at Harefield Hospital (Middlesex, UK) between November 2011 and January 2013. | Frailty in COPD could be mitigated through pulmonary rehabilitation |
| | | Marenzoni et al., 2019 | Level IV/ Cohort study | High | Participants were recruited to this prospective cohort study from respiratory outpatient and pulmonary rehabilitation clinics at Harefield Hospital (Middlesex, UK) between November 2011 and January 2013. | Frailty in COPD could be mitigated through pulmonary rehabilitation |
| | | Moza & Benson, 2017 [25] | Level V/ Qualitative study | High | This review described seven clinically meaningful COPD phenotypes that can be identified by the primary care provider as well as the specialist, and that carry specific management and prognostic implications. | Frailty in COPD may be prevalent especially in the elderly patients |
### Table 2. Data extraction and appraisal for studies evaluating association of COPD and frailty, IPF and frailty, asthma and frailty (n=31)

| Study Reference                  | Design                  | Frailty Level | COPD/ILD Level | IPF/Frailty Study | COPD/Frailty Study | Asthma/Frailty Study | Results/Implications                                                                 |
|---------------------------------|-------------------------|---------------|----------------|-------------------|-------------------|----------------------|----------------------------------------------------------------------------------|
| Mora & Benzo, 2017[25]          | Level IV/Qualitative study | High          | High           |                   |                   |                      | Frailty in COPD could be mitigated through pulmonary rehabilitation               |
| Mittal et al., 2016[7]          | Cohort study/Level IV   | High          | High           |                   |                   |                      | Frailty in COPD may be prevalent especially in the elderly patients                 |
| Park et al., 2013[8]            | Level IV/cross-sectional study | High          | High           |                   |                   |                      | Frailty in COPD could be mitigated through pulmonary rehabilitation               |
| Guler et al., 2019[40]          | Level IV/Cohort study   | High          |                |                   |                   |                      | Patients with COPD and frailty have lower levels of physical activity             |
| Sheth et al., 2019[15]          | Level IV/Cohort study   | High          |                |                   |                   |                      | Frailty in COPD could be mitigated through pulmonary rehabilitation               |
| Meine et al., 2017[38]          | Level IV/Cohort study   | High          |                |                   |                   |                      | Frailty in COPD could be mitigated through pulmonary rehabilitation               |
| Hadlon et al., 2018[3]          | Level IV/Cohort study   | High          |                |                   |                   |                      | Frailty increased from asthma severity and suggests that mechanisms related to the ageing process are involved |
| Kim et al., 2020[42]            | Level IV/cross-sectional study | High          |                |                   |                   |                      | Frailty increased from asthma severity and suggests that mechanisms related to the ageing process are involved |
| Lande et al., 2020[41]          | Level IV/Cohort study   | High          |                |                   |                   |                      | Frailty increased from asthma severity and suggests that mechanisms related to the ageing process are involved |
| Rincon & Irwin, 2012[43]        | Level IV/Qualitative study | High          |                |                   |                   |                      | Frailty increased from asthma severity and suggests that mechanisms related to the ageing process are involved |

Asthma was significantly related to frailty in community-dwelling older adults (aged >65 years) and patients with asthma had increased risk of frailty.

IPF drug treatments could be made more feasible by an adequate clinical management of comorbidities, more attention should be devoted to the identification of the malnutrition (undernutrition) and overnutrition, as well as of low muscle strength (dynamess) and low physical performance.

Frailty in COPD could be mitigated through pulmonary rehabilitation.

Frailty in IPF could be mitigated through pulmonary rehabilitation.

Frailty in COPD may be prevalent especially in the elderly patients.

Frailty in IPF may be prevalent especially in the elderly patients.

IPF: Interstitial Pulmonary Fibrosis, ILD: Interstitial Lung Disease.
(40) and survival (14,40). As IPF drug treatments could be more effective with an adequate clinical co-morbidity management, more attention should be devoted to imbalanced nutrition, as well as to (early) occurrence of low muscle strength (dynapenia) and low physical performance (39).

**Frailty and asthma**

Six studies reported information on frailty in patients with asthma. Landré et al. (41) demonstrated that the patients with asthma had increased risk of frailty (41). Additionally, in four studies, asthma was related to frailty in community-dwelling older adults (aged >65 years) (3,42-44). Furthermore, a recent study showed that when asthma combined with the exposure to the toxic effects of smoke could increase the burden of respiratory dysfunction and make older individuals more vulnerable to developing frailty (44). Finally, one study highlighted that the prevalence of frailty and asthma was increased among cancer survivors and also this combination adds limitations to their usual activities (45).

**Discussion**

This systematic review identified 31 articles, mostly prospective cohort studies, related to the prevalence, severity, and impact of frailty in patients with chronic lung disease. Our review revealed some key findings. Firstly frailty can have a negative impact on pragmatic and perceived functionality and has also an effect to increase death risk, especially in older patients with COPD, IPF and asthma. Additionally, our review summarises that frailty, in these patients, with respiratory dysfunction, expressed as dyspnea worsening.

Frailty is significantly higher among older adults. Fried et al. (2) identified frailty in 3.9% of older adults aged 65 to 74 years, 11.6% among those aged 75 to 84 years, and 25% in individuals aged 85 years or older (2). Collard et al. (46) also detected a high frailty occurrence among older adults aged 80 to 84 years (15.7%) and among those older than 84 years of age (26.1%) (46). As the world’s population ages, frailty is likely to increase in prevalence. Thus, unfavourable health determinants as reduced physical capacity, increased risk of falls with their causal care episodes, impaired cognitive function, and poor nutrition (28) will rise in conjunction with frailty (15,34,47).

Frailty appears as a ‘satellite’ expression of an ageing mechanism, but it is also associated with multiple chronic diseases and independently increases risk of disability, hospitalization, and mortality (26,32). According to recent evidence, frailty will affect more than half patients with interstitial lung diseases (ILD) and is strongly associated with respiratory impairment, accelerated biological aging, and the presence of comorbidities (48). Farooqi et al. (49) emphasize in their study that physical frailty is prevalent in patients with ILD and is independently associated with an increased risk of death (49). Assessment of physical frailty provides additional prognostic value to tested risk estimation tools, such as the ILD-GAP score, and may be seen as a modifiable target for future intervention (49).

Frailty is associated with quality of life (40) and survival in older patients (>65 years) with IPF (40,50) and not surprisingly, its prevalence is greater compared to same age persons in general population groups (14,15,51). Additionally, the combination of comorbidities and complications, such as IPF with frailty and osteoporosis (14,52), can have a profound

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| Asthma & Frailty | 6 | Smitherman et al.,2018[45] | Level IV/cross-sectional study | High | Using a cross-sectional survey at a tertiary medical center-based cancer survivorship cohort, they determined the prevalence of specific comorbidities and frailty using the survey-based FRAIL assessment. In separate models adjusting for age, they estimated prevalence ratios (PRs) for the associations between patient characteristics and (1) any comorbidity and (2) frailty or prefrailty using log-binomial models. The prevalence of frailty and asthma is high among cancer survivors and also this combination causes limitations to their usual activities. |
|---|---|---|---|---|---|
| | 6 | Trevisan et al.,2019[44] | Level IV/Cohort study | High | Data come from 2039 community-dwelling participants (aged ≥ 60 years) of the Swedish National Study on Ageing and Care in Kungsholmen (SNAC-K) and survival (14,40). As IPF drug treatments could be more effective with an adequate clinical co-morbidity management, more attention should be devoted to imbalanced nutrition, as well as to (early) occurrence of low muscle strength (dynapenia) and low physical performance (39). |

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*Level of evidence based on the adapted Hierarchy of Evidence Rating System (19,20); **Appraisal based on the GRADE guidelines: 3. Rating the quality of evidence. (22).
impact on patients’ quality of life (14). As expected, the incurable and progressive nature of IPF - as well as the burdensome symptoms of breathlessness, cough and fatigue - are additional factors that affect their lives (53). Supportive interventions could thus contribute to helping patients maintain their quality of life despite the increasing physical constraints (53).

The increased prevalence of frailty in patients with asthma is supported by little evidence. However, asthma may also interplay with other chronic diseases associated with frailty (53), especially in geriatric populations (8,54). Older patients diagnosed with asthma present unique characteristics, including severe symptoms, uncontrolled response to standard therapy, and higher mortality (54), which are different from those of younger asthma patients. As Kang et al. (55) proposed, major changes take place in the respiratory tract as a part of the ageing process (55). These changes include immunosenescence, which results in gradual and various alterations in the immune system brought on by advancing age (55). This is expressed through imbalance in lymphocyte subsets, with decreased production of new T cells, apoptosis and mitochondrial dysregulation, and impaired function of immune regulatory cells (56). These age-related changes increase susceptibility to infections, and lead to a status of subclinical, sustained inflammation (56). Other alterations include age-associated changes in lung physiology (57), such as decreased strength of respiratory muscles (54), decreased lung recoil (8) and increased chest wall stiffness (58). As a result, elderly patients breathe at higher lung volumes than younger patients, which poses an additional load on their respiratory muscles (59,60). The abovementioned changes can affect the pathogenesis and the development of asthma in older people (55). Moreover, asthma is a comorbidity that can concur with COPD, affecting elderly patients as well (61,62). Some of the common comorbid disorders that complicate asthma and aging are osteoporosis (61) and frailty (41).

The results of our study are consistent with previous suggestions of an association between frailty, respiratory impairment, and health status. Results from recent studies demonstrated that frail patients with COPD had a poorer quality of life, suggesting that their health condition considerably impairs their everyday life (29-33,35). Lahousse et al. (27) suggested that frail elderly patients with COPD have an almost threefold increased risk of mortality (27). According to the literature, COPD is closely correlated to frailty, having shared risk factors such as aging and exposure to smoke, as well as common mechanisms of respiratory and endocrine dysfunction (24,25,29,44). Additionally Chen et al. in their results, highlight that frailty, which is common among patients with COPD with dyspnea, it does not only affect the maintenance of health-related quality of life but also increases the frequency of medical service utilization (35). A possible reason might be that aging-related changes affected pharmacokinetics (35), such as reduced drug clearance and increased drug accumulation (63) and disease-related distress increased the chances of taking multiple medications among COPD patients (64). Another effect of frailty and COPD in patients’ health, is that they are both associated with common systemic comorbidities, including osteoporosis (65-69). The high prevalence of osteoporosis in COPD patients is due to risk factors, such as older age, inactivity, smoking, systemic inflammation, vitamin D deficiency and use of oral or inhaled corticosteroids (65-67). Osteoporosis may cause fragility fractures such as rib cage and vertebral compression fractures, which further decrease mobility, reduce pulmonary function and thus increase morbidity and mortality in both women and men (65-67). The parameter of coexisting frailty further increases the vulnerability of COPD patients for osteoporosis, as it acts as a predictor of decrease in bone mineral density and osteoporotic fractures (68,69). Early detection of osteoporosis in frail COPD patients is, therefore, important and can be based on routine screening for osteoporosis using dual photon absorptiometry measurements in hip and spine and risk assessment of fractures using tools such as the Fracture Risk Assessment Tool (FRAX), which takes into account bone mineral density, history of fragility fractures, and population-specific clinical features (67,69). These imaging and risk assessment tools will enable general physicians and pneumologists to diagnose frail COPD patients with comorbid osteoporosis at an early stage and allow early prevention and treatment strategies to develop (67,69).

Moreover, patients suffering from chronic respiratory diseases, are immediately listed to be at risk for severe forms of COVID-19 (70,71). COVID-19
is responsible for various respiratory manifestations, from cough with dyspnea to acute respiratory distress syndrome (ARDS) in cases with most severe suffering (72). Implications for patients’ health may longly persist after infectious period. Wong et al. suggested the assessment need for quality of life, frailty, dyspnea, mood and sleep in patients after hospitalisation for COVID-19 (73). Nalbandian et al. (74) describe a post-acute outpatient service established in Italy and report symptom persistence in 9 out of 10 recovered patients, following acute COVID-19 hospitalization, averagely two months after first symptom onset (74). Fatigue, dyspnea, joint pain and chest pain remain common symptoms, within almost 6 out of 10 patients, continuing to experience three or more symptoms, as another study suggests (75). In a Chinese study, most patients report at least one symptom; fatigue/muscular weakness was the most commonly described, followed by sleep difficulties and anxiety/depression (76). Additionally, COVID-19 infected, old and frail persons tend to experience substantially more severe symptoms and lethality (77,78). Effects of accelerated aging and the development of age-related disorders have been plausibly described as post-COVID-19 consequences (78). Moreover, post-infectious interstitial lung alterations may mimic tissue inflammation or fibrosing, ILD-like, patterns, deserving attention in pathophysiology terms and by treating them as a new source for building knowledge.

Returning to the general concept, at an interventional level, as summarized by Torres-Sanchez et al. (79), some systematic reviews (80,81) have provided evidence that exercise interventions have a benefit for frail older adults. There is evidence (79-81), that exercise improves cardiorespiratory function, muscle function, balance, performance of activities of daily living, and functional ability in frail older adults. Additionally, exercise interventions should be offered to older people during social isolation to reduce the risk of frailty, sarcopenia, cognitive and emotional impairment; and tele-rehabilitation may represent an option for people at home (82,83). Patients with frailty have to adapt to a number of limitations and participate in the treatment process. Upon frailty diagnosis and loss of health, patients have to go through multidimensional and continuous changes introduced in the scope of physical, mental, and social functioning (28). Decision making process should be, in parallel, focused on mental health and emotional status, since a psycho–eco–social background may play an important role in disease progression for several chronically built disorders (84,85). From this perspective, it is optimistic that consensus documents endorse frailty as an ‘entity’ to be integrated in the management of cardiovascular morbidity, opening new pathways within theragnostic choices and interdisciplinary care (86).

**Limitations**

The results of this review should be interpreted in the context of some limitations. In the general population, frailty has been associated with multimorbidity and the fact that fewer studies have reported frailty in patients with COPD, IPF and asthma, may imply an overlapping causality. However, our search strategy and data extraction were conducted using specific methodological tools, and we attempted a balanced approach based on our findings, to highlight the need for well-designed proposals aimed to discriminate to what extend frailty is the cause, result or concurrence in the context of specific morbidity. Narrow conformity was also noticed between different methodologies and nature of chronic conditions, being parameters that deserve attention when collection and analysis of information might lead to strict conclusions. For this reason, we have tabulated some relevant descriptive information in order to offer more clarity.

**Conclusion**

This study shows that the link between frailty and chronic respiratory diseases (COPD, IPF and asthma) leads to a decline of functional ‘readiness’ and capacity in elderly. A greater understanding of the implications of ‘frail phenotype’ across different ages, as well as in a range of long-term conditions, is of great necessity. The early detection of frailty represents a needed strategy in the management of chronic respiratory diseases. A well designed plan of frailty-based tailored management for the older population groups, involving primary care and secondary respiratory care services, may help to prevent an overwhelming tertiary care demand. However, there is a need for a more thorough evaluation of frailty in order to identify this syndrome and intervene much
earlier. Clinicians and policy makers are in need of an evidence base regarding the effective interventions so as to reduce frailty or buffer its effects. Future research should explore the consequences of frailty across a wider age range and in patients with multimorbidity by using specific research questions and advanced methodology. This will provide more evidence promoting interventions, which should be targeted at modifying or reversing the frailty installation as process. Interventions should be tailored to patients’ clinical contexts, as no single intervention is likely to be applicable to all those meeting the criteria for frailty. By intervening earlier, not only individuals, but also health-care systems, have more potential to gain benefits. All health professionals involved need evidence and mindful interventions to buffer the impact of frailty.

Authors’ contributions: EKS conceived the study idea, invited team members and offered a guidance to search topic. AK performed the literature search and composed results section by appraising findings for the studies included. AK and EKS cross-checked the emerged literature information. KA critically reviewed literature information and offered clinical input when this was necessary. AK, EKS and KA contributed to the first draft preparation. ED and CJR offered intellectual input and contributed in the draft writing and revision based on the field of their expertise. All authors read and approved final manuscript.

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