1. Population Needs

1.1 National/local context and evidence base

The interstitial lung diseases (ILD) comprise a broad spectrum of conditions all of which are characterised by inflammation or fibrosis of the alveolar wall with impairment of gas exchange. The commonest of these conditions are idiopathic pulmonary fibrosis (IPF), extrinsic allergic alveolitis (EAA) and sarcoidosis. In addition, there is also a large group of patients with connective tissue diseases (also known as collagen vascular diseases or CTD) such as rheumatoid arthritis and scleroderma with up to 30% of these patients thought to have ILD, and a myriad of less common ILDs (non-specific interstitial pneumonitis, desquamative interstitial pneumonitis, respiratory bronchiolitis interstitial lung disease, acute interstitial pneumonia, lymphocytic interstitial pneumonitis, histiocytosis X and lymphangioleiomyomatosis - for which there exists a nationally commissioned service - to name but a few).

The relative rarity of the individual ILDs makes diagnosis difficult and the emergence of novel, often highly specialised treatments (e.g. pirfenidone, rapamycin and rituximab) has increased the need for delivery of care by dedicated centres. Furthermore, existing national and international guidelines emphasise the need for a multi-disciplinary approach to diagnosis of ILD – this therefore requires the involvement of respiratory physicians with an ILD interest, thoracic radiologists, thoracic pathologists and, in a proportion of cases, a thoracic surgeon. Growing evidence points to the importance of combined multi-disciplinary team (MDT) input...
for assigning correct diagnoses and initiating appropriate therapy in individuals with ILD. Misdiagnosis contributes to increased morbidity and mortality in this patient group. A recent US study has demonstrated that care delivered in a specialist ILD centre improved outcomes in patients with IPF independent of their disease severity at diagnosis. In addition to the importance of diagnosis, the progressive nature of many of the ILDs, particularly the most frequently occurring, IPF, necessitates that the appropriate delivery of care to this patient group requires the integration of Respiratory, Palliative Care and Transplant services. In the case of ILDs such as lymphangioleiomyomatosis (LAM), histiocytosis X and connective tissue disease associated ILD, the use of cytotoxic and immunosuppressive agents (in some cases intravenously) requires that centres treating these diseases have in place appropriate systems and guidelines for monitoring both drug levels and for potential signs of drug toxicity. For these reasons, the diagnosis and management of ILDs should be considered a specialised service.

Clinical trial data are emerging to support the value of a number of therapies in the various ILDs. The novel anti-fibrotic drug pirfenidone slows disease progression in IPF. Rapamycin results in improved lung function and quality of life in individuals with LAM. Intravenous cyclophosphamide improves outcomes in individuals with CTD associated ILD and, observational data suggests that the monoclonal antibody rituximab has a beneficial effect in individuals with disease resistant to cyclophosphamide. In individuals with severe, progressive sarcoidosis, the monoclonal anti-TNF-α antibody infliximab has been shown to improve outcomes and reduce disease activity. Appropriate use and monitoring of all these therapies requires the integration of several disciplines and is therefore best suited to regionally delivered specialist centres.

Estimates of the incidence of the different ILDs vary. The commonest, IPF and sarcoidosis, have an incidence of between 2000 – 4000 in the UK per annum. Whilst the prognosis for individuals with sarcoidosis is reasonably good, the median survival for those with IPF is only 3 – 3.5 years and the disease now accounts for more than 3000 deaths in the UK each year. Rarer conditions such as LAM and histiocytosis X have an incidence of 2 – 6 per million per annum whilst a recent epidemiological study utilising the UK GPR database identified only 563 new cases of CTD-ILD diagnosed in the last decade. Importantly however, mortality for those with CTD-ILD was 40% higher than for those with CTD alone.

2. Scope

2.1 Aims and objectives of service

The interstitial lung diseases comprise a broad spectrum of over 200 conditions all of which are characterised by inflammation or fibrosis of the alveolar wall with impairment of gas exchange.

The commonest of these conditions are:
- idiopathic pulmonary fibrosis (IPF),
- extrinsic allergic alveolitis (EAA)
- sarcoidosis

In addition there is also a large group of patients with connective tissue diseases (also known as collagen vascular diseases) such as:
- rheumatoid arthritis
- idiopathic inflammatory myositis
- Sjogren’s disease
- scleroderma with up to 30% of these patients thought to have ILD

Plus a myriad of less common ILDs:
- non-specific interstitial pneumonitis,
- desquamative interstitial pneumonitis,
- respiratory bronchiolitis interstitial lung disease,
- acute interstitial pneumonia,
- lymphocytic interstitial pneumonitis,
- histiocytosis X
- lymphangioleiomyomatosis (for which there exists a nationally commissioned service)
- pulmonary arterio-venous malformations.

The overall aim of the specialist service is to ensure equality of patient access to multi-disciplinary team diagnosis, to guarantee that patients with ILD have equal access to current treatment modalities and that their disease-specific management plans are drawn up following MDT assessment at regional specialist units. Networks of care need developing so that the majority of subsequent follow up is provided in local secondary care units.

The objectives of the service are to:
- provide a specialist multi-disciplinary service for diagnosis thus improving diagnostic accuracy for individuals with ILD
- initiate appropriate pharmacological and non-pharmacological treatment for individuals with ILD
- reduce morbidity and mortality due to ILD, including reducing hospitalisation
- ensure equity of access to specialised therapies for all patients with ILD in England
- identify individuals requiring referral to lung transplant centres
- oversee those aspects of care that fall out with the expertise of local units (e.g. administration of cytotoxic chemotherapy, monitoring blood levels of immunosuppressants etc.).

The purpose of the service will be to:
- develop an equitable national ILD service whereby individuals with ILD will have access to specialist ILD-MDT diagnosis.
- where appropriate, provide personal management plans for each patient
annually, the provision of which will, in most cases, be delivered locally.

- provide specialist advice and support to local providers of care, and in difficult cases to review patients between annual visits
- provide equitable access to specialist therapies and to provide appropriate support and ancillary services (e.g. drug level monitoring) to ensure the safe local management of individuals requiring cytotoxic or immunosuppressant therapy
- develop and share national ILD protocols and guidelines. Ensure local clinical teams are provided with management guidelines, and have access to specialist advice when needed.
- provide a national forum to discuss difficult management decisions.
- improve awareness and management of ILD within the UK by education and provision of an excellent service.
- raise standards of care for patients with ILD in the UK so as to improve prognosis and reduce disease and treatment related morbidity.
- offer patient centred assessment and management regarding the disease complications and organ specific problems associated with certain ILDs (e.g. sarcoidosis, CTD-associated ILD)
- minimise the disease impact of ILDs on the patient and their family life and work practice
- enable integration of clinical services with clinical trials and translational research to ensure on going developments in the care of individuals with these rare diseases.
- ensure equitable patient access to related services e.g. lung transplant assessment, end-of life palliative care input etc.

2.2 Service description/care pathway

The Map of Medicine has also developed guidance on the diagnosis and management of ILD and this document is currently undergoing peer-review:


Currently management and diagnosis of the ILDs is guided by a number of guidelines:

- The 2008 British Thoracic Society SIGN guidelines on interstitial lung disease
- The diagnosis of IPF has been formalised in a consensus guideline developed by the American Thoracic Society (ATS) and European Respiratory Society (ERS) (published in 2011).
- NICE are developing a clinical guideline for IPF (currently under consultation [http://bit.ly/Y1hvob](http://bit.ly/Y1hvob))
- NICE are undertaking a technology appraisal of the novel anti-fibrotic agent, pirfenidone.
- The Map of Medicine
- Sarcoidosis is covered by the 1999 ATS/World Association of Sarcoidosis and other Granulomatous Disorders (WASOG) guidelines
LAM is addressed by 2010 ERS management and diagnosis guidelines

The ICD 10 codes to be used for interstitial lung disease are given in the table below:

<table>
<thead>
<tr>
<th>ICD-10 codes for interstitial lung disease</th>
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<tr>
<td>D76.0</td>
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<td>J67</td>
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<td>D86.0</td>
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<td>D86.2</td>
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<td>J84.0 - J84.9</td>
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Therapies associated with the diagnostic codes will also be identified for pirfenidone, rapamycin, rituximab, cyclophosphamide, infliximab and cladribine.

Sarcoidosis will only be considered for specialist centre assessment in cases where there is extensive multi-organ involvement (to include lungs, heart or brain and other organ involvement) or in individuals who develop progressive pulmonary fibrosis despite standard therapy.

The flows and pathways required at specialist centres will be those centred around 1) diagnosis, 2) treatment planning, 3) in some cases, treatment administration and 4) disease monitoring.

**Diagnostic assessment**

Patients will be referred to the centre that is geographically most convenient for them and will then be systematically assessed over the course of two to three day case visits (depending on the need for bronchoscopy). In approximately 10-15% of cases, diagnostic video assisted surgical lung biopsy will be necessary. For individuals assessed at specialist centres the following investigations will be required:

- Full pulmonary function tests (PFT) including carbon monoxide diffusing capacity (DLco) and estimation of total lung capacity (either by plethysmography or helium dilution).
- 6 minute walk test (or equivalent).
- High Resolution Computed Tomography of the thorax.
- Bone densitometry (dual energy X-ray absorptiometry (DEXA)).
- Full Blood Count, Erythrocyte Sedimentation Rate, C-Reactive Protein, Autoimmune profile, Anti-neutrophil Cytoplasmic Antibody and serum precipitins.
- Echocardiogram with right heart assessment.
- Overnight oximetry.
- In selected cases bronchoscopy with bronchoalveolar lavage with or without transbronchial biopsy.
- In 10-15% of cases surgical lung biopsy (pre-operative planning to include a case conference between physician, surgeons and, when necessary, thoracic radiologist).
• In suspected LAM patients will require tuberous sclerosis genotyping and pelvic and abdominal ultrasound.
• In multi-organ sarcoid, patients require cardiac magnetic resonance imaging (MRI), abdominal ultrasound, upper airway assessment, 24 hour urinary calcium estimation and, in selected cases, brain MRI.
• Patients with a confirmed diagnosis of pulmonary langerhan’s histiocytosis should have screening for systemic disease to include; dermatology review, MRI pituitary and bone scan.
• For patients with pulmonary alveolar proteinosis, testing for anti granulocyte/macrophage colony stimulating factor (anti-GM CSF) antibodies.

Following the completion of the assessments the results of test will be discussed at a diagnostic multi-disciplinary team (MDT) meeting. A fully constituted MDT will consist of a respiratory physician with a specialist interest in ILD, a thoracic radiologist, a thoracic pathologist, an ILD Specialist Nurse and an MDT co-ordinator.

**Treatment planning**

Following diagnosis, treatment will be planned in accordance with national and international guidelines. This will involve input from respiratory physicians with an interest in ILD, an ILD specialist nurse and where necessary respiratory physiotherapists, occupational therapists and physicians from other disciplines (e.g. rheumatologists, ear, nose and throat (ENT); cardiology, transplant, pulmonary hypertension, palliative care etc.). Provision should be made to ensure patient access to pulmonary rehabilitation. In most cases, it is envisaged that treatment will be delivered locally and reviewed annually at specialist centres.

**Treatment Administration**

In certain cases, it will be necessary for specialist centres to administer therapy to patients rather than rely on local services. Such treatments include:
• parental cytotoxic agents (intravenous cyclophosphamide, intra muscular methotrexate)
• biological agents (rituximab, infliximab)
• chemotherapeutic agents (e.g. cladrabine for Langerhans Cell Histiocytosis)
• plasmapharesis
• intra venous immunoglobulins
• whole lung lavage for pulmonary alveolar proteinosis
• nebulised granulocyte macrophage colony stimulating factor (GM-CSF)
• monitoring of immunosuppressant serum levels (rapamycin, cyclosporine, tacrolimus)
• embolisation of arteriovenous malformations.

**Disease monitoring**

For patients receiving treatment at specialist centres, follow up and monitoring of disease (in most cases through clinical assessment and full lung function testing) will
be dictated by disease severity and treatment regimen, but is likely to be once every months. For the majority of individuals for whom care is being delivered locally, specialist centre review will occur annually. These reviews will comprise clinical assessment, full lung function and chest radiograph. Patients will also, where necessary, be seen at the same visit by other members of the multi-disciplinary team.

Discharge

Individuals will be discharged from specialist centre care in the following circumstances:
- if diagnostic assessment fails to confirm a diagnosis of an ILD
- patients with disease that remains stable at 2 consecutive visits following withdrawal of treatment.
- individuals with end stage disease transitioning to palliative care services
- individuals with end-stage disease who have undergone lung transplantation.

Additional roles of specialist centres

- Patient education
- Patient support groups
- Outreach support to local centres (electronically or by teleconference).
- Inpatient care and transfer of individuals with treatment responsive ILD or patients requiring emergency, inpatient assessment following first presentation of acute onset ILD
- Intensive care support for ILD inpatients.
- Education of health care professionals

2.3 Population covered

The service outlined in this specification is for patients ordinarily resident in England; or otherwise the commissioning responsibility of the NHS in England\(^1\) (as defined in Who Pays?: Establishing the responsible commissioner, and other Department of Health guidance relating to patients entitled to NHS care or exempt from charges).

Specifically individuals to be assessed at specialist centres will fulfil the following criteria,
- all adult patients with suspected rare interstitial lung disease (estimated incidence < 1 per 500,000) e.g. LAM, Langerhans cell histiocytosis. The very rare disorders will only be cared for at a small number (c. 1 to 3) nominated specialist centres.
- all adult patients with ILD of uncertain aetiology (for specialist multi-disciplinary team diagnosis)

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\(^1\) Note: for the purposes of commissioning health services, this EXCLUDES patients who, whilst resident in England, are registered with a GP Practice in Wales, but INCLUDES patients resident in Wales who are registered with a GP Practice in England.
• all adult patients fulfilling criteria for treatment with specialist drugs (e.g. pirfenidone for IPF, infliximab for sarcoidosis) or interventions (e.g. treatment of AVMs)
• patients with multi-organ or progressive sarcoidosis requiring specialist MDT input.

2.4 Any acceptance and exclusion criteria

Acceptance criteria
• Individuals with ILD of unknown aetiology – to be identified by local secondary care physician
• Individuals with a known or suspected rare ILD – as identified through ICD-10 codes and registries
• Individuals with progressive or multi-organ sarcoid requiring assessment for specialist therapies or multi-disciplinary assessment
• All individuals fulfilling criteria for specialist pharmacological therapy (e.g. pirfenidone for idiopathic pulmonary fibrosis (IPF), rapamycin for LAM) or specialist interventions e.g. embolization of pulmonary-Arteriovenous Malformations

Exclusion criteria
• This specification does not cover paediatric interstitial lung disease

2.5 Interdependencies with other services

3. Applicable Service Standards

3.1 Applicable national standards e.g. NICE, Royal College

BTS ILD Guidelines 2008
NICE IPF Guidelines (expected 2013)

| Service Standards Core Standards | • Fully constituted ILD MDT (to consist Respiratory physician with dedicated specialist interest in ILD, Thoracic radiologist, thoracic pathologist, ILD Nurse Specialist and MDT co-ordinator).
• Dedicated ILD nurse specialist to provide patient education and supervision of immunosuppressant therapy.
• Able to undertake full lung function including spirometry, |

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plethysmography and measurement of gas transfer
• Able to undertake bronchoscopy with cytology service able to perform cell differential counts
• Access to immunological laboratory services for testing of autoimmune serology
• Facilities to administer cytotoxic and biological therapies
• Facilities for monitoring immunosuppressant serum levels
• Links with thoracic surgery for diagnostic biopsy
• Where appropriate, centres will be able to undertake whole lung lavage for pulmonary alveolar proteinosis and/or embolisation of pulmonary arterio-venous malformations
• Access to pulmonary rehabilitation services
• Clearly defined pathways of care with regional transplant centre
• Intensive care services and inpatient beds to support the assessment of new cases of ILD presenting with acute onset respiratory failure
• Access to pulmonary hypertension services
• Dedicated link with palliative care services
• Dedicated ILD pharmacist to handle dispensing and accountability of cytotoxic drugs and specialist therapies

**Recommended Standards**

- Multi-disciplinary service for multi-organ sarcoid including; neurology, cardiology, dermatology and ENT
- Links with rheumatology services for management of multi-system connective tissue disease
- Availability of specific investigations for sarcoidosis including; PET scanning, Gallium Scanning and Cardiac MRI
- Integrated clinical trials unit (linked with CLRN network) offering trial access for patients with IPF and other ILDs

**4. Key Service Outcomes**

The following data will be collected annually to monitor clinical outcomes:

- Lung function (% predicted forced expiratory volume in 1 second (FEV1), Forced Vital Capacity and DLco).
- Health related quality of life, disease-specific and generic.
- Mortality data.