Improving understanding of disability in activities of daily living among adults with advanced cancer or respiratory disease and implications for clinical care

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Improving understanding of disability in activities of daily living among adults with advanced cancer or respiratory disease and implications for clinical care

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Abstract

Background

The population living with advanced cancer or respiratory disease is aging, resulting in changing care needs. Difficulty or inability to perform daily activities, known as disability in activities of daily living (ADLs) is one of the most common unmet needs in these populations. The prevalence of disability in ADLs is set to rise, resulting in a greater demand for care and rehabilitation. Rehabilitation interventions targeting disability in ADLs could help people maintain independence and delay or reduce need for care, but rehabilitation provision is currently inadequate across cancer and respiratory services. A better understanding of disability in ADLs and factors influencing change over time would help improve timing and delivery of rehabilitation interventions and equity in service provision.

Aim

To understand and compare disability in activities of daily living (ADLs) among adults with advanced cancer or respiratory disease, thereby informing future rehabilitation intervention(s).

Method

An observational study was conducted consisting of two components with convergent design.

Component 1: Secondary analysis of data from the International Access Rights and Empowerment programme (IARE), pooled from two studies relating to older people receiving palliative care (IARE I) or frail elderly (IARE II). The selected sample consisted of people with advanced solid cancer or Chronic Obstructive Pulmonary Disease (COPD). Measures assessed

disability in basic ADLs (Barthel Index), symptom severity (Palliative care Outcome Scale), and assistive device use (self-reported).

Component 2: A multi-site prospective cohort study in people with advanced non-small cell lung cancer (NSCLC), COPD or Interstitial Lung Disease (ILD). Self-reported questionnaires were completed at baseline and then monthly over 6-months. Primary measures for basic and instrumental ADLs were assessed using the Barthel Index and the Lawton–Brody IADL Scale respectively. Explanatory variables included difficulty in daily activities (World Health Organization Disability Assessment Schedule-2.0), symptom severity (Palliative care Outcomes Scale - Symptoms), and physical and social isolation (self-reported). The latter measure was introduced in response to the Covid-19 pandemic.

Analysis

Univariable and multiple variable logistic regression analysis was used to examine factors associated with disability in ADLs cross-sectionally at baseline, in components 1 and 2. Visual graphical analysis explored individual disability trajectories. Longitudinal data from the cohort study were analysed prospectively over six months and summary statistics were used to determine trajectories of ADL disability at group level. Univariable associations for variables recorded at baseline, between each basic ADL and instrumental ADL disability trajectory (increasing, decreasing, fluctuating) compared to the stable trajectory were explored using the Mann-Whitney-u test and chi-square test of independence. Multiple variable logistic regression analysis was used to examine factors associated with increasing disability in basic and instrumental ADLs over 6-months. Significance levels were set at 0.01 to account for multiple testing.

Results

Component 1: The pooled sample consisted of 159 participants (140 (94%) cancer, 19 (6%) COPD). 79% had disability in basic ADLs, which was most prevalent in stair climbing (65%), bathing (48%), dressing (39%), and mobilising (36%). Greater disability was independently associated with increased symptom burden (odds ratio, 1.08 [95% CI:1.02-1.15], P=0.01) and walking unaided (z=2.35, P=0.02), but not with primary diagnosis (z=0.47, P=0.64). There was wide inter-individual variation for change in disability in basic ADLs over time.

Component 2: Between March 2020 and January 2021, 110 NSCLC, 72 COPD, 19 ILD (121 (60%) had stage IV disease) participants were recruited, during the first year of the UK Covid-19 pandemic. At baseline, 104 (52%) and 142 (71%) were not fully independent in basic and instrumental ADLs, respectively. One-hundred-and-ninety-seven (96%) had difficulty in undertaking daily activities.

In the cross-sectional analysis, disability in basic ADLs was independently related to prolonged physical and social isolation (odds ratio [OR], 1.17 [95% CI: 1.03– 1.33], p=0.01), COPD or ILD (OR, 4.00 [95% CI: 1.20–8.14], p<0.001), and increased symptom severity (OR, 1.12 [95% CI: 1.06–1.19], p<0.001). Disability in instrumental ADLs was independently related to COPD or ILD (OR, 3.6 [95% CI: 1.41–7.10], p=0.005) and increased symptom severity (OR, 1.14 [95% CI: 1.07–1.22], p<0.001).

In the longitudinal sample (n=151), individual trajectories of ADL disability revealed wide variation in individual change, which were masked at group-level. Four different patterns emerged: increasing, decreasing, fluctuating, or stable. No independent predictors of basic ADL disability were identified. The only independent predictor of increasing disability in instrumental ADLs was difficulty mobilising (controlling for baseline diagnosis, symptom

severity, disability in ADLs, age, sex, living status, assistive device use, and physical activity). Every increase of 1 point on the WHODAS-2.0. mobility domain, increases the odds of a person following a trajectory of increasing disability in instrumental ADLs compared to a stable trajectory (odds ratio, 1.41 [CI: 1.14-1.74], p=0.002).

Conclusion

Disability in ADLs affects over half of people with advanced cancer or respiratory disease. Instrumental ADLs are more commonly affected than basic ADLs. Greater symptom severity and Covid-19-related physical and social isolation are associated with increased ADL disability at baseline. There is wide individual variability in disability over time, however, an increasing disability trajectory can be predicted by mobility limitation, which could be used to prompt referral to rehabilitation services. In clinical care, screening for mobility limitation is indicated among people with increased symptom severity, and people who have been physically or socially isolated. When assessing ADL disability, the measurement of difficulty and dependency is recommended, and disability management should be aligned with good symptom control. Further investment into rehabilitation is required to implement these recommendations and improve services for these groups.

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Statement of contribution

The contents of this thesis represent work conceived, planned, and undertaken by me, under the supervision of Matthew Maddocks, Irene Higginson, and Stephen Ashford. I conceived the research aims and objectives and was responsible for the design of this PhD study. I conducted all aspects of the primary study, including obtaining ethical approvals, development of study materials, co-ordination of multiple recruitment sites, data collection, and analysed the data for all findings presented within. The thesis represents my own original ideas and was written by me.

Members of the Cicely Saunders Institute Public Involvement Forum supported the cohort study design, advising on the choice of outcome measures and providing guidance on the development of study materials. Research Nurses employed within the NIHR Clinical Research Network supported recruitment at seven NHS Trusts, including King's College London, Nottingham University Hospital, Macclesfield District Hospital, South Tyneside and Sunderland, Royal Cornwall Hospital, Medway Hospital, York Hospital, and Western Sussex NHS Foundation Trust. Clinical staff at Guy's and St Thomas' NHS Foundation Trust, St Christophers Hospice, St Michaels Hospice and St Barnabas Hospice, assisted with participant identification. Administrative support was received for data entry.

My contribution to each of the three papers included in this thesis are specified below:

Incorporated publication 1 (background):

I developed the aims and objectives, systematic review protocol and search strategy, undertook the search, screened, and selected relevant papers. I extracted relevant data, conducted the narrative synthesis, and wrote the manuscript as first author.

Incorporated publication 2 (results):

I conducted a secondary analysis of data from the International Access Rights and Empowerment programme of research. I was responsible for writing the manuscript as first author.

Incorporated publication 3 (results):

I developed the protocol, applied for ethical approval, set up and co-ordinated recruitment sites, undertook data collection, analysed quantitative data, and wrote the manuscript as first author.

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Publications, presentations, and awards

Publications in peer reviewed journals

The following publications have been incorporated as chapters in this thesis:

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(Chapter 3)

Fettes L, Bone AE, Etkind SN, Ashford S, Higginson IJ, Maddocks M. Disability in Basic Activities of Daily Living Is Associated With Symptom Burden in Older People With Advanced Cancer or Chronic Obstructive Pulmonary Disease: A Secondary Data Analysis. Journal Pain Symptom Manage. 2021;61(6):1205-1214. doi: 10.1016/j.jpainsymman.2020.10.012.

(Chapter 6)

Fettes L, Bayly J, de Bruin LM, Patel M, Ashford S, Higginson IJ, Maddocks M. Relationships between prolonged physical and social isolation during the COVID-19 pandemic, reduced physical activity and disability in activities of daily living among people with advanced respiratory disease. Chronic Respiratory Disease. 2021;18:14799731211035822. doi: 10.1177/14799731211035822.

(Chapter 7)

Presentations and published abstracts

Trajectories of disability in Activities of Daily Living in advanced cancer or respiratory disease, including towards end-of-life: a systematic review. 19th World Congress of the European Association for Palliative Care (EAPC), Oct 2020

Awards and prizes

- Chartered Society of Physiotherapy (CSP) Educational Award, 2018
- NIHR CLHARC South London PhD Fees Award, 2018

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Abbreviations

Abbreviation	Meaning
ADL	Activities of daily living
A&E	Accident and emergency
AKPS	Australian Karnofsky Performance Status
BADL	Basic activities of daily living
BI	Barthel Index
BLF	British Lung Foundation
CFD	Compression of functional decline
CFS	Clinical Frailty Scale
CI	Confidence Interval
CDSE	Chronic Disease Self-Efficacy Scale
COPD	Chronic Obstructive Pulmonary Disease
COVID-19	Coronavirus disease 2019
CSRI	Client Service Receipt Inventory
EOL	End of Life
FEV1	Forced expiratory volume in 1 second
FT	Foundation Trust
FVC	Forced vital capacity
GCP	Good clinical practice
GOLD	Global Strategy for Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease
HRA	Health Research Authority
IADL	Instrumental activities of daily living
IARE	International Access Rights and Empowerment programme
ILD	Interstitial Lung Disease
IPOS	Integrated Palliative care Outcome Scale
IQR	Interquartile range
IRAS	Integrated Research Application System
ISRCTN	International Standard Randomised Controlled Trial Number - Registry
LB	Lawton Brody Instrumental ADL Scale
LGCM	Latent growth curve modelling
MCID	Minimal clinically important difference
MRC	Medical Research Council
NICE	National Institute for health and social care
NHS	National Health Service
NIHR	National Institute of Health Research
NSCLC	Non-small-cell lung cancer
POS-S	Palliative care Outcome Scale - Symptoms
PPI	Patient and Public Involvement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
OACC	The Outcome Assessment and Complexity Collaborative
OT	Occupational therapy
SCLC	Small-cell lung cancer
STROBE	STrengthening the Reporting of OBservational studies in Epidemiology
TLCO	Carbon monoxide transfer factor
VGA	Visual graphical analysis
UK	United Kingdom
USA	United States of America
WHO	World Health Organization
WHO-ICF	World Health Organization - International Classification of Functioning, Disability and Health
WHODAS-2.0.	World Health Organization Disability Assessment Schedule

Chapter 1

Introduction

Disability is defined by The World Health Organization (WHO) as 'any condition of the body or mind (impairment) that makes it more difficult for the person with the condition to do certain activities (activity limitation) and interact with the world around them (participation restrictions) [1]. Activities of daily living (ADLs) describe a collection of skills required to live independently [2]. Disability in ADLs describes a person having difficulty or becoming unable to perform ADLs independently. This difficulty or inability to perform ADLs is referred to in this thesis as "ADL disability".

Functional decline is common in advanced cancer or respiratory disease and becomes almost universal towards the end of life [3]. Resulting disability in ADLs is highly prevalent, affecting at least half of all patients with cancer [4] and COPD [5], though people with advanced disease are under-represented in studies to date. Currently, there is unprecedented population aging at a global level [6]. This increased life-expectancy means people with advanced cancer or respiratory disease will potentially be living with disability in ADLs for longer periods [7]. This in turn increases the demand on health and social care services and potentially need for formal care [8].

The symptoms and care needs of patients with advanced cancer or respiratory disease towards the end of life has been the focus of many palliative care studies [9]. However, these give more attention to distressing symptoms, psychosocial needs and carer support and few focus on physical function [10]. There is an evolving body of evidence supporting rehabilitation in palliative care, but provision of specialist services targeting functional decline

is poor [11]. Consequently, disability in ADLs is among the most common unmet supportive care needs in patients with advanced cancer or respiratory disease [4, 12].

Disability in ADLs towards the end of life remains poorly understood. This results in unsatisfactory delivery and timing of rehabilitation interventions and services targeting disability in ADLs, which aim to maintain independence and delay need for care [13]. Longitudinal studies have described functional trajectories of unselected patients retrospectively from death [14], but study of ADL disability trajectories are predominantly in community-dwelling older people [15, 16], and not specific to advanced cancer or respiratory disease. An understanding of prospective trajectories of ADL disability in advanced cancer or respiratory disease to inform clinical care is lacking.

This knowledge gap led me to design a longitudinal study to compare the prevalence of disability of patients with advanced lung cancer or respiratory disease, describe the course of disability in ADLs over time, and identify predictors of disability in ADLs to inform clinical care.

Chapter 2

Background

2.1. Introduction

This chapter defines cancer or respiratory disease and advanced disease criteria and outlines the epidemiology and prognosis for these conditions. It will provide an overview of the course (or trajectory) of disease, and how advanced cancer or respiratory disease affect the lives of individuals, with a particular focus on symptom experience, and the impact of the Covid-19 pandemic. This chapter goes on to introduce the concept of disability and its current management with rehabilitation.

2.2. Cancer and respiratory disease

2.2.1. Definitions and epidemiology

Cancer is a disease in which abnormal or damaged cells in the body grow uncontrollably and spread into or invade nearby tissues, or travel to other parts of the body [17]. Cancer can affect any part of the body. In the United Kingdom, nearly 3 million people are living with cancer [18]. The most common cancers are breast, prostate, lung, and bowel cancers, which together accounted for around half of all new cancer cases (53%) and cancer deaths (45%) in the UK in 2016-2018 [19].

Lung cancer is one of the most common cancer types. There are two types of lung cancer. Non-small cell lung cancer (NSCLC) is the most common type accounting for approximately 83% of patients diagnosed with lung cancer, as opposed to 13% with small cell lung cancer

(SCLC) [20]. NSCLC is defined as a malignant epithelial tumour and can be subdivided into adenocarcinomas and squamous cell carcinomas representing approximately 38.5% and 20% of all lung cancers, respectively [20]. Lung cancer can also be considered a type of respiratory disease.

Respiratory disease is any disease that obstructs or restricts the respiratory system, which can be malignant (e.g., lung cancer) or non-malignant (e.g., chronic obstructive pulmonary disease (COPD) or Interstitial lung disease (ILD)) [21]. Among common life-limiting respiratory diseases, an estimated 85,000 people are living with lung cancer, 1.2 million people living with chronic obstructive pulmonary disease (COPD) and 32,500 people living with interstitial lung disease (ILD). Collectively these conditions are responsible for more than 60% of UK deaths from respiratory disease each year [21].

2.2.2. Recognising advanced disease

Advanced disease can be identified by disease-based parameters (e.g., diagnosis or disease categorisation), timed-based parameters (e.g., chronicity or time to death) or needs-based parameters (e.g., recurrent hospital admissions, or palliative care needs) [22, 23]. Needs-based and time-based parameters are limited by their subjective or retrospective nature respectively [24]. Therefore, disease-based parameters are more commonly used. For most conditions advanced disease is commonly defined using disease categorisation criteria.

2.2.2.1. Cancer

For cancer the TNM Classification of Malignant Tumours (TNM) is a globally recognised standard for classifying the extent of spread [25] which helps the identification of advanced disease. There are four stages of cancer (I, II, III, and IV) defined by the size of the tumour (T),

extent of spread to the lymph nodes (N), and metastatic spread (M) to other parts of the body, as illustrated for lung cancer in table 2.1. Cancer is deemed advanced stage if the disease is stage III (locally advanced and unrespectable), or stage IV (defined as metastatic spread, distant spread).

Table 2.1. TNM Classification of Malignant Tumours (TNM) in lung cancer [25]

Tumour size / metastases	Subcategory	Nodes			
		N0	N1	N2	N3
T1	T1a	IA1	IIB	IIIA	IIIB
	T1b	IA2	IIB	IIIA	IIIB
	T1c	IA3	IIB	IIIA	IIIB
T2	T2a	IB	IIB	IIIA	IIIB
	T2b	IIA	IIB	IIIA	IIIB
T3	T3	IIB	IIIA	IIIB	IIIC
T4	T4	IIIA	IIIA	IIIB	IIIC
M1	M1a	IVA	IVA	IVA	IVA
	M1b	IVA	IVA	IVA	IVA
	M1c	IVB	IVB	IVB	IVB

Fifty percent of people with cancer survive the disease for ten years or more, but there is huge variation in survival between cancer types. Of the four most common cancers: breast, prostate, and bowel cancers have a five-year survival of 50% or more, but lung cancer remains difficult to diagnose and/or treat, and five-year survival is less than 20% [26], which is reduced to less than 13% in advanced disease [27]. SCLC is also known for progressing faster than NSCLC, in part because 60-65% of patients are diagnosed with stage IV metastatic disease [28].

2.2.2.2. Chronic Obstructive Pulmonary Disease (COPD)

For COPD, The Global Initiative for chronic obstructive pulmonary disease (GOLD) [29, 30] provides standardised classification using severity of airflow limitation with specific

spirometry cut-offs (grade 1 to 4) to distinguish between mild, moderate, severe, and very severe disease (table 2.2). GOLD also recommend assessment is extended to incorporate symptom burden and risk of exacerbation leading to hospitalisation, represented by groups A-D, as illustrated in figure 2.1.

Table 2.2: The Global Initiative for chronic obstructive pulmonary disease (GOLD) criteria for classification of COPD [29]

Classification of airflow limitation severity in COPD (based on post-bronchodilator FEV1)		
In patients with FEV1/FVC<0.70:		
GOLD 1:	Mild	FEV1 ≥ 80% predicted
GOLD 2:	Moderate	50% ≤ FEV1 < 80% predicted
GOLD 3:	Severe	30% ≤ FEV1 < 50% predicted
GOLD 4:	Very Severe	FEV1< 30% predicted

FEV1: Forced expiratory volume in 1 second FVC: Forced vital capacity

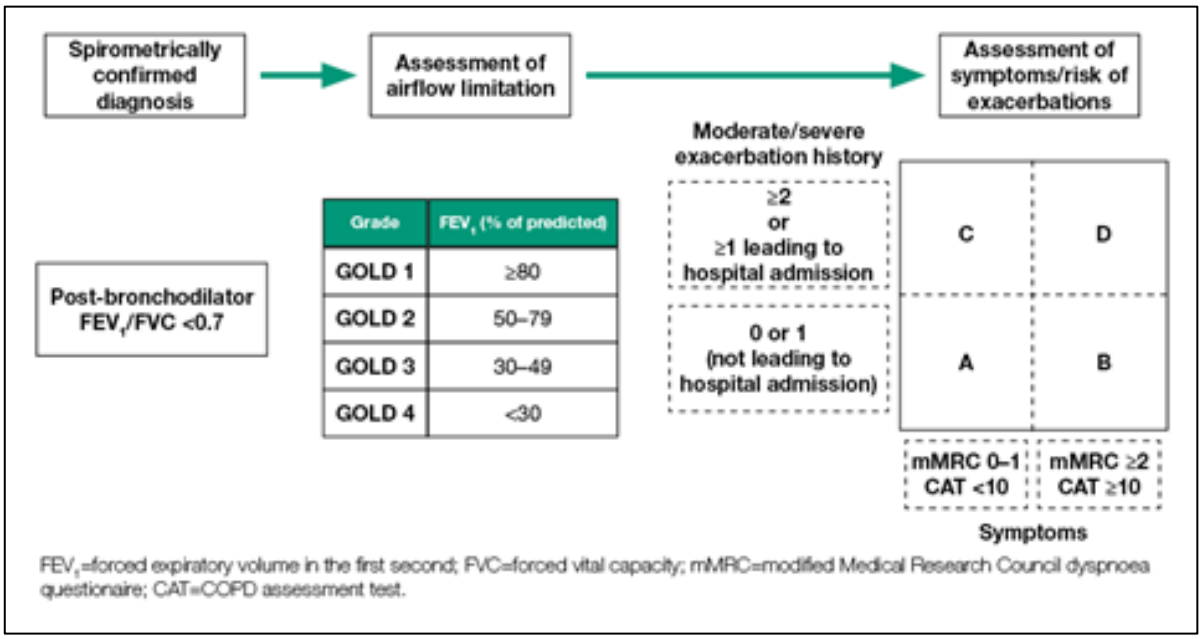


Figure 2.1. The refined ABCD assessment tool for the diagnosis, management, and prevention of COPD [30]

[Credit: GOLD, 2017, published with permission from The American Thoracic Society [30]]

People diagnosed with COPD generally have a greater life-expectancy than people diagnosed with cancer, due to its less aggressive nature, but the disease follows an indeterminate course with variable prognosis [3, 31]. The four-year life expectancy for people with COPD ranges from 64% in mild disease to 4% in very severe disease [32].

2.2.2.3. Interstitial lung disease (ILD)

Interstitial lung disease (ILD) is a broad category of respiratory diseases that includes over one-hundred disorders. Historically staging of ILD from different causes has been challenging, but progress in prognoses has been made over the last decade [33]. Common characteristics of ILD are unexplained scarring (idiopathic pulmonary fibrosis) and/or inflammation of the lungs. Disease severity in patients with ILD can be established using resting spirometry and gas transfer measurement at presentation [34].

Forced vital capacity (FVC), the maximum volume of air a person can forcefully exhale from the lungs, is used as a standard spirometry measure [35]. A >10% absolute decline in FVC %predicted over six months indicates a significant decline in pulmonary function, signifying disease progression [34]. However, FVC has been shown to be stable in a proportion of patients prior to death either because of missing values due to patients being unable to perform the test, or because of acute exacerbation or pulmonary hypertension, rather than declining lung capacity being the ultimate cause of death [36]. Carbon monoxide transfer factor (TLCO) levels at presentation offer a more reliable guide to predicted life-expectancy than other lung function tests, where a TLCO level of less than 40% is indicative of advanced disease, and a decline of >15% in TLCO in the first 6–12 months identifies patients with a much higher mortality [34].

The median life expectancy in ILD is three to five years from the time of diagnosis, although there is considerable heterogeneity with some patients living longer than ten years [37]. Prognosis is unpredictable, as ILD can follow a stable slow progressive course; a rapidly progressive trajectory; or a course with repeated acute exacerbations [38]. Acute exacerbations of unknown cause may lead to a life-threatening crisis [37].

2.2.3. Changing demography

People are living longer with advanced cancer or respiratory disease due to a combination of earlier identification and diagnosis, and advances in treatment leading to improved survival rates [6, 39]. The Global Burden of Disease study 2019 [7], confirms longer life-expectancy is found on a global level, and identifies a shift away from mortality and towards morbidity, focusing on disability as a major contributor to morbidity. In people aged over fifty, lung cancer and respiratory disease are recognised as the third and fourth leading cause of death and productive life lost due to disability respectively in the United Kingdom in 2019 [7]. This is higher than any other country with similar health system performance [7].

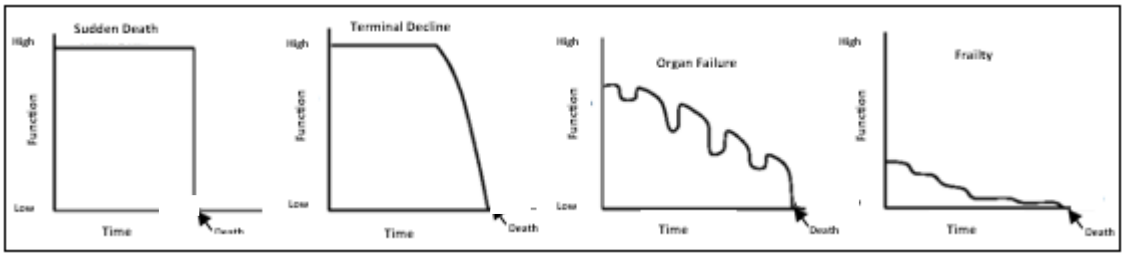
The profiles of people living and dying with advanced cancer or respiratory disease are becoming more diverse, bringing a new dimension to the healthcare needs of this population. By 2030, almost 50% of all people who die will be aged over 85 years [40]. Older age is associated with multi-morbidity, which in turn leads to a greater risk of poor functional status and prolonged disability [41]. It is important to understand how people live with advanced disease, to reduce disability, including through controlling the severity of disease related symptoms [42].

2.3. Living with advanced cancer or respiratory disease

2.3.1. Disease trajectories

Functional decline is a common consequence of advanced disease, becoming almost universal at the end of life. Lunney et al [3], described four patterns of functional decline towards death (figure 2.2). Firstly, the cancer trajectory (terminal decline) reflects a substantial period of high function followed by a sudden and sharp decline in function over the last few months or weeks of life. In contrast, patients with organ failure, including respiratory disease, often live for months or years with functional limitations, interrupted by intermittent bouts of worsening function, without fully regaining their previous functional ability. These deteriorations are generally related to illness exacerbations and worsening symptoms, and associated with hospital admissions, where any exacerbation can result in death or recovery, making prognosis difficult to predict [43]. Finally, sudden death is described by a sudden drop in function at the time of death, and patients with frailty or dementia follow a prolonged dwindling trajectory, usually dying at an older age [3].

Figure 2.2: Graphical Representation of Proposed Trajectories of Dying [3]



[Credit: Lunney et al, 2003, published with permission from the American Medical Association [3]]

It is important to note that disease trajectories in this instance are studied with a means to predicting death, rather than understanding functional decline with a view to changing the course of that trajectory [14]. As the demography of the population changes, so may the trajectory of advanced cancer or respiratory disease. As these patients live longer with advanced disease it could be possible to positively influence the trajectory in terms of function or disability prior to death.

2.3.2. Implications of disease-related symptoms

People with advanced cancer or respiratory disease often live with multiple symptoms. On average, people with advanced cancer report between three [44] and eleven [45] symptoms, and people with severe respiratory disease report between six [46] and eleven [47] symptoms. A systematic review of symptom prevalence across advanced cancer and non-cancer conditions showed a prevalence of 50% or higher for symptoms of fatigue, anorexia, and pain in both advanced cancer or COPD, and breathlessness, insomnia, and depression in advanced COPD but not cancer [9]. In a cohort study of people with lung cancer published following this review, 68-80% of participants reported feeling tired, shortness of breath, cough, feeling sleepy in the day and weight loss [48]. Further, fatigue and pain have been found to be the most distressing symptoms to people following cancer treatment [49]. In severe ILD the most prevalent symptoms are breathlessness (54-98%) and cough (59-100%) followed by heartburn (25-65%) and depression (10-49%) [50].

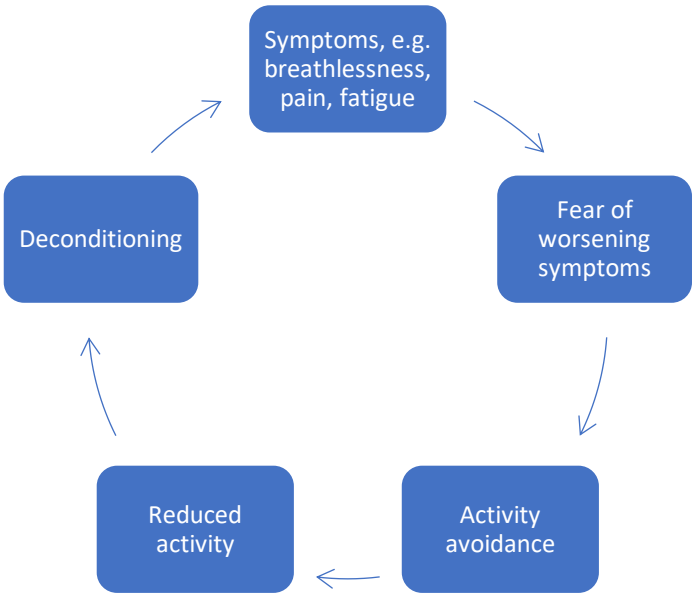
Symptoms in advanced cancer or respiratory disease can be persistent and difficult to control, which have a negative effect on functional independence [51, 52], and cause high levels of symptom-related distress [46, 49, 53]. Physical activity can aggravate exertional symptoms,

resulting in fear of activity [54]. Similarly, severe pain and breathlessness interfere with general activity in people with advanced lung cancer [55]. It is also recognised that breathlessness is a major contributor to reduced mobility for patients with COPD in the last year of life and severe ILD, causing housebound status and an increased likelihood of dying in hospital [53, 56].

Infection or exacerbation of disease may account for a flare-up of symptoms. Patients with COPD report a broad range of symptoms during acute exacerbations, including breathlessness, depression and fatigue [57]. An exacerbation in ILD causes increased breathlessness, coughing, increased sputum production, fever, and flu-like symptoms [58]. Acute exacerbations in COPD and ILD can be managed with antibiotics [29, 58], but are often associated with hospital admission and subsequent functional decline [59, 60].

Resulting physical inactivity from symptoms and/or exacerbation, causes a spiral of deconditioning (figure 2.3.) characterised by muscle weakness and declining function [61]. This cumulative functional loss accompanied with disease progression, eventually reduces an individual's ability to perform daily activities and participate in daily life.

Figure 2.3. Deconditioning in advanced disease



2.3.3. Impact of the Covid-19 pandemic on people with advanced cancer or respiratory disease

Covid-19 was declared a global pandemic on the 11th of March 2020 [62]. About one in five individuals worldwide were considered at increased risk of severe Covid-19 infection, due to underlying health conditions including cancer and respiratory disease, and many countries put policies in place to protect those at increased risk [63]. In the UK, as part of government policy, individuals fulfilling this high-risk criteria were classed as 'extremely clinically vulnerable' and physical and social isolation (shielding) was advised [64]. This directly affected people living with advanced cancer or respiratory disease.

Physical and social isolation refers to a complete or near-complete lack of contact with society [65]. It adversely affects psychosocial and mental health functioning [66], contributes to a reduction in physical activity and an increase in sedentary behaviour [67]. This escalates the deconditioning process associated with advanced disease and functional decline [59, 66]. Long term, physical and social isolation have also been found to be associated with an increase in mortality, and people who are socioeconomically disadvantaged or in poor physical or mental health are at higher risk [68]. This could potentially speed up the rate of deterioration in many people with advanced cancer or respiratory disease.

Furthermore, Covid-19 guidance has caused disruption to treatment, or disease management delivery, including reduced access to cancer therapies and rehabilitation [69]. Rehabilitation is reported to have been the most disrupted health service, often deemed non-essential [70]. In addition, individuals considering themselves extremely clinically vulnerable were reluctant to seek medical attention or receive support from others [71], which may account for a reduction in hospitalisation for exacerbation in COPD patients [72]. At the same time, social

support was lacking considerably [73], denying people access to a support system that is known to act as a protective psychological factor against a decline in mental and physical health–related quality of life [74].

People with advanced cancer or respiratory disease are at increased risk of developing disability in daily activities because of the pandemic [75, 76]. The first aim of post-pandemic rehabilitation would be to reverse the effects of deconditioning and prevent further harm [77]. This includes helping people to regain or maintain independence in ADLs and prevent or delay dependency [76]. This subsequently increases the need for rehabilitation in people with advanced cancer or respiratory disease. However, usual rehabilitation services have been disrupted and changed during the pandemic, adopting remote delivery where possible [78]. There is emerging evidence that interventions provided during this time may be delivered differently, with both positive [79-81], and negative [82] implications.

The next section will outline the concept of disability and rehabilitation provision will be discussed further in section 2.6.2.

2.4. Disability in advanced cancer or respiratory disease

2.4.1. Beyond assessment of functional limitation

When considering the assessment of functional loss, it is important to distinguish between functional limitation and disability. Functional limitation is defined as limitation in performance at the level of the whole person [83], whereas disability is defined as any restriction or lack of ability to perform a task or an activity [84]. Functional limitation can be measured in several different ways, including through use of impairment measures, physical performance measures (PPMs), self-report measures [83], and clinician-completed measures

[85]. Although, functional limitation is identified, these measures do not typically identify how functional impairment affects an individual's ability to perform a specific task or activity (disability), and the impact this has on their daily lives. Therefore, assessment of a person's function needs to go beyond limitation and include measurement of disability in daily activities.

2.4.2. Defining and measuring disability in ADLs

Activities of daily living (ADL) are defined as activities that constitute a person's daily life, which can be considered either basic ADLs (e.g. washing, dressing, bathing, toileting, feeding), or as more complex instrumental ADLs (e.g. shopping, housework, use of public transportation) [86]. Disability in ADLs can be considered in terms of ADL dependency; requiring assistance from others or assistive devices, or ADL difficulty; where an activity is managed independently but with increased difficulty as described by the person [87]. If a person develops disability in instrumental ADLs this may indicate need for domestic support with household tasks. Disability in basic ADLs usually requires a greater need for support at home particularly with personal care and often leads to an admission to a nursing home. For some people, disability in ADLs can be overcome by use of an assistive device for a particular task. If a task is found to be difficult an intervention at this point could prevent or delay dependency in that task.

Most validated measures for capturing disability in ADLs are self-reported by the patient or proxy [88, 89]. The most common used measures are the Barthel Index, Lawton Brody Instrumental Activities of Daily Living Scale, and Katz Index of Activities of Daily Living [89], but none of these measures assess both basic and instrumental ADLs. These measures assess

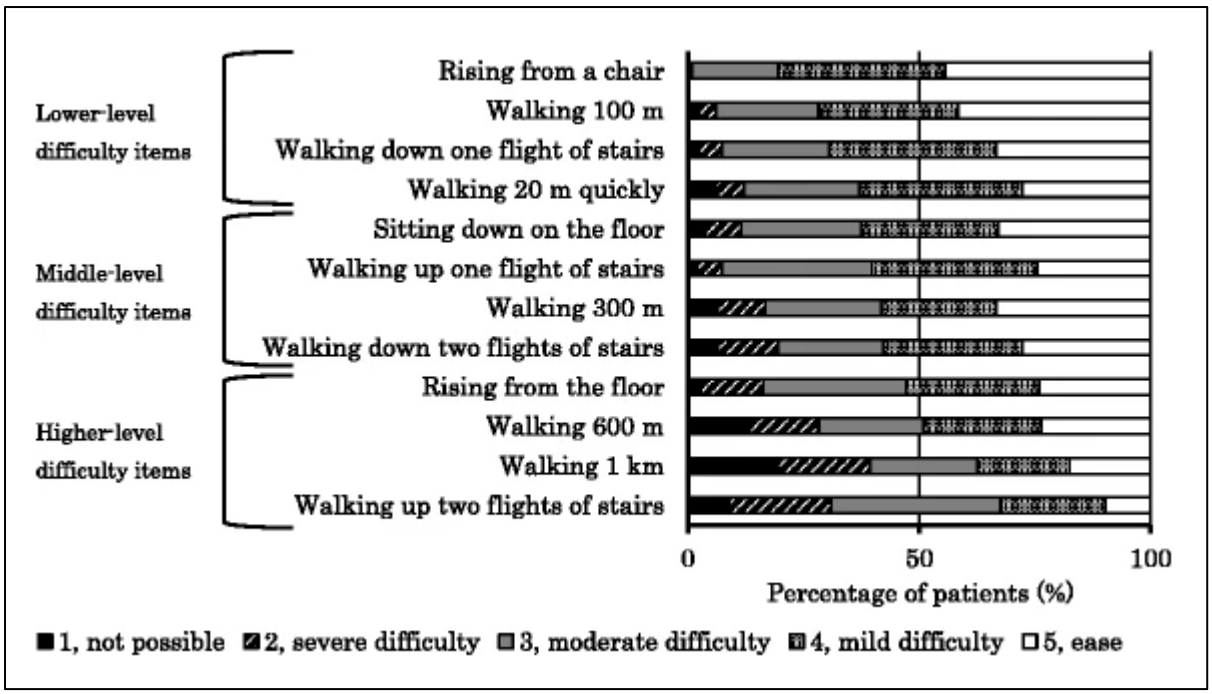
disability in terms of dependency but do not account for difficulty. This may generate a ceiling effect by excluding difficulty, as individuals scoring the highest score, indicating full independence, may still have difficulty performing that activity. The World Health Organization Disability Assessment Schedule (WHODAS-2.0.) is a globally recognized measure of disability in terms of difficulty. Strong evidence exists that including questions about difficulty and dependency provide complementary information, that together can more fully depict the continuum of disability. No one questionnaire can meet all the assessment and evaluation needs of the population, and a combination of existing questionnaires is recommended for fully assessing ADL disability [90]. In addition, use of assistance and perceptions of difficulty are inextricably interwoven. In order to ensure a comprehensive assessment of disability in ADLs, additional questions about assistive device use are recommended, and these should not be limited to people who report current problems in ADLs [91].

2.4.3. Prevalence of disability in ADLs

A meta-analysis identified 37% and 55% of adults with cancer have difficulty performing basic and instrumental ADLs, respectively [4], and a systematic review found disability in ADLs was prevalent in up to half of COPD patients [5]. Patients with advanced disease were under-represented in the studies included in these reviews. Included studies also use a range of different measurement scales. It is known that differences in the number of activities included in an ADL scale affect the prevalence estimates, as the greater the number of activities included, the higher is the probability of reporting ADL disability [92]. Therefore, measuring only one component of ADL (basic or instrumental) or using a binary measure could bias towards an underestimate in the extent of and change in disability.

Measures of difficulty and dependency may also provide conflicting estimates. Measures of difficulty have been found to give estimates from specific ADLs 1.2 to 5 times greater than dependency scales [93]. In one study, 24.1% of people surveyed experienced difficulty in performing one or more ADLs and 13.2% required human assistance in performing one or more ADLs [93]. Watanabe et al [94] explored levels of mobility difficulty in ambulatory patients undergoing haemodialysis, which describes increasing task difficulty from 'easy', through 'mild', 'moderate', and 'severe' difficulty, leading to 'not possible', the latter being a threshold where dependency occurs (figure 2.4). The figure also shows, difficulty progresses from higher-level difficulty tasks (e.g., walking 1km), where prevalence of difficulty and dependency is greater, to lower-level difficulty tasks (e.g., rising from a chair), where prevalence of difficulty is lower, and all participants are independent.

Figure 2.4. Difficulty levels and distribution of 12 items of the questionnaire on perceived mobility difficulty [94]



[Credit: Watanabe et al, 2018, published with permission from Springer Nature BV (Springer) [94]]

In addition, disability has been found to be underestimated in national surveys due to participants not reporting difficulty performing an activity despite using an assistive device, which in itself can be an indicator of disability [91]. Therefore, task modification or modified ability, needs to be considered to ascertain disability beyond task difficulty and dependence [95]. If assistive device use and rates of difficulty or personal help were combined, the prevalence of disability would significantly increase [91]. Therefore, large prevalence studies need to be interpreted with caution. Prevalence of disability in ADLs is difficult to assess, implying disability in ADLs could potentially be a more widespread problem in advanced cancer or respiratory disease than currently estimated.

2.4.4. Impact of disability in ADLs

Disability in ADLs impacts greatly on an individual's daily life. Patients often report not being able to perform daily activities independently and feeling a burden on others are among the most distressing things towards the end of their lives [96, 97]. ADL disability has been linked directly to poorer quality of life [98]. Even when deteriorating health hinders an individual's ability, they still maintain a desire to partake in daily activities [99]. Despite this, disability in ADLs remains among the most common unmet supportive care needs in patients with cancer or respiratory disease [4, 12]. Some patients with advanced COPD have been found to lack confidence in community-based services often leading them to seek hospital admission in the last year of life [100]. This leads to increased dependency on others and has been associated with extended hospital admissions and discharge to a nursing home [8]. Patients in the last year of life have an increased likelihood of hospice admission the greater the number of

disabilities in ADLs they have [101], and difficulty bathing is a strong predictor of nursing home placement [102].

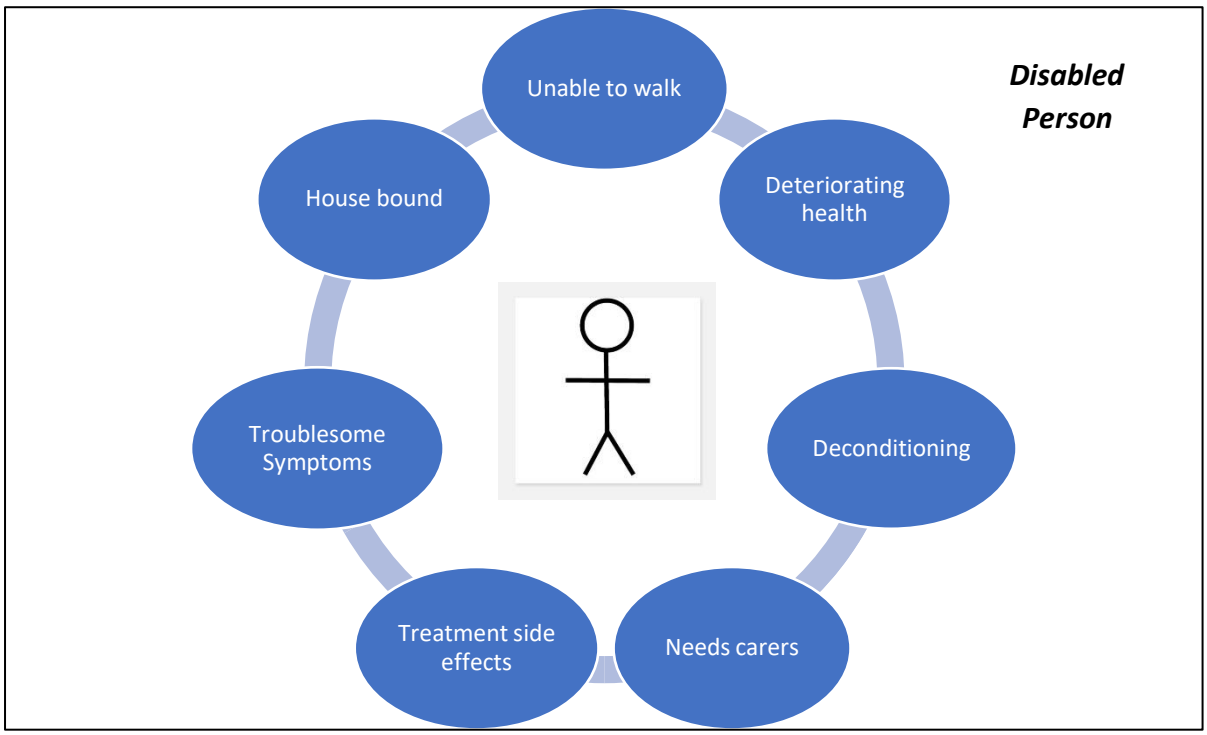
2.5. Models of disability

Conceptual models can be used to define and understand the impact of disability in context. The models have applications for assessment of disability and functioning, to inform patient needs and address disability by optimising clinical care. The three most common models of disability referred to in the literature are outlined below:

2.5.1. The medical model of disability

In the medical model of disability [103], disability is linked to an individual's physical impairments which can be diminished or corrected by medical management. It focuses on what is wrong with the person and not what the person needs, ignoring the personal experience of disability. In this model, resources to address disability are directed almost exclusively towards medical interventions, where adaption of a disabled person's environment could potentially be more beneficial to the individual and society at large, as well as financially cheaper and physically more attainable [104]. A worked example of the medical model of disability is presented in figure 2.5. [105].

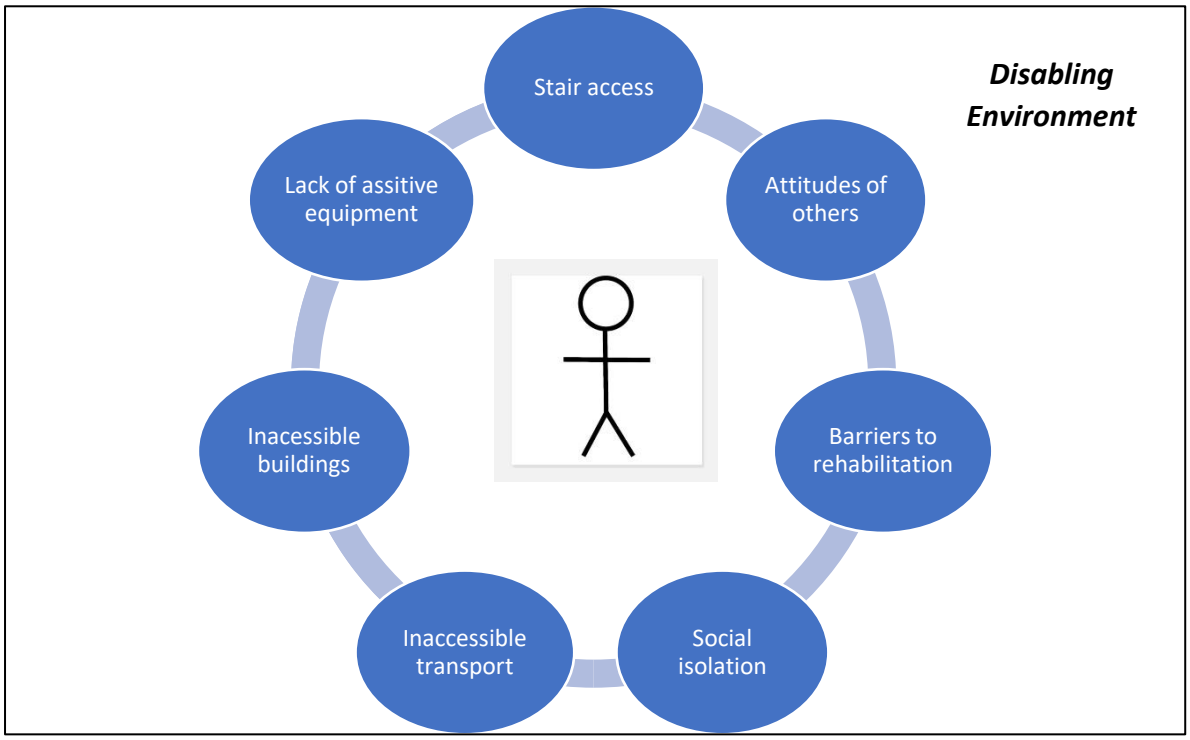
Figure 2.5. The medical model of disability



2.5.2. The social model of disability

The social model of disability [103] challenges the medical model and proposes that what makes someone disabled is not their medical condition, but the attitudes and structures of society. It attempts to understand disability by looking at the relationship between impairment (such as the inability to walk) and disability (restrictions caused when society does not accommodate individuals with impairments). The social model identifies barriers that restrict an individual's independence and how the environment can increase independence and overcome disability. It proposes that people can become disabled by lack of resources to address an individual's impairments [104], such as lack of funding for assistive devices to help someone unable to walk independently, which could make an individual disabled by society. A worked example of the social model of disability is presented in figure 2.6. [105].

Figure 2.6. The social model of disability



2.5.3. The biopsychosocial model of disability

This thesis adopts the biopsychosocial model of disability, which integrates both the medical and social models of disability, where health and illness are determined by a dynamic interaction between biological, psychological, and social factors [106] (Figure 2.7.). This model is the basis of The World Health Organizations International Classification of Functioning, Disability and Health (WHO-ICF) which provides a standard language framework for the description of health and disability [84, 107] (Figure 2.8.). Within the WHO-ICF, biological and psychological factors are represented by 'Health Condition' and 'Body Functions & Structures', social factors are represented by 'Environmental' and 'Personal' factors, 'Activity' and 'Participation' are both considered aspects of a person's functioning and therefore disability.

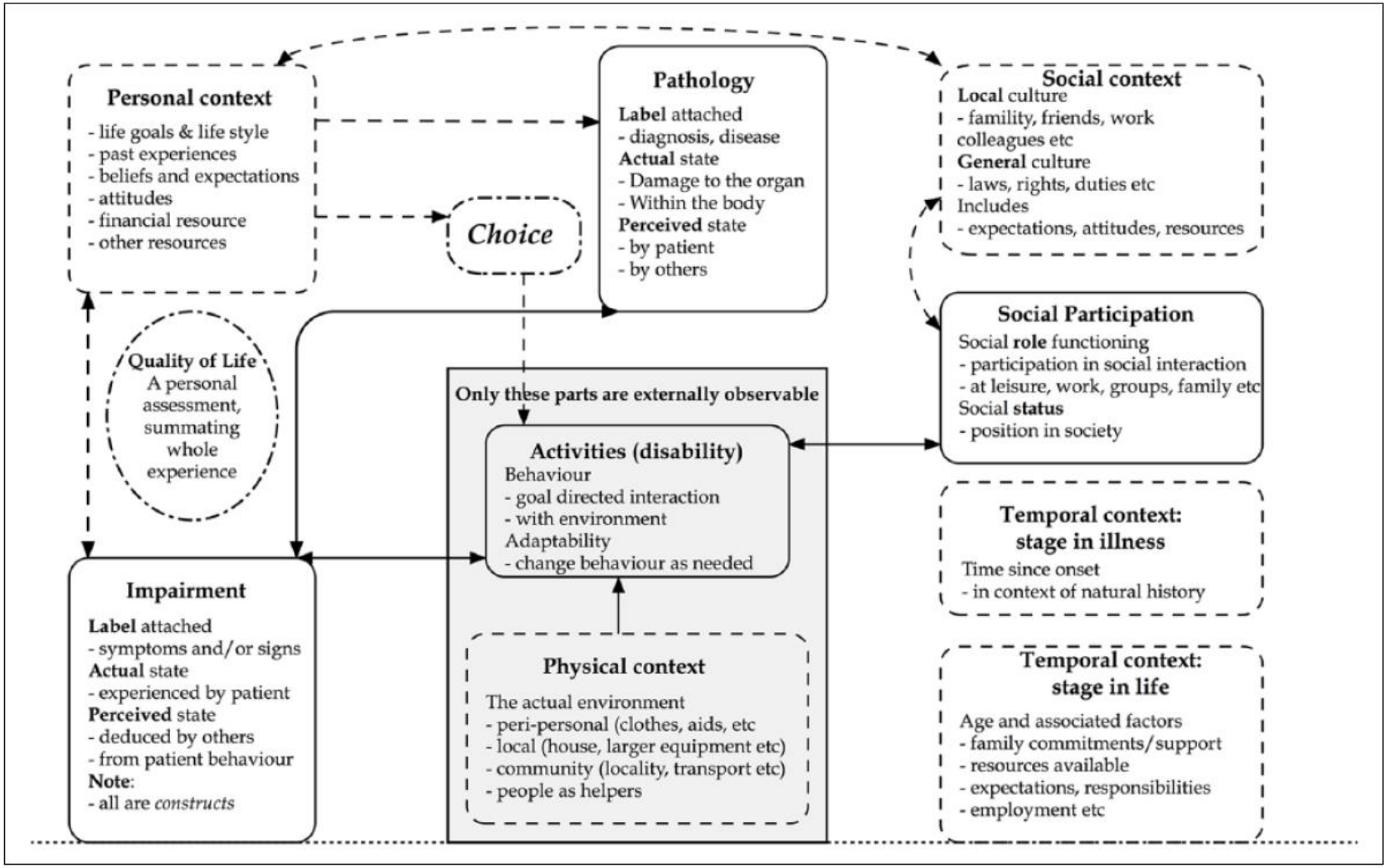
In the WHO-ICF, the term functioning is an umbrella term for all body functions, activities, and participation, while disability refers to all functional limitations, resulting in difficulties in doing certain activities (activity limitation), and participate in the world around them (participation restriction) [84]. In this model, emphasis is put on health and functioning rather than disability and it sees disability as interactive and multi-dimensional where all components of disability are important and any one may impact on another [108]. This is characterised by a complex relationship between an individual's health condition, impairments to body functions and structures, and contextual factors including personal attributes and the environment in which a person lives, as defined below [84]:

- *Health condition* – defined as diseases, disorders or injuries which can be physical or psychological. For instance, the health condition of interest in this thesis is advanced cancer or respiratory disease.
- *Body functions and structures* – Impairments to body functions and structures can be any problem with the physiological or psychological function of the body or mind such as symptom burden, or significant deviation or loss, often resulting from the health condition itself or an indirect consequence of treatment.
- *Personal factors* – internal personal factors relate to the background of an individual's life comprising individual features that are not part of a health condition but can influence how disability is experienced by an individual. These factors may include gender, ethnicity, education, social background, age, other health conditions, fitness, lifestyle, coping styles, overall behaviour pattern and individual psychological characteristics.

- *Environmental factors* – external environmental factors make up the physical, social, and attitudinal environment in which people live and conduct their lives, whether these factors are barriers or facilitators of disability. For example, a person's living situation, infrastructure, social attitudes, social support, health services, and available resources or equipment.

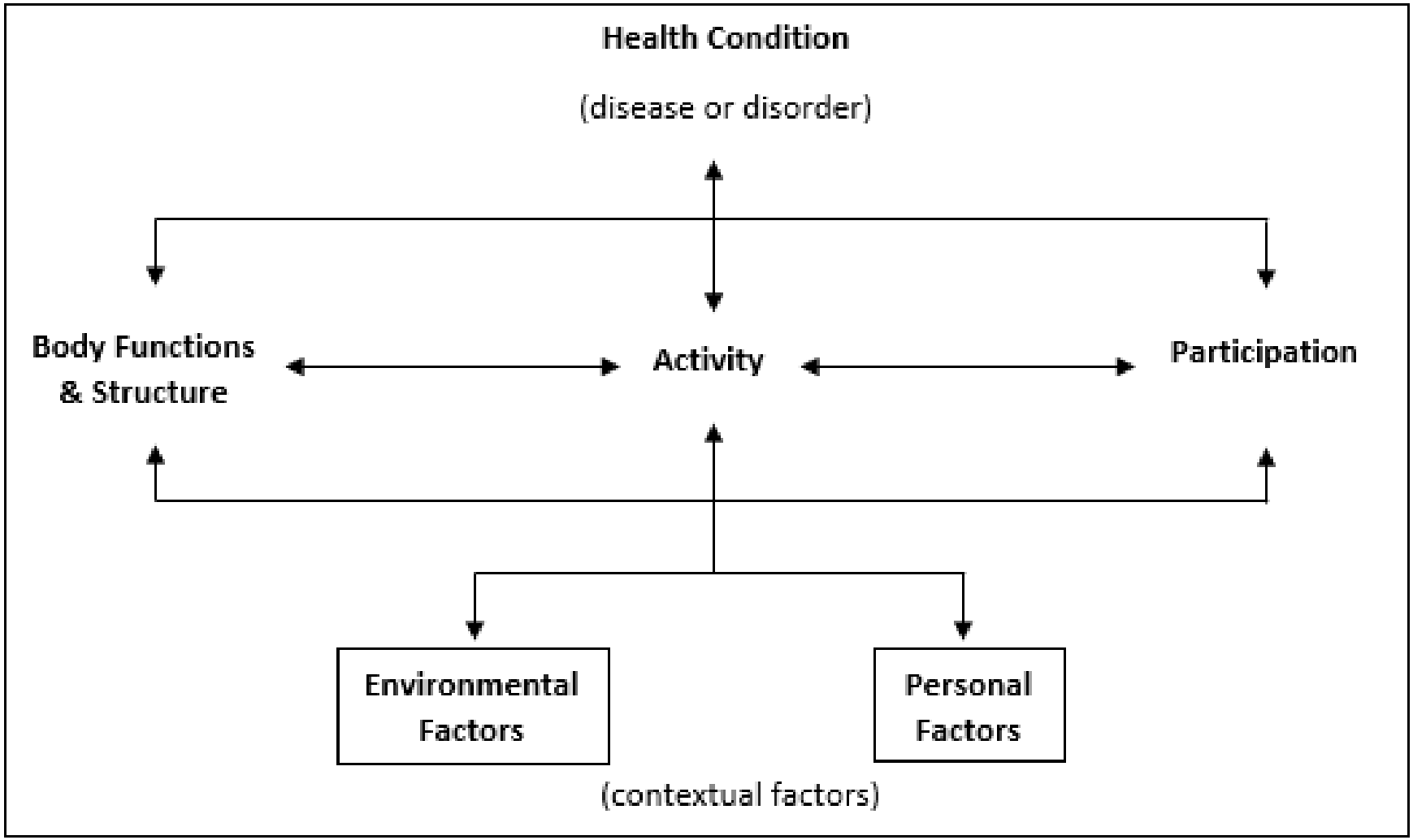
Reduced function at one or more of these levels contributes to disability in activity and participation. By identifying disability in terms of health-related bodily impairments (health-related factors), personal or environment factors, a person can potentially be enabled to overcome activity limitation or participation restrictions through rehabilitation interventions.

Figure 2.7: Biopsychosocial model of disability [107]



[Credit: Wade & Halligan, 2017, published with permission from Sage Publications Limited [107]]

Figure 2.8. The WHO International Classification of Function, Disability and Health Framework (WHO-ICF) [84]



[Credit: The World Health Organization, 2001, published with permission from WHO Press [84]]

2.6. Rehabilitation in advanced cancer or respiratory disease

2.6.1. The process of rehabilitation

The World Health organization defines rehabilitation as “a set of interventions designed to optimize functioning and reduce disability in individuals with health conditions in interaction with their environment” [110]. Rehabilitation seeks to reduce disability in ADLs, and increase independence, by helping people to maintain their optimal levels of physical, sensory, intellectual, and social functioning with minimum dependence on others for as long as possible, while optimizing their ability to adapt and respond to changes in circumstances [109, 110]. The World Health Organization states that rehabilitation should aim to achieve the following broad objectives [13]:

- Prevent the loss of function
- Slow down the rate of loss of function
- Improve or restore function
- Compensate for lost function
- Maintain current function

The conceptual process of rehabilitation may benefit any person with continuing disability, arising from any cause, at any age, at any stage of illness, and may be delivered in any setting [110]. This process is person-centred, comprising of a comprehensive holistic assessment of the patients’ current impairments and goals, and contributing personal and environmental factors, which may be modifiable by intervention.

Rehabilitation interventions are multi-factorial addressing individual impairment, personal factors, and their interaction with the environment as appropriate. In advanced disease, rehabilitation interventions aim to enable the patient to remain active and productive in their

daily lives, and with minimum dependence on others [111]. Rehabilitation interventions include non-pharmacological symptom management, exercise prescription, task modification, self-management, carer training, and provision of assistive devices [112-114]. These interventions are delivered by a range of allied health professionals including physiotherapists, occupational therapists, speech and language therapists, dietitians, and rehabilitation assistants, as well as nurses, and health care assistants, often working within a multi-disciplinary team [115, 116].

Disability may be addressed on the individual level, for example, by using techniques to manage symptoms such as breathlessness management, education to optimise function such as pacing, or give confidence through repetition of functional tasks to combat fear. Alternatively, disability may be addressed on the social level by adjusting the environment to enable them to function within it, such as through the provision of assistive devices. The aim and context of the rehabilitation service will determine the combination of professionals involved and availability of specific activities or interventions [117, 118].

2.6.2. Rehabilitation service provision

The World Health Organization Rehabilitation 2030 initiative, draws attention to the unmet need for rehabilitation worldwide, acknowledging the need to prioritise rehabilitation as a health strategy to address disability, as considering population aging, demand for rehabilitation will continually increase [13]. In the UK the NHS commissioning guidance for rehabilitation states three key messages [119]:

- Rehabilitation intervention underpins all conditions
- Rehabilitation is everyone's business

- Rehabilitation intervention runs through the life course

Patients with advanced cancer or respiratory disease, may have their condition managed by disease-specific specialists, general practitioners in primary care teams or hospital-based generalists (e.g. elderly care), or by palliative care specialists in hospices, hospitals and community settings [120]. Patients may receive rehabilitation within a disease specialism as an inpatient or outpatient, or they may be referred to a rehabilitation service or receive rehabilitation as part of multi-disciplinary palliative care. However, traditionally, respiratory disease has a strong bias towards rehabilitation over cancer [121]. Outside of acute settings, there are different rehabilitation services which may be offered to patients with advanced cancer or respiratory disease throughout their disease trajectory, with varying guidance and access. These include pulmonary rehabilitation, cancer rehabilitation, intermediate care, and rehabilitation in palliative care, as outlined below.

2.6.2.1. Pulmonary rehabilitation

Pulmonary rehabilitation is a nationally commissioned exercise and education programme designed for people with lung disease who experience symptoms of breathlessness. It is recognised as best practice in the British Thoracic Society guideline on pulmonary rehabilitation in adults for the management of respiratory disease, including after exacerbation [122], and recommended within national guidance for the diagnosis and management of COPD [123] and ILD [124]. National guidelines on the diagnosis and management of lung cancer [125] do not recommend pulmonary rehabilitation despite potential observed benefits of exercise for patients with lung cancer [126].

Delivery of pulmonary rehabilitation has its challenges. It needs to be held in buildings which are easily accessible to people with disabilities, and places need to be available within a

reasonable time of referral [123]. Barriers to enrolment are multifactorial and include not recognising rehabilitation needs in routine primary and secondary care practice; failure to recommend and refer patients to pulmonary rehabilitation services; poor communication with patients about potential benefits; as well as individuals comorbidities, logistical and financial challenges, and competing personal demands that make participation difficult [127, 128]. Dropout rates of 20–40% are common in pulmonary rehabilitation programmes [54] suggesting it is not universally beneficial to all who attend.

2.6.2.2. Cancer Rehabilitation

National guidelines on the rehabilitation management of cancer specialties mainly focus on curative management. Cancer rehabilitation has evolved in recent years, where it has moved beyond recovery after cancer treatment to supporting people to live with the impact of cancer from diagnosis through to end of life. Although there is not currently a national guideline for cancer rehabilitation, there is a growing body of evidence supporting rehabilitation in advanced cancer. A systematic review evaluating the effectiveness of exercise interventions for individuals with advanced cancer found exercise can maintain or improve fitness and physical function, and may reduce fatigue and enhance quality of life [129].

The report Achieving World Class Cancer Outcomes: a strategy for England 2015-2020, published by Cancer Research UK [130], sets out recommendations for rehabilitation to become fully embedded in the care pathway. The strategy stipulates that access to adequate and appropriate rehabilitation services is essential in order that people living with cancer achieve optimum function and quality of life, encompassing appropriately skilled allied health professionals to support their individual needs throughout the whole cancer pathway.

However, there is likely to be variation in the commissioning of cancer rehabilitation services across the UK [131], suggesting inequity in implementation of the strategy's vision.

2.6.2.4. Intermediate care

In the UK, intermediate care refers to a range of integrated multidisciplinary services that help people to be as independent as possible at home [132]. Intermediate care aims to prevent unnecessary admissions to hospital and care homes or aid discharge from hospital through a person-centred approach to rehabilitation [133]. This may be as:

- Reablement: aims to help patients recover skills and confidence and maximise their independence in their home (or care home). This is a time-limited service of up to 6 weeks to prevent admission or aid discharge from hospital and may be delivered alongside homecare.

- Crisis response: an urgent short-term (usually up to 48 hours) community-based intervention which aims to avoid imminent hospital admissions.

- Bed-based intermediate care: offered when more intensive rehabilitation is required to prevent unnecessary admissions to acute hospitals or premature admissions to long-term care, and to support timely discharge from hospital. For most people, interventions last up to 6 weeks.

The national guidance on intermediate care including reablement [133] specifies that a rehabilitation referral is indicated if: it would improve a person's ability to live independently; they are at risk of hospital admission; have been in hospital and need help to regain independence; are living at home and having increasing difficulty with daily life through illness or disability. The guideline states people should not be excluded from intermediate

care based on their diagnosis. However, neither cancer nor respiratory disease is listed as common conditions managed by intermediate care teams, despite recommendation of occupational therapy and potential benefits of hospital at home or early discharge in the management of COPD [123]. Intermediate care staff should be able to recognise and respond to deterioration in the person's health or circumstances [133], but these services do not specifically target advanced disease. More often these are short-term reactive services that respond to a crisis, such as a fall or a hospital admission, rather than responding to forthcoming functional decline and preventing a potential crisis occurring.

2.6.2.5. Rehabilitation in Palliative and End-of-Life Care

End-of-life care is the care provided to people with advanced disease, which may be delivered by disease-specific specialists, general practitioners in primary care teams or hospital-based generalists (e.g. elderly care), or by palliative care specialists in hospices, hospitals, and community settings. These patients may receive 'supportive care' which is given alongside disease modifying and potentially life-prolonging therapies, particularly in cases of advanced cancer, which is not curable but responds to treatment such as chemotherapy, radiotherapy, or immunotherapy. Alternatively, they may receive 'palliative care' aimed at giving comfort to distressing symptoms and maintain quality of life by integrating the psychological, social, and spiritual aspects of the person's care, and continue to offer a support system to help people to live as actively as possible until they die [120]. Historically, palliative care provision has a strong bias towards advanced cancer over other life-limiting conditions [135], but the benefits of palliative care for non-cancer conditions including respiratory disease has been recognised in the more recent national guidelines on End of life care for adults [136].

Rehabilitation is recognised in the national guidelines for Improving Supportive and Palliative Care for Adults with Cancer (2004) [134], highlighting patients may benefit from rehabilitation whatever their stage of illness and wherever the care is provided. This complements the palliative care approach. Despite the holistic essence of palliative care, services do not routinely assess function or disability, giving more attention to relieving distressing symptoms, psychosocial needs and carer support [10], and usually in people recognised to have a short prognosis. Although the guideline on End of life care for adults [136] recognises the importance of a multi-disciplinary team, it does not expand on the make-up of that team, and explicit recognition of rehabilitation is lacking. The benefits of early integration of palliative care with respiratory, primary care, and rehabilitation services, with referral based on the complexity of symptoms and concerns, rather than prognosis, is now being recognised [137], as well as a key component of cancer care [138].

However, rehabilitation services in palliative care are generally confined to specialist centres, and staff with specific rehabilitation expertise tend to be employed in cancer centres and hospices [11]. There are barriers to access of rehabilitation services for people with advanced cancer or respiratory disease, including poor detection of rehabilitation problems; inadequate training; waiting lists; delays in accessing equipment; and frontline practitioners are often unaware of the benefits of rehabilitation at the end-of-life preventing referral or acceptance of referrals [128, 134, 139-141].

2.6.2.6. Gaps in rehabilitation provision

Existing models of rehabilitation across malignant and non-malignant diagnoses are similar in their patient centred approach, but all present barriers to access for patients with advanced disease. The main difference in rehabilitation across diagnoses is that pulmonary

rehabilitation is a well-formed fixed programme which is nationally commissioned, whereas cancer rehabilitation is ad-hoc and varies by cancer type. A nationally commissioned model of cancer rehabilitation does not currently exist. As highlighted above, there is potential inequity in the provision and access of rehabilitation across sectors (pulmonary rehabilitation, cancer rehabilitation, intermediate care, palliative care), that are suitable and/or accessible for patients with advanced cancer or respiratory disease. This is in part because current service provision is not structured around forthcoming functional decline and/or fluctuating needs. Although pulmonary rehabilitation is nationally commissioned, other rehabilitation services specifically targeting the needs of patients with deteriorating health conditions and anticipated functional loss are not. This highlights unmet palliative care and rehabilitation needs in this population, fitting the rehabilitation initiative of the World Health Organization for 2030 [119], outlined above.

2.7. Summary

This chapter highlights disability as a major and growing concern for people with advanced cancer or respiratory disease, which often impacts on their ability to manage ADLs independently. Disability in daily activities is recognised as an unmet care need, likely made worse by the impact of the Covid-19 pandemic. This thesis adopts the biopsychosocial model of disability, where health, illness and disability are determined by a dynamic interaction between biological, psychological, and social factors.

The rehabilitation process resonates powerfully with the definitions of palliative care, since palliative care is an approach that focuses not on the disease (which can no longer be cured) but on the best ways to improve quality of life and other outcomes. Despite current services,

there is a gap in rehabilitation provision for people with advanced cancer or respiratory disease. Rehabilitation could be integrated earlier in the disease trajectory along with earlier palliative care, with the joint focus of enabling people to live until they die. How disability can be better understood to address this change in approach will be introduced in the next chapter.

Chapter 3

Rationale for thesis

3.1. Introduction

This chapter provides a rationale for the thesis. It will summarise the key issues surrounding the importance of addressing disability in ADLs in advanced cancer or respiratory disease to help improve clinical care. Based on evidence outlined in the previous chapter, the need to develop rehabilitation interventions and service provision for people with advanced cancer or respiratory disease, based on better understanding of disability in ADLs, will be justified. The importance of longitudinal study of disability will be introduced, with reference to the Medical Research Council (MRC) framework for complex interventions. This chapter incorporates a published systematic review of trajectories of disability in ADLs in advanced cancer or respiratory disease (incorporated publication 1) and closes by highlighting key gaps in the current evidence.

3.2. Key Issues for clinical care

Chapter 2 highlighted how people with advanced cancer or respiratory disease are living longer with disability reducing their quality of life and ability to live independently. This in turn, increases the demand and requirement for health and social care services and formal care. Rehabilitation could address this need, but there are currently gaps in service provision for people with advanced cancer or respiratory disease across care sectors. As disability becomes an increasingly large component of disease burden and health expenditure, research investment is needed to identify effective intervention strategies [7].

Identifying rehabilitation interventions or services that can prevent or delay disability in daily activities is becoming essential to keep people independent and reduce the pressure on health and social care services. All healthcare services need to consider patients holistically, giving equal attention to disease, disability, and distress, working in parallel to achieve this purpose, as well as structural and organisational change, to meet the needs of patients [142]. This is becoming increasingly important as health service costs are primarily related to levels of impairment and/or disability and dependence, but healthcare funding remains primarily based on pathological diagnosis [107].

In the UK, the NHS 10-year plan [143] is driving this change with an investment of £4.5 billion into community multi-disciplinary teams, which aim to help people live independently at home for longer and prevent unnecessary hospital admissions or institutional care [140]. This brings the opportunity to develop rehabilitation services in advanced disease which are integrated with other healthcare services. This requires establishing referral protocols to rehabilitation services for patients with advanced disease and multi-disciplinary working, both within a hospital and across acute, community and specialist services to enable continuity of rehabilitation throughout the broader care pathway [39].

3.3. Importance of longitudinal study of disability in ADLs

Rehabilitation interventions and services exist that could potentially benefit people with advanced cancer or respiratory disease who have disability in ADLs (section 2.6.2.). However, due to the complex and deteriorating nature of advanced disease, patients often present with difficult problems and vary considerably in their level of function, prognosis, and reasons for engaging with services [41-43].

To improve appropriate service delivery, an understanding of the context in which to adapt or deliver rehabilitation targeting ADL disability in people with advanced cancer or respiratory disease is required. This is underscored in the 2021 version of the MRC guidance [144], where context is defined as any feature of the circumstances (physical, spatial, organisational, social, cultural, political, or health-economical) in which an intervention is conceived, developed, evaluated, and implemented.

In the population of advanced cancer or respiratory disease, the context of the required rehabilitation intervention is to manage declining function in patients with deteriorating health. By thinking about rehabilitation in this context it may be possible to target intervention towards changing the disability trajectory, aiming to prevent or delay further decline, maintain current function, or temporary improvements in disability.

Misunderstanding the context of the intervention may lead to ineffective delivery. For example, a randomized controlled trial evaluating the efficacy of occupational therapy (OT) in people with advanced cancer on disability in ADLs showed no significant effects [145]. A process evaluation of this trial identified that beneficial effect could be limited by lack of continual disability in the sample over time, and inadequate timing of the intervention and follow-up procedure [146]. Also, the OT intervention may only help one component of care and may need to be complimented by other interventions [110]. By paying attention to the biopsychosocial models of disability and rehabilitation, the reach, timing, and delivery of the intervention in this context might have been improved.

The context of declining function and potential change in trajectories of disability in ADLs can be better understood through longitudinal study. Understanding disability, at just one point in time, provides a limited perspective. Longitudinal study of disability is needed to elucidate

the epidemiology of disability, to help inform the development of effective components of rehabilitation to maintain and restore independent function [16]. Gill et al found in a longitudinal cohort study in older people, that the disabling process is characterized by multiple and possibly interrelated disability episodes, even over short periods of time, and that disability often results when a vulnerable person is affected by an intervening event [16].

Intervening events or crisis, such as a fall, could be prevented or modified by intervention if there is a better understanding of how different health-related, personal, and environmental factors contribute towards the event(s) that cause or change levels of disability. The longitudinal study of disability in ADLs is an effective and appropriate way to observe change in ADL disability over time and allows for as many variables as required to be studied, to determine the timing of determinants and outputs [147].

Trajectories are characterised by three or more timepoints. They can be drawn prospectively from study entry (forward trajectory) or retrospectively from death (backwards trajectory). A retrospective study of functional performance status in the last four months of life within specialist palliative care services, identified two trajectories, one with a slow decline, the other with stable functional impairment, but both were followed by a rapid decline in the last two weeks of life [148]. Prospective study of trajectories is required to understand clinical implications of ADL disability in the deteriorating patient, which might be more helpful in making recommendations for appropriate and timely interventions and services than retrospective trajectories.

The following systematic review introduces the need for exploring trajectories of ADL disability in this population, followed by aims and methods of the review. It identifies common trajectories of disability in ADL. Causes and consequences of increasing disability are

identified and mapped using the WHO-ICF framework of disability introduced in chapter 2. By applying the WHO-ICF framework in this way, the contribution of health-related factors, personal attributes, and environmental factors, and how they relate to or cause ADL disability in this population and possible impact can be better understood. The discussion highlights limitations of this work and implications for future research.

3.4. Incorporated paper 1: Trajectories of disability in ADLs

Fettes L, Neo J, Ashford S, Higginson IJ, Maddocks M. Trajectories of disability in activities of daily living in advanced cancer or respiratory disease: a systematic review. Disabil Rehabil. 2022 May;44(10):1790-1801. doi: 10.1080/09638288.2020.1820587. Epub 2020 Sep 22. PMID: 32961067.

Title:
Trajectories of disability in activities of daily living in advanced cancer or respiratory disease: A systematic review

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Abstract
Introduction: Advanced cancer and/or respiratory disease threaten a person's independence in activities of daily living. Understanding how disability develops can help direct appropriate and timely interventions.
Aim: To identify different trajectories and associations of disability in activities of daily living and appraise its measurement.
Methods: Medline, Embase, PsychINFO, and CINAHL databases were searched for cohort studies with measures of disability in activities of daily living in advanced cancer or respiratory disease at three or more timepoints. Data were narratively synthesized to produce a typology of disability trajectories and a model of factors and outcomes associated with increasing disability.
Results: Of 5702 publications screened, 11 were included. Seventy-four disability trajectories were categorized into typologies of unchanging (n=20), fluctuating (n=21) and increasing disability (n=33). Respiratory disease did not predict any particular disability trajectory. Advanced cancer frequently followed trajectories of increasing disability. Factors associated with increasing disability included: frailty, multi-morbidity, cognitive impairment, and infection. Increased disability led to recurrent hospital admissions, long-term care and/or death. Methodological limitations included use of non-validated measures.
***Conclusions*:** Increasing disability trajectories in advanced cancer and/or respiratory disease is related to potentially modifiable personal and environmental factors. We recommend future studies using validated disability instruments.

Implications for Rehabilitation
- Disability in activities of daily living (ADL) is a common unmet need in advanced cancer or respiratory disease and represents an important outcome for patients, caregivers and health and social care services.
- Trajectories of ADL disability can be categorized into increasing, fluctuating and unchanging disability, which could help planning of rehabilitation services in advanced cancer or respiratory disease.
- Increasing disability in advanced cancer or respiratory disease relates to personal and environmental factors as well as bodily impairments, which can all be modifiable by intervention.
- This review highlights implications for the measurement of ADL disability in advanced cancer or respiratory disease and recommends use of validated measures of ADL to understand what factors can be modified through rehabilitation interventions.

Key words
Activities of daily living; Cancer; Disability; Functional trajectories; Occupational Therapy; Rehabilitation; Respiratory disease; Systematic review

Introduction

Due to progressions in treatment and an aging population, people are often living longer with advanced cancer or respiratory disease [1]. Functional decline is a common consequence of both conditions, caused by symptom burden, muscle weakness, and/or multi-morbidity, which results in prolonged dependency and high service use [2-4]. This is becoming increasingly important as health service costs are primarily related to levels of impairment and/or disability and dependence, but healthcare funding is still primarily based on pathological diagnosis [5]. Compared to other conditions, management of advanced cancer or respiratory disease is heavily focused on medical management and acute response to exacerbations [6-8], possibly with the belief that functional decline towards the end of life is inevitable and irreversible as there is no cure for their illness [9].

The ultimate concern in declining physical function is resulting disability. Current work in this field in advanced disease has a broad focus on functional limitation but not specifically disability [10], and studies generally aim to determine functional decline as a predictor of approaching death [11,12]. Disability is defined as *"limitation in performance of socially defined roles and tasks within a sociocultural and physical environment"*[13]. The World Health Organization (WHO) International Classification of Functioning, Disability and Health (ICF) provides a universal language and framework for the description of health and health-related states [14]. In addition to health conditions and associated impairments, this model recognizes the environmental and personal factors in disability, acknowledging the equally important goal of maximizing participation in daily life despite expected health outcomes. Disability in activities of daily living (ADL) is among the most common unmet supportive care needs in cancer patients [15,16] and equally important to patients with advanced respiratory disease [17,18]. This difficulty to perform ADLs is referred to in this paper as *"ADL disability".*

Lunney and colleagues [11] seminal work suggested functional trajectories based on proxy-reported measures of ADLs in the year before death were disease specific, with cancer following a trajectory of high functioning then a period of rapid decline and respiratory disease following a more unpredictable pattern. This work was limited as it did not follow the same participants longitudinally over time, which could ultimately affect the accuracy of future service planning. There is very limited investigation to elucidate the magnitude of decline in ADLs or factors that contribute to it in advanced cancer or respiratory disease in the context of the ICF [2,15]. This all-encompassing approach of the ICF leads to fundamentally different goals for interventions and services, which could potentially guide policies to address disability in advanced cancer or respiratory disease [19].

In order to identify appropriate interventions to prevent or restore ADL disability in advanced cancer or respiratory disease, an in-depth understanding of trajectories specifically focusing on ADL disability is required. We therefore aimed to provide a comprehensive synthesis around trajectories, influencing factors and assessment of ADL disability in advanced cancer or respiratory disease. Our objectives were to: (i) identify trajectories of ADL disability and variation across specific populations, settings and individual ADLs; (ii) determine factors and outcomes associated with increasing ADL disability; and (iii) identify methods used to assess ADL disability including measurement instruments, timing, outcomes, and analysis.

Methods

We conducted a systematic review in accordance with the recommendations from the Centre for Reviews and Dissemination [20], and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement [21]. The protocol was registered and published on PROSPERO (ID: CRD42019126713).

Eligibility Criteria

We included studies of cohort design with no date limitations. Studies could be prospective or retrospective, measuring ADL disability over at least 3 time-points for a minimum of one-month follow-up. ADL disability outcomes included measures of basic activities of daily living (BADL) and/or instrumental activities of daily living (IADL). We included studies of adults, which include reference to participants with advanced cancer or respiratory disease. We defined advanced disease using either traditional markers of advanced disease: incurable/irreversible cancer (stage III or IV) or treatment with palliative intent; respiratory disease with severe/very severe obstruction (FEV1 <50% predicted) or restriction (CVF< 40% / DLCO < 40%), breathlessness at rest or on minimal exertion, exacerbation requiring hospitalization, or recurrent hospital admissions (>3 admissions in 12 months); participants' accessing specialist palliative care, hospital, hospice or nursing home; or in the case of retrospective studies a deceased population. Papers not published in the English language were excluded.

Search strategy
Electronic databases were searched from inception until August 2020. We devised an electronic search strategy within MEDLINE (Ovid) (see Appendix A), adapted to the MeSH terms of all other databases (EMBASE, CINAHL, PsychINFO). MeSH terms included "Terminally ill", "palliative care", "end of life", "advanced disease", "nursing home", or "hospital" for the population; "Function limitation", "activities of daily living", "activity restriction", or "mobility" for the outcome; and restricted to cohort studies, adults and English language. All search terms were written in full text, with known alternatives and abbreviations, plus use of truncation symbols used to retrieve variations in the terminology. The Boolean operators 'OR' and 'AND' were used for MeSH terms within and across population, outcome and applied restrictions. We searched grey literature using the database OpenGrey; hand searching; scanning reference lists of included studies; and contacting experts in the field.

Selection of studies
Search results were managed in reference software (EndNote version x7) to remove duplicates. LF identified potentially relevant studies by screening titles and abstracts from the search using the inclusion and exclusion criteria. Full papers were retrieved for all potentially eligible papers and full texts were assessed independently by LF and MM. Any uncertainty over eligibility was resolved by discussion.

Data extraction
We developed and piloted a standardized form to extract data on study design and methodology (country, publication details, dates and length of study, methods, and analysis); population (diagnosis, advanced disease or end-of-life indicators, participant demographics, and setting); outcomes (ADLs measured, outcome measurement, timing of measures, and identified disability trajectories); and exposures (e.g. symptom, multi-morbidities, hospital admission, health service utilization, acute events, treatment, deterioration in health, transitions of care, and rehabilitation). One reviewer (LF) extracted data and a second (JN) checked data from one-third of the included studies.

Data analysis
Data are reported using description, tabulation, and narrative synthesis. Meta-analysis was not considered appropriate due to heterogeneity of included studies. Study characteristics were tabulated according to diagnosis (cancer, respiratory disease, or mixed diagnosis) and sub-categorized by setting (community, hospital, or both).

Trajectories of ADL disability
Trajectories of ADL disability were identified from descriptions of each of the functional trajectory categories within each study. They were grouped overall into nine functional trajectory classifications of ADL disability according to their description and/or graphical presentation and categorized further into three typologies of "unchanging", "fluctuating" or "increasing" disability. These were pooled according to diagnosis, setting and type of ADL (basic (BADL), instrumental (IADL), or mobility) to identify any variation in trajectories.

Model of influencing factors
Factors associated with increasing ADL disability and consequent outcomes were identified from all trajectories categorized as "increasing" disability. These were then synthesized into a model and weighted according to prevalence across studies. The model displays influencing factors and outcomes of increasing disability based on categorization using universal language from the WHO ICF [14], which includes health-related factors, body functions and structures, environmental and personal factors. We distinguished the most common factors identified in the model as those identified in four or more trajectories of "increasing" disability.

Measurement of ADL disability
Methods used to measure ADL disability described in the studies were summarized in a table according to the type of ADL, measurement tool, response categories, level of validation, method and timing of collection, and length of follow-up.

Quality Assessment
Quality assessment was conducted using the Critical Appraisal Skills Programme (CASP) tool designed for cohort studies [29]. The published guideline 'Strengthening the Reporting of Observational Studies' (STROBE) Statement [30], was used to support narrative on methodological quality of included studies.

Results

Study retrieval

Our search retrieved 4574 articles from electronic databases, and 1128 articles from the grey literature. After screening titles and abstracts, and removal of duplicates, 431 full texts were retrieved for further appraisal, of which 19 articles reporting 11 studies were eligible (figure 1). Reason for exclusion of full texts included: no reference to cancer or respiratory disease (n=70); no reference to or indicator of advanced disease (n=76); no ADL instrument (n=75); ADL not measured at ≥3 time-points (n=187); follow-up for <1 month (n=2); abstract only (n=2).

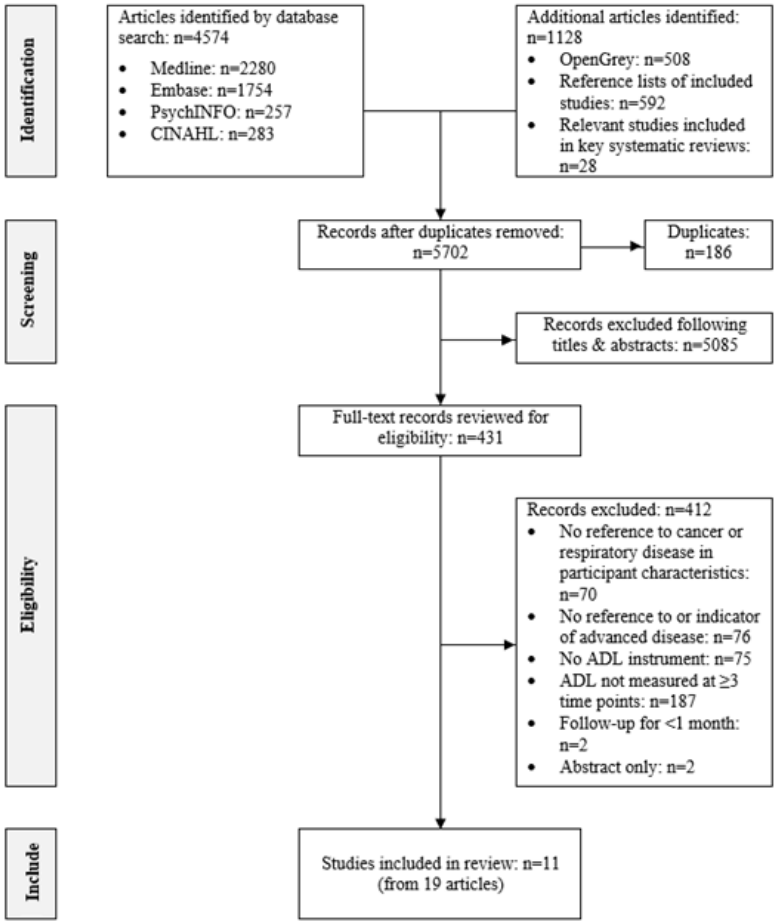


Figure 1. PRISMA flow diagram

Study characteristics

Of the eleven included studies [22-40] (table 1), eight were from the USA, two from the Netherlands, one each from Spain and Australia. The combined sample size ranged from 15,966 to 17,904 participants. The Precipitating Events Project (PEP Project) [41] of community dwelling elders in the USA, used data to produce seven reports, and Nusselder [37,38] published two reports from the same study, totaling nineteen included reports in this review. All studies used a prospective cohort design, although some used analyses retrospective from death. Most studies (n=8) recruited a mixed-disease population including participants with cancer (0-35%) or respiratory disease (0-21%). Two studies recruited only patients with advanced cancer and one study recruited patients with COPD. The type of cancer or respiratory disease was reported in only five analyses. Seven studies reported mean age which ranged from 71 to 91 years and the PEP Project (7 reports) intentionally over-sampled for frailty. Data was reported from the community (n=8), hospitals (n=6), nursing homes (n=3) and hospice (n=1) settings, with follow-up duration ranging from 3 months to 10 years.

Table 1. Study characteristics

Study ID (first author, date and country)	Study design	Disease groups	Sample of interest for analysis	Analytical sample size (n)	Population characteristics	Subgroups identified for comparison of functional trajectories of ADL disability (% of study population)
Cancer						
Hospital setting						
McCarthy 2000 – USA [41]	Prospective cohort (1989-1991 & 1992-1994)	Cancer (advanced colon cancer and advanced non-small cell lung cancer)	Last 6 months of life in advanced colon or lung cancer admitted to hospital	1063	Mean age (SD): NR Female: 43% White ethnicity: 85% Frailty: NR	Illness-related: - Advanced colon cancer - died in hospital (3%) - Advanced colon cancer - did not die in hospital (27%) - Advanced non-small cell lung cancer - died in hospital (11%) - Advanced non-small cell lung cancer - did not die in hospital (59%)
Community setting						
Covinsky 2003 – USA [32]	Prospective cohort (1989-1998)	Cancer	Last 2 years of life in the community	917	Mean age (SD): 83 (8.4) Female: 68.8 White ethnicity: 46.1% Frailty: NR	Illness-related: - Cognitive impairment (64%) - No cognitive impairment (36%)
Chronic Obstructive Pulmonary Disease (COPD)						
Hospital setting						
Medina-Mirapeix 2016 – Spain [42]	Prospective cohort (dates not reported)	COPD	Post-hospitalization after exacerbation of advanced COPD	101	Mean age (SD): 71 (9.1) Female: 6.8%) White ethnicity: NR Frailty: 55.3%	Disability-related: - Gradual decline during admission and post admission (16.1%) - No change during admission and rapid decline post admission (26%) - Declined during admission and returned to baseline (12%) - No change throughout admission and post admission (50%) - Improved during admission and returned to baseline (2%) - Improvement during admission and post admission (6%)

Mixed disease groups						
Hospital setting						
Buurman 2016 – USA [30] – *(The PEP Project)*	Prospective cohort (1998-2012)	Mixed, including: Cancer 5.8%; Respiratory disease 4.8%	Year after skilled nursing facility (SNF) admission following hospitalization	393	Mean age (SD): 85 (5.5) Female: 67.8% White ethnicity: 90.4% Frailty: 70.8%	Disability-related: - Substantial improvement (26%) - Modest improvement (36.5%) - No improvement (37.5%)
Gill 2004 – USA [34] – *(The PEP Project)*	Prospective cohort (1998-2003)	Mixed, including: Cancer 16.4%; Respiratory disease 10.2%	Effect of hospitalization in the elderly	754	Mean age (SD): 78 (5.3) Female: 64.6% White ethnicity: 90.5% Frailty: NR	Disability-related: - Any disability (55.3%) - Persistent disability (36.9%) - Disability with nursing home admission (26.4%)
Gill 2013 – USA [38] – *(The PEP Project)*	Prospective cohort using matched cohort design (1998-2010)	Mixed, including: Cancer NR; Respiratory disease NR	Comparing disability in fall and non-fall related hospital admissions	363	Mean age (SD): 86 (5.8) Female: 69.7% White ethnicity: 83.6% Frailty: 68%	Illness-related: - Hip fracture related to fall (16%) - Fall related injury (other than hip fracture) (17%) - Non-fall related admission (66%)
Gill 2015 – USA [37] – *(The PEP Project)*	Prospective cohort (1998-2013)	Mixed, including: Cancer 10%; Respiratory disease NR	Effect of hospitalization on last year of life	552	Mean age (SD): 86 (6.0) Female: 61.6% White ethnicity: 91.3% Frailty: 86.1%	Disability-related: - No disability (17.2%) - Catastrophic disability (11.1%) - Accelerated disability (9.6%) - Progressively mild disability (11.1%) - Progressively severe disability (23%) - Persistently severe disability (28%)
Somogyi-Zalud 2000 – USA [46]	Prospective cohort (1993-1994)	Mixed, including: Cancer 7%; Respiratory disease 10%	Patients' who died within 1 year of hospital enrolment	417	Mean age (SD): NR Female: 58% White ethnicity: NR Frailty: NR	Illness-related: - Died during hospitalization (17%) - Died after hospitalization (83%)
Stabenau 2015 – USA [47] – *(The PEP Project)*	Prospective cohort (1998-2012)	Mixed, including: Cancer 34.7%; Respiratory disease 5.2%	Last year of life following hospice admission	213	Mean age (SD): 86 (5.8) Female: 64.8% White ethnicity: 90.1% Frailty: 9.4%	Disability-related: - Persistently severe disability (32.4%) - Progressively severe disability (24.9%) - Moderate disability (21.5%) - Accelerated disability (10.8%) - Late decline (10.8%)

Community setting						
Ailshire 2015 – USA [29]	Prospective cohort (1993-2010)	Mixed, including: Cancer 12%; Respiratory disease 7%	Patterns of disability in adults aged over 80 who did or did not survive to 100 years	1141	Mean age (SD): 87 Female: 69.3% White ethnicity: 95.4% Frailty: NR	Illness-related: - Survivor (2%) - Delayer (5%) - Escaper (2%) - Non-survivors (91%)
Chen 2007 – USA [31]	Prospective cohort study (1994-2004)	Mixed, including: Cancer 14.6%; COPD 9.9%	Last year of life	747	Mean age (SD) 91 (6.1) Female: 74% White ethnicity: NR Frailty: NR	Illness-related: - Advanced dementia (42%) - Terminal cancer (8%) - Organ failure (50%)
Ferrucci 1997 – USA [33]	Prospective cohort (1981-1983 to 1988-1990)	Mixed, including: Cancer NR Respiratory disease NR	Developing disability in the elderly	6070	Mean age (SD): NR Female: 64.3% White ethnicity: 95.5% Frailty: NR	Disability-related: - Catastrophic disability (3%) - Progressive disability (3.5%) - Stable without disability (84.5%) - Stable with disability (8%)
Gill 2009 – USA [35] – *(The PEP Project)*	Prospective cohort (1998-2007)	Mixed, including: Cancer 16.6%; Respiratory disease 21.3%	Disability in patients newly admitted to nursing home following acute hospitalization	295	Mean age (SD) 77 (5.4) Female: 63.9% White ethnicity: 89.2% Frailty: 11.4%	Disability-related: - Discharge home without disability (22%) - Discharge home with disability (46%) - Continuous disability in nursing home (27%) - Non-continuous disability in nursing home (4%)
Gill 2010 – USA [36] – *(The PEP Project)*	Prospective cohort (1998-2008)	Mixed, including: Cancer 19.3%; Organ failure 21.4%	Last year of life	383	Mean age (SD): 85 (5.8) Female: 59.8% White ethnicity: 91.6% Frailty: NR	Disability-related: - No disability (17%) - Catastrophic disability (19.8%) - Accelerated disability (17.5%) - Progressive disability (23.8%) - Persistently severe disability (21.9%)
Lawrence 2017 – USA [40]	Prospective cohort (1997-2008)	Mixed, including: Cancer 13%; Organ failure 19%	Disability in nursing home residents prior to death	257	Mean age (SD): 84 (NR) Female: 69% White ethnicity: NR Frailty: 58%	Illness-related: - Cancer (13%) - Organ failure (19%) - Frailty (58%) - Other (10%)

Janssen 2014 – The Netherlands [39]	Prospective cohort (2008-2010)	Organ Failure, including COPD (GOLD III or IV) 41%	Comparing patterns of disability in advanced organ failure	270	Mean age (SD): NR Female: NR White ethnicity: NR Frailty: NR	Illness-related: - COPD (41%) - Chronic Heart Failure (29.5%) - Chronic Renal Failure (29.5%)
Nagurney 2017 – USA [43]	Prospective cohort with matched cohort design (1998-2012)	Mixed including: Cancer NR; Respiratory disease 4%	Disability within the 6 months following an Emergency department visit, which may or may not result in hospitalization	2257	Mean age (SD): 83 (5.6) Female: 66.8% White ethnicity: 88.5% Frailty: NR	Service-related: - Emergency department visit only (36%) - Emergency department visit resulting in hospitalization (28%) - Control group (did not attend emergency department) (36%)
Nusselder 2005 and 2006 – The Netherlands [44, 45]	Prospective cohort (1991 - 1997)	Mixed, including: Cancer NR; Asthma or COPD 8.4%	Time course of disability in Dutch population, including death trajectory	1711	Mean age (SD) NR Female: 50.7% White ethnicity: NR Frailty: NR	Disability-related: - Non-disabled (53%) - Permanent mild disability (13%) - Mild but increasing disability (6%) - Mild but decreasing disability (3%) - Sudden increase in disability (1%) - Moderately disabled with partial regain in functional loss (4%) - Moderately disabled with strong fluctuations (1%) - Permanently severely disabled (2%) - Severely disabled with large increase in disability (1%) - Death trajectory (13%)

NR: Not reported; COPD: Chronic obstructive pulmonary disease

Trajectories of ADL disability

A total of 74 trajectories of ADL disability were identified across all reports and sub-groups within them. The number of sub-groups in each article ranged from 2 to 10. Nine papers sub-categorized by illness-related factors (diagnosis, symptom or survival), eight by disability, and one by setting. These were classified into 9 different trajectories according to the description used in primary studies and collectively grouped into three final trajectories: unchanging disability (n=20); fluctuating disability (n=21); and increasing disability (n=33) (Table 2). In some studies, more than one functional trajectory with the same classification was identified.

Table 2. Development of classifications of functional trajectories of ADL disability

Identified functional trajectories in study subgroups	→	**Classification of functional trajectories of ADL disability**
No disability (n=7)	→	Unchanging disability (n=20)
Stable (n=7)		
Persistently severe (n=6)		
Improving disability (n=5)	→	Fluctuating disability (n=21)
Partial Improvement (n=11)		
Unpredictable (n=5)		
Progressive disability (n=19)	→	Increasing disability (n=33)
Accelerated (n=5)		
Catastrophic (n=9)		

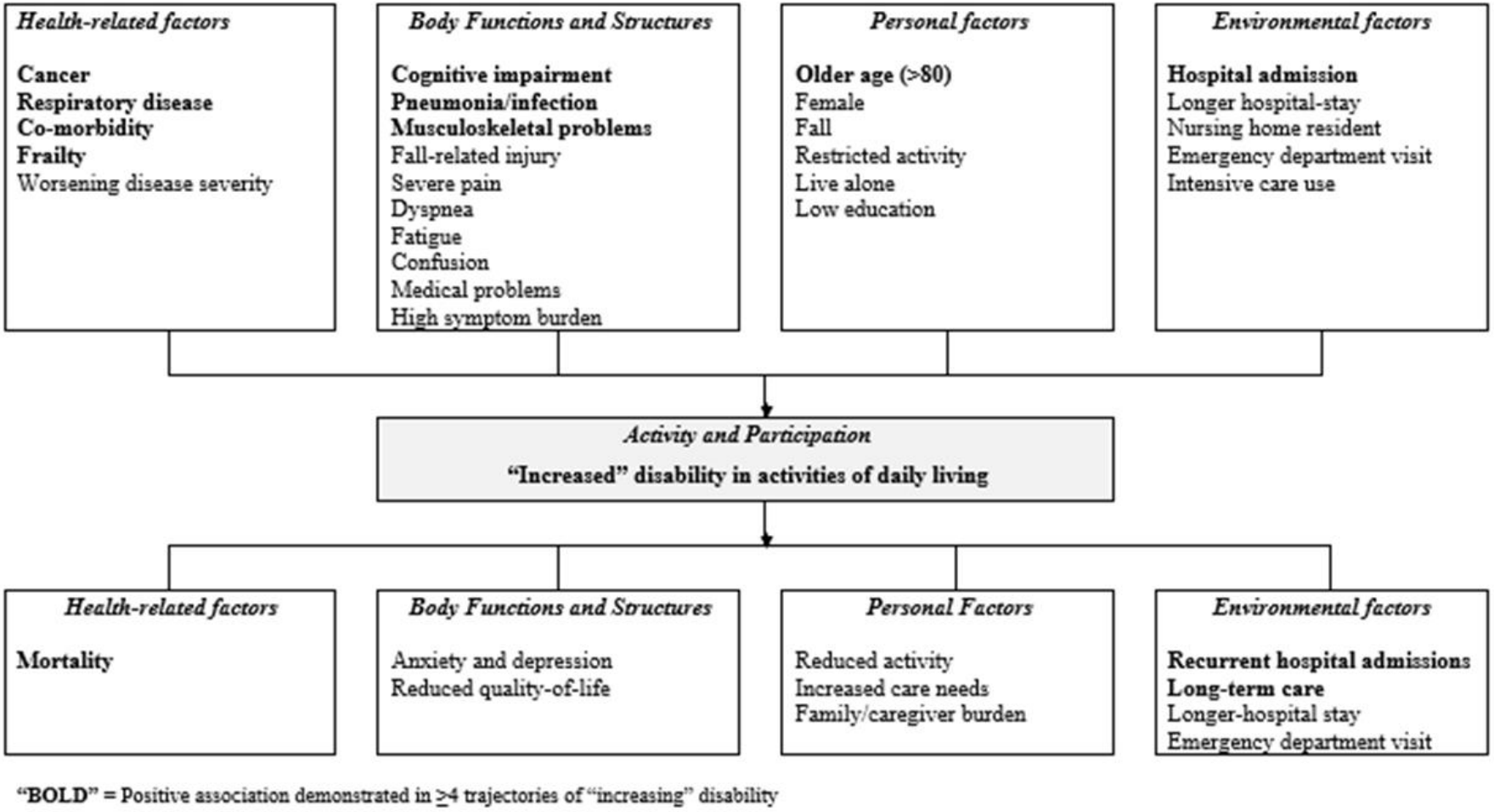
Unchanging disability describes a constant unchanging level of disability, which can occur at any level of severity on the ADL scale. 'Fluctuating disability' describes a pattern of disability that declines, improves or plateaus over time points. Changes occur throughout the trajectory but do not follow a consistent direction. Fluctuations were more often observed when measures were made more often or frequently. Functional trajectories for progressive, accelerated and sudden disability follow a pattern of increasing disability, which occur at different rates. These trajectories were commonly observed in studies examining patterns of disability retrospectively from death.

A primary diagnosis of respiratory disease did not consistently predict any particular disability trajectory. The two studies exclusively in the cancer population identified trajectories of progressive or sudden decline, but all trajectory classifications were associated with cancer among studies with a mixed disease population. No pattern suggesting the ADL disability trajectory differed by setting or whether BADL, IADL, or/and mobility was measured could be discerned.

Associated factors and outcomes of ADL disability

Factors and outcomes associated with increasing ADL disability are shown in figure 2. Of the twenty-six influencing factors, nine were prevalent in four or more of the thirty-three trajectories of increasing disability, each ranging from one to eleven trajectories overall. We found older age to be the most commonly identified personal factor associated with increasing disability; cancer, respiratory disease or co-morbidity are the most commonly associated health-related factors; bodily functions and structures are mostly frailty, cognitive impairment, pneumonia/infection, or musculoskeletal problems; and exposure to hospitalization is the most prevalent environmental factor. Following an increase in ADL disability, ten different outcomes were identified which each occurred in up to nine trajectories of increasing disability. These included reduced physical activity, increased care needs and family/caregiver burden. Increased disability was associated with recurrent hospital admissions, a long-term care placement, longer hospital stays, emergency department attendance and/or reduced survival. In the 5 trajectories where ADL disability improved (not included in figure) this was a result of nursing home admission prompting rehabilitation input, leading to shorter admission duration and an increased likelihood of discharge home.

Figure 2. Model of influencing factors associated with increasing disability in activities of daily living and consequent outcomes in advanced cancer or respiratory disease



"**BOLD**" = Positive association demonstrated in ≥4 trajectories of "increasing" disability

Measurement of ADL disability

Table 3 summarizes the methods used to assess ADL disability. We found wide variation in measurement practice across included studies. Studies measured change in ADL disability over a median (range) period of 1 year (3 months to 10 years), at intervals ranging from 1 month to 2 years. The most common method of data collection was a comprehensive assessment by interview on study enrolment followed by follow-up telephone calls (n=9 reports). ADL disability was usually self-reported by the participant or a proxy (n=12 reports), using a binary response as to whether or not the participant could perform that activity without needing assistance (n=14 reports). Two reports used separate ADL measures to capture BADLs and IADLs.

Table 3. ADL measurement across studies

ADL measurement	Overall findings from 19 reports n, or median (range)
Length of follow-up, months	12 (3-120)
Number of assessments	6 (3-54)
Frequency of assessments, months	1.5 (1-24)
Method of data collection	
Comprehensive assessment with telephone follow-up interview	9
Face to face interviews	3
Patient records	3
Interview on enrolment and postal survey follow-up	2
Medicare database	1
Method of reporting	
self-reported	15
Proxies for cognitively impaired only	8
Proxies for all participants available	4
Minimum data set	1
Survey completed by study coordinator	1
Not reported	1
Outcome measure	
List of BADL	8
List of BADL, IADL and mobility	6
KATZ Activities of daily living index	3
Duke activity status index	2
Care dependency scale	1
Validation of measure	
Non-validated	15
Validated	3
Definition of disability	
Specified	13
Not specified	5
Scoring of measure	
Binary (yes or no)	14
Categorical (5-point, 0-4)	1
Categorical (6-point, 0-5)	2
Unspecified	3
Type of ADL	
BADL	9
BADL, IADL + mobility	5
BADL + IADL	2
BADL + mobility	1
Unspecified	1
Total number of ADLs assessed	7 (4-14)
No of individual BADL items assessed	4 (0-10)
No of individual IADL items assessed	0 (0-5)
No of individual mobility items assessed	0 (0-5)

ADL: Activities of daily living; BADL: Basic activities of daily living; IADL: Instrumental activities of daily living

However, a validated assessment tool was used in only 3 reports (Katz Activities of daily living index), and 14 reports used questionnaires specifically designed for the study. The majority of reports (n=15) used a non-validated list of individual ADLs with a median (range) of 7 (4-14) items. Compared to BADLs measured in all 19 reports, IADLs were measured in only 9 reports, the most prevalent activities being walking inside the home (n=17 reports), dressing (n=16 reports), transferring (n=15 reports) and bathing (n=15 reports). For a detailed list of individual ADLs assessed see Appendix B. Disability was usually defined as the inability to perform that task (n=13 reports) and scoring severity of ADL disability was most commonly calculated by totaling the number of ADL disabilities (n=14 reports), where a higher score indicated greater disability.

Methodological quality assessment

Methodological limitations and lack of reporting was common across studies (see Appendix C). These included: lack of validated outcome measures; unaccounted potential confounders despite use of multi-variate analysis or trajectory modelling; selection bias and attrition particularly relating to chronic conditions and mortality; and lack of handling of missing data in the analysis and reporting of relative-risk ratios. Participant characteristics were generally well described, but nearly all studies recruited participants predominantly of white ethnicity, were female dominated, and most were conducted in the USA.

Discussion

Main Findings

This systematic review of 19 reports from 11 prospective cohort studies, with over 15,000 participants with advanced cancer or respiratory disease, reveals nine classifications of trajectories of ADL disability following three ultimate typologies: unchanging disability, fluctuating disability, and increasing disability. We extend understanding of ADL disability in this population through a model of influencing factors associated with increasing disability and consequent outcomes, relating to body functions and structures, health-related, personal and environmental factors. We found the most common influencing factors associated with increasing disability in ADLs include older age, frailty, co-morbidity, cognitive impairment, pneumonia/infection or musculoskeletal problems, as well as hospitalization. As an outcome of increasing disability, patients develop increased care needs, reduced activity, and increased family/caregiver burden, which may also result in recurrent hospital admissions, long-term care placement, emergency department attendance, or/and death.

Risk factors for increasing disability in ADL's (e.g., in elderly inpatients) may be modified by using interventions that target ADL disability. In studies when ADL disability improved, this was a result of nursing home admission with rehabilitation input, leading to shorter admission duration and more likelihood of discharge home, which suggests services can be modified to improve ADL disability and consequent outcomes. However, which interventions are used (e.g., assistive devices) and how they are delivered (e.g., professional input/intensity) is not reported in included studies, which limits understanding of how environmental factors can be modified in order to efficiently address ADL disability in this population.

Trajectories of ADL disability

Our findings are supported by work from Gill et al [42] who widely explored trajectories of ADL disability in the elderly including towards the end-of-life, in domains of disability severity. Heterogeneity of these trajectories was generally found across disease groups including cancer or respiratory disease, but it is not possible to identify whether these vary according to type of cancer or respiratory condition. A recent systematic review [10] of trajectories of terminal decline distinguished four different functional trajectories in disease domains in line with work from Lunney et al [11], which found that cancer follows a pattern of increasing disability, whereas respiratory disease can by unpredictable in nature. However, this review looks at functional limitation in its broadest sense, with the majority of studies assessing cognitive decline. It does not specifically explore trajectories of ADL disability or influencing factors, which is where our review is incremental to the field.

Factors influencing ADL disability

Studies included in this review are selective over which influencing factors and outcomes of disability they investigated, some of which were specified inclusion criteria. Overall, there is lack of studies accounting for all body functions and structures, personal and environmental factors that we identified as potentially being associated with increasing disability in advanced cancer or respiratory disease.

Personal factors
By identifying personal characteristics associated with ADL disability, it may be possible to predict who is at greatest risk of increasing disability. Older age and falls are known to increase the risk of disability in advanced disease [43,44], which is identified in our model, however, some individual characteristics may not have been identified in included study samples such as ethnic minority or social deprivation, the latter being known to be associated with disability [45].

Body functions and structures
Work from Gill et al [4] found symptoms restricting disability are common during the last year of life, increasing substantially in the last 5 months before death. The likelihood of a hospice admission increases in patients with a greater burden of restricting symptoms and number of disabilities in ADL, which is particularly associated with older age and multi-morbidity [46]. The prevalence of restricting symptoms was found to reduce substantially upon hospice admission [47], indicating a link between symptoms and disability, which have the potential to improve upon intervention even towards the end-of-life. Currently, there is a gap in knowledge of how different symptoms particularly relate to disability in advanced cancer or respiratory disease. This is important to fully understand in order to provide interventions or services particularly tailored to these conditions or related symptoms and to identify when in the disability trajectory it is possible to prevent or restore ADL disability in order to influence outcomes.

Environmental Factors
Identifying the influence of environmental factors on disability is important in order to identify which services or interventions will potentially help or hinder disability and how these can be modified to improve the outcome. Emergency admission is associated with advanced cancer [48] and non-cancer conditions [49] and lack of social support at home is a large contributor to hospital-based death [50]. The prevalence of disability in cancer as inpatients is known to be greater than as outpatients [51]. However, it is not fully understood how disability influences hospital admissions or discharge home in advanced cancer or respiratory disease and what type of interventions targeting ADL disability (e.g., assistive devices) may help reduce admissions or length of inpatient stay.

Outcomes of ADL disability
Mortality is commonly reported as an outcome of increased ADL disability in advanced disease where decline in function is often seen as a predictor of approaching death [11]. A recent study explored trajectories of functional performance status in the last 4-months of life using routine clinical data from a sample of 55,954 patients across 115 specialist palliative care services in Australia [12]. It identified reduced function as an indicator of approaching death where approximately 70% of patients with cancer or COPD died in hospital. However, there are other outcomes of disability that can occur prior to death, which need to be recognized. Disability is known to increase dependency and need for care, potentially bringing feelings of distress, loss and inadequacy in patients and caregivers, reduce quality of life and increase the likelihood of hospitalization or long-term care placement [8,50,52-56].

As well as identifying consequent outcomes of ADL disability it is important to recognize what could potentially improve these outcomes. Palliative care is known to reduce emergency admission [49] and there is growing evidence that rehabilitation increases independence in advanced disease by helping people to maintain their optimal levels of physical, sensory, intellectual and social functioning with minimum dependence on others for as long as possible [57,58]. However, despite being at risk of worsening disability, patients with advanced disease are often considered too unwell to benefit from rehabilitation interventions which prevents referral [9,59,60]. Consequently, our model does not include such interventions, due to lack of consideration in included studies, warranting further investigation.

Methodological considerations for future research
We have learnt from this review that functional trajectories of ADL disability are varied; accuracy of study findings are limited by study design and use of non-validated ADL instruments; and the sample is not convincingly representative of advanced cancer or respiratory disease. More research is required using robust study design and validated instruments to determine trajectories of ADL disability in this population and to understand: who is at risk of developing ADL disability; when ADL disability is likely to occur; how disability in ADLs is affected by symptom or treatment burden; what services may impact positively or negatively on ADL disability; and consequent outcomes, in order to appropriately modify services targeting ADL disability. Findings from this work will provide a grounding for further study of the effectiveness of preventative and restorative interventions for ADL disability and ultimately have implications for the planning and provision of health and social care services.

Identification of methodological limitations from this review enable development of a robust study protocol to explore trajectories of ADL disability in advanced cancer or respiratory disease and associating factors and outcomes, for which we make the following recommendations.

Study design and sample
A prospective cohort study is an effective and appropriate way to observe trajectories of ADL disability as it allows for as many variables as required to be studied in order to determine any association with the outcome and allow all relevant confounding variables to be rigorously collected [61]. The sample should accurately reflect advanced cancer or respiratory disease using appropriate inclusion criteria [61], and use of multiple sites helps to widen recruitment and generalizability, and small samples can be pooled for increased power [62-64]. It is important to be aware that the efficiency of a prospective cohort study increases as the incidence of a particular outcome increases [61], which means it is necessary to recruit participants who are at risk of functional loss. Gatekeeping of the more unwell or disabled participants by clinicians can be prevented by use of a trained research assistant to screen for eligible participants [65].

Data collection and measurement
In terms of data collection, face-to-face interviews are not always feasible for research staff or patients due to logistics and disease burden, therefore an interview on enrolment followed by telephone interviews would suffice. It is important to have an allocated proxy if available, in order to continue to capture change in deteriorating patients, which will also limit attrition and selection bias [66]. Use of a validated ADL measure(s) capturing BADL, IADL and mobility are recommended [61], preferably using a categorical measure in order to capture sensitivity to change in a deteriorating population [67]. To ensure change is captured over time, ADL disability should be measured monthly over a period of at least six months. Although a question about any change in disability within that time window may aim to capture any short-term fluctuations [68], it can be found to be of little benefit and increase the burden of assessment [69]. Confounding variables are a major problem in analyzing cohort studies [61], which need to be identified and adjusted for in a multivariable analysis or trajectory modelling, and sample size should be calculated accordingly. Any missing data should be reported and included in the analysis as well as identifying characteristics of non-completers to establish generalizability [62,66,70].

Strengths and limitations
This review follows recommendations from the Centre for Reviews and Dissemination [20], and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement [21]. Transparency of reporting was ensured by development and publication of a detailed study protocol. Publication bias was minimized by widely searching for published and unpublished papers, and errors in the review process were limited by utilizing a second reviewer to independently extract and review data. The model of influencing factors associated with increasing disability is viewed through the broad lens of the ICF framework which extends understanding beyond bodily impairments to personal and environmental factors.

This systematic review has several limitations. English language restrictions add selection bias. The broad inclusion criteria meant that the population was not exclusive to advanced cancer or respiratory disease and the lack of advanced disease specification meant it was unclear how advanced in their disease participants were. This limits the generalizability of our findings within the advanced cancer or respiratory disease population. It is also important to consider that the majority of included studies were conducted around a decade ago and with progress in life-pro-longing cancer treatments, people may be living longer with disability which have a different effect on trajectories of ADL disability to those identified in our review. Synthesis of the findings was narrative, and a meta-analysis was deemed inappropriate due to population heterogeneity, and variation in methodology and ADL measurement. This also limited interpretation of associations and outcomes of ADL disability in the model to be explanatory in nature rather than quantifiable.

Conclusion

Trajectories of ADL disability in advanced cancer or respiratory disease can be categorized into typologies of “increasing”, “fluctuating” and “unchanging” disability. A trajectory of “increasing” disability is not always an indication of approaching death and may be responsive to intervention. The model of influencing factors associated with “increasing” disability demonstrates that these factors move beyond bodily impairments to include personal and environmental factors, which could potentially be targeted with rehabilitation interventions and inform service planning. Studies in this field are limited by methodological weaknesses in the measurement of ADL disability. We recommend future studies using validated ADL measurement instruments to understand

which specific factors may be modified through intervention to prevent, maintain or improve disability in ADLs in advanced cancer or respiratory disease.

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Declaration of conflicts of interests

None of the authors have any conflicts of interests to declare.

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3.5. Gaps in evidence and justification of thesis

As the systematic review of trajectories of disability in ADL has highlighted, there is currently limited understanding of how disability in ADLs change over time in advanced cancer or respiratory disease. The review suggests different health-related, personal, and environmental factors contribute to the development of disability in ADLs, but findings are not exclusive to patients with advanced cancer or respiratory disease and the changing demography of this population may produce different findings to studies conducted over a decade ago. Studies included in the review paid little attention to the impact of symptom burden or to interventions or services that help overcome disability. There were also few studies assessing instrumental ADLs, and a lack of validated measures was noted.

The broad population of any type of cancer or respiratory disease with a wide variation of disease stages within included studies in this review, make it difficult to accurately compare trajectories of disability. In addition, it was not possible to account for drop out and retention bias in this review. Inclusion of drop out and retention data in future studies is recommended, especially due to the high risk of healthy patient bias in longitudinal studies. The lack of UK studies in this review further strengthens the case for further study.

Future study of trajectories of disability in ADLs would benefit from the incorporation of theoretical frameworks such as the WHO-ICF [84] within the study design. This would help to identify the populations who could benefit most from rehabilitation; understand the process of disability in ADLs and influencing or predicting factors; determine components of rehabilitation interventions that may help address health-related, personal, or environmental factors, to overcome ADL disability; and identify timing and delivery of appropriate

interventions or services. Understanding this complexity in the development of disability may help reinforce a biopsychosocial approach towards the management of disability in the context of declining function in advanced cancer or respiratory disease and an integrated multi-disciplinary approach to clinical care across the broader care pathway. This in turn would support the need for further intervention studies and service development to effectively implement this approach.

3.6. Summary

To summarise, this research is timely and appropriate due to:

- An aging population and changing demography leading to an increased burden of disability in advanced cancer or respiratory disease, leading to loss of independence in ADLs and increased need for care, potentially escalated by the impact of the Covid-19 pandemic.
- Current gaps in rehabilitation provision, which could address disability in people with advanced cancer or respiratory disease but is limited across care sectors.
- A lack of study of trajectories of disability, specifically in people with advanced cancer or respiratory disease using validated measures, across basic and instrumental ADLs, making it difficult to accurately identify potential risk factors.
- An increased understanding of predictors of disability trajectories in ADLs and influencing factors in this population would help to inform anticipatory clinical care, including rehabilitation interventions and service delivery.

Chapter 4

Aims and objectives

4.1. Aim

To understand and compare disability in activities of daily living (ADLs) among adults with advanced cancer or respiratory disease, to inform future rehabilitation intervention(s).

4.2. Objectives

In patients with advanced cancer or respiratory disease:

1. To describe the prevalence of disability in basic and instrumental ADLs.
2. To determine relationships between disability in ADLs, and health-related and environmental factors.
3. To identify and compare trajectories of disability in ADLs over time and associated or predicting health-related and environmental factors.
4. Based on findings, to make recommendations for rehabilitation intervention components and timing of services to address ADL disability in clinical care.

Chapter 5

Methodological Overview

5.1. Introduction

This chapter outlines the methodological considerations of this PhD study. Firstly, it considers the underpinning epistemology and choice of overall study design, which comprises two main components: a secondary data analysis, and a prospective cohort study. Methods relating to the secondary data analysis are presented in the incorporated publication 2, and specific methods for the prospective cohort study are detailed in this chapter. The final section will discuss methodological modifications, made in response to the Covid-19 pandemic.

5.2. Methodological considerations

5.2.1. Ontological and epistemological considerations

The philosophical perspective of pragmatism [149] underpins this thesis, which acknowledges there are different and complementary ways to identify multiple realities (ontology), and methodological decisions for acquiring knowledge (epistemology) can be based on what is most suited to answer the research question [150]. The focus of this thesis; disability in ADLs, is characterised by a complex relationship between an individual's health condition, the environment in which they live, and their personal attributes [84], so it represents a complex real-world health problem. From the ontological perspective this complex relationship acknowledges multiple realties, where truth comes in different forms, lending itself to the philosophy of pragmatism. Clinical implications of disability in ADLs will be addressed in this thesis, including consideration of interventions or services to modify disability. This further

supports a pragmatic approach when designing and/or recommending interventions or services, as the goal of research in this instance is to bring about the optimal level of improvement in the patients' lives [151].

Research strategies based on pragmatism can be qualitative, quantitative, or mixed design [152]. The choice of research design depends on the aim of the research. To address the main overall aim of this thesis, a cross-sectional and prospective cohort study design was selected. Cross-sectional study allows for identification of factors associated with disability at one point in time, whereas in prospective cohort studies, a variety of variables are measured that might predict or relate to the development of the outcome of interest, which is monitored over time [152]. The latter allows for temporal relationships to be identified, as well as the comparison of two disease groups: advanced cancer and respiratory disease. Therefore, health-related, and environmental factors and their relationship with disability within the theoretical framework of the WHO-ICF, can be better understood using these methods. The aim does not include identifying how people perceived they are affected by disability, therefore a qualitative or a mixed methods approach was not considered to be appropriate.

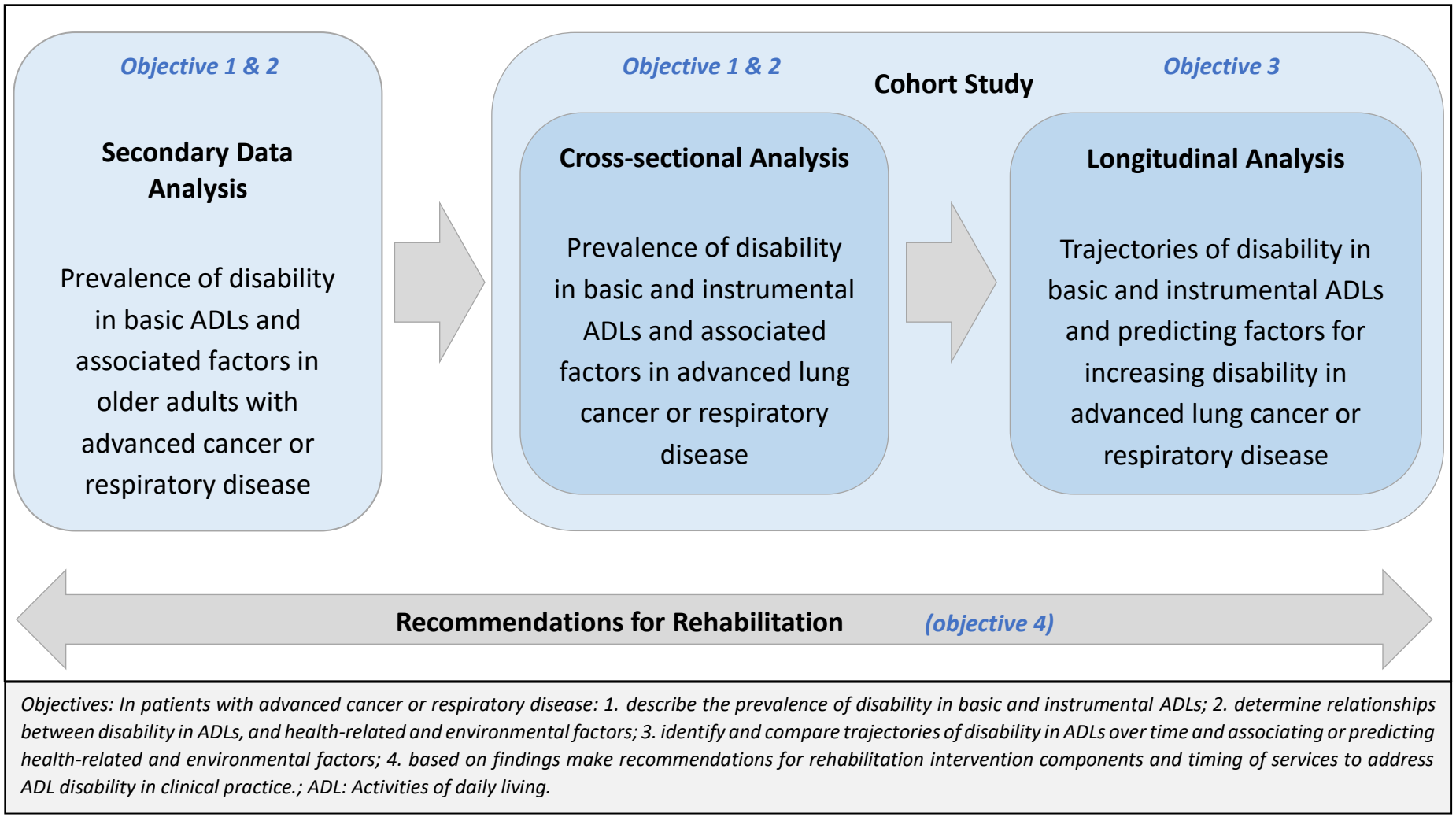
5.2.2. Overview of study design

To meet the aim and objectives of this thesis, the study design comprised of two components:

i) A secondary data analysis of pooled survey data from the International Access, Rights and Empowerment (IARE) studies.
ii) A prospective cohort study involving patient-reported surveys using monthly repeated measures over a 6-month period.

The overview of the design of this work is presented in Figure 5.1.

Figure 5.1. Overview of study design



Objectives: In patients with advanced cancer or respiratory disease: 1. describe the prevalence of disability in basic and instrumental ADLs; 2. determine relationships between disability in ADLs, and health-related and environmental factors; 3. identify and compare trajectories of disability in ADLs over time and associating or predicting health-related and environmental factors; 4. based on findings make recommendations for rehabilitation intervention components and timing of services to address ADL disability in clinical practice.; ADL: Activities of daily living.

5.2.2.1. Secondary data analysis

Component 1 is a secondary analysis of pooled data from the International Access, Rights and Empowerment (IARE) studies. These two studies were designed to be compatible using similar inclusion criteria and measurement. IARE I [153] was a cross-sectional patient survey of older patients accessing palliative care services across UK, Ireland, and the USA between November 2012 and August 2014 (inclusion criteria: age ≥65; under the care of a palliative care team). IARE II [154] was a prospective cohort study to identify and understand service use, preferences, and palliative care needs of frail older people with advanced disease in the UK between February 2017 and January 2019 (inclusion criteria: age ≥65; Rockwood Clinical Frailty Scale score ≥5; one or more unplanned hospital admission or two or more unplanned emergency department attendances in the last 6 months; not currently receiving specialist palliative care). Participants with solid advanced cancer or advanced respiratory disease were included in the cross-sectional analysis and exploratory longitudinal analysis.

This component aimed to i) describe the prevalence of disability in basic ADLs; ii) examine factors associated with disability in basic ADLs; and iii) explore disability trajectories. Component 1 was therefore planned to generate knowledge that contributed to thesis objectives 1 and 2 and identified recommendations for clinical care (objective 4), as well as where further exploration was required. Full methods for this secondary data analysis are presented in incorporated publication 2 (chapter 6).

5.2.2.2 Prospective cohort study

The second component of the study design is a multi-centre prospective cohort study in patients with advanced respiratory disease, including lung cancer, comprising both a cross-

sectional and longitudinal analysis. Component 2 was planned to generate knowledge that contributed to all four thesis objectives. It specifically aimed to describe and compare in adults with advanced lung cancer or respiratory disease: i) prevalence of disability in basic and instrumental ADLs and individual activities; ii) change in disability in ADLs over time; iii) the extent to which different health-related and environmental factors relate to or predict disability in ADLs, including symptoms, assistive devices, and social isolation. The underlying hypotheses within this work were that:

1. Patients with advanced lung cancer develop greater ADL disability over time than people with advanced respiratory disease.
2. Symptom severity is positively associated with subsequent ADL disability.
3. Social isolation is positively associated with increased dependence in ADLs.

Section 5.3 outlines specific methodology and the study protocol in Appendix B gives full details of study procedures. Methodological challenges and amendments surrounding the conduction of this work in the context of the Covid-19 pandemic are discussed in section 5.4.

5.3. Prospective cohort study methods

5.3.1. Study design

A prospective cohort study was chosen as an effective and appropriate way to observe trajectories of ADL disability as it identifies change over time and allows for as many variables as required to be studied, to determine timing of determinants and outputs [147, 152].

5.3.2. Setting

To increase generalisability of the study population, multi-site recruitment was adopted across the UK from both the National Health Service (NHS) and charity sector. Patients with advanced lung cancer or respiratory disease may access different clinical services in the advanced stages of their disease depending on local provision. Therefore, recruiting from a broad range of clinical services enables ADL disability to be captured in patients receiving a range of interventions and services, across different settings and trusts.

NHS acute trusts recruited from hospital medical, respiratory or oncology wards, and/or outpatient respiratory or lung cancer clinics including chemotherapy units. Hospice services included inpatients, outpatients, community teams, day hospices and rehabilitation services. The British Lung Foundation advertised the study on the members forum, acting as a participant identification site, allowing members to self-refer to the study. The twelve participating centres and their specific recruitment strategy is outlined in table 5.1.

Table 5.1. Details of participating centres recruiting participants for the prospective cohort study

	Site	Diagnoses	Setting	Services recruited from
1	Princess Royal University Hospital, London	NSCLC COPD ILD	NHS	Respiratory outpatient clinics Oncology outpatient clinics Medical wards
2	Nottingham University Hospital NHS Foundation Trust	NSCLC COPD	NHS	Respiratory outpatient clinics Oncology outpatient clinics
3	Macclesfield District Hospital, East Cheshire NHS Foundation Trust	NSCLC	NHS	Oncology outpatient clinics
4	South Tyneside and Sunderland NHS Foundation Trust	NSCLC COPD ILD	NHS	Respiratory outpatient clinics Oncology outpatient clinics Medical wards Database of oncology and respiratory patients agreeing to be contacted
5	Royal Cornwall Hospital NHS Foundation Trust	NSCLC COPD	NHS	Respiratory outpatient clinics Oncology outpatient clinics Chemotherapy unit
6	Medway NHS Foundation Trust, Kent	NSCLC COPD	NHS	Respiratory outpatient clinics Oncology outpatient clinics
7	York Hospital NHS Foundation Trust	NSCLC COPD ILD	NHS	Respiratory outpatient clinics. Oncology outpatient clinics. Chemotherapy unit
8	Guy's and St Thomas' NHS Foundation Trust, London	ILD	NHS	Respiratory outpatient clinic (ILD)
9	Western Sussex NHS Foundation Trust and St Barnabas Hospice	NSCLC COPD ILD	NHS and Hospice	Respiratory outpatient clinic (ILD) Hospice outpatient clinic
10	St Christopher's Hospice, South London	COPD ILD	Hospice	Hospice self-management programme
11	St Michael's Hospice, East Sussex	NSCLC COPD ILD	Hospice	Hospice self-management programme Hospice outpatient clinics ILD support group
12	British Lung Foundation (BLF), UK	COPD ILD	Charity	BLF members forum

NSCLC: Non-small cell lung cancer; COPD: Chronic obstructive pulmonary disease; ILD: Interstitial lung disease; NHS: National Health Service; BLF: British Lung Foundation.

5.3.3. Participants

5.3.3.1. Inclusion criteria

The inclusion criteria for the study were:

- Patients aged ≥ 18.
- Advanced lung cancer or respiratory disease as defined by one of the following:

  - *Lung cancer:* Inoperable stage III or IV non-small cell lung cancer (NSCLC)

  - *Chronic Obstructive Lung Disease (COPD):* Severe or very severe stages of COPD according to the criteria set by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage III (FEV1/FVC < 70%. 30% ≤ FEV1 < 50% predicted with or without chronic symptoms (cough, sputum production)) and stage IV (FEV1/FVC < 70%. FEV1 < 30% predicted plus chronic respiratory failure)

  - *Interstitial lung disease (ILD):* Carbon monoxide transfer factor (TLCO/DLCO) level of <40% or FVC <50% predicted [34, 155]

The over-riding population for this thesis was '*advanced cancer or respiratory disease'* with a focus on disease-based criteria. Due to similarity in pathology the population within the prospective cohort study was further limited to advanced malignant or non-malignant respiratory disease, using conventional disease progression markers [22] as specified above.

Small cell lung cancer (SCLC) was excluded as this affects only 10-15% of lung cancers and tends to progress faster than NSCLC, often over weeks or a short number of months [156]. Therefore, NSCLC follows a similar disease trajectory to non-malignant respiratory disease, as described in chapter 2. The respiratory diseases were limited to chronic obstructive pulmonary disease (COPD) or Interstitial Lung Disease (ILD), which are life-limiting conditions,

known to have unmet healthcare needs in the advanced stages of the disease like that of cancer patients [9].

Therefore, the two disease groups consisted of i) malignant respiratory disease (NSCLC), and ii) non-malignant respiratory disease (COPD or ILD). Participants with both a malignant and non-malignant diagnosis were classified in the malignant group as this is the most aggressive disease. Exploring difference in trajectories of disability in ADLs between NSCLC and COPD or ILD will confirm or deny differences in functional decline [3], supporting whether all these conditions would benefit from rehabilitation and challenge the bias towards respiratory disease outlined in chapter 2.

5.3.3.2. Exclusion criteria

The exclusion criteria for the study were defined as:

- Patients who lack capacity to consent.
- Patients who lack ability to understand and complete a questionnaire in English.
- Life expectancy of <1 month as assessed by the clinician taking consent.

It was considered that the minority of this population would be affected by cognitive impairment as the study is not exclusively conducted in older people. Also, in previous studies recruiting participants with advanced lung cancer or advanced respiratory disease, the number of participants ineligible or withdrawn due to lack of capacity was very low [157, 158]. Therefore, it was justified not to include people who lack the capacity to consent to participate in the study. It would however have been useful to include patients who do not speak English, as disability is prevalent across ethnic groups [159] and this would increase generalisability of the findings, but this was not possible due to limited resources. It was

important to balance the likelihood of completing the study follow-up with including participants in the advanced stages of their disease. To address this, patients with a life-expectancy of <1 month were excluded. However, predicting prognosis in advanced disease remains challenging [160], and attrition prior to any follow-up was to be expected.

5.3.4. Recruitment and consent

Before recruitment commenced, LF (researcher) visited all participating sites either in person or virtually, to meet with colleagues and identify a key contact person who supported the study by helping to identify potential participants. LF also gave presentations introducing the aims and methods of the study and provided simple study materials (Appendix C) outlining the eligibility criteria and recruitment process.

Consecutive sampling was used and included all patients who are screened as eligible and willing to take part in the study. All members of the available population were considered for participation in the study. Potential participants were identified by clinical staff from medical records, admissions-lists and multi-disciplinary team meetings and screened against the inclusion and exclusion criteria. A member of the clinical team asked potential participants if they were interested in taking part in the study at a routine face to face or virtual consultation.

Names of interested patients were given to the local researcher via secure NHS email. The local researcher contacted participants by telephone to explain the study in more detail, and if in agreement participants were sent a patient information sheet and consent form in the post. A convenient time was then arranged to complete consent and the baseline questionnaire either face to face or verbally over the telephone. More details surrounding

verbal consent can be found in section 5.4. The participant was then formally enrolled in the study and their contact details were passed on to LF via secure NHS email for follow-up and their GP was informed. All patient facing documents and the standardised GP letter can be found in Appendix D.

Progress of recruitment at participating centres was closely monitored to encourage the sites to recruit as rapidly as possible. This included regular contact via email or telephone to offer support if needed; being available to receive questions as required; repeat introduction of the study for new staff; collection of monthly recruitment figures; and circulation of a monthly newsletter providing a recruitment update, offering encouragement, and ensuring all sites received the same information relating to any questions or concerns that may have been raised that month.

5.3.5. Data collection tools

The primary variable for this study of ADL disability includes basic ADLs, and instrumental ADLs. It has been highlighted that one questionnaire cannot meet all the assessment and evaluation needs of one population and a combination of existing questionnaires is recommended for fully assessing ADL disability [90]. The choice of measurement instrument for this study was influenced by the following criteria:

i) Closely met the aims of the study.

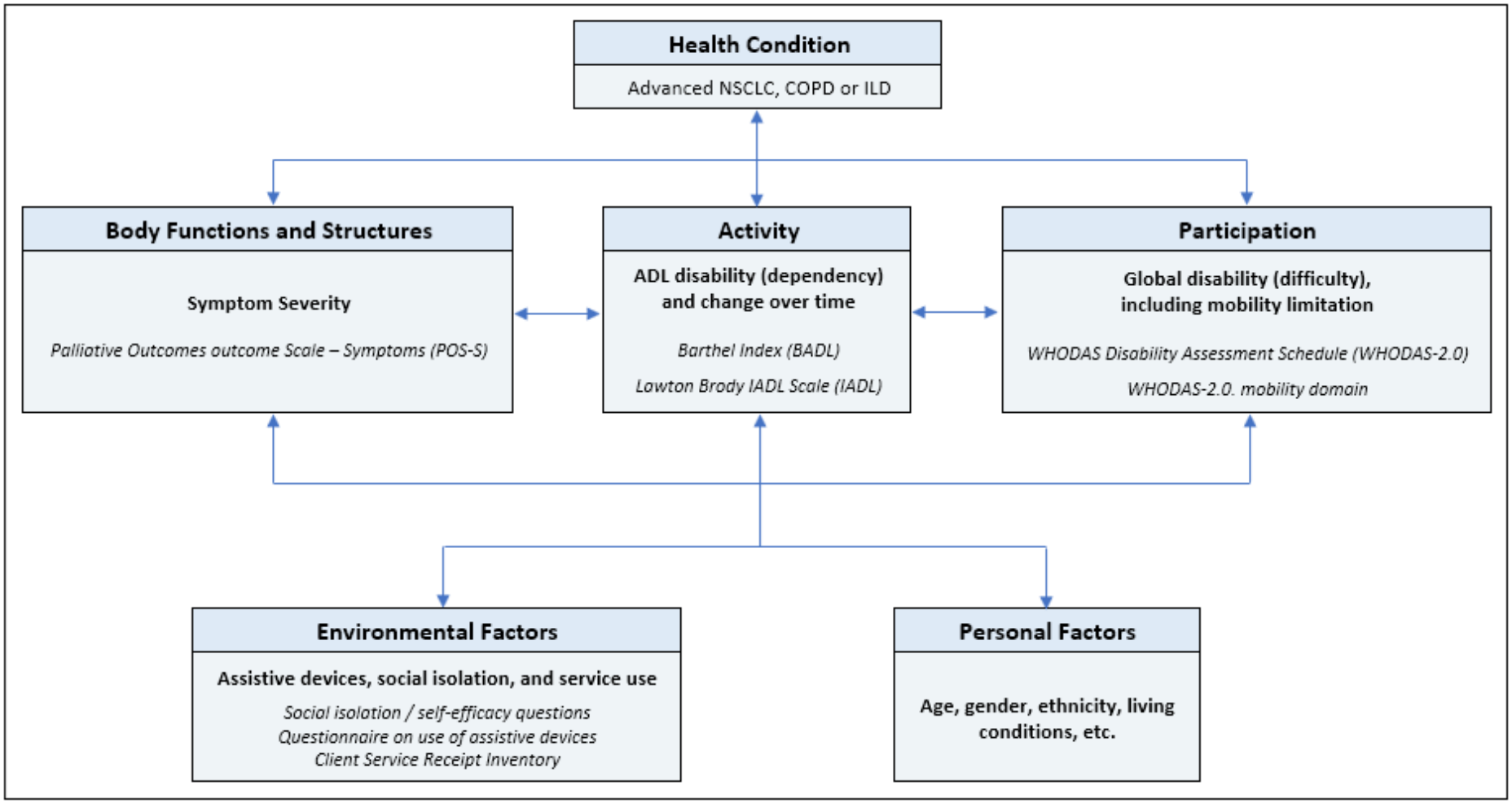
ii) Validated or tested in patients with advanced cancer or respiratory disease.

iii) The measure had a continuous scale with categorical responses.

Based on this criterion, the Barthel Index, and the Lawton Brody Instrumental ADL scale were selected as the primary measures of ADL disability, which are widely accepted for the measurement of disability in basic and instrumental ADLs respectively [88, 92]. The World Health Organization Disability Assessment Schedule (WHODAS 2.0.) [161] was selected as a secondary measure. The WHODAS 2.0., based on the WHO-ICF framework, measures disability in terms of difficulty and is considered the leading measure of disability worldwide [89]. It was also felt to be important to capture mobility limitation within this population, that could be linked to ADL disability, which is assessed within the mobility domain of the WHODAS 2.0.

As explained in chapter 2 the WHO-ICF framework is the theoretical underpinning of this thesis. The WHO-ICF helped frame findings from the systematic review (incorporated publication 1, chapter 3), which informed selection of explanatory variables for further study. From the review it was identified that there was lack of understanding of the relationship between ADL disability and symptoms and assistive devices. It was also deemed important to collect information on the use of clinical services to identify how these affects or are affected by disability. In the WHO-ICF model these come under health-related bodily functions and environmental factors. Measuring these variables alongside ADL disability will enable exploration of how these domains relate to ADL disability. How these can be mapped onto the WHO-ICF model with ADL disability and other co-variables, is illustrated in Figure 5.2. An overview of the instruments selected to measure the primary and explanatory variables are presented in table 5.2 and outlined in more detail below. All collected demographic data and outcome measures can be found in the questionnaires within the patient-facing documents in Appendix D.

Figure 5.2. Study variables and measures mapped onto the WHO International Classification of Function, Disability and Health Framework (WHO-ICF) [84].



NSCLC: non-small-cell lung cancer; COPD: chronic obstructive pulmonary disease; ILD: Interstitial lung disease; POS-S: Palliative care Outcome Scale- Symptoms (POS-S); ADL: activities of daily living; BADL: basic activities of daily living measured as dependency on the Barthel Index; IADL: Instrumental activities of daily living measured as dependency on the Lawton Brody Instrumental ADL Scale; WHODAS-2.0.: World Health Organization Disability Assessment Schedule measures difficulty in activity and participation.

Table 5.2. Measurement instruments used in the study: domains, items, and scoring systems

Instrument	Domain	Items assessed	Scoring	Reason for inclusion
Barthel Index [162, 163]	Basic activities of daily living	10-item questionnaire rated: unable; dependent; needs some help; or independent, as appropriate. The number of item responses ranges from 2 to 4, where 0 = fully dependent.	A summary score of 0 (fully dependent) to 20 (independent), where <20 = mild disability, <15 = moderate disability and <10 = severe disability.	Primary variable
Lawton Brody Instrumental ADL Scale [88, 164, 165]	Instrumental activities of daily living	8-item questionnaire, rated from independent (1), requiring some assistance (0), to fully dependent (0).	A summary score ranges from 0 (low function, dependent) to 8 (high function, independent).	Primary variable
Total score of WHODAS 2.0 [89, 166, 167]	Global disability and participation	36-item questionnaire with 6 domains: cognition, mobility, self-care, getting along, life activities (home and work), and participation. All rated from 1 (no difficulty) to 5 (extreme difficulty/unable).	A combined summary score ranges from 36 (no difficulty) to 180 (extreme difficulty). The work domain can be excluded limiting the summary score to 36 to 160.	Secondary variable
Mobility domain of WHODAS 2.0 [89, 166, 167]	Mobility limitation	5-item domain rated from 1 (no difficulty) to 5 (extreme difficulty/unable).	A summary domain score ranges from 5 (no difficulty) to 25 (extreme difficulty).	Explanatory variable
Questions on use of assistive devices [91]	Assistive device use	10 questions with yes/no answers and descriptive responses.	A summary score of the total number of assistive devices used, ranging from 0-10.	Explanatory variable
Palliative care Outcome Scale – Symptoms (POS-S) [168]	Symptom severity	10-item questionnaire with option to add additional symptoms, rated from 0 (not affected) to 4 (overwhelmingly affected).	Summary score ranges from 0 (not affected) to 52 (overwhelmingly affected).	Explanatory variable
Client Service Receipt Inventory (CSRI) [169]	Service utilization	Inpatient stays, outpatient consultations and home visits with medical, nursing, and allied health professionals, and formal and informal care input.	Items assessed individually using a yes/no response and recorded as prevalence.	Explanatory variable

IADL: instrumental activities of daily living; WHODAS-2.0: World Health Organization Disability Assessment Schedule

5.3.5.1. Barthel Index

The Barthel Index [163] is a 10-item measure of basic ADLs including: bowel continence, toilet use, grooming, feeding, mobility, bladder continence, dressing, bathing, stairs, and transfers. Each item has a range of two to four categorical responses rated on a 0-4 scale, ranging from dependent/unable, to minor help, major help, or independent, depending on the activity. A lower score indicates greater disability in terms of dependence on others and a higher score indicates greater independence. A summary score ranges from 0-20 where a score of 20 represents no disability, a score of <20 represents mild disability, <15 represents moderate disability, a score <10 represents severe disability, and a score <5 represents very severe disability [162]. A change of ≥3.6 points in total score reflects a minimal clinically important difference (MCID) in ability to perform ADLs in older people, in relation to discharge home [170]. A change in total score of ≥1.85 indicates a MCID in patient reported ability to perform ADLs in stroke patients [171].

5.3.5.2. Lawton Brody Instrumental ADL scale

The Lawton Brody Instrumental ADL scale is a 8-item measure of instrumental ADLs including: ability to use the telephone, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility for own medication, ability to manage finances [165]. Each item has a range of three to five categorical responses ranging from fully independent to fully dependent. Each response is scored 1 if independent or 0 for anything other than independent. A summary score ranges from 0 (low function, dependent) to 8 (high function, independent), therefore a lower score indicates greater disability [165, 172]. The MCID for the Lawton Brody Instrumental ADL scale lies around half a point [173].

5.3.5.3. World Health Organization Disability Assessment Schedule

The World Health Organization Disability Assessment Schedule (WHODAS-2.0) [161] consists of six domains (cognition, mobility, self-care, getting along with others, life activities, societal participation). Life activities consist of 2 sections: household activities and work activities; the latter is optional to include in the analysis. All items are scored on a scale of activity difficulty ranging from 1 to 5: none (1), mild (2), moderate (3), severe (4), and extreme or cannot do (5). The cognition domain is made up of six items; mobility and getting along with others, each have five items; self-care and household activities, each have four items; and societal participation has seven items.

Domain scores were totalled to produce a WHODAS summary score, where 32 reflects no difficulty and 180 extremely difficult (160 excluding the work domain) [161]. A higher score indicates higher levels of disability [167]. A WHODAS summary score of 32 = no difficulty, 33-64 = mild difficulty, 65-96 = moderate difficulty, 97-128 = severe difficulty, 129-160 = extreme difficulty or cannot do [161]. A MCID for the WHODAS 2.0 has not yet been established [174].

The WHODAS-mobility domain [167] is selected to capture mobility limitation not accounted for in the Barthel Index or the Lawton Brody Instrumental ADL scale. This is a 5-item categorical measure, where the patient rates difficulty in each mobility task (standing for long periods, standing up from sitting down, moving around inside the home, getting out of your home, walking a long distance), on a 5-point scale from none (1) to extreme or unable (5). A simple summary score totalling the scores of all five items ranges from 5-25 where the lowest score indicates no disability and the highest score indicates extreme disability [166, 167]. A score of 6 or more indicates disability.

5.3.5.4. Palliative care Outcome Scale – Symptoms

Palliative care Outcome Scale - Symptoms (POS-S) is a measure of symptom severity and is part of the POS family of measures [175]. It is a 10-item measure listing ten symptoms (pain, shortness of breath, weakness or lack of energy, nausea, vomiting, poor appetite, constipation, mouth problems, drowsiness, immobility, and up to three other symptoms). The patient rates the severity of each symptom on a 5-point scale from not at all (0) to overwhelmingly affected (4). A summary score ranges from 0-52, where a higher score indicates greater severity of overall symptoms. According to the scale a change in individual symptom severity is identified by a change of 1 point or more in any direction (improving or worsening).

5.3.5.5. Use of ADL assistive devices

The use of ADL assistive devices is measured using a list of ten questions about assistive devices to help with several ADL tasks (eating, transfers, getting around indoors, dressing, bathing, toileting, getting around outside, using steps or stairs, domestic task and any other activity), which have been used in previous surveys investigating use of assistive devices [91]. Patients answer yes or no to the use of equipment for each ADL task, followed by a question asking them to specify what equipment they use. This was measured on a binary scale (yes: 1, no: 0), making a combined summary score of 0-10 where a higher total score indicates a higher use of assistive devices and greater disability [91].

5.3.5.6. Clinical service receipt inventory

Service utilization was collected using the Clinical Service Receipt Inventory (CSRI). Questions were asked regarding inpatient admissions, outpatient or remote consultations, and home visits, with medical, nursing, or allied health professionals, and formal and informal care. A

yes/no response was required with the option to include further information about the nature, quantity, and length of time of the visits.

5.3.5.7. Co-variables

A demographic questionnaire was used to collect participant characteristics including age, gender, living situation, current location, caregiver details, diagnosis and staging, current treatment, and physical and social isolation. The Charlson Co-morbidity Index [176], and Australian Karnofsky Performance Scale (AKPS) [85] were used to collect information on co-morbidities and functional status respectively. The Chronic Disease Self-Efficacy Scale was used to collect participants confidence in managing chores, receiving social support and participation in society [177, 178]. In addition, change in levels of physical activity indoors and outdoors was collected using a Likert Scale [179]. Details of measures included in the demographic questionnaire are presented in table 5.3.

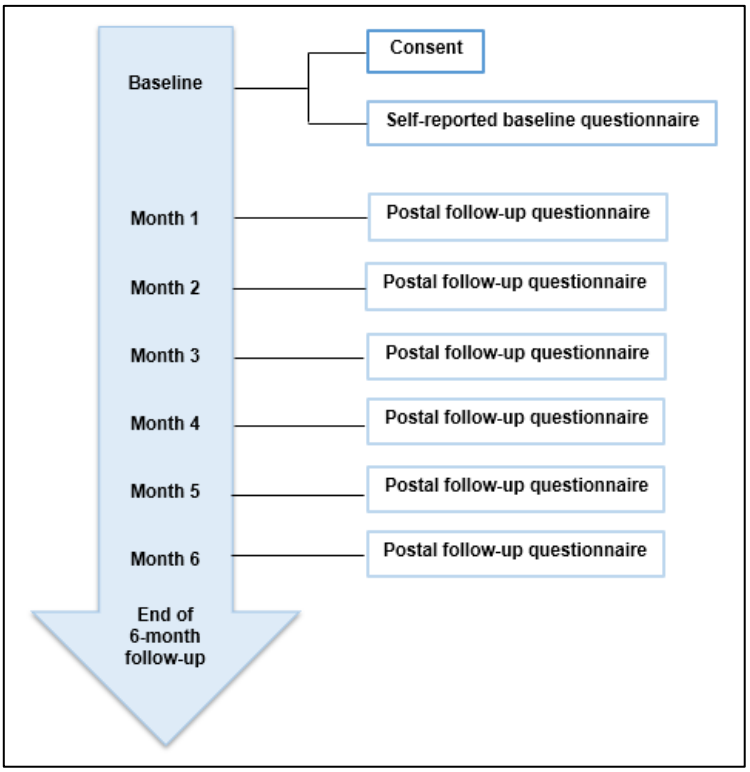
Table 5.3: Measurement instruments used for collection of co-variables

Co-variable	Measure	Scoring
Co-morbidity	Charlson Co-morbidity Index [176]	A 20-item measures of common co-morbidities each rated 1-6 depending on associated prognosis. A higher score on the scale (0-42), indicates a greater burden of co-morbidities.
Functional performance status	Australian Karnofsky Performance Scale (AKPS) [85]	A 10-point scale ranging from 0 (dead) to 100 (fully independent).
Confidence managing daily activities	Chronic Disease Self-Efficacy Scale (CDSE): confidence in managing chores, receiving social support and participation in society domain [177, 178]	A 4-item domain each assessing confidence on a 1-10 scale (1 no confidence, 10 fully confident) in: a) Help with daily activities from (i) family and friends, (ii) formal resources b) Emotional support from (i) family and friends, (ii) formal resources.
Change in levels of physical activity	Likert Scale [179]	A 5-point Likert scale: a lot less, a little less, no change, a little more or a lot more in: (i) physical activity indoors (ii) physical activity outdoors.

5.3.6. Follow-up

Prospective data collection consists of seven timepoints: baseline and every month (4-6 weeks) for the next 6-months (figure 5.3). Data were collected using repeated measures including the Barthel Index, Lawton Brody Instrumental ADL Scale, WHODAS-2.0, POS-S, use of ADL devices, and the CSRI at all timepoints. A demographic questionnaire was used to collect co-variables at baseline only. Monthly follow-up was preferable as regular assessment ensures that change in ADL disability is captured over time while balancing likelihood of attrition, burden of assessment, and quality data collection [16]. Although a question about any change in disability within the monthly time window may aim to capture any short-term fluctuations [180], it was found to often be of little benefit and increases the burden of assessment [181]. To aid timely recruitment the baseline questionnaire was completed in person with the local researcher where possible or over the telephone.

Figure 5.3. Schedule of prospective data collection



All follow-up was conducted by LF. The follow-up questionnaire was in the form of a self-reported postal survey as resources did not permit telephone follow-up for all participants. However, to minimise missing postal questionnaire data, a telephone call was made prior to posting to remind participants to expect a questionnaire, and the option to complete the questionnaire over the telephone was offered if preferred, which proved popular among house-bound individuals. Participants also had the opportunity to withdraw at this time if they wished to do so. Proxy-completion was considered to reduce drop-out but discrepancies in reporting physical limitations between patient and proxy responses are known [182], and therefore decided against. It was anticipated that not all postal surveys would be completed in a timely fashion and loss to follow-up in surveys was to be expected. Appendix E presents rules regarding inclusion and continuation of follow-up, and study completion.

5.3.7. Patient and public involvement

The public engagement forum at the Cicely Saunders Institute was utilized to engage patients and members of the public in the planning of the study and screening of all study documents to ensure appropriateness. During the planning stage of the study design, valuable input from the patient and public involvement (PPI) group was utilized in three main ways:

i. *To facilitate choice of outcome measures:* An overview of the study design was presented to the PPI group at a monthly dragon's den session, which facilitates input on research studies from PPI members. Two different tools for measuring basic ADLs (Barthel Index and the Katz Index of Independence in ADL) and instrumental ADLs (Lawton Brody Instrumental ADL Scale and the Nottingham Extended ADL Scale) were discussed within the group. Feedback from the PPI members within this session

contributed to the selection of the Barthel Index for measuring basic ADLs, and the Lawton Brody Instrumental ADL Scale for measuring instrumental ADLs, mainly due to preference over included items in the tool and categorical options.

ii. *To feedback on patient facing documents and clinical materials:* PPI members were approached via the PPI forum to assist with refining patient facing documents and clinical materials. Three PPI members expressed interest via email to the PPI co-ordinator. They were contacted individually by the researcher via email and asked to read and comment on the patient information sheet, and a crib sheet for helping clinicians to introduce the study to interested patients. Feedback was communicated via email or a telephone discussion. This helped to adopt language that was easily understood by potential participants and to encourage participation in the study.

iii. *To reflect on the data collection process and tools (pilot):* The questionnaires and data collection methods were planned to be piloted using a brief discussion with the first five consecutively recruited participants following completion of the baseline questionnaire, to refine chosen questionnaires and methods. Consent to being included in the pilot was taken when completing the baseline questionnaire. In a pre-arranged telephone call, participants were asked to reflect on the questions, questionnaire layout and length, and means of completion of follow-up (post, telephone, or email). This helped to identify any possible barriers to recruitment and enable the researcher to check the practicality and patients' understanding of the questionnaire, to facilitate completion. Further information on the pilot phase and proceeding modifications can be found in section 5.4.2.

5.3.8. Ethical considerations and approval

Ethical approval for the study was obtained from the London Camberwell St Giles Research Ethics Committee (ref 19/LO/1950). The study was subsequently registered on the ISRCTN registry (ISRCTN14159936). All ethical approval documents can be found in Appendix F. There were three main ethical issues that were considered in the construction of this study, relating to consent, data collection, and data management.

There were several issues surrounding consent to participate. Firstly, the process of consent for adults with impaired or lack of capacity can be an ethical concern. However, numbers of participants lacking capacity to consent was anticipated to be very low based on previous studies recruiting participants with advanced lung cancer or respiratory disease [157, 158], and therefore justified excluding participants who lacked capacity to consent. Secondly, identifiable data about patients who did not consent to participate in the study were not collected, in line with the data protection act 2018 [183]. Finally, verbal consent procedures were required in response to Covid-19 (section 5.4), for which approval of required amendments was granted.

This study recruited patients with advanced illness, who may be considered a "vulnerable population" [184], and particular care needed be taken when conducting research with this population. This included ensuring patients were not burdened by the study during data collection, whilst also ensuring that those who wished to take part were included. This was addressed by: minimising questionnaire burden by keeping the survey as short as possible; structuring the questionnaires so that the most important questions were at the beginning of the survey; follow-up questionnaires were self-completed and could be completed at the patient's convenience; participants completing questionnaires over the telephone were

offered flexibility to complete it at a suitable time with regular breaks if required. As standard, participants were also offered the opportunity to withdraw without reason.

Participants were recruited from multiple sites throughout the UK which required transference of data. To ensure confidentiality, all data were processed and stored in line with the principles of the data protection act 2018 [183]. This included transferring patient identifiable information from local sites to the researcher (LF) by secure NHS email and anonymising all participant data for analysis. As this was a multi-site study, it was crucial to ensure data from all sites were collected and recorded in the same way, which was ensured by using a standardised database for recording data. Further details on the handling of data in line with data protection, is outlined in section 5.3.10.

5.3.9. Sample size

A sample size calculation was carried out for the prospective cohort study considering the following points. To compare the severity of disability between the two diagnostic groups (lung cancer and respiratory disease) at one point in time with power of 80% at a 5% significant level, and an expected MCID of 4 on the Barthel Index [170], a sample size of 78 (39 per group) was required. An attrition rate of 40% was estimated [185], meaning a sample size of 120 was needed (60 per group). 120 would also achieve a precision of + or - 9% in the estimation of prevalence of ADL disability, based on assumed prevalence of disability in ADLs in this patient population to be around 50% [4, 186]. However, to adjust for up to 20 co-variables in planned multiple regression analysis, 200 participants were planned to be included in this study. This sample size was also sufficient to detect a significant correlation

with co-variables based on a medium effect size (0.5) and 80% power at a 5% significance level.

5.3.10. Data handling

5.3.10.1. Data storage

All personal data were managed according to the principles established in the Data Protection Act 2018 [183]. All the researchers undertook GCP training, and current research governance processes were followed. Completed questionnaires including demographic data were anonymised using a unique study identification number and contained no patient identifiable data. The participant identification number and linkage with the participant's name only occurred on the consent form and participant log. Consent forms were kept securely at participating recruitment sites and where electronic consent forms were used for verbal consent these were filed with password protection. The participant log was held in a password protected Excel spread sheet. Data was transferred via a secure NHS email account. Participant questionnaires were stored separately to the consent forms, in a secure location.

5.3.10.2. Recruitment, follow-up, and attrition

The number of eligible participants who were approached, including those who died before recruitment, who moved out of area, or who declined participation, were reported, along with reason for decline. As the inclusion criteria specified a life-expectancy of ≥1 month, drop-out prior to 6-month completion or missing timepoints due to ill-health was expected. Length of follow-up (median and range) and study outcome (whether participants completed 6-month follow-up) were reported. The number of participants completing each timepoint and reasons for study withdrawal or missing timepoint was recorded. The proportion of patients

completing 6-month follow-up or withdrawing from data collection and the characteristics of these groups were examined in and between the two diagnostic groups.

5.3.10.3. Missing data

Missing data in the final dataset is defined as: 'whole questionnaire missing' (when the complete questionnaire was missing, either because of late completion, or it was not returned); or 'single item missing' (when one of several items in a completed survey were missing). Patterns of missing data could be either: 'terminal' when no further data were available for a participant who had been withdrawn from the study; or 'intermittent' when one or more observation was missing for a participant who had completed 6-month follow-up [187].

There are specific statistical methods for handling missing data, including complete case analysis, imputation, or modelling [187]. As 'terminal' missing data was most likely to be 'not missing at random' due to death or ill health, imputation methods were not appropriate. Complete case analysis would apply to only those participants' that complete 6-month follow-up. However, those completing three or more time points were included in the analysis, as these data would provide important information for the description of trajectories. On individual trajectory plots (section 5.3.12.1.), missing timepoints were not connected to illustrate where data were missing.

5.3.10.4. Data entry and cleaning

All data from the baseline and follow-up questionnaires were entered into a spreadsheet in Microsoft Excel by LF and an administrative assistant, using a pre-prepared coding sheet based on scoring systems from the included measurement instruments (Appendix G). Missing data were entered as '999' and unclear answers were highlighted in colour, which were

addressed during the cleaning process as outlined below. All additional text was included as additional information to aid interpretation if required.

On completion of data collection, LF cleaned and checked all the data for anomalies and prepared it for transference into STATA 16 for analysis. This approach was chosen due to the amount of data and time constraints. A more rigorous approach would have been for a second researcher to enter the data into an identical spreadsheet and compare the two data sets.

As part of the cleaning process, missing demographic data were recovered from the medical notes by local research staff and sent to LF by secure NHS email, who inputted it into the dataset. On the Barthel Index and Lawton Brody Instrumental ADL Scale, unclear answers and some missing responses could be replaced with an appropriate response derived from a written explanation by the participant as to how they manage that activity (e.g., “no change”, “need help”, “someone else does it”, “shielding”). Online shopping was classed as being independent. Where up to two items in each WHODAS-2.0 domain were missing, the mean score across all items within that domain were assigned to the missing items [161].

Missing items on the POS-S were only replaced if there was a clear response from the participant written elsewhere. When checking use of assistive devices for ADLs, oxygen was commonly recorded as equipment for several ADLs, but it was decided to remove this from the responses as it is considered a medical intervention rather than an assistive device. Equipment used for “getting in and out of bed” or “standing up from a chair” were grouped as transfers. On the CSRI a response to whether the participant received that service was assumed to be “no” if at least one item in that section had been selected and was only considered to be missing if the whole section had been left unanswered.

5.3.11. Cross-sectional analysis

Descriptive statistics using non-parametric tests for unevenly distributed data were used to describe participant characteristics and to compare demographic characteristics of participants who withdrew or were lost to follow-up prior to 6-month follow-up and those who did not. When describing participant characteristics, the significance level of the p-value was set to, $p \leq 0.01$ to account for multiple testing [188]. A cross-sectional analysis at baseline was used to answer objectives 1 and 2 of the study and contribute towards objective 4.

The analysis plan for objectives 1 and 2 are specified as follows:

5.3.11.1. Objective 1: To describe the prevalence of disability in basic and instrumental ADLs

Disability in basic and instrumental ADLs were categorised at baseline into groups of disability severity: no disability, mild disability, moderate disability, severe disability, and very severe disability, with the outlined cut-offs on their corresponding scales presented in table 5.4. Details of the scoring for the Barthel Index and Lawton Brody Instrumental ADL Scale are reported in section 5.3.5.1. and 5.3.5.2 respectively, and full scoring guidelines of each measure can be found in Appendix G. The prevalence of disability severity for basic and instrumental ADLs was described using summary statistics. Comparisons were made between NSCLC and COPD or ILD.

Table 5.4. Categorisation of ADL disability severity

Severity of disability	Basic ADLs (Barthel Index)	Instrumental ADLs (Lawton Brody IADL Scale)
No disability	Score = 20	Score = 8
Mild disability	Score = 15-19	Score = 6-7
Moderate disability	Score = 10-14	Score = 4-5
Severe disability	Score = 5-9	Score = 2-3
Very severe disability	Score = <5	Score = <2

IADL: instrumental activities of daily living

The prevalence (yes/no) of each individual basic ADL and instrumental ADL item was described and compared by diagnosis at baseline using summary statistics. The individual items of each measure are outlined in section 5.3.5.1. and 5.3.5.2. Prevalence of disability in each domain is classed as follows:

- Basic ADL: Barthel index score = needs help/dependent/unable (scores vary per item).
- Instrumental ADL: Lawton Brody Instrumental ADL scale item score = 0 (dependent)

5.3.11.2. Objective 2: To determine relationships between disability in ADLs, and health-related and environmental factors

Details of the cross-sectional analysis to identify health-related (e.g., symptoms) and environmental factors (e.g., physical and social isolation; use of assistive devices) at baseline can be found in incorporated publication 3 in chapter 7.

5.3.12. Longitudinal analysis

Longitudinal data analysis in this study describes the course of trajectories of disability in ADLs of patients with advanced NSCLC or COPD or ILD over the course of 6 months. As data were collected prospectively, forward trajectories are appropriate for this study. To model change over-time, at least three waves of data were required, therefore, participants who completed repeated measures at 3 or more timepoints are included in the longitudinal analysis. The demographic characteristics of patients providing sufficient follow-up data and those who do not was compared using appropriate non-parametric tests for unevenly distributed data. The analysis of the longitudinal data aims to answer objectives 3 and 4 of the study.

The analysis plan for objective 3 is specified as follows:

5.3.12.1. Objective 3: To identify and compare trajectories of disability in ADLs over time and associating or predicting health-related and environmental factors

There were several parts to the analysis of objective 3. Firstly, differences between participants who completed three or more timepoints and included in the longitudinal analysis and those who were not, were compared using appropriate non-parametric tests. Trajectories were then analysed on the group and individual level, and associations with individual trajectories and predictors of increasing disability were tested, as outlined below. To account for multiple testing the significance level of the p-value was set to, $p \leq 0.01$ [188].

- Group-level (summary) trajectories

ADL disability trajectories were determined using summary statistics for the whole sample (group-level) with medians [IQR] for unevenly distributed data, at each time-point and plotted over time, separately for basic and instrumental ADLs. These were then compared by diagnostic group (NSCLC and COPD or ILD). It was anticipated that statistical analysis of longitudinal data such as multi-level modelling or latent growth curve modelling may not be possible due to insufficient numbers of participants and unevenly distributed data.

- Individual trajectories

Individual trajectories of ADL disability were explored using visual graphical analysis (VGA) to identify variances in common patterns and develop categories of trajectories of ADL disability [189]. This enables identification of individual change which can be masked by summary trajectories at group level. Individual trajectory plots were drawn for participants who completed three or more timepoints. Missing timepoints were not connected within these plots to illustrate where data were missing.

Change at each time point in an individual's trajectory is indicated by the MCID for each measure. The American Thoracic Society defines MCID as "the smallest difference that clinicians and patients would care about" [190]. In older adults, the Lawton Brody Instrumental ADL scale has an established MCID of ≥0.5 [173]. The Barthel Index has an established MCID of ≥1.85 in stroke patients [171] and ≥3.6 in older people [170]. However, the MCID for the Barthel index in these studies is associated with improvement following rehabilitation and does not take decline in disability into account as meaningful change. There is no established MCID for either measure in a deteriorating population. In the original reliability study for the Barthel Index, a change in one item from dependent to independent or vice versa (change of 1 point) is likely to be reliable, and a measurement error of 1 point was identified [162]. Bearing in mind that the study sample in this analysis have advanced disease, and the aim is to identify any change in either direction that may be important to the patient, a change of ≥2 on the Barthel Index and ≥1 on the Lawton Brody Instrumental ADL scale was used to identify change in basic ADL and instrumental ADL disability trajectories, respectively.

Individual trajectories for disability in basic and instrumental ADLs were examined separately. Changing trajectories could either change in one direction (only increasing in score or decreasing in score) or fluctuate. To categorise individual trajectories, each participants trajectory was prepared for inspection on a line graph using identical scales to reduce subjectivity, and reviewed by two independent researchers to enhance reliability [189]. The individual line graphs were independently grouped into categories of ADL disability trajectories identified in the recent systematic review presented in chapter 2 [191]. This review condensed the ADL disability trajectories into three groups: increasing, fluctuating, and unchanging disability. Due to limited numbers of trajectories in the review paper, no

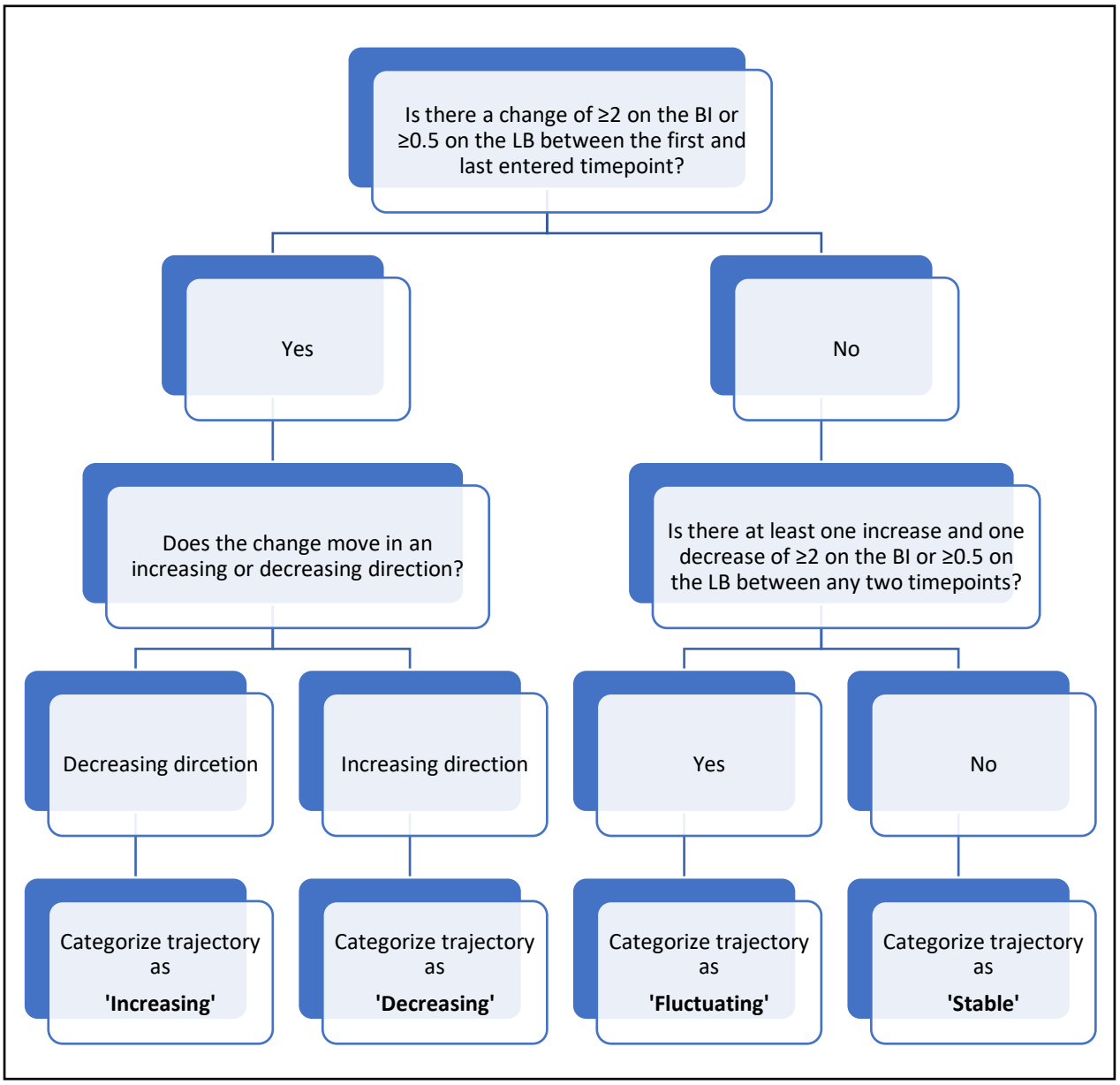
disability and unchanging disability trajectories were combined, and decreasing and fluctuating disability trajectories were combined. However, to enhance generalisability, this analysis identified four ADL disability trajectory groups (increasing, decreasing, fluctuating, and stable (includes no disability and unchanging disability).

The ADL disability trajectory groups (increasing, decreasing, fluctuating, and stable) are defined by distinct rules as outlined in table 5.5., and categorised via eyeballing using the process outlined in the flow diagram (Figure 5.4). The stable group was inspected further and was divided into: i) independent, where participants presented with no disability in ADLs, which did not change; and ii) persistent: where the participants presented with constant unchanging ADL disability on any other level in the scale. However, the whole stable group consisting of both independent and persistent ADL disability trajectories was used for the statistical analysis.

Table 5.5. Characteristics of individual trajectory groups of ADL disability

Trajectory Sub-group	**Variable criteria**	
	Basic ADLs (Barthel Index: 0-20)	**Instrumental ADLs (Lawton Brody IADL Scale: 0-8)**
Increasing disability	Decrease in score over 6-months (including downwards fluctuation) of ≥2.	Decrease in score over 6-months (including downwards fluctuation) of ≥0.5.
Decreasing disability	Increase in score over 6-months (including upwards fluctuation) of ≥2.	Increase in score over 6-months (including upwards fluctuation) of ≥0.5.
Fluctuating disability	At least one increase and one decrease (or vice versa) between any two timepoints of ≥2.	At least one increase and one decrease (or vice versa) between any two timepoints of ≥0.5.
Stable	Difference in score between first and last recorded timepoint is <2 (includes no disability).	Difference in score between first and last recorded timepoint is <0.5 (includes no disability).

Figure 5.4. Flow diagram for identifying trajectory classification in basic and instrumental ADLs



BI: Barthel Index; LB: Lawton Brody Instrumental ADL scale

- Characteristics and association with ADL disability trajectory groups

Descriptive statistics were used to describe participant baseline characteristics of each trajectory group (increasing, decreasing, fluctuating, and stable). These were compared across the groups using the Kruskal Wallis test for continuous variables and the Chi-squared test of independence for categorical variables. Univariable associations for variables recorded at baseline, between each basic and instrumental ADL disability trajectory (increasing, decreasing, fluctuating) compared to the stable trajectory were explored using the Mann-Whitney-u test for continuous variables and chi-square test of independence for categorical variables**.** This means three groups are tested consisting of: i) increasing and stable trajectories; ii) decreasing and stable trajectories; iii) fluctuating and stable trajectories.

- Predictors of increasing trajectories of ADL disability

Univariable logistic regression and multiple-variable logistic regression were used to identify baseline associations with the increasing disability trajectory, separately for basic and instrumental ADLs. Participants included in the analysis have either an increasing or stable disability trajectory, where the constant variable is increasing disability compared to stable disability. The number of variables included in the multi-variable model were determined by the sample size of the group. It is advisable to have around at least 10 participants per variable in the model, but more variables were added one by one and remained in the model if they did not alter the findings dramatically.

The main explanatory variables included in the models are diagnosis, symptom severity and ADL device use at baseline. Covariables considered for the model are selected based on findings from the systematic review (chapter 3) or if they have a p-value of ≤0.01 in the univariable analysis. The covariables considered for the model were Charlson Comorbidity

Index Score, functional performance status (AKPS), Barthel Index and Lawton Brody Instrumental ADL total scores, difficulty managing daily activities in WHODAS-2.0 or sub-domains, receiving cancer treatment or oxygen therapy, age, gender, living alone, ethnicity, level of education, reduced physical activity, months spent in physical and social isolation, and under hospice care. They were eliminated from the models if there was collinearity between explanatory and/or confounding variables identified in scatter plots between continuous variables, or if there were not enough observations to carry out univariable logistic regression.

5.4. Impact of Covid-19 pandemic on cohort study

Coronavirus (Covid-19) was declared a global pandemic by the World Health Organization on 11th March 2020 [62]. An emergency bill to strengthen the Covid-19 response was put in place by the UK Government on the 17th March 2020 and enforced on the 24th March 2020 [64]. The prospective cohort study was subsequently suspended for nearly 4-months from the 18th of March 2020, in response to the public health measures in the coronavirus emergency bill. This led to modification to prospective cohort study procedures outlined below:

5.4.1. Study modifications and their rationale

To open the prospective cohort study during the Covid-19 pandemic, amendments were required to give it a coronavirus focus and abide by public health measures [192]. It was acknowledged that it may be opportunistic to explore the effect physical and social isolation has on disability. About one in five individuals worldwide were considered at increased risk of

severe Covid-19 infection, due to underlying health conditions including cancer and respiratory disease, encouraging countries to put policies in place to protect those at increased risk [63]. In the UK, as part of government policy, individuals fulfilling this high-risk criteria were classed as 'extremely clinically vulnerable' and physical and social isolation (shielding) was advised [64]. Physical and social isolation refers to a complete or near-complete lack of contact with society [65].

The importance of investigating the effect of physical and social isolation was highlighted in the Patient Experience Research Centre at the Imperial College London online survey that aimed to rapidly capture the opinions, experiences, preferences and concerns of people in the UK during the early phase of the Covid-19 outbreak [193]. Of the 414 people who responded, 399 (95%) agreed that research exploring the public's experiences, risk perceptions and behaviours during this outbreak was necessary and important. Some respondents wanted to specifically understand the impact of social-distancing and self-isolation on people's lives, the activities people adopt during these periods, and factors that influence whether they can comply. The most frequent suggestions for research were for people who are believed to be at risk of more severe infection because of their age or other underlying health conditions, and continuing to track the long-term impact, both physically and socially.

5.4.2. Pilot

5.4.2.1. Important questions surrounding Covid-19 and its impact

Pilot participants highlighted concerns around reduced professional support and increased demand on informal carers while physically and socially isolating. In addition, they expressed

concerns around lack of government support, uncertainty of not knowing how long the situation will last and increasing anxiety around loss of function and ability to cope at home during this period.

5.4.2.2. Refinement of survey questions and length

It was acknowledged by the pilot participants that the survey was already very long prior to adding questions regarding Covid-19. However, they thought all the questions were relevant and the extra time would not be a problem as-long-as it was well explained when the study is introduced.

5.4.2.3. How to maintain participation over 6-months

The pilot participants expressed that completing questionnaires by post may be problematic if a participant feels unwell and/or lacks support to return the questionnaire, the latter being particularly limited under the government restrictions. It was suggested that giving participants the option to complete the questionnaire over the telephone may encourage participants to continue follow-up for the study entity, especially if feeling unwell or unsupported. Although completing the questionnaire via email could be an option, not all participants would have access to the internet or compatible software.

5.4.3. Study amendments

Taking on board the pilot findings and to conduct the study in line with public health policy related to the Covid-19 pandemic, the following amendments were made to the study: i) changes to research aim and objectives, ii) additional questions relating to physical and social isolation, iii) procedural changes, iv) additional recruitment sites. These amendments were

approved by London Camberwell St Giles Research Ethics Committee (ref 19/LO/1950) (Appendix E).

5.4.3.1. Changes to research aim and objectives

Understanding trajectories of disability in the context of Covid-19 may enable services to plan accordingly for potential rehabilitation and social care needs outlined in chapter 2. Therefore, an additional objective was added to the study protocol as follows:

"To describe, determine and compare in people with advanced lung cancer or respiratory disease the extent to which social isolation during the Covid-19 pandemic impacts on ADL function and its recovery".

This objective is addressed in incorporated publication 3 in chapter 7.

5.4.3.2. Additional questions relating to physical and social isolation

Questions were added to the demographic questionnaire to identify how long participants had been physically and socially isolating. This included asking participants whether they are, and/or have been physically or socially isolating and how long for, including dates of isolation period based on their dated government letter. Further information was collected on change in physical activity and social support, and self-management strategies. The Chronic Disease Self-Efficacy Scale was used to measure confidence in managing chores, receiving social support and participation in society [177, 178], and change in physical activity inside and outside the home was also collected using a Likert Scale [179]. See section 5.3.5. for further details on these measures.

5.4.3.3. Procedural changes

The methodology of this study did not change significantly. However due to social distancing rules enforced by the government, remote practices were developed and adopted according

to HRA guidelines [194]. This included, ensuring all contact between the researcher and the participant was by telephone, email, or post, and adopting verbal consent over the telephone. Verbal consent was permissible as this was not a clinical trial and not considered high-risk to participants [194]. Baseline questionnaires were also completed over the telephone. The researcher recorded the participants answers so there was no need to return the questionnaire by post. This was done in more than one telephone call if the participant needed flexibility. The monthly follow-up questionnaires continued to be delivered by post, but telephone follow-up was offered if participants preferred.

5.4.3.4. Additional recruitment sites

Due to the temporary closure of the study, and anticipated slower recruitment while using remote practices, additional sites were required to ensure the study met the required sample size. Sites that expressed interest via the NIHR portfolio with access to patients with advanced NSCLC, COPD or ILD were added as participating centres. There were twelve sites in total, which opened in two waves, once local approvals and set-up was complete, at the convenience of the site. The challenge associated with multiple sites was that government restrictions varied over time and by region across the UK, depending on the number of coronavirus infections, therefore local recruitment was affected differently.

Chapter 6

Results - Secondary Data Analysis

6.1. Introduction

This chapter presents findings from a secondary data analysis of data from the International Access, Rights and Empowerment study of older adults with advanced disease in the UK, Ireland, and the United States. Within incorporated publication 2, data were presented on the prevalence of disability in basic ADLs, and factors associated with this disability, and explores trajectories of disability, to contribute towards the thesis objectives 1, 2 and 4.

6.2. Incorporated publication 2: secondary data analysis

Fettes L, Bone AE, Etkind SN, Ashford S, Higginson IJ, Maddocks M. Disability in Basic Activities of Daily Living Is Associated With Symptom Burden in Older People With Advanced Cancer or Chronic Obstructive Pulmonary Disease: A Secondary Data Analysis. J Pain Symptom Manage. 2021 Jun;61(6):1205-1214. doi: 10.1016/j.jpainsymman.2020.10.012. Epub 2020 Oct 21. PMID: 33096219.

Title:

Disability in basic activities of daily living is associated with symptom burden in older people with advanced cancer or chronic obstructive pulmonary disease: A secondary data analysis

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Abstract

Context: Managing activities of daily living is important to people with advanced cancer or chronic obstructive pulmonary disease (COPD). Understanding disability in activities of daily living may inform service planning.

Objective: To identify the prevalence of disability in activities of daily living, associations and change over time, in older people with advanced cancer or COPD.

Methods: Secondary analysis of International Access, Rights and Empowerment (IARE) studies in adults aged ≥65 years with advanced disease in the UK, Ireland, and USA. Cross-sectional (IARE I & II) and longitudinal (IARE II, 3 timepoints over 6-months) data. Measures: disability in activities of daily living (Barthel Index), symptom severity (Palliative Outcome Scale), assistive device use (self-reported). Logistic regression was used to identify relationships between disability and age, sex, living alone, diagnosis, and symptom burden; Visual Graphical Analysis explores individual disability trajectories.

Results: 159 participants were included (140 cancer, 19 COPD). 65% had difficulty climbing stairs, 48% bathing, 39% dressing, 36% mobilising. Increased disability was independently associated with increased symptom burden (odds ratio [OR], 1.08 [95% CI:1.02-1.15], p=0.01) and walking unaided (z=2.35, p=0.02), but not with primary diagnosis (z=-0.47, p=0.64). Disability generally increased over time but with wide inter-individual variation.

Conclusion: Disability in activities of daily living in advanced cancer or COPD is common, associated with increased symptom burden, and may be attenuated by use of assistive devices. Individual disability trajectories vary widely, with diverse disability profiles. Services should include rehabilitative interventions, guided by disability in individual activities of daily living.

Key message

Disability in activities of daily living is highly prevalent in older people with advanced cancer or chronic obstructive pulmonary disease and is associated with greater symptom burden. Individual disability profiles and trajectories are diverse and require individualised rehabilitation intervention.

Key words

activities of daily living; functional performance; neoplasms; palliative care; pulmonary disease; rehabilitation

Introduction

People are living longer with advanced cancer or chronic obstructive pulmonary disease (COPD) due to earlier identification and diagnosis, advances in treatment, and an aging population (1). This may lead to greater levels of functional loss and prolonged dependency on others over a longer period of time (2, 3), thus increasing the demand for health and social care services (4). Symptom burden is similar between advanced cancer or respiratory disease diagnoses (5), which have a profound effect on functional independence (6). Despite these similarities, clinical management differs where palliative care has a strong bias towards cancer (5), and rehabilitation has a strong bias towards COPD (7). However, towards the end of life, management of advanced conditions in acute care is heavily focused on medical management with little attention to disability (8).

The World Health Organization (WHO) International Classification of Functioning, Disability and Health (ICF) characterizes disability as the result of a complex relationship between an individual's health condition, personal factors, and external (environmental) factors, such as the circumstances in which the individual lives (9). Activities of daily living are defined as activities that constitute a person's daily life, which can be considered either basic activities of daily living (e.g. washing, dressing, bathing, toileting, feeding), or more complex tasks known as instrumental activities of daily living (e.g. shopping, housework, use of public transportation). Disability in activities of daily living is among the most common unmet supportive care need in cancer patients (10), and equally important to patients with COPD (11).

Associations and individual patterns of disability in activities of daily living, specifically in advanced cancer or COPD are under-investigated. Measuring disability in activities of daily living may shed light on how functional decline affects an individual's independence. Self or proxy-reported disability in the year before death suggests disability trajectories of activities of daily living are disease specific, with cancer following a trajectory of high functioning then a period of rapid decline and respiratory disease following a more unpredictable pattern (3). However, whilst this approach helps to understand disability in relation to death, prospective individual-level trajectories are needed to provide a more clinical perspective and inform service planning.

Addressing disability is increasingly important as health service costs are primarily related to levels of impairment and/or disability and dependence, but service planning is primarily disease specific (12). Current gaps in the literature include an understanding of causes and consequences of disability in activities of daily living in advanced cancer or COPD, including how disability changes over time, can help establish appropriate services and interventions to reduce functional dependence. This study aimed to: i) describe the prevalence of disability in activities of daily living overall and by each individual activity; ii) examine factors associated with disability in activities of daily living; and iii) explore change in disability over time, in older people with advanced cancer or COPD.

Methods

Data source – the IARE studies

This is a secondary analysis of data from the International Access, Rights and Empowerment (IARE) studies. These two studies were designed to be compatible using similar inclusion criteria and measurement. IARE I (13) was a cross-sectional patient survey of older patients accessing specialist palliative care services across UK, Ireland, and the USA between November 2012 and August 2014. IARE II (14) was a prospective cohort study to identify and understand service use, preferences, and palliative care needs of frail older people with advanced disease in the UK between February 2017 and January 2019. Recruitment was from specialist palliative care services at two large London hospitals, and one hospital in Dublin and one in New York in IARE I, and from two

acute hospitals, one sub-acute hospital, and one acute community service in South London (UK) in IARE II. IARE I inclusion criteria were: 1. aged ≥65, and2. under the care of a palliative care team. IARE II inclusion criteria were: 1. Age≥65 years; 2. Frailty (Rockwood Clinical Frailty Scale score ≥5 (15)); 3. one or more unplanned hospital admission or two or more unplanned emergency department attendances in the last 6 months; 4. Not currently receiving specialist palliative care. Exclusion criteria were patients with cognitive impairment (IARE I) and without an allocated proxy (IARE II). Participants in IARE II were studied at baseline and followed up at 3 and 6 months. Ethical approval was granted by the Dulwich, and Camberwell and St Giles Research Ethics Committee(s), (Refs: 12/LO/0044 and 16/LO/2048).

Selected sample

From the pooled sample of IARE I and II participants (n = total IARE I and II sample), we included participants with solid advanced cancer or respiratory disease. Respiratory disease was further limited to COPD due to lack of cases with other respiratory conditions in the dataset. This study is reported following STROBE guidelines for reporting of observational studies (16).

Outcome variable

The primary outcome for this study was basic disability in activities of daily living, measured using the Barthel Index (17, 18). This is a 10-item categorical measure which includes ten basic activities of daily living items (bowel incontinence, toilet use, grooming, feeding, mobility, bladder incontinence, dressing, bathing, stairs, and transfers). The values assigned to each item in the Barthel Index are based on the amount of physical assistance required to perform the task. Items have between two and four responses, rated on a 0-1, 0-2, or 0-3 scale, ranging from dependent/unable, to minor help, major help, or independent (17). A total score ranges from 0-20 where 0 represents fully dependent and 20 fully independent (17, 18). A minimal important clinical difference in total disability is identified by a change of 3 or more in any direction (19). Scores from the original Barthel Index using a 0-100 scale were transferred onto the comparable Barthel Index using the recommended 0-20 scale (17, 18), in order to pool data. On the 0-100 scale a total Barthel Index score of 0-20 suggests total dependence, 21-60 severe dependence, 61-90 moderate dependence, 91-99 slight dependence, and 100 fully independent (20). Comparatively on the 0-20 scale, very severe disability is identified by a score of <5, severe 5-9, moderate 10-14, mild 15-19, and 20 no disability.

Explanatory variables

Explanatory variables were selected based on findings from a recent systematic review of trajectory studies of disability in activities of daily living in advanced cancer or respiratory disease (21). In the pooled data analysis these included age, gender, living alone, diagnosis, symptom burden, and comorbidity. Symptom burden was measured using the Palliative Outcomes Scale family of measures which calculate a total score ranging from 0-40 where a higher score equals greater symptom burden (22). Co-morbidities were collected using the Charlson Comorbidity Index or the Elixhauser Comorbidity Measure and reported as counts. Further explanatory variables were considered that were only collected in IARE II, including performance status, frailty, and use of an assistive device (yes/no) including walking aid, wheelchair, commode, raiser recliner chair, and chair raisers. Performance status was measured using the Australian Functional Performance Scale which is a 10-point scale ranging from 0 (dead) to 100 (fully independent) (23). The Rockwood Clinical Frailty Scale was used to measure frailty using a 9-point scale from 1 (very fit) to 9 (terminally ill) (15).

Data Analysis

Cross-sectional analysis

Descriptive statistics were used to summarise participant characteristics. Medians and interquartile ranges for unevenly distributed data or counts (percentages) were used where appropriate. Disability in activities of daily living was reported as prevalence for total disability and for each individual item on the Barthel Index for the whole sample (combined diagnoses), if disability scores are similar across diagnoses and separately by diagnosis if not. Associations between the total Barthel Index score and explanatory variables were calculated using non-parametric tests: Mann-Whitney-U, or Spearman's rho for binary and continuous variables, respectively.

Associations with age, gender, living alone, diagnosis, symptom burden, and comorbidity were calculated. Assistive devices, performance status and frailty were calculated for IARE II only. Our primary dependent variable in logistic regression analysis was whether the participant had ≥ moderate disability (Barthel Index<15) (24) or not (Barthel Index ≥15) and included complete cases only. Explanatory variables considered for the model were age, gender, living status, diagnosis, symptom severity, and comorbidity, as identified above (21)

STATA version 16 was used for all analyses, where all available data were used in complete case analysis. Based on assumed prevalence of disability in activities of daily living in this patient population to be around 50% (10, 25) a sample size of 150 would achieve a precision of + or - 8% in the estimation of prevalence of ADL disability. This sample size would also be sufficient to detect a significant correlation (based on a medium effect size and 80% power at a 5% significance level, a sample of 84 is required), and for us to enter ≤10 planned variables in regression analysis.

Longitudinal analysis

Longitudinal analysis was exploratory. Change in disability in activities of daily living over time using total Barthel Index score and symptom burden (Palliative Outcomes Scale) was plotted using medians and interquartile ranges at baseline, 3 and 6 months. Visual graphical analysis (26) was used to discover common patterns of individual change in total Barthel Index score over the three timepoints. Four trajectory groups were identified where a change of ≥1 point was used to discriminate the different trajectories. An increase or decrease of ≥1 would represent a decreasing or increasing trajectory respectively, and a combination of at least one increase and one decrease of ≥1 would represent a fluctuating trajectory. A change of <1 in either direction would represent a trajectory of no change.

Results

Cross-sectional Analysis

159 participants were included in the cross-sectional analysis (table 1): 94% cancer (n=140); 6% COPD (n=19). The median [IQR] total Barthel Index score for the whole sample was 17 [14-19], which was numerically higher in cancer (18 [13-19]) indicating less disability than COPD (17 [14-19]), but was not significantly different (z=-0.47, p=0.64). Forty-eight percent of all participants had mild, 18% moderate, 12% severe and 1% very severe disability. 21% had no disability. The univariate relationship between explanatory variables and total Barthel Index score is presented in table 2. More severe disability is associated with greater symptom burden (R = -0.24, p=0.01). The multivariable analysis shows that ≥ moderate disability (Barthel Index<15) in activities of daily living (n= 44 (31%)) is independently associated with increasing symptom burden (odds ratio [OR], 1.08 [95% CI:1.02-1.15], p=0.01) (table 3).

Australian Karnofsky Performance Status, frailty, and use of a walking aid were reported by the 31 participants in IARE II. At baseline higher function on the Australian Karnofsky Performance Status was associated with less disability (R=0.73, p<0.001). Increased frailty is related to increased disability (R = -0.44, p=0.01). Use of a walking aid was associated with less severe disability (z=2.35, p=0.02) and higher functional performance (z=1.96, p=0.05).

Longitudinal Analysis

Eighteen participants completed activity of daily living measures (Barthel Index) at all three time points for longitudinal analysis (8 cancer, 10 COPD). Total disability in activities of daily living slightly increased over 6 months (median -2 [IQR -3 – 0]) (figure 2a) and there was little change in symptom burden (median -1 [IQR -3 - 3] (figure 2b). Figure 3 shows wide variation in the pattern and speed of change in individual trajectories of total disability in activities of daily living on the Barthel Index, which are grouped into trajectories of no change (n=4); decreasing disability (n=2); increasing disability (n=6); and fluctuating disability (n=6), which vary across diagnoses. Overall, there was a bigger change in disability between baseline and 3 months (0 to 9 points) than between 3 months and 6 months (0 to 7 points). At 3 months, 7 patients showed a change beyond the minimal important clinical difference, of which 3 improved and 4 had more disability, and 1 patient showed increased disability beyond the minimal important clinical difference between 3 and 6 months.

Table 1: Participant characteristics

Pooled dataset (n=159)	**All (n=159)**	**Cancer (n=140)**	**COPD (n=19)**
Total Barthel Index score [median, IQR]	17 [14-19]	18 [13-19]	17 [14-19]
Age [median, IQR]	74 [69-81]	73 [68-80]	79 [72-85]
Female, n (%)	86 (54)	74 (53)	12 (63)
White British, n (%)	140 (88)	106 (83)	17 (90)
Lives alone, n (%)	72 (45.3)	61 (44)	11 (58)
Co-morbidities [median, IQR]:			
Number of comorbidities included in Charlson Co-morbidity Index	1 [0-2]	1 [0-2]	4 [1-7]
Number of comorbidities included in Elixhauser Comorbidity Measure	4 [3-6]	4 [3-5]	5 [3-6]
Symptom burden (Palliative Outcomes Scale) [median, IQR]	11 [5-16]	11 [5.5-16]	9.5 [4-18]
IARE II (N=31)	**All (N=31)**	**Cancer (N=17)**	**COPD (N=14)**
Total Barthel Index score [median, IQR]	16 [14-19]	16 [13-19]	16 [13-19]
Australian Karnofsky Performance Status [median, IQR]	50 [50-60]	50 [50-60]	50 [50-60]
Frailty [median, IQR]	6 [5-6]	6 [5-6]	6 [5-6]
Current equipment, n (%):			
Walking aid	28 (90)	15 (88.2)	13 (92.9)
Wheelchair	17 (55)	7 (41)	10 (71)
Commode	11 (36)	5 (29)	6 (43)
Raiser recliner chair	13 (42)	7 (41)	6 (43)
Chair raisers	4 (13)	4 (24)	14 (100)

COPD: chronic obstructive pulmonary disease; Comorbidity was measured using the Charlson comorbidity index in 128 participants (123 Cancer, 5 COPD), and the Elixhauser Comorbidity Measure in 31 participants (17 Cancer, 14 COPD)

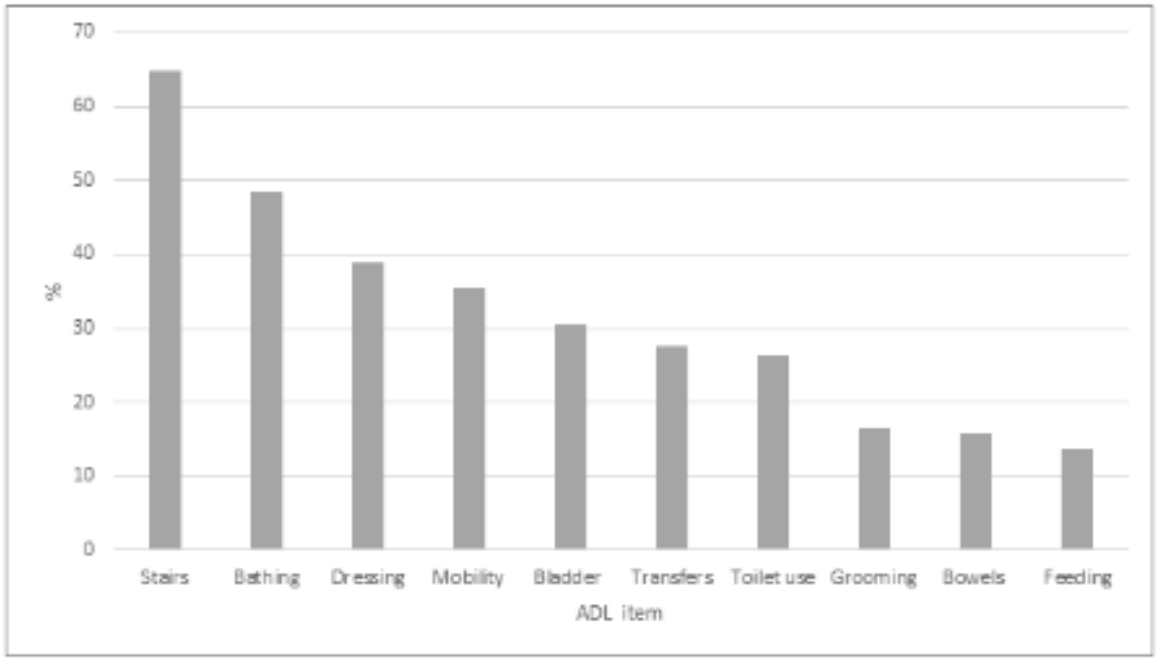

Figure 1. Prevelance of disability in activities of daily living

Table 2: Univariate relationship between explanatory variables and total Barthel Index score

Pooled dataset (n=159)	**Z**	**R**	**P**
Cancer	-0.47	-	0.64
Age	-	-0.24	0.66
Female	0.44	-	0.66
White British	-0.01	-	0.99
Lives alone	-0.46		0.64
Number of Co-morbidities	-	-0.02	0.88
Symptom burden	-	-0.24	0.01
IARE II (N=31)			
Australian Karnofsky Performance Status	-	0.73	<0.001
Frailty	-	-0.44	0.01
Current equipment: Uses w*alking aid*	2.35	-	0.02
Uses wheelchair	-1.36	-	0.18
Uses commode	0.64	-	0.52
Uses raiser recliner chair	-1.71	-	0.09
Uses chair raisers	-0.77	-	0.44

Z = Mann-Whitney-U; R = spearman's rho; P = p-value; All variables in this table have been dichotomised, except symptom burden and age which were treated as continuous variables.

Table 3: Adjusted associations with moderate/severe disability in activities of daily living using multivariable logistic regression (n=139)

Disability severity	Odds ratio	[95% Conf. Interval]		P-value
Symptom burden	1.08	1.02	1.15	0.01
Age	1.02	0.97	1.08	0.36
Cancer	0.92	0.24	3.43	0.90
Female	0.97	0.44	2.13	0.94
Live alone	0.77	0.34	1.70	0.51
IARE I	1.02	0.31	3.34	0.97
_cons	0.04	0.00	3.58	0.16

Reference group is moderate/severe disability in activities of daily living (Barthel Index <15); All variables in this table have been dichotomised, except symptom burden and age which were treated as continuous variables.

a) **b)**

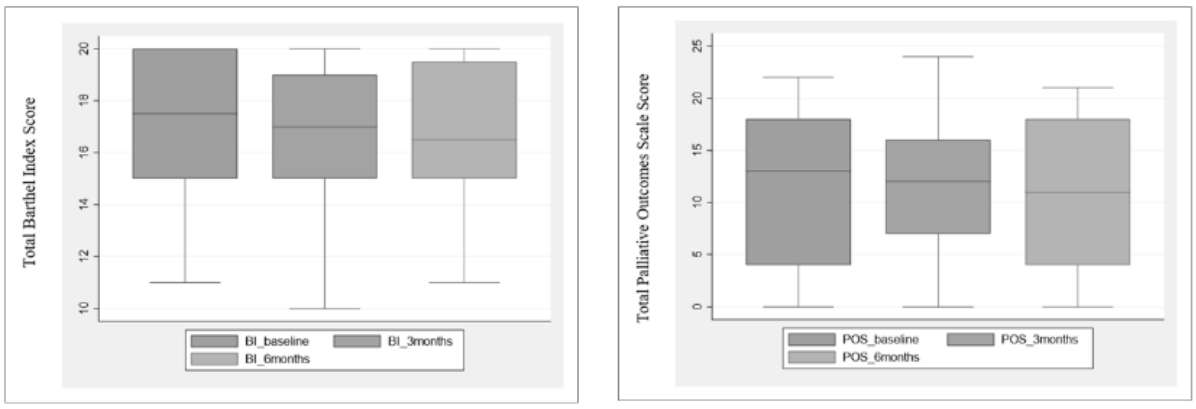

Figure 2. Change in total disability and symptom burden over 6 months (N=18). a) Total disability in Barthel Index (BI) (lower score equals greater dependency). b) Total symptom burden in Palliative Outcomes Scale (POS) (higer score equals greater symptom burden).

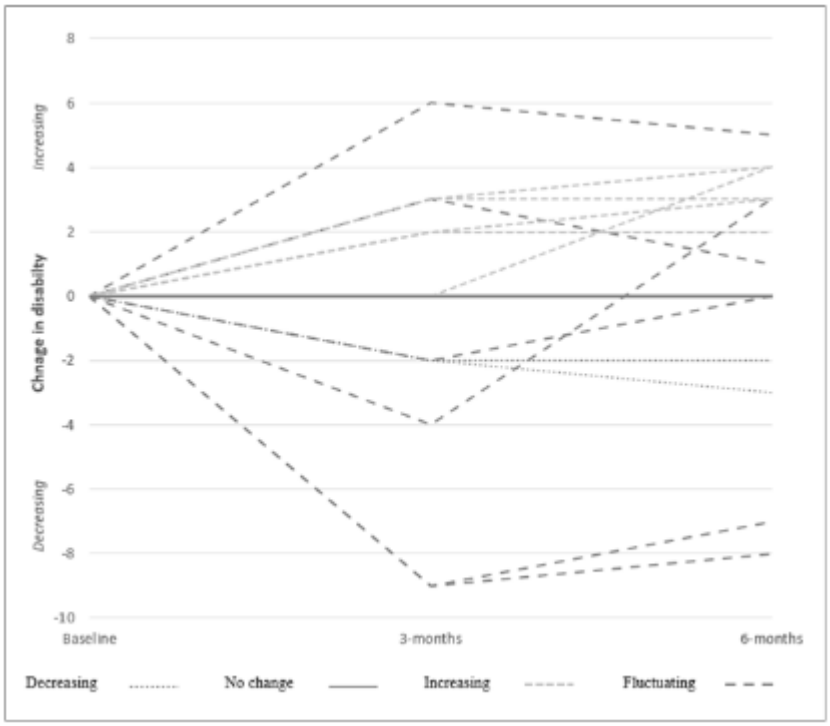

Figure 3. Individual trajectories of change in total disability in activities of daily living on the Barthel Index over 6months (N=18)

Discussion

Main Findings

In our analysis of older people with advanced cancer or COPD, disability was highly prevalent. Our main findings were that: i) More severe disability in this population independently related to greater symptom burden but not age or primary diagnosis; ii) Less disability related to use of a walking aid; iii) The most disabling activities of daily living were stairs, bathing, and dressing; iv) wide variability in disability in activities in daily living and symptom burden over 6 months; v) Individual trajectories were variable across all four patterns of ADL disability: no change, increasing, decreasing, and fluctuating disability.

Prevalence of disability in activities of daily living

Our findings show that disability in basic activities of daily living is prevalent in three-quarters of older people with advanced cancer or COPD. This is greater than identified in a systematic review that found disability in activities of daily living was prevalent in 7.4-49.8% of those with COPD (27), and a meta-analysis that identified one-third and half of adults with cancer have difficulty or require assistance to perform basic and instrumental activities of daily living respectively (10). This suggests disability may be greater in an older or/and sicker population. The Chinese Longitudinal and Health Longevity Study of 4621 oldest-old (≥80 years old) (28), found independent associations between COPD and disability in basic and instrumental activities of daily living in the community. However, it is known that disability is more prevalent in inpatient compared to outpatient settings in advanced cancer (10), particularly relating to basic activities of daily living, which can lead to increased length of hospital stay and discharge to a care facility (29). Comparatively, in a cohort study of 164 patients with advanced cancer living at home, heavy housework was found to be the most problematic of daily activities and engagement in leisure and social activities was considered a priority (30).

We propose that functional assessment should include both basic and instrumental activities of daily living with a focus on individual activities rather than overall decline. Although there can be a hierarchical pattern in loss of independence in activities of daily living, the order can be affected by: the sample studied, the choice of response

options for each item, the selection and number of items in the scale, and the type of scaling procedure (31). This is supported by a population based longitudinal study of 51,338 older adults which found that physical function measured by performance tests was significantly associated with self-reported disability in activities of daily living, and risk of disability was higher when the number of activity of daily living domains increased (32). However, one validated questionnaire cannot meet all the assessment and evaluation needs of one population and a combination of existing questionnaires is recommended to fully assess disability in both basic and instrumental activities of daily living (33). The Katz Index and the Lawton Brody Instrumental Activities of Daily Living Scale are popular for measuring basic and instrumental activities of daily living respectively (10).

Factors associated with disability in activities of daily living

Our study found symptom burden relates to disability in activities of daily living in advanced cancer or COPD, which is supported by a prospective analytical study of 638 patients referred to a Home Care Support Team (34). Symptoms restricting disability are common during the last year of life and the likelihood of a hospice admission increases in patients with a greater burden of restricting symptoms and number of disabilities in activities of daily living (35). Our findings showed that use of a walking aid is associated with less disability. As the Barthel Index allows the use of an assistive device to be independent (17), this does not necessarily mean that the person has changed their underlying functional impairment or has less severe symptoms, but rather the environment has been manipulated to enable them to function. This is supported by the Health and Retirement study (36) that identified difficulty bathing to be a strong and independent predictor of nursing home placement in older people and difficulty walking was not associated despite being common in this population, possibly due to use of mobility devices. This highlights the importance of considering environmental factors (9) (e.g. assistive devices or place of care) in the causation of disability. However, it is not clear if there is a more specific relationship between a certain symptom (e.g., breathlessness) and a specific disability in certain activities (e.g. bathing) and whether this could be modified by an adaption to the environment (e.g. shower stool). Research is needed to fully understand relationships between individual symptoms, different basic and instrumental activities, and environmental adaptation. This would help to pre-empt loss of independence and inform timely preventative interventions rather than wait for irreversible functional decline or crisis.

Our study did not identify a relationship between disability in activities of daily living and age or comorbidity. A cross-sectional study of 6973 cancer survivors identified an association between greater disability in activities of daily living and people aged ≥85 as well as those with metastatic cancer (37). A prospective cohort study of 9058 older adults found complex multimorbidity to be strongly related to the need for assistance in instrumental activities of daily living and need for assistance in basic activities of daily living was related to a lesser extent (38). In addition, older people with frailty are less likely to recover from disability in activities of daily living than people who were not frail (39). Extending measurement of disability to instrumental activities of daily living could identify associations which may be missed by focusing on basic activities of daily living.

Clinical implications

Healthcare organizations are designed to address acute problems which might explain the medical emphasis in advanced disease (40). Prolonged survival in advanced cancer or COPD has implications for health care services to stretch beyond acute management and recovery which may not be possible in advanced illness, to adopting an anticipatory, preventative and adaptive approach to persisting symptoms and functional decline (41), and avoid hindrance of an individual's performance (e.g. unavailability of assistive devices) (9).

A focus on symptom management and maximisation of function is essential to improve quality of life in advanced illness, albeit in older adults non-pharmacological interventions should be considered in the first line of treatment to minimize drug-drug interactions and serious side-effects (42). Rehabilitation has a role to play in the non-pharmacological management of symptoms, as well as by helping people to maintain their optimal levels of physical, sensory, intellectual and social functioning with minimum dependence on others for as long as possible (43, 44).

Utilization of interventions targeting disability in activities of daily living in advanced illness, such as occupational therapy, remain low, possibly due to weak evidence (45) and lack of referral (46). A randomised controlled trial evaluating the efficacy of an occupational therapy-based intervention on disability in activities of daily living in people with advanced cancer showed no significant effects (47). A process evaluation of this trial identified that beneficial effect could be limited by: lack of presenting disability in the recruited sample; insufficient dosage; and inadequate timing of the intervention and follow-up procedures, which could be potentially overcome by

improving the reach, timing and delivery of the intervention (48). Robust prospective studies exploring disability trajectories in activities of daily living could help identify when, where, for whom and how to intervene, to inform future trial design.

Limitations of study and data

This study is limited by data collected in the primary studies from the IARE project. Firstly, the population was restricted to people aged ≥65 either receiving palliative care or frail, which may not be generalisable to everyone with advanced cancer or COPD. The sample consisted mostly of cancer patients, compromising comparison across diagnoses. Secondly, measurement of disability in activities of daily living was limited to basic activities and did not collect data on instrumental activities, underestimating the prevalence of disability. Thirdly, it is difficult to fully understand all factors that may relate to disability due to the choice of explanatory variables explored in the primary studies, the differing measures used across the two studies and use of complete case analysis. Fourth, the Palliative care Outcome Scale includes mobility as a symptom overlapping with several items of the Barthel Index (stairs, mobility, and transfers), and it is unknown how this could influence the findings. Finally, the small sample size in the longitudinal analysis means analysis is exploratory and is limited by completion bias.

Conclusion

Disability in activities of daily living is common in advanced cancer or COPD. Increased disability relates to greater symptom burden and may be attenuated by use of adaptive interventions. Disability increases over time, but trajectories vary among individuals with differing disability profiles. To directly address disability in activities of daily living, services need to be modified to include rehabilitative interventions which are guided by disability in individual activities of daily living rather than a total disability score. Further investigation is required to understand the patterns of decline over time in basic and instrumental activities of daily living, and the complexity of factors that contribute to this change in people living with advanced cancer or COPD. This includes symptom management and adaptive interventions. Greater understanding of these relationships prospectively and retrospective from death will provide the opportunity to robustly test rehabilitative interventions and positively influence policy and clinical practice.

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None of the authors have any conflicts of interests to declare.

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6.3. Summary of secondary data analysis

This secondary data analysis found disability in basic ADLs was highly prevalent in older people with advanced cancer or COPD and was associated with increased symptom burden. Assistive devices may attenuate the impact of disability. Further research was indicated to increase generalizability to people with advanced lung cancer or respiratory disease, and to extend understanding of disability across a broader range of ADLs and how it changes over time. These findings contributed to the design of the prospective cohort study, which led to: i) narrowing the population of interest to NSCLC, COPD and ILD; ii) including study of both basic and instrumental ADLs; iii) following participants prospectively with more regular assessment.

Chapter 7

Results - Cohort study recruitment, follow-up, participant characteristics, and cross-sectional analysis

7.1. Introduction

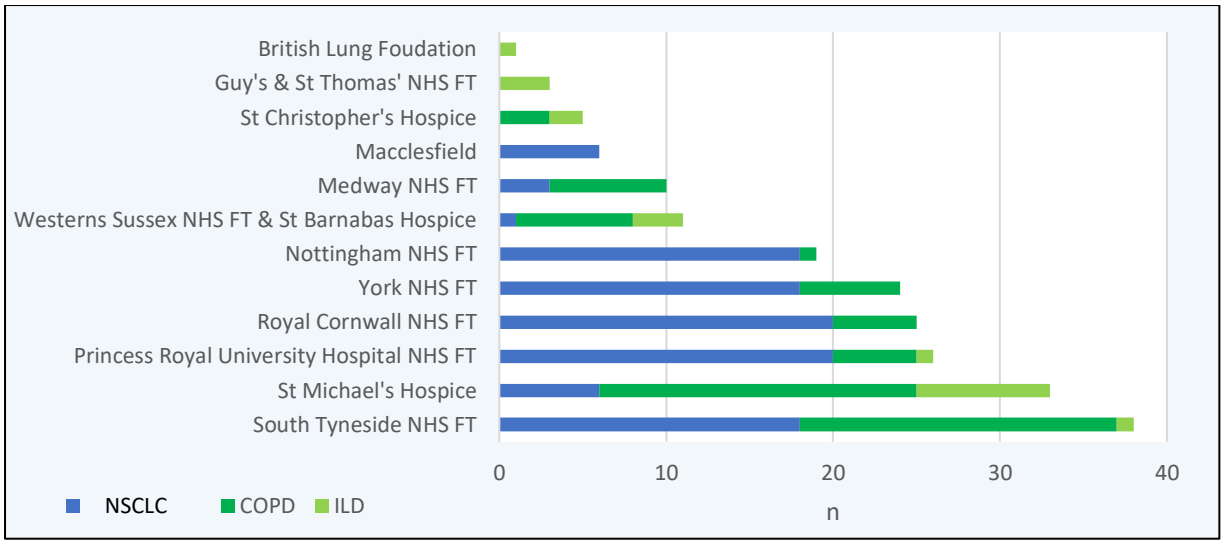
This chapter for the cohort study puts the findings into context to consider the generalizability of the study population and representativeness of the findings. Incorporated publication 3 presents baseline data from the prospective cohort study to place the study in the context of the Covid-19 pandemic and identify associations with baseline disability in basic and instrumental ADLs.

7.2. Recruitment, follow-up, and attrition

7.2.1. Recruitment

Across twelve participating sites in England, 475 patients with NSCLC, COPD or ILD who met the inclusion criteria were approached between March 2020 and January 2021. Three of these participants were recruited during the pilot phase, prior to closure of the study for nearly four months from the 18th of March 2020, due to the Covid-19 pandemic. One-hundred-and-fifty-two (76%) participants were recruited from acute NHS trusts, 48 (24%) were recruited from hospice services, and one participant was recruited through the British Lung Foundation members forum. As shown in figure 7.1, recruitment varied across sites, mainly due to local implications of the Covid-19 pandemic, which restricted access to potential participants or required redeployment of research staff.

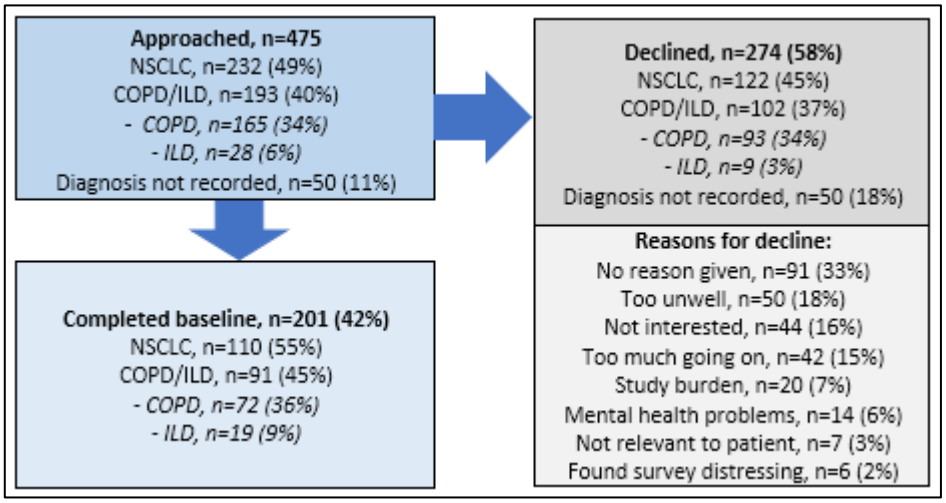
Figure 7.1: Recruitment from participating sites across England



NHS FT: National Health Service Foundation Trust, COPD: Chronic Obstructive Pulmonary Disease, ILD: Interstitial Lung Disease

The recruitment flow is outlined in figure 7.2. The overall response rate was 42%: 201 participants consented to participate in the study and 274 participants declined to participate. Of those who consented, 110 (55%) had NSCLC and 91 (45%) had COPD or ILD. One third (33%) of those who declined did not give a reason. Where provided, reasons included: feeling too unwell (18%); not being interested (16%); or having too much going on (15%).

Figure 7.2: Recruitment flow

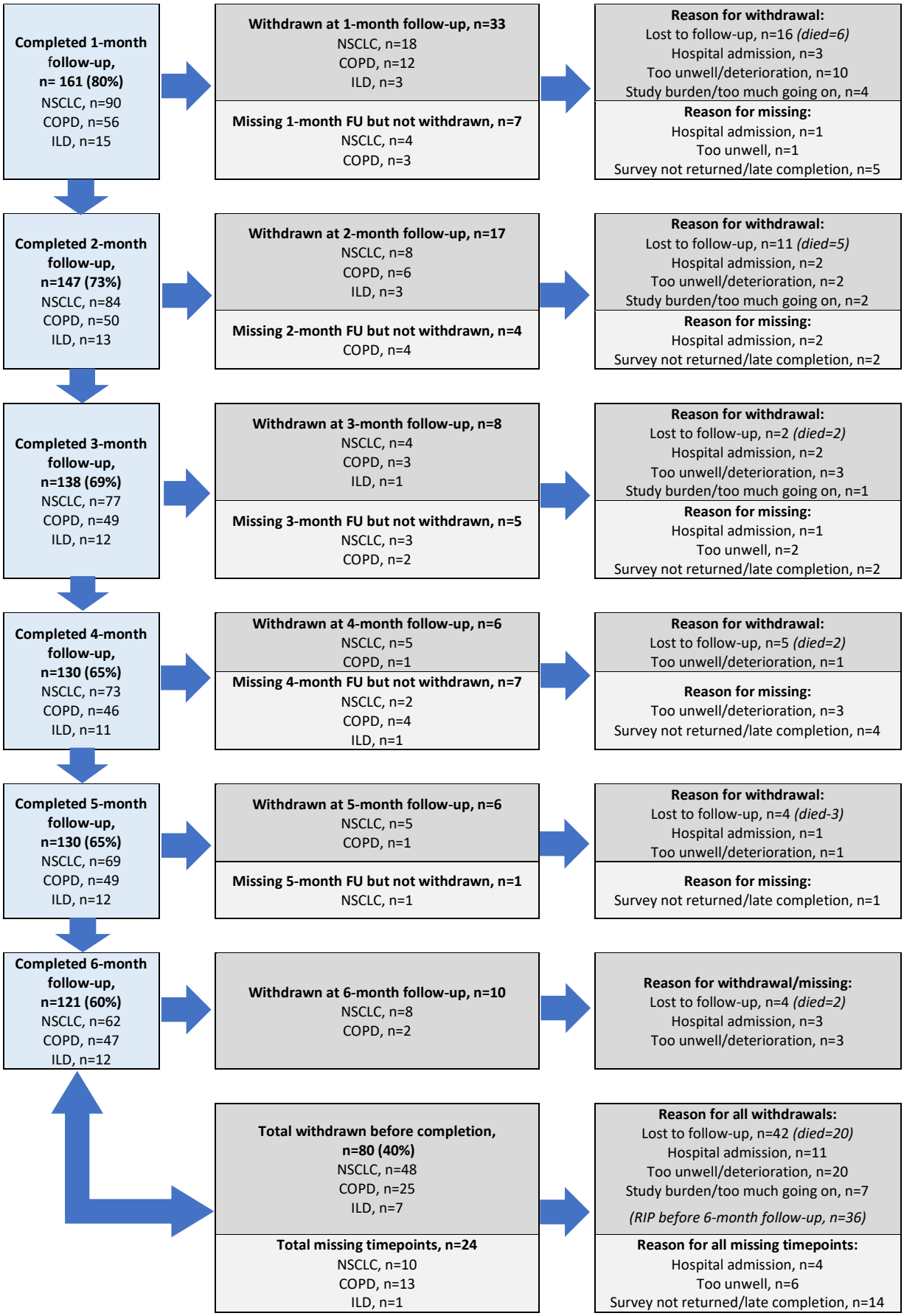


NSCLC: non-small-cell lung cancer; COPD: chronic obstructive pulmonary disease; ILD: Interstitial lung disease (ILD)

7.2.2. Follow-up and attrition

The study flow of follow-up, attrition and missing timepoints is presented in figure 7.3. This illustrates 121 (60%) participants completed 6-month follow-up, of which 62 (51%) had NSCLC and 59 (49%) had COPD or ILD. The overall attrition to 6-months was 80 participants (40%), most of whom had a primary diagnosis of NSCLC (n=48, 60%). Attrition was greatest at 1-month follow-up (n=33, 16%). Withdrawal from the study across all timepoints occurred either due to being lost to follow-up (n=42, 52%), or voluntary withdrawal (n=38, 48%). Lost to follow-up included instances when patients were unable to be contacted, either due to death or an unknown reason. Where participants were contacted and expressed a wish to withdraw, reasons given included feeling too unwell or deterioration of their condition (n=20, 25%); admission to hospital (n=11, 14%); or they found continuing in the study too burdensome (n=7, 9%). Medical notes were checked at 6-month follow-up which clarified that 36 (45%) participants who withdrew or were lost to follow-up had died within six months following consent (before 6-month follow-up), which reflects the general mortality of this population. Most participants who died had NSCLC (n=25, 69%).

Figure 7.3: Study flow of follow-up and attrition



NSCLC*: non-small-cell lung cancer; COPD: chronic obstructive pulmonary disease; ILD: Interstitial lung disease; FU: follow-up*

7.3. Missing data

Out of a possible 1206 monthly follow-up questionnaires, 931 questionnaires were due to be sent to participants across all timepoints, excluding those participants known to have been withdrawn from the study at an earlier timepoint. 851 (91%) of these questionnaires were sent to participants who were contactable and wished to continue participating in the study, and 827 (88%) were completed.

7.3.1. Missing questionnaires due to withdrawal or lost to follow-up

As the study flow (figure 7.3) shows, missing data were mostly due to withdrawal or loss to follow-up, which accounts for 355 (94%) of the 379 missing questionnaires. This missing data represents 'attrition due to death or illness' [195] that occurs during follow-up where participants did not provide any further data.

7.3.2. Intermittent missing questionnaires

Intermittent missing data occurred when participants missed a follow-up timepoint but completed a subsequent time point. Of the 121 participants who completed 6-month follow-up there were 24 missing follow-up questionnaires out of a possible 726 (figure 7.3.) The most common reason for missing a timepoint was either late or no return of the questionnaire (n=14), often due to Covid-19 restrictions preventing postage or delays to the postal service.

7.3.3. Missing items

Episodes of missing data also occurred when participants missed a single questionnaire in the survey or an item within a single questionnaire (table 7.1).

Table 7.1: Missing data in follow-up questionnaires

Questionnaire	Total no. of questionnaires	No. of missing single questionnaires	% of missing single questionnaires	No. of main items per questionnaire	Total no. of items	No. of missing items	% of missing items	Explanations for missing data
Barthel Index (BADL)	814	1	0.1	10	8140	52	0.6	Explanations include: "no change", "someone else does it", "have help", "use an aid", "don't do it", "don't have stairs"
Lawton Brody IADL Scale (IADL)	814	0	0	8	6512	50	0.8	Explanations include: "no change", "someone else does it", "shop online", "microwave meals", "don't go out", "shielding"
WHODAS-cognition	814	7	0.9	6	4884	29	0.6	Explanations include: “don’t need to”, “varies”
WHODAS-mobility	814	8	1	5	4070	40	1	Explanations include: "don't go out", "shielding"
WHODAS-self-care	814	6	0.7	4	3256	37	1	Explanations include: “I live on my own”, "have to stay in by myself due to covid"
WHODAS-getting along with others	814	15	1.8	5	4070	191	4.7	Explanations include: “Unable to due to shielding / Covid-19 restrictions”, “not applicable”, “don’t want to answer”
WHODAS-household activities	814	8	1	4	3256	13	0.4	Explanations include: “takes time”, “varies”
WHODAS-work	814	694	85	4	-	-	-	This section was optional and missed out if the participant was not working. It is therefore not included in the analysis.
WHODAS-participation	814	6	0.7	7	5698	143	2.5	Explanations include: “Unable to due to shielding / Covid-19 restrictions”
Palliative care outcomes scale - symptoms (POS-S)	814	4	0.5	10	8140	16	0.2	Explanations include: “depends on activity”, “varies”
Use of assistive devices for ADLs	814	1	0.1	10	8140	29	0.4	Explanations include: "don't go out", "shielding"
CSRI - overnight stays	814	4	0.5	5	4070	3	0.1	Items were often only missed if another option was ticked, e.g., hospital admission or specialist oncology visit, and therefore assumed to be a “no” response” if not ticked and not considered missing, unless the whole section was missing. This was the last questionnaire in the survey and some sections may appear repetitive or missed due to questionnaire fatigue.
CSRI - specialist services	814	11	1.4	5	4070	31	0.8	
CSRI - other services	814	13	1.6	18	14652	78	0.5	

ADL: Activities of daily living; BADL Basic activities of daily living- measured using the Barthel Index; IADL: Instrumental activities of daily living – measured using the Lawton Brody Instrumental ADL Scale; WHODAS: World Health Organization Disability Assessment Schedule; CSRI: Client Service Receipt Inventory; The main missing items were the items that contributed to the total score and excluded the ‘other’ option in the questionnaire; Explanations of missing data were recorded by the participant next to an unanswered response in the questionnaire; ‘Shielding’ is the term participants generally used to describe physical and social isolation.

Nearly all 201 baseline questionnaires were completed in full. Data were only missing on physical and social isolation and difficulty in daily activities (WHODAS-2.0) for one participant each. In total, 814 follow-up questionnaires were returned, all of which were at least partially completed. Missing items mostly affected postal surveys rather than those completed over the telephone with the researcher.

7.3.3.1. Missing single questionnaires

Across all follow-up timepoints, of the single questionnaires within the survey, only one Barthel index and none of the Lawton Brody Instrumental ADL Scales were missing in full. Participants missed individual domains on the WHODAS-2.0, which was highest in the 'work' domain (85%), as most participants did not work. As the work domain was optional it could be excluded from the analysis. Out of all the questionnaires, there were less than 2% missing for each of the remaining WHODAS-2.0. domains, the POS-S, use of assistive devices, and CSRI questionnaires, some of which may be accounted for by participants accidently missing pages in the survey or questionnaire fatigue.

7.3.3.2. Missing item responses

The frequency of missing item responses for each follow-up questionnaire in the survey are presented in figures H1 to H6 in Appendix H. Missing responses to items within the single questionnaire were low for the Barthel Index (0.6%) and Lawton Brody Instrumental ADL scale (0.8%). However, an explanation as to how they manage this activity (e.g., "no change", "need help", "someone else does it", "shielding") was provided for nearly all missing items from which the correct response to the item could be applied.

One participant did not answer the individual item 'bowels', or 'bladder' with no explanation on the Barthel Index on all six follow-up questionnaires and was therefore excluded from the

analysis. Where the whole section was missing (n=1) or where it was not possible to allocate an appropriate response (n=5) that timepoint was not included in the longitudinal analysis. On the Lawton Brody Instrumental ADL Scale, 'shopping' was the most frequent missing item (n=30, 4%), along with the comment 'online shopping', which was rectified by classing this response as independent.

On the WHODAS-2.0, most missing items were from the 'getting along with others' (4.7%) and 'participation' domains (2.5%), which reflected where participants were uncomfortable responding to the item 'sexual activities' (n=136) or were impacted by Covid-19 restrictions on physical and social isolation (n=118). Missing items did not affect the total score for use of ADL assistive devices or the CSRI, but a missed symptom would invalidate the total POS-S score and therefore the whole questionnaire would be considered missing. The only measure that outlined methods for handling missing data was the WHODAS-2.0, which could be applied where less than three items were missing on a single domain.

It is probable that missing data is 'missing not at random', as current or future observations are unknown and cannot be predicted [195]. Given the overall nature and levels of missing data, complete case analysis was used. Imputation of missing data (such as last value carried forward, simple mean imputation, or other techniques) were not deemed appropriate.

7.4. Participant characteristics

7.4.1. Demographics and clinical characteristics

The demographic and clinical characteristics of study participants are presented in table 7.2. Ninety-one women and 110 men were included in the study, with a median [IQR] age of 69 [63-75]. Nearly all participants were white British (95%) and almost half (46%) were educated above secondary school education. One-hundred-and-ten participants had NSCLC, and 91 had COPD or ILD (72 COPD, 19 ILD), 121 (60%) of whom had stage IV disease. Thirty-one (28%) participants with NSCLC also had COPD or ILD of any staging. The median [IQR] score on the Charlson Comorbidity Index, AKPS, and symptom severity was 7 [3-10], 70 [60-80], and 10 [5.5-15], respectively. This showed most of the sample often had multiple long-term conditions, were able to care for themselves and were mildly affected by their symptoms. Ninety-one percent of participants with NSCLC were receiving cancer treatment (chemotherapy, radiotherapy, immunotherapy), and 20% of all participants were prescribed ambulatory oxygen.

Nearly all participants (97%) actively chose to physically and socially isolate due to the Covid-19 pandemic for a median [IQR] of 5 [3-8] months at the time of recruitment, despite only 87% receiving a government letter requesting them to. Confidence to receive support from community services, family or friends was extremely low (median 2 [IQR 1.5-3]), despite only 68 (34%) of participants living alone. Reduced physical activity indoors and outdoors affected 94 (47%) and 129 (65%) participants respectively, and 144 (72%) lived in a property with stairs. Over half of participants had an informal carer (n=112, 56%), and 29 participants (14%) received care from a formal care provider.

Table 7.2: Participant characteristics and comparisons between participants who completed 6-month follow-up and those who withdrew

Participant characteristics and outcomes at baseline	Whole sample n=201	Completed 6-month follow-up (n=121)	Withdrawn before 6-month follow-up (n=80)	Difference between groups (p value)
❖ **Health-related factors**				
NSCLC, n (%)	110	33 (41%)	47 (59%)	0.35
COPD or ILD, n (%)	91	58 (48%)	63 (52%)	
Stage III, n (%)	80 (40%)	53 (44%)	27 (34%)	0.14
Stage IV, n (%)	121 (60%)	68 (66%)	53 (66%)	
Charlson comorbidity Index score, median [IQR]	7 [3-10]	6 [3-10]	7 [4-10]	0.38
❖ **Body Functions and Structures**				
Australian Karnofsky Performance Status (AKPS), median [IQR]	70 [60-80]	70 [60-80]	60 [55-80]	**0.002**
Symptom severity (Palliative care Outcome Scale-symptoms), median [IQR]	10 [5.5-15]	9 [4-14]	11 [7-16]	**0.01**
Receiving cancer treatment, n (%)	100 (50%)	60 (49.6%)	40 (50.6%)	0.1
On oxygen therapy, n (%)	40 (20%)	24 (19.8%)	16 (20.3%)	0.1
❖ **Activity and participation**				
Total Barthel Index score (BADLs), median [IQR]	19 [17-20]	20 [17-20]	19 [16.5-20]	0.15
Lawton Brody Instrumental ADL score (IADLs), median [IQR]	7 [5-8]	7 [5-8]	6 [4-7]	**0.001**
WHODAS Summary score, median [IQR]	57 [46-79]	52 [43-70]	71 [51-86]	**0.0001**
Cognition, median [IQR]	7 [6-10]	7 [6-9	8 [6-14]	**0.0003**
Mobility, median [IQR]	13 [7-17]	11 [7-15]	14.5 [10.5-19]	**0.0005**
Self-Care, median [IQR]	5 [4-9]	4 [4-8]	7 [4-9.5]	**0.009**
Getting along with people, median [IQR]	9 [5-11]	7.[5-10]	9 [6-13]	**0.01**
Household activities, median [IQR]	9 [4-13]	7 [4-12]	11.5 [8-17]	**0.0001**
Societal participation, median [IQR]	17 [12-21]	15 [11-20]	19 [14-22]	**0.002**
❖ **Personal factors**				
Age, median [IQR]	69 [63-75]	70 [64-76]	69 [61-75]	0.21
Female, n (%)	91 (45%)	53 (43.8%)	38 (47.5%)	0.61
White British, n (%)	191 (95%)	116 (96%)	75 (94%)	0.5
Education above secondary school, n (%)	93 (46%)	63 (52%)	29 (36.3%)	0.03
CDSE: Confidence to receive help, median [IQR]	2 [1.5-3]	2.5 [1.5-3]	2 [1-3]	0.25
❖ **Environmental factors**				
Lives alone, n (%)	68 (34%)	37 (30.6%)	31 (38.8%)	0.23
Inpatient/residential care, n (%)	4 (2%)	1 (1%)	3 (4%)	0.15
Property with stairs, n (%)	144 (72%)	88 (73%)	56 (70%)	0.68
Formal caregiver, n (%)	29 (14%)	13 (11%)	16 (20%)	0.07
Informal caregiver, n (%)	112 (56%)	65 (53.7%)	47 (59.5%)	0.51
Physiotherapy input within the last month, n (%)	20 (10%)	8 (7%)	12 (15%)	0.09
Occupational therapy input within the last month, n (%)	10 (5%)	4 (3.3%)	6 (7.5%	0.32
Received GOV letter to physically and socially isolate, n (%)	174 (87%)	107 (88.4)	67 (83.8%)	0.34
Currently physically and socially isolating, n (%)	143 (71%)	85 (70.25%)	58 (72.5%)	0.73
Have spent time in physical and social isolation, n (%)	194 (97%)	117 (96.7%)	78 (97.5%)	0.74
Months spent in physical and social isolation, median [IQR]	5 [3-8]	4.5 [3-8]	5 [3-8]	0.76
Hospital admission in the last month, n (%)	27 (13.5%)	14 (11.7%)	13 (16.3%)	0.47
Accident & Emergency (A&E) visit in the last month, n (%)	7 (3.5%)	1 (1%)	6 (7.5%)	**0.01**
Hospice patient, n (%)	48 (23.9%)	24 (19.8%)	24 (30%)	0.1
Total use of ADL devices, median [IQR]	1 [0-4]	1 [0-3.5]	2 [0-4]	**0.009**
Reduced physical activity inside the home, n (%)	94 (47%)	49 (41%)	45 (57%)	0.03
Reduced physical activity outside the home, n (%)	129 (65%)	77 (64%)	52 (66%)	0.73

NSCLC: non-small-cell lung cancer; COPD: chronic obstructive pulmonary disease; ILD: Interstitial lung disease; ADL: activities of daily living; BADL: Basic activities of daily living; IADL: instrumental activities of daily living; WHODAS: World Health Organization disability assessment Schedule; CDSE: Chronic Disease Self-Efficacy subscale; GOV: government; Reduced physical activity includes responses of 'little less' or a 'lot less'; IQR: inner quartile range; Statistical comparisons between the two groups was conducted using the Mann Whitney-U test for continuous variable and the Chi square test for categorical variables.; the significance level is set at p≤0.01.

Only four participants were in hospital or residential care at the time of recruitment, but 48 (23.9%) were under the care of a hospice in the community. In the last month, 27 (13.5%) participants had been admitted to hospital, 7 (3.5%) had visited an accident and emergency department (A&E), 20 (10%) had received physiotherapy, and 10 (5%) had received occupational therapy. The median [IQR] number of ADLs that required use of assistive devices was 1 [0-4].

7.4.2. Differences between participants who withdrew or were lost to follow-up and participants who completed 6-month follow-up

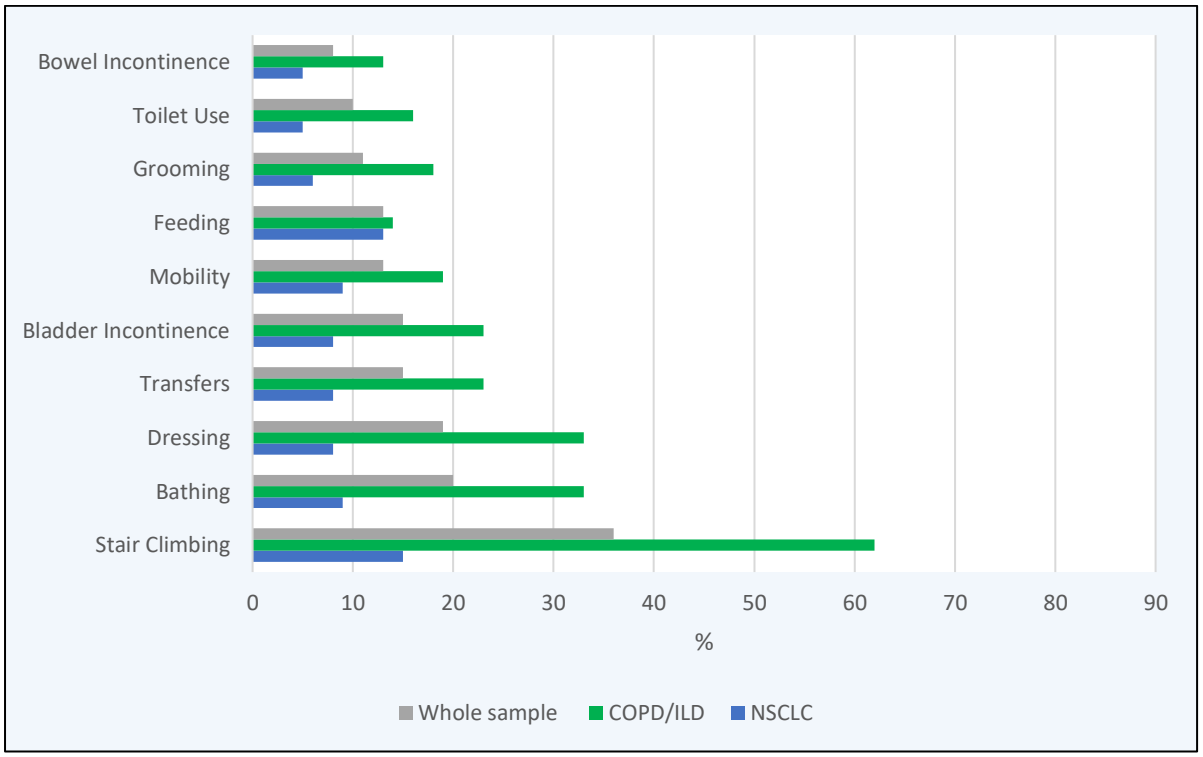
Participants who withdrew from the study at any timepoint or were lost to follow-up were significantly more disabled in instrumental ADLs at baseline (p=0.001), had greater difficulty in managing daily activities (p=0.0001) across all domains (cognition (p=0.0003), mobility (p=0.0005), self-care (p=0.009), getting along with people (p=0.001), household activities (p=0.0001), and societal participation (p=0.002)), had lower AKPS (p=0.002), and greater symptom severity (p=0.01). They were also less likely to have visited A&E in the last month (p=0.01) and used assistive devices for a greater number of ADLs (p=0.009). This finding reflects selective attrition where less healthy participants at the time of recruitment were more likely to not complete longitudinal follow-up. Statistical differences between participants with NSCLC and COPD or ILD are presented in the cross-sectional analysis in the following section, 7.5.

7.4.3. Prevalence of disability in basic and instrumental ADLs

Overall, recruited participants reported mild disability (median [IQR]) in basic (19 [17-20]), and instrumental ADLs (7 [5-8]). Some participants had difficulty managing daily activities (57 [46-79]) across all domains (cognition (7 [6-10]), mobility (13 [7-17]), self-care (5 [4-9]), getting along with people (9 [5-11]), household activities (9 [4-13]), and societal participation (17 [12-21])). On categorization of disability severity, in all participants, 104 (52%) participants had mild to very severe disability in basic ADLs, and 142 (71%) participants had mild to very severe disability in instrumental ADLs (Appendix I). The most prevalent disability in basic ADL items (figure 7.4a) were stair climbing (n=47, 31%), bathing (n=28, 19%), and dressing (n=26, 17%). The most prevalent disabilities in instrumental ADL items (figure 7.4b) were shopping (n=92, 61%), food preparation (n=53, 35%), and transportation (n=37, 27%). Participants with COPD or ILD were more disabled in nearly all individual ADLs compared to participants with NSCLC.

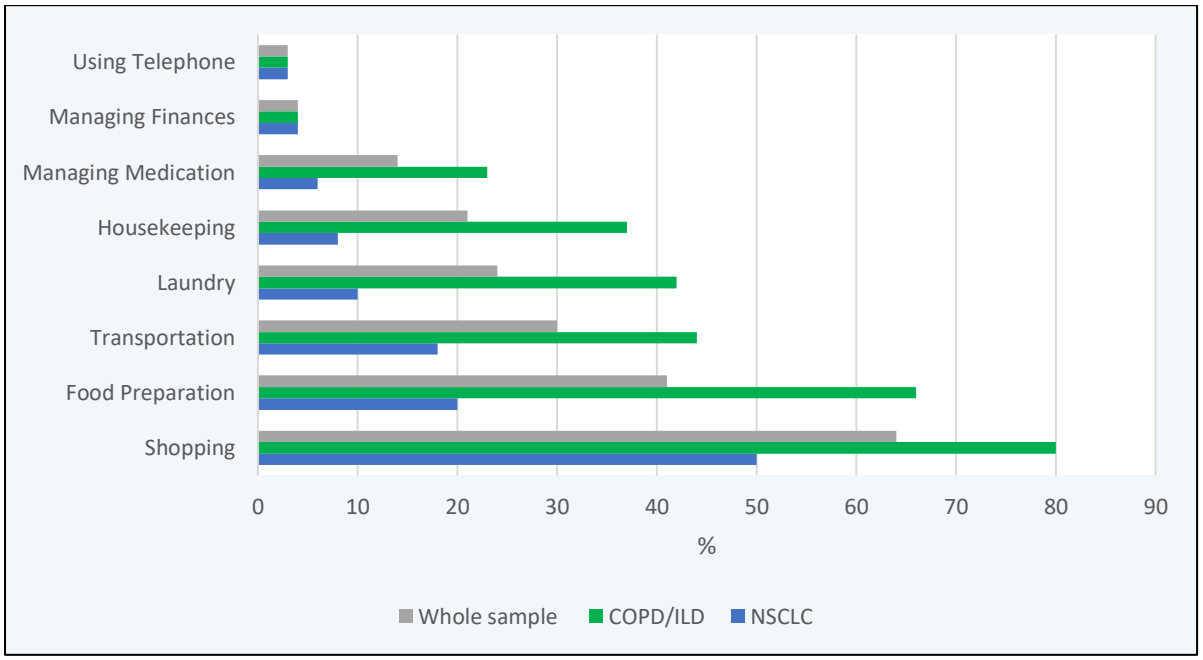
Figure 7.4. Prevalence of disability in individual ADLs

7.4a. Prevalence of disability in individual basic ADLs



Basic activities of daily living measured using the Barthel Index; NSCLC: Non-small cell lung cancer; COPD: Chronic Obstructive Pulmonary Disease; ILD: Interstitial Lung Disease

7.4b. Prevalence of disability in individual instrumental ADLs



Instrumental activities of daily living measured using the Lawton Brody ADL: activities of daily living; ADL Scale; NSCLC: Non-small cell lung cancer; COPD: Chronic Obstructive Pulmonary Disease; ILD: Interstitial Lung Disease

7.5. Incorporated publication 3: cohort study - cross-sectional analysis

COVID-19 and Chronic Respiratory Disease

Chronic Respiratory Disease

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Relationships between prolonged physical and social isolation during the COVID-19 pandemic, reduced physical activity and disability in activities of daily living among people with advanced respiratory disease

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Abstract

In people with advanced respiratory disease, we examined (i) the impact of COVID-19–related physical and social isolation on physical activity and (ii) relationships between time spent in isolation and disability in activities of daily living. Cross-sectional analysis was conducted in adults with advanced non-small cell lung cancer, chronic obstructive lung disease or interstitial lung disease. Measures included change in physical activity since physically and socially isolating (Likert scale) and disability (Barthel Index and Lawton–Brody IADL scale) or difficulty (World Health Organisation Disability Assessment Schedule-2.0) in daily activities. Multiple logistic regression was used to examine factors associated with disability in daily activities. 194/201 participants were isolating for a median [IQR] 5 [3–8]-month period, often leading to lower levels of physical activity at home (n = 94, 47%), and outside home (n = 129, 65%). 104 (52%) and 142 (71%) were not fully independent in basic and instrumental activities of daily living, respectively. 96% reported some degree of difficulty in undertaking daily activities. Prolonged physical and social isolation related to increased disability in basic ($r = -0.28$, $p < 0.001$) and instrumental ($r = -0.24$, $p < 0.001$) activities of daily living, and greater difficulty in daily activities ($r = 0.22$, $p = 0.002$). Each month spent in physical or social isolation was independently related to disability in basic activities of daily living (odds ratio [OR], 1.17 [95% CI: 1.03–1.33], p = 0.013). These findings suggest disability in daily activities is associated with prolonged physical or social isolation, which may present as difficulty in people who are fully independent. Post-isolation recovery and rehabilitation needs should be considered for all people deemed extremely clinically vulnerable.

Keywords

Activities of daily living, COVID-19, disability, rehabilitation, respiratory disease, social isolation

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Introduction

Coronavirus (COVID-19) was declared a global pandemic by the World Health Organization on 11th March 2020.[1] About one in five individuals worldwide are considered at increased risk of severe COVID-19 infection due to underlying health conditions including respiratory disease, encouraging countries to put policies in place to protect those at increased risk.[2] In the United Kingdom, as part of

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government policy, individuals fulfilling these high-risk criteria were classed as 'extremely clinically vulnerable' and physical and social isolation (shielding) was advised.[3] This included many of the estimated 85,000 people living with lung cancer, 1.2 million people living with chronic obstructive pulmonary disease (COPD) and 32,500 people living with interstitial lung disease (ILD).[4] The Global Burden of Disease Study reports non-malignant and malignant respiratory disease to be the third and fourth leading cause of death and productive life lost due to disability in the United Kingdom in 2019, respectively, which is higher than any other country with similar health system performance.[5] Therefore, protecting this population from the severe risk of COVID-19 and preventing disability is a particular concern in the United Kingdom.

Physical and social isolation refers to a lack of contact with society[6] and has been found to decrease physical activity and increase sedentary behaviour.[7] Physical and social isolation adversely affects psychosocial and mental health functioning[8] and results in functional impairments[6] and deconditioning.[9] In people with advanced respiratory disease, it is currently unclear how prolonged physical and social isolation may impact disability, and health- and social-care services post-pandemic, whether or not they contract the virus.[10]

Furthermore, COVID-19 guidance has caused disruption to treatment or disease management delivery, including reduced access to cancer therapies and rehabilitation.[11] On the other hand, there has been a significant reduction in exacerbations and improvement in symptoms in COPD patients, possibly relating to less exposure to respiratory viruses, and/or a strict adherence to physical and social isolation.[12] However, there was also a reluctance to seek medical attention during the pandemic by individuals considering themselves clinically vulnerable.[13]

The World Health Organization (WHO) defines disability as 'any condition of the body or mind (impairment) that makes it more difficult for the person with the condition to do certain activities (activity limitation) and interact with the world around them (participation restrictions)'.[14] This is characterised by a complex relationship between an individual's health condition, the environment in which they live and personal attributes.[14] Activities of daily living (ADLs) describe a collection of skills required to live independently.[15] Activities of daily livings can be classified as basic (e.g. feeding, dressing and continence) or instrumental (e.g. shopping, housework and transportation).[15] Activities of daily living disability can be considered in terms of ADL dependency; a reliance on others, or ADL difficulty, which describes an increased difficulty to manage ADLs independently. Both have been linked to poorer clinical outcomes and quality of life.[16]

This study aimed to (i) describe the impact of physical and social isolation on an individual's level of physical activity; (ii) examine the relationship between time spent in physical and social isolation, disability in basic and instrumental ADLs and difficulty managing daily activities; and (iii) examine factors associated with disability in ADLs in people with advanced respiratory disease during the COVID-19 pandemic.

Methods

Study design

We report baseline data of a prospective cohort study, following the STROBE guidelines.[17] The study was registered on the ISRCTN registry (ISRCTN14159936), and ethical approval was granted by the London Camberwell St Giles Research Ethics Committee (ref 19/LO/1950).

Recruitment setting

We recruited from 12 sites across England from July 2020 to January 2021, including eight acute NHS trusts, three hospices and the British Lung Foundation. Recruitment settings included hospital medical, respiratory or oncology wards; outpatient lung cancer or respiratory clinics; and hospice/palliative care inpatient, outpatient and community services. The study was advertised through the British Lung Foundation members' forum.

Eligibility criteria

Inclusion criteria were adults with a diagnosis of either (i) inoperable stage III or IV non-small cell lung cancer; (ii) severe or very severe COPD, defined by $FEV_1 < 50\%$ predicted[18]; or (iii) advanced ILD, defined by carbon monoxide transfer factor (TLCO/DLCO) level of < 40% or FVC < 50% predicted.[19] Patients were excluded if they lacked capacity to consent, were unable to complete the survey in English or had a clinician-estimated life expectancy of less than 1 month.

Recruitment strategy

Eligible patients were identified from their medical notes and approached by a member of their clinical team at a routine face-to-face or telephone consultation. Verbal consent was taken for the research team to contact them about the study. Alternatively, members of the British Lung Foundation could self-refer directly to the researcher. Study information was posted to the participant and followed a week later by a telephone call to take informed verbal consent and complete the baseline questionnaire if they agreed to participate.

Variables and measures

Demographic data and participant characteristics were collected, including diagnosis, age, gender, ethnicity, education level, living status and location, carer support, Charlson Co-morbidity Index score,[20] Australian Karnofsky Performance Status[21], and symptom severity (Palliative Outcomes Scale-symptoms),[22] along with the following patient-reported variables of interest.

Time spent in physical and social isolation (in months): This was collected by asking participants whether they are, or/and have been physically or socially isolating and how long for, including dates of isolation period based on dated government letters.

Change in physical activity since physically or socially isolating: This was *measured* using a 5-point Likert scale: a lot less, a little less, no change, a little more or a lot more in (i) physical activity inside the home and (ii) physical activity outside the home. The Likert scale is one of the most fundamental and frequently used psychometric tools for scaling responses in survey research where response to change is common.[23,24]

Disability in carrying out basic ADLs: This was measured using the Barthel Index, consisting of 10 items (bowel incontinence, toilet use, grooming, feeding, mobility, bladder incontinence, dressing, bathing, stairs, and transfers).[25] Domains are scored according to the level of physical assistance required to perform the daily task with individual scores varying between 0–1, 0–2 and 0–3, depending on the number of options per item. A combined total score of all 10 items ranges from 0 to 20. A score of zero corresponds to full ADL dependence, whilst 20 reflects full independence.[25] A change of 1.85 in stroke and 3.6 in older people indicates a minimal clinically important difference (MCID) in patient reported Barthel Index score.[26]

Disability in carrying out instrumental ADLs: This was measured using the Lawton–Brody IADL scale, an 8-item categorical measure (ability to use the telephone, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility for own medication and ability to manage finances).[27] Each item has a range of three to five responses ranging from fully independent to fully dependent. Each response is scored one if independent or 0 for anything other than independent. A summary score ranges from 0 (low function, dependent) to 8 (high function, independent); a lower score indicates greater disability.[27] The MCID for the Lawton–Brody IADL scale lies around half a point.[28]

Difficulty in managing daily activities: This was measured using the World Health Organisation Disability Assessment Schedule (WHODAS-2.0).[29] The WHODAS-2.0 measures disability in terms of difficulty managing ADLs independently, as opposed to the Barthel Index and Lawton–Brody IADL scale which measure disability in terms of dependency on others. This index consists of six domains (cognition, mobility, self-care, getting along with people, life activities and societal participation). Life activities consist of two sections: household activities and work activities; the latter is optional to include and was therefore excluded from this analysis. All items are scored on a scale of activity difficulty ranging from 1 to 5: none [1], mild [2], moderate [3], severe [4] and extreme or cannot do [5]. The cognition domain is made up of six items; mobility and getting along with people, each have five items; self-care and household activities, each have four items; and societal participation has seven items. Domain scores were totalled to produce a WHODAS summary score, where 32 reflects no difficulty and 160 extremely difficult (excluding the work domain).[29] A WHODAS summary score of 32 = no difficulty, 33–64 = mild difficulty, 65–96 = moderate difficulty, 97–128 = severe difficulty and 129–160 = extreme difficulty or cannot do.[29] The WHODAS-2.0 is the current leading measure of disability worldwide; however, a MCID for the WHODAS-2.0 has not yet been established.[30]

Sample size

A sample size of 200 is sufficient to achieve a precision of at least 8% in the estimation of prevalence of ADL disability, based on assumed prevalence to be around 50%.[31,32] This sample size would also be sufficient to detect a significant correlation of ≥ 0.20.[33]

Data analysis

Participant characteristics and change in physical activity during physical and social isolation were summarised using descriptive statistics. Diagnosis was split into two groups: malignant (lung cancer) or non-malignant (COPD or ILD). Participants with both a malignant and non-malignant diagnosis were classified in the malignant group. The Mann–Whitney U-test was used to compare the two diagnostic groups and differences between those who did and did not receive a government (GOV) letter of request to physically and socially isolate.

Univariate associations between (i) months spent physically and socially isolating, (ii) Barthel Index total score, (iii) Lawton–Brody IADL Scale total score and (iv) WHODAS-2.0 summary score were calculated using the Spearman's rho test. Disability in basic ADLs and instrumental ADLs were each split into two groups: (i) fully independent (Barthel Index = 20/Lawton–Brody = 8) and (ii) disability (Barthel Index < 20/Lawton–Brody < 8). Difficulty in managing ADLs measured by the WHODAS

summary score was defined by level of disability (fully independent/disabled) in basic and instrumental ADLs separately.

Our primary dependent variable in logistic regression analysis was (a) whether the participant had disability in basic ADLs (Barthel Index < 20) or was fully independent (Barthel Index = 20) and (b) whether the participant had disability in instrumental ADLs (Lawton–Brody IADL Scale < 8) or was fully independent (Lawton Brody IADL Scale = 8). Explanatory variables considered for the model were based on a recent systematic review[34] and included diagnosis, time spent physically and socially isolating, age, gender, living status and symptom severity. The model included complete cases only.

Results

201 participants were recruited, 110 (55%) with malignant respiratory disease and 91 (45%) with non-malignant (72 (36%) COPD and 19 (9%) ILD), respectively. The study flow and participant characteristics are presented in Figure 1 and Table 1. Data were missing on physical and social isolation and disability in daily activities (WHODAS-2.0) for one participant each. For all participants, the median [IQR] disability in independence in basic ADLs, instrumental ADLs and difficulty in daily activities was 19 [17–20], 7 [3–10] and 57 [46–79], respectively, illustrating overall mild disability (Table 1).

Participants with non-malignant respiratory disease had significantly greater dependency in basic ADLs, instrumental ADLs and increased difficulty in daily living (all $p < 0.001$), compared with participants with malignant respiratory disease. They were also significantly older, had a lower functional performance status and higher symptom severity.

During the first wave of the COVID-19 pandemic, 174 (87%) participants received a letter of request from the government to physically and socially isolate, which was not significantly different between those with malignant or non-malignant respiratory disease ($p = 0.14$). Differences between participants who did and did not receive this letter are presented in Supplementary Table 1. We found those who received the letter were more symptomatic ($p = 0.003$), more likely to physically and socially isolate ($p < 0.001$) and reduce their participation in society ($p = 0.002$) than those who did not receive the letter.

Almost all participants (194/97%) had spent time physically and social isolating for a median [IQR] period of 5 [3–8] months at the time of assessment. During physical and social isolation, 94 (47%) participants were less physically active at home (Figure 2(a)). Physical activity outside the home was lower in 129 (65%) participants (Figure 2(b)). Patients with non-malignant respiratory disease were significantly less physically active than patients with malignant respiratory disease, inside ($p = 0.02$) and outside ($p = 0.004$) the home.

97 (48%) participants were fully independent in basic ADLs, and 59 (29%) were fully independent in instrumental ADLs. 197 (96%) participants had difficulty managing daily activities (median [IQR]) including those fully independent in basic ADLs (48 [39–57]) or instrumental ADLs (43 [37–54]) (Figure 3). Only 10% and 5% of participants received physiotherapy or occupational therapy interventions, respectively, within the last month.

A longer time in physical or social isolation was weakly associated with increased disability (lower Barthel Index or

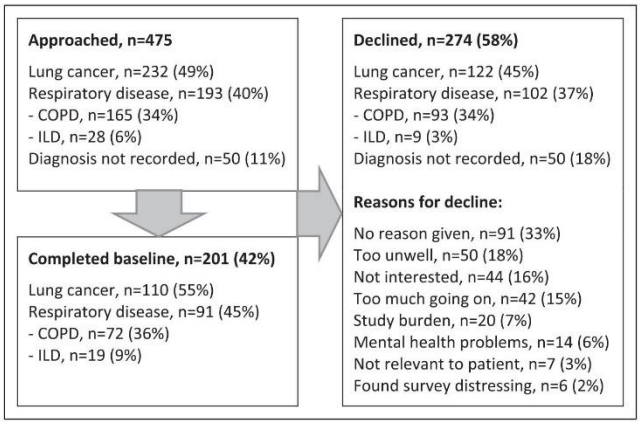

Figure 1. Study flow diagram.

Table 1. Participant characteristics.

	All diagnoses n = 201	Malignant respiratory disease, n = 110 (55%)	Non-malignant respiratory disease, n = 91 (45%)	Difference between groups (p value)
Age	69 [63–75]	68 [61–72]	72 [66–77]	< 0.001
Female	91 (45%)	51 (46%)	40 (44%)	0.73
White British	191 (95%)	105 (95%)	86 (95%)	0.76
Education above secondary school	93 (46%)	52 (48%)	41 (45%)	0.85
Lives alone	68 (34%)	36 (33%)	32 (35%)	0.72
Inpatient/residential care	4 (2%)	0	4 (2%)	0.03
Formal caregiver	29 (14%)	11 (10%)	18 (20%)	0.05
Informal caregiver	112 (56%)	54 (50%)	58 (64%)	0.05
Physiotherapy input within the last month	20 (10%)	6 (5%)	14 (16%)	0.02
Occupational therapy input within the last month	10 (5%)	3 (3%)	7 (8%)	0.10
Charlson Co-morbidity Index score	7 [3–10]	9 [7–13]	3 [2–5]	< 0.001
Australian Karnofsky Performance Status	70 [60–80]	80 [60–90]	60 [60–70]	< 0.001
Received GOV letter to physically and socially isolate	174 (87%)	91 (84%)	83 (91%)	0.14
Currently physically and socially isolating	143 (71%)	72 (65%)	71 (78%)	0.05
Have spent time in physical and social isolation	194 (97%)	104 (95%)	90 (99%)	0.15
Months spent in physical and social isolation	5 [3–8]	4 [3–6]	6.5 [4–9]	< 0.001
Total Barthel Index score (basic ADLs)	19 [17–20]	20 [19–20]	18 [15–19]	< 0.001
Lawton–Brody IADL score (instrumental ADLs)	7 [5–8]	7 [6–8]	5 [4–7]	< 0.001
WHODAS summary score	57 [46–79]	49 [40–62]	73 [57–87]	< 0.001
Cognition	7 [6–10]	6 [6–8]	8 [6–12]	< 0.001
Mobility	13 [7–17]	9 [6–13]	17 [13–19]	< 0.001
Self-Care	5 [4–9]	4 [4–5]	6 [5–11]	< 0.001
Getting along with people	9 [4–13]	7 [5–9]	10 [8–13]	< 0.001
Household activities	9 [4–13]	6 [4–10]	12 [9–18]	< 0.001
Societal participation	17 [12–21]	15 [11–20]	19 [14–22]	< 0.001
Symptom severity (Palliative Outcomes Scale-symptoms)	10 [5.5–15]	7 [4–13]	11.6 [8–18]	< 0.001

ADLs: Activities of daily livings; WHODAS: World Health Organisation Disability Assessment Schedule; GOV: Government.
Values are n (%) or [median, IQR]; Missing data: physical and social isolation, n = 1, WHODAS-2.0, n = 1.

Lawton–Brody total score) in basic (r = −0.28, $p < 0.001$) and instrumental ADLs (r = −0.24, $p < 0.001$), and greater difficulty (higher WHODAS summary score) in daily activities (r = 0.22, $p = 0.002$) (Figure 4). Moderate relationships were found between less independence in basic ADLs, less independence in instrumental ADLs and greater difficulty in daily activities.

The multivariable analysis (Table 2) showed that disability in basic ADLs was related to prolonged physical and social isolation (odds ratio [OR], 1.17 [95% CI: 1.03–1.33], $p = 0.01$), non-malignant respiratory disease (odds ratio [OR], 4.00 [95% CI: 1.20–8.14], $p < 0.001$) and increased symptom severity (odds ratio [OR], 1.12 [95% CI: 1.06–1.19], $p < 0.001$). Disability in instrumental ADLs was related to non-malignant respiratory disease (odds ratio [OR], 3.6 [95% CI: 1.41–7.10], $p = 0.005$) and increased symptom severity (odds ratio [OR], 1.14 [95% CI: 1.07–1.22], $p < 0.001$). Both models were adjusted for months spent in physical and social isolation, diagnosis, age, gender, living status and symptom severity.

Discussion

Main findings

In our cross-sectional analysis of 201 participants with advanced respiratory disease, physical and social isolation was highly prevalent. We report several main findings. Firstly, physical and social isolation has resulted in lower levels of physical activity. Secondly, disability in activities of daily living is common in advanced respiratory disease and even those who are fully independent in ADLs have difficulty managing daily activities independently. Finally, disability in basic activities of daily living independently relates to increased time spent in physical or social isolation, and both basic and instrumental activities

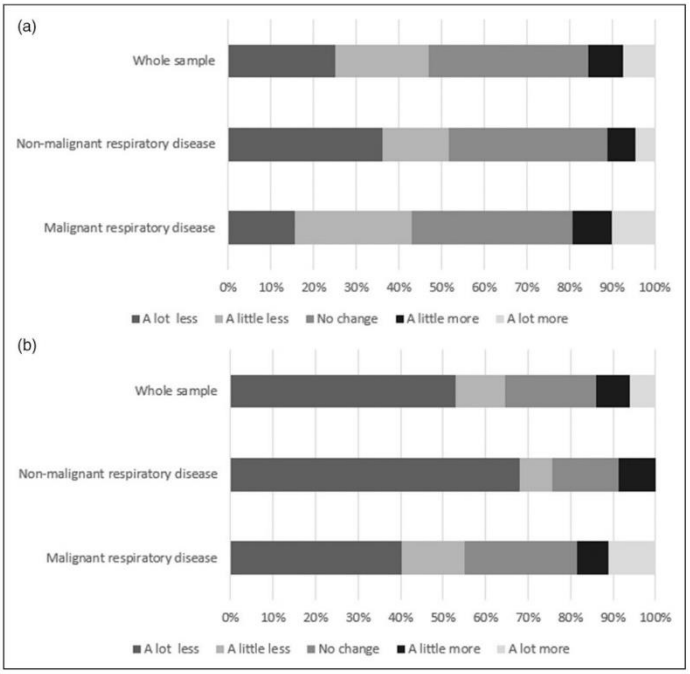

Figure 2. Change in physical activity during physical and social isolation. (a) Change in physical activity inside the home; (b) Change in physical activity outside the home

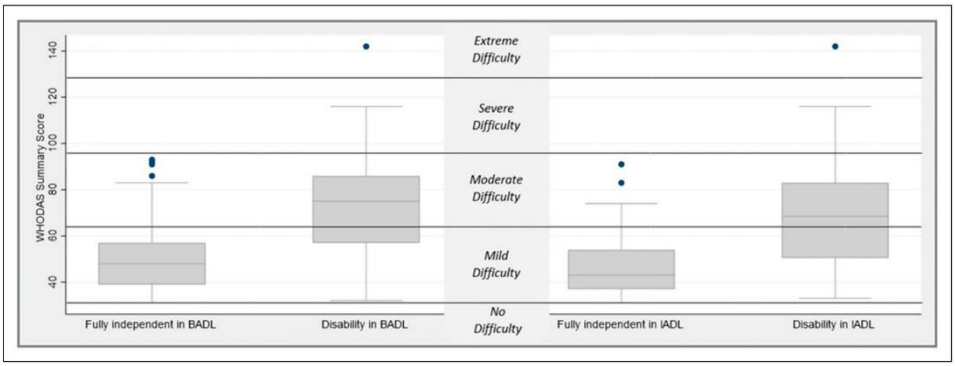

Figure 3. Difficulty in daily activities (WHODAS summary score (median [IQR])) in patients with advanced respiratory disease who have full independence or disability in basic (BADL) and instrumental (IADL) activities of daily living. WHODAS: World Health Organisation Disability Assessment Schedule.

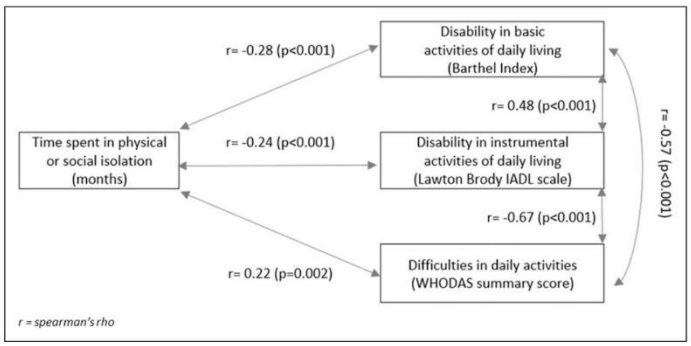

Figure 4. Univariate associations between time spent in physical or social isolation, disability in basic activities of daily living, disability in instrumental ctivities of daily living, and difficulties in daily activities.

Table 2. Adjusted associations with disability in activities of daily living using multivariable logistic regression.

a) Disability in basic activities of daily living (n = 199)	Odds ratio [OR]	[95% conf. Interval]		p value
Months spent in physical and social isolation	1.17	1.03	1.33	0.01
Non-malignant respiratory disease (COPD or ILD)	4.00	1.20	8.14	< 0.001
Symptom severity (Palliative Outcomes Scale-symptoms)	1.12	1.06	1.19	< 0.001
Age	1.02	0.98	1.06	0.32
Female	1.48	0.74	2.96	0.26
Live alone	1.70	0.82	3.52	0.15
_Cons	0.01	0.0006	0.25	0.004
b) Disability in instrumental activities of daily living (n = 200)	Odds ratio [OR]	[95% conf. Interval]		p value
Months spent in physical and social isolation	1.19	0.59	2.41	0.63
Non-malignant respiratory disease (COPD or ILD)	3.16	1.41	7.10	0.005
Symptom severity (Palliative Outcomes Scale-symptoms)	1.14	1.07	1.22	< 0.001
Age	1.03	0.99	1.07	0.21
Female	1.19	0.59	2.41	0.63
Live alone	0.68	0.33	1.41	0.30
_Cons	0.08	0.004	1.35	0.08

COPD: chronic obstructive pulmonary disease; ILD: interstitial lung disease.
Reference group (a) is disability in basic activities of daily living (Barthel Index < 20); Reference group (b) is disability in instrumental activities of daily living (Lawton–Brody IADL Scale < 8); All variables in this table have been dichotomised, except months spent in physical and social isolation, symptom burden and age, which were treated as continuous variables.

of daily living independently relate to non-malignant respiratory disease and increased symptom severity.

Contributions to the literature

Our findings contribute to the literature in several ways. Firstly, we identified that nearly all participants with advanced respiratory disease spent time in physical and social isolation due to the pandemic, resulting in a reduction in their usual physical activity. This corroborates a small cohort study of 10 COPD patients who had a significant reduction in their level of physical activity during the first 3 months of the pandemic while under instructions to physically and socially isolate following a course of pulmonary rehabilitation.[35] Furthermore, we found the impact on reduced activity in non-malignant respiratory disease was significantly greater than malignant respiratory disease. However, even pre-pandemic, over time, physical activity in COPD has been shown to follow a downwards trajectory and exacerbated by sedentary behaviour.[36] In older patients with advanced cancer, perceptions of physical activity are positive, and periods of reduced activity usually occur during cancer treatment.[37]

Secondly, we identified people who may be indirectly affected by the pandemic. People who spend longer in physical and social isolation experience greater disability in basic ADLs. Also, those with disability in basic and instrumental ADLs have a higher symptom severity and/or a non-malignant respiratory diagnosis. This may arise from feelings of vulnerability from COVID-19[13] where reduced confidence to participate in normal daily activities leads to deconditioning and functional impairment.[6,9] Symptoms restricting disability are common in advanced disease,[38] and higher symptom severity is associated with a housebound status, significantly limiting a persons' ability to carry out activities involving socialising and participating in the community.[39] This highlights the contribution of health, environmental and personal factors in the development of disability.[14]

Thirdly, we found that despite some participants being fully independent in activities of daily living they often experienced 'difficulty' in managing their daily activities independently. Participants in our study may be struggling independently due to lack of or reluctance to accept help due to restrictions on social contact, particularly if living alone. This may be missed by only measuring dependency. It is also plausible that difficulty pre-empts disability, therefore recognising and addressing difficulty in daily activities may help to maintain independence and prevent dependency. Helping people to continue to live independently at home as their condition progresses could potentially reduce or delay the need for social care. This is supported by the Health and Retirement Study that identified nursing home placements could be strongly predicted by difficulty bathing.[40]

Clinical implications

It is important to recognise the effect limited access to rehabilitation may have had on disability in daily activities in advanced respiratory disease. During the pandemic, rehabilitation is reported to have been the most disrupted health service, often being deemed non-essential.[11] This is reflected in our findings where less than a fifth of participants received physiotherapy or occupational therapy interventions despite most participants reporting difficulty in managing daily activities independently. Online delivery has been found to be acceptable during this time,[41,42] but there are access challenges for patients who have limited knowledge or availability to these resources.[43]

In addition, social support provision is likely to have been impacted by COVID-19 guidelines. This included difficulty getting the necessary basics such as food, difficulty accessing healthcare services for support and feelings of loneliness.[44] Social support can be considered a protective psychological factor against a decline in mental and physical health–related quality of life.[45] Two cohort studies have identified that poorer satisfaction with social support is associated with greater difficulties in instrumental activities of daily living in people with chronic conditions, where the quality of social support was identified to be of greater importance than the quantity.[46] Among COPD patients, low support levels have been associated with depression and physical symptom deterioration.[47] Positively, physical and social isolation may reduce hospitalisation due to reduction in exacerbations in COPD patients.[12] However, patients with cancer may have suffered delays in treatment and less access to support due to restrictions on visitors, which may accelerate decline.[48]

Consequently, physical and social isolation and reduced rehabilitation threatens a post–COVID-19 wave of disability in people with advanced respiratory disease. Addressing disability is important as it is known to lead to increased hospital stay and discharge to a care facility,[49] putting increased strain on already stretched health- and social-care services. Moving forward, health- and social-care services need to consider post–COVID-19 recovery and rehabilitation for all people deemed extremely clinically vulnerable.[50] To help identify need, we recommend consideration is given to the following individual risk factors: (i) length of time spent in physical and social isolation, (ii) presenting difficulty and not only disability in daily activities, (iii) symptom severity and (iv) level of social support, with a heightened awareness in non-malignant respiratory disease. Further, we propose strategies are considered to (i) minimise time spent in isolation, (ii) maintain physical activity, (iii) continue rehabilitation services or/and offer online alternatives, and (iv) increase social support. More research is required to ensure their success.

Study strengths and limitations

We recruited a large sample of patients with advanced respiratory disease across multiple sites to increase generalisability of the findings. We report baseline data only, identifying associations and not causative relationships. Potential bias includes varying time of individual data collection, fluctuating COVID-19 guidelines over the recruitment time period, use of subjective measures over objective measurement and response or recall from self-reported measures. In addition, instrumental ADLs were compromised by the context of COVID-19 lockdown restrictions themselves and therefore this regression analysis should be interpreted with caution. Analysis of the longitudinal data from the ongoing cohort study will add a valuable understanding of the impact of physical and social isolation on disability over time.

Conclusion

Evidence from this study suggests that disability is associated with prolonged physical or social isolation. This implies this population with advanced respiratory disease is deconditioning as an indirect result of the pandemic. Consideration needs to be given to post–COVID-19 recovery and rehabilitation for all people deemed extremely clinically vulnerable. Strategies to better handle the rehabilitation needs of those in physical and social isolation in light of future pandemics need to be prepared.

Supplemental material

Supplemental material for this article is available online.

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Supplemental material

Supplemental material for this article is available online.

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Supplementary Table 1: Differences between participants who did and did not receive a Government (GOV) letter of request to physically and socially isolate.

	Received GOV Letter	Did not receive GOV letter	Difference between groups (p value)
Age	69 [63-77]	69 [65-77]	0.77
Female	80 (46%)	11 (44%)	0.85
White British	164 (94%)	25 (100%)	0.22
Education above secondary school	77 (44%)	13 (52%)	0.47
Lives alone	58 (33%)	10 (40%)	0.66
Inpatient/residential care	4 (100%)	0	0.44
Formal caregiver	28 (16%)	1 (4%)	0.11
Informal caregiver	100 (58%)	12 (48%)	0.36
Charlson comorbidity Index score	7 [3-10]	1 [6-12]	0.24
Australian Karnofsky Performance Status	70 [60-80]	80 [60-90]	0.08
Currently physically and socially isolating	127 (73%)	15 (60%)	0.18
Have spent time in physical and social isolation	173 (99%)	20 (80%)	<0.001
Months spent in physical and social isolation	5 [3.5-8]	3.5 [0-7]	0.02
Total Barthel Index score (basic ADLs)	19 [17-20]	20 [18-20]	0.14
Lawton Brody IADL score (instrumental ADLs)	6 [5-8]	7 [6-8]	0.06
WHODAS Summary score	60 [47-81]	46.5 [40-56.5]	0.002
Symptom severity (Palliative Outcomes Scale-symptoms)	10 [6-16]	6 [4-9]	0.003

7.6. Summary

This prospective cohort study was successful in recruiting 110 patients with advanced NSCLC, and 91 patients with advanced COPD or ILD from across twelve participating sites throughout England. Sixty percent of study participants completed 6-month follow-up. Although a greater number of participants with NSCLC were recruited than participants with COPD or ILD, attrition was also slightly greater in the NSCLC group. Missing data were anticipated in this study due to advanced disease, which resulted from attrition due to death or illness in patients who withdrew or were lost to follow-up. Intermittent missing data occurred in participants who completed the study but selectively missed a follow-up timepoint. Missing items were relatively low and highest in items that participants either felt uncomfortable answering or appeared unable to answer due to the impact of Covid-19 restrictions and physical and social isolation. Participants who withdrew, were lost to follow-up, or completed less study timepoints, had poorer clinical outcomes at baseline than participants who remained in the study. Almost half of withdrawn participants died, suggesting selective attrition. Therefore, missing data occurred not at random. This requires careful consideration in interpretation of the findings.

At baseline, disability was highly prevalent and affected over 50% of the study population. Overall, participants presented with mild disability in basic and instrumental ADLs. Most participants with respiratory disease presented with disability. The prevalence of disability in basic ADLs was in keeping with findings from the secondary data analysis (chapter 6), where the most affected basic ADL items were stair climbing followed by bathing and dressing. This study identified that participants were more affected in instrumental ADLs than basic ADLs, with over two thirds of the study population reporting disability. This showed overall

participants required more assistance with instrumental ADLs and less help with personal activities. This highlights the importance of identifying and understanding disability in instrumental ADLs as well as basic ADLs in this population. Disability in some instrumental ADLs, such as shopping, may be an implication of physical and social isolation, which meant participants were not able to shop in person. It was not clear to participants whether to class online shopping as independent. It is possible participants would respond differently to certain ADL items under normal circumstances.

This cross-sectional analysis of baseline data in incorporated publication 3 attempts to put findings into the context of the Covid-19 pandemic. It identified that nearly all participants were affected by Covid-19 restrictions, causing them to spend considerable time in physical and social isolation. This resulted in reduced physical activity, particularly outdoors. It became apparent from this baseline data that even participants presenting with no disability in basic or instrumental ADLs still had difficulty managing ADLs independently, which could be due to a reduction in social contact and support from health care services or from within the community.

Findings support the association between greater symptom burden and disability identified in the secondary data analysis, extending this association to instrumental ADLs. Novel contributions of this analysis expose the relationship between advanced COPD or ILD and disability in both basic and instrumental ADLs, and between increased time spent in physical and social isolation and disability in basic ADLs. Therefore, people with advanced NSCLC or COPD or ILD may be indirectly impacted by the Covid-19 pandemic, affecting their ability to live independently at home, and potentially increasing demand for rehabilitation.

Chapter 8

Results - Longitudinal Analysis

8.1 Introduction

This last results chapter for the cohort study presents findings from the longitudinal analysis. It aims to address objective 3 and contribute towards objective 4 of the thesis. It describes longitudinal data and identifies trajectories of disability in basic and instrumental ADLs. This analysis tests the hypotheses that an increasing disability trajectory in ADLs can be predicted by: a diagnosis of NSCLC; greater symptom severity; and/or lower usage of ADL assistive devices. This chapter presents findings on:

- Characteristics of the longitudinal sample, with statistical comparison of participants who completed ≥3 timepoints with participants who did not.
- Description of group-level trajectories in disability in basic and instrumental ADLs in people with advanced NSCLC or COPD or ILD, across the whole sample.
- Visual graphical analysis of individual trajectories in disability in basic and instrumental ADLs in people with advanced NSCLC or COPD or ILD.
- Characteristics of participants according to disability trajectory group for both basic and instrumental ADLs, and statistical comparisons of characteristics between groups.
- Relationships of health-related and environmental factors with increasing disability trajectories in basic and instrumental ADLs, including findings from univariable and multi-variable logistic regression.

8.2. Longitudinal sample characteristics

8.2.1. Description of participant characteristics in the longitudinal sample

One-hundred-and fifty-one participants contributed data at ≥3 timepoints during 6-month follow-up and were included in the longitudinal analysis (table 8.1). Eighty-five (56%) participants had NSCLC, and 66 (44%) had COPD or ILD. Eighty-eight (58%) participants had stage IV disease. Eighty-six (55%) were men and 65 (45%) were women, with a median [IQR] age of 70 years [64-76]. Nearly all participants were white British (n=143, 95%) and almost half (n=74, 49%) were educated above secondary school education.

Nearly all participants had spent time in physical and social isolation (n=146, 97%). Despite only 45 (30%) participants were living alone, and over half were receiving informal care (82, 55%), confidence in receiving help from community services, family, or friends was extremely low (median 2 [IQR:1.5-3]). Physical activity indoors and outdoors was reduced in 65 (43%) and 95 (63%) participants, respectively, and 110 (73%) had stairs at home.

The Charlson Comorbidity Index score (median: 7 [IQR:3-11]) showed participants in the longitudinal sample presented with multiple long-term conditions. They were also able to care for themselves, which was reflected by the AKPS score (median: 70 [IQR:60-80]). The Palliative care Outcome Scale score indicated participants were mildly affected by their symptoms at baseline (median: 9 [IQR:5-14]). There was no difference in prevalence of disability in ADLs between the longitudinal sample and the whole sample (section 7.3.2.).

Table 8.1: Differences in characteristics between participants included in the longitudinal analysis (completed ≥3 timepoints) and participants excluded from the longitudinal analysis (completed <3 timepoints)

Participant characteristics and outcomes at baseline	Whole sample n=201	Completed 3 or more timepoints (n=151)	Completed <3 timepoints (n=50)	Difference between groups (p value)
❖ **Health-related factors**				
NSCLC, n (%)	110 (55%)	85 (56.3%)	25 (50%)	0.44
COPD or ILD, n (%)	91 (45%)	66 (43.7%)	25 (50%)	
Stage III, n (%)	80 (40%)	63 (42%)	7 (34%)	0.27
Stage IV, n (%)	121 (60%)	88 (58%)	33 (66%)	
Charlson comorbidity Index score, median [IQR]	7 [3-10]	7 [3-11]	7 [3-9]	0.83
Died, n (%)	35 (17.4)	12 (8%)	23 (46%)	**<0.0001**
❖ **Body Functions and Structures**				
Australian Karnofsky Performance Status (AKPS), median [IQR]	70 [60-80]	70 [60-80]	60 [50-70]	**0.0002**
Symptom severity (Palliative care Outcome Scale-symptoms), median [IQR}	10 [5.5-15]	9 [5-14]	13 [8-19]	**0.0002**
Receiving cancer treatment, n (%)	100 (50%)	78 (51.7%)	22 (44.9%)	0.51
On oxygen therapy, n (%)	40 (20%)	29 (19.2%)	11 (22.5%)	0.76
❖ **Activity and participation**				
Total Barthel Index score (BADLs), median [IQR]	19 [17-20]	20 [15-20]	19 [16-20]	0.14
Lawton Brody Instrumental ADL score (IADLs), median [IQR]	7 [5-8]	7 [5-8]	5.5 [3-7]	**0.002**
WHODAS Summary score, median [IQR]	57 [46-79]	53.5 [44-72]	82 [53-92]	**<0.0001**
Cognition, median [IQR]	7 [6-10]	7 [6-9]	9 [7-16]	**<0.0001**
Mobility, median [IQR]	13 [7-17]	12 [7-16]	16 [11-19]	**0.0001**
Self-Care, median [IQR]	5 [4-9]	4 [4-8]	8 [4-10]	**0.0001**
Getting along with people, median [IQR]	9 [4-13]	8 [5-10]	9 [7-14]	**0.002**
Household activities, median [IQR]	9 [4-13]	8 [4-12]	14 [8-20]	**<0.0001**
Societal participation, median [IQR]	17 [12-21]	16 [11-20]	20 [14-24]	**0.001**
❖ **Personal factors**				
Age, median [IQR]	69 [63-75]	70 [64-76]	68 [61-74]	0.12
Female, n (%)	91 (45%)	65 (43.1%)	26 (52%)	0.27
White British, n (%)	191 (95%)	143 (94.7%)	48 (96%)	0.72
Education above secondary school, n (%)	93 (46%)	74 (49%)	18 (36%)	0.11
CDSE: Confidence to receive help, median [IQR]	2 [1.5-3]	2 [1.5-3]	2 [1-3]	0.17
❖ **Environmental factors**				
Lives alone, n (%)	68 (34%)	45 (30%)	23 (46%)	0.04
Inpatient/residential care, n (%)	4 (2%)	1 (0.7%)	3 (6%)	0.02
Property with stairs, n (%)	144 (72%)	110 (73%)	34 (68%)	0.51
Formal caregiver, n (%)	29 (14%)	18 (12%)	11 (22%)	0.08
Informal caregiver, n (%)	112 (56%)	82 (55%)	30 (60%)	0.62
Physiotherapy input within the last month, n (%)	20 (10%)	14 (9.3%)	6 (12%)	0.76
Occupational therapy input within the last month, n (%)	10 (5%)	5 (3.3%)	5 (10%)	0.15
Received GOV letter to physically and socially isolate, n (%)	174 (87%)	131 (86.8%)	43 (86%)	0.89
Currently physically and socially isolating, n (%)	143 (71%)	108 (71.5%)	35 (70%)	0.84
Have spent time in physical and social isolation, n (%)	194 (97%)	146 (96.7%)	49 (98%)	0.64
Months spent in physical and social isolation, median [IQR]	5 [3-8]	5 [3.5-8]	5 [3-8]	0.97
Hospital admission in the last month, n (%)	27 (13.5%)	19 (12.7%)	8 (16%)	0.7
Accident & Emergency (A&E) visit in the last month, n (%)	7 (3.5%)	2 (1.3%)	5 (10%)	**0.004**
Hospice patient, n (%)	48 (23.9%)	31 (20.5%)	17 (34%)	0.05
Total use of ADL devices, median [IQR]	1 [0-4]	1 [0-3]	3 [1-5]	**0.001**
Reduced physical activity inside the home, n (%)	94 (47%)	65 (43%)	28 (57%)	0.06
Reduced physical activity outside the home, n (%)	129 (65%)	95 (63%)	34 (69%)	0.6

NSCLC: non-small-cell lung cancer; COPD: chronic obstructive pulmonary disease; ILD: Interstitial lung disease; ADL: activities of daily living; BADL: Basic activities of daily living; IADL: instrumental activities of daily living; WHODAS: World Health Organization disability assessment Schedule; CDSE: Chronic Disease Self-Efficacy subscale; GOV: government; Reduced physical activity includes responses of 'little less' or a 'lot less'; IQR: inner quartile range; Statistical comparisons between the two groups was conducted using the Mann Whitney-U test for continuous variable and the Chi square test for categorical variables.; the significance level is set at p≤0.01.

8.2.2. Difference between participants included in, and excluded from, the longitudinal sample

The longitudinal sample had a significantly higher AKPS, lower symptom severity, less disability in instrumental ADLs, and lower use of ADL assistive devices than those not included in this analysis. These participants also presented with less difficulty in daily activities across all domains (cognition, mobility, self-care, getting along with people, household activities, and societal participation), had lower AKPS, and greater symptom severity. They were also more likely to have attended the A&E department in the last month.

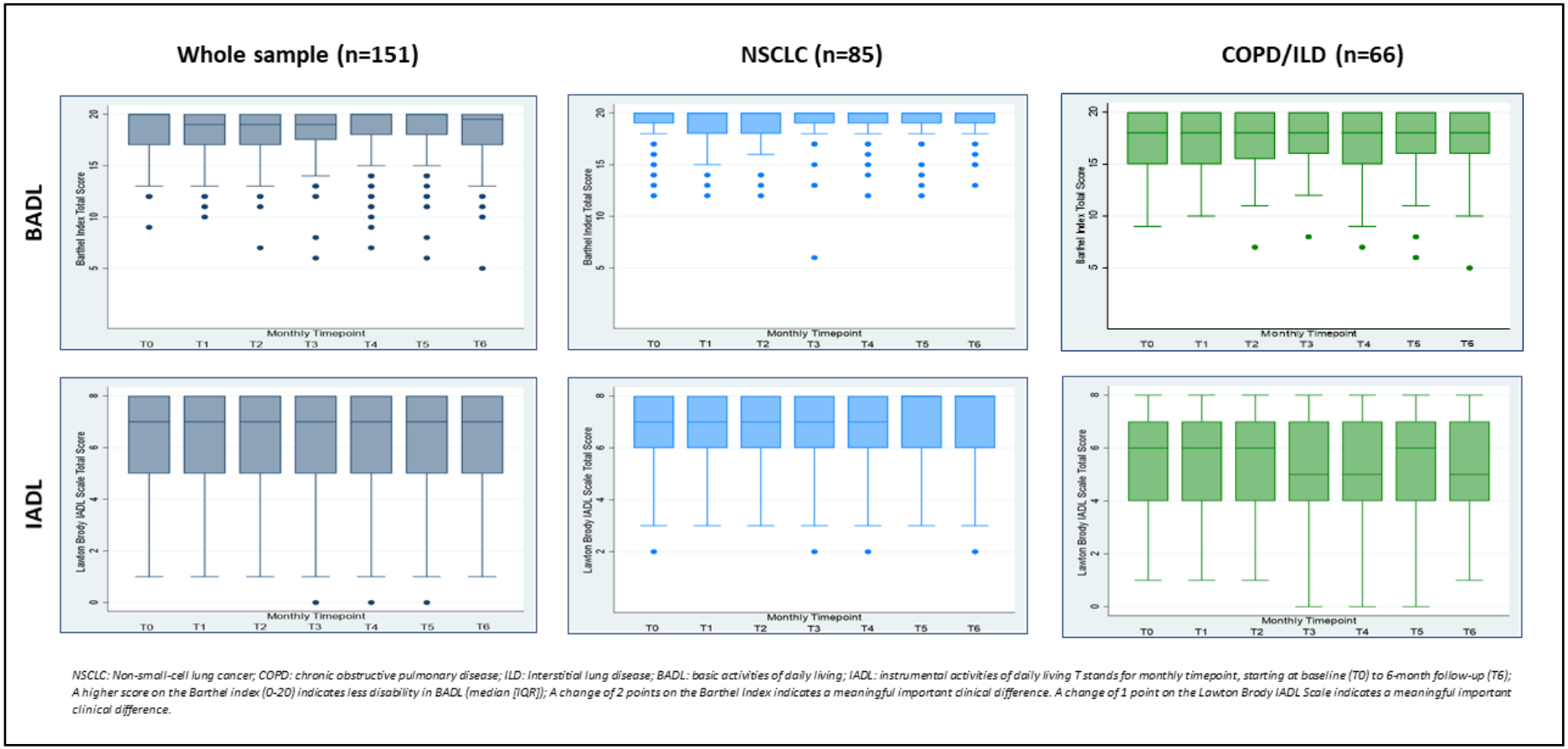
Attempts to mitigate healthy patient bias were made by including participants in the analysis who completed at least three timepoints rather than the full 6-month follow-up: twelve (8%) of whom had died before completion and 31 (20.5%) who were under the care of a hospice. Despite this, there still appeared to be selective attrition, where participants who did not complete three or more timepoints were potentially less healthy at the time of recruitment.

8.3. Group-level trajectories of disability in ADLs

8.3.1. Group-level ADL disability trajectories across the whole sample

Figure 8.1. illustrates the group-level trajectories of basic ADL and instrumental ADL disability over 6-month follow-up. For participants overall, the median disability in basic ADLs is shown to fluctuate by 0.5 to 1 point on the Barthel index between baseline (median 20 [1QR 17-20]), 1-month follow-up (median 19 [1QR 17-20]), 4-month follow-up (median 20 [1QR 18-20]), and 6-month follow-up (median 19.5 [1QR 17-20]).

Figure 8.1: Summary trajectories of disability in ADLs over 6 months



NSCLC: Non-small-cell lung cancer; COPD: chronic obstructive pulmonary disease; ILD: Interstitial lung disease; BADL: basic activities of daily living; IADL: instrumental activities of daily living T stands for monthly timepoint, starting at baseline (T0) to 6-month follow-up (T6); A higher score on the Barthel index (0-20) indicates less disability in BADL (median [IQR]); A change of 2 points on the Barthel Index indicates a meaningful important clinical difference. A change of 1 point on the Lawton Brody IADL Scale indicates a meaningful important clinical difference.

Disability (median) in instrumental ADL did not change over 6-months and was maintained at a median [IQR] of 7 [5-8] at all follow-up timepoints. This suggests that there is no change in the median disability in basic and instrumental ADLs over time at group level, but there remains variation in the range of disability within the whole sample.

8.3.2. Comparison of group-level ADL disability trajectories between NSCLC and COPD or ILD

Group-level ADL disability trajectories for NSCLC and COPD or ILD follow slightly different patterns. For basic ADLs, participants with NSCLC remained independent with a median Barthel Index score of 20 throughout 6-month follow-up. Patients with COPD or ILD also followed a stable trajectory, but mild disability in basic ADLs persisted with a median Barthel Index score of 18 maintained over six months.

Group-level instrumental ADL disability trajectories for NSCLC participants showed decreasing disability in the median Lawton Brody Instrumental ADL Scale score, where they presented with mild disability over the first five months (median 7 [IQR 6-8]), which decreased by one point on the scale to fully independent at 5-month follow-up (median 8 [IQR 6-8]). Participants with COPD or ILD followed a fluctuating trajectory in instrumental ADLs at group level: the median Barthel Index score, decreased by one point between 2-month follow-up (median 6 [IQR 4-7] and 3-month follow-up (median 5 [IQR 4-7]), then increased by one point at 5-month follow-up (median 6 [IQR 4-7]), followed by a decrease of one point at 6-month follow-up (median 5 [IQR 4-7]).

Ultimately group-level disability trajectories showed participants with NSCLC presented with a lower median disability in ADLs over time and were less likely to experience worsening episodes of disability in daily activities than participants with COPD or ILD. There remains

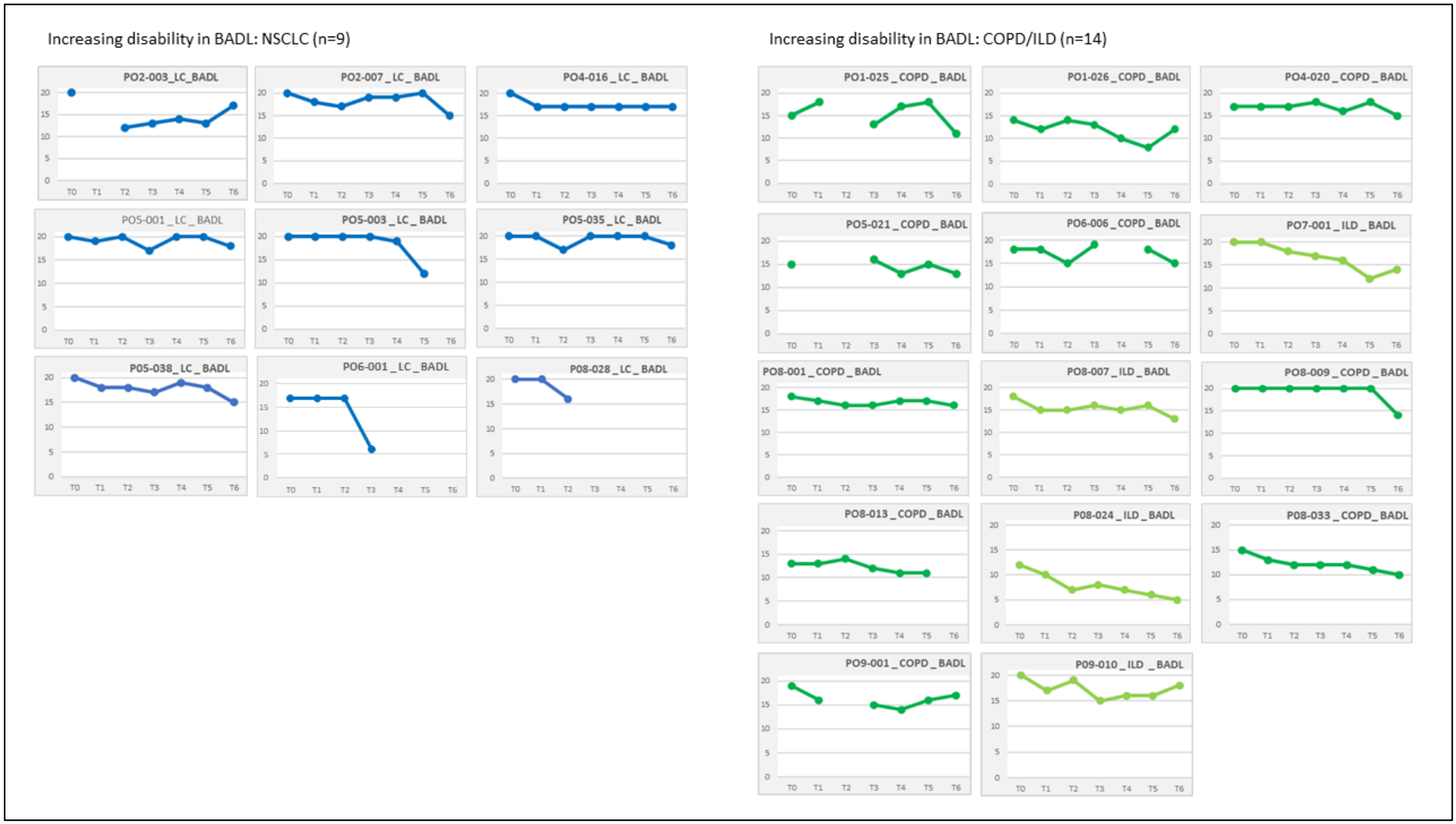
variation in the range of disability in both diagnoses, which is slightly wider ranging in the COPD or ILD group. However, group-level trajectory charts need to be interpreted with caution as the data is limited to disability trajectories of participants alive and well enough to complete follow-up questionnaires and supresses individual change. As previously noted, attrition is most apparent in participants with NSCLC, and the group-level disability trajectories may differ if these participants were able to contribute longitudinal data.

8.4. Individual trajectories of disability in ADLs

Individual disability trajectory charts are presented in figures 8.2a (basic ADLs) and 8.2b (instrumental ADLs), arranged according to disability trajectory and sub-grouped by diagnosis. Half of participants had basic ADL disability trajectories categorised as 'stable' (n=74, 50%), and the remainder had increasing (n=23, 15%), decreasing (n= 23, 15%), and fluctuating (n=30, 20%) disability trajectories. For instrumental ADL disability, increasing disability (n=50, 33%) was the most common trajectory, with little difference between the decreasing (n=33, 22%), fluctuating (n=35, 23%) and stable (n=33, 22%) trajectory groups. The rate of change within each of the disability trajectories varied considerably, and linear change in increasing or decreasing disability was very rare. Trajectories of increasing or decreasing disability mostly had fluctuations within them.

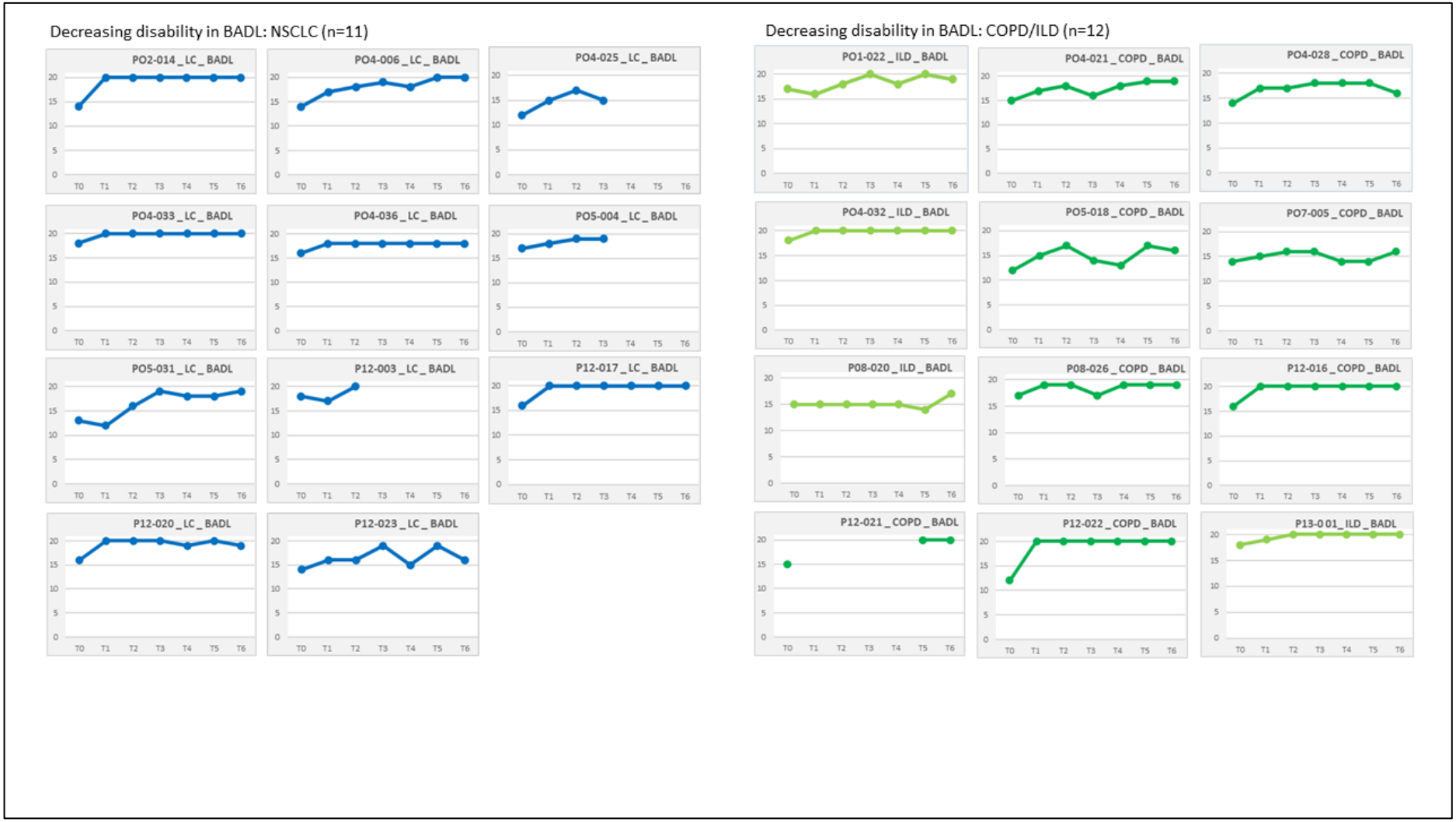
Figure 8.2a: Individual disability trajectory charts in basic ADLs (n=150)

i) Increasing disability trajectories in basic ADL (n=23)



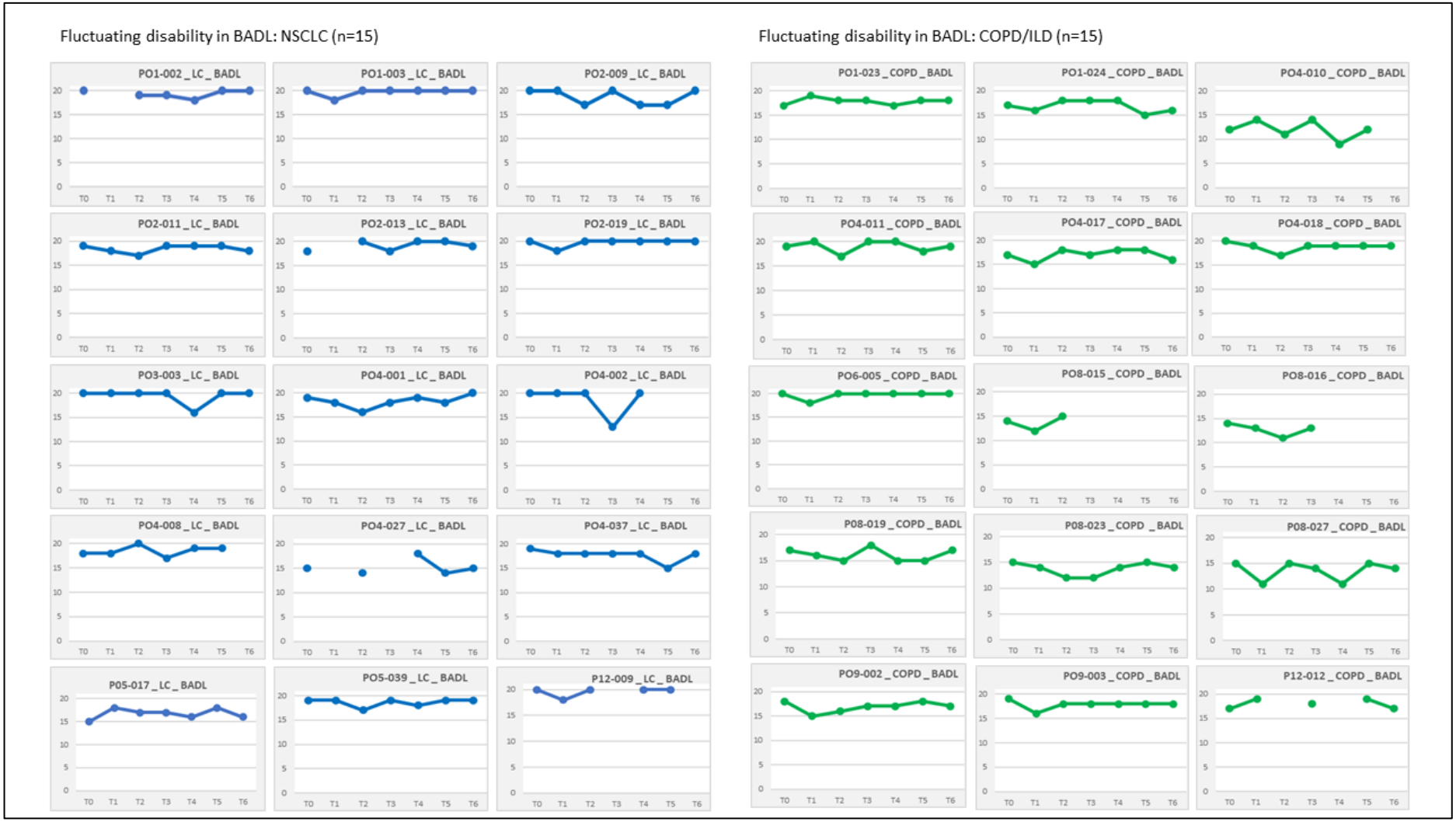
*BADL = basic activities in daily living; P**-*** = participant study ID number; NSCLC: non-small-cell lung cancer; LC = non-small-cell lung cancer (blue chart); COPD = Chronic Obstructive Pulmonary Disease (dark green chart); ILD = Interstitial Lung Disease (light green chart); X-axis = monthly timepoint from baseline (T0) to 6-month follow-up (T6); Y-axis = total score in Barthel Index for BADL (0-20); A higher score on the Barthel Index indicates less disability, and a lower score indicates greater disability. A decreasing score of ≥2 points between baseline and the last follow-up timepoint shows increasing disability; A gap in the trajectory indicates a missing timepoint.*

ii) Decreasing disability trajectories in basic ADLs (n=23)



*BADL = basic activities in daily living; P**-*** = participant study ID number; NSCLC: non-small-cell lung cancer; LC = non-small-cell lung cancer (blue chart); COPD = Chronic Obstructive Pulmonary Disease (dark green chart); ILD = Interstitial Lung Disease (light green chart); X-axis = monthly timepoint from baseline (T0) to 6-month follow-up (T6); Y-axis = total score in Barthel Index for BADL (0-20); A higher score on the Barthel Index indicates less disability, and a lower score indicates greater disability. An increasing score of ≥2 points between baseline and the last follow-up timepoint shows decreasing disability; A gap in the trajectory indicates a missing timepoint.*

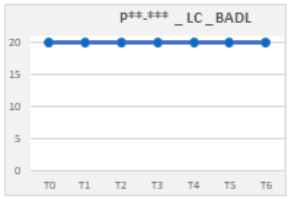
iii) Fluctuating disability trajectories in basic ADLs (n=30)



*BADL = basic activities in daily living; P**-*** = participant study ID number; NSCLC: non-small-cell lung cancer; LC = non-small-cell lung cancer (blue chart); COPD = Chronic Obstructive Pulmonary Disease (dark green chart); ILD = Interstitial Lung Disease (light green chart); X-axis = monthly timepoint from baseline (T0) to 6-month follow-up (T6); Y-axis = total score in Barthel Index for BADL (0-20); A higher score on the Barthel Index indicates less disability, and a lower score indicates greater disability. A fluctuating score of least one increase and one decrease (or vice versa) between any two timepoints of ≥2points, but a change <2 points between the first and last timepoint shows fluctuating disability; A gap in the trajectory indicates a missing timepoint*

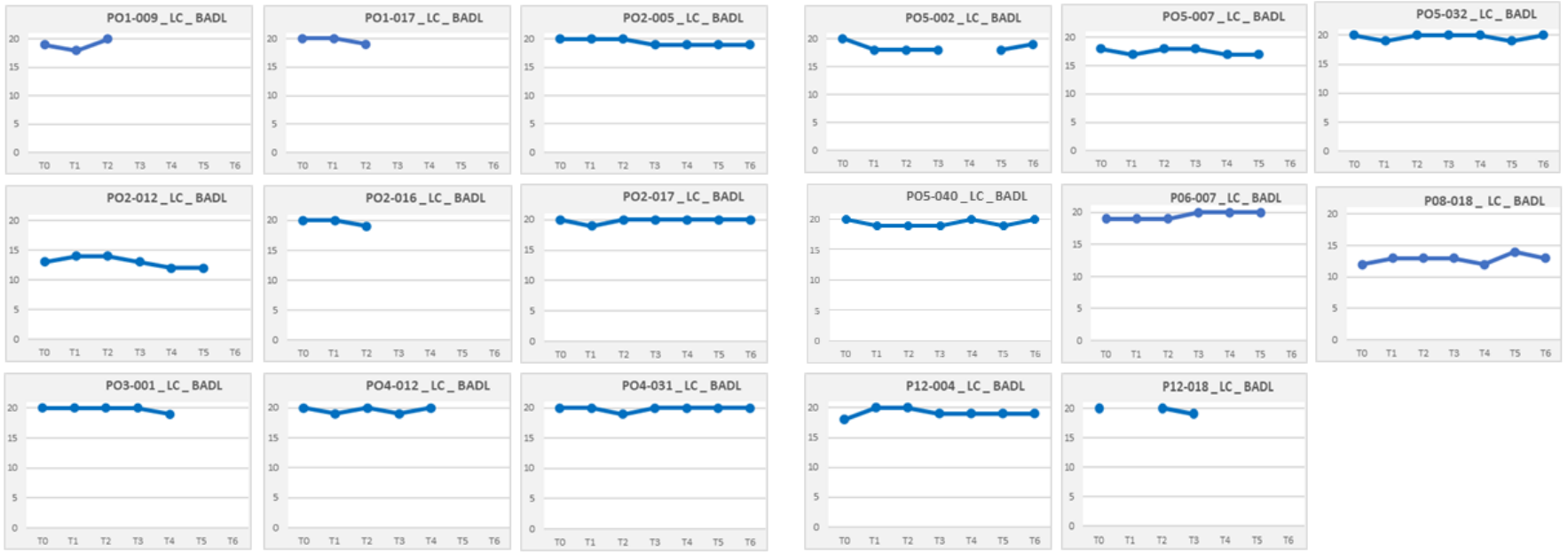
iv) Stable disability trajectories in basic ADLs (n=74)

Stable disability in BADL (independent): NSCLC (n=33)



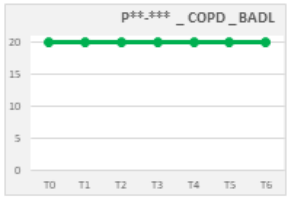
Independent in BADL (completed all timepoints), n-27									Independent in BADL (missing 1 or 2 timepoints), n=6	
P01-004	P01-010	P02-008	P03-004	P04-004	P04-014	P05-027	P05-036	P12-005	P01-001 (missing T2)	P08-012 (missing T5/T6)
P01--006	P01-019	P02-010	P03-005	P04-009	P05-009	P05-029	P05-044	P12-011	P01-007 (missing T6)	P09-007 (missing T5/T6)
P01-008	P02-002	P03-002	P03-006	P04-013	P05-011	P05-033	P08-025	P12-025	P01-018 (missing T6)	P12-14 (missing T5/T6)

Stable disability in BADL (persistent): NSCLC (n=17))



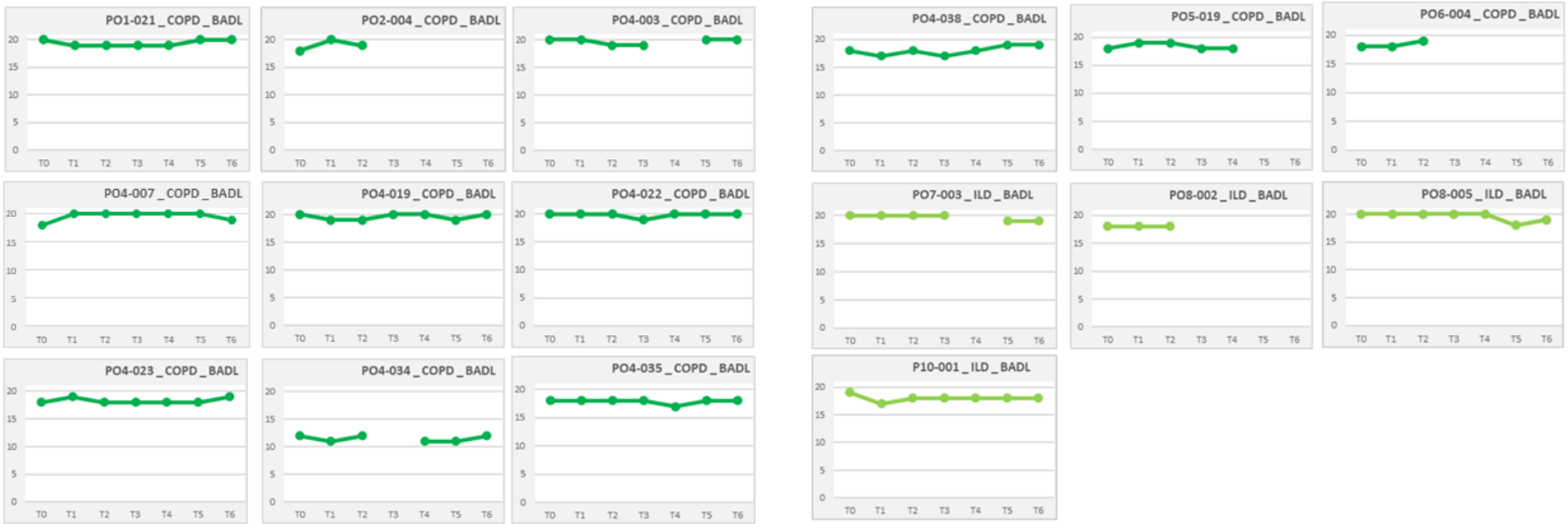
*BADL = basic activities in daily living; P**-*** = participant study ID number; NSCLC: non-small-cell lung cancer; LC = non-small-cell lung cancer (blue chart); X-axis = monthly timepoint from baseline (T0) to 6-month follow-up (T6); Y-axis = total score in Barthel Index for BADL (0-20); A higher score on the Barthel Index indicates less disability, and a lower score indicates greater disability. A no change in score is indicated by a difference in score of <2 points between the first and last recorded timepoint, showing stable disability; The stable disability trajectory group is sub-grouped into' independent' where the chart shows no disability in ADLs and 'persistent' where the chart shows constant disability in ADLs; A gap in the trajectory indicates a missing timepoint.*

Stable disability in BADL (independent): COPD/ILD (n=8)



Independent in BADL (completed all timepoints), n-8			
P04-005 (COPD)	P06-003 (COPD)	P08-021 (ILD)	P12-006 (COPD)
P04-024 (COPD)	P08-008 (COPD)	P09-005 (COPD)	P09-006 (COPD)

Stable disability in BADL (persistent): COPD/ILD (n=16)

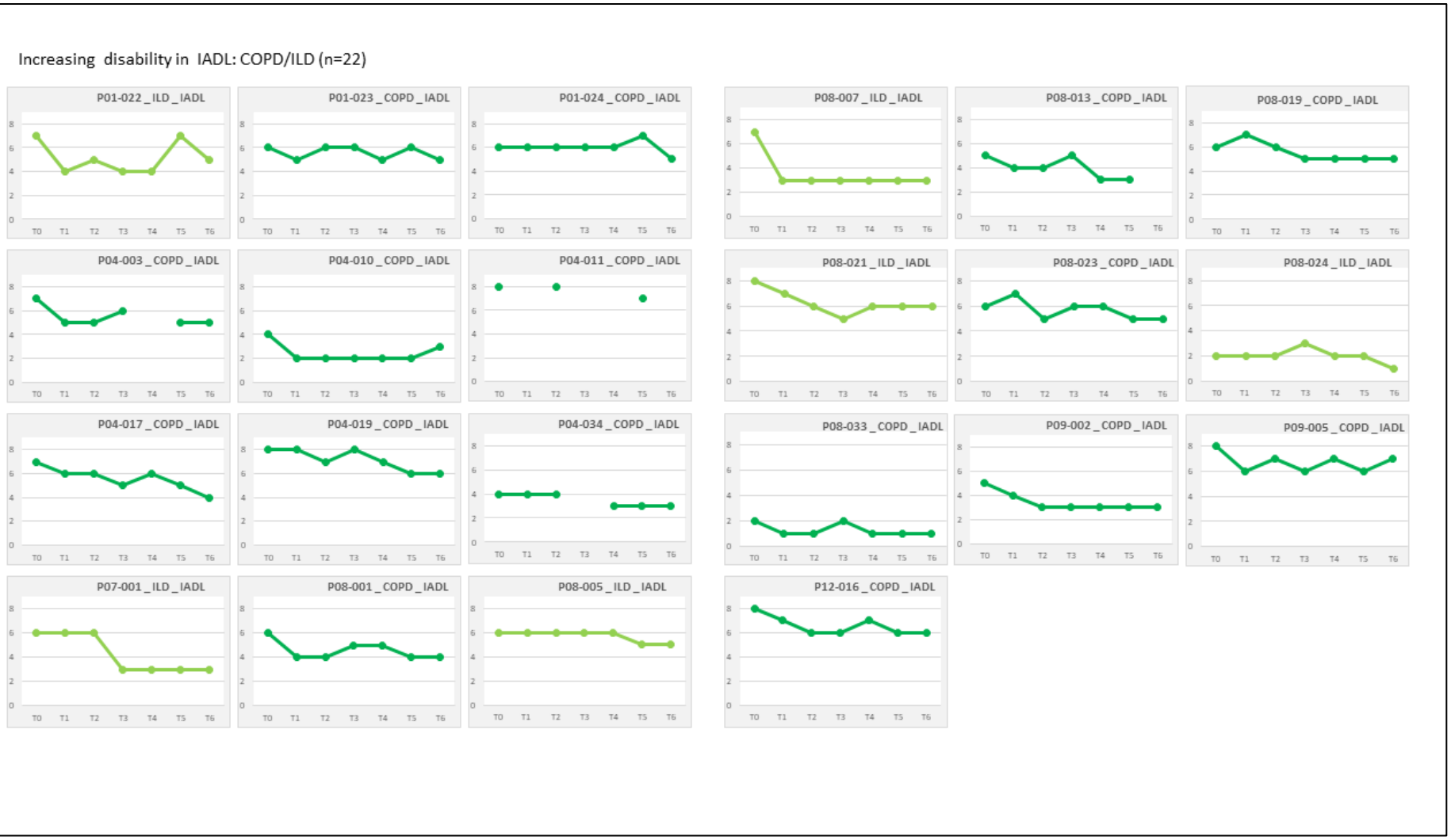


*BADL = basic activities in daily living; P**-*** = participant study ID number; COPD = Chronic Obstructive Pulmonary Disease (dark green chart); ILD = Interstitial Lung Disease (light green chart); X-axis = monthly timepoint from baseline (T0) to 6-month follow-up (T6); Y-axis = total score in Barthel Index for BADL (0-20); A higher score on the Barthel Index indicates less disability, and a lower score indicates greater disability. A no change in score is indicated by a difference in score of <2 points between the first and last recorded timepoint, showing stable disability; The stable disability trajectory group is sub-grouped into' independent' where the chart shows no disability in ADLs and 'persistent' where the chart shows constant disability in ADLs; A gap in the trajectory indicates a missing timepoint*

Figure 8.2b: Individual disability trajectory charts in instrumental ADLs (n=151)

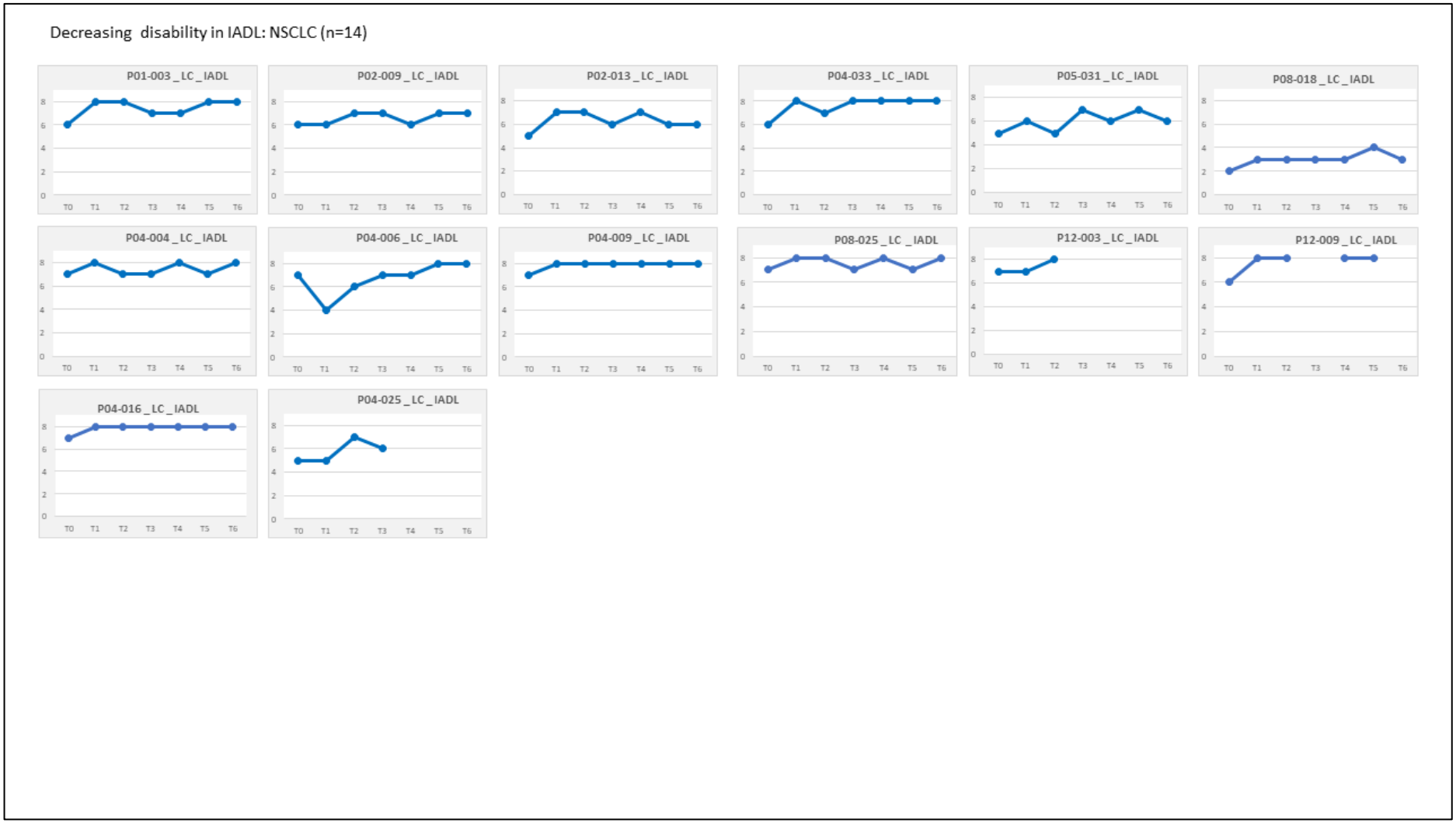
i) Increasing disability trajectories in instrumental ADL (n=50)

*IADL = instrumental activities in daily living; P**-*** = participant study ID number; NSCLC: non-small-cell lung cancer; LC = non-small-cell lung cancer (blue chart); X-axis = monthly timepoint from baseline (T0) to 6-month follow-up (T6); Y-axis = total score in Lawton Brody Instrumental ADL Scale for IADL (0-8); A higher score on the Lawton Brody Instrumental ADL Scale indicates less disability, and a lower score indicates greater disability. A decreasing score of ≥2 points between baseline and the last follow-up timepoint shows increasing disability; A gap in the trajectory indicates a missing timepoint.*



*IADL = instrumental activities in daily living; P**-*** = participant study ID number; COPD = Chronic Obstructive Pulmonary Disease (dark green chart); ILD = Interstitial Lung Disease (light green chart); X-axis = monthly timepoint from baseline (T0) to 6-month follow-up (T6); Y-axis = total score in Lawton Brody Instrumental ADL Scale for IADL (0-8); A higher score on the Lawton Brody Instrumental ADL Scale indicates less disability, and a lower score indicates greater disability. A decreasing score of ≥2 points between baseline and the last follow-up timepoint shows increasing disability; A gap in the trajectory indicates a missing timepoint.*

ii) Decreasing disability trajectories in instrumental ADLs (n=33)

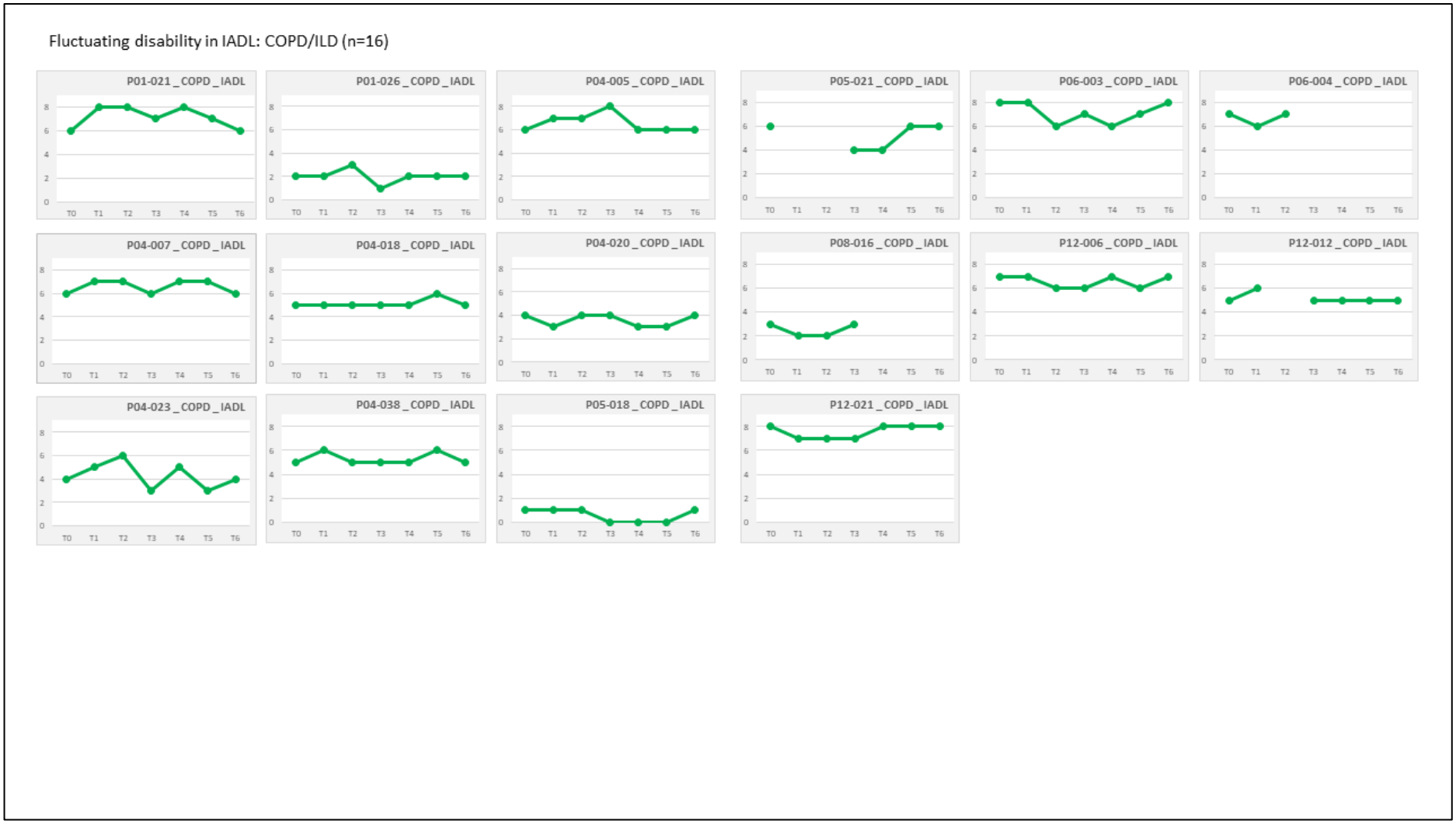


*IADL = instrumental activities in daily living; P**-*** = participant study ID number; NSCLC: non-small-cell lung cancer; LC = non-small-cell lung cancer (blue chart); X-axis = monthly timepoint from baseline (T0) to 6-month follow-up (T6); Y-axis = total score in Lawton Brody Instrumental ADL Scale for IADL (0-8); A higher score on the Lawton Brody Instrumental ADL Scale indicates less disability, and a lower score indicates greater disability. An increasing score of ≥2 points between baseline and the last follow-up timepoint shows decreasing disability; A gap in the trajectory indicates a missing timepoint*

*IADL = instrumental activities in daily living; P**-*** = participant study ID number; Chronic Obstructive Pulmonary Disease (dark green chart); ILD = Interstitial Lung Disease (light green chart); X-axis = monthly timepoint from baseline (T0) to 6-month follow-up (T6); Y-axis = total score in Lawton Brody Instrumental ADL Scale for IADL (0-8); A higher score on the Lawton Brody Instrumental ADL Scale indicates less disability, and a lower score indicates greater disability. An increasing score of ≥2 points between baseline and the last follow-up timepoint shows decreasing disability; A gap in the trajectory indicates a missing timepoint*

iii) Fluctuating disability trajectories in instrumental ADLs (n=35)

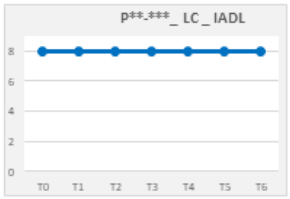
*IADL = instrumental activities in daily living; P**-*** = participant study ID number; NSCLC: non-small-cell lung cancer; LC = non-small-cell lung cancer (blue chart); X-axis = monthly timepoint from baseline (T0) to 6-month follow-up (T6); Y-axis = total score in Lawton Brody Instrumental ADL Scale for IADL (0-8); A higher score on the Lawton Brody Instrumental ADL Scale indicates less disability, and a lower score indicates greater disability. A fluctuating score of least one increase and one decrease (or vice versa) between any two timepoints of ≥1points, but with a change <1 points between the first and last timepoint shows fluctuating disability; A gap in the trajectory indicates a missing timepoint*



*IADL = instrumental activities in daily living; P**-*** = participant study ID number; COPD = Chronic Obstructive Pulmonary Disease (dark green chart); ILD = Interstitial Lung Disease (light green chart); X-axis = monthly timepoint from baseline (T0) to 6-month follow-up (T6); Y-axis = total score in Lawton Brody Instrumental ADL Scale for IADL (0-8); A higher score on the Lawton Brody Instrumental ADL Scale indicates less disability, and a lower score indicates greater disability. A fluctuating score of least one increase and one decrease (or vice versa) between any two timepoints of ≥1points, but with a change <1 points between the first and last timepoint shows fluctuating disability; A gap in the trajectory indicates a missing timepoint*

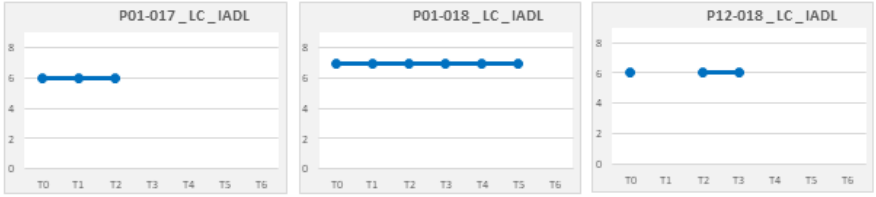
iv) Stable disability trajectories in instrumental ADLs (n=3)

Stable disability in IADL (independent): NSCLC (n=21)

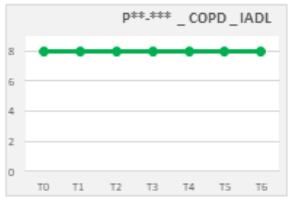


Independent in IADL (completed all timepoints), n=20				Independent in IADL (missing one timepoint), n=1
P01-004	P02-017	P04-013	P05-039	P01-001 (missing T2)
P01-006	P03-002	P05-011	P05-040	
P02-002	P03-003	P05-027	P05-044	
P02-005	P03-004	P05-035	P12-017	
P02-010	P03-005	P05-036	P12-025	

Stable disability IADL (persistent): NSCLC (n=3)

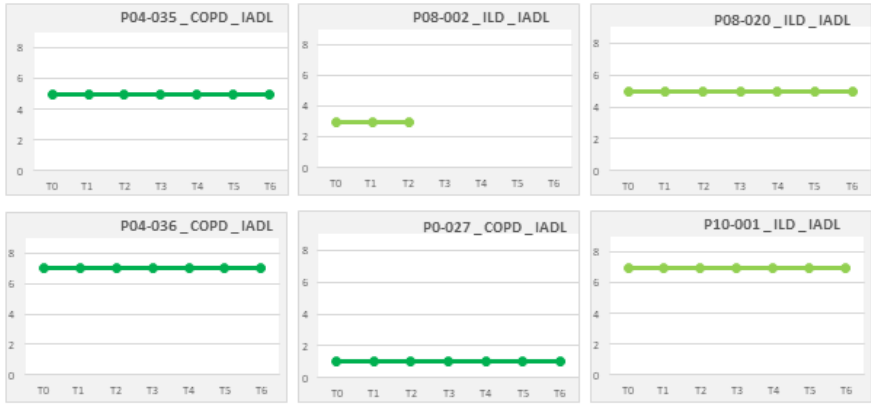


Stable disability IADL (independent): COPD/ILD (n=3)



Independent in IADL (completed all timepoints), n-3		
P04-024 (COPD)	P06-005 (COPD)	P12-022 (COPD)

Stable disability in IADL (persistent): COPD/ILD (n=6)



*IADL = instrumental activities in daily living; P**-*** = participant study ID number; NSCLC: non-small-cell lung cancer; LC = non-small-cell lung cancer (blue chart); COPD = Chronic Obstructive Pulmonary Disease (dark green chart); ILD = Interstitial Lung Disease (light green chart); X-axis = monthly timepoint from baseline (T0) to 6-month follow-up (T6); Y-axis = total score in Lawton Brody IADL Scale (0-8); A higher score on the Lawton Brody Instrumental ADL Scale indicates less disability, and a lower score indicates greater disability. A no change in score is indicated by a difference in score of <2 points between the first and last recorded timepoint, showing stable disability; The stable disability trajectory group is sub-grouped into' independent' where the chart shows no disability in ADLs and 'persistent' where the chart shows constant disability in ADLs; A gap in the trajectory indicates a missing timepoint.*

8.5. Characteristics of ADL disability trajectory groups

8.5.1. Differences in characteristics across ADL disability trajectory groups

Participant characteristics for each trajectory group for basic and instrumental ADLs are presented in tables 8.2 and 8.3 respectively. When comparing baseline characteristics across the disability trajectory groups (increasing, decreasing, fluctuating, stable), basic ADL disability trajectories were found to have significantly different baseline disability in basic ADLs. The basic ADL disability trajectory groups also differed by AKPS, difficulty in daily activities (specifically mobility, self-care, and household activities), as well as receipt of occupational therapy, hospice care, and use of ADL assistive devices. The instrumental ADL disability trajectory groups significantly differed by baseline disability in instrumental ADLs, AKPS, and difficulty in daily activities (specifically mobility). Symptom severity, reduced physical activity outdoors, and whether participants received hospice care or died, was also significantly different across instrumental ADL disability trajectory groups.

Table 8.2: Participant characteristics and differences between disability trajectories in basic ADLs

Participant characteristics and outcomes at baseline	Increasing (n=23)	Decreasing (n-23)	Fluctuating (n=30)	Stable (n=74)	Difference between groups (p value)
❖ **Health-related factors**					
NSCLC, n (%)	9 (39%) *	11 (48%)	15 (50%)	50 (68%)	0.03
COPD or ILD, n (%)	14 (61%)	12 (52%)	15 (50%)	24 (32%)	
Stage IV, n (%)	14 (59%)	8 (35%)	22 (73%)	43 (59%)	0.05
Charlson comorbidity Index score, median [IQR]	4 [2-7] *	6 [3-10]	7 [4-13]	7 [6-12]	0.03
Died, n (%)	3 (13%)	2 (9%)	1 (3%)	6 (8%)	0.67
❖ **Body Functions and Structures**					
Australian Karnofsky Performance Status (AKPS), median [IQR]	65 [60-70] *	60 [60-80] *	60 [60-80] *	80 [70-90]	**0.0005**
Symptom severity (Palliative care Outcome Scale-symptoms), median [IQR}	11 [6-18]	11 [6-15] *	10 [4-16]	7 [4-11]	0.02
Receiving cancer treatment, n (%)	8 (33%) *	12 (52%)	12 (40%)	46 (63%)	0.04
On oxygen therapy, n (%)	8 (33%)	4 (17%)	7 (23%)	10 (14%)	0.18
❖ **Activity and Participation**					
Total Barthel Index score (BADLs), median [IQR]	19 [16-20] *	15 [14-17] *	18 [16-20] *	20 [20-20]	**0.0001**
Lawton Brody Instrumental ADL score (IADLs), median [IQR]	6 [4-7] *	6 [5-7] *	6 [5-7] *	7 [6-8]	**0.0004**
WHODAS Summary score, median [IQR]	64 [47-81] *	57 [45-75]	61 [51-79] *	49 [40-62]	**0.003**
Cognition, median [IQR]	7 [6-10]	6 [6-7]	7 [6-10]	6 [6-9]	0.44
Mobility, median [IQR]	16 [10-20] *	13 [7- 16]	15 [7-18] *	9 [6-13]	**0.0001**
Self-Care, median [IQR]	6 [4-9] *	5 [4-9]	5 [4-10] *	4 [4-6]	**0.009**
Getting along with people, median [IQR]	8 [5-10]	8 [5-10]	8 [4-12]	6 [5-10]	0.38
Household activities, median [IQR]	11 [5-17] *	9 [5-13]	8 [4-12]	6 [4-10]	**0.008**
Societal participation, median [IQR]	16 [12-22]	18 [13-21]	17 [13-21]	15 [11-18]	0.11
❖ **Personal factors**					
Age, median [IQR]	74 [71-79] *	70 [62-74]	69 [64-75]	69 [64-75]	0.03
Female, n (%)	8 (33%)	10 (43%)	18 (60%)	28 (38%)	0.17
White British, n (%)	22 (92%)	23 (100%)	29 (97%)	68 (93%)	0.51
Education above secondary school, n (%)	10 (42%)	12 (52%)	15 (50%)	36 (49%)	0.89
CDSE: Confidence to receive help, median [IQR]	2.5 [1.5-3]	3 [2-3]	2 [1.5-2.5]	2 [1.5-3]	0.63
❖ **Environmental factors**					
Lives alone, n (%)	9 (38%)	6 (26%)	8 (27%)	22 (30%)	0.81
Inpatient/residential care, n (%)	0	0	1 (3%)	0	0.26
Property with stairs, n (%)	16 (67%)	18 (78%	18 (60%)	57 (78%)	0.23
Formal caregiver, n (%)	6 (25%)	1 (4%)	5 (17%)	6 (8%)	0.08
Informal caregiver, n (%)	14 (61%)	15 (63%)	18 (62%)	34 (47%)	0.32
Physiotherapy input within the last month, n (%)	4 (17%)	2 (9%)	3 (10%)	5 (7%)	0.1
Occupational therapy input within the last month, n (%)	4 (17%) *	0	0	1 (1%)	**0.001**
Received GOV letter to physically and socially isolate, n (%)	21 (88%)	19 (83%)	25 (83%)	65 (89%)	0.8
Currently physically and socially isolating, n (%)	19 (79%)	18 (78%)	29 (63%)	51 (70%)	0.52
Have spent time in physical and social isolation, n (%)	23 (96%)	23 (100%)	28 (93%)	71 (97%)	0.58
Months spent in physical and social isolation, median [IQR]	7 [4-10]	6 [4-9]	5 [3-7]	5 [4-6]	0.08
Hospital admission in the last month, n (%)	3 (13%)	7 (30%) *	3 (10%)	6 (8%)	0.05
Accident & Emergency (A&E) visit in the last month, n (%)	0	0	0	2 (3%)	0.54
Hospice patient, n (%)	11 (46%) *	3 (13%)	7 (23%)	10 (14%)	**0.006**
Total number of ADL devices, median [IQR}	2 [1-5] *	2 [1-4] *	2 [0-4] *	0 [0-2]	**0.0007**
Reduced physical activity indoors, n (%)	10 (42%)	9 (39%)	13 (43%)	33 (45%)	0.96
Reduced physical activity outdoors, n (%)	14 (58%)	14 (61%)	21 (70%)	45 (62%)	0.81

*NSCLC: non-small-cell lung cancer; COPD: chronic obstructive pulmonary disease; ILD: Interstitial lung disease; ADL: activities of daily living; BADL: Basic activities of daily living; IADL: instrumental activities of daily living; WHODAS: World Health Organization disability assessment Schedule; CDSE: Chronic Disease Self-Efficacy subscale; GOV: government; Reduced physical activity includes responses of 'little less' or a 'lot less'; IQR: inner quartile range; Statistical comparisons between groups were conducted using the Kruskal-Wallis test for continuous variables between four groups, the Mann Whitney-U test for continuous variables between two groups, and the Chi square test for categorical variables. * Indicates significant differences of p≤0.01 between the decreasing, increasing, or fluctuating disability trajectory groups and the 'stable' trajectory group.*

Table 8.3: Participant characteristics and differences between disability trajectories in instrumental ADLs

Participant characteristics and outcomes at baseline	Increasing (n=50)	Decreasing (n=33)	Fluctuating (n=35)	Stable (n=33)	Difference between groups (p value)
❖ **Health-related factors**					
NSCLC, n (%)	28 (56%)	14 (42%) *	19 (54%)	24 (73%)	0.1
COPD or ILD, n (%)	22 (44%)	19 (58%)	16 (46%)	9 (27%)	
Stage IV, n (%)	28 (56%)	23 (70%)	16 (46%)	21 (64%)	0.21
Charlson comorbidity Index score, median [IQR]	7 [5-11]	6 [2-8] *	6 [3-12]	8 [6-13]	0.04
Died, n (%)	9 (18%)	2 (6.1%)	0	1 (3%)	0.01
❖ **Body Functions and Structures**					
Australian Karnofsky Performance Status (AKPS), median [IQR]	70 [60-80] *	70 [60-80] *	70 [60-80] *	80 [70-90]	**0.0001**
Symptom severity (Palliative care Outcome Scale-symptoms), median [IQR}	12 [6-15]	9 [6-14]	8 [4-11]	6 [3-10]	**0.007**
Receiving cancer treatment, n (%)	23 (46%)	14 (42.4%)	19 (54.3%)	22 (66.7%)	0.18
On oxygen therapy, n (%)	9 (18%)	9 (27.3%)	8 (22.9%)	3 (9.1%)	0.27
❖ **Activity and Participation**					
Total Barthel Index score (BADLs), median [IQR]	19 [17-20]	18 [15-20] *	19 [17-20]	20 [19-20]	0.04
Lawton Brody Instrumental ADL score (IADLs), median [IQR]	7 [6-8] *	6 [4-7] *	7 [5-8] *	8 [7-8]	**0.0001**
WHODAS Summary score, median [IQR]	60 [48-79] *	52 [47-74] *	57 [47-72] *	42 [37-54]	**0.0007**
Cognition, median [IQR]	7 [6-10]	7 [6-9]	6 [6-7]	7 [6-8]	0.71
Mobility, median [IQR]	13 [9-17] *	13 [7-18] *	12 [7-15] *	7 [5-10]	**0.0001**
Self-Care, median [IQR]	5 [4-8] *	4 [4-8]	5 [4-8]	4 [4-4]	0.05
Getting along with people, median [IQR]	9 [7-11] *	8 [5-10]	7 [5-10]	5 [5-9]	0.02
Household activities, median [IQR]	9 [5-12] *	9 [5-12]	8 [4-12]	5 [4-9]	0.03
Societal participation, median [IQR]	18 [13-22] *	15 [13-20]	16 [11-19]	13 [10-17]	0.02
❖ **Personal factors**					
Age, median [IQR]	71 [65-78]	70 [63-75]	68 [64-76]	69 [67-73]	0.77
Female, n (%)	21 (42%)	18 (54.6%)	14 (40%)	12 (36.4%)	0.47
White British, n (%)	46 (92%)	32 (97%)	33 (94.3%)	32 (97%)	0.7
Education above secondary school, n (%)	23 (46%)	15 (45.5%)	14 (40%)	22 (66.7%)	0.13
CDSE: Confidence to receive help, median [IQR]	2 [1.5-3]	2 [1.5-3]	2.5 [1.5-3]	3 [2-3]	0.1
❖ **Environmental factors**					
Lives alone, n (%)	13 (26%)	7 (21.2%	11 (31.4%)	14 (42.4%)	0.25
Inpatient/residential care, n (%)	1 (2%)	0	0	0	0.57
Property with stairs, n (%)	35 (70%)	23 (70%)	25 (71%)	27 (82%)	0.63
Formal caregiver, n (%)	10 (20%) *	3 (9%)	5 (14.3%)	0	0.05
Informal caregiver, n (%)	28 (56%)	22 (68.8%)	20 (57.1%)	12 (36.4%)	0.07
Physiotherapy input within the last month, n (%)	8 (16.3%)	5 (15%)	1 (2.9%)	0	0.03
Occupational therapy input within the last month, n (%)	2 (4.1%)	2 (6.1 %)	1 (2.9%)	0	0.57
Received GOV letter to physically and socially isolate, n (%)	45 (90%)	29 (87.9%)	30 (85.7%)	27 (81.8%)	0.75
Currently physically and socially isolating, n (%)	40 (80%) *	23 (69.7%)	27 (77.1%)	18 (54.6%)	0.07
Have spent time in physical and social isolation, n (%)	49 (98%)	33 (100%)	35 (100%)	29 (87.9%)	**0.01**
Months spent in physical and social isolation, median [IQR]	4.75 [3-6.5]	5 [4-8]	6 [4-9] *	4 [3-5.5]	0.03
Hospital admission in the last month, n (%)	6 (12.2%)	5 (15%)	8 {22.9%] *	0	0.04
Accident & Emergency (A&E) visit in the last month, n (%)	0	0	2 (5.7%)	0	0.08
Hospice patient, n (%)	15 (30%)	12 (36.4%) *	1 (2.9%)	3 (9.1%)	0.001
Total number of ADL devices, median [IQR]	2 [0-4] *	1 [0-3]	1 [0-4] *	0 [0-1]	0.02
Reduced physical activity indoors, n (%)	29 (58%)	14 (42%)	12 (34%)	11 (33%)	0.08
Reduced physical activity outdoors, n (%)	38 (76%) *	25 (76%)	16 (46%)	16 (48%)	**0.004**

*NSCLC: non-small-cell lung cancer; COPD: chronic obstructive pulmonary disease; ILD: Interstitial lung disease; ADL: activities of daily living; BADL: Basic activities of daily living; IADL: instrumental activities of daily living; WHODAS: World Health Organization disability assessment Schedule; CDSE: Chronic Disease Self-Efficacy subscale; GOV: government; Reduced physical activity includes responses of 'little less' or a 'lot less'; IQR: inner quartile range; Statistical comparisons between groups were conducted using the Kruskal-Wallis test for continuous variables between four groups, the Mann Whitney-U test for continuous variables between two groups, and the Chi square test for categorical variables. * Indicates significant differences of p≤0.01 between the decreasing, increasing, or fluctuating disability trajectory groups and the 'stable' trajectory group.*

8.5.2. Differences in characteristics between stable disability and increasing, decreasing, or fluctuating disability

Significant differences in baseline characteristics between each individual disability trajectory (increasing, decreasing, fluctuating) and the stable disability trajectory for basic ADLs, are presented in Appendix J. At baseline, all basic ADL and instrumental ADL disability trajectories (increasing, decreasing, fluctuating) were significantly associated with having poorer AKPS, more disabled in instrumental ADLs, greater difficulty mobilising**,** and ADL assistive device use for a greater number of ADLs.

8.5.2.1.Differences in characteristics between stable disability and increasing disability

Participants with increasing disability trajectories appeared to portray a less well population at baseline. For increasing disability in basic ADLs, participants presented with significantly greater prevalence of COPD or ILD, were more disabled in basic ADLs, had difficulty managing daily activities (specifically self-care, and household activities), reduced physical activity outdoors, and were more likely to be receiving hospice care, or occupational therapy, but not cancer treatment. Increasing instrumental ADL disability trajectories were significantly associated with difficulty managing daily activities (including self-care, getting along with people, household activities, and societal participation), in receipt of formal care, and current physical and social isolation.

8.5.2.2. Differences in characteristics between stable disability and decreasing disability

Participants with a decreasing basic ADL disability trajectory, had significantly higher symptom severity, greater disability in basic ADLs, and an increased likelihood of a hospital admission in the last month. Participants with a decreasing instrumental ADL disability

trajectory were more likely to have NSCLC, were more disabled in basic ADLs, had difficulty managing daily activities, and were under the care of a hospice.

8.5.2.3. Differences in characteristics between stable disability and fluctuating disability

Participants with a fluctuating disability trajectory in basic ADLs, were more disabled in basic ADLs at baseline. Participants with both a fluctuating basic ADL and instrumental ADL disability trajectory presented with general difficulty in daily activities and an increased likelihood of a hospital admission in the last month, the latter of which may be responsible for a temporary improvement in disability.

8.6. Relationships with the increasing disability trajectory

The univariable and multi-variable analyses between explanatory variables and the increasing disability trajectory in basic ADLs (n=97) and instrumental ADLs (n=82) are presented in tables 8.4 and 8.5 respectively. Functional performance status (AKPS) and total difficulty (WHODAS-2.0) were therefore eliminated from the models due to collinearity with symptom severity (POS-S). The WHODAS-2.0. summary score was replaced with the WHODAS-2.0. mobility domain.

Table 8.4: Associations with an increasing disability trajectory in basic ADLs

Participant characteristics and outcomes at baseline	Univariable associations (n=97)			Multi-variable associations (n=97)		
	odds ratio	95% CI	p-value	odds ratio	95% CI	P-value
❖ **Health-related factors**						
NSCLC	0.28	0.11 - 0.72	**0.009**	0.82	0.72 – 9.38	0.87
Stage IV	0.98	0.38 – 2.49	0.96	-	-	-
Charlson comorbidity Index score	0.85	0.75 - 0.98	**0.01**	0.9	0.72 – 1.11	0.33
❖ **Body Functions and Structures**						
Australian Karnofsky Performance Status (AKPS)	0.96	0.92 - 0.99	0.02	-	-	-
Symptom severity (Palliative care Outcome Scale-symptoms)	1.1	1.02 - 1.19	**0.01**	1.05	0.93 - 1.18	0.72
Pain	1.03	0.64 - 1.63	0.91	-	-	-
Shortness of breath	1.62	1.06 - 2.49	0.03	-	-	-
Weakness or lack of energy	1.41	0.90 - 2.19	0.13	-	-	-
Nausea	1.24	0.71 - 2.15	0.44	-	-	-
Vomiting	2.19	0.81 - 5.92	0.12	-	-	-
Poor appetite	1.69	1.02 - 2.82	0.04	-	-	-
Constipation	1.99	1.09 - 3.64	0.03	-	-	-
Mouth problems	1.17	0.64 - 2.12	0.61	-	-	-
Drowsiness	1.27	0.83 - 1.93	0.27	-	-	-
Immobility	2.92	1.84 - 4.66	**<0.001**	-	-	-
Receiving cancer treatment	0.29	0.11 - 0.77	**0.01**	6.57	0.54-79.83	0.14
On oxygen therapy	3.15	1.07 - 9.27	0.04	-	-	-
❖ **Activity and participation**						
Total Barthel Index score (BADLs)	0.74	0.59 - 0.92	**0.007**	1.06	0.72-1.55	0.77
Lawton Brody Instrumental ADL score (IADLs)	0.64	0.49 - 0.84	**0.001**	0.92	0.59-1.47	0.75
WHODAS Summary score	1.04	1.01 - 1.06	**0.008**	-	-	-
Cognition	1.11	0.97 - 1.27	0.12	-	-	-
Mobility	1.25	1.12 - 1.39	**<0.001**	1.13	0.96 - 1.33	0.15
Self-Care	1.18	1.02 - 1.37	0.03	-	-	-
Getting along with people	1.04	0.92 - 1.16	0.55	-	-	-
Household activities	1.17	1.06 - 1.29	**0.001**	-	-	-
Societal participation	1.06	0.97 - 1.15	0.2	-	-	-
❖ **Personal Factors**						
Age	1.07	1.01 - 1.14	**0.01**	1.07	0.99 - 1.15	0.09
Female	0.8	0.30 – 2.12	0.66	0.89	0.26 – 3.08	0.86
White British	0.81	0.14 - 4.47	0.81	-	-	-
Education above secondary school	0.73	0.29 – 1.86	0.5	-	-	-
CDSE: Confidence to receive help	1.1	0.74 – 1.63	0.64	-	-	-
❖ **Environmental factors**						
Lives alone	1.39	0.53 – 3.65	0.5	1.1	0.27- 4.49	0.9
Property with stairs	0.56	0.2 – 1.55	0.26	-	-	-
Months spent in physical and social isolation	1.21	1.04-1.43	0.02	-	-	-
Hospice patient	5.33	1.87- 15.14	**0.002**	3.05	0.54 – 17.21	0.21
Total number of ADL devices	1.49	1.17 - 1.90	**0.001**	1.34	0.89 – 3.02	0.17
Reduced physical activity indoors	0.87	0.34 – 2.2	0.77	-	-	-
Reduced physical activity outdoors	0.87	0.34 – 2.23	0.77	-	-	-
Constant (Increasing disability trajectory)	-	-	-	**0.00009**	**2.75e-09 – 3.02**	**0.08**

NSCLC: non-small-cell lung cancer; ADL: activities of daily living; BADL: Basic activities of daily living; IADL: instrumental activities of daily living; WHODAS: World Health Organization disability assessment Schedule; CDSE: Chronic Disease Self-Efficacy subscale; Reduced physical activity includes responses of 'little less' or a 'lot less'; Variables included in the multi-variable logistic regression were either continuous or dichotomous; Variables were selected for the multi-variable model if they had significance level of p≤0.01 in univariable logistic regression, were considered important factors in the systematic review, and did not show collinearity with other variables in the model.

Table 8.5: Associations with an increasing disability trajectory in instrumental ADLs

Participant characteristics and outcomes at baseline	Univariable associations (n=82)			Multi-variable associations (n=82)		
	odds ratio	95% CI	P-value	odds ratio	95% CI	P-value
❖ **Health-related factors**						
NSCLC	0.48	0.18 - 1.23	0.13	6.02	1.01 – 35.84	0.05
Stage IV	0.73	0.29 – 1.79	0.49	-	-	-
Charlson comorbidity Index score	0.93	0.83 - 1.04	0.18	-	-	-
❖ **Body Functions and Structures**						
Australian Karnofsky Performance Status (AKPS)	0.92	0.88 - 0.96	**<0.001**	-	-	-
Symptom severity (Palliative care Outcome Scale-symptoms)	1.15	1.05 - 1.27	**0.002**	1.03	0.89 - 1.2	0.69
Pain	1.9	1.23 - 3.25	**0.005**	-	-	-
Shortness of breath	1.59	1.08 - 2.3	0.02	-	-	-
Weakness or lack of energy	1.53	1.03 - 2.29	0.03	-	-	-
Nausea	2.38	1.06 - 5.32	0.04	-	-	-
Vomiting	-	-	-	-	-	-
Poor appetite	2.38	1.28 -4.39	**0.006**	-	-	-
Constipation	1.82	1 - 3.46	0.07	-	-	-
Mouth problems	1.56	0.82 - 2.96	0.17	-	-	-
Drowsiness	1.16	0.77 - 1.76	0.48	-	-	-
Immobility	2.11	1.36 - 3.27	**0.001**	-	-	-
Receiving cancer treatment	0.43	0.17 - 1.06	0.07	-	-	-
On oxygen therapy	2.2	0.55 - 8.8	0.27	-	-	-
❖ **Activity and participation**						
Total Barthel Index score (BADLs)	0.8	0.64 - 1.0	0.05	0.86	0.62 - 1.21	0.4
Lawton Brody Instrumental ADL score (IADLs)	0.67	0.47 - 0.96	0.03	1.38	0.8 - 2.37	0.25
WHODAS Summary score	1.05	1.02 - 1.08	**0.001**	-	-	-
Cognition	1.15	0.96 - 1.36	0.12	-	-	-
Mobility	1.28	1.14 - 1.45	**<0.001**	1.41	1.14 - 1.74	**0.002**
Self-Care	1.22	1.02 - 1.46	0.03	-	-	-
Getting along with people	1.23	1 - 1.28	0.06	-	-	-
Household activities	1.18	1.03 - 1.31	**0.01**	-	-	-
Societal participation	1.11	1.03 - 1.21	**0.009**	-	-	-
❖ **Personal Factors**						
Age	1.01	0.97 - 1.06	0.6	0.99	0.93 - 1.05	0.76
Female	1.27	0.51 - 3.13	0.61	0.98	0.29 - 3.25	0.96
White British	0.36	0.04	0.37	-	-	-
Education above secondary school	0.43	0.17 - 1.06	0.07	-	-	-
CDSE: Confidence to receive help	0.89	0.65 – 1.21	0.46	-	-	-
❖ **Environmental factors**						
Lives alone	0.48	0.19 - 1.22	0.12	0.49	0.14 - 1.72	0.27
Property with stairs	0.52	0.18 – 1.51	0.23	-	-	-
Months spent in physical and social isolation	1.07	0.92 - 1.28	0.31	-	-	-
Hospice patient	4.29	1.13 - 16.24	0.03	-	-	-
Total number of ADL devices	1.42	1.08 - 1.87	**0.01**	1.06	0.68 - 1.64	0.81
Reduced physical activity indoors	2.76	1.1 – 6.9	0.03	-	-	-
Reduced physical activity outdoors,	3.36	0.34 – 1.48	**0.01**	2.02	0.62 – 6.61	0.25
Constant (Increasing disability trajectory)	**-**	**-**	**-**	**0.02**	**3.47e-06 – 148.07**	**0.4**

NSCLC: non-small-cell lung cancer; ADL: activities of daily living; BADL: Basic activities of daily living; IADL: instrumental activities of daily living; WHODAS: World Health Organization disability assessment Schedule; CDSE: Chronic Disease Self-Efficacy subscale; Reduced physical activity includes responses of 'little less' or a 'lot less'; Variables included in the multi-variable logistic regression were either continuous or dichotomous; Variables were selected for the multi-variable model if they had significance level of p≤0.01 in univariable logistic regression, were considered important factors in the systematic review, and did not show collinearity with other variables in the model.

8.6.1. Relationships with the increasing disability trajectory in basic ADLs

The univariable logistic regression identified that participants with increasing disability trajectories in basic ADLs were more likely to have COPD or ILD. This was reflected by a lower Charlson Co-morbidity Index score, which gives participants a higher score if they have a cancer diagnosis and metastases. At baseline, participants in this group were older, had greater disability in basic ADLs, had more difficulty managing daily activities (specifically mobility and household activities), and higher symptom severity (specifically immobility). In addition, these participants were less often undergoing cancer treatment (chemotherapy, radiotherapy, or immunotherapy), more often under the care of a hospice and used assistive devices for a greater number of ADLs. None of these associations remained significant in multi-variable analysis (n=97), therefore no independent predictors of increasing disability trajectories in basic ADLs were identified.

8.6.2. Relationships with the increasing disability trajectory in instrumental ADLs

Participants with increasing instrumental ADL disability trajectories were found by univariable analysis to be significantly associated with lower AKPS, greater difficulty in daily activities (specifically mobility, household activities, and participating in society), and use of assistive devices for a greater number of ADLs. Higher symptom severity, particularly from a combination of symptoms (immobility, pain, and poor appetite), contributed to increasing disability in instrumental ADLs. The multi-variable logistic regression model (n=82) adjusting for these factors showed that difficulty mobilising (odds ratio, 1.41 [95%CI: 1.14-1.74], p=0.002) was associated with an increasing instrumental ADL disability trajectory.

8.7. Summary

In this chapter, group-level and individual trajectories of disability in basic and instrumental ADLs have been presented. Group-level trajectories did not show any change in disability in ADLs over time across the whole sample but appeared to show patients with NSCLC maintain greater independence than patients with COPD or ILD. Individual trajectories uncover change in disability that is missed at a group-level, where patients with either NSCLC, COPD or ILD may present with a trajectory of increasing, decreasing, fluctuating, or stable disability.

It appears change in disability occurs more in instrumental ADLs more than basic ADLs in this population. Almost half of individual disability trajectories in basic ADLs presented as stable, and a third of individual disability trajectories in instrumental ADLs presented increasing disability. Compared to a stable disability trajectory in basic ADLs, increasing disability trajectories represent a less well population, decreasing disability trajectories often occur following clinical intervention, and fluctuating disability trajectories may be in response to Covid-19 restrictions on social interaction. Approximately one third of participants had missing timepoints due to withdrawal or loss to follow-up, not specific to any one disability trajectory. Although including participants with a minimum of three completed timepoints attempts to increase generalisability, important change may have been missed which could have potentially altered a participants disability trajectory classification.

Findings fit the WHO-ICF model, where increasing disability in basic or instrumental ADLs resulted from a combination of health-related factors, and personal and environmental factors. Difficulty mobilising was the only independent predictor of increasing disability in ADLs. Associations with increasing disability identified in this study should be interpreted with caution. Participants who were less healthy were likely to be excluded from the longitudinal

analysis (which mostly affected NSCLC patients), or present missing timepoints in the individual trajectories where a change in disability would potentially be missed. Comparisons are made to the stable disability trajectory which may have some similarities to the increasing trajectory group relating to the impact of Covid-19 restrictions, and therefore disguise possible relationships with increasing disability. It is apparent in participants not included in the longitudinal analysis, that they present with greater mobility limitation and symptom severity than included participants, which might have strengthened these associations with increasing disability if they contributed longitudinal data.

The dependent variable in this longitudinal analysis is a trajectory of disability in basic or instrumental ADLs. It might be enlightening in future analysis of these data to explore incidence of increasing or decreasing disability (month by month) to discover predictors along the trajectory rather than being limited to predictors at the beginning of the trajectory. This type of analysis could uncover factors associated with an individual episode of change in disability rather than consistent increase in disability over time. This may be subject to a change in symptom severity, or an increased use of assistive devices for ADLs. These longitudinal data may also be used to identify the impact of a trajectory or incidence of increasing disability in ADLs, such as hospital admission or increased formal or informal care.

The implication of findings from the cohort study, study limitations, and recommendations for clinical care will be discussed in chapter 9.

Chapter 9

Discussion

9.1. Introduction

This chapter will present a summary of the main findings arising from the thesis in relation to objectives 1, 2 and 3, which will be discussed in the context of the wider literature. Strengths and limitations of this work will be considered along with methodological reflections. The chapter then considers the implications of these findings for clinical care to meet objective 4.

9.2. Summary of main findings

Until now, trajectories of disability in ADLs in advanced cancer or respiratory disease were understudied and poorly understood. This has led to challenges in the delivery and timing of rehabilitation interventions to help prevent, maintain, or improve independence, and reduce or delay the need for formal care. The body of research presented in this thesis has generated new knowledge to help address this evidence gap. Ten main findings are highlighted below in relation to the first three objectives.

9.2.1. Prevalence of disability in ADLs (objective 1)

1. Disability in ADLs is present in over half of participants with advanced cancer or respiratory disease. Instrumental ADLs (71%) are more commonly affected than basic ADLs (52%).
2. People with advanced NSCLC, COPD or ILD presenting without disability in ADLs often report difficulty managing ADLs independently.

9.2.2. Cross-sectional associations with disability in ADLs (objective 2)

3. Symptom severity is consistently associated with disability in ADLs. This was evident for basic ADLs in the secondary data analysis of the IARE studies and the cross-sectional analysis of the cohort study. The latter also found an association with disability in instrumental ADLs.
4. In the cohort study, people with COPD or ILD were more likely than people with NSCLC to be affected by disability in both basic and instrumental ADLs.
5. During the Covid-19 pandemic, disability in basic ADLs was associated with longer time spent in physical and social isolation, directly related to government-imposed restrictions in the UK at the period of recruitment between March 2020 and January 2021.

9.2.3. Trajectories of ADL disability (objective 3)

6. Group-level trajectories show that disability in basic ADLs remained stable over time in this population, but people with COPD or ILD often followed a fluctuating trajectory in instrumental ADLs, whilst in people with NSCLC most often reported improving disability.
7. Individual trajectories show wide variation in ADL disability that is missed at group-level. These can be categorised into one of four identified trajectories of ADL disability: increasing, decreasing, fluctuating, or stable (incorporating independent or persistent trajectories).
8. Compared to people with stable ADL disability over time, people with increasing ADL disability trajectories have more advanced disease, decreasing ADL disability trajectories often occur following clinical intervention related to hospice care or a hospital admission, and fluctuating ADL disability trajectories may be in response to Covid-19 restrictions on social interaction.

9.2.4. Associations with increasing disability (objective 3)

9. Disability is complex and arises from a combination of personal, health and environmental factors.
10. Mobility limitation was an independent predictor of increasing disability in instrumental ADLs over the subsequent 6 months, after adjusting for diagnosis and baseline symptom severity, disability in basic and instrumental ADLs, age, sex, living alone, assistive device use, and reduced physical activity.

9.3. Discussion of main findings and contribution

9.3.1. Prevalence of disability

Prevalence of disability can be difficult to establish due to variations in the definition and measurement of disability in ADLs outlined in chapter 2. The novel contribution of this thesis was to differentiate and assess disability in terms of dependency and difficulty, and to extend current knowledge around prevalence in early-stage cancer or respiratory disease [4, 5] to the advanced stages of disease, in both basic and instrumental ADLs.

Firstly, in the cohort study, prevalence of disability in basic ADLs in terms of dependency affected 52% of people with advanced NSCLC, COPD or ILD. In NSCLC participants, findings in the cohort study reflected findings in a systematic review [5], affecting 31% and up to 35% of participants with cancer, respectively. In the secondary analysis of older people in the IARE studies, which included predominantly participants with advanced cancer, 79% of the population presented with disability in basic ADLs, which was considerably greater than the cohort study or the systematic review. Comparatively, prevalence of disability in basic ADLs in advanced COPD or ILD was found to be a lot greater in the cohort study than identified in

the systematic review [5], affecting 77% and up to 50% of participants with respiratory disease, respectively. This suggests older people with advanced cancer, or people with advanced respiratory disease are more likely to present with disability in basic ADLs than people with early-stage disease. Greater disability in the older population (IARE) could also be due to purposeful sampling of older frail individuals in the IARE studies, a clinical syndrome known to be associated with, and sometimes defined by, disability [196, 197].

Secondly, the cohort study extends knowledge of prevalence of disability (dependency) beyond basic ADLs in the IARE studies, to instrumental ADLs. Disability in instrumental ADLs (71%) was more prevalent than disability in basic ADLs (52%), supporting findings from a meta-analysis of disability in ADLs in cancer [4], but both seen to a greater extent in the advanced stages of disease. These findings confirm this level of disability to also be apparent in people with advanced COPD or ILD. The comparative data in disability prevalence also suggest that independence in instrumental ADLs may be lost prior to basic ADLs, but not explicitly so. In the community, housework is the most problematic type of disability [198], but it is not until disability affects basic ADLs, particularly bathing, that need for formal care is indicated [8, 102]. If disability is identified earlier by measuring disability in instrumental ADLs, timely intervention may delay disability in basic ADLs and potentially need for care [199].

Thirdly, participants who did not present with disability in terms of dependency, often had difficulty managing those activities independently. This supports observations in older populations where difficulty managing ADLs was found to be more prevalent than dependency [93]. People with advanced illness often wish to remain independent, for example to maintain their dignity or remain at home, no matter how difficult this may be [99],

which puts them at risk of a crisis such as a fall. Falls have been found to strongly relate to difficulty using the toilet and transfers [200]. Therefore, ADL disability may be missed if only measured as dependency. This is important to recognise as measuring dependency enables assessment of need for care but measuring difficulty may indicate need for an intervention that might prevent a future potential crisis or delay need for care.

9.3.2. Cross-sectional associations with disability in ADLs

Symptom severity was measured in the IARE studies and the cohort study and was consistently associated with disability in basic and instrumental ADLs. A prospective analytical study of 638 patients referred to a home care support team, supports this finding, where an individual's ability to manage at home prompting a referral was linked to symptom burden [52]. During the last year of life, symptoms restricting disability are common, and patients with a greater burden of restricting symptoms and number of disabilities in ADLs are increasingly likely to receive hospice care [101]. Higher symptom severity is also associated with a housebound status, reducing a persons' ability to carry out activities involving socialising and participating in the community [201]. This highlights the importance of understanding how symptoms may be restricting an individual's function when assessing disability.

As the secondary data analysis recruited predominantly cancer patients, any association with diagnosis was not observed. This came into light in the cohort study, where people with COPD or ILD were more likely to be affected by disability in ADLs than people with NSCLC. However, the prognosis of participants is unknown, and this finding may relate to where individuals were on their trajectory of disability at the point of study entry. Lunney et al 2003 [3] has

previously identified that people with organ failure including respiratory disease may experience fluctuating disability over a longer period than cancer patients, who present with sudden and rapidly progressive disability closer to death, as outlined in chapter 2, which may explain this finding.

Greater prevalence of disability in COPD or ILD compared to NSCLC may also be linked to the impact of the Covid-19 pandemic, where reduced activity in COPD or ILD was significantly greater than in NSCLC during the study recall period. However, even pre-pandemic, over time, physical activity in COPD has been shown to follow a downwards trajectory and exacerbated by sedentary behaviour [202], whereas reduced activity in advanced cancer is more often specifically related to cancer treatment [203]. During the pandemic, reduced physical activity was aggravated by physical and social isolation, known to be associated with functional decline [66]. These data reveal a relationship between disability in basic ADLs and time spent in physical and social isolation. This highlights the impact Covid-19 restrictions have had on this population, initially portrayed as feelings of vulnerability about catching Covid-19 [71], even after restrictions were lifted or removed. This reduced confidence to participate in normal daily activities transpires as deconditioning and functional impairment, leading to disability [59, 65]. Findings, highlight a potential escalation of deconditioning and disability in the study populations, making it an even greater concern than it may have been pre-pandemic.

9.3.3. Trajectories of ADL disability

9.3.3.1. Group-level trajectories of ADL disability

In advanced disease, population trajectories of disability have been mostly explored at group level, retrospectively from the time of death [3, 204, 205]. When looking at trajectories prospectively, at group-level, findings from the cohort study show that people with advanced NSCLC mostly maintained full independence and people with advanced COPD or ILD most often had persistent disability, in basic ADLs over time. Comparatively, the advanced NSCLC group most often follow an improving trajectory in instrumental ADLs, whereas advanced COPD or ILD followed a fluctuating trajectory at group level. This raises some speculation over findings from a systematic review of trajectories of terminal decline [14], where organ failure including respiratory disease follow a fluctuating trajectory and cancer follows a stable trajectory followed by sudden decline, as first suggested by Lunney et al 2003 [3]. Bearing in mind, trajectories of disability in the cohort study were prospective rather than retrospective from death, theses data may have represented the stable phase of the Lunney cancer trajectory. This may reflect the more chronic nature of NSCLC resulting from advances in cancer treatment keeping patients on a stable or even improving disability trajectory for a longer period, prior to sudden decline.

The 95% confidence intervals, when compared to the size of the median change over time in both diagnostic groups in the cohort study, were relatively wide, indicating variation in change in disability over time within the sample. Using disease-based criteria for study inclusion may be a limiting factor, as it is likely to increase the heterogeneity of the study population. In terms of prognosis some participants may be close to death, and some may not. This potentially leads to a range and diversity of symptoms and functional limitation. Changes over

time may be effectively diluted by this heterogeneity and eventual deterioration be less easy to identify using a prospective approach, unless participants are followed up until death.

However, the aim of this thesis is to improve the management of disability prior to death, not to understand the dying phase, which has been the aim of longitudinal studies in palliative care or the end of life [14]. As well as identifying different dying trajectories, these studies have been used to demonstrate the effectiveness of palliative care services to show that symptoms can be stabilised by these services in the last weeks of life [206].

Population-level ageing studies have shed some light on understanding disability over a longer period, using latent trajectory modelling. The Precipitating Events Project (PEP Project) of 747 community dwelling elders [16] assessed disability in ADLs monthly and drew trajectories in the last year of life [207]. Lunney's recent work on mobility trajectories in a population-based sample of 3075 participants aged over seventy [15], carried out 6-monthly assessments over three years. Despite differences in study design and data collection, both these studies have challenged the usefulness of clinical groupings for categorising disability trajectories. The authors argue that clinical diagnosis does not adequately predict the trajectory of ADL disability or decline in mobility in the last years of life. This supports findings from the systematic review in chapter 3 [191], reinforced by the cohort study analysis of individual trajectories of ADL disability, which do not follow a predictable pattern based on a diagnosis of advanced NSCLC or COPD or ILD.

9.3.3.2. Individual trajectories of ADL disability

The novel contribution of work from the cohort study is the exploration of individual trajectories of ADL disability. Individual trajectories in advanced disease populations are found to be more sensitive to individual change and variation over time than the population

mean or median [208]. Importantly, these show that people with a diagnosis of NSCLC or COPD or ILD can follow any one of the four main types of ADL disability trajectory (increasing, decreasing, fluctuating, or stable). This highlights the importance of studying the patterns of an individual's experience, as opposed to averaging all individuals' responses over time [189].

Lunney et al 2018 [15], identified five trajectories of decline in mobility over three years prior to death in older people: late decline, progressive disability, moderate disability, early decline, and persistent disability, which were not associated by diagnosis as previously discussed. Although these portray change in mobility, strong comparisons were made with change in three basic ADLs (transferring, bathing, and dressing). The late decline group were more likely to be younger and die in hospital, and the persistent disability group were more likely to be older, female, have multimorbidity, and die in a nursing home. However, trajectories were drawn from 6-monthly assessments and could possibly miss fluctuations that occurred within these 6-months, between assessments. Trajectories of ADL disability in this cohort study were drawn from monthly assessments over 6-months which fills this window and uniquely identifies four types of trajectories within it. However, the timing of the 6-month window for each participant prior to death is unknown due to heterogeneity of prognosis within the sample.

The majority of the 6-month trajectories of ADL disability (other than the stable trajectory) identified in this study, have fluctuations within them, which either fluctuate in an increasing or decreasing direction, or end with the same score as baseline (fluctuating trajectory). These may be important to consider as an intervening event may be responsible for a short-term deterioration (e.g. worsening symptoms) or improvement (e.g. medication review or provision of an assistive device).

Data from the cohort study uncovered notable differences between the ADL disability trajectory groups (increasing, decreasing, fluctuating) when compared to the stable group. Compared to people with stable disability over time, people with increasing disability trajectories have more advanced disease, for which declining function may be inevitable [201]. Decreasing ADL disability trajectories often occurred following clinical intervention, particularly relating to hospice care in the community or a hospital admission. This improvement may be due to the possibility that a hospital admission may have prompted a referral to intermediate care [133], or hospice services with access to specialist rehabilitation teams [11]. This may also be the case for temporary improvements along the fluctuating ADL disability trajectory, although these may also be in response to fluctuation in Covid-19 restrictions on social interaction.

The classifications of ADL disability trajectories were not without their limitations. Missing timepoints within individual trajectories could potentially affect the accuracy of classification. Also, trajectories of increasing or decreasing disability often had fluctuations within them and rarely follow a linear pattern of decline or improvement, which therefore goes unaccounted for. These could potentially be linked to other factors that intervene negatively or positively along the trajectory, rather than to a particular predictor earlier in the trajectory. The PEP project identified that the disabling process is characterized by multiple and possibly interrelated disability episodes, even over relatively short periods of time, and that disability often results when a vulnerable person is affected by an intervening event [16].

9.3.4. Associations with increasing disability in ADLs

The cohort study examined factors that predict a subsequent increasing disability trajectory in basic or instrumental ADLs, and found health-related, personal, and environmental factors were related, fitting the WHO-ICF framework [84]. Most influencing factors arising from these data are exploratory (univariable), signalling a potential relationship, and less robust than the mobility limitation finding. This confirms that disability is complex and generally the product of a combination of factors. However, healthy patient bias in the data may underestimate the effect some factors have on disability. Participants who were not included in the longitudinal analysis due to withdrawal or loss to follow-up presented with greater symptom severity and mobility limitation at baseline than included participants, which may possibly strengthen the relationship if these participants were included in the analysis.

9.3.4.1. Complexity of ADL disability

Increasing disability in ADLs was more likely to be associated to certain health-related factors, including a COPD or ILD diagnosis, greater symptom severity, lower AKPS, and participants who were not receiving cancer treatment. The latter finding may be due to not being fit for or having exhausted cancer treatment but could also reflect a COPD or ILD diagnosis as 91% of participants with NSCLC were receiving cancer treatment. The study did highlight specific univariable relationships between individual symptoms on the POS-S and increasing disability, including, immobility, pain, and poor appetite. There is a need for further investigation to fully comprehend the relationship between individual symptoms and disability as they could not be included in the multivariate analysis.

Older age was the only personal factor associated with increasing disability. Older age could be linked to other variables, such as frailty, falls, or multi-morbidities [2, 41, 200], all found to

be associated with increasing disability in the systematic review in chapter 3 [191]. Our study contradicted the systematic review by identifying a relationship between lower co-morbidity and increasing disability in this population, but this could be due to selected measurement. The Charlson Co-morbidity Index [176], used in the cohort study, grades severity of co-morbidity based on prognosis and scores cancer and metastases considerably higher than any other condition which may bias the findings. This finding may therefore reflect primary diagnosis rather than the number of co-morbidities. This measure may also be considered out-of-date, where prognosis and therefore weightings of some conditions approximately thirty years ago may differ to today, due to advances in treatments, survival, and an aging population. There is now an age-adjusted Charlson Co-morbidity Index (ACCI), but the weighting of conditions such as AIDS, cancer and respiratory diseases remains the same. An alternative approach to capturing multi-morbidity would be to use disease counts. Using a cut-off of two or more conditions as part of the definition of multimorbidity is widely adopted, however, this would not account for severity of disease.

Environmental factors relating to increasing disability were use of ADL assistive devices for a greater number of ADLs at baseline and being under hospice care, reflecting a less healthy population. This mirrors the health-related factors above, reinforcing the complexity of disability determinants. Further work is required to understand environmental factors that may cause, be a consequence of, or attenuate disability. Hospital admissions are known to be associated with declining function, as well as an implication of disability [191]. However, the cohort study identified an association between decreasing disability and hospital admission, which could be due to clinical intervention, rehabilitation referral, and/or provision of

assistive equipment, but further exploration of the data is warranted. It is possible that manipulation of the environment, such as use of a mobility aid, may enable a person to function within it, rather than an actual change to their functional impairment, as identified in the secondary data analysis (chapter 6) [209], and supported by the Health and Retirement Study [102].

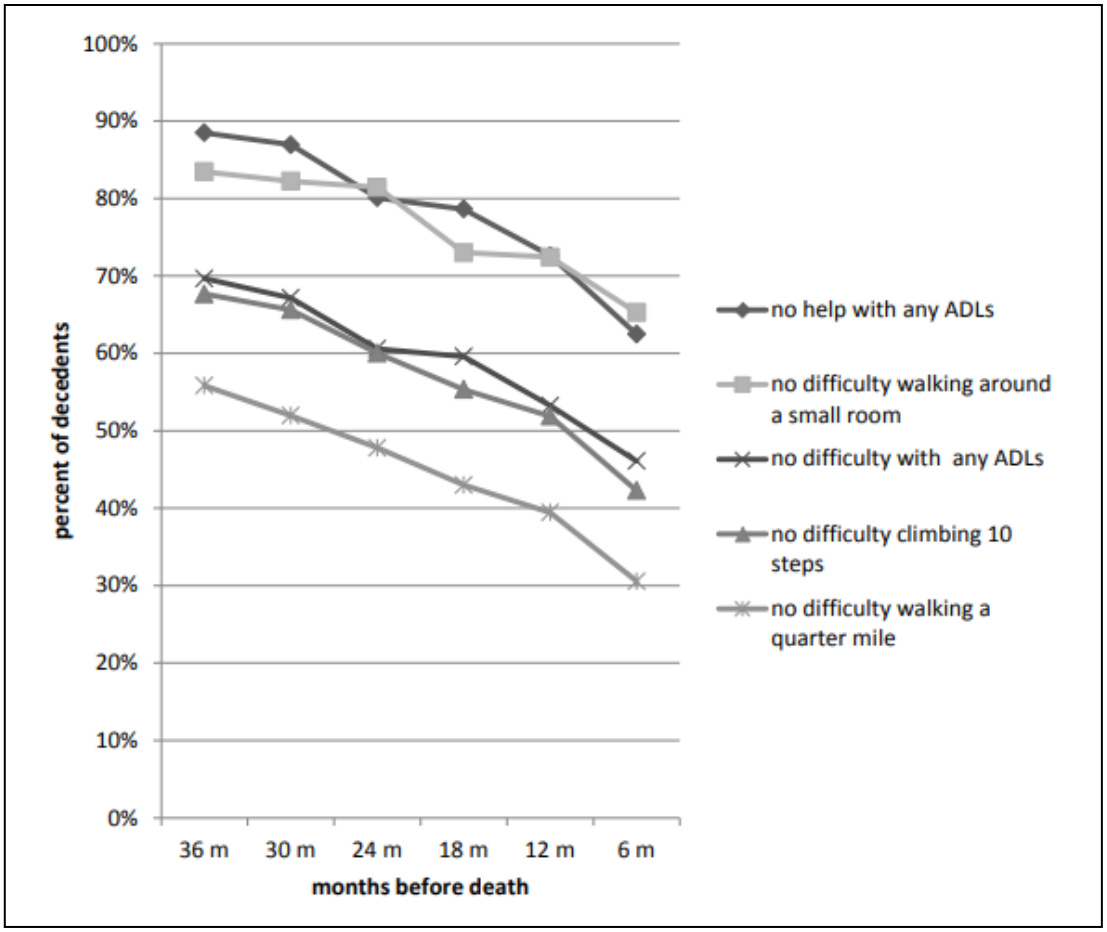
9.3.4.2. Mobility limitation

Mobility limitation is the only independent predictor of increasing disability in ADLs. Mobility limitation as a possible predictor of disability is supported by findings in a population study of trajectories of mobility over three years [15]. In this study, in addition to mobility trajectories, Lunney and colleagues explored several further trajectories, five in total, which included disability in three basic ADLs (transferring, bathing, and dressing). These were: i) no help with ADLs; ii) no difficulty walking around a small room; iii) no difficulty with any ADLs; iv) no difficulty climbing 10 steps; v) no difficulty walking a quarter mile (figure 9.1). At baseline, the most prevalent type of disability trajectory was difficulty walking a quarter mile, followed by difficulty with any ADLs and difficulty climbing 10 steps, which were both approximately 20% more prevalent than help with ADLs and difficulty walking round a small room. Over three years, the prevalence of each trajectory increased by approximately 30% and followed a similar pattern of decline. This suggests that the explicit order of loss of function or development of disability is: 1. Difficulty mobilising outside the home; 2. Difficulty with basic ADLs including stairs; 3. Dependency in basic ADLs.

The novel contribution of work in this thesis, is the ability to highlight mobility limitation as an independent predictor of increasing disability. Consequently, mobility limitation may be viewed as a 'tipping point' for declining function. Understanding 'tipping points' as times of

change or transition when care can be maximized to improve outcomes most effectively can only be uncovered by longitudinal research. Mobility limitation may be such a 'tipping point' or transition, where rehabilitation interventions can be targeted to provide most benefit. This is supported by a systematic review [210] which found that identifying risk for mobility limitation in older adults can be accomplished through routine screening, and functional deficits and environmental barriers can be addressed with proprioceptive exercise and mobility devices, leading to improved function, safety, and quality of life. Findings in this thesis suggests that screening for mobility limitation should be extended to people with advanced cancer or respiratory disease and not limited to older age.

Figure 9.1. Decline compared among function variables for the entire sample (n=1410) [15].



[Credit: Lunney et al, 2018, published with permission from John Wiley and Sons Limited (Journals) [15]]

The concept of difficulty preceding dependency aligns with Gore et al [199], who proposed the framework of, compression of functional decline (CFD), based on the latest understanding of the hierarchy of age-related functional decline [211, 212]. In the CFD model, the trajectory of disability in ADLs represents the stages through which an individual progresses through the disablement process, encountering difficulty with, or inability to perform each of the fifteen activities in the hierarchy, independently [199]. The model highlights that use of preventative interventions at the right time, can potentially compress the trajectory of disability into a shorter timeframe.

The CFD model is demonstrated in healthy aging and may be slightly different in advanced cancer or respiratory disease, where compression of disability could potentially fluctuate in line with episodes of deterioration. In addition, although there can be a hierarchical pattern in loss of independence in ADLs, the order can be affected by the sample studied, the choice of response options for each item, the selection and number of items in the scale, and the type of scaling procedure [213]. This is reflected in data from our cohort study which showed a slightly different hierarchical pattern than the one used in the CFD model.

9.4. Methodological reflections

This section evaluates the quality of the primary research, to fully understand the contribution and implications of the prospective cohort study. The strengths and limitations of this study are discussed and reflected on below, identifying learning points for future research.

9.4.1. Planning and design

9.4.1.1. Study design

A prospective cohort study design was the most appropriate design choice to distinguish cause of ADL disability and its change over time, and the cross-sectional element could most efficiently determine prevalence of ADL disability [147]. The design of the prospective cohort study was strengthened by preliminary work in the form of a systematic review (chapter 3) which helped select the most appropriate methodology, that would also be feasible within the time available. The 6-month follow-up is shorter than other large longitudinal studies, but longer follow-up was impractical in the timeframe. Trajectories of disability may differ if follow-up was longer or continued until death. Follow-up till death is very challenging and is often drawn from retrospective data [3], proxy-reported [204], or from less regular assessment [15]. A strength of this study is that prospective trajectories are drawn from patient-reported outcomes, at regular monthly intervals, allowing for identification of short-term change.

Concentrating on only quantitative methods rather than a mixed methods approach has allowed for a larger sample size. Additional qualitative methods may have created a dialogue between the different methods and enabled a deeper understanding of what the quantitative findings mean to participants, but this was beyond the aim of the thesis. In the IARE programme [214], a mixed-methods approach was used to explore stability of preferences using a combination of ranking and in-depth qualitative interviews. Stability of preferences was reinforced by care experiences and the presence of family support [214].

9.4.1.2. Population

It is important to consider the generalisability of the study population. The overall population of this thesis is advanced cancer or respiratory disease. Due to the wide variation of trajectories in different cancers and respiratory diseases, diagnoses were confined to NSCLC, COPD and ILD for the cohort study. Due to small numbers of ILD participants these were grouped with COPD as non-malignant respiratory disease and compared to NSCLC as malignant respiratory disease. Grouping the diagnoses in this way potentially limited comparisons between malignant (NSCLC) and non-malignant (COPD or ILD) respiratory disease, as COPD is known to be a long-term chronic condition [32], whereas ILD patients can have a much shorter prognosis [37].

Despite controlling for diagnosis in multiple regression analysis, there are various similarities and differences between NSCLC and COPD or ILD which may have affected study findings. Similarities include symptoms such as breathlessness, and physical and social isolation during the pandemic. Differences may occur if patients with NSCLC have an exacerbation of symptoms related to cancer treatment such as immunotherapy which may have a short-term impact on disability. A chest infection in COPD or ILD patients may cause an exacerbation of their condition which often results in unrecoverable disability. This makes it difficult to clearly identify differences in associations or predictors of disability in ADLs across and between diagnoses.

Disease-based criteria were used as an inclusion criterion for advanced disease. Disease-based criteria was chosen over prognosis, as estimating prognosis over 6-months is unreliable [215]. We had an exclusion criterion of an estimated life-expectancy of <1 month based on requiring repeated measures to study change in disability trajectories. This was reflected in

the sample, where 33 participants withdrew from the study in the first month, six of which were known to have died. Many of the participants would not have been included in the study if the life-expectancy was six-months in line with the length of follow-up. This would have reduced attrition but potentially worsened selective attrition and healthy patient bias.

Recruiting across twelve participating centres, from a range of clinical settings increased generalisability of study findings. This was reflected by the variation in social deprivation in the sample, where about half of all participants were educated above, or below secondary education. However, as this was a multi-site study use of postal code may have been a better indicator of social deprivation and this could have been considered when selecting recruitment sites to ensure that all social classes were included in the sample.

Despite effort to increase diversity of the sample, participants from ethnic minorities were under-represented. This was mainly due to limited resources which prevented the availability of questionnaires in different languages and development of culturally acceptable materials and specific targeting of ethnic minorities across sites. Consequently, the sample was almost entirely white-British, and disability in this group may be socially different to other ethnic groups [159]. Representation of ethnic minorities may have been improved through community outreach, closer engagement with these groups, and potentially availability of interpreters.

Unfortunately, it was not always possible to establish the reasons that potential participants declined participation, since the initial invitation was undertaken by the clinical teams, and reasons were not routinely given by those people declining. A further limitation in assessing representativeness was the inability to report clinical outcomes of non-participants. Non-participants may have greater disability and higher symptom prevalence. This limitation may

have biased the study conclusions towards slightly lower levels of disability and symptom severity.

9.4.1.3. Primary outcomes and measurement

The primary outcome measures of this study were the Barthel Index and Lawton Brody Instrumental ADL Scale. These measures were carefully selected based on the required criteria identified in the systematic review (chapter 3), which were to be, well validated, and consist of categorical responses. Selection was also strengthened by PPI feedback on several different instruments, confirming the Barthel Index and Lawton Brody Instrumental ADL Scale as the most appropriate measures for this study. However, the subjective nature of these measures over objective assessment, and response or recall from self-reported measures, may bias findings. Each of these tools have limitations which affect sensitivity to change. Issues with any scale that simply sums activities to form an overall disability score are that it suppresses valuable information on the order and timing in which individual activity loss accumulates and is unable to identify the specific ADL deficits [199]. To address this, the cohort study explored prevalence of individual ADL items and examined individual trajectories as well as summary trajectories at group-level.

Both outcome measures assess disability in terms of dependency but do not account for difficulty, so may underestimate disability. This implies that the Barthel Index and the Lawton Brody Instrumental ADL Scale may have a ceiling effect by excluding difficulty, as participants scoring the highest score, indicating full independence, may still have difficulty performing that activity. This was addressed in this study by including the WHODAS-2.0. questionnaire in the survey which measures disability in terms of difficulty. Strong evidence exists that

including questions about difficulty and dependency provide complementary information, that together can more fully depict the continuum of disability [216].

Items on the Barthel Index vary regarding whether being 'independent' includes the use of an assistive device. This is the case for 'mobility' on the Barthel Index but is not specified for the other ADL items on the measure, and therefore open to interpretation, potentially causing variation and inconsistency in responses. A systematic review [91] of approaches to measuring assistive device use in late life in National Surveys found that people often report using an assistive device but report no difficulty with that activity. If assistive device use and rates of difficulty or dependency were combined, the prevalence of disability would significantly increase [91]. Despite collecting assistive device use these data were not used in the estimates of disability prevalence in this study.

The Lawton Brody Instrumental ADL Scale presented some missing items, mostly in relation to online shopping. This highlights the need to modernise some responses in this measure to accommodate new technologies that may help people to manage daily activities independently. Where indicated, the researcher (LF) classed online shopping as independent, but to other participants, interpretation of whether online shopping is 'independent' is subjective, again possibly causing an inaccurate response. Also, participants may have responded differently to certain instrumental ADL items if they were not affected by Covid-19 restrictions.

9.4.1.4. Explanatory variables

The use of the WHO-ICF framework in combination with findings from the systematic review (chapter 3), strengthened selection of the most relevant or under-researched variables. The systematic review identified an evidence gap in how symptoms and use of assistive devices

relate to disability. The POS-S was selected to measure symptom severity, which is a validated and widely used measure for assessing symptoms in palliative care [217]. Collection of assistive device use was strengthened by using an approach used in national surveys of assistive devices, where the device is linked to a particular ADL activity [91], rather than a listing approach which does not identify which ADL activities the device is used for. However, this was analysed as a collective (devices used for a total number of ADLs). It may have been enlightening to look at relationships between whether equipment was used for an individual activity (e.g., mobility aid used for walking) and disability. This would help to support the finding in the IARE study (chapter 6) which suggested disability could be attenuated by use of a mobility aid and increase understanding of environmental factors.

There are several variables highlighted by the systematic review which could potentially relate to disability in ADLs but were not investigated due to feasibility. These include frailty, weight-loss, falls, depression, and infection or exacerbation [191]. Of relevance to this study, findings showed that increasing disability relates to reduced appetite which could imply weight loss, and a measure of sarcopenia may have identified this. Symptom severity was collected but this does not include any information regarding exacerbation, which is highly relevant in a respiratory disease population and potentially related to disability.

9.4.2. Data collection

9.4.2.1. Recruitment

Opening of recruitment sites was initially delayed due to ethical approval taking longer than expected. The study opened the first two sites on the 1st of March 2020 but closed two weeks later due to the declaration of the Covid-19 pandemic. The study design meant it could be

easily adapted into a study investigating the impact of Covid-19, and adopt remote practices required to conduct research during this time. This enabled the study to re-open four months later, allowing collection of unique data related to the impact of the pandemic in this population. Accordingly, knowledge from this study is of relevance to the Covid-19 pandemic (incorporated publication 3) [218]. It was highlighted in a journal editorial [219] as one of the first primary studies into the indirect effects of the pandemic on disability in advanced respiratory disease.

Due to the delay in opening study recruitment, to recruit the required sample size by the end of 2020 as prespecified, the number of participating centres was increased to twelve. Setting up and co-ordinating twelve sites was time consuming. Identifying and recruiting participants over the telephone was also more challenging than face-to-face at a clinical appointment. Fluctuating Covid-19 restrictions over the recruitment period meant local research staff were not always available to assist due to deployment and prioritization of Covid-19 vaccination studies. This led to varying recruitment across sites.

Despite the above challenges, the required sample size of 200 participants was reached within six months of the study re-opening. This was achieved through close regular engagement with the research sites. Additionally, the researcher (LF) assisted with recruitment where required. It was also evident that sites where LF engaged directly with the clinical team, had a much better participant identification rate than other sites, proving these relationships are essential to successful study recruitment. Recruitment was also strengthened by PPI involvement, where PPI members assisted with designing clinical materials and patient facing documents. This helped to engage potential participants, and to ensure that study materials were easily understood.

9.4.2.2. Follow-up

Follow-up assessment was conducted monthly over 6 months. Attrition was no more than expected in longitudinal studies in an advanced disease population [195], demonstrating the success of efforts to reduce missing data. This was partly due to feedback from the pilot participants, which influenced follow-up procedures. Work with participants to explain the importance of correctly completed questionnaires to improve their completion and return was time-consuming and demanded sensitivity but was ultimately fruitful. The researcher (LF) came to know most participants (and some family members) quite well, and the monthly telephone calls often included a social element, which was particularly appreciated by participants who were physically and socially isolated during the pandemic. This personal contact is likely to have helped considerably to maximize and maintain follow-up [220].

Covid-19 restrictions indirectly affected the return of postal surveys. The postal service was often unreliable during this time, and participants who were physically or socially isolating were unable to get to a post box and reluctant to ask for help to do so, which affected the timing of follow-up and sometimes caused a missed timepoint. These restrictions led to the number of participants requesting telephone follow-up to be higher than expected. Regardless of the pandemic, as identified in the systematic review (chapter 3), study completion may have been greater if all follow-up questionnaires were completed over the telephone instead of by postal survey, but this was not feasible in the time available. Some participants wrote additional comments next to questions in the survey, indicating a desire to elaborate. Including a free-text section at the end of the survey may have made participants feel that their opinions were valued, and possibly help reduce study withdrawal.

9.4.3. Analysis of longitudinal data

9.4.3.1. Trajectories of ADL disability

This study contributes to the understanding of longitudinal research of disability in advanced cancer or respiratory disease. Previous studies describing trajectories of disability in patients in the last years of life considered to be longitudinal studies, are in fact a collection of cross-sectional data calculated retrospectively from death [3, 221]. Formal longitudinal methods such as latent growth curve modelling (LGCM) have been used in large population-level studies of disability trajectories [15, 16]. LGCM is advocated as a better method of identifying individual change over time and can establish nonlinear growth trajectories (show increases or decreases over time), allowing more flexibility to estimate patterns of change [222]. However, it was not possible to conduct a large population-level study with a sample of sufficient size to utilize this method reliably.

The approach used to analyse the longitudinal data was visual graphical analysis (VGA), which can be useful for smaller sample populations [189]. This technique has been used successfully in this study to describe for the first-time individual trajectories of ADL disability in advanced NSCLC, COPD or ILD. This allows valuing the richness of the data and describing the change over time in individual participants. Although limited by its descriptive nature, VGA delineates the considerable difference between conclusions drawn from the trajectory of group-level statistics over several time points (based on averages of the whole study population), and conclusions drawn from individual trajectories in this study. Summary statistics reflect the average scores of the whole sample (group level), and the variation of the scores in the sample in reducing data to one single value. This is helpful to describe the characteristics of the whole sample but implies there is only one trajectory of ADL disability and masks the experience or trajectory of individual participants.

Missing data is common in longitudinal studies in advanced disease [195] and the 40% attrition rate in this study was anticipated [185] and considered in the sample size calculation. To attempt to reduce healthy patient bias, participants who completed three or more time points were included in the longitudinal analysis. However, participants not included in the analysis had worse symptom severity and mobility limitation at baseline than the included participants, which may have reduced the strength of this association. Greater withdrawal of participants with NSCLC than COPD or ILD was also apparent, affecting comparisons made across diagnoses. This would move rehabilitation in advanced disease away from reactive crisis management. Preventing a potential crisis such as a fall or hospital admission may not only help improve a patient's quality of life but reduce the burden on informal carers and health and social care services. However, the timing and delivery of preventative services for optimal outcomes need to be established.

In addition, missing timepoints in individual trajectories may be misleading. Reasons for missing a timepoint were collected, which mostly related to participants feeling unwell or being admitted to hospital. Therefore, important change may have been missed which could have potentially altered the classification of individual disability trajectories, potentially leading to inaccuracy in the analysis and subsequent associations and interpretations.

The strength of predictors of increasing disability may also be limited by comparisons made to the stable group. This group consisted of participants following either a trajectory of no disability (independent) or persistent disability, who could potentially have different characteristics. Participants with persistent disability may not differ greatly from participants with other disability trajectories. Also, given the blanket restrictions on social interaction at this time, it might not be possible to identify a relationship between increasing disability and

physical and social isolation. Identified predictors are also restricted by selected explanatory variables based on collinearity between co-variables. Functional performance status, and co-morbidity were excluded due to their collinearity with symptom severity, which could have been associated with ADL disability if included instead.

9.4.3.2. Additional data analysis

The primary variable in this analysis is the trajectory of disability in ADLs. Given the recognised differences between dependency and difficulty in measuring disability [15], it may have been helpful to compare individual trajectories of dependency to individual trajectories of difficulty using the WHODAS-2.0 domains [167]. However, there is no identified meaningful important clinical difference for the WHODAS-2.0. [174], making it difficult to identify what would be a meaningful change in score to categorise each trajectory. Also, findings showed a strong relationship between symptom severity and ADL disability at baseline, but a weaker association with increasing disability over time. Trajectories of symptom severity could have been drawn to see if an association exists between increasing symptom severity and increasing ADL disability over time.

The primary outcome variable: ADL disability trajectory, allows for predictors of an increasing ADL disability trajectory to be identified but does not allow exploration of intervening events along the trajectory which may account for the change [16]. To understand prospective data that due to lack of an anchor (other than study entry) has immense variation within the sample, other methods of analysing and interpreting these data could be beneficial. A secondary data analysis could be conducted on these data using alternative variables as the primary outcome, such as 'incidence' of disability in ADLs, or 'impact' of disability in ADLs. Incidence of disability would identify factors that contribute to change in disability between

each timepoint along the trajectory, to understand fluctuations in either direction. Impact of disability relates to associations between disability at baseline or increasing disability and the consequences of that disability, such as a hospital admission. As mobility limitation is the only independent predictor of disability, it might be particularly helpful to identify whether greater mobility limitation results in a rehabilitation referral or use of a new assistive device. This would help to further comprehend the relationship between disability and health-related and environmental factors.

9.5. Implications for clinical care

This research provides a better understanding of risk factors relating to disability in ADLs, how disability can be measured, and when intervention may be indicated in people with advanced lung cancer or respiratory disease. Based on findings, we would recommend: i) early referral to rehabilitation based on mobility limitation; ii) measurement of disability (dependency and difficulty) in both basic and instrumental ADLs; iii) integrated management of symptoms and function; and iv) investment in and further commissioning of specialist rehabilitation services. These clinical recommendations are discussed further in the subsequent sections.

9.5.1. Identifying risk of disability and referral to rehabilitation services

In advanced cancer or respiratory disease, it is important to identify risk of disability to prompt referral for intervention. Current rehabilitation services for people with advanced disease are often reactive rather than preventative, e.g., intermediate care post hospital discharge [133]. Clinical conditions are only one of many factors that influence the course of functional decline and disability, suggesting a need for interventions targeting function irrespective of diagnosis

or prognosis [15, 84]. Moving to a preventative model of rehabilitation, considering forthcoming decline in function, could help maintain independence or prevent or delay potential disability in daily activities. This would move rehabilitation in advanced disease away from reactive crisis management. Preventing a potential crisis such as a fall or hospital admission may not only help improve a patient's quality of life but reduce the burden on informal carers and health and social care services. However, the timing and delivery of preventative services for optimal outcomes need to be established.

This study has identified that mobility limitation in advanced cancer or respiratory disease, predicts increasing disability and this could therefore serve to identify a population in which to target preventative interventions, regardless of specific diagnosis or prognosis. Mobility limitation could be used to identify the right time to refer to rehabilitation services. The mobility domain of the WHODAS-2.0. [161] used in the cohort study, consists of five items of difficulty in: i) standing for long periods, such as 30 minutes; ii) standing up from sitting down; iii) moving around inside the home; iv) getting out of the home; v) walking a long distance, such as a kilometer. Every increase of one-point (scale of 5-25), significantly increases the likelihood of developing disability in ADLs. At baseline the median [IQR] score was 13 [9-17] for increasing ADL disability, 7 [5-10] for stable ADL disability and 13 [7-18] and 12 [7-15] for participants with decreasing or fluctuating ADL disability respectively. A score of 11 is greater than the upper-quartile of the stable trajectory and within the IQR of trajectories that do change and may be an appropriate cut-off for referral. As this is a deteriorating population, functional decline despite intervention identified by an increase of 1 in the WHODAS-2.0. mobility domain may prompt a review or re-referral.

Other mobility limitation measures are available [223] including, self-reported preclinical mobility limitation [224] and the Life-Space Assessment tool [225]. Lunney at el 2018 [15], found difficulty mobilising a quarter mile preceded difficulty in basic ADLs, and this single question may suffice to identify need for intervention. As identifying need for rehabilitation and lack of referral in advanced disease is a known barrier to receiving rehabilitation interventions [139], keeping the referral criteria as simple as possible is paramount. Careful work is required to understand thresholds for screening (e.g., severity of symptoms, and time spent in physical and social isolation), as well as to select appropriate screening tools and develop cut-offs for referral criteria (e.g., mobility limitation tools, items, or questions). Decisions regarding choice of tools and/or thresholds, may also depend on what available clinical services can offer, and adaptability may be essential for such a system to work effectively in clinical care.

9.5.2. Assessment of disability in ADLs

Findings have highlighted the importance of measuring disability in both basic and instrumental ADLs. Measurement of basic ADLs is currently encouraged in palliative care but not for instrumental ADLs [217]. However, if disability in ADLs is not fully measured then it may go undetected and therefore not be addressed.

When choosing measurement tools is it important to consider the aim of the intervention, which would be to: i) improve or maintain independence, ii) prevent or delay dependency and need for care, iii) prevent a crisis. As in this study, dependency in ADLs is often used to measure disability. However, as findings have suggested, difficulty in ADLs may pre-empt dependency. This has also been highlighted by Lunney and colleagues [15], who identified greater prevalence in difficulty managing ADLs than dependency in ADLs. Therefore, it is

important to consider difficulty in ADLs as well as dependency. By measuring difficulty, intervention to make that activity easier for the individual would be indicated, which would potentially delay dependency or avoid a crisis such as a fall [200]. If need for intervention is identified earlier this dependency could possibly be avoided or reduced (e.g., number of carers or frequency of visits), especially if individuals are reluctant to accept help from others.

Including questions about both difficulty and dependency in clinical care is recommended [95]. As discussed earlier, dependency measures such as the Barthel Index [163] and the Lawton Brody Instrumental ADL Scale [165] will underestimate a person's level of disability. Including a measure of difficulty such as the WHODAS-2.0. [166] would allow for a more thorough assessment. However, this is a lengthy tool, and some items on the measure were difficult for participants to answer in this study. There is a short version of the WHODAS-2.0. consisting of only 12 items, but this may not be a suitable alternative as many of the ADL items included in the full version are not included. A measure incorporating difficulty and dependency, while covering both basic and instrumental ADLs for this population, may be more practical to use within clinical care. Measurement of ADL disability including wording and structure, also needs to be consistent across major surveys, to ensure robust data are available to estimate needs of the population and the resources required to meet them [90].

9.5.3. Integrated management of symptoms and function

A combination of health-related factors, personal, and environmental factors likely contribute towards disability in ADLs supporting both the assumptions of the biopsychosocial model of disability and a comprehensive approach to rehabilitation [110]. The novel contribution of this work is the consistent relationship between symptom severity and disability in ADLs, implying assessment and management of symptoms and function need to go hand in hand.

Rather than treating symptoms in isolation to function, the impact each symptom has on a patient's daily activities needs to be considered to optimise active participation in essential and valued activities [99]. The impact of symptoms on function needs to be uncovered in the clinical assessment and rehabilitation as an intervention should be implemented alongside pharmacological management. Disability relating to restrictive symptoms has been found to significantly reduce in patients receiving multi-disciplinary care following a hospice admission [51]. This highlights the importance of the multidisciplinary team when approaching management of disability in advanced cancer or respiratory disease.

The IARE study also identified that greater disability was related to increased symptom burden, but disability could still be attenuated by the use of a mobility aid. This could apply to other types of assistive devices, such as a shower stool, to help ease breathlessness when washing. Also, with advances in technology this may also apply to systems such as online shopping, which may be a very welcome option in the event of fatigue. Therefore, an assistive device would enable an individual to continue to manage that task independently, despite persisting symptoms, and delay dependency on another person. This highlights the need to identify and address environmental factors in relation to a patient's restrictive symptoms, particularly the usefulness of an assistive device. However, implementation of assistive devices is not always appropriate due to small, cramped living spaces, and may not always be accepted by patients or carers, or not considered safe to use due to cognitive impairment or memory loss, rapid deterioration, or other hazards in the home. They also require patient and/or carer training to use, and self-management of symptoms often needs to be incorporated, such as breathing control exercises and pacing while using adapted railings to climb steps or stairs safely. Assessment and implementation of assistive devices therefore

requires advanced communication and problem-solving skills on behalf of the allied health professional.

9.5.4. Improved rehabilitation service provision

Based on the clinical implications discussed above, figure 9.2. presents an overview of clinical recommendations for the provision of rehabilitation services in advanced cancer or respiratory disease, to provide better care for these patients, to meet objective 4. This could include, targeted population, screening and referral criteria, rehabilitation assessment, approach, and targeted outcome.

Ultimately, rehabilitation requires more investment and existing services may not be able to cope with existing or anticipated demand. Pulmonary rehabilitation and cancer rehabilitation services could extend reach to patients with advanced disease, though this may require adaption of current programme delivery to accommodate fluctuating needs [226], including after hospitalisation [227], and during cancer treatment [228]. A randomised control trial of early rehabilitation in COPD patients admitted to hospital did not enhance recovery of physical function or reduce the risk of subsequent readmission following acute exacerbation over twelve months [229]. This indicates progressive exercise rehabilitation should not be started during the early stages of acute illness [229].

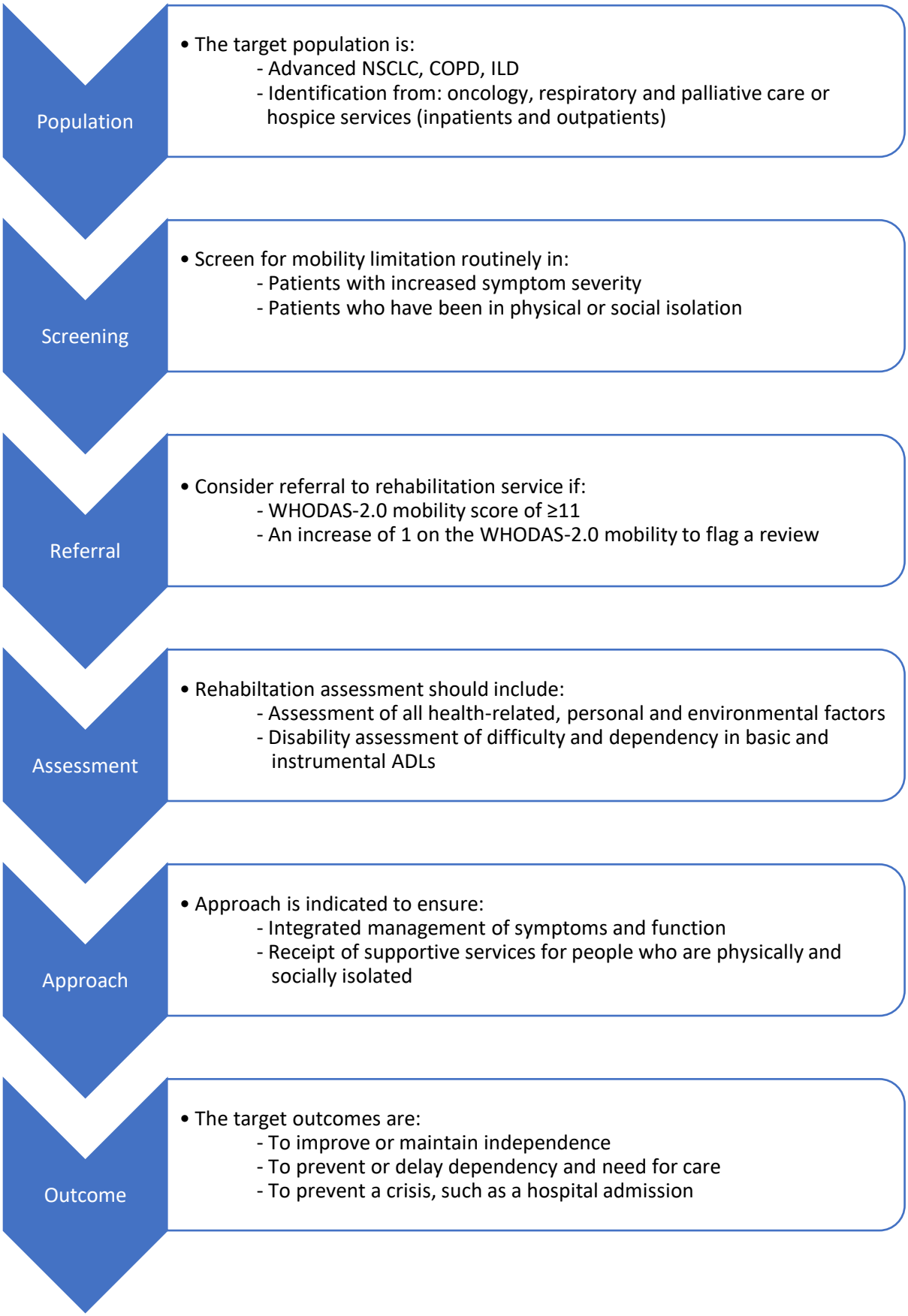
Intermediate care which focuses intervention on independence in ADLs to promote hospital discharge could also be more inclusive of advanced cancer or respiratory disease, but these short-term interventions have mixed effectiveness [132], and may not be appropriate for people with declining function. It has been highlighted that ‘a one size fits all’ approach to discharge bundles may not be appropriate for people with COPD and an individualised

approach may be required [230], which is likely to be echoed in cancer and other respiratory conditions. However, it should not take a crisis such as a hospital admission to prompt a rehabilitation referral in this population, by which time it may be too late to make a difference to a person's independence. It is much harder to regain loss of function than to prevent functional loss.

Addressing forthcoming functional decline in advanced disease before function is lost, can prevent or delay disability in daily activities. This is becoming essential to help people maintain independence, prevent a crisis, and reduce the pressure on health and social care services [231]. Developing services to target functional decline in advanced disease should be a priority. As the NHS-10-year plan [143] drives to improve the provision of community services, with the aim of keeping people at home for as long as possible, it may be opportunistic to support investment in new or improved services. This could be commissioned within palliative care services across acute trusts and hospices, adopting rehabilitation professionals as part of core palliative care teams rather than an optional extra.

Following a pragmatic approach, the goal of this research was to bring about the optimal level of improvement in patients' lives, by recommending development of the above interventions or services. The reality of implementing this vision will be limited by resources available in local health services and will require engagement from stakeholders including commissioners, service providers, and clinicians, across the care pathway, to ensure equity of service provision. Ultimately, further research is required to provide valuable evidence to support specific referral criteria and the effectiveness of rehabilitation interventions specifically targeting ADL disability, to be incorporated into national guidelines, in order for services to be nationally commissioned.

Figure 9.2. Clinical recommendations for provision of rehabilitation services in advanced NSCLC, COPD or ILD based on study findings



NSCLC: non-small cell lung cancer; COPD: Chronic Obstructive Pulmonary Disease; ILD: Interstitial Lung Disease; WHODAS-2.0: World Health Organization Disability Assessment Schedule, ADL: Activities of Daily Living

Chapter 10

Conclusion

This study makes a substantial contribution to the improved understanding of ADL disability in advanced cancer or respiratory disease, with implications for clinical care.

In the prospective cohort study, disability in ADLs was more often present than not in advanced NSCLC, COPD or ILD, affecting more than half of participants. Instrumental ADLs were more greatly affected than basic ADLs. Even participants presenting with no disability often reported difficulty managing some activities independently. Disability in ADLs is independently associated with increased symptom severity, non-malignant respiratory disease (COPD or ILD), and physical and social isolation. These findings are uniquely related to the Covid-19 pandemic, reflecting the real-world situation. The relationship between symptom severity and ADL disability is also supported by findings in the secondary data analysis.

Individual disability profiles and trajectories were diverse and participants with NSCLC, COPD or ILD could follow one of four individual trajectories: increasing, decreasing, fluctuating and stable ADL disability. These patient level differences were masked when looking at group-level disability trajectories. The prospective cohort study identified a range of health-related, personal, and environmental factors which contribute towards the development of disability. Mobility limitation was identified as an independent predictor of increasing disability, following adjustment for relevant factors.

Considering implications for clinical care, timing of rehabilitation interventions targeting disability in ADLs can be responsive to earlier indications of functional decline. A mobility

limitation tool could be used as a referral criterion. Screening for mobility limitation is especially indicated among people with advanced NSCLC, COPD or ILD who have increased symptom severity and/or have been physically or socially isolated. Measurement of difficulty and dependency is recommended in both basic and instrumental ADLs, as difficulty can identify need for intervention and dependency can identify need for care. The co-management of symptoms and disability should occur within rehabilitation services. Further investment into rehabilitation is required to address major unmet need in advanced cancer or respiratory disease.

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Appendices

Appendix A

Supplementary material for incorporated publication 1

Supplemental online material for:

Trajectories of disability in activities of daily living in advanced cancer or respiratory disease: A systematic review

Appendices

Appendix A: Search Strategy:

1 Palliative*.tw./

2 Exp "Terminal care"

3 "Terminally ill"

4 "End of life"

5 "Last year of life"

6 Advanced*.tw

7 Progressive*.tw

8 Hospi*/

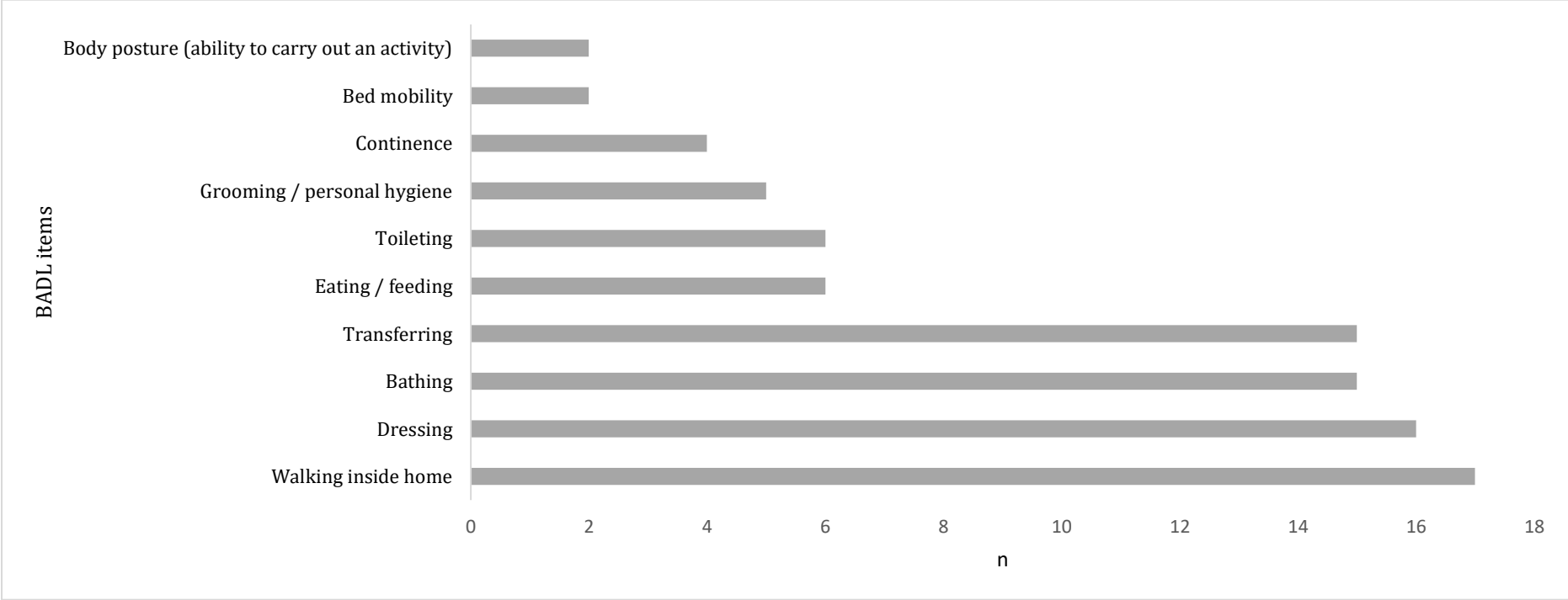
9 "Long term care"

10	“Nursing home”
11	Inpatient
12	Exp Bereavement/
13	Exp “attitude to death”
14	Trajectory/
15	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 12 OR 15
16	“Functional disabilities”
17	“Functional outcomes”
18	“Functional limitation”/ or restriction
19	“Functional performance”
20	“Functional status”
21	“Activities of daily living”
22	ADL/ or BADL/ or IADL
23	“International Classification of functioning, disability and health”/ or ICF
24	“Activity restriction”
25	“Participation Restriction”
26	“Performance status”
27	Mobility
28	Weakness
29	“Muscle weakness”
30	16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29

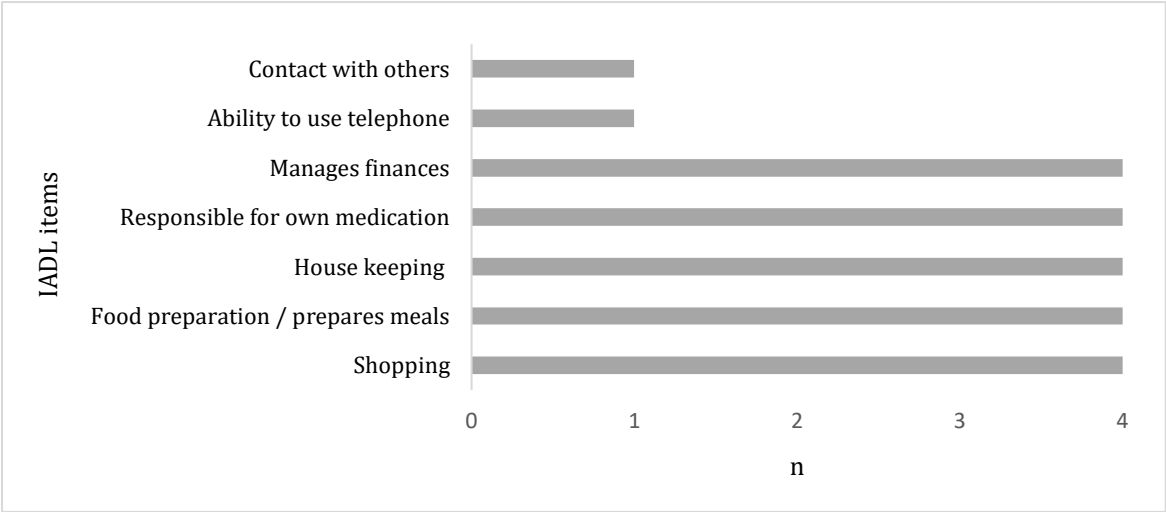
31	Longitudinal studies/ or Cohort
32	Adults
33	English only
34	31 AND 32 AND 33
35	15 AND 30 AND 34

Appendix B: Activities of daily living (ADLs) collected across studies

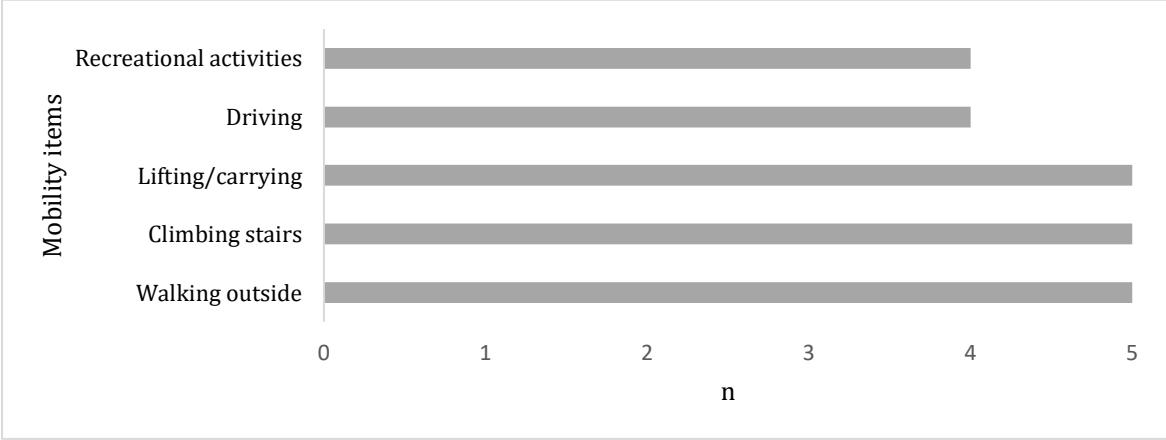
Appendix B1: Basic activities of daily living (BADL)



Appendix B2: Instrumental activities of daily living (IADLs)



Appendix B3: Mobility items



Appendix C: Critical Appraisal Skills Programme (CASP): (1a: Section A; 1b: Section B; 1c: Section C)

Appendix C1: CASP Section A: Are the results of the study valid? (Answer: Yes; No; Can't tell)

Study ID (first author and date)	1. Did the study address a clearly focused issue?	2. Was the cohort recruited in an acceptable way?	3. Was the exposure accurately measured to minimize bias?	4. Was the outcome accurately measured to minimize bias?	5.a) Have the authors identified all important confounding factors?	5.b) Have they taken account of the confounding factors in design/or analysis?	6.a) Was the follow up of subjects complete enough?	6.b) Was the follow-up regular enough
Ailshire 2015	Yes	Yes	Can't tell	Yes	Can't tell	Can't tell	Can't tell	No
Buurman 2016	Yes	Yes	Can't tell	No	Yes	Yes	Can't tell	Yes
Chen 2007	Yes	Yes	Can't tell	No	No	Yes	Yes	No
Covinsky 2003	Yes	Yes	No	No	Yes	Yes	No	No
Ferrucci 1997	Yes	Yes	No	No	Can't tell	No	No	No
Gill 2004	Yes	Yes	Can't tell	No	Yes	Yes	No	Yes
Gill 2009	Yes	Yes	Can't tell	No	Can't tell	Can't tell	Yes	Yes
Gill 2010	Yes	Yes	Can't tell	No	Yes	Yes	Can't tell	Yes
Gill 2013	Yes	Yes	Can't tell	No	Yes	Yes	Yes	Yes
Gill 2015	Yes	Yes	Can't tell	No	Yes	Yes	Yes	Yes

Janssen 2014	Yes	Yes	Can't tell	No	Yes	Yes	No	No
Lawrence 2017	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	No
McCarthy 2000	Yes	Yes	Can't tell	Yes	Can't tell	Can't tell	Can't tell	Can't tell
Medina-Mirapeix 2016	Yes	Yes	Can't tell	No	Yes	Yes	Yes	Can't tell
Nagurney 2017	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Can't tell	Yes
Nusselder 2005 and 2006	Yes	Yes	Can't tell	No	No	Can't tell	No	No
Somogyi-Zalud 2000	Yes	Yes	Can't tell	Yes	Can't tell	Can't tell	Can't tell	Can't tell
Stabenau 2015	Yes	Yes	Can't tell	No	No	Yes	Yes	Yes

Appendix C2: CASP Section B. What are the results? (Answer: Yes; No; Can't tell)

Study ID (first author and date)	7. What are the results of this study?	8. How precise are the results?	9. Do you believe the results?
Ailshire 2015	While some centenarians have poor health and functioning upon reaching 100 years of age, others can achieve exceptional longevity in relatively good health and without losing function.	No	Can't tell
Buurman 2016	Among older persons, distinct disability trajectories were observed in the year before and after admission to a skilled nursing facility.	Yes	Yes
Chen 2007	Dementia severity worsens in last year of life with little opportunity for improvement as death approaches. Cancer and organ failure show moderate disability until the last 3 months before death when patients experience rapid decline.	Yes	Can't tell
Covinsky 2003	Patients with advanced frailty, with or without cognitive impairment, have an end-of-life functional course marked by slowly progressive functional deterioration. Patients with cognitive impairment have particularly high rates of functional impairment at the time of death.	Yes	Yes
Ferrucci 1997	In the year when older persons become severely disabled, a large proportion are hospitalized for a small group of diseases.	No	Can't tell
Gill 2004	The likelihood of developing disability following illness or injury that leads to hospitalization was greater among people who were not physically frail than those who were physically frail. The likelihood of developing disability following an intervening event is higher in the physically frail.	Yes	Yes
Gill 2009	Older persons admitted to hospital following hospitalization are generally poor and only 20% are discharged home without disability.	No	Can't tell
Gill 2010	There was heterogeneity of disability trajectories within each disease classification group among older people in the last year of life.	Can't tell	Yes
Gill 2013	Relative to other disabling conditions, injurious falls are associated with worsening disability and a higher likelihood of a nursing home admission.	Yes	Yes
Gill 2015	Disability at the end-of life does not follow a predictable pattern, raising issues of cause of disability at the end-of-life.	Yes	Yes
Janssen 2014	Patients with advanced Chronic obstructive pulmonary disease (COPD), elderly patients, patients with frequent hospital admissions, and patients with an increased number of co-morbidities are at risk of an increase in care dependency.	No	Can't tell
Lawrence 2017	It is possible to use cause of death to shape trajectories of ADL disability. The research has demonstrated that changes in level of care need can be measured over time in populations of older nursing home residents.	No	No

McCarthy 2000	Patients dying with cancer become increasingly ill and experience functional decline as they approach death.	Can't tell	No
Medina-Mirapeix 2016	More than one third of patients hospitalized for acute exacerbation of COPD declined during the subsequent 12 weeks post discharge from hospital, with most decline occurring by 6-weeks post-discharge.	Yes	Can't tell
Nagurney 2017	Patients presenting to the emergency department and discharged had a worse functional course and higher nursing home admission than patients not presenting to the emergency department, but they had better outcomes than those who visited the emergency department and were hospitalized.	Yes	Can't tell
Nusselder 2005 and 2006	Findings suggest that disability is a dynamic process, and that important differences exist within the disabled population. .	Yes	No
Somogyi-Zalud 2000	Patients over 80 years who died within 1 year of enrolment had substantial comorbidity and reported a limited quality of life along with significant and increasing functional impairment.	Can't tell	No
Stabenau 2015	The care needs of many older persons especially those with a non-cancer diagnosis are substantial in the year before hospice admission.	Yes	Yes

Appendix C3: CASP Section C: Will the results help locally? (Answer: Yes; No; Can't tell)

Study ID (first author and date)	10. Can the results be applied to the local population?	11. Do the results of this study fit with other available evidence?	12. What are the implications of this study for practice?
Ailshire 2015	No	Yes	People may live longer if they have less disability and disease in their 80's. Disability is linked with disease burden.
Buurman 2016	No	Yes	Disability trajectories are associated with transitions of care. People with greater disability have a higher risk of re-admission to hospital and likelihood of dying in a nursing home. People with less severe disability are more likely to be allocated rehabilitation.
Chen 2007	No	Yes	The terminal trajectories of functional decline among long-term-care residents vary by underlying diseases. An understanding of these trajectories may be useful for clinicians and families caring for long-term-care residents near end-of life.
Covinsky 2003	No	Yes	Findings have important implications for the care provided for advanced cancer patients at the end-of life. Medicare limits benefits of palliative care to the last 6 months of life which may not be of benefit to patients with a long prolonged declining functional trajectory, and it would be difficult to predict when a patient enters the last 6 months of life.
Ferrucci 1997	No	Yes	Reduction of severe disability in the older population will depend on both prevention of diseases that cause disability and interventions in persons who develop these diseases. Such interventions range from routine medical care to intensive medical treatment and rehabilitation.
Gill 2004	No	Yes	Illnesses and injuries leading to either hospitalization or restricted activity represent important sources of disability for older persons living in the community regardless of physical frailty. These intervening events may be suitable targets for the prevention of disability.
Gill 2009	No	No	Only 20% of patients return home after a nursing home admission following hospitalization.
Gill 2010	No	Can't tell	The absence of a predictable disability trajectory based on the condition leading to death for most decedents poses challenges for the proper allocation of resources to care for older persons at end-of life. This also raises concerns about policies that establish benefits for end-of life care primarily on the basis of disease-specific criteria.
Gill 2013	No	Can't tell	Patients who were hospitalized following a fall injury had worse disability outcomes than those hospitalized for non-fall related reasons over a 6-month period and a higher likelihood of a long-term-care admission. Therefore, the prevention and treatment of injurious falls should be a high priority when decisions are made to allocate resources aimed at reducing the burden of disability in older persons.

Gill 2015	No	Can't tell	Knowledge of the course of disability influencing intervening events may facilitate clinical decision making at the end-of life regarding prevention and management of disability, particularly restorative interventions in the community and especially among patients who had previous disability.
Janssen 2014	No	Yes	Regular assessment of the level of care dependency is necessary in patients with organ failure to develop and adjust an individualized palliative care program that addresses the needs of patients with advanced chronic obstructive pulmonary disease (COPD), chronic heart failure and chronic renal failure and their families and improve quality of life.
Lawrence 2017	No	Yes	Further analysis is required to determine the degree to which individual characteristics, not included in the analysis are required to develop a predictive tool to assist clinicians when determining the optimal time to implement advanced care planning (ACP). Such knowledge will enhance the ACP conversation.
McCarthy 2000	No	Yes	Findings highlight shortcomings in the care of patients dying with cancer and important opportunities for improving the care of cancer patients at end-of life.
Medina-Mirapeix 2016	No	Yes	Findings have implications for hospital physicians and rehabilitation services. Efforts should be prioritized to rehabilitate frail patients. For patients who decline rehabilitation and don't recover, social services should be applied.
Nagurney 2017	No	Yes	Findings should encourage efforts to provide functional assessments and appropriate interventions for older people who present at the emergency department, and they support the need for further research to evaluate new models of care for this population.
Nusselder 2005 and 2006	No	Yes	Identifies care needs in disabled population and suggests possibilities for reducing the burden of disability in society.
Somogyi-Zalud 2000	No	Yes	Physical and emotional suffering, reduced quality of life, depression and caregiver burden are consequences of disability in activities of daily living.
Stabenau 2015	No	Yes	Progressive and persistent levels of severe disability substantially increase the care needs and rate of mortality of older persons. Greater access to palliative care could address these needs, while also offering symptom management, family support and advanced care planning.

Appendix B

Cohort study protocol

Comparing disability in activities of daily living over time
among adults with advanced lung cancer or respiratory disease
during the COVID-19 Pandemic:
Study Protocol (DIScOVER)

Investigators/ Researchers	**Chief Investigator**: Dr Matthew Maddocks Cicely Saunders Institute, Kings College London e-mail: matthew.maddocks@kcl.ac.uk Tel: 02078485242 **Co-investigator:** Lucy Fettes Cicely Saunders Institute, Kings College London e-mail: lucy.fettes@kcl.ac.uk Tel: 02078485385 Dr Stephen Ashford Cicely Saunders Institute, Kings College London e-mail: stephen.ashford@kcl.ac.uk Tel: 02078485564 Prof Irene Higginson Cicely Saunders Institute, Kings College London e-mail: irene.higginson@kcl.ac.uk Tel: 02078485585
Sponsor **Co-Sponsor:**	Prof Reza Razavi, Director of Research Management & Director of Administration (Health Schools) Address: Room 5.31, James Clerk Maxwell Building, 57 Waterloo Road, London SE1 8WA Tel: +44 (0)207 8483224 Email: reza.razavi@kcl.ac.uk Rahman Ahmed, Research & Innovation Governance Manager Address: King's College Hospital NHS Foundation Trust, 161 Denmark Hill, LONDON, SE5 8EF. Tel: 020 3299 6625 e-mail: rahman.ahmed1@nhs.net
Funder (s):	National Institute for Health Research
IRAS Reference:	271894

Contents

STUDY SUMMARY

STUDY OVERVIEW	
Full title	Comparing disability in activities of daily living over time, among adults with advanced lung cancer or respiratory disease **during the COVID-19 pandemic**
Objectives	**Aim:** To compare and contrast trajectories of disability in activities of daily living (ADLs) over time, among adults with advanced lung cancer or respiratory disease **Objectives:** To describe and compare in people with advanced lung cancer or respiratory disease the following: 1. Trajectories of symptom severity and ADL disability over 6 months. 2. Extent to which different disability items of BADL, IADL, and mobility are limited and how they change over time. 3. Extent to which different symptoms relate to ADL disability. 4. Extent to which assistive devices are used and relate to ADL disability. 5. **Determine the extent to which social isolation during the COVID-19 pandemic impacts on ADL function and its recovery**
Type of trial	Multi-site prospective cohort study
Trial design and methods	- Sample: advanced cancer or respiratory disease (COPD or ILD) - Recruitment sites: hospital lung cancer and respiratory inpatients and outpatient clinics; hospice inpatients, outpatients, or community teams. - Outcome variable: ADL disability (BADL, IADL and mobility) - Explanatory variables: symptoms; assistive devices; **social isolation** - Outcome measures: Modified Barthel Index; Lawton Brody IADL scale; WHO Disability Assessment Scale (WHODAS 2.0); Palliative Outcomes Scale-Symptoms; SARC-F; Frailty measure; **Chronic Disease Self-Efficacy Scales** - Data collection: Baseline self-reported questionnaire **via telephone** and monthly postal survey for 6-months or until death.
Health condition(s) or problem(s) studied	Advanced lung cancer or respiratory disease (COPD or ILD)
Target sample size	200
Trial duration per participant:	6 months or until death/deterioration
Main inclusion/exclusion criteria:	Inclusion: - Patients aged >18 - Advanced lung cancer or respiratory disease (COPD or ILD) defined by advanced disease markers Exclusion: - Patients who lack capacity to consent - Patients who lack ability to understand and complete a questionnaire in English - Life expectancy of <1 month, assessed by the person taking consent
Statistical methodology and analysis:	- Descriptive statistics will be used to describe the population and changes in ADL disability over time. - Visual graphical analysis (VGA) will be used to categorise individual trajectories and compare patterns. - Regression analysis will be used to test associations between ADL disability and the explanatory variables of symptoms, assistive devices, and **social isolation**. - Comparisons will be made across disease groups.
STUDY TIMELINES	
Study Duration/length	18 months (recruitment over 1 year)
Expected Start Date	November 2019
End of Study definition and anticipated date	May 2021
Key Study milestones	**Recruitment opened in March 2020 for 1 year**

One Page Summary

This study 'comparing and contrasting trajectories of disability in activities of daily living (ADL) in advanced lung cancer or respiratory disease' during the COVID-19 pandemic' (DIScOVER) is a prospective cohort study, which aims to compare and contrast trajectories of ADL disability in advanced lung cancer or respiratory disease and their relationship with symptom severity, use of assistive devices and social isolation during the COVID-19 pandemic.

This study will compare how ADL disability changes over time between patients with advanced lung cancer or respiratory disease throughout 2020 during COVID-19 pandemic. It will recruit patients with a diagnosis of advanced lung cancer or respiratory disease (chronic obstructive pulmonary disease (COPD) or Interstitial lung disease (ILD)) from hospital or hospice inpatient, outpatient or community services and compare the differences in ADL disability and influencing factors, particularly symptom severity, use of assistive devices and social isolation. By following people prospectively over time, we will be able to evaluate how ADL disability changes, what influences these changes, who it affects, and whether ADL disability can be modified and how.

This will enable us to better understand how ADL disability affects people with advanced lung cancer or respiratory disease, and where in the trajectory of ADL disability services could potentially be modified and how, in order to improve outcomes for these disease groups. This will inform development and delivery of appropriate interventions and trial design, which will ultimately inform appropriate and timely services addressing ADL disability in advanced disease. It will also identify the impact social isolation has on a person ability to manage their daily activities and subsequent recovery which may aid future crisis planning.

*Note on definitions

- ADL disability: the difficulty an individual has in managing everyday activities known as activities of daily living (ADLs), which can be basic (BADL) such as washing or dressing, instrumental (IADL) such as shopping or housework, or mobility-related such as walking or climbing stairs.

Background and Rationale

- **Epidemiology of advanced cancer or respiratory disease:**

Globally, 9.8 million people died from cancer in 2018 [1], and a further 3 million people died from chronic respiratory disease in 2015 [2]. Living with advanced cancer or respiratory disease brings different challenges. Cancer is often of rapid onset with a severe treatment related symptom burden, whereas respiratory disease is slower to develop but unpredictable in nature [3] and particularly associated with lower social deprivation linked with poor disability-free-life-expectancy [4]. Traditionally palliative care provision differs between the two populations with a strong bias towards cancer [3, 5], as does rehabilitation, with a strong bias towards respiratory disease [6], despite a potential need for both in the two disease groups. Due to an aging population people with a diagnosis of cancer or respiratory disease have an increased likelihood of multi-morbidity [7-10], adding to their complexity and severity of disability [11]. In addition, due to advances in treatment, particularly in lung cancer, people are now living with advanced disease over a longer period-of-time, which may change the illness trajectory in terms of pro-longing symptoms and disability which accompany a chronic condition. This means the needs of people with advanced lung cancer or respiratory disease may be changing, requiring additional strategies for their successful management. Lung cancer is also the most comparable cancer type to respiratory disease which makes for a good comparison of the needs of these two disease groups.

Disability in activities of daily living in advanced cancer or respiratory disease:

ADL disability is defined as the difficulty an individual has in managing everyday activities known as activities of daily living (ADLs), which can be basic (BADL) such as washing or dressing, instrumental (IADL) such as shopping or housework, or mobility-related such as walking or climbing stairs. Disability in advanced disease has a specific effect on ADLs, limiting a patient's independence and quality of life [12]. A recent systematic review identified that trajectories of ADL disability in advanced cancer or respiratory disease can be unchanging, fluctuating or increasing in nature. Increasing ADL disability can be associated with individual factors such as age or gender, illness-related factors such as diagnosis or symptoms, or services such as hospitalization. Towards the end of life disability is often limited by a high burden of symptoms [13], but little is known of the relationship between severity of symptoms and ADL disability specific to lung cancer or respiratory disease and how they compare. Understanding this relationship would enable application of timely and appropriate interventions that modify ADL disability in these populations, such as rehabilitation. Rehabilitation in advanced disease, aims to optimise a patient's independence, ability to remain active and improve quality of life during the dying process, by helping people to maintain their optimal levels of physical, sensory, intellectual, and social functioning with minimum dependence on others for as long as possible [14-16]. Rehabilitation interventions are very broad making for a difficult comparison. However, there is particularly a lack of study of how assistive devices relate to ADL disability, when, where and for who, which would demonstrate whether ADL disability is modifiable along its trajectory in this population.

- Need for development work to inform trial design and rehabilitation service provision:

Rehabilitation interventions towards the end-of-life are complex, comprising multiple component treatments that are adapted to the patient or setting, to target different outcomes. This complexity demands a better understanding of the needs of people receiving rehabilitation, to enable modelling of interventions prior to formal testing and evaluation, in line with the MRC guidelines for developing complex interventions [17]. Development work is particularly important in advanced disease because people present with difficult problems and vary considerably in their level of function, prognosis, and reasons for engaging with services [18, 19]. This study will observe trajectories of ADL disability over time, which will enable identification of parameters for rehabilitation, in order to inform development and delivery of an appropriate intervention targeting ADL disability and future trial design. Testing the effectiveness of such an intervention will allow standardization of rehabilitation in advanced disease in order to guide equitable service provision.

- Adapting study to the COVID-19 Pandemic

Coronavirus (COVID-19) was declared a global pandemic by the World Health Organization on 11th March 2020 and as of the 10th April 2020 there have been 60,737 confirmed cases and 7,097 confirmed deaths in the UK [20]. An emergency bill to strengthen the COVID-19 response was put in place on the 17th March 2020 and enforced on the 24th March 2020 [21]. As part of this response, the government enforced social distancing rules on everyone in society and patients with lung cancer or respiratory disease have been advised to stay at home and socially isolate for 12 weeks [22]. Social isolation refers to a complete or near-complete lack of contact with society [23].There are two levels of social isolation imposed on people considered to be at risk of dying from Coronavirus:

- Self-isolation: people who are in a high-risk group (e.g. aged over 70, respiratory disease, cancer, diabetes or pregnancy) are advised to stay at home for 12 weeks except for essential errands and avoid contact with others [22].

- Shielding: people who are in a very-high risk group including those with severe respiratory disease are strongly advised to stay at home, avoid contact with others including household members and not go out at all for at least 12 weeks from the day they receive a letter from the government which defines them as a vulnerable person (24th March 2020) [24].

PPI members have highlighted concerns around reduced professional support and increased demand on informal carers while socially isolating. Pilot participants have added concerns around discrepancies in government support available between high-risk and very-high-risk groups, uncertainty of not knowing how long the situation will last and increasing anxiety around loss of function and ability to cope at home during this period.

Social isolation is known to be strongly associated with functional impairments in older people and persons with cancer [23, 25], and is a major contributor of mortality in older adults [26]. If a person is contained to home for a long time, this physical inactivity may cause them to decondition in the same way they would if they had a long stay in hospital. In a study of advanced COPD patients admitted to hospital 50% showed functional decline throughout the six-week admission of which only 16.7% recovered functional loss six weeks post discharge [27]. Functional limitation, living alone, and lack of social support are also predictors of emergency attendance and hospital admission in COPD and older

people [28-30], which could put increased strain on an already stretched health and social care services during this public health crisis.

It is currently unclear what the consequences of enforced social isolation in people with advanced lung cancer or respiratory disease will be on their daily function and the impact decline in function may have on health and social care services during and after the COVID-19 pandemic, whether or not they contract the virus [31]. It is important to understand functional trajectories in the community in the context of COVID-19 and consider the magnitude and long-term impact of functional decline in order to help us to understand how this population is affected by the covid pandemic and plan accordingly for rehabilitation and social care needs.

Aims and Objectives

Aim:

To compare and contrast trajectories of disability in activities of daily living (ADLs) over time, among adults with advanced lung cancer or respiratory disease (COPD or ILD) during the COVID-19 pandemic

Objectives:

To describe and compare in people with advanced lung cancer or respiratory disease the following:

1. Trajectories of symptom severity and ADL disability over 6 months.
2. Extent to which different disability items of BADL, IADL, and mobility are limited and how they change over time.
3. Extent to which different symptoms relate to ADL disability.
4. Extent to which assistive devices are used and relate to ADL disability.
5. Determine the extent to which social isolation during the COVID-19 pandemic impacts on ADL function and its recovery

Hypotheses:

- People with advanced lung cancer develop greater ADL disability over time than people with advanced respiratory disease.
- Symptom severity is positively associated with subsequent ADL disability.
- Use of assistive device is positively associated with increased independence in ADLs.
- Social isolation is positively associated with increased dependence in ADLs.

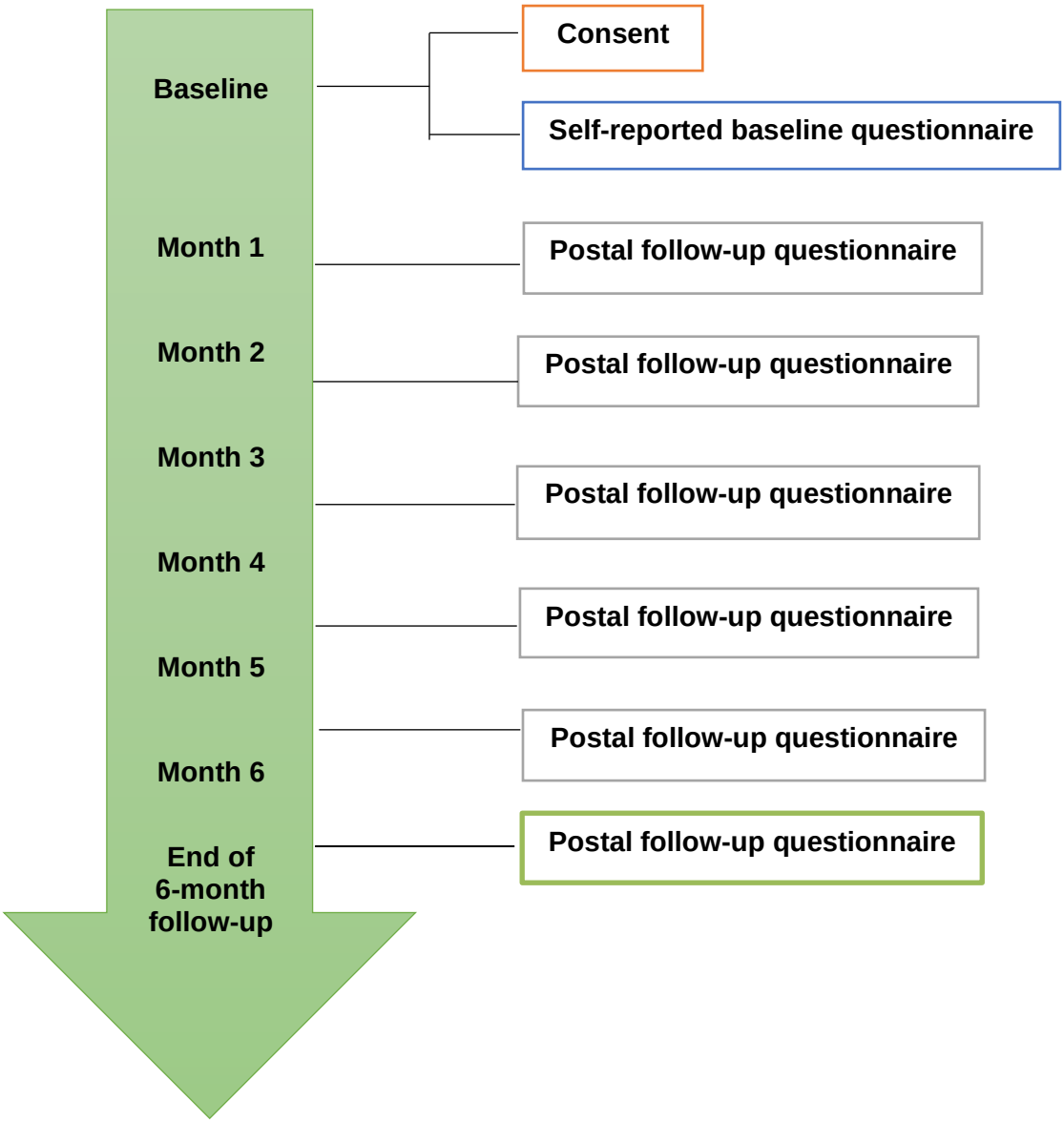
Methods

a) Overview of study design:

This is a multicentre prospective cohort study to observe ADL disability in patients with advanced cancer or respiratory disease. Data will be collected prospectively for 6 months, in a total of 7 monthly assessments including baseline. Figure 1 summarises the study schedule. The data collection booklet will consist of a variety of questionnaires asking patients about disability in ADLS, functioning,

symptoms, health care usage and use of assistive devices. These will be collected at all time-points. Demographic and clinical variables will also be collected in the baseline questionnaire only.

Figure 1: Schedule of prospective data collection



b) Study population and sample:

The study population is patients with advanced cancer or respiratory disease defined as below in section c). Consecutive sampling will be used and include all patients that have been screened eligible and are willing to take part. A convenience sample of patients at local sites will be used for piloting the questionnaire.

c) Inclusion & exclusion criteria

Inclusion:

- Patients aged >18
- Advanced lung cancer or respiratory disease as defined by one of the following:

    - *Lung cancer:* Inoperable stage III or IV non-small cell lung cancer
    - *Chronic Obstructive Lung Disease (COPD):* Severe or very severe stages of COPD according to the criteria set by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [32]: stage III (FEV1/FVC < 70%. 30% ≤ FEV1 < 50% predicted with or without chronic symptoms (cough, sputum production)) and stage IV (FEV1/FVC < 70%. FEV1 < 30% predicted plus chronic respiratory failure)
    - *Interstitial lung disease (ILD):* Carbon monoxide transfer factor (TLCO/DLCO) level of <40% or FVC <50% predicted [33, 34]

Exclusion:

- Patients aged <18
- Patients who lack capacity to consent
- Patients who lack ability to understand and complete a questionnaire in English
- Life expectancy of <1 month as assessed by the person taking consent

d) Recruitment of Participants

i. Setting and identification of participants

Patients will be recruited in the UK from: hospital medical, respiratory or oncology wards; outpatient lung cancer or respiratory clinics; or hospice/palliative care services, including inpatients, outpatients, community teams, day hospices and rehabilitation services. We will open 5 recruitment sites as follows:

1. King's College Hospital NHS Foundation Trust, London: lung cancer and COPD
2. Guys' and St Thomas' Hospital, London: lung cancer, COPD, and ILD
3. Nottingham University Hospitals NHS Trust: lung cancer
4. St Christopher's Hospice, London: lung cancer, COPD, and ILD
5. St Michael's Hospice, East Sussex: lung cancer, COPD, and ILD
6. Macclesfield Hospital, East Cheshire NHS Trust: lung cancer, COPD, and ILD
7. South Tyneside and Sunderland NHS Foundation Trust: lung cancer, COPD, and ILD
8. Medway Foundation Trust, Kent: lung cancer, COPD, and ILD
9. The British Lung Foundation Charity, National: lung cancer, COPD, and ILD

The study will start by opening at locally at Kings College Hospital NHS FT to collect pilot data. Following the pilot, the study will formally open for recruitment and the remaining sites will open. In addition, the study will be added to the NIHR portfolio which if needed will enable interested sites with access to this population to volunteer to recruit participants. Each site will recruit approximately 25 participants over the course of 1 year at the rate of approximately 2-3 patients per month per site and followed for six

months. The study will therefore be open for 18 months to complete follow-up. Potential participants will be screened and identified by the patients' direct clinical team at the recruitment sites and asked if they would like to participate in the study. These would be:

- *Inpatient approaches:*

    - Identification of patients from hospital/hospice admissions lists
    - Identification of patients from ward rounds on suitable inpatient wards
    - Identification of patients via ward multidisciplinary meeting discussions

- *Outpatient approaches:*

    - Clinicians in oncology and respiratory outpatient clinics at hospital sites including remote consultations
    - Clinical research nurses where available to attend above clinics to help clinicians screen clinic lists
    - Clinicians in hospice outpatients, community services, day hospices and rehabilitation services

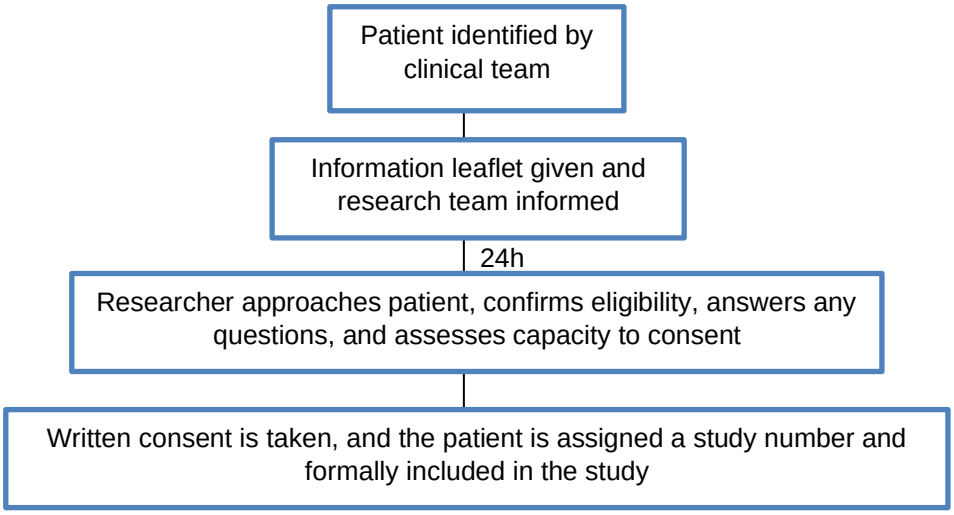
In order to understand which of the patients identified by the clinical team as eligible are included, we will record reason for not being approached or reason for decline for non-participants identified by the clinical teams. We will not record any identifiable information for non-participants.

ii. a) Usual Consent Procedure

Figure 1a outlines the usual consent procedure. Potentially eligible patients will be identified by the clinical team. A member of the participating clinical teams will approach eligible patients and give them a participant information sheet, which details the aim of the study and clearly describes what participation involves. The clinician will ask for verbal consent for the research team to contact the patient, and if this is given will inform the researcher of a potential participant in the study. Patients and their families are given at least 24 hours to read the information before they are contacted by the researcher unless they prefer to discuss the study with a researcher sooner.

The researcher will be informed of any potential participants and will follow up in-person or via telephone or email, as per the patients' preference. At this point, the researcher will address any questions or concerns and ascertain the patient's intention to participate or not during this meeting. If they are happy to take part, completion of the consent form and baseline questionnaires will be scheduled at a time and place convenient for the participant. They will be asked to give written informed consent once they have understood the benefits, risks and burdens associated with the study, had all information about the study and are aware that they can withdraw at any time. For patients who are visually impaired or unable to write, there is an option for a witness signature to confirm the patient gives informed consent.

Figure 1a: Usual consent procedure



ii. b) Remote Consent during COVID-19 pandemic

Figure 2 outlines the remote consent procedure during the COVID-19 pandemic when nonessential patient contact is prohibited. Due to social distancing rules enforced by the government, procedures of consent will move to remote practices and follow HRA guidelines [35], using the process outlined below:

- Potentially eligible patients will be identified by one of two new routes:

  i) An advertisement will be emailed to members of the British lung Foundation (BLF) and to potential participants at recruitment sites already consenting to be contacted by researchers. Interested people are invited to contact the researcher and request an information sheet.

  ii) The clinical team at open recruitment sites, will approach eligible patients, during a routine telephone consultation and introduce the study. The clinician will ask for verbal consent for the research team to contact the patient. If consent is given, they will inform the researcher of a potential participant and email the participants contact details to the researchers NHS email account. The research team will post or email a study pack including a participant information sheet, consent form and the baseline questionnaire and allow at least 24 hours for them to consider participation.

- The research team will post or email (as per their preferred option) a study pack including a participant information sheet, consent form and the baseline questionnaire and allow at least 24 hours for them to consider participation.

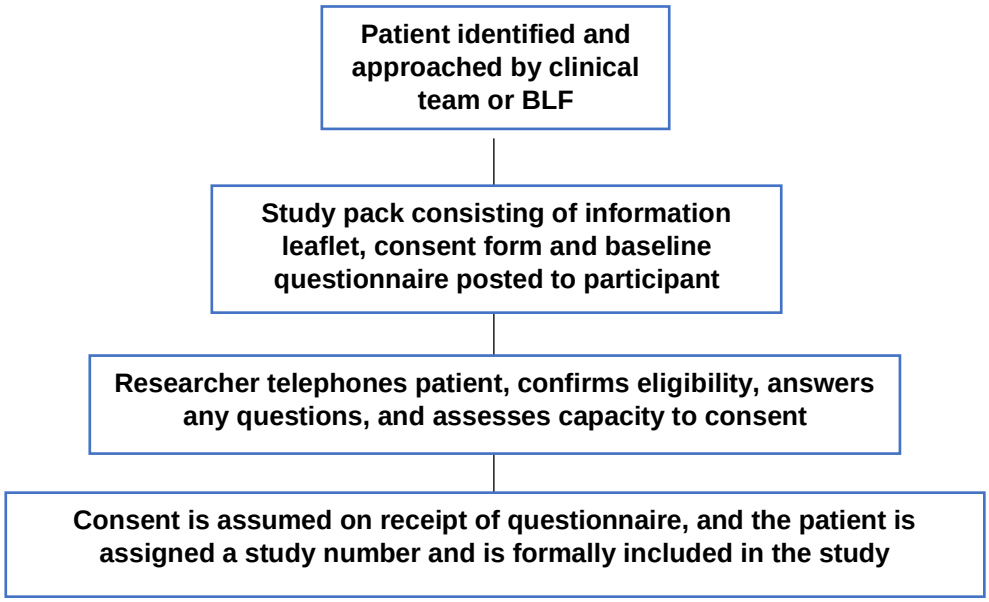
- The researcher will telephone the patient to introduce the study and address any questions or concerns and ascertain the patient's intention to participate or not during this call.

- If the participant is happy to take part, the researcher will verbally consent the participant to be recruited to the study once they have understood the benefits, risks and burdens associated with the study, had all information about the study and are aware that they can withdraw at any time. Verbal consent is permissible as this is not a clinical trial and not considered high-risk to participants [35].

- The participant will be asked to return the completed questionnaire in separate stamped addressed envelopes or to the researchers NHS email address. If the participant requires help to complete the questionnaire this will be ascertained at the time of verbal consent and a convenient time to complete the questionnaire over the telephone with the researcher will be arranged. Full consent will be assumed upon receipt of the questionnaire.

- The monthly follow-up questionnaires will be delivered either by post or email as per the participants preference. RIP status will be checked where possible prior to follow-up. The postal follow-up procedures have not changed.

Figure 1b: Remote consent procedure



e) Data collection schedule

- Study enrolment and baseline assessment

For those participants who meet the inclusion criteria and who consent to participate they will be enrolled in the study by the researcher. Each participant will be provided with an enrolment ID and added to the recruitment log. The researcher will approach the participant to arrange a convenient time to complete the consent form and baseline questionnaire over the telephone which will take approximately 60 minutes to complete. Following consent, the researcher will send a standard letter to the participants' GP informing them of their involvement in the study.

- Follow-up questionnaires and continued consent

There will be six monthly follow-up questionnaires for up to six months from study enrolment. Participants will receive a reminder phone-call a couple of days prior to posting each questionnaire. A couple of days prior to this phone-call clinical teams will inform the researcher of the participants health status, and if they are reported to have died, they will be withdrawn from the study. If the participant is happy to continue in the study, follow-up questionnaires will be posted out to the participants desired address by the researcher at monthly intervals for 6 months from the date of enrolment. There will be no financial incentive for participants to complete follow-up questionnaires. All follow-up questionnaires will take approximately 30-60 minutes to complete. Those who require help to complete the questionnaires can request assistance from the researcher over the telephone or face-to-face depending on the capacity of the recruitment site. A pre-paid envelope will be supplied for returning all questionnaires ideally within 7 days of receipt. If the questionnaire is not returned within the timeframe the participant will receive a telephone call to remind them. Patients will exit the study at 6 months or at the point of death. Information on withdrawal or loss to follow-up will be recorded (e.g., death, deterioration, hospital admission) from the medical notes.

f) Data collection measures

The outcome variable of interest is ADL disability consisting of BADL, IADL and mobility. There is no one measure of ADL disability that includes all desired components of BADL, IADL and mobility, therefore individual measures for each are recommended [36]. These are measured using validated outcome measures: Modified Barthel Index (BI) for BADL [37, 38], Lawton Brody IADL Scale (LB) for IADL [39-41] and the mobility domain of the WHO Disability Assessment Schedule 2.0 (WHO DAS mob.) for mobility [42-44]. **The main three explanatory variables of interest are (i) symptoms, (ii) assistive devices, (iii) social isolation measured by the Palliative Outcomes Scale - Symptoms (POS-S) [45] and specific assistive device questions [46], and description of social isolation and self-efficacy using the Chronic Disease Self-Efficacy Scale on Social support respectively.** It is also important to collect all potential confounding variables. All potential variables and data collection measures to be used in prospective data collection are identified in Table 2. Where possible, data will be extracted from clinical notes on enrolment to reduce questionnaire burden.

Table 2: Data collection measures to be used in prospective data collection

2a) Outcome variable – ADL Disability (BADL, IADL, mobility)

Outcome	Outcome measure	Reason for inclusion	Use in analysis
Basic activities of daily living (BADL)	Modified Barthel Index (BI)	To understand disability aspects and changes over time in each ADL domain	Primary outcome variable
Instrumental activities of daily living (IADL)	Lawton Brody IADL scale (LB)		Secondary outcome variable
Mobility	Mobility domain of WHODAS 2.0 (WHODAS mob)		
Global disability	WHO Disability Assessment Schedule 2.0 (WHO DAS 2.0)	To describe and understand relationship between ADL disability and global disability	Secondary outcome variable

2b) Potential explanatory variables

Variable	Method of collection	Reason for inclusion	Use in analysis
Individual factors			
Demographic data: - Age - Gender - Ethnicity - Marital status - Education - Living status - Co-morbidities	List of participant characteristics from participant or medical records Charlson co-morbidity index	Understand study population and to account for confounding variables	Descriptive – to describe population Independent variables in analysis
Functional performance status	Australian Karnofsky Performance Status (AKPS)	Measure of function	Descriptive – second measure of function which is useful to understand population recruited
Illness-related factors			
Disease and stage	Diagnosis, date of diagnosis and staging recorded in medical records	Understand study population	Descriptive – to describe population
Symptoms	Palliative outcomes scale - Symptoms (POS-S) – 7-day version	To understand relationship between symptoms and ADL disability and change over time	Descriptive – to describe population Analytic – associations with ADL disability and to compare between groups
Environmental factors			
Social Isolation	**Specific questions on COVID-19 and social isolation and the Chronic Disease Self-Efficacy scale on social support**	**To understand relationship between social isolation and ADL disability and change over time**	**Descriptive – to describe population** **Analytic – associations with ADL disability and to compare between groups**
Assistive devices	Specific questions on type of assistive device used for different ADL tasks	To understand use of assistive devices and how they relate to ADL disability	Descriptive – to describe use Analytic – associations with ADL disability and to compare between groups
Service-related factors			
Service utilisation	Client service receipt inventory – service receipt section	To understand which services influence ADL disability or are an outcome of ADL disability	Descriptive – to describe use of services Independent variable in analysis
Place of care / death	Reported by participant or proxy or medical records	To understand impact of ADL disability on place of care or death	Descriptive – to describe location of care or death Independent variable in analysis

g) Study Procedure

i. Pilot phase

The questionnaires and data collection methods will be piloted using a brief discussion with the first five consecutively recruited patients following completion of the baseline questionnaire, in order to refine chosen questionnaires and methods. Patients will be asked whether they think the questions work, are understandable and how they would prefer to be contacted, using a semi-structured topic guide. This will allow for sites to test the feasibility of recruiting this patient group and identify any barriers to recruitment. It will also enable the researcher to check the practicality and patients' understanding of the questionnaire. Any concerns identified with the questionnaire tools will then be quickly relayed to other sites and amendments sought in order to maximise the quality of the data to be collected.

ii. Documentation of participation

All participants who consent to participate in the study will be given a copy of the information sheet to keep. The research team will retain the original signed consent form. A copy of the signed consent form will be filed in the patient's medical notes, and they will be offered a signed copy to keep if they wish.

h) Safety & reporting

This is an observational study. There will be no intervention or changes to the patient care for the participant if they agree to participate. The steps below will be taken to minimise any distress the participant may experience from completing the survey.

i. Steps to prevent harm

The researcher will make every effort to complete all questionnaires in a private place. The purpose and intent of the study will be explained to participants and the participants will be advised that they are under no obligation to take part. Patients will be made aware that they can withdraw from the study at any time, with no adverse implications for their clinical care.

It is possible that participants may raise issues during the baseline questionnaires which raise clinical concerns or warrant a change in their medical management. Should this be the case, then a member of the research team will gain consent from the participant to discuss matters with the relevant member(s) of the patient's medical team or their general practitioner, as appropriate. All returned questionnaires will be screened immediately following completion to check their content for any areas of clinical concern. This screening will be done by the researcher at the return address (King's College London). Additionally, if participants disclose any ideation of self-harm or other risk to themselves or others, then this will be dealt with as an urgent matter for discussion with the PI and a senior member of the treating medical team. Provision will be made to ensure the researchers have PI or senior back up available by phone whenever they are undertaking data collection.

ii. Distress protocol

We are aware of the possibility that despite measures to prevent harm, completion of the study questionnaires may be distressing to potential participants. We expect significant distress to be uncommon, since most of the questionnaire deals with routine or day to day issues. Nevertheless, a

series of measures will be in place to deal with the any additional distress which may arise in the course of the study as outlined below:

- Study contact telephone number will be made available for participants to contact with any questions or concerns about the study process or in the event of any distress.
- Contact number to be included on all study information and participants to be informed of this during participation.
- Senior clinical staff members will be available to support the researcher and to deal with more complex distress or concerns.

iii. Withdrawal of participants

In consenting to participate in the survey, participants are consenting to completing a baseline questionnaire with the researcher and 6 follow-up postal surveys.

A participant may withdraw from the study at any time with no effect to their routine care. The decision to withdraw will be included if the participant volunteers that information and will be recorded in the main study database.

i) Data handling and management

All personal data will be managed according to the principles established in the Data Protection Act 2018. All of the researchers will undertake, and update GCP training, and current research governance processes will be followed. Completed demographic forms, questionnaires and interview transcripts will be anonymised using a unique study identification number and contain no patient identifiable data. The participant identification number and linkage with the participant's name will only occur on the consent form and participant log. The participant log will be held in a password protected Excel Spread sheet, stored on an encrypted memory stick at KCL in a locked filing cabinet, and backed up on an NHS computer in a separate location. Data will be transferred via NHS or other secure email account. Questionnaires, demographics forms, and transcripts will be stored separately to the consent forms, each in a separate locked cabinet.

ALL personal data held by the research team will be stored for seven years after the study has ended. This is to allow enough time for clarification and validation following reporting and publications. Data will be stored in locked cabinets in a locked office in the Department of Palliative Care, Policy & Rehabilitation in accordance with the requirements of the Data Protection Act 2018 [47] and local Data Management Guidelines.

Data quality will be monitored throughout the study at the local sites, and centrally monitored at the lead site. All data will be de-identified before being transferred to the lead site (King's College London).

j) Statistical Analysis

i. Proposed sample size

The sample size of 200 participants, 100 advanced lung cancer and 100 advanced respiratory disease and/or an allocated proxy (as outlined in consent section above) will be recruited for the prospective questionnaire. This is not a trial, so in the quantitative data we are not estimating a sample size

sufficient to determine a difference between one intervention and another. The basis of this sample size estimate is based on a combination of the following factors:

- *Precision:*

The changing trajectories of ADL disability in advanced lung cancer or respiratory disease are not known, therefore descriptive analysis will provide useful new information. Thurs we will be aiming to estimate these with a level of precision and to describe them over time. Based on assumed prevalence of ADL disability in this patient population to be around 50% [2, 12], a sample size of 150 would achieve a precision of 8% in the estimation of prevalence of ADL disability characteristics.

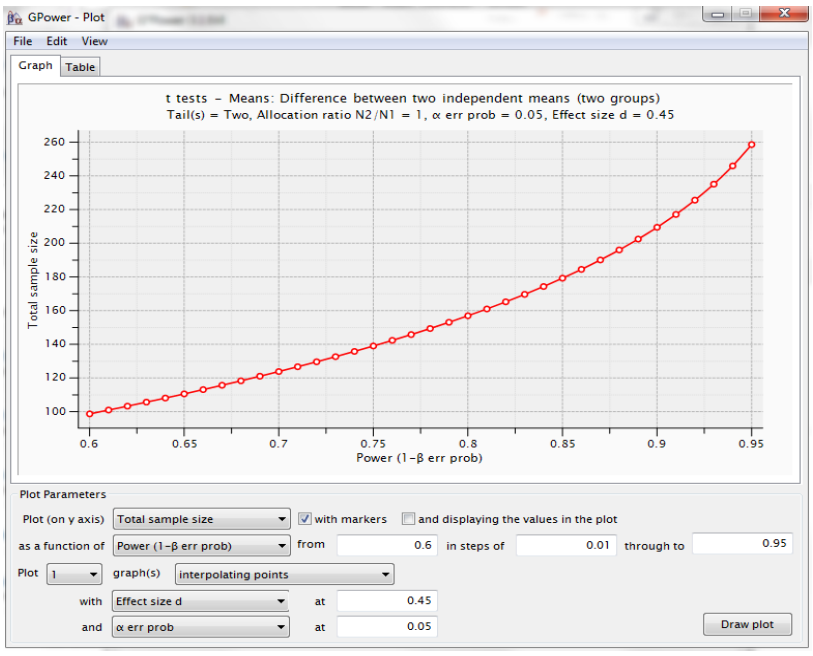
- *Power:*

Comparative analysis will be used to investigate changes over time between the two disease groups (lung cancer and respiratory disease). A recent study within the department investigating trajectories of need, experience, and priorities over time in older adults with serious illness (IARE2), collected ADL data using the Modified Barthel index (BI) at three time-points over 6 months. IARE2 has a similar advanced illness population to this study and included patients with a diagnosis of cancer or respiratory disease. Therefore in order to work out our sample size it was possible to use cases of cancer (solid tumours) and COPD that had BI scores at baseline and 6 months from this data to calculate an effect size using the following formula by Cohen 1988 [48]:

$$d \text{ (effect size)} = \frac{M1 \text{ (mean of group 1)} - M2 \text{ (mean of group 2)}}{\sqrt{(SD1^2 + SD2^2) / 2}}$$

A sample size was then calculated using G-power software. Based on a difference between two independent groups and an effect size of 0.45 on the BI (primary outcome) at the primary end point of 6 months with power of 80% at a 5% significance level, a sample size of 158 would be required.

Figure 3: Sample size calculation



- *Adjustment for co-variates in regression analysis:*

We will be using regression analysis to test the association between the outcome variable of ADL disability and the explanatory variable (co-variate). As a rule of thumb in regression analysis there should be ten cases for each co-variate. A sample size of 200 allows for up to 20 co-variates in the analysis. The co-variates that need to be accounted for in this study are age, gender, ethnicity, martial-status, education level, living status, co-morbidities, performance status, diagnosis, symptom severity, cognitive function, assistive devices, service utilization, place of care, place of death, and mortality. Therefore, a minimum sample size of 160 is required.

- *Attrition:*

An attrition rate of 20% over 6 months was estimated in this study population. This is based on a local study in the advanced disease population that experienced 36% attrition over 12 months [49]. This means by recruiting 200 participants by the end of the study our sample size will be 160. Therefore, our estimated sample size will be sufficient to account for a precision of 8%, power of 80% at a 5% significance level, and adjustment of the required co-variates in the analysis.

ii. Principles of analysis and data usage:

Questionnaires will be checked after completion for any concerning clinical features. All questionnaire data will be entered into a standardised spreadsheet using Microsoft Excel, which will be standardised across sites. Data will be checked for missing values. Statistical software will be used to support descriptive and comparative analysis. This will be done by the researcher.

iii. Specific analysis plan

- Assessment of disability

ADL disability is the primary outcome and will be measured using three measures: Modified Barthel Index (BI) for BADL (main primary), Lawton Brody IADL Scale (LB) for IADL and the World Health Organization Disability Assessment Schedule 2.0 (WHOSDAS 2.0) mobility domain (WHODAS-mob) for mobility. Disability is defined on each of these measures as follows:

- BI: A 10-item categorical measure, where each item has a range of two to four responses rated on a 0-4 scale, ranging from dependent/unable, to minor help, major help, or independent, depending on the activity. Therefore, a lower score indicates greater disability. A summary score ranges from 0-20 where a score <15 represents moderate disability and a score <10 represents severe disability [37]. Changes of more than 2 points in total score reflect a probable genuine change in ability to perform ADLs [37].

- LB: An 8-item categorical measure, where each item has a range of three to five responses ranging from fully independent to fully dependent. Each response is scored 0 if independent or 1 for anything other than independent. A summary score ranges from 0 (low function, dependent) to 8 (high function, independent), therefore a lower score indicates greater disability [41, 50]. A change of 1 or more in total score indicates a change in ADL disability.

- WHODAS-mob: A 5-item categorical measure, where the patient rates difficulty in each task on a 5-point scale from none (1) to extreme or unable (5). A simple summary score totalling the scores of all five items ranges from 5-25 where the lowest score indicates no disability and the highest score indicates extreme disability [43, 44]. A score of 5 or more indicates moderate disability. A more comprehensive scoring method will also be used (see WHODAS 2.0 below).

- WHODAS 2.0: All domain scores rated as above (see WHODAS-mob) on the WHODAS 2.0 are combined to give a global disability score, with higher scores indicating higher levels of disability [44]. To enable easy comparison each domain score can be transformed to a 0-100 scale using the complex WHODAS method of scoring [51]. Global disability scores are categorized according to ICF severity ranges (no problem, 0-4; mild disability, 5-24; moderate disability, 25-49, severe/extreme disability, 50-100). Based on the WHODAS ICF, 'disability' is indicated by a disability score of 25 or higher.

The individual items measured in each ADL tool (BI, LB, and WHODAS-mob) are listed in Table 3. For individual items in line with the scale metric a change in disability on any measure is identified by a change of 1 point or more in any direction (improvement or decline).

Table 3: Individual items of each outcome measure for use in analysis

Modified Barthel Index	Lawton-Brody IADL Scale	WHODAS-Mob	POS-S	Assistive devices
Bowels	Ability to use telephone	Standing for long periods (>30mins)	Pain	Special utensils/dishes to help eating
Bladder	Shopping	Standing up from sitting down	Shortness of breath	Equipment to help getting in or out of bed
Grooming	Food preparation	Moving around inside the home	Weakness or lack of energy	Equipment to help getting around inside
Toilet use	Housekeeping	Getting out of the home	Nausea	Special clothing or use equipment to get dressed
Feeding	Laundry	Walking long distances (1km)	Vomiting	Equipment to help bathe
Transfer (bed to chair and back)	Mode of transportation		Poor appetite	Equipment to help use the toilet
Mobility	Responsibility of own medication		Constipation	Equipment to help getting around outside
Dressing	Ability to handle finances		Mouth Problems	Equipment to help use the stairs or steps
Stairs			Drowsiness	Equipment to help with domestic tasks
Bathing			Immobility	Anything else (e.g., transport adaptations or communication aids)

- Assessment of symptom severity

Symptom severity will be measured using the POS-S which is a 10-item categorical measure listing ten symptoms (Table 3). The patient rates the severity of each symptom on a 5-point scale from not at all (0) to overwhelmingly affected (4). A summary score ranges from 0-20, where a higher score indicates greater severity of overall symptoms. According to the scale a change in individual symptom severity is identified by a change of 1 point or more in any direction (improving or worsening).

- Assessment of assistive devices

This is measured using a list of ten questions about assistive devices to help with several ADL tasks (Table 3), which have been used in previous surveys [46]. Patients answer yes or no to the use of equipment for each task, followed by a question asking them to specify what equipment they use. This can be measured on a binary scale (yes: 1, no: 0), making a combined summary score of 0-7 where a higher total score indicates a higher use of assistive devices and greater disability.

- Assessment of Social Isolation and self-efficacy

Questions will be added around COVID-19 and social isolation including information on how the participant's daily activity and support changed while self-isolating or shielding. Strategies used to manage physical well-being will also be collected. The 'receiving social support' scale from the validated Chronic Disease Self-Efficacy Scales will be used to measure confidence in managing receiving social support in society' [52, 53]. This scale contains 4 questions which are scored on a numerical rating scale of 1 to 10 where 1 is 'not at all confident' and 10 is 'totally confident'. The total score is the mean of the 4 items. A higher score indicates higher self-efficacy in that scale.

- Descriptive analysis:

The data from patient questionnaires will initially be summarised using descriptive statistics to describe the population in detail and make comparisons between the two disease groups. This will include demographic characteristics, baseline performance status, symptom severity, assistive device use, social isolation, service utilization, and place or care or/and death (Table 2). The significance of variations will be determined using X^2 tests or Fishers Exact Test when required for categorical data, Mann Whitney U tests for ordinal data and t-tests/ANOVA for continuous data. A significance value of $p < 0.05$ will be used.

- Analysis by objectives:

To describe and compare in people with advanced lung cancer or respiratory disease the following:

1. *Trajectories of symptom severity and ADL disability over 6 months.*

Summary trajectories:

We will describe changes in ADL disability (BADL, IADL, mobility) using total scores on each of the three measures (BI, LB, and WHODAS-mob) and for symptom severity (POS-S total score) over time using repeated measures from point of study entry (forward trajectory) and from point of death (backwards trajectory). Forward trajectories are useful to understand clinical implications of ADL disability and symptom severity and backward trajectories allow understanding of how these change prior to death. Trajectories of ADL disability and symptom severity will be determined separately for lung cancer and respiratory disease using summary statistics with means and 95% confidence intervals at each time-point and will be presented graphically.

Individual trajectories:

Individual trajectories using the primary outcome of ADL disability (BADL, IADL, mobility) using visual graphical analysis (VGA) [54] which allows patterns to emerge for visual inspection of each individual report which have completed data from repeated measures at three or more time-points. These trajectories will be plotted separately for lung cancer and respiratory disease to identify variances in common patterns and develop categories of trajectories of ADL disability (e.g., increasing, decreasing, stable or fluctuating). The clinical and demographic characteristics of each trajectory group will be described and compared using X^2 tests or Fishers Exact Test for categorical variables and appropriate non-parametric analysis of variance for continuous variables (t-test, Mann-Whitney U, or Kruskal-Wallis test). If appropriate latent growth curve modelling may be used.

2. *Extent to which different disability items of BADL, IADL, and mobility are limited and how they change over time.*

The prevalence disability in each individual ADL item (Table 3) for all three measures (BI, LB, and WHODAS-mob) will be calculated by dividing the number of participants with disability in that item in each specific month by the total of completed questionnaires that month, which will be tabulated. Disability is classed in the individual items of each measure as:

- BI: needs help/dependent/unable (scores vary per item)
- LB: score of 1 point or more
- WHODAS-mob: score of 1 point or more

Change in monthly prevalence of each item can be plotted over time using summary statistics with means and 95% confidence intervals at each time-point and presented graphically. Lung cancer and respiratory disease will be analysed separately in order to make comparisons between the two disease groups.

3. *Extent to which different symptoms limit ADL disability.*

Symptoms recorded using POS-S will be described using descriptive statistics and tabulated. We will undertake regression analysis using overall change in each ADL measure (BI, LB, and WHODAS-mob) as the outcome variable to test associations with change in each individual symptom score on the POS-S over time using summary statistics with means and 95% confidence intervals at each time-point. Lung cancer and respiratory disease will be analysed separately in order to make comparisons between the two disease groups.

4. Extent to which assistive devices are used and relate to ADL disability.

The types of assistive devices (Table 3) used by participants will be described using descriptive statistics. The prevalence of assistive devices will be calculated by dividing the number of participants using any assistive device in a specific month by the total of completed questionnaires that month and change can be plotted over time using summary statistics with means and 95% confidence intervals at each time-point. This can also be done for each individual assistive device to compare popularity/availability. We will undertake regression analysis using overall change in each ADL measure to test associations with use of assistive devices as measured by change in prevalence over time. Lung cancer and respiratory disease will be analysed separately in order to make comparisons between the two disease groups.

5. Determine the extent to which social isolation during the COVID-19 pandemic impacts on ADL function and its recovery

The level of social isolation, length of time spent socially isolating, effect on physical activity and support with daily living, and self-efficacy score in the 'chores', 'receiving social support' and 'participation in society' scales, will be described using descriptive statistics and presented as frequencies, means or medians as appropriate. We will undertake regression analysis using overall change in each ADL measure to test associations with level of social isolation and change in self-efficacy score over time. Lung cancer and respiratory disease will be analysed separately in order to make comparisons between the two disease groups.

- Adjustments in analysis

Adjustments will be made in the analysis for multiple testing, missing data and confounding variables as follows:

- Multiple testing: To adjust for multiple comparisons in this analysis a multiple testing correction such as the Bonforroni, Holm, Hochberg or Hommel adjustment can be used [55]. As a compromise the significance level will be set to a p-value of 0.01.
- Missing data: Analysis will test the pattern of missing data and depending on the nature of missingness (at random, not at random, completely not at random) will use and contrast findings using sensitivity analysis [56].
- Confounding variables: Adjustments will be made in the multivariate analysis for covariates as appropriate (e.g., time, age, gender, ethnicity, martial-status, education level, living status, co-morbidities, performance status, diagnosis, symptom severity, cognitive function, assistive devices, service utilization, place of care, social isolation, self-efficacy).
-

k) Patient and public involvement (PPI)

The public engagement forum at the Cicely Saunders Institute will be utilized to engage patients and members of the public in the planning of the study and screening of all study documents to ensure

appropriateness. They will be updated on the progress of the study and involved in the dissemination of findings.

l) Ethical and regulatory approval

This study will be conducted in line with principles of research ethics as outlined in the declaration of Helsinki and Good Clinical Practice (GCP) guidance. This protocol and study documents will be submitted to the Health Research Authority for approval.

m) Dissemination

Knowledge will be presented through the project (within 3 years) to:

- researchers and clinicians within the project group
- clinicians involved with the research at recruitment sites as findings emerge
- participants/caregivers who express interest
- at Institutional open seminar programmes

Learning will be shared (within 5 years):

- in peer reviewed publications in high impact journals
- at national (e.g., CSP Congress, SRR) and international conferences (e.g. European Association of Palliative Care)
- with clinicians at speciality study events (e.g., ACPOPC (Association of chartered physiotherapists in oncology and palliative care) seminars)
- with students on KCL's longstanding physiotherapy and Palliative Care programmes
- via our department website and other online channels including YouTube and Twitter

n) Funding and costings

Funder: NIHR grant to the value of £565,413, covering:

- 3-year research assistant salary (£32,548 per annum)
- Printing and posting of questionnaires with pre-paid return envelopes (£5000)

o) Revised Project timeline

2019				2020												2021									
Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apri	Ma	Jun	July	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apri	Ma	Jun	July	Aug	Sep	Oct
Ethics																									
					Site set up																				
						Pilot																			
								Recruitment																	
								Prospective follow-up																	
																			Data Analysis						
																							Write up		
																								Paper	

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Appendix C

Study materials for clinicians

C.1. Outline of study for clinicians

Comparing disability in activities of daily living (ADL) over time among adults with advanced lung cancer or respiratory disease (DIScOVER)

Study summary for clinicians

What is DIScOVER about?

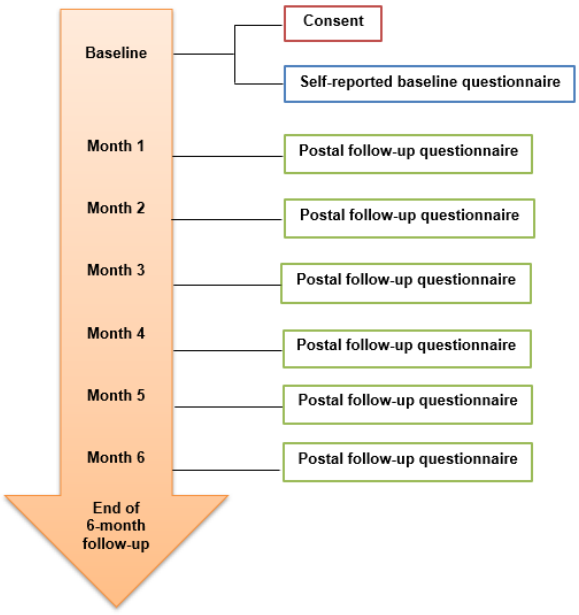
This is an observational study of patients with advanced lung cancer or respiratory disease looking at how **disability changes over time** in ADLs (e.g., washing, dressing, shopping, walking) and associated factors. This will enable us to understand how disability changes towards end-of-life, and what, where and for whom services or interventions can be modified to target disability in ADLs.

Where are we recruiting from?

We are recruiting from hospital and hospice in/outpatient settings over a 12-month period and will be following participants for 6-months.

What is involved?

Following consent, participants will complete a baseline questionnaire upon enrolment with the researcher and a series of monthly postal questionnaires over 6 months as outlined in the diagram below:



What do you need to do?

1. We are asking if you can identify possible participants that meet the inclusion criteria.

The key inclusion criteria are:

- Patients aged >18
- Advanced lung cancer or respiratory disease as defined by one of the following:
  - *Lung cancer:* Inoperable stage III or IV non-small cell lung cancer.
  - *Chronic Obstructive Lung Disease (COPD):* Severe or very severe stages of COPD according to the criteria set by the Global Initiative for Chronic Obstructive Lung Disease (GOLD):
    - Stage III (FEV1/FVC < 70%, 30% ≤ FEV1 < 50% predicted with or without chronic symptoms (cough, sputum production)) OR
    - Stage IV (FEV1/FVC <70%, FEV1 < 30% predicted plus chronic respiratory failure).
  - *Interstitial lung disease (ILD):* Carbon monoxide transfer factor (TLCO/DLCO) level of <40% or FVC <50% predicted
- Patients with capacity to consent
- Patients with the ability to understand and complete a questionnaire in English
- Life expectancy of > 1 month as assessed by the person taking consent

2. Once you have identified a potential participant, we ask you to:
   - Tell them a little bit about the study using the script available if needed.
   - If they are interested, please give them a participant information leaflet, and ask if it is okay for a researcher to contact them.
   - Phone or email the research nurses (if available) to let them know if they have agreed to be approached (using the study referral form).
   - If the research nurse is attending clinics, they can be informed immediately, and the patient can be approached straight away if they are willing.
   - If the participant declines participation, please complete the table of declining participants, and return this to the KCL research team at the end of each month.
3. The researcher will arrange to meet the potential participant to complete the consent process and the baseline questionnaire. Once consented they will add the participant to the recruitment log and send the standard GP letter stating that the patient is participating in this study.
   - This will be the research nurse in your area (if available) or the main investigator (Lucy) if local.
   - If your site does not have access to research nurses or not local this will be the principal investigator or a delegated member of staff with GCP training.
4. Participant contact details will be emailed to the research team at KCL using the study referral form, who will conduct monthly follow-up phone-calls and posting of follow-up questionnaires. The local research nurses (if available) will keep track of when monthly follow-up is required for each participant and inform the research team at KCL at each time-point as to whether or not the participant has died.
5. The recruitment log and follow-up tracking in the Excel spreadsheet will be emailed to the research team at KCL at the end of each month for our records.

Comparing disability in activities of daily living over time among adults with advanced lung cancer or respiratory disease (DIScOVER)

Introducing the study: guidance for clinicians

The team here is involved in a research study to find out about how people with 'advanced' lung cancer or respiratory disease manage daily activities (such as washing, dressing, shopping, and walking) and how this changes over several months.

This will help to identify when people with these conditions may find it more difficult to manage everyday activities, what may cause this such as being breathless or anxious, and what might help to improve their independence and well-being.

We will be grateful for your contribution which will involve completing a series of monthly questionnaires for 6 months. These includes questions about how you manage your daily activities, your symptoms, health services you have been accessing, and equipment you have been using to help you.

The first questionnaire will be completed with myself or the researcher at the start of the study and might take about 45-60 minutes to complete.

You will then receive follow-up questionnaires in the post every month for the next 6 months. This will help us to better understand how your daily activities are managed over time. These questionnaires can be completed at home or in a place of your convenience and might take about 30-45 minutes to complete. You simply need to return the completed questionnaire in the pre-paid envelope provided.

If you participate in this study, your usual care will not change, and you will not need to come to the hospital for any extra visits.

We have an information sheet for you to read and we will give you at least 24 hours to think about participating in this research unless you want to decide sooner.

If you are interested, please let me know and I will inform the research team at King's College London. Either the researcher or I will get in touch with you to arrange a meeting to get your consent, to enrol you in the research study and complete the first questionnaire. Do you have any questions?

Comparing disability in activities of daily living over time among adults with advanced lung cancer or respiratory disease (DIScOVER)

Referral to the research team

To complete following participant identification:

The following person who attends *(name of site)* has agreed to be contacted by the research team for DIScOVER and is happy to receive more information about this research study.

- **Please provide potential participant's preferred contact details below:**

Name:

Address:

Telephone Number:

Email:

- **Please provide contact details for the participants GP below:**

GP:

GP Practice:

Address:

Telephone Number:

- **Please provide referrer details below:**

Name:
(of person completing referral)

Signature:

Designation:

Contact number/email:

Date:

- **Please return this form to your local research nurses:**

Research Nurse:

Tel:

Email:

Research Nurse:

Tel:

Email:

To complete following participant consent:

- **Please provide the following details:**

Participant ID (e.g., PRUH001, PRUH002, PRUH003 etc.):

- **Please send this form to the KCL Research team below:**

Researcher:	**Research nurse:**	**Research nurse:**
Lucy Fettes	Evelyne Burssens	Paramjote Kale
Tel: 0207 848 5385	*Tel:* 020 3299 5240	*Tel:* 0203 299 5239
Email:	*Email:*	*Email:*
l.fettes@nhs.net	evelyne.burssens@nhs.net	p.kaler@nhs.net

Comparing disability in activities of daily living over time among adults with advanced lung cancer or respiratory disease (DIScOVER)

Distress Protocol

We are aware of the possibility that despite measures to prevent harm, completion of the study questionnaires may be distressing to potential participants. We expect significant distress to be uncommon, since most of the questionnaire deals with routine or day to day issues. Nevertheless, a series of measures will be in place to deal with the any additional distress which may arise in the course of the study as outlined below:

- Study contact telephone number will be made available for participants to contact with any questions or concerns about the study process or in the event of any distress.
- Contact number to be included on all study information and participants to be informed of this during participation.
- Senior clinical staff members will be available to support the researcher and to deal with more complex distress or concerns.

C.5. Screening log template

Site code: P0

Date	Contact	Referring department / ward or clinic	Hospital Number	Date of birth	Initials	Diagnosis (NSCLC, COPD, ILD)	Reason not approached *(insert code)*	Date approached	Date PIS given or sent	Reason for exclusion *(insert code)*	Date of decision to/not to participate	Reason for decline *(insert code)*	Notes

NSCLC: Non-small-cell lung cancer; COPD: Chronic Obstructive Pulmonary Disease; ILD; Interstitial Lung Disease; PIS: patient information sheet

Code	Reason	Code	Reason
Exclusion criteria		*Other reasons*	
1	Not advanced disease	5	Died
2	Doesn't have capacity	6	Admitted to hospital
3	Insufficient English	7	Too unwell
4	Life expectancy of <1month	8	Too much 'going on'
		9	Not interested
		10	Other (please specify)

Appendix D

Patient facing documents

D.1. Participant information sheet

Comparing disability in activities of daily living over time among adults with advanced respiratory disease during the COVID-19 pandemic (DIScOVER)

Participant Information Sheet

We are inviting you to take part in a research study. Before you decide, it is important that you understand why the research is being done and how it may involve you.

Please take time to read this information carefully and discuss it with friends or relatives if you wish. We will talk through this with you and answer any questions you might have. Feel free to ask if there is anything that is unclear or if you would like more information and take your time to decide whether or not you wish to take part.

This study has been approved by the London-Camberwell St Giles Research Ethics Committee (REC reference: 19/LO/1950).

What is the purpose of this study?

We are very interested in finding out more about how people with advanced lung cancer or respiratory disease manage daily activities (e.g., washing, dressing, shopping, and walking) and how this changes over several months during the Coronavirus (COVID-19) pandemic. This is so we can identify when people with these conditions may become unable to manage everyday activities, what may cause them to have more difficulty (e.g., breathlessness) and what might help to improve their independence, in order to guide clinical practice and service provision.

Why have I been chosen to take part?

You have been chosen because of your diagnosis of either respiratory disease or lung cancer. The information you can provide about managing daily activities is very important.

What is the survey about?

The survey will be about how you manage your daily activities, and includes questions about caring for yourself, how you walk around, the symptoms you experience, services you have been accessing, the equipment you have been using to help you, and social isolation during the COVID-19 pandemic. To collect all this information, the survey will be made up of several different questionnaires. Some of the questions may appear repetitive but it is important to complete all the questionnaires in the survey as each questionnaire will tell us something different.

We will also collect information regarding your diagnosis, mobility, age, gender, ethnicity, martial-status, and health service usage such as hospital admissions. You may be asked some of these questions when you complete the first questionnaire with the researcher. We may also ask to look at your healthcare record to find out this information at the time of enrolment and at the end of the study.

What do I have to do if I agree to take part?

In this study pack you will receive this information sheet, a consent form and the first questionnaire. The researcher will contact you by telephone to explain the study and ask you for your consent to participate. You will then complete the first questionnaire with the researcher when they call and be enrolled in the study.

There will then be six identical follow-up postal questionnaires at monthly intervals for up to six months. This is so we can identify how a person's ability to perform daily activities may change over time. If you need help to complete the follow-up questionnaires this can be arranged if you let the researcher know. You will receive a telephone call a few days before each monthly questionnaire booklet is due to be sent to remind you to expect a questionnaire in the post, and to ask if you are still happy to continue in the study.

Will I be identifiable?

You will be given a unique study identification number which will be on all your questionnaires so that you are not identifiable, and your answers will be fully anonymised.

Where and when will the survey take place?

The researcher will call you at the agreed time to get your consent to participate in this study and to complete the first questionnaire over the telephone. Please have the consent form and questionnaire to hand when the researcher calls. The researcher will be available to help you and explain any questions if you wish.

Follow-up questionnaires will be posted to your desired address at monthly intervals for up to 6 months unless other arrangements have been made with the researcher. You will be asked to return each questionnaire within the next 7 days of receipt if possible, using the pre-paid envelope provided.

How long will it take to complete?

The first questionnaire will take about 45-60 minutes. After this, the questionnaires will be shorter and will take about 30-45 minutes each.

Are there any other benefits to taking part?

This research doesn't involve any changes to your care, and so you are unlikely to benefit personally from taking part, though your participation may help us to improve the care of others in future.

Are there any risks to taking part?

The risks to taking part are very small, this research will not in any way affect the standard of care you or any person related to you might receive, care options, or any relationships you have with any staff or researchers.

Some people may find some of the questions upsetting, but you can choose not to answer questions if you do not want to. We will offer you support if you feel you need it. A telephone number for support will be available.

Do I have to take part?

No. It is entirely up to you to decide whether or not to take part. We will give you at least 24 hours to decide whether to take part unless you wish to decide sooner.

Who will know about my involvement in the study?

All information about you will be treated confidentially and we will follow guidelines to make sure this happens. Your information will be anonymised which means no one will be able to identify you from what you have shared. The information you share will be stored in a safe place with any information that identifies you kept separately. Information about you which leaves the hospital or hospice will have your name and address removed so that you cannot be recognised. Anonymised information that you provide may also be used for education and teaching and to inform future research.

We will ask you whether you want your GP or consultant(s) to know about your involvement in this study. We can contact them on your behalf if you want them to know, but we will not tell them about your involvement if you don't want us to.

Could patient confidentiality ever be broken?

If the researcher becomes concerned about your health or welfare your clinical team or GP may be informed in order for you to receive the care, you may need.

What if I decide to withdraw?

You may withdraw at any time. If you do withdraw, we will ask you if information that has already been collected may be included in the results for the study.

What happens at the end of the study?

After the study, your care will continue as normal under the guidance of your care team.

What happens to the results of this study?

The findings of this study will be published in scientific journals. A summary of the results for wider distribution will be sent to policy makers, staff, and individual users of services, their caregivers, and charities. If you wish, we can send you a copy of the results. Please be reminded that all personal details will be removed from the results so you and your family will not be identified from the findings.

Who is organising the study?

The study is organised by Lucy Fettes a researcher from King's College London who will be working on the study as part of a higher degree.

Who is funding the study?

This study is funded by a grant from The National Institute of Health research (NIHR).

Will I get paid?

There are no funds available for payment to those participating in the study.

Who and what is the sponsor of the study?

King's College London is the sponsor (we) for this study based in the United Kingdom. We will be using information from you and/or your medical records in order to undertake this study. This information will include your NHS number, name, and contact details. People will use this information to do the research or to check your records to make sure that the research is being done properly.

We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study. You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you. King's College London will keep identifiable information about you for 7 years.

To safeguard your rights, we will use the minimum personally identifiable information possible.

You can find out more about how we use your information:

- https://www.kch.nhs.uk/about/corporate/data-protection
- www.hra.nhs.uk/information-about-patients/

Need more information and want to talk to someone else?

All research is looked at by an independent committee of people called a 'Research Ethics Committee', to protect your interests. However, if you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. Their contact details are included at the end of this information sheet.

What if there is a problem?

If you wish to make a complaint about any aspect of the way you have been approached or treated during the study, normal NHS / local complaint procedures will be available to you. If you disclose information leading to safeguarding concerns or allegations of bad practice, action will be taken in line with the local policy where you are receiving your care. If you are harmed due to someone's negligence, then you may have grounds for a legal action, but you may have to pay for it.

If you wish to complain formally you can do this via the Patient Advice and Liaison Service (PALS) at:

- King's College Hospital, London - Tel: 020 3299 3601
- St Thomas' Hospital, London - Tel: 020 7188 8801
- Guy's Hospital, London - Tel: 020 7188 8803
- Princess Royal University Hospital, Kent - Tel: 01689 863252
- Nottingham University Hospital - Tel: 0800 183 0204
- Conquest Hospital, St Leonards-on-sea - Tel: 01424 758090
- Medway NHS Foundation Trust - Tel: 01634 825004
- Macclesfield District General Hospital - Tel: 01625 661111
- South Tyneside & Sunderland NHS Foundation Trust - Tel: 0191 5699549
- Royal Cornwall Hospital - Tel: 01872 252793

Independent advice and specific concerns:

Independent advice about taking part in research can be found at:

- INVOLVE
  Tel: 023 8065 1088 or Email: www.involve.org.uk

Becoming involved:

We welcome any suggestions that you have to improve this research. We are happy to share the findings of the research with you regardless of whether you participate or not.

Our contact details:

Please contact us with any questions or concerns.

Researchers:
Lucy Fettes lucy.fettes@kcl.ac.uk / l.fettes@nhs.net

Work address:
Cicely Saunders Institute, King's College London, Bessemer Road, London, SE5 9PJ

Telephone: 02078485385 / 07854 607441

Website: www.csi.kcl.ac.uk

Thank you very much for taking the time to read this information sheet and consider this study

D.2. Baseline cover letter

Comparing disability in activities of daily living over time among adults with advanced respiratory disease during the COVID-19 pandemic (DIScOVER)

Researchers

Lucy Fettes, Research Assistant/PhD student, King's College London
Dr Matthew Maddocks, Lecturer in Health Services Research in Palliative Care, King's College London
Professor Irene Higginson, Professor of Palliative Care and Policy, King's College London
Dr Stephen Ashford, Clinical Senior Lecturer and Consultant Physiotherapist, King's College London

[insert date]

Dear *[insert patient name]*

Thank you very much for considering to participate in our study to explore disability in activities of daily living over time in people with advanced respiratory disease during the Coronavirus (COVID-19) pandemic.

We are asking you to complete the same questionnaire every month for six months. This will help us to identify how a persons' ability to manage daily activities may change over several months and what interventions or health services could help someone to maintain their independence.

The study pack you received previously contained an information sheet, a consent form, and the baseline questionnaire. Please complete the baseline questionnaire as soon as possible and return by post in the enclosed envelope. Consent to participate will be assumed upon receipt of the completed questionnaire.

Thank you very much for your time, it is very much appreciated. If you have any questions regarding this study, please contact:

Ms Lucy Fettes
King's College London, c/o 59 North Street, Scalby, Scarborough, North Yorkshire. YO13 0RP.
Email: l.fettes@nhs.net; Tel: 07854 607441

Yours sincerely

Lucy Fettes

To be completed with the researcher over the telephone

Comparing disability in activities of daily living over time, among adults with advanced respiratory disease during the COVID-19 pandemic (DIScOVER)

Consent form for patients

Patient Name:	**Participant ID:**
Consent for: Pilot / Questionnaire (circle)	

		Please initial
1	I confirm that I have read and understood the information sheet version 3.0 dated 06/05/20 for the above research study and that the nature, purpose, duration, and foreseeable effects and risks of the research study and my involvement have been explained.	☐
2	I have had time to consider whether to take part in this research study. My questions have been answered satisfactorily.	☐
3	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	☐
4	I consent to my General Practitioner being informed that I am taking part in this research study *(optional).*	☐
5	I consent to the processing of personal information for the purposes of this research study. I understand that such information will be treated strictly confidentially and handled in accordance to the Data Protection Act 2018.	☐

P.T.O.

6 I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from King's College London, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐

7 I agree that appropriately qualified researchers, trained and supervised by the research team, will have access to my anonymised information for the current study and for future related research. ☐

8 I confirm that the information I provide can be used for teaching or educational purposes if the information is anonymised *(optional)*. ☐

9 I agree to being contacted during the time of the study. ☐

10 I agree to take part in this study and I understand that I will receive a copy of this consent form and a copy will be kept on file by the researcher and in my medical records. ☐

Name of Patient (in block letters)	Date	Signature
……	…….	……
Name of Person taking consent	Date	Signature
……	…….	……
Name of Witness (*if verbal consent*)	Date	Signature
……	……	……

King's College London, Cicely Saunders Institute, Faculty of Nursing, Midwifery, & Palliative Care, 6 Bessemer Road, Denmark Hill, London SE5 9PJ; Telephone: +44 (0)20 7848 5385

Thank you.

Comparing disability in activities of daily living over time among adults with advanced respiratory disease during the COVID-19 pandemic

(DIScOVER)

Participant survey booklet

BASELINE

Study ID: _____

Date survey completed *(please insert)*: _____

To be completed with the researcher over the telephone

This is a research study. This means that we may ask about some issues more than once, but in a different way.

Please answer all questions if possible. If you cannot remember, do not know the answer, or are unable to answer a particular question, please write that in.

Thank you very much.

Please feel free to contact us if you have any questions or concerns:

Lucy Fettes, Cicely Saunders Institute, Kings College London, Bessemer Road, Denmark Hill, London, SE5 9PJ.

Tel: 02078485385; Email: lucy.fettes@kcl.ac.uk / l.fettes@nhs.net

What is this survey about?

This survey will be about how you manage your daily activities, and includes questions about caring for yourself, how you walk around, the symptoms you experience, services you have been accessing, the equipment you have been using to help you, and how you have been affected by social isolation during the COVID-19 pandemic.

In order to collect all this information, the survey will be made up of several different questionnaires. Some of the questions may appear repetitive but it is important to complete all the questionnaires in the survey as each questionnaire will tell us something different.

You will be invited to complete the same questionnaire each month for six months. This will help us to identify how a persons' ability to manage daily activities may change over several months.

Please complete this questionnaire with the researcher when they telephone, who will fill in and return the questionnaire. It should take about 45 to 60 minutes to complete. You do not have to complete the questions in one go, it can be arranged to be finished another time if you need to.

Thank you very much for the time you take to answer this questionnaire, it is very much appreciated.

Information about you

Please answer the following questions about yourself.

How old are you?

How would you describe your ethnic background?

How would you describe your gender?			
☐	Male	☐	Female
☐	Other *(please describe)*	☐	Prefer not to say

What is your highest level of completed education?			
☐	Primary	☐	Vocational
☐	Secondary	☐	Undergraduate
☐	College	☐	Postgraduate

Where in the UK do you live?			
☐	Scotland	☐	West Midlands
☐	Northern Island	☐	East Midlands
☐	Wales	☐	South West
☐	North East	☐	South East
☐	North West	☐	East of England
☐	Yorkshire and the Humber	☐	Greater London

Please answer the following questions about your living situation.

Where is your current overnight location?			
☐	Home	☐	Nursing home
☐	Hospital	☐	Residential home
☐	Hospice	☐	Other *(please specify):* ……

What is your usual type of accommodation?			
☐	House	☐	Nursing home
☐	Flat with stairs access	☐	Residential home
☐	Bungalow or flat with disabled access	☐	Other *(please specify):* ……

Who do you live with? *(please tick all that apply)*			
☐	I live alone	☐	Other family member
☐	Husband/wife/partner	☐	Friend
☐	Child/children	☐	Formal caregiver
☐	Other *(please specify):*		

Do you have a formal care package or paid caregiver?			
☐	Yes	☐	No

Do you have an informal or unpaid caregiver (e.g., a family member, friend, neighbour)?			
☐	Yes	☐	No

Please answer the following questions about your condition.

What is your primary diagnosis? *(please tick all that apply)*	
☐	Non-small-cell lung cancer (NSCLC)
☐	Chronic obstructive pulmonary disease (COPD)
☐	Interstitial lung disease (ILD)
☐	Other *(please specify):*

What stage of disease do you have?	
☐	Stage 1 (mild)
☐	Stage 2 (moderate)
☐	Stage 3 (severe)
☐	Stage 4 (very severe)
☐	Don't know

When were you diagnosed? *(please insert date, month, and year if possible)*

Which of the following treatments are you receiving for your condition? *(please tick all that apply)*	
☐	Immunotherapy or targeted therapy
☐	Chemotherapy
☐	Radiotherapy
☐	Anti-fibrotic medicine
☐	Oxygen
☐	Other *(please specify):*

Which, if any, of the following conditions have you been diagnosed with *(please tick all that apply)*	
☐	Myocardial infarct
☐	Peripheral vascular disease
☐	Cerebrovascular disease (stroke)
☐	Connective tissue disease
☐	Chronic liver disease
☐	Hemiplegia
☐	Diabetes with end organ damage
☐	Leukemia
☐	Moderate or severe liver disease
☐	Malignant tumor
☐	Metastasis
☐	Congestive heart failure
☐	Dementia
☐	Chronic lung disease
☐	Ulcer
☐	Diabetes
☐	Moderate or severe kidney disease
☐	Benign tumor
☐	Lymphoma
☐	AIDS

Do you have any other conditions *(please specify)*

Which one of the following statements best describes your current level of physical activity?	
☐	100% - Normal activity, no complaints, no evidence of disease
☐	90% - Able to carry out normal activity, minor signs or symptoms of disease
☐	80% - Normal activity with effort, some signs or symptoms of disease
☐	70% - Care for self, but unable to carry on normal activity or to do active work
☐	60% - Able to care for most needs, but require occasional assistance
☐	50% - Considerable assistance and frequent medical care required
☐	40% - In bed more than 50% of the time
☐	30% - Almost completely bedfast
☐	20% - Totally bedfast and requiring extensive nursing care by professionals and/or family

Social Isolation

During the Coronavirus (COVID-19) pandemic, government guidance for social isolation was set for the general public, also known as 'lock down' as follows:

- **Social distancing:** everyone to stay at home except for essential work or errands and daily exercise (1 hour maximum) and avoid contact with others.
- **Self-isolation:** people who are in a high-risk group (e.g., aged over 70, respiratory disease, cancer, diabetes, or pregnancy) are advised to stay at home for 12 weeks except for essential errands and avoid contact with others.
- **Shielding:** people who are in a very-high risk group including those with severe respiratory disease are strongly advised to stay at home, avoid contact with others including household members and not go out at all for at least 12 weeks.

Please answer the following questions relating to how you have been affected by COVID-19 and the government 'lock down' since the beginning of the pandemic.

Have you had COVID-19 (Coronavirus), or do you think you may have had symptoms of COVID-19 (e.g., fever/high temperature, persistent cough)?	
☐	No
☐	Yes, I have had symptoms, but I've not been tested
☐	Yes, I tested positive for COVID-19
If Yes, please insert date of illness:	
How long did your illness last?	
Any further information *(e.g., hospitalization, treatment):*	

Are you currently:			
☐	Shielding	☐	Social distancing
☐	Self-isolating	☐	None of the above

Did you receive a letter from the government requesting you to stay at home as a vulnerable person for 12 weeks due to your health condition?			
☐	Yes	☐	No

To date, how long have you spent self-isolating or shielding?			
☐	Not at all	☐	12 weeks exactly
☐	Occasionally/sporadic	☐	More than 12 weeks *(please state how long):* ……
☐	Less than 12 weeks		
Please insert dates of isolation period(s):			
Any further information:			

Compared to before 'lock down', while you have been self-isolating or shielding, was your physical activity inside your home:			
☐	A lot less	☐	A little more
☐	A little less	☐	A lot more
☐	No change	☐	Not applicable

Compared to before 'lock down', while you have been self-isolating or shielding, was your physical activity outside your home:			
☐	A lot less	☐	A little more
☐	A little less	☐	A lot more
☐	No change	☐	Not applicable

Compared to before 'lock down', while you have been self-isolating or shielding, was the help you received with personal care (e.g., bathing, walking, getting in and out of bed):			
☐	A lot less	☐	A little more
☐	A little less	☐	A lot more
☐	No change	☐	Not applicable

Compared to before 'lock down', while you have been self-isolating or shielding, was the help you received with daily activities inside your home (e.g., cooking, housework):			
☐	A lot less	☐	A little more
☐	A little less	☐	A lot more
☐	No change	☐	Not applicable

Compared to before 'lock down', while you have been self-isolating or shielding, was the help you received with daily activities outside your home (e.g., shopping, collecting medication):			
☐	A lot less	☐	A little more
☐	A little less	☐	A lot more
☐	No change	☐	Not applicable

During 'lock down', how confident are you that you can get family and friends to help you with the things you need (such as household chores like shopping, cooking, or transport), if needed?											
Not at all confident	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Totally confident

During 'lock down', how confident are you that you can get help with your daily tasks (such as housekeeping, meals, or personal hygiene) from resources other than friends or family, if needed?											
Not at all confident	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Totally confident

During 'lock down', how confident are you that you can get emotional support from friends and family (such as listening or talking over your problems), if needed?											
Not at all confident	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Totally confident

During 'lock down', how confident are you that you can get emotional support from resources other than friends or family, if needed?											
Not at all confident	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Totally confident

During 'lock down', what strategies have you been doing to help maintain your well-being? *(please tick all that apply)*	
☐	I do not have any strategies
☐	Prescribed exercise programme
☐	Self-exercises
☐	Exercise/dance classes online or on TV
☐	Walk around house or garden
☐	Walk outside home
☐	Housework/domestic tasks
☐	Gardening
☐	Self-management strategies (e.g., breathlessness management, pacing)
☐	Relaxation exercises
☐	Creative activities
☐	Social support via phone or video link
☐	Other (please specify):

Personal daily activities

These questions are intended to help us find out how much help you require with day-to-day activities. For each of the activities below, **please tick** the statement that most closely matches your **current** level of ability.

Bowels	
☐ ☐ ☐	I am incontinent (or I need to be given enemas) I have occasional accidents (e.g., once per week) I am continent
Toilet Use	
☐ ☐ ☐	I am dependent on help to use the toilet I need some help, but I can do things alone I am independent (getting on and off, dressing and wiping)
Grooming	
☐ ☐	I need help with personal care I am independent (face/hair/teeth/shaving etc.)
Feeding	
☐ ☐ ☐	I am unable to feed myself I need help cutting, spreading butter etc. I am independent in feeding myself

Mobility	
☐	I am immobile
☐	I am wheelchair independent, including corners, etc.
☐	I walk with help of one person (verbal or physical)
☐	I am independent (but may use an aid, e.g., a stick)
Bladder	
☐	I am incontinent or catheterized and unable to manage
☐	I have occasional accidents (max once per 24 hours)
☐	I am continent for over 7 days at a time
Dressing	
☐	I am dependent on help to get dressed
☐	I need some help but can do about half unaided
☐	I am independent (including buttons, zips, laces etc.)
Bathing	
☐	I am dependent on help to bathe
☐	I am independent in bathing (or in shower)
Stairs	
☐	I am unable to use stairs
☐	I need help to use stairs (verbal/physical/carrying aid)
☐	I am independent going up and down
Transfers (from standing to sitting or vice versa)	
☐	I am unable – no sitting balance
☐	I need major help (one or two people), I can sit
☐	I need minor help (verbal or physical)
☐	I am independent

Day to day activities

For each question, please tick the answer that best applies to your **current** situation.

Ability to use telephone	
☐	I can operate the telephone on my own initiative – look up and dial number etc.
☐	I can dial a few well-known numbers
☐	I can answer telephone but do not dial
☐	I do not use the telephone at all
Shopping	
☐	I take care of all shopping needs independently
☐	I can shop independently for small purchases
☐	I need to be accompanied on any shopping trips
☐	I am completely unable to shop
Food preparation	
☐	I can plan, prepare, and serve adequate meals independently
☐	I can prepare adequate meals if supplied with the ingredients
☐	I can heat, serve, and prepare meals, or prepare meals but do not maintain adequate diet
☐	I need to have meals prepared and served
Housekeeping	
☐	I can maintain my house alone or with occasional assistance (e.g., “heavy work domestic help”)
☐	I can perform light daily tasks but cannot maintain acceptable level of cleanliness alone
☐	I need help with all home maintenance tasks
☐	I can perform light daily tasks such as dish washing, bed making
☐	I do not participate in any housekeeping tasks

Laundry	
☐	I do all my personal laundry completely
☐	I can wash small items (e.g., rinses stocks etc.)
☐	All my laundry must be done by others
Mode of transportation	
☐	I can travel independently on public transport or drive my own car
☐	I can arrange my own travel via taxi, but do not otherwise use public transport
☐	I can travel on public transport when accompanied by another
☐	My travel is limited to taxi or automobile with assistance of another
☐	I do not travel at all
Responsibility for own medication	
☐	I am responsible for taking medication in correct dosages at correct time
☐	I take responsibility if medication is prepared in advance in separate dosage
☐	I am not capable of dispensing own medication
Ability to manage finances	
☐	I can manage financial matters independently (budgets, writes cheques, pays rent, bills, goes to Bank), collect and keep track of income
☐	I can manage day-to-day purchases, but need help with banking, major purchases etc.
☐	I am incapable of handling money

Difficulties in everyday activities

This questionnaire asks about difficulties due to health/mental health conditions. Health conditions include diseases or illnesses, other health problems that may be short or long lasting, injuries, mental or emotional problems, and problems with alcohol or drugs.

Think back over the **past 30 days** and answer these questions thinking about how much difficulty you had doing the following activities. For each question, **please circle** only **one** response.

Understanding and communicating					
In the last 30 days, how much difficulty have you had in:					
Concentrating on doing something for ten minutes?	None	Mild	Moderate	Severe	Extreme or cannot do
Remembering to do important things?	None	Mild	Moderate	Severe	Extreme or cannot do
Analyzing and finding solutions to problems in day-to-day life?	None	Mild	Moderate	Severe	Extreme or cannot do
Learning a new task, for example learning how to get to a new place?	None	Mild	Moderate	Severe	Extreme or cannot do
Generally understanding what people say?	None	Mild	Moderate	Severe	Extreme or cannot do
Starting and maintaining a conversation?	None	Mild	Moderate	Severe	Extreme or cannot do

Getting around					
In the last 30 days, how much difficulty have you had in:					
Standing for long periods, such as 30 minutes?	None	Mild	Moderate	Severe	Extreme or cannot do
Standing up from sitting down?	None	Mild	Moderate	Severe	Extreme or cannot do
Moving around inside your home?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting out of your home?	None	Mild	Moderate	Severe	Extreme or cannot do
Walking a long distance, such as a kilometer (or equivalent)?	None	Mild	Moderate	Severe	Extreme or cannot do

Self-care					
In the last 30 days, how much difficulty have you had in:					
Washing your whole body?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting dressed?	None	Mild	Moderate	Severe	Extreme or cannot do
Eating?	None	Mild	Moderate	Severe	Extreme or cannot do
Staying in by yourself for a few days?	None	Mild	Moderate	Severe	Extreme or cannot do

Getting along with people					
In the last 30 days, how much difficulty have you had in:					
Dealing with people you do not know?	None	Mild	Moderate	Severe	Extreme or cannot do
Maintaining a friendship?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting along with people who are close to you?	None	Mild	Moderate	Severe	Extreme or cannot do
Making new friends?	None	Mild	Moderate	Severe	Extreme or cannot do
Sexual activities?	None	Mild	Moderate	Severe	Extreme or cannot do

Life activities – Household					
In the last 30 days, how much difficulty have you had in:					
Taking care of your household responsibilities?	None	Mild	Moderate	Severe	Extreme or cannot do
Doing most important household tasks well?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting all the household work done that you needed to do?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting all the household work done as quickly as needed?	None	Mild	Moderate	Severe	Extreme or cannot do

Life activities – work					
If you work (paid, non-paid, self-employed) answer the questions below, otherwise skip to the next section (participation in society).					
Because of your health condition, in the last 30 days how much difficulty have you had in:					
Your day-to-day work?	None	Mild	Moderate	Severe	Extreme or cannot do
Doing your most important work tasks <u>well</u>?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting all the work <u>done</u> that you need to do?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting your work done as <u>quickly</u> as needed?	None	Mild	Moderate	Severe	Extreme or cannot do

Participation in society					
In the last 30 days?					
How much of a problem did you have in joining in community activities (for example, festivities, religious, or other activities) in the same way as anyone else?	None	Mild	Moderate	Severe	Extreme or cannot do
How much of a problem did you have because of barriers or hindrances around you?	None	Mild	Moderate	Severe	Extreme or cannot do
How much of a problem did you have living with dignity because of attitudes and actions of others?	None	Mild	Moderate	Severe	Extreme or cannot do
How much time did you spend on your health condition or its consequences?	None	Mild	Moderate	Severe	Extreme or cannot do
How much have you been emotionally affected by your health condition?	None	Mild	Moderate	Severe	Extreme or cannot do
How much has your health been a drain on the financial resources of you or your family?	None	Mild	Moderate	Severe	Extreme or cannot do
How much of a problem did your family have because of your health problems?	None	Mild	Moderate	Severe	Extreme or cannot do

Symptoms

Below is a list of symptoms, which you may or may not have experienced. Please **put a tick** in the box to show how you feel each of these symptoms has affected you and how you have been feeling in the **past week.**

	Not at all No effect	**Slightly** But not bothered to be rid of it	**Moderately** Limits some activity or concentration	**Severely** Activities or concentration markedly affected	**Over-whelming** Unable to think of anything else
Pain	☐	☐	☐	☐	☐
Shortness of breath	☐	☐	☐	☐	☐
Weakness or lack of energy	☐	☐	☐	☐	☐
Nausea (feeling like you are going to be sick)	☐	☐	☐	☐	☐
Vomiting (being sick)	☐	☐	☐	☐	☐
Poor appetite	☐	☐	☐	☐	☐
Constipation	☐	☐	☐	☐	☐

	Not at all No effect	**Slightly** But not bothered to be rid of it	**Moderately** Limits some activity or concentration	**Severely** Activities or concentration markedly affected	**Over-whelming** Unable to think of anything else
Mouth problems	☐	☐	☐	☐	☐
Drowsiness	☐	☐	☐	☐	☐
Immobility	☐	☐	☐	☐	☐
Any other symptoms *(please specify):*					
……	☐	☐	☐	☐	☐
……	☐	☐	☐	☐	☐
……	☐	☐	☐	☐	☐

Which symptom has affected you most?	

Which symptom has improved the most?	

Equipment

Please answer the following questions about assistive equipment that you may use to help you with daily activities.

Do you use special utensils or special dishes to help you eat?			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

Do you use special equipment like a bed rail, zimmer-frame, leg-lifter, or hoist to help you get in or out of bed?			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

Do you use special equipment like a wheelchair, walker, walking stick or other device to help you get around inside?			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

Do you wear special clothing or use special equipment to get dressed?			
☐	Yes	☐	No
What kind of special clothing or equipment did you use?			
Anything else?			

Do you use special equipment like a shower seat, bath stool, or grab rail to help you bathe?			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

Do you use special equipment like a raised toilet seat, bedside commode, or grab rail to help you to use the toilet?			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

When you go outside, do you use special equipment like a walking stick, walker, or mobility scooter to help you get around outside?			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

Do you use any special equipment like rails, walking stick/crutch or stair lift to help you to ascend/descend stairs or/and steps			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

Do you use any special equipment to help you to manage domestic tasks such as cooking, housework or shopping?			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

Do you use any other special equipment to help with any other daily activities not already mentioned?			
☐	Yes	☐	No
What kind of special equipment did you use?			
What do you use it for?			
Anything else?			

Service use

These final questions are intended to help us to find out what services you have been accessing over the last month. If you tick yes, please complete all the other columns.

Please provide details of the **overnight stays** you have had over the last **month.**

Service	**In the last month have you stayed overnight in the following?**		**Number of nights in the last month**	**Any other information** E.g., reason for admission *(i.e., fall, flare-up or worsening symptoms, not coping at home)* etc.
	Yes	**No**		
Hospital	☐	☐	……. nights	
Hospice	☐	☐	……. nights	
Nursing home	☐	☐	……. nights	
Residential home	☐	☐	……. nights	
Rehabilitation facility	☐	☐	……. nights	
Other *(specify)* ……	☐	☐	……. nights	

Please provide details of any **outpatient services** that you have used over the last **month.**

Service	**In the last month have you attended the following?**		**Number of visits in the last month**	**Any other information** E.g., Reason for visit (*i.e., routine, fall, flare-up, or worsening symptoms)*; Type of rehabilitation *(i.e. community, pulmonary rehab, breathlessness service);* Location *(i.e. home, hospital, hospice);* Delivery *(e.g. remotely by telephone/video link or face to face) e*tc.
	Yes	**No**		
Specialist oncology visit	☐	☐	……. visits	
Specialist respiratory visit	☐	☐	……. visits	
Specialist palliative care visit	☐	☐	……. visits	
Day care centre	☐	☐	……. visits	
Rehabilitation	☐	☐	……. visits	
Other *(specify)* ……..	☐	☐	……. visits	

Please provide details of **other services** that you have used over the last **month.**

Service	**In the last month have you had contact with the following?**		**Number of visits in the last month**	**Average duration of each visit**	**Any other information** E.g., reason for visit *(i.e., routine, fall, flare-up or worsening symptoms, not coping);* Location *(i.e., home, hospital, hospice)*; Delivery *(e.g., remotely by telephone/video link or face to face) e*tc.
	Yes	**No**			
GP or family doctor	☐	☐	……. times		
District nurse, or community nurse, or GP practice nurse	☐	☐	……. times		
Specialist oncology nurse	☐	☐	……. times		
Specialist respiratory nurse	☐	☐	……. times		
Specialist palliative care nurse	☐	☐	……. times		
Palliative care or hospice at home team	☐	☐	……. times		
Physiotherapist	☐	☐	……. times		
Occupational therapist	☐	☐	……. times		

Service	**In the last month have you had contact with the following?**		**Number of visits in the last month**	**Average duration of each visit**	**Any other information** E.g., reason for visit *(i.e., routine, fall, flare-up or worsening symptoms, not coping);* Location *(i.e., home, hospital, hospice)*; Delivery *(e.g., remotely by telephone/video link or face to face) e*tc.
	Yes	**No**			
Rehabilitation or therapy assistant	☐	☐	……. times		
Psychologist or counsellor	☐	☐	……. times		
Social worker	☐	☐	……. times		
Dietitian	☐	☐	……. times		
Speech and language therapist	☐	☐	……. times		
Complementary therapist	☐	☐	……. times		
Paid formal carer	☐	☐	……. times		
Night sitters	☐	☐	……. times		
Informal carer (e.g., relative, friend, neighbour)	☐	☐	……. times		
Volunteer	☐	☐	……. times		
Other *(specify)* ……..	☐	☐	…… times		

Thank you very much.

If you completed this questionnaire over the telephone with the researcher, there is no need to return this questionnaire.

Otherwise, please return the completed questionnaire in the stamped addressed envelope provided, which will be addressed to either:

Ms Lucy Fettes
Cicely Saunders Institute,
Kings College London,
Bessemer Road,
Denmark Hill,
London.
SE5 9PJ

Ms Lucy Fettes
King's College London
c/o 59 North Street,
Scalby,
Scarborough,
North Yorkshire.
YO13 0RP

Ms Lucy Fettes
King's College London
c/o 50 Albemarle Road,
York
North Yorkshire.
YO23 1ER

Tel: 0207 848 5385 / 07854 607441

Email: lucy.fettes@kcl.ac.uk / l.fettes@nhs.net

Comparing disability in activities of daily living over time, among adults with advanced respiratory disease during the COVID-19 pandemic (DIScOVER)

GP Letter

Investigators: Lucy Fettes, Research Assistant/PhD student, King's College London
Dr Matthew Maddocks, Lecturer in Health Services Research in Palliative Care, King's College
Professor Irene Higginson, Professor of Palliative Care and Policy, King's College London
Dr Stephen Ashford, Clinical Senior Lecturer and Consultant Physiotherapist, King's College

[insert date]

Dear *[insert GP name]*

Re: *[insert patient name]*

Your patient has agreed to participate in an observational study to explore disability in activities of daily living over time in patients with advanced lung cancer or respiratory disease during the Coronavirus (COVID-19) pandemic. This will enable us to understand how disability changes towards end-of-life, and what, where and for whom services or interventions can be modified to target disability in activities of daily living.

Following consent, participants will complete a baseline questionnaire upon enrolment and a series of repeated postal questionnaires at monthly intervals over 6 months. These questionnaires will ask participants how they are managing their daily activities as well as symptoms they are experiencing, services they are accessing and use of assistive devices.

I enclose a participant information leaflet for your reference. If you have any questions regarding this study, please contact:

Lucy Fettes (research assistant)
Cicely Saunders Institute
Bessemer Road
London SE5 9PJ

Tel: 07854 607441
Email: lucy.fettes@kcl.ac.uk

Yours sincerely

D.6. Follow-up cover letter

Comparing disability in activities of daily living over time among adults with advanced respiratory disease during the COVID-19 pandemic (DIScOVER)

Researchers
Lucy Fettes, Research Assistant/PhD student, King's College London
Dr Matthew Maddocks, Lecturer in Health Services Research in Palliative Care, King's College London
Professor Irene Higginson, Professor of Palliative Care and Policy, King's College London
Dr Stephen Ashford, Clinical Senior Lecturer and Consultant Physiotherapist, King's College London

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[insert date]

Dear *[insert patient name]*

Thank you very much for agreeing to participate in our study to explore disability in activities of daily living over time in people with advanced lung cancer or respiratory disease during the Coronavirus (COVID-19) pandemic.

We are asking you to complete the same questionnaire every month for six months. This will help us to identify how a persons' ability to manage daily activities may change over several months and what interventions or health services could help someone to maintain their independence.

Please complete the enclosed questionnaire for *[insert one, two etc.]* month follow-up as soon as possible and return in the stamped addressed envelope provided. This questionnaire will take about 30 to 60 minutes to complete.

Thank you very much for the time you take to do this, it is very much appreciated.

If you have any questions regarding this study, please contact:

Ms Lucy Fettes
King's College London, c/o 59 North Street, Scalby, Scarborough, North Yorkshire. YO13 0RP.
Email: l.fettes@nhs.net; Tel: 07854 607441

Yours sincerely

D.4. Follow-up questionnaire

Comparing disability in activities of daily living over time among adults with advanced respiratory disease during the COVID-19 pandemic

(DIScOVER)

Participant survey booklet

Study ID:

Month of follow-up *(researcher to please circle):*

1	2	3	4	5	6

Date survey completed *(participant to please insert):*

This is a research study. This means that we may ask about some issues more than once, but in a different way.

Please answer all questions if possible. If you cannot remember, do not know the answer, or are unable to answer a particular question, please write that in.

Thank you very much.

Please feel free to contact us if you have any questions or concerns:

Lucy Fettes, Cicely Saunders Institute, Kings College London, Bessemer Road, Denmark Hill, London, SE5 9PJ.

Tel: 02078485385; Email: lucy.fettes@kcl.ac.uk / l.fettes@nhs.net

What is this survey about?

This survey will be about how you manage your daily activities, and includes questions about caring for yourself, how you walk around, the symptoms you experience, services you have been accessing, the equipment you have been using to help you, and how you have been affected by social isolation during the COVID-19 pandemic.

In order to collect all this information, the survey will be made up of several different questionnaires. Some of the questions may appear repetitive but it is important to complete all the questionnaires in the survey as each questionnaire will tell us something different.

You will be invited to complete the same questionnaire each month for six months. This will help us to identify how a persons' ability to manage daily activities may change over several months.

Please complete this questionnaire as soon as possible and return in the stamped addressed envelope provided or to the researchers NHS email address. It should take about 30 to 60 minutes to complete. You do not have to complete the questions in one go, you can come back later if you need to. If you need help to complete the questionnaire, please let the researcher know and this can be arranged.

Thank you very much for the time you take to answer this questionnaire, it is very much appreciated. Please fill in the date you complete the questionnaire on the front cover, thank you.

Social Isolation

During the Coronavirus (COVID-19) pandemic, government guidance for social isolation was set for the general public, also known as 'lock down' as follows:

- **Social distancing:** everyone to stay at home except for essential work or errands and daily exercise (1 hour maximum) and avoid contact with others.
- **Self-isolation:** people who are in a high-risk group (e.g., aged over 70, respiratory disease, cancer, diabetes, or pregnancy) are advised to stay at home for 12 weeks except for essential errands and avoid contact with others.
- **Shielding:** people who are in a very-high risk group including those with severe respiratory disease are strongly advised to stay at home, avoid contact with others including household members and not go out at all for at least 12 weeks.

Please answer the following questions relating to how you have been affected by COVID-19 and the government 'lock down' since the beginning of the pandemic.

Have you had COVID-19 (Coronavirus), or do you think you may have had symptoms of COVID-19 (e.g., fever/high temperature, persistent cough)?	
☐	No
☐	Yes, I have had symptoms, but I've not been tested
☐	Yes, I tested positive for COVID-19
If Yes, please insert date of illness:	
How long did your illness last?	
Any further information *(e.g., hospitalization, treatment):*	

Are you currently:			
☐	Shielding	☐	Social distancing
☐	Self-isolating	☐	None of the above

Personal daily activities

These questions are intended to help us find out how much help you require with day-to-day activities. For each of the activities below, **please tick** the statement that most closely matches your **current** level of ability.

Bowels	
☐	I am incontinent (or I need to be given enemas)
☐	I have occasional accidents (e.g., once per week)
☐	I am continent
Toilet Use	
☐	I am dependent on help to use the toilet
☐	I need some help, but I can do things alone
☐	I am independent (getting on and off, dressing and wiping)
Grooming	
☐	I need help with personal care
☐	I am independent (face/hair/teeth/shaving etc.)
Feeding	
☐	I am unable to feed myself
☐	I need help cutting, spreading butter etc.
☐	I am independent in feeding myself

Mobility	
☐	I am immobile
☐	I am wheelchair independent, including corners, etc.
☐	I walk with help of one person (verbal or physical)
☐	I am independent (but may use an aid, e.g., a stick)
Bladder	
☐	I am incontinent or catheterized and unable to manage
☐	I have occasional accidents (max once per 24 hours)
☐	I am continent for over 7 days at a time
Dressing	
☐	I am dependent on help to get dressed
☐	I need some help but can do about half unaided
☐	I am independent (including buttons, zips, laces etc.)
Bathing	
☐	I am dependent on help to bathe
☐	I am independent in bathing (or in shower)
Stairs	
☐	I am unable to use stairs
☐	I need help to use stairs (verbal/physical/carrying aid)
☐	I am independent going up and down
Transfers (from standing to sitting or vice versa)	
☐	I am unable – no sitting balance
☐	I need major help (one or two people), I can sit
☐	I need minor help (verbal or physical)
☐	I am independent

Day to day activities

For each question, please tick the answer that best applies to your **current** situation.

Ability to use telephone	
☐	I can operate the telephone on my own initiative – look up and dial number etc.
☐	I can dial a few well-known numbers
☐	I can answer telephone but do not dial
☐	I do not use the telephone at all
Shopping	
☐	I take care of all shopping needs independently
☐	I can shop independently for small purchases
☐	I need to be accompanied on any shopping trips
☐	I am completely unable to shop
Food preparation	
☐	I can plan, prepare, and serve adequate meals independently
☐	I can prepare adequate meals if supplied with the ingredients
☐	I can heat, serve, and prepare meals, or prepare meals but do not maintain adequate diet
☐	I need to have meals prepared and served
Housekeeping	
☐	I can maintain my house alone or with occasional assistance (e.g., “heavy work domestic help”)
☐	I can perform light daily tasks but cannot maintain acceptable level of cleanliness alone
☐	I need help with all home maintenance tasks
☐	I can perform light daily tasks such as dish washing, bed making
☐	I do not participate in any housekeeping tasks

Laundry	
☐	I do all my personal laundry completely
☐	I can wash small items (e.g., rinses stocks etc.)
☐	All my laundry must be done by others
Mode of transportation	
☐	I can travel independently on public transport or drive my own car
☐	I can arrange my own travel via taxi, but do not otherwise use public transport
☐	I can travel on public transport when accompanied by another
☐	My travel is limited to taxi or automobile with assistance of another
☐	I do not travel at all
Responsibility for own medication	
☐	I am responsible for taking medication in correct dosages at correct time
☐	I take responsibility if medication is prepared in advance in separate dosage
☐	I am not capable of dispensing own medication
Ability to manage finances	
☐	I can manage financial matters independently (budgets, writes cheques, pays rent, bills, goes to Bank), collect and keep track of income
☐	I can manage day-to-day purchases, but need help with banking, major purchases etc.
☐	I am incapable of handling money

Difficulties in everyday activities

This questionnaire asks about difficulties due to health/mental health conditions. Health conditions include diseases or illnesses, other health problems that may be short or long lasting, injuries, mental or emotional problems, and problems with alcohol or drugs.

Think back over the **past 30 days** and answer these questions thinking about how much difficulty you had doing the following activities. For each question, **please circle** only **one** response.

Understanding and communicating					
In the last 30 days, how much difficulty have you had in:					
Concentrating on doing something for ten minutes?	None	Mild	Moderate	Severe	Extreme or cannot do
Remembering to do important things?	None	Mild	Moderate	Severe	Extreme or cannot do
Analyzing and finding solutions to problems in day-to-day life?	None	Mild	Moderate	Severe	Extreme or cannot do
Learning a new task, for example learning how to get to a new place?	None	Mild	Moderate	Severe	Extreme or cannot do
Generally understanding what people say?	None	Mild	Moderate	Severe	Extreme or cannot do
Starting and maintaining a conversation?	None	Mild	Moderate	Severe	Extreme or cannot do

Getting around					
In the last 30 days, how much difficulty have you had in:					
Standing for long periods, such as 30 minutes?	None	Mild	Moderate	Severe	Extreme or cannot do
Standing up from sitting down?	None	Mild	Moderate	Severe	Extreme or cannot do
Moving around inside your home?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting out of your home?	None	Mild	Moderate	Severe	Extreme or cannot do
Walking a long distance, such as a kilometer (or equivalent)?	None	Mild	Moderate	Severe	Extreme or cannot do

Self-care					
In the last 30 days, how much difficulty have you had in:					
Washing your whole body?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting dressed?	None	Mild	Moderate	Severe	Extreme or cannot do
Eating?	None	Mild	Moderate	Severe	Extreme or cannot do
Staying in by yourself for a few days?	None	Mild	Moderate	Severe	Extreme or cannot do

Getting along with people					
In the last 30 days, how much difficulty have you had in:					
Dealing with people you do not know?	None	Mild	Moderate	Severe	Extreme or cannot do
Maintaining a friendship?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting along with people who are close to you?	None	Mild	Moderate	Severe	Extreme or cannot do
Making new friends?	None	Mild	Moderate	Severe	Extreme or cannot do
Sexual activities?	None	Mild	Moderate	Severe	Extreme or cannot do

Life activities – Household					
In the last 30 days, how much difficulty have you had in:					
Taking care of your household responsibilities?	None	Mild	Moderate	Severe	Extreme or cannot do
Doing most important household tasks well?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting all the household work done that you needed to do?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting all the household work done as quickly as needed?	None	Mild	Moderate	Severe	Extreme or cannot do

Life activities – work					
If you work (paid, non-paid, self-employed) answer the questions below, otherwise skip to the next section (participation in society).					
Because of your health condition, in the last 30 days how much difficulty have you had in:					
Your day-to-day work?	None	Mild	Moderate	Severe	Extreme or cannot do
Doing your most important work tasks well?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting all the work done that you need to do?	None	Mild	Moderate	Severe	Extreme or cannot do
Getting your work done as quickly as needed?	None	Mild	Moderate	Severe	Extreme or cannot do

Participation in society					
In the last 30 days?					
How much of a problem did you have in joining in community activities (for example, festivities, religious, or other activities) in the same way as anyone else?	None	Mild	Moderate	Severe	Extreme or cannot do
How much of a problem did you have because of barriers or hindrances around you?	None	Mild	Moderate	Severe	Extreme or cannot do
How much of a problem did you have living with dignity because of attitudes and actions of others?	None	Mild	Moderate	Severe	Extreme or cannot do
How much time did you spend on your health condition or its consequences?	None	Mild	Moderate	Severe	Extreme or cannot do
How much have you been emotionally affected by your health condition?	None	Mild	Moderate	Severe	Extreme or cannot do
How much has your health been a drain on the financial resources of you or your family?	None	Mild	Moderate	Severe	Extreme or cannot do
How much of a problem did your family have because of your health problems?	None	Mild	Moderate	Severe	Extreme or cannot do

Symptoms

Below is a list of symptoms, which you may or may not have experienced. Please **put a tick** in the box to show how you feel each of these symptoms has affected you and how you have been feeling in the **past week.**

	Not at all No effect	**Slightly** But not bothered to be rid of it	**Moderately** Limits some activity or concentration	**Severely** Activities or concentration markedly affected	**Over-whelming** Unable to think of anything else
Pain	☐	☐	☐	☐	☐
Shortness of breath	☐	☐	☐	☐	☐
Weakness or lack of energy	☐	☐	☐	☐	☐
Nausea (feeling like you are going to be sick)	☐	☐	☐	☐	☐
Vomiting (being sick)	☐	☐	☐	☐	☐
Poor appetite	☐	☐	☐	☐	☐
Constipation	☐	☐	☐	☐	☐

	Not at all No effect	**Slightly** But not bothered to be rid of it	**Moderately** Limits some activity or concentration	**Severely** Activities or concentration markedly affected	**Over-whelming** Unable to think of anything else
Mouth problems	☐	☐	☐	☐	☐
Drowsiness	☐	☐	☐	☐	☐
Immobility	☐	☐	☐	☐	☐
Any other symptoms *(please specify):*					
……	☐	☐	☐	☐	☐
……	☐	☐	☐	☐	☐
……	☐	☐	☐	☐	☐

Which symptom has affected you most?	

Which symptom has improved the most?	

Equipment

Please answer the following questions about assistive equipment that you may use to help you with daily activities.

Do you use special utensils or special dishes to help you eat?			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

Do you use special equipment like a bed rail, zimmer-frame, leg-lifter, or hoist to help you get in or out of bed?			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

Do you use special equipment like a wheelchair, walker, walking stick or other device to help you get around inside?			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

Do you wear special clothing or use special equipment to get dressed?			
☐	Yes	☐	No
What kind of special clothing or equipment did you use?			
Anything else?			

Do you use special equipment like a shower seat, bath stool, or grab rail to help you bathe?			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

Do you use special equipment like a raised toilet seat, bedside commode, or grab rail to help you to use the toilet?			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

When you go outside, do you use special equipment like a walking stick, walker, or mobility scooter to help you get around outside?			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

Do you use any special equipment like rails, walking stick/crutch or stair lift to help you to ascend/descend stairs or/and steps			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

Do you use any special equipment to help you to manage domestic tasks such as cooking, housework or shopping?			
☐	Yes	☐	No
What kind of special equipment did you use?			
Anything else?			

Do you use any other special equipment to help with any other daily activities not already mentioned?			
☐	Yes	☐	No
What kind of special equipment did you use?			
What do you use it for?			
Anything else?			

Service use

These final questions are intended to help us to find out what services you have been accessing over the last month. If you tick yes, please complete all the other columns.

Please provide details of the **overnight stays** you have had over the last **month.**

Service	**In the last month have you stayed overnight in the following?**		**Number of nights in the last month**	**Any other information** E.g., reason for admission *(i.e., fall, flare-up or worsening symptoms, not coping at home)* etc.
	Yes	**No**		
Hospital	☐	☐	……. nights	
Hospice	☐	☐	……. nights	
Nursing home	☐	☐	……. nights	
Residential home	☐	☐	……. nights	
Rehabilitation facility	☐	☐	……. nights	
Other *(specify)* ……..	☐	☐	……. nights	

Please provide details of any **outpatient services** that you have used over the last **month.**

Service	**In the last month have you attended the following?**		**Number of visits in the last month**	**Any other information** E.g., Reason for visit (*i.e. routine, fall, flare-up, or worsening symptoms)*; Type of rehabilitation *(i.e. community, pulmonary rehab, breathlessness service);* Location *(i.e. home, hospital, hospice);* Delivery *(e.g. remotely by telephone/video link or face to face) e*tc.
	Yes	**No**		
Specialist oncology visit	☐	☐	……. visits	
Specialist respiratory visit	☐	☐	……. visits	
Specialist palliative care visit	☐	☐	……. visits	
Day care centre	☐	☐	……. visits	
Rehabilitation	☐	☐	……. visits	
Other *(specify)* ……..	☐	☐	……. visits	

Please provide details of **other services** that you have used over the last **month.**

Service	**In the last month have you had contact with the following?**		**Number of visits in the last month**	**Average duration of each visit**	**Any other information** E.g., reason for visit *(i.e., routine, fall, flare-up or worsening symptoms, not coping);* Location *(i.e., home, hospital, hospice)*; Delivery *(e.g., remotely by telephone/video link or face to face) e*tc.
	Yes	**No**			
GP or family doctor	☐	☐	……. times		
District nurse, or community nurse, or GP practice nurse	☐	☐	……. times		
Specialist oncology nurse	☐	☐	……. times		
Specialist respiratory nurse	☐	☐	……. times		
Specialist palliative care nurse	☐	☐	……. times		
Palliative care or hospice at home team	☐	☐	……. times		
Physiotherapist	☐	☐	……. times		
Occupational therapist	☐	☐	……. times		

Service	**In the last month have you had contact with the following?**		**Number of visits in the last month**	**Average duration of each visit**	**Any other information** E.g., reason for visit *(i.e., routine, fall, flare-up or worsening symptoms, not coping);* Location *(i.e., home, hospital, hospice)*; Delivery *(e.g., remotely by telephone/video link or face to face) e*tc.
	Yes	**No**			
Rehabilitation or therapy assistant	☐	☐	……. times		
Psychologist or counsellor	☐	☐	……. times		
Social worker	☐	☐	……. times		
Dietitian	☐	☐	……. times		
Speech and language therapist	☐	☐	……. times		
Complementary therapist	☐	☐	……. times		
Paid formal carer	☐	☐	……. times		
Night sitters	☐	☐	……. times		
Informal carer (e.g., relative, friend, neighbour)	☐	☐	……. times		
Volunteer	☐	☐	……. times		
Other *(specify)* ……..	☐	☐	…… times		

Thank you very much.

Please return the completed questionnaire in the stamped addressed envelope provided, which will be addressed to either:

Ms Lucy Fettes Cicely Saunders Institute, Kings College London, Bessemer Road, Denmark Hill, London. SE5 9PJ	Ms Lucy Fettes King's College London c/o 59 North Street, Scalby, Scarborough, North Yorkshire. YO13 0RP	Ms Lucy Fettes King's College London c/o 50 Albemarle Road, York North Yorkshire. YO23 1ER

Tel: 0207 848 5385 / 07854 607441

Email: lucy.fettes@kcl.ac.uk / l.fettes@nhs.net

Appendix E

Rules regarding inclusion and continuation of follow-up and completion

E.1. Rules regarding inclusion and continuation of follow-up in the cohort study

Rule	FU status alive and ok to contact	Received last questionnaire	Able to contact within 3 phone calls	Action
1	no	no	NA	Withdraw from study
2	no	yes	NA	i) Withdraw if participant has died or is dying. ii) If unwell or an inpatient check with the local researcher, the following week: - if died or dying withdraw - if ok continue - if still unwell miss timepoint (record reason) and review next month
3	yes	yes	Yes	i) Send follow up if participant wishes to continue. ii) If participant does not wish to continue, withdraw, and record reason.
4	yes	yes	No	Send follow up and withdraw if not returned
5	yes	no	Yes	i) If participant wishes to continue, send follow up and record reason for missing timepoint. ii) If participant does not want to continue, withdraw, and record reason.
6	yes	no	No	Withdraw from study
7	unknown	yes	Yes	i) send follow up if participant wishes to continue. ii) If participant does not wish to continue, withdraw, and record reason.
8	unknown	no	Yes	i) send follow up if participant wishes to continue. ii) If participant does not wish to continue, withdraw, and record reason.
9	unknown	yes	No	Withdraw from study
10	unknown	no	No	Withdraw from study

E.2. Rules regarding completion of the cohort study

Rule	Returned Questionnaire	Action
1	Participant completed < 1 week of expected completion date	Record date of completion - no change to follow-up
2	Participant completed within a week of next months' completion date	Class as the next months' follow-up and record reason for missing timepoint.
3	Participant completed >1 week later than expected completion date but < 1 week before next one is due	Delay sending next questionnaire by i) 1 week if 1-2 weeks late ii) 2 weeks if 2-3 weeks late
4	Questionnaire not returned	Attempt to telephone up to 3 times to chase questionnaire: i) if unable to contact - withdraw. ii) Able to contact but does wish to participate - withdraw. iii) Able to contact, participants unable to do this timepoint but does not wish to withdraw - class as missing and record reason. iv) Able to contact participant is in the process of returning the questionnaire – refer to follow-up rules.

Appendix F

Ethical Approval

NHS
Health Research Authority

London - Camberwell St Giles Research Ethics Committee
Level 3, Block B
Whitefriars
Lewins Mead
Bristol
BS1 2NT

Telephone: 0207104 8204

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

11 February 2020

Dr Matthew Maddocks
Cicely Saunders Institute
King's College London
Bessemer Road, London
SE5 9PJ

Dear Dr Maddocks

Study title:	**Comparing disability in activities of daily living over time among adults with advanced lung cancer or respiratory disease**
REC reference:	**19/LO/1950**
Protocol number:	**N/A**
IRAS project ID:	**271894**

Thank you for your reply received on the 26th January 2020, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation [as revised], subject to the conditions specified below.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.
Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations

Registration of Clinical Trials

It is a condition of the REC favourable opinion that **all clinical trials are registered** on a publicly accessible database. For this purpose, 'clinical trials' are defined as the first four project categories in IRAS project filter question 2. Registration is a legal requirement for clinical trials of investigational medicinal products (CTIMPs), except for phase I trials in healthy volunteers (these must still register as a condition of the REC favourable opinion).

Registration should take place as early as possible and within six weeks of recruiting the first research participant at the latest. Failure to register is a breach of these approval conditions, unless a deferral has been agreed by or on behalf of the Research Ethics Committee (see here for more information on requesting a deferral: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/research-registration-research-project-identifiers/

As set out in the UK Policy Framework, research sponsors are responsible for making information about research publicly available before it starts e.g. by registering the research project on a publicly accessible register. Further guidance on registration is available at: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/transparency-responsibilities/

You should notify the REC of the registration details. We will audit these as part of the annual progress reporting process.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

After ethical review: Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol

- Progress and safety reports
- Notifying the end of the study, including early termination of the study
- Final report

The latest guidance on these topics can be found at https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/.

Ethical review of research sites

NHS/HSC sites

The favourable opinion applies to all NHS/HSC sites listed in the application subject to confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or management permission (in Scotland) being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Sponsor insurance]	1	23 July 2019
IRAS Application Form [IRAS_Form_19112019]		19 November 2019
IRAS Checklist XML [Checklist_26012020]		26 January 2020
Letter from funder [Funding confrimation]	1	27 November 2017
Letter from sponsor [sponsorhip authorasation request]	1	11 November 2019
Non-validated questionnaire [demographic questionnaire]	1	11 November 2019
Non-validated questionnaire [Questionnaire booklet baseline]	1	11 November 2019
Other [signed funding confirmation]	1	27 November 2017
Other [Sponsor indemnity insurance]	1	02 August 2019
Other [Supervisor CV - IH]	1	21 November 2019
Other [Supervisor CV - SA]	1	21 November 2019
Other [Response to Ethical review]	1	13 January 2020
Other [GP letter]	1	13 January 2020
Other [The Frail Scale]	1	13 January 2020
Other [SARC-F]	1	13 January 2020
Other [Partcipating Organisations]	1	13 January 2020
Participant consent form [consent form]	1	11 November 2019
Participant consent form [consent form]	2	10 January 2020
Participant information sheet (PIS) [Participant information sheet]	1	11 November 2019
Participant information sheet (PIS) [Participant information sheet]	2	10 January 2020
Research protocol or project proposal [Study protocol]	1	11 November 2019
Summary CV for Chief Investigator (CI) [Cheif Investigator CV]	1	12 November 2019
Summary CV for student [Student CV]	1	11 November 2019
Summary CV for supervisor (student research) [Supervisor CV - MM]	1	11 November 2019

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

19/LO/1950	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

Pp

Mr John Richardson
Chair

Email: nrescommittee.london-camberwellstgiles@nhs.net

Enclosures: "After ethical review – guidance for researchers"
Copy to: Prof Reza Razavi

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Dr Matthew Maddocks
Cicely Saunders Institute
King's College London
Bessemer Road, London
SE5 9PJ

Email: hra.approval@nhs.net
HCRW.approvals@wales.nhs.uk

11 February 2020

Dear Dr Maddocks

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Comparing disability in activities of daily living over time among adults with advanced lung cancer or respiratory disease**
IRAS project ID:	**271894**
Protocol number:	**N/A**
REC reference:	**19/LO/1950**
Sponsor	**King's College London**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The standard conditions document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **271894**. Please quote this on all correspondence.

Yours sincerely,

Natalie Wilson
Approvals Manager

Email: nrescommittee.london-camberwellstgiles@nhs.net

Copy to: *Professor Reza Razavi, KCL, Sponsor contact*
Miss Lucy Fettes, KCL, Student researcher

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Sponsor insurance]	1	23 July 2019
IRAS Application Form [IRAS_Form_19112019]		19 November 2019
IRAS Checklist XML [Checklist_26012020]		26 January 2020
Letter from funder [Funding confrimation]	1	27 November 2017
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Non-validated questionnaire [Questionnaire booklet baseline]	1	11 November 2019
Organisation Information Document [Organisation information document]	1	
Other [signed funding confirmation]	1	27 November 2017
Other [Sponsor indemnity insurance]	1	02 August 2019
Other [Supervisor CV - IH]	1	21 November 2019
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Other [The Frail Scale]	1	13 January 2020
Other [SARC-F]	1	13 January 2020
Other [Partcipating Organisations]	1	13 January 2020
Participant consent form [consent form]	2	10 January 2020
Participant information sheet (PIS) [Participant information sheet]	2	10 January 2020
Research protocol or project proposal [Study protocol]	1	11 November 2019
Schedule of Events or SoECAT [Final]	1	26 November 2019
Summary CV for Chief Investigator (CI) [Cheif Investigator CV]	1	12 November 2019
Summary CV for student [Student CV]	1	11 November 2019
Summary CV for supervisor (student research) [Supervisor CV - MM]	1	11 November 2019

IRAS project ID	271894

Information to support study set up

The below provides all parties with information to support the arranging and confirming of capacity and capability with participating NHS organisations in England and Wales. This is intended to be an accurate reflection of the study at the time of issue of this letter.

Types of participating NHS organisation	Expectations related to confirmation of capacity and capability	Agreement to be used	Funding arrangements	Oversight expectations	HR Good Practice Resource Pack expectations
Research activities and procedures.as per the protocol and other study documents will take place at participating NHS organisations.	Research activities should not commence at participating NHS organisations in England or Wales prior to their formal confirmation of capacity and capability to deliver the study.	An Organisation Information Document has been submitted and the sponsor is not requesting and does not expect any other site agreement to be used.	Sponsor is not providing funding to participating NHS organisations.	A Principal Investigator (PI) is expected at participating NHS organisations.	Where arrangements are not already in place, research staff not employed by the NHS host organisation undertaking any of the research activities listed in the research application would be expected to obtain an honorary research contract from one NHS organisation (if university employed), followed by Letters of Access for subsequent organisations. This would be on the basis of a Research Passport (if university employed) or an NHS to NHS confirmation of pre-engagement checks letter (if NHS employed). These should confirm enhanced DBS checks, including appropriate barred list checks, and occupational health clearance. For research team members only administering questionnaires or surveys, a Letter of Access based on standard DBS checks and occupational health clearance would be appropriate.

Other information to aid study set-up and delivery

This details any other information that may be helpful to sponsors and participating NHS organisations in England and Wales in study set-up.
The applicant has indicated that they intend to apply for inclusion on the NIHR CRN Portfolio.

NHS
Health Research Authority

London - Camberwell St Giles Research Ethics Committee

Level 3, Block B
Whitefriars
Lewins Mead
Bristol
BS1 2NT

Tel: 02071048103

23 June 2020

Miss Lucy Fettes
Research assistant/PhD student
Cicely Saunders Institute
King's Colege London
Bessemer Road
London
SE5 9PJ

Dear Miss Fettes,

Study title:	**Comparing disability in activities of daily living over time among adults with advanced lung cancer or respiratory disease**
REC reference:	**19/LO/1950**
Protocol number:	**N/A**
Amendment number:	**Substantial Amendment 1**
Amendment date:	**11 June 2020**
IRAS project ID:	**271894**

The above amendment was reviewed at the meeting of the Sub-Committee held in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Completed Amendment Tool [271894_Substantial Amendment 1]	1	11 June 2020
Covering letter on headed paper [Baseline cover letter]	1	06 May 2020

Covering letter on headed paper [Follow up cover letter]	1	06 May 2020
GP/consultant information sheets or letters [GP letter]	2	06 May 2020
Letters of invitation to participant [Study invitation]	1	06 May 2020
Participant consent form [Consent form]	3	06 May 2020
Participant information sheet (PIS) [Participant information sheet]	3	06 May 2020
Research protocol or project proposal [Study Protocol]	2	06 May 2020
Validated questionnaire [Participant questionnaire]	2	06 May 2020

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Amendments related to COVID-19

We will update your research summary for the above study on the research summaries section of our website. During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you have not already done so, please register your study on a public registry as soon as possible and provide the HRA with the registration detail, which will be posted alongside other information relating to your project.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

19/LO/1950:	**Please quote this number on all correspondence**

Yours sincerely,
PP

Chair

E-mail: camberwellstgiles.rec@hra.nhs.uk

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Miss Lucy Fettes, Cicely Saunders Institute*

London - Camberwell St Giles Research Ethics Committee

Attendance at Sub-Committee of the REC meeting held via correspondence

Committee Members:

Name	*Profession*	*Present*	*Notes*
Dr Michael Millar (Chair)	Consultant in Infection (Barts Health)	Yes	
Mr James Uwalaka	Regulatory Compliance Officer	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Miss Yasmin King	Approvals Administrator

Appendix G

Scoring of Measurement Instruments

G.1. Charlson Co-morbidity Index scoring

Co-morbidity	Score
Myocardial Infarction	1
Peripheral Vascular Disease	1
Cerebrovascular Disease (stroke)	1
Connective Tissue Disease	1
Hemiplegia	2
Diabetes with End Organ Damage	2
Leukemia	2
Moderate/Severe Liver Disease	3
Malignant Tumour	6
Metastasis	6
Congestive Heart Failure	1
Dementia	1
Chronic Lung Disease	1
Ulcer	1
Diabetes	1
Moderate/Severe Kidney Disease	2
Benign Tumour	2
Lymphoma	2
AIDS	6
Total co-morbidity	Sum of co-morbidities
Interpretation	Higher score = greater burden of co-morbidities
Missing	Insert 999
NB. Ensure the diagnosis is included in the Charlson: Lung cancer = *'malignant tumour'*; COPD/ILD = *'chronic lung disease'*. If recorded cancer spread/mets in additional info this should be classed as *'metastasis'*.	

G.2. Australian Karnofsky Performance Status (AKPS) scoring

Functional performance status (AKPS)	
100	100% - Normal activity, no complaints, no evidence of disease
90	90% - Able to carry out normal activity, minor signs or symptoms of disease
80	80% - Normal activity with effort, some signs or symptoms of disease
70	70% - Care for self, but unable to carry on normal activity or to do active work
60	60% - Able to care for most needs, but require occasional assistance
50	50% - Considerable assistance and frequent medical care required
40	40% - In bed more than 50% of the time
30	30% - Almost completely bedfast
20	20% - Totally bedfast and requiring extensive nursing care by professionals and/or family
Missing	insert 999

G.3. Physical Activity scoring

physical activity inside your home:			
1	A lot less	4	A little more
2	A little less	5	A lot more
3	No change	6	No Change
physical activity outside your home:			
1	A lot less	4	A little more
2	A little less	5	A lot more
3	No change	6	No Change
help you received with personal care			
1	A lot less	4	A little more
2	A little less	5	A lot more
3	No change	6	No Change
help you received with daily activities inside your home			
1	A lot less	4	A little more
2	A little less	5	A lot more
3	No change	6	No Change
help you received with daily activities outside your home			
1	A lot less	4	A little more
2	A little less	5	A lot more
3	No change	6	No Change
NB. We can assume 'not applicable' (6) is no change so we can change all the 6's to a 3			
Missing	insert 999		

G.4. Chronic Disease Self-Efficacy Scale (CDSE) scoring

	Obtain Help from Community, Family, Friends Scale	**Confidence**
1	During 'lock down', how confident are you that you can get family and friends to help you with the things you need (such as household chores like shopping, cooking, or transport), if needed?	insert 1 to 10
2	During 'lock down', how confident are you that you can get help with your daily tasks (such as housekeeping, meals, or personal hygiene) from resources other than friends or family, if needed?	insert 1 to 10
3	During 'lock down', how confident are you that you can get emotional support from friends and family (such as listening or talking over your problems), if needed?	insert 1 to 10
4	During 'lock down', how confident are you that you can get emotional support from resources other than friends or family, if needed?	insert 1 to 10
Total	total subscale score is the mean of the 4 items	mean
Interpretation	Total score ranges from 4 to 10. Higher score = greater confidence in receiving social support	
Missing	For scales with 3-4 items, do not score the scale if more than 1 item is missing, in which case total score would be classed as 999	

G.5. Barthel Index scoring for basic ADLs (BADL)

1	**Bowels**	**Score**
	I am incontinent (or I need to be given enemas)	0
	I have occasional accidents (e.g., once per week)	1
	I am continent	2
2	**Toilet Use**	**Score**
	I am dependent on help to use the toilet	0
	I need some help, but I can do things alone	1
	I am independent (getting on and off, dressing and wiping)	2
3	**Grooming**	**Score**
	I need help with personal care	0
	I am independent (face/hair/teeth/shaving etc.)	1
4	**Feeding**	**Score**
	I am unable to feed myself	0
	I need help cutting, spreading butter etc.	1
	I am independent in feeding myself	2
5	**Mobility**	**Score**
	I am immobile	0
	I am wheelchair independent, including corners, etc.	1
	I walk with help of one person (verbal or physical)	2
	I am independent (but may use an aid, e.g., a stick)	3
6	**Bladder**	**Score**
	I am incontinent or catheterized and unable to manage	0
	I have occasional accidents (max once per 24 hours)	1
	I am continent for over 7 days at a time	2
7	**Dressing**	**Score**
	I am dependent on help to get dressed	0
	I need some help but can do about half unaided	1
	I am independent (including buttons, zips, laces etc.)	2
8	**Bathing**	**Score**
	I am dependent on help to bathe	0
	I am independent in bathing (or in shower)	1
9	**Stairs**	**Score**
	I am unable to use stairs	0
	I need help to use stairs (verbal/physical/carrying aid)	1
	I am independent going up and down	2
10	**Transfers (from standing to sitting or vice versa)**	**Score**
	I am unable – no sitting balance	0
	I need major help (one or two people), I can sit	1
	I need minor help (verbal or physical)	2
	I am independent	3
	Total Barthel Index score	Sum of domains 1 to 10
	Interpretation - total score ranges from 0 to 20. Higher score = less disability in personal ADLs. <15 – usually represents moderate disability, <10 – usually represents severe disability	
	Missing - insert 999 for missing value and total score	

G.6. Lawton Brody Instrumental ADL (IADL) Scale scoring

A	**Ability to use telephone**	Score
	I can operate the telephone on my own initiative – look up and dial number etc.	1
	I can dial a few well-known numbers	1
	I can answer telephone but do not dial	1
	I do not use the telephone at all	0
B	**Shopping**	Score
	I take care of all shopping needs independently	1
	I can shop independently for small purchases	0
	I need to be accompanied on any shopping trips	0
	I am completely unable to shop	0
C	**Food preparation**	Score
	I can plan, prepare, and serve adequate meals independently	1
	I can prepare adequate meals if supplied with the ingredients	0
	I can heat, serve, and prepare meals, or prepare meals but do not maintain adequate diet	0
	I need to have meals prepared and served	0
D	**Housekeeping**	Score
	I can maintain my house alone or with occasional assistance (e.g., “heavy work domestic help”)	1
	I can perform light daily tasks but cannot maintain acceptable level of cleanliness alone	1
	I need help with all home maintenance tasks	1
	I can perform light daily tasks such as dish washing, bed making	1
	I do not participate in any housekeeping tasks	0
E	**Laundry**	Score
	I do all my personal laundry completely	1
	I can wash small items (e.g., rinses stocks etc.)	1
	All my laundry must be done by others	0

F	**Mode of transportation**	Score
	I can travel independently on public transport or drive my own car	1
	I can arrange my own travel via taxi, but do not otherwise use public transport	1
	I can travel on public transport when accompanied by another	1
	My travel is limited to taxi or automobile with assistance of another	0
	I do not travel at all	0
G	**Responsibility for own medication**	Score
	I am responsible for taking medication in correct dosages at correct time	1
	I take responsibility if medication is prepared in advance in separate dosage	0
	I am not capable of dispensing own medication	0
H	**Ability to manage finances**	Score
	I can manage financial matters independently (budgets, writes cheques, pays rent, bills, goes to Bank), collect and keep track of income	1
	I can manage day-to-day purchases, but need help with banking, major purchases etc.	1
	I am incapable of handling money	0
	Total IADL disability	Sum of domains A to H
	Interpretation - total score ranges from 0-8. Higher score = less disability in IADL	
	Missing - insert 999 for missing value and total score	

G.7. World Health Organization Disability Assessment Schedule (WHODAS-2.0) scoring

1	**Understanding and communicating**	None	Mild	Moderate	Severe	Extreme or cannot do
	In the last 30 days, how much difficulty have you had in:					
	Concentrating on doing something for ten minutes?	1	2	3	4	5
	Remembering to do important things?	1	2	3	4	5
	Analysing and finding solutions to problems in day-to-day life?	1	2	3	4	5
	Learning a new task, for example learning how to get to a new place?	1	2	3	4	5
	Generally understanding what people say?	1	2	3	4	5
	Starting and maintaining a conversation?	1	2	3	4	5
	Total cognition score	Total sum of communicating items ranging from 7 to 35				
	Interpretation	Higher score = greater disability: <8=none, 8-14=mild, 15-21=moderate, 22-28=severe, 29-35= extreme or cannot do				

2	**Getting around**	None	Mild	Moderate	Severe	Extreme or cannot do
	Standing for long periods, such as 30 minutes?	1	2	3	4	5
	Standing up from sitting down?	1	2	3	4	5
	Moving around inside your home?	1	2	3	4	5
	Getting out of your home?	1	2	3	4	5
	Walking a long distance, such as a kilometre (or equivalent)?	1	2	3	4	5
	Total mobility score	Total sum of getting around items, ranging from 5 to 25				
	Interpretation	Higher score = greater disability: <6=none, 6-10=mild, 11-15=moderate, 16-20=severe, 21-25= extreme or cannot do				

3	**Self-care**	None	Mild	Moderate	Severe	Extreme or cannot do
	Washing your whole body?	1	2	3	4	5
	Getting dressed?	1	2	3	4	5
	Eating?	1	2	3	4	5
	Staying in by yourself for a few days?	1	2	3	4	5
	Total self-care score	Total sum of self-care items ranging from 4 to 20				
	Interpretation	Higher score = greater disability: <5=none, 5-8=mild, 9-12=moderate, 13-16=severe, 17-20= extreme or cannot do				

4	**Getting along with people**	None	Mild	Moderate	Severe	Extreme or cannot do
	Dealing with people you do not know?	1	2	3	4	5
	Maintaining a friendship?	1	2	3	4	5
	Getting along with people who are close to you?	1	2	3	4	5
	Making new friends?	1	2	3	4	5
	Sexual activities?	1	2	3	4	5
	Total getting along score	Total sum of getting along with people items ranging from 5 to 25				
	Interpretation	Higher score = greater disability: <6=none, 6-10=mild, 11-15=moderate, 16-20=severe, 21-25= extreme or cannot do				

5a	**Life activities – Household**	None	Mild	Moderate	Severe	Extreme or cannot do
	Taking care of your household responsibilities?	1	2	3	4	5
	Doing most important household tasks well?	1	2	3	4	5
	Getting all the household work done that you needed to do?	1	2	3	4	5
	Getting all the household work done as quickly as needed?	1	2	3	4	5
	Total household activity score	Total sum of household activities, ranging from 4 to 20				
	Interpretation	Higher score = greater disability: <5=none, 5-8=mild, 9-12=moderate, 13-16=severe, 17-20= extreme or cannot do				

5b	**Life activities – work**	None	Mild	Moderate	Severe	Extreme or cannot do
	Your day-to-day work?	1	2	3	4	5
	Doing your most important work tasks well?	1	2	3	4	5
	Getting all the work done that you need to do?	1	2	3	4	5
	Getting your work done as quickly as needed?	1	2	3	4	5
	Total work activity score	Total sum of work activity items ranging from 4 to 20				
	Interpretation	Higher score = greater disability: <5=none, 5-8=mild, 9-12=moderate, 13-16=severe, 17-20= extreme or cannot do				

6	**Participation in society**	None	Mild	Moderate	Severe	Extreme or cannot do
	How much of a problem did you have in joining in community activities (for example, festivities, religious, or other activities) in the same way as anyone else?	1	2	3	4	5
	How much of a problem did you have because of barriers or hindrances around you?	1	2	3	4	5
	How much of a problem did you have living with dignity because of attitudes and actions of others?	1	2	3	4	5
	How much time did you spend on your health condition or its consequences?	1	2	3	4	5
	How much have you been emotionally affected by your health condition?	1	2	3	4	5
	How much has your health been a drain on the financial resources of you or your family?	1	2	3	4	5
	How much of a problem did your family have because of your health problems?	1	2	3	4	5
	Total participation score	Total sum of all participation in society items ranging from 7 to 35				
	Interpretation	Higher score = greater disability: <8=none, 8-14=mild, 15-21=moderate, 22-28=severe, 29-35= extreme or cannot do				

WHODAS summary score	The sum of all domains apart from 5b (work) - total ranges from 32 to 160
Interpretation	Higher score = greater disability: <33=none, 33-64=mild, 65-96=moderate, 97-128=severe, 129-160= extreme or cannot do
Missing	The mean score across all items within the domain should be assigned to the missing items. This method should not be used if more than two items are missing in that domain.

G.8. Palliative care Outcomes Scale (POS-S) scoring

Symptom Severity	Not at all	Slightly	Moderately	Severely	Overwhelming
Pain	0	1	2	3	4
Shortness of breath	0	1	2	3	4
Weakness or lack of energy	0	1	2	3	4
Nausea	0	1	2	3	4
Vomiting	0	1	2	3	4
Poor appetite	0	1	2	3	4
Constipation	0	1	2	3	4
Mouth problems	0	1	2	3	4
Drowsiness	0	1	2	3	4
Immobility	0	1	2	3	4
Other symptom 1	0	1	2	3	4
Other symptom 2	0	1	2	3	4
Other symptom 3	0	1	2	3	4
Total POS score	Total score = sum of all symptoms, including other symptoms 1 to 3				
Interpretation	Total score ranges from 0 to 52. Higher score = greater symptom burden				
Missing	insert 999 for missing value and total score				

G.9. Assistive devices scoring

Eating equipment			
1	yes	0	No
Equipment for getting in and out of bed			
1	yes	0	No
Equipment for walking indoors			
1	yes	0	No
Dressing equipment			
1	yes	0	No
Bathing equipment			
1	yes	0	No
Toileting equipment			
1	yes	0	No
Equipment for walking outdoors			
1	yes	0	No
Equipment for climbing stairs			
1	yes	0	No
Equipment for domestic tasks			
1	yes	0	No
Other equipment			
1	yes	0	No

G.10. Client Service Receipt Inventory (CSRI) scoring

Service	**In the last month have you stayed overnight in the following?**				**Number of nights in the last month**
For each service	1	yes	0	No	Insert number

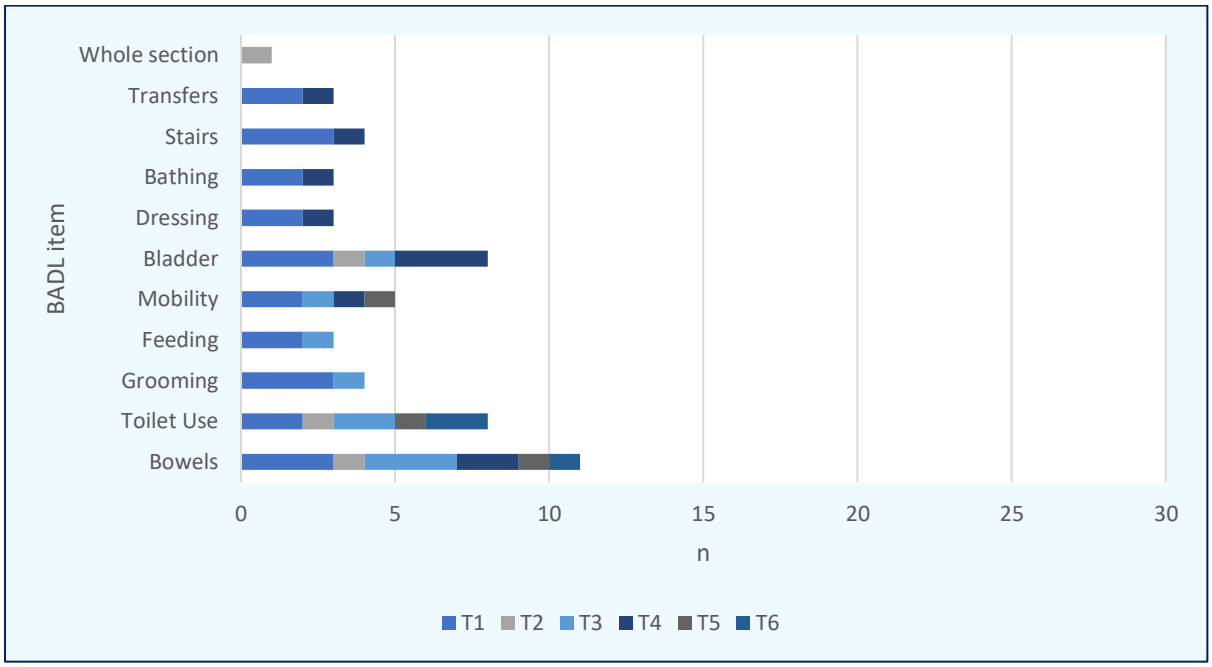
Service	**In the last month have you attended the following?**				**Number of visits in the last month**
For each service	1	yes	0	No	Insert number

Service	**In the last month have you had contact with the following?**				**Number of visits in the last month**	**Average duration of each visit**
For each service	1	yes	0	No	Insert number	insert duration in minutes (if there is a range put the average)

Appendix H

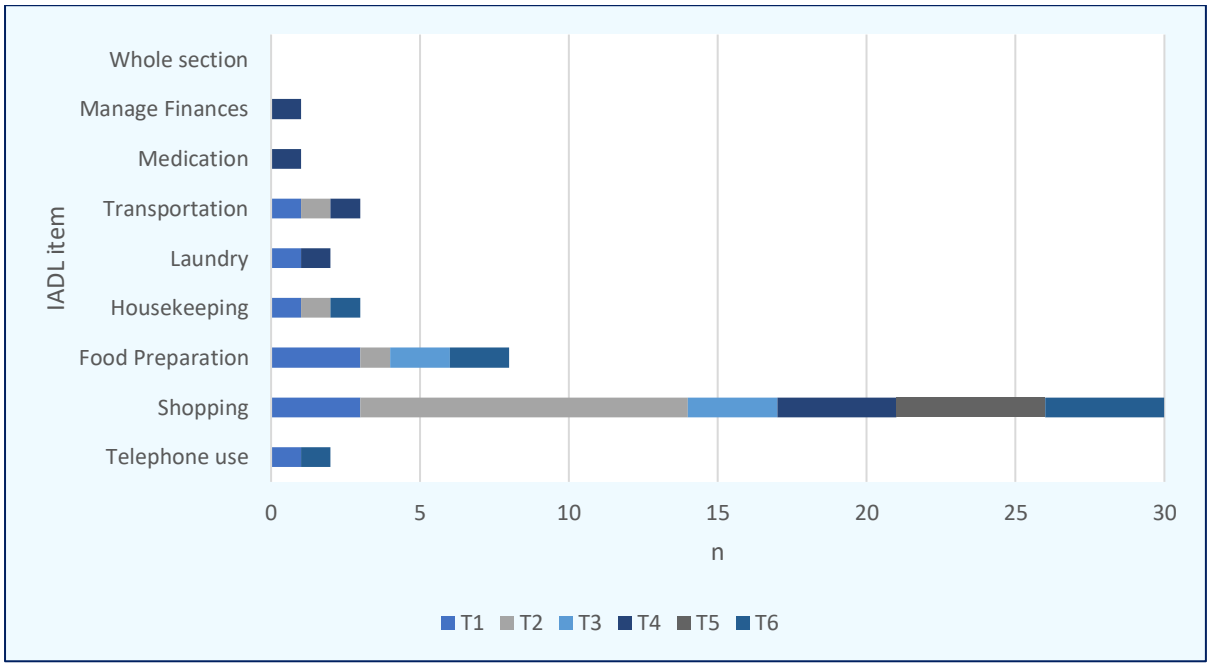
Missing item responses on each follow-up questionnaire

H.1. Missing items on the Barthel Index measuring disability in basic ADLs



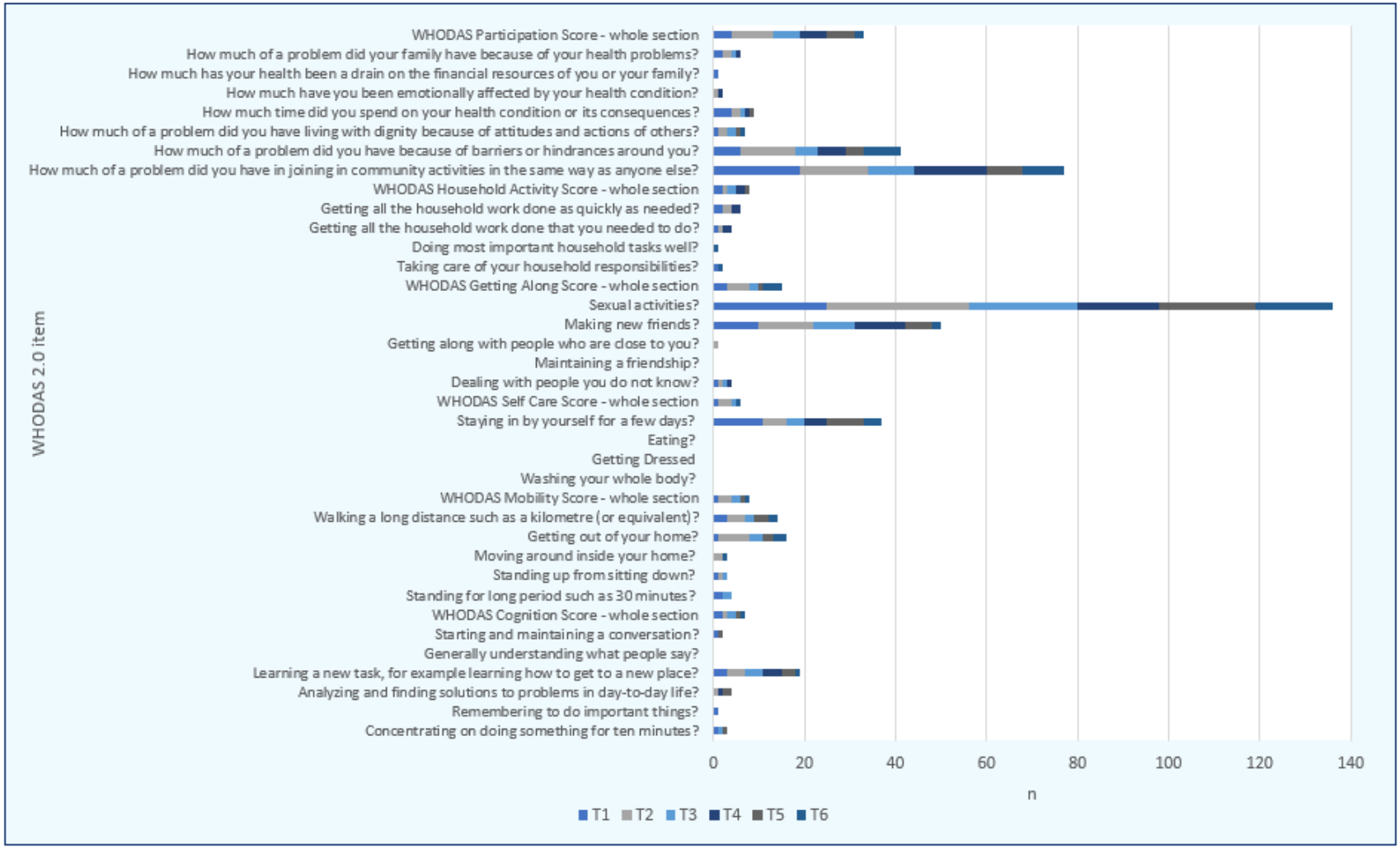
BADL: basic activities of daily living; T stands for monthly timepoint, starting at 1-month follow-up (T1) to 6-month follow-up (T6); n refers to the number of missing items or section (where indicated) out of a total of 814 questionnaires over all follow-up timepoints.

H.2. Missing items on the Lawton Brody Instrumental ADL Scale measuring disability in instrumental ADLs



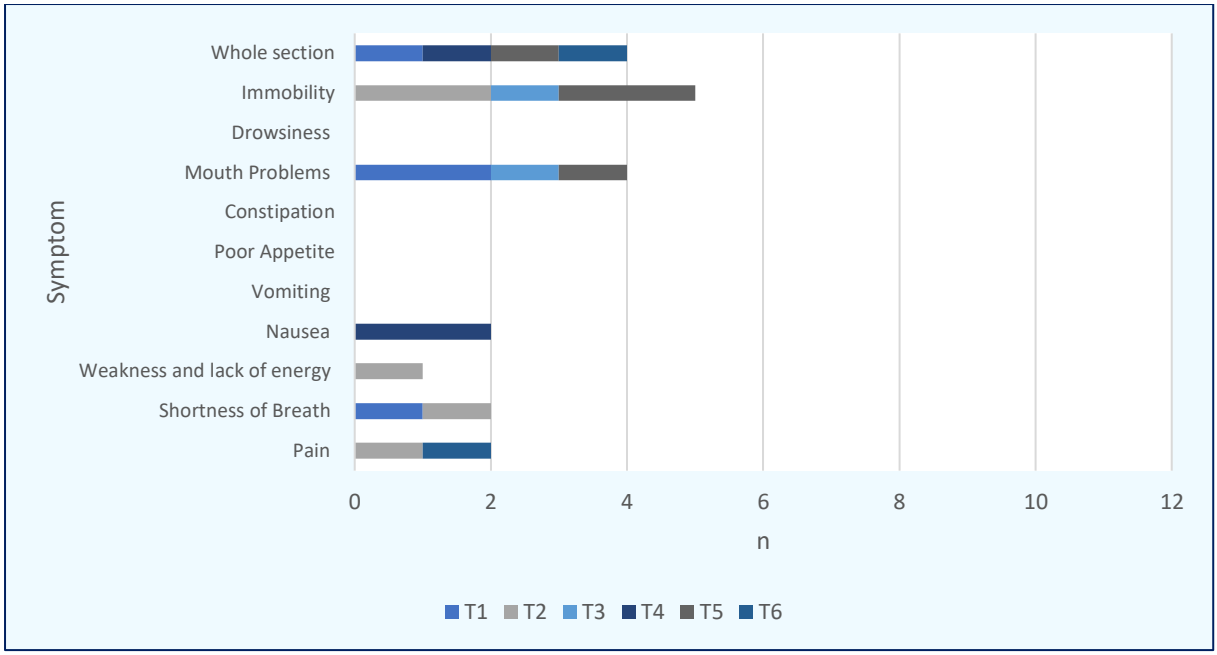
IADL: instrumental activities of daily living; T stands for monthly timepoint, starting at 1-month follow-up (T1) to 6-month follow-up (T6); n refers to the number of missing items or sections (where indicated) out of a total of 814 questionnaires over all follow-up timepoints.

H.3. Missing items on the World Health Organization Disability Assessment Schedule (WHODAS-2.0) measuring difficulty in daily activities



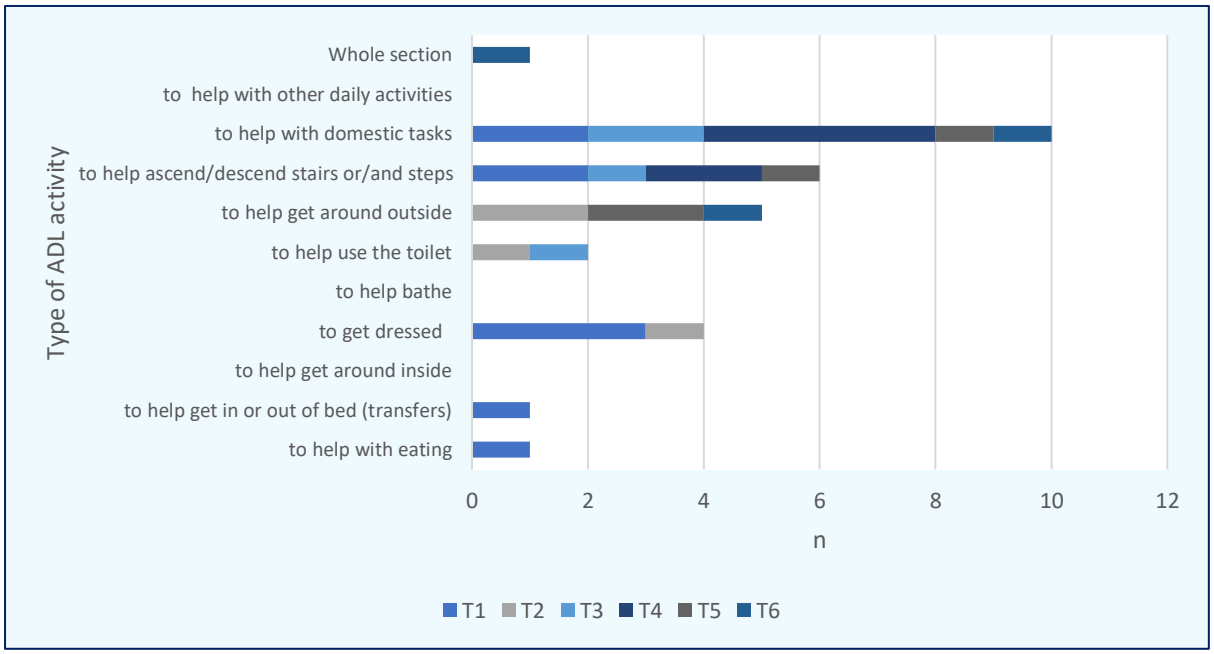
WHODAS-2.0; World Health Organization Disability Assessment Schedule; T stands for monthly timepoint, starting at 1-month follow-up (T1) to 6-month follow-up (T6); n refers to the number of missing items or sections (where indicated) out of a total of 814 questionnaires over all follow-up timepoints. Each question (item) on the WHODAS-2.0 refers to difficulty in the last 30 days.

H.4. Missing items on the Palliative Care Outcomes Scale (POS-S) – Symptoms



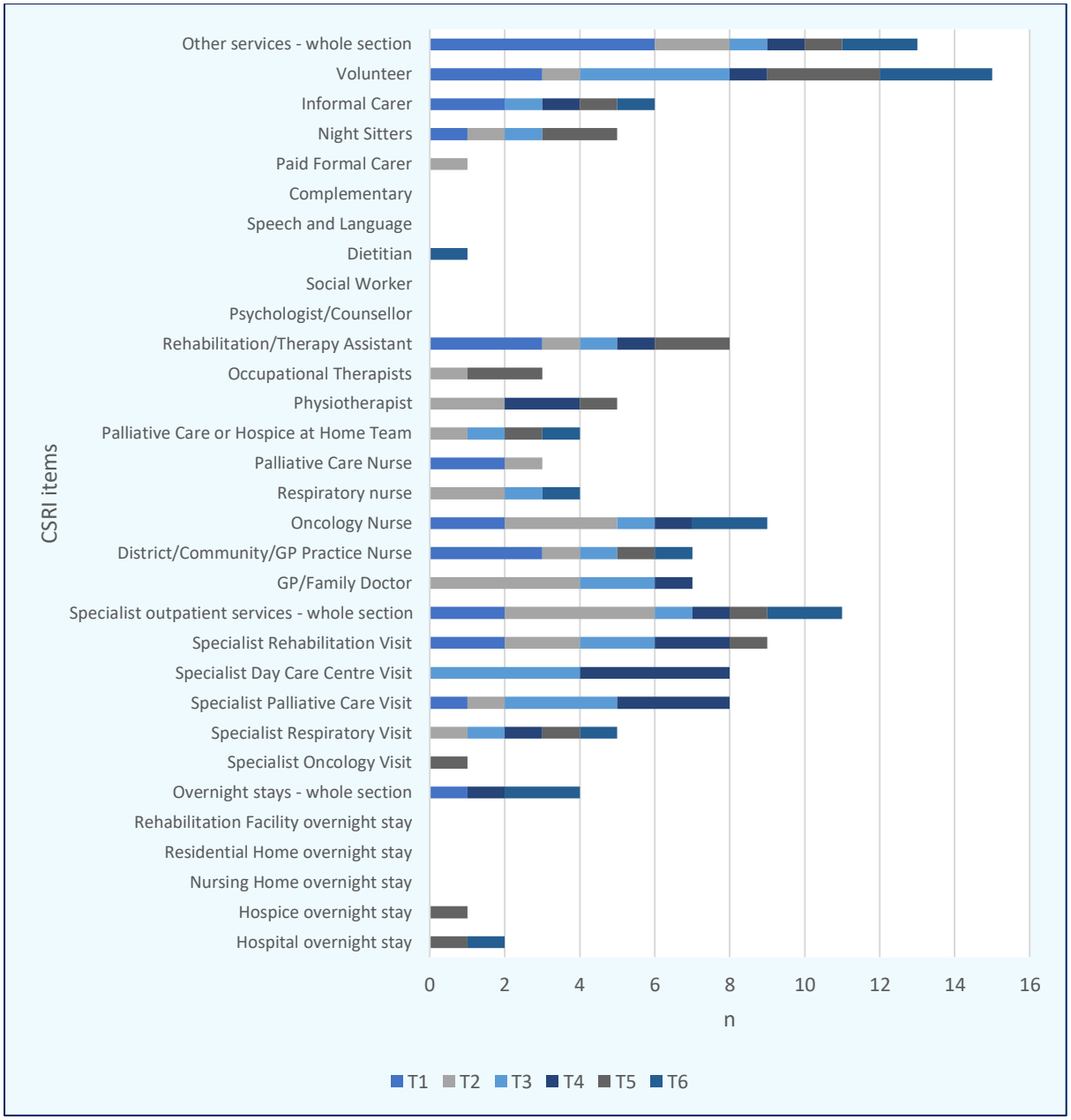
T stands for monthly timepoint, starting at 1-month follow-up (T1) to 6-month follow-up (T6); n refers to the number of missing items or sections (where indicated) out of a total of 814 questionnaires over all follow-up timepoints.

H.5. Missing items on the use of ADL assistive devices questionnaire



ADL; activities of daily living; T stands for monthly timepoint, starting at 1-month follow-up (T1) to 6-month follow-up (T6); n refers to the number of missing items or sections (where indicated) out of a total of 814 questionnaires over all follow-up timepoints.

H.6. Missing items on the Client Service Receipt Inventory (CSRI) measuring service use

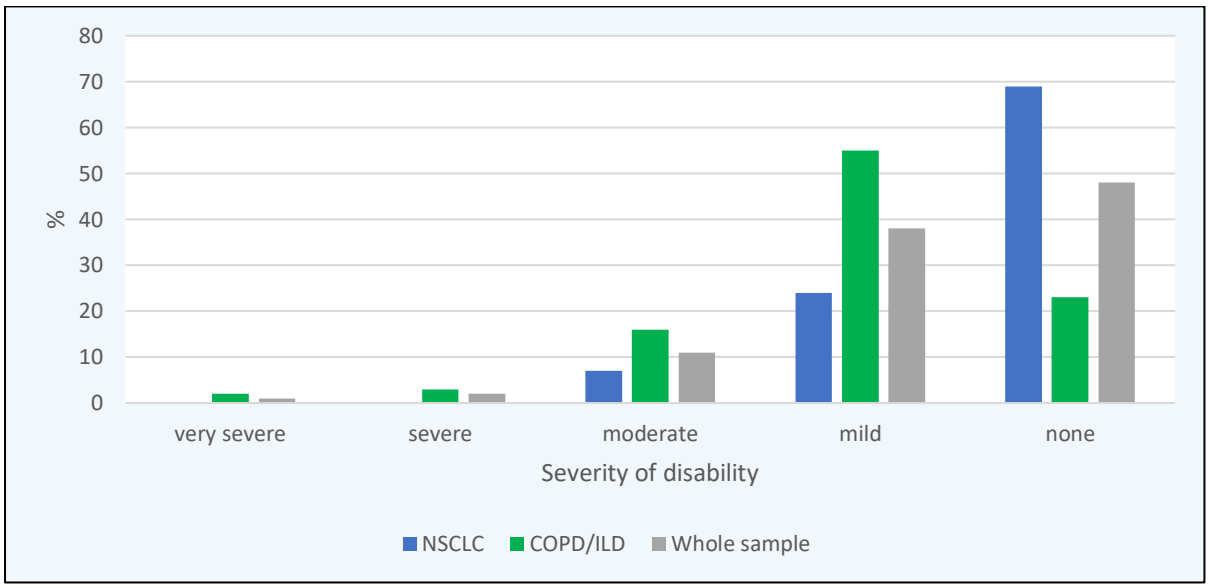


CSRI: client service receipt inventory; T stands for monthly timepoint, starting at 1-month follow-up (T1) to 6-month follow-up (T6); n refers to the number of missing items or sections (where indicated) out of a total of 814 questionnaires over all follow-up timepoints; Items were often only missed if another option was ticked, e.g., hospital admission or specialist oncology visit, and therefore assumed to be a "no" response" if not ticked and not considered missing, unless the whole section was missing; This was the last questionnaire in the survey and some sections may appear repetitive or missed due to questionnaire fatigue.

Appendix I

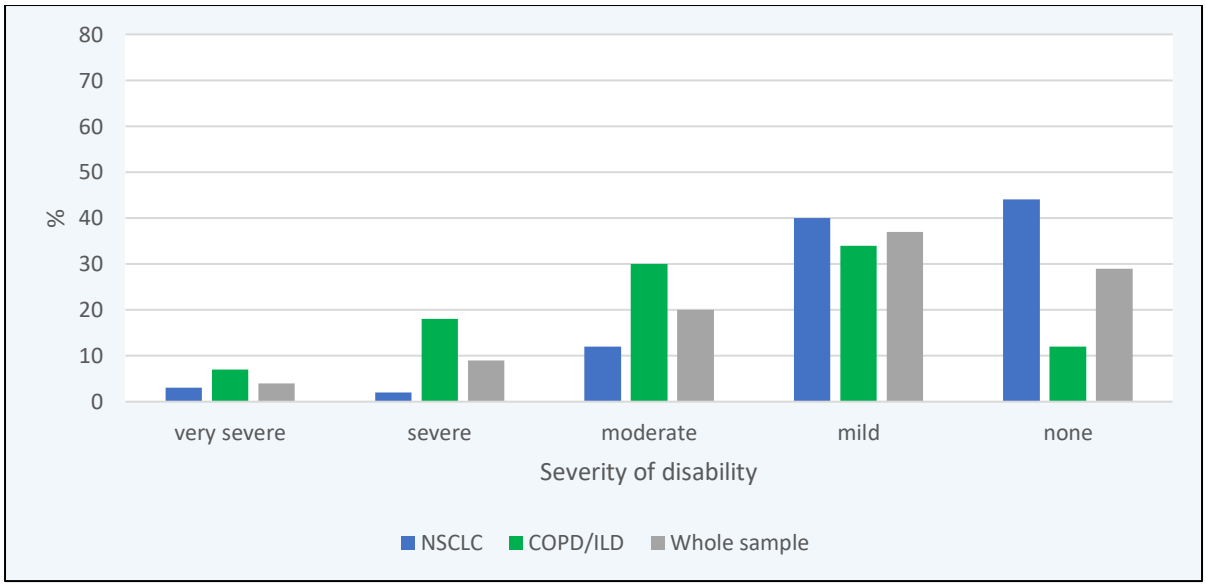
Prevalence of disability severity in ADLs

I.1. Severity of disability in basic ADLs



ADL: activities of daily living; Disability severity categorization in basic activities of daily living measured on the Barthel Index (0-20): no disability=20; mild=15-19; moderate=10-14; severe=5-9; very severe=<5; NSCLC: non-small cell lung cancer; COPD: Chronic Obstructive Pulmonary Scale; IDL: Interstitial Lung Disease.

I.2. Severity of disability in instrumental ADLs



ADL: activities of daily living; Disability severity categorization in instrumental activities of daily living measured on the Lawton Brody IADL Scale (0-8): no disability=8; mild=6-7; moderate=4-5; severe=2-3; very severe=<2; NSCLC: non-small cell lung cancer; COPD: Chronic Obstructive Pulmonary Scale; IDL: Interstitial Lung Disease.

Appendix J

Relationships between disability trajectory groups in ADLs and the stable trajectory

J.1. Relationships between basic ADL disability trajectory groups and the stable trajectory

Participant characteristics and outcomes at baseline	Increasing Disability (n=24)			Decreasing Disability (n=23)			Fluctuating disability (n=30)		
	X2 (1df)	z	p	X2 (1df)	z	p	X2 (1df)	z	p
❖ **Health-related factors**									
NSCLC	7.28	-	**0.007**	3.22	-	0.07	3.12	-	0.08
Stage IV	0.002	-	0.96	4.09	-	0.04	1.9	-	0.17
Charlson comorbidity Index score	-	2.72	**0.007**	-	1.6	0.11	-	0.14	0.89
❖ **Body Functions and Structures**									
Australian Karnofsky Performance Status (AKPS)	-	2.98	**0.003**	-	3.25	**0.001**	-	2.78	**0.005**
Symptom severity (Palliative Outcomes Scale-symptoms)	-	-2.18	0.03	-	-2.62	**0.009**	-	-1.66	0.1
Receiving cancer treatment	6.45	-	**0.01**	0.86	-	0.35	4.58	-	0.03
On oxygen therapy	4.61	-	0.03	0.19	-	0.66	1.43	-	0.23
❖ **Activity and participation**									
Total Barthel Index score (BADLs)	-	2.85	**0.004**	-	7.27	**<0.0001**	-	4.68	**<0.0001**
Lawton Brody Instrumental ADL score (IADLs)	-	3.16	**0.002**	-	2.66	**0.008**	-	3.31	**0.0009**
WHODAS Summary score	-	-2.62	**0.009**	-	-1.85	0.06	-	-3.08	**0.002**
Cognition	-	-1.02	0.31	-	0.47	0.64	-	-1.3	0.19
Mobility	-	-3.95	**0.0001**	-	-2.24	0.03	-	-2.96	**0.003**
Self-Care	-	-2.62	**0.009**	-	-1.63	0.1	-	-2.82	**0.005**
Getting along with people	-	-0.82	0.41	-	-0.10	0.92	-	-1.61	0.11
Household activities	-	-2 9	**0.004**	-	-2.33	0.02	-	-1.64	0.1
Societal participation	-	-1.05	0.3	-	-1.72	0.09	-	-2.16	0.03
❖ **Personal factors**									
Age	-	-2.71	**0.007**	-	-0.10	0.92	-	0.13	0.9
Female	0.2	-	0.7	0.19	-	0.66	4.03	-	0.05
White British	0.06	-	0.81	1.66	-	0.2	0.48	-	0.49
Education above secondary school	0.42	-	0.52	0.06	-	0.81	0.00 4	-	0.95
CDSE: Confidence to receive help	-	0.18	0.86	-	-0.58	0.56	0.89	-	0.37
❖ **Environmental factors**									
Lives alone	0.45	-	0.5	0.2	-	0.71	0.12	-	0.73
Property with stairs	1.26	-	0.26	0.0003	-	0.99	3.51	-	0.06
Formal caregiver	4.69	-	0.03	0.39	-	0.53	1.59	-	0.21
Informal caregiver	1.83	-	0.18	1.43	-	0.23	1.99	-	0.16
Physiotherapy input within the last month	2.07	-	0.15	0.09	-	0.77	0.35	-	0.55
Occupational therapy input within the last month	8.64	-	**0.003**	0.31	-	0.57	0.4	-	0.52
Received GOV letter to physically and socially isolate	0.04	-	0.84	0.66	-	0.42	063	-	0.43
Currently physically and socially isolating	0.78	-	0.38	0.61	-	0.44	0.42	-	0.52
Have spent time in physical and social isolation	0.12	-	0.72	0.64	-	0.42	0.88	-	0.35
Months spent in physical and social isolation	-	-2.05	0.04	-	-1.33	0.18		0.41	0.68
Hospital admission in the last month	0.39	-	0.53	7.37	-	**0.007**	0.12	-	0.73
Hospice patient	11.0	-	**0.001**	0.01	-	0.94	1.43	-	0.23
Total number of ADL devices	-	-3.27	**0.001**	-	-2.9	**0.004**	-	-3.12	**0.002**
Reduced physical activity indoors	0.09	-	0.76	0.26	-	0.61	0.03	-	0.86
Reduced physical activity outdoors	4.08	-	0.04	0.004	-	0.95	0.65	-	0.42

NSCLC: non-small-cell lung cancer; ADL: activities of daily living; BADL: Basic activities of daily living; IADL: instrumental activities of daily living; WHODAS: World Health Organization disability assessment Schedule; CDSE: Chronic Disease Self-Efficacy subscale; GOV: government; Reduced physical activity is dichotomous ('little/lot less' or not); Statistical comparisons between the two groups were conducted separately against stable for increasing, increasing, and fluctuating trajectories using the Mann Whitney-U test for continuous variables and the Chi square test for categorical variables; the significance level is set at p≤0.01.

J.2. Relationships between instrumental ADL disability trajectory groups and the stable trajectory

Participant characteristics and outcomes at baseline	Increasing disability (n=50)			Decreasing disability (n=33)			Fluctuating disability (n=35)		
	X2 (1df)	Z	p	X2 (1df)	Z	P	X2 (1df)	Z	p
❖ **Health-related factors**									
NSCLC	2.38	-	0.12	6.2	-	**0.01**	2.48	-	0.12
Stage IV	0.48	-	0.49	0.27	-	0.6	2.2	-	0.14
Charlson comorbidity Index score	-	1.39	0.16	-	2.66	**0.008**	-	1.89	0.06
❖ **Body Functions and Structures**									
Australian Karnofsky Performance Status (AKPS)	-	4.46	**<0.0001**	-	3.08	**0.002**	-	3.14	**0.002**
Symptom severity (Palliative Outcomes Scale-symptoms)	-	-3.23	0.001	-	-2.2	0.03	-	-1.49	0.14
Receiving cancer treatment	3.42	-	0.06	3.91	-	0.05	1.09	-	0.3
On oxygen therapy	1.28	-	0.26	3.67	-	0.06	2.37	-	0.12
❖ **Activity and participation**									
Total Barthel Index score (BADLs)	-	2.36	0.02	-	2.7	**0.007**	-	2.03	0.04
Lawton Brody Instrumental ADL score (IADLs)	-	3.4	0.0007	-	5.29	**<0.0001**	-	3.17	**0.002**
WHODAS Summary score	-	-3.8	**0.0001**	-	-3.2	**0.001**	-	-2.6	**0.009**
Cognition	-	-0.63	0.53	-	-0.17	0.86	-	0.71	0.48
Mobility	-	-4.69	**<0.0001**	-	-3.14	**0.002**	-	-3	**0.003**
Self-Care	-	-2.69	0.007	-	-1.97	0.05	-	-2.16	0.03
Getting along with people	-	-2.96	0.003	-	-1.22	0.22	-	-1.2	0.23
Household activities	-	-2.82	0.005	-	-2.35	0.02	-	2.07	0.04
Societal participation	-	-2.79	0.005	-	-1.1	0.05	-	-1.49	0.14
❖ **Personal factors**									
Age	-	-0.64	0.52	-	0.29	0.77	-	0.18	0.85
Female	0.26	-	0.61	2.2	-	0.14	0.06	-	0.76
White British	0.87	-	0.35	0	-	1	0.29	-	0.59
Education above secondary school	3.42	-	0.06	3.01	-	0.08	4.84	-	0.03
CDSE: Confidence to receive help	-	2.22	0.03	-	1.55	0.12	-	0.52	0.6
❖ **Environmental factors**									
Lives alone	2.44	-	0.11	3.42	-	0.06	0.88	-	0.35
Property with stairs	1.47	-	0.23	1.32	-	0.25	1.02	-	0.31
Formal caregiver	7.5	-	**0.006**	3.14	-	0.08	5.09	-	0.03
Informal caregiver	3.07	-	0.08	6.83	-	**0.01**	2.94	-	0.09
Physiotherapy input within the last month	5.97	-	0.02	5.41	-	0.02	0.96	-	0.33
Occupational therapy input within the last month	1.38	-	0.24	2.06	-	0.15	0.96	-	0.33
Received GOV letter to physically and socially isolate	1.16	-	0.28	0.47	-	0.5	0.19	-	0.66
Currently physically and socially isolating	6.12	-	0.01	1.61	-	0.21	3.88	-	0.05
Have spent time in physical and social isolation	3.6	-	0.06	4.26	-	0.04	4.51	-	0.04
Months spent in physical and social isolation	-	-1.21	0.22	-	-1.76	0.08	-	-2.26	**0.008**
Hospital admission in the last month	4.36	-	0.04	5.41	-	0.02	8.55	-	**0.003**
Hospice patient	5.12	-	0.02	6.99	-	**0.008**	1.19	-	0.28
Total number of ADL devices	NA	-3.12	**0.002**	-	-2.12	0.03	-	-2.48	**0.01**
Reduced physical activity indoors	4.84	-	0.03	0.58	-	0.45	0.007	-	0.93
Reduced physical activity outdoors	6.62	-	**0.01**	5.22	-	0.02	0.05	-	0.82

NSCLC: non-small-cell lung cancer; ADL: activities of daily living; BADL: Basic activities of daily living; IADL: instrumental activities of daily living; WHODAS: World Health Organization disability assessment Schedule; CDSE: Chronic Disease Self-Efficacy subscale; GOV: government; Reduced physical activity is dichotomous ('little/lot less' or not); Statistical comparisons between the two groups were conducted separately against stable for increasing, increasing, and fluctuating trajectories using the Mann Whitney-U test for continuous variables and the Chi square test for categorical variables; the significance level is set at p≤0.01.