



King's Research Portal

DOI:

[10.1097/SPC.0000000000000523](https://doi.org/10.1097/SPC.0000000000000523)

Document Version

Peer reviewed version

[Link to publication record in King's Research Portal](#)

Citation for published version (APA):

Brighton, L. J., Bone, A. E., & Maddocks, M. (2020). Supportive and palliative care for people with chronic respiratory disease and frailty. *Current Opinion in Supportive and Palliative Care*, 14(3), 206-212. <https://doi.org/10.1097/SPC.0000000000000523>

Citing this paper

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

General rights

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

Take down policy

If you believe that this document breaches copyright please contact librarypure@kcl.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

Supportive and palliative care for people with chronic respiratory disease and frailty

Lisa Jane Brighton, Anna E Bone, Matthew Maddocks

King's College London, Cicely Saunders Institute of Palliative Care, Policy and Rehabilitation,
Bessemer road, London, SE5 9PJ, UK

Correspondence to:

Lisa Jane Brighton, Cicely Saunders Institute of Palliative Care, Policy and Rehabilitation, King's College London, London, SE5 9PJ, United Kingdom.

Tel: +44 (0)202 7848 5041.

E-mail: lisa.brighton@kcl.ac.uk

Word count: 2969

ABSTRACT

Purpose of review: Frailty is a multidimensional syndrome associated with increased risk of poor outcomes. It is estimated that at least one in five people with chronic respiratory disease is also living with frailty. In this review we consider recent advances in how frailty can be recognised, and its associated impact on people with chronic respiratory disease. We then discuss advances in supportive and palliative care for those with both chronic respiratory disease and frailty.

Recent findings: The interconnectedness of chronic respiratory disease and frailty is being better understood. An increasing number of factors associated with frailty in respiratory disease have been identified, from increased symptom burden (e.g. breathlessness, fatigue) to increased exacerbations and higher mortality. These contribute to accumulating multidimensional losses in reserve, and unpredictable health. Recent advances in respiratory research, while not always with people with frailty, may inform supportive and palliative care to address frailty in chronic respiratory disease. These include rehabilitation interventions to strengthen reserves, advance care planning interventions to help manage unpredictable trajectories, and integrated models of care (e.g. incorporating respiratory, geriatric, and palliative care) to address multidimensional needs.

Summary: Recent evidence supporting the role of rehabilitation, advance care planning, and early palliative care, may be of benefit to people living with chronic respiratory disease and frailty. Models showing integration across multiple specialities and professionals may have the most potential to meet the multidimensional needs of this group. Future research should develop and test models of care that address frailty and/or explore the role of frailty in triggering integrated multidisciplinary input.

Keywords: Palliative care, supportive care, chronic respiratory disease, Frailty, review

Introduction

Frailty is broadly understood to be a multidimensional syndrome characterised by decreases in reserve and diminished resistance to stressors(1), and is present in between 20-50% of people living with chronic respiratory disease(2-4). The mechanisms underlying the link between respiratory disease and frailty are likely multifactorial, for example due to sedentary behaviour, mobility impairments, sarcopenia and malnutrition, in addition to having shared risk factors with frailty (e.g. age, socioeconomic status, chronic inflammation, immune dysfunction)(4).

In this review we consider recent advances in our understanding of frailty, how it might be recognised, and its associated impact on people with chronic respiratory disease. We then discuss advances in supportive and palliative care for those with respiratory disease and frailty, including rehabilitation, advance care planning, and integrated care approaches. To identify literature, we searched Medline for articles published between September 1st 2018 and March 3rd 2020. We combined relevant MeSH terms and free text synonyms using the following structure: chronic respiratory disease AND (frailty OR palliative care). Searches were restricted to articles published in English.

Understanding and recognising frailty in chronic respiratory disease

Since our earlier review (5), the interconnectedness of chronic obstructive pulmonary disease (COPD) and frailty (6), and the crosstalk between frailty, comorbidity and other age-related syndromes are better understood and articulated (7). A distinction between age-related and disease-related frailty has been suggested (8), though in the context of respiratory illness frailty is likely to be a combination of both. Marengoni et al (4) published a meta-analysis showing a pooled prevalence using the Fried frailty phenotype, which comprises five criteria: unintentional weight loss, self-reported exhaustion, weakness, slow gait speed, and low energy expenditure. In people with COPD, pooled prevalence estimates were 56% for pre-frailty (people meeting one or two of the criteria) and 19% for frailty (people meeting three or more of the criteria). COPD led to a two-fold increased odds of frailty, and the few included longitudinal studies suggested a bidirectional association.

Guan and Niu (9) provide an excellent summary of frailty assessment tools and areas of practice where frailty may add value, including for screening, stratification or to prompt intervention. Their review shows, through empirical studies, how different tools fit different situations. For example, they unpick the Fried frailty phenotype and show utility across outpatient and community rehabilitation services. Through a stakeholder consensus event, outcomes for a combined exercise rehabilitation programme for people with COPD and heart failure were proposed (10). Profiling of frailty was ranked as at least moderately important for clinical purposes, and as one of the most important outcomes for research purposes. In this context, assessment of physical frailty was deemed appropriate. The Timed Up and Go Test, 4-metre gait speed and Short Physical Performance Battery (SPPB) were flagged as candidate measures, though ceiling and floor effects were acknowledged (10).

Frailty screening and assessment in the acute setting is also gaining traction. In the review period, Ospina et al (11) incorporated frailty screening in a proposed evidence-based discharge bundle for people with acute exacerbations of COPD. Most experts recommended a frailty and comorbidity screen during their nominal group meeting, though suggestions on which tool(s) to use were lacking.

Chin et al (12) reported on the feasibility of implementing the Clinical Frailty Scale among hospitalised people with COPD. Frailty assessments were completed on 46/50 people hospitalised over a 10-month period. Increasing severity of frailty was associated with trends in increased cost, length of stay, and discharge to another facility. Interestingly, in a blinded rating compared to nurses, physicians classified people as frailer in about half of cases. This highlights a need to ensure education and training to better standardise routine frailty assessments.

Impact of living with frailty and chronic respiratory disease

Frailty, disease and disability are known to coexist, with causal interrelationships between each(13). There is evidence of this in COPD, where frailty is associated with comorbidities(14), disability(15) and geriatric conditions, such as malnutrition(16). There is emerging evidence that these associations are also observed in idiopathic pulmonary fibrosis (IPF)(17). In people with COPD or IPF, frailty increases with age(14, 17). Alongside this, within COPD, a cross-sectional study found disease severity and exacerbations are also associated with frailty(14), and a prospective observational study found dyspnoea was associated with worsening frailty over a two year period(15).

Frailty in chronic respiratory disease is associated with poor outcomes, including increased healthcare utilisation and mortality. Among people with COPD and IPF, frailty was associated with higher rate of hospitalisation(18-20) and longer hospital stay(18, 20). In people with COPD, frailty was also significantly associated with unfavourable discharge disposition and 30-day readmission(21). There is consistent evidence that increased severity of frailty in respiratory disease is associated with higher likelihood of mortality(18-20, 22, 23).

There is also evidence that frailty is associated with higher symptom burden, which may contribute to increased use of non-elective care. A pilot study of 50 people with IPF found that frailty was associated with higher fatigue and shortness of breath(17). A study of 540 people with fibrotic interstitial lung disease (ILD) also found that frailty was associated with worse quality of life, even when adjusting for age, sex, ILD severity and IPF diagnosis(18). Many of these quantitative outcomes chime with the qualitative experiences captured in a recent study of people with both COPD and frailty attending pulmonary rehabilitation, who described accumulating, multidimensional losses as part of an unpredictable health trajectory (Figure 1)(24). Together, these findings corroborate previous evidence that people with chronic respiratory disease and frailty experience worse physical and psychological outcomes in comparison to their non-frail counterparts(25, 26).

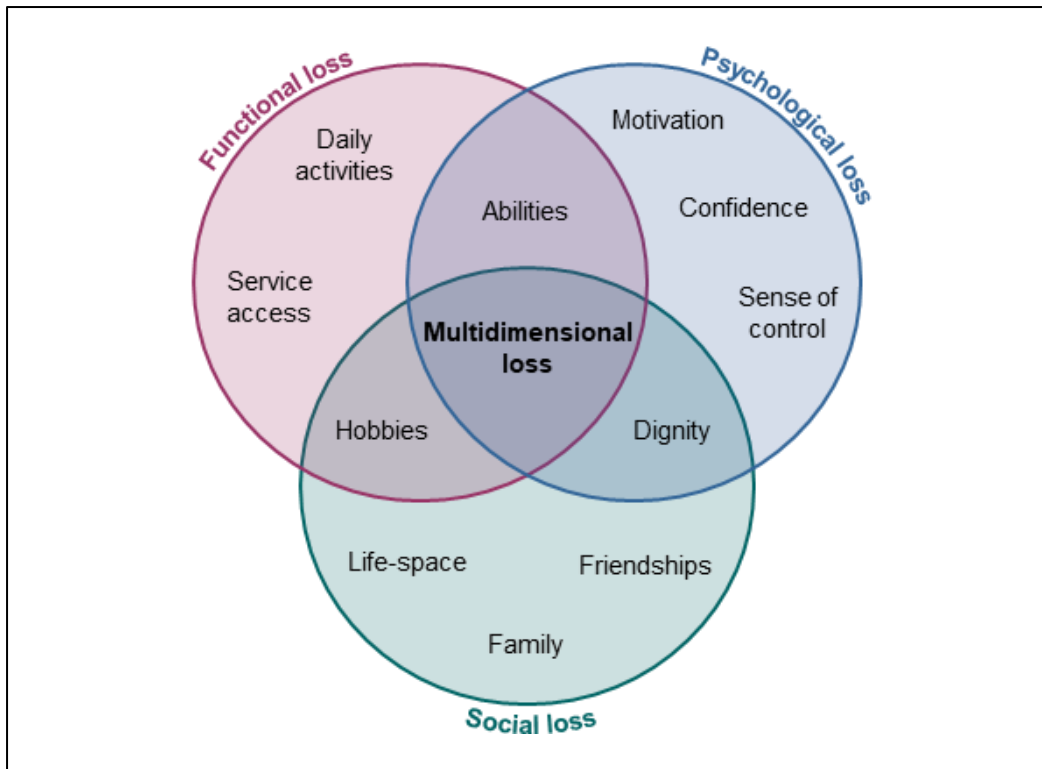


Figure 1: Multidimensional losses reported by people with frailty and chronic respiratory disease

Advances in palliative and supportive care

Interventions to address frailty and its correlates in chronic respiratory disease are increasingly important. Recent advances, while not always with populations identified as frail, may inform provision of optimal supportive and palliative care for this group. These include exercise and nutritional interventions to directly address frailty(7), advance care planning interventions to help manage unpredictable health, and addressing multidimensional losses through integrated models of care.

Strengthening reserves through rehabilitation

Two recent literature reviews explore the potential benefits of exercise in strengthening reserves in people with chronic respiratory disease, including those living with frailty. Neder et al.(27) outline how some with advanced COPD and frailty may not show significant physiological improvements from exercise-based interventions (e.g. pulmonary rehabilitation). However, these interventions can still alter the affective component of dyspnoea and improve capacity to tolerate physical activity in this population. Meanwhile, Tanner et al.(28) unpick how the anti-inflammatory effects of exercise may be a mechanism by which many of the positive outcomes of pulmonary rehabilitation are achieved. Given the association of systemic inflammation with ageing and chronic conditions, including COPD, they suggest a role for pulmonary rehabilitation programmes as a generic intervention to reduce risk of frailty.

With these benefits in mind, an abstract from Kennedy et al.(29) in the United States assesses the impact of pulmonary rehabilitation on frailty in 63 people who are potential lung transplant candidates and recipients. Preliminary results showed post-rehabilitation reductions in presence of the Fried frailty phenotype, particularly through improvements in gait speed and exhaustion. This

builds on previous UK work that suggested the potential role of pulmonary rehabilitation in reducing frailty, but also showed frailty was a strong independent risk factor for not completing the intervention(26). Acknowledging these challenges, Brighton et al.(30) conducted a realist review to understand how exercise-based approaches may be better adapted for those with COPD and frailty. Five key principles were identified to help adapt rehabilitation for this group: 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.

Alongside exercise-based approaches, there is growing work to explore nutritional adjuncts. Billingsley et al.(31) conducted a literature review of the role of nutritional strategies to increase cardiorespiratory fitness in a range of conditions, including chronic respiratory disease, and sarcopenia and frailty. There was insufficient evidence to recommend a nutritional adjunct to pulmonary rehabilitation, although these approaches showed promise. Kuniaki et al.(32) also report a case where they explore the potential benefits of the traditional Japanese medicine Ninjin'yoeito to address frailty in a person with COPD. The person's frailty had persisted despite using bronchodilators, nutrition support, and pulmonary rehabilitation over four months, but showed improvement in both physical and psychological domains one month after these measures were supplemented with Ninjin'yoeito taken three times a day. The authors suggest further clinical studies to determine effectiveness.

Managing unpredictability with advance care planning

Adequate care planning will also be important to help manage the unpredictable disruptions to health and subsequent deterioration characteristic of frailty. A scoping review of advance care planning practices within COPD by Meehan et al.(33) identified few trials of advance care planning interventions. The most recent was a multicentre cluster randomised-controlled trial by Houben et al.(34), testing a nurse-led one and a half-hour home-based advance care planning session in the Netherlands. They recruited 165 people with advanced COPD post-hospitalisation for an acute exacerbation. Their intervention was associated with increased advance care planning discussions and significantly lower family anxiety at six months, in comparison to usual care. This builds on evidence from a previous Australian trial of a hospital-based nurse-led intervention that helped to increase uptake of advance care planning(35). However, Houben et al. also reported high numbers of people with COPD declining to participate and gatekeeping by professionals, suggesting a need for careful work to implement into routine practice.

New approaches to advance care planning have also been tested in pulmonary rehabilitation and long-term care facilities. Grossman et al.(36) evaluated two one-hour group-based discussions of advance care planning with people attending pulmonary rehabilitation, facilitated by palliative care specialists. Thirty people who attended at least one session found the content relevant and appreciated the opportunity to share their thoughts. Two participants found some of the discussion difficult. Within long-term care facilities, Sussman et al.(37, 38) used condition-specific pamphlets to support communication around end of life care for people affected by dementia, heart failure, COPD, renal failure, and frailty. Residents and family members reported that the pamphlets supported reflections on future care, but that discussions with each other remained difficult(38).

While staff who had read the pamphlets (n=105) felt the information was useful, more staff reported using the pamphlets for self-education than for educating residents and their families. The authors suggested a need for accompanying communication training and a clearer distribution strategy to support implementation.

Perceived challenges from professionals around when and how to implement advance care planning, and feeling inadequately trained to undertake these conversations, are well-documented(33). To guide such training, Burgess et al.(39) asked 38 experienced medical, nursing and allied healthcare professionals to identify priority topics for advance care planning education. Areas of strongest consensus included identifying who with COPD might benefit from palliative care interventions and when, identifying changing care needs, addressing mismatches in patient/family expectations, and talking about poor prognosis. Respiratory and palliative medicine specialists across Australia, New Zealand and the United Kingdom (n=400) also agree on the need for advance care planning in COPD, suggesting a readiness for greater collaboration and multidisciplinary models of care(40).

Addressing multidimensional losses through integrated care

Calls for integrated models of respiratory care are well-aligned with what is known about the multidimensional losses experienced by those with respiratory disease and frailty(24). As such, approaches that seek to integrate palliative care may be of benefit to this population. For example, a recent systematic review(41) found that holistic breathlessness services, which typically integrate palliative and respiratory care, are effective in reducing distress and depression symptoms in people with advanced disease and chronic breathlessness. One suggested role of these services was as a bridge to, or step down from, rehabilitation services, for those who are more unwell. However, the authors also acknowledged that triggering these services as part of an earlier palliative care approach might be important. The role for early palliative care in respiratory disease is supported by Iyer et al.'s recent work with 10 people with COPD and 10 family caregivers(42): they responded positively to a standardised description of early palliative care, and they felt integration could occur from moderate COPD (GOLD stage II) onwards. This was echoed by 12 clinicians from pulmonary and palliative care(43), who agreed on the potential added value of palliative care alongside respiratory care.

Several recent trials have now sought to determine acceptable and effective models to deliver early palliative care, but not without challenges. One intervention with promising qualitative feedback was the new outpatient 'CAPTAIN' care model in Denmark(44). This involved community management of those with severe COPD through needs-based (rather than routine quarterly) contacts with the respiratory team, and annual advance care planning dialogues. People who received the CAPTAIN model reported improved quality of care and more continuous and natural advance care planning discussions. Feeling 'known' by their CAPTAIN nurse was key to this success. Doctors and nurses delivering the service(45) also felt care was more person-centred and holistic. However, increased continuity of care came with increased exposure to suffering, making professionals' roles more stressful and mentally exhausting. Multidisciplinary support and ongoing supervision were suggested as important in ameliorating this.

Other new trials of home-based approaches also show potential for success. Vitacca et al.(46) conducted a before-after feasibility study of a home-based tele-assisted palliative care intervention with 10 people with severe COPD in Italy. Each received a 60-minute advance care planning discussion in hospital, followed by post-discharge monthly telephone support from a nurse specialist. Their intervention was deemed feasible and participants expressed their satisfaction, yet in many cases the person's preferences were not fulfilled when an acute event later arose. In another pilot RCT of early home-based palliative care for people with COPD(47), people in the intervention group (n=26) received monthly support from a community palliative care team, while those in the control group (n=23) received usual care. Again, the intervention and data collection were deemed feasible, however significant problems with recruitment meant the planned sample size (n=80 per group) could not be reached. Finally, Scheerens et al. conducted a pilot RCT of a home-based approach for people with COPD in Belgium(48). People in the intervention group (n=20, usual care control group n=19) received on average 3.4 visits from palliative home care nurses over six months. The nurses provided protocolised symptom management and support, care plans, and leaflets on coping mechanisms. Their intervention was also deemed largely feasible and acceptable, but did not show anticipated effects on participant health outcomes. The study was likely underpowered, but the team also suggested a need for increased training of the palliative nurses in COPD management, and greater integration across teams.

Challenges around delivering holistic care and integrated working across relevant professional groups have been commonly noted. This raises the questions as to whether models of care that support integration beyond respiratory and palliative care may have most potential, particularly in addressing the multidimensional losses seen in those with frailty. For example, Van Dam van Isselt et al.(49) report a cohort study of their inpatient geriatric rehabilitation service for people with COPD in the Netherlands. The service comprises a six-week inpatient multidisciplinary rehabilitation programme, beginning with a comprehensive geriatric assessment and incorporating expertise from respiratory, geriatric and palliative care. Their intervention group (n=78) showed a significant and clinically meaningful improvement on disease-specific health-status, and experienced significantly fewer exacerbations than the control group who declined the service (n=80), at three-month follow-up. Although some caution in interpretation is needed due natural differences in the groups and risk of confounding, some of these differences were addressed through use of propensity scores. Barratt et al.(50) also report a retrospective cohort study in the UK, where people with ILD and palliative care needs are reviewed by a multidisciplinary team. This team includes a palliative care consultant and nurse, a psychologist, an ILD consultant, nurse, and pharmacists, and an MDT coordinator who meet every six weeks. In comparison to those seen prior to creation of the MDT (n=26), those seen by the MDT (n=46) showed increased: documentation of cardiopulmonary resuscitation decisions, referrals to fatigue and breathlessness support and specialist palliative care, recommendations for GPs to add them to a supportive care register, and referrals to community matrons. This preliminary work shows the promise of multidimensional integrated care approaches for those with respiratory disease at risk of poor outcomes, although further controlled studies focusing on those identified as living with frailty are still needed.

Future research

People living with respiratory disease and frailty are at risk of poor outcomes, and likely to benefit from recent advances in supportive and palliative care. Heterogenous trial designs and populations have been cited as a particular challenge in this area of research(31). However, it might be that more explicit theoretical modelling and consideration of intervention mechanisms would help overcome some of these challenges and support transferable learning across different contexts(30). It is also notable that few studies reported involving people with COPD and their informal carers in priority settings activities, or research and intervention design. Working more collaboratively with service users may be an important part of improving both research and intervention acceptability.

Lack of agreement over appropriate criteria for early palliative care is evidenced from both stakeholder feedback and varying trial entry criteria (e.g. incorporating long-term oxygen use(47), MRC dyspnoea(48), and/or the 'surprise' question(46)). Considering the utility of measuring frailty regardless of diagnosis/comorbidities, and the poor and unpredictable health that often accompanies it, using frailty as an indicator to prompt additional integrated supportive and palliative care may be worth exploring. With little work specifically addressing frailty and respiratory disease, this may be an efficient way to respond to calls for proactive integration of geriatrics and palliative care in respiratory disease(51).

Conclusions

Recent advances in supportive and palliative care, including rehabilitation, advance care planning, and early palliative care, may be of benefit to people living with both chronic respiratory disease and frailty. Models showing integration across multiple specialities and professionals (e.g. respiratory, geriatrics, palliative care) may have the most potential to strengthen reserves and meet the multidimensional needs of this group. Future research should develop and test models of care that specifically address frailty in respiratory disease, including exploring the role of frailty in triggering integrated multidisciplinary input.

KEY POINTS

- People with both respiratory disease and frailty experience high symptom burden (e.g. breathlessness, fatigue, exacerbations) and multidimensional losses (e.g. physical and psychological health) as part of an unpredictable health trajectory
- Recent developments in rehabilitation, advance care planning and integrated models of care are highly relevant to building reserves and addressing multidimensional needs in people with respiratory disease and frailty
- Identification of frailty may be an important trigger for integrated care approaches that incorporate respiratory, geriatric and palliative care
- Future research should develop and test models of care that specifically address frailty in respiratory disease

ACKNOWLEDGEMENTS

None.

FINANCIAL SUPPORT AND SPONSORSHIP

MM is funded by, and LB is supported by, a National Institute for Health Research (NIHR) Career Development Fellowship (CDF-2017-10-009). MM is supported by the National Institute for Health Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust. The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care. AEB is supported by Dunhill Medical Trust and Cicely Saunders International.

CONFLICTS OF INTEREST

Of the 41 papers included in the review period, LJB is an author on three and MM is an author on five. The authors declare no other conflicts of interest.

REFERENCES & RECOMMENDED READING

Papers of particular interest, published within the period of review have been highlighted as: * of special interest, ** of outstanding interest.

- (4) *A systematic review and meta-analysis of observational studies, showing pooled prevalence of frailty and pre-frailty in COPD at 19% and 56% respectively.
- (9) * Provides a succinct overview of a range of frailty measures and their application to chronic respiratory disease.
- (24) * The first qualitative study of the experiences needs and preferences of people with both COPD and frailty referred for pulmonary rehabilitation.
- (30) *A realist review of how exercise-based interventions might be optimised for people living with both COPD and frailty, suggesting core principles including: building trusting relationships, understanding priorities, using individualised and multidisciplinary approaches, and flexible service delivery.
- (36)*A small feasibility study of group teaching and discussion of advance care planning for people attending pulmonary rehabilitation, which suggests it might be acceptable to participants.
- (42)**Mixed methods exploratory study with people with COPD and their family caregivers to understand acceptability of, and needs relevant to, early palliative care. Shows perceived acceptability of early palliative care, and highlights priority areas of support.
- (45)*A qualitative study of health professionals' experiences of a new model of outpatient care intended to better address palliative care needs of people with COPD. They note perceived benefits for quality of care, but also potential emotional impacts on staff providing palliative care support.
- (48)**Pilot randomised controlled trial of the feasibility, acceptability, and effect of early integrated palliative home care for people with COPD. They found that the intervention was feasible and acceptable, but did not detect anticipated effects on participant health outcomes.
- (47)**Pilot randomised controlled trial to determine the feasibility of early home-based palliative care for people with COPD found that while the service was feasible, there were significant challenges with recruitment to the trial.
- (49)**Prospective cohort study testing the effects of an inpatient geriatric rehabilitation program incorporating input from respiratory, palliative and geriatric care for people with COPD found positive impacts on disease-specific health status and exacerbations.
- (50)**Service evaluation of the impact of an integrated model of care for people with ILD incorporating expertise from respiratory care, palliative care and psychology, which found positive impacts on subsequent care processes (e.g. referrals to hospice-based support).

1. Rodriguez-Manas L, Feart C, Mann G, Vina J, Chatterji S, Chodzko-Zajko W, et al. Searching for an operational definition of frailty: a Delphi method based consensus statement: the frailty operative definition-consensus conference project. *J Gerontol A Biol Sci Med Sci.* 2013;68(1):62-7.
2. Milne KM, Kwan JM, Guler S, Winstone TA, Le A, Khalil N, et al. Frailty is common and strongly associated with dyspnoea severity in fibrotic interstitial lung disease. *Respirology.* 2017;22(4):728-34.
3. Mittal N, Raj R, Islam EA, Nugent K. The Frequency of Frailty in Ambulatory Patients With Chronic Lung Diseases. *Journal of primary care & community health.* 2016;7(1):10-5.
4. Marengoni A, Vetrano DL, Manes-Gravina E, Bernabei R, Onder G, Palmer K. The Relationship Between COPD and Frailty: A Systematic Review and Meta-Analysis of Observational Studies. *Chest.* 2018;154(1):21-40.
5. Bone AE, Hepgul N, Kon S, Maddocks M. Sarcopenia and frailty in chronic respiratory disease: Lessons from gerontology. *Chronic Respiratory Disease.* 2017;14(1):85-99.
6. Cicutto LC. Frailty: Is This a New Vital Sign? *Chest.* 2018;154(1):1-2.
7. Charbek E, Espiritu JR, Nayak R, Morley JE. Editorial: Frailty, Comorbidity, and COPD. *The journal of nutrition, health & aging.* 2018;22(8):876-9.
8. Bottiger BA, Nicoara A, Snyder LD, Wischmeyer PE, Schroder JN, Patel CB, et al. Frailty in the End-Stage Lung Disease or Heart Failure Patient: Implications for the Perioperative Transplant Clinician. *Journal of cardiothoracic and vascular anesthesia.* 2019;33(5):1382-92.
9. Guan C, Niu H. Frailty assessment in older adults with chronic obstructive respiratory diseases. *Clinical interventions in aging.* 2018;13:1513-24.
10. Jones AV, Evans RA, Man WDC, Bolton CE, Breen S, Doherty PJ, et al. Outcome measures in a combined exercise rehabilitation programme for adults with COPD and chronic heart failure: A preliminary stakeholder consensus event. *Chronic respiratory disease.* 2019;16:1479973119867952.
11. Ospina MB, Michas M, Deuchar L, Leigh R, Bhutani M, Rowe BH, et al. Development of a patient-centred, evidence-based and consensus-based discharge care bundle for patients with acute exacerbation of chronic obstructive pulmonary disease. *BMJ open respiratory research.* 2018;5(1):e000265.
12. Chin M, Voduc N, Huang S, Forster A, Mulpuru S. Practical lessons in implementing frailty assessments for hospitalised patients with COPD. *BMJ open quality.* 2020;9(1).
13. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *The journals of gerontology Series A, Biological sciences and medical sciences.* 2004;59(3):255-63.
14. Ierodiakonou D, Kampouraki M, Poulonirakis I, Papadokostakis P, Lintovoi E, Karanassos D, et al. Determinants of frailty in primary care patients with COPD: the Greek UNLOCK study. *BMC pulmonary medicine.* 2019;19(1):63.
15. Bernabeu-Mora R, Oliveira-Sousa SL, Sanchez-Martinez MP, Garcia-Vidal JA, Gacto-Sanchez M, Medina-Mirapeix F. Frailty transitions and associated clinical outcomes in patients with stable COPD: A longitudinal study. *PLoS One.* 2020;15(4):e0230116.

16. Ter Beek L, van der Vaart H, Wempe JB, Krijnen WP, Roodenburg JLN, van der Schans CP, et al. Coexistence of malnutrition, frailty, physical frailty and disability in patients with COPD starting a pulmonary rehabilitation program. *Clinical nutrition* (Edinburgh, Scotland). 2019.
17. Sheth JS, Xia M, Murray S, Martinez CH, Meldrum CA, Belloli EA, et al. Frailty and geriatric conditions in older patients with idiopathic pulmonary fibrosis. *Respiratory medicine*. 2019;148:6-12.
18. Guler SA, Kwan JM, Leung JM, Khalil N, Wilcox PG, Ryerson CJ. Functional ageing in fibrotic interstitial lung disease: the impact of frailty on adverse health outcomes. *The European respiratory journal*. 2020;55(1).
19. Nolan CM, Maddocks M, Maher TM, Banya W, Patel S, Barker RE, et al. Gait speed and prognosis in patients with idiopathic pulmonary fibrosis: a prospective cohort study. *The European respiratory journal*. 2019;53(2).
20. Kennedy CC, Novotny PJ, LeBrasseur NK, Wise RA, Sciruba FC, Benzo RP. Frailty and Clinical Outcomes in Chronic Obstructive Pulmonary Disease. *Annals of the American Thoracic Society*. 2019;16(2):217-24.
21. Ehsani H, Mohler MJ, Golden T, Toosizadeh N. Upper-extremity function prospectively predicts adverse discharge and all-cause COPD readmissions: a pilot study. *International journal of chronic obstructive pulmonary disease*. 2019;14:39-49.
22. Burtin C, ter Riet G, Puhan MA, Waschki B, Garcia-Aymerich J, Pinto-Plata V, et al. Handgrip weakness and mortality risk in COPD: a multicentre analysis. *Thorax*. 2016;71(1):86-7.
23. Quinn TM, Hill AT. Non-cystic fibrosis bronchiectasis in the elderly: current perspectives. *Clinical interventions in aging*. 2018;13:1649-56.
24. Brighton LJ, Bristowe K, Bayly J, Ogden M, Farquhar M, Evans CJ, et al. Experiences of pulmonary rehabilitation in people living with COPD and frailty: a qualitative interview study. *Annals of the American Thoracic Society*. In Press.
25. Kusunose M, Oga T, Nakamura S, Hasegawa Y, Nishimura K. Frailty and patient-reported outcomes in subjects with chronic obstructive pulmonary disease: are they independent entities? *BMJ Open Respir Res*. 2017;4(1):e000196.
26. Maddocks M, Kon SS, Canavan JL, Jones SE, Nolan CM, Labey A, et al. Physical frailty and pulmonary rehabilitation in COPD: a prospective cohort study. *Thorax*. 2016;71(11):988-95.
27. Neder JA, Marillier M, Bernard A-C, James MD, Milne KM, O'Donnell DE. The Integrative Physiology of Exercise Training in Patients with COPD. *COPD*. 2019;16(2):182-95.
28. Tanner A, Vassallo M, Kwan J, Allen SC. The pulmonary rehabilitation regimen: a treatment for frailty and 'inflammaging'? *British journal of hospital medicine* (London, England : 2005). 2018;79(8):432-7.
29. Kennedy C, Novotny P, Stevens E, Kirsch J, Garrett J, LeBrasseur N, et al., editors. Prospective Trial Using Pulmonary Rehabilitation to Treat Frailty. 2018 American Transplant Congress; 2018; Seattle, WA, USA: ATS Meeting Abstracts.
30. Brighton LJ, Evans CJ, Man W, Maddocks M. Improving exercise-based interventions for people living with both COPD and frailty: a realist review. *International journal of chronic obstructive pulmonary disease*. 2020(15):841-55.

31. Billingsley H, Rodriguez-Miguel P, Del Buono MG, Abbate A, Lavie CJ, Carbone S. Lifestyle Interventions with a Focus on Nutritional Strategies to Increase Cardiorespiratory Fitness in Chronic Obstructive Pulmonary Disease, Heart Failure, Obesity, Sarcopenia, and Frailty. *Nutrients*. 2019;11(12).
32. Kuniaki H, Akihiko T, Tetsuya H, Hatsuko M, Tomoko K, Shin O, et al. Improvement in Frailty in a Patient With Severe Chronic Obstructive Pulmonary Disease After Ninjin'yoeito Therapy: A Case Report. *Frontiers in nutrition*. 2018;5:71.
33. Meehan E, Foley T, Kelly C, Burgess Kelleher A, Sweeney C, Hally RM, et al. Advance Care Planning for Individuals With Chronic Obstructive Pulmonary Disease: A Scoping Review of the Literature. *Journal of pain and symptom management*. 2019.
34. Houben CHM, Spruit MA, Luyten H, Pennings H-J, van den Boogaart VEM, Creemers JPHM, et al. Cluster-randomised trial of a nurse-led advance care planning session in patients with COPD and their loved ones. *Thorax*. 2019;74(4):328-36.
35. Sinclair C, Auret KA, Evans SF, Williamson F, Dormer S, Wilkinson A, et al. Advance care planning uptake among patients with severe lung disease: a randomised patient preference trial of a nurse-led, facilitated advance care planning intervention. *BMJ Open*. 2017;7(2):e013415.
36. Grossman D, Katz A, Lock K, Caraiscos VB. A Retrospective Study Reviewing Interprofessional Advance Care Planning Group Discussions in Pulmonary Rehabilitation: A Proof-of-Concept and Feasibility Study. *J Palliat Care*. 2019:825859719896421.
37. Sussman T, Kaasalainen S, Lee E, Akhtar-Danesh N, Strachan PH, Brazil K, et al. Condition-Specific Pamphlets to Improve End-of-life Communication in Long-term Care: Staff Perceptions on Usability and Use. *Journal of the American Medical Directors Association*. 2019;20(3):262-7.
38. Sussman T, Kaasalainen S, Bui M, Akhtar-Danesh N, Mintzberg S, Strachan P. "Now I Don't Have to Guess": Using Pamphlets to Encourage Residents and Families/Friends to Engage in Advance Care Planning in Long-Term Care. *Gerontol Geriatr Med*. 2017;3:2333721417747323-.
39. Burgess Kelleher A, Sweeney C, Foley T, Hally RM, Meehan E, Savage E, et al. An e-Delphi Study to Identify Priority Areas for Education on Advance Care Planning in COPD Management. *Respiratory care*. 2020;65(3):347-54.
40. Smallwood N, Currow D, Booth S, Spathis A, Irving L, Philip J. Attitudes to specialist palliative care and advance care planning in people with COPD: a multi-national survey of palliative and respiratory medicine specialists. *BMC palliative care*. 2018;17(1):115.
41. Brighton LJ, Miller S, Farquhar M, Booth S, Yi D, Gao W, et al. Holistic services for people with advanced disease and chronic breathlessness: a systematic review and meta-analysis. *Thorax*. 2019;74(3):270-81.
42. Iyer AS, Dionne-Odom JN, Ford SM, Crump Tims SL, Sockwell ED, Ivankova NV, et al. A Formative Evaluation of Patient and Family Caregiver Perspectives on Early Palliative Care in Chronic Obstructive Pulmonary Disease across Disease Severity. *Annals of the American Thoracic Society*. 2019;16(8):1024-33.
43. Iyer AS, Dionne-Odom JN, Khateeb DM, O'Hare L, Tucker RO, Brown CJ, et al. A Qualitative Study of Pulmonary and Palliative Care Clinician Perspectives on Early Palliative Care in Chronic Obstructive Pulmonary Disease. *Journal of palliative medicine*. 2019.

44. Bove DG, Jellington MO, Lavesen M, Marsa K, Herling SF. Assigned nurses and a professional relationship: a qualitative study of COPD patients' perspective on a new palliative outpatient structure named CAPTAIN. *BMC palliative care*. 2019;18(1):24.
45. Bove DG, Lavesen M, Jellington MO, Marsaa KB-M, Herling SF. First year experiences with a palliative out-patients structure for patients with COPD: a qualitative study of health professionals' expectations and experiences. *BMC palliative care*. 2018;17(1):113.
46. Vitacca M, Comini L, Tabaglio E, Platto B, Gazzi L. Tele-Assisted Palliative Homecare for Advanced Chronic Obstructive Pulmonary Disease: A Feasibility Study. *Journal of palliative medicine*. 2019;22(2):173-8.
47. Janssens J-P, Weber C, Herrmann FR, Cantero C, Pessina A, Matis C, et al. Can Early Introduction of Palliative Care Limit Intensive Care, Emergency and Hospital Admissions in Patients with Severe Chronic Obstructive Pulmonary Disease? A Pilot Randomized Study. *Respiration; international review of thoracic diseases*. 2019;97(5):406-15.
48. Scheerens C, Pype P, Van Cauwenberg J, Vanbutsele G, Eecloo K, Derom E, et al. Early Integrated Palliative Home Care and Standard Care for End-Stage COPD (EPIC): A Phase II Pilot RCT Testing Feasibility, Acceptability, and Effectiveness. *Journal of pain and symptom management*. 2020;59(2):206-24.e7.
49. van Dam van Isselt EF, van Eijk M, van Geloven N, Groenewegen-Sipkema KH, van den Berg J-WK, Nieuwenhuys CMA, et al. A Prospective Cohort Study on the Effects of Geriatric Rehabilitation Following Acute Exacerbations of COPD. *Journal of the American Medical Directors Association*. 2019;20(7):850-6.e2.
50. Barratt SL, Morales M, Spiers T, Al Jboor K, Lamb H, Mulholland S, et al. Specialist palliative care, psychology, interstitial lung disease (ILD) multidisciplinary team meeting: a novel model to address palliative care needs. *BMJ open respiratory research*. 2018;5(1):e000360.
51. Iyer AS, Curtis JR, Meier DE. Proactive Integration of Geriatrics and Palliative Care Principles Into Practice for Chronic Obstructive Pulmonary Disease. *JAMA Internal Medicine*. 2020.