NEW YORK STATE OF OPPORTUNITY.

Workers' Compensation Board

Medical Treatment Guidelines

Occupational Interstitial Lung Disease

Effective May 2, 2022

Contributors

Medical Advisory Committee

The NYS Workers' Compensation Board would like to thank the members of the New York Workers' Compensation Board Medical Advisory Committee (MAC). The MAC served as the Board's advisory body to adapt the American College of Occupational and Environmental Medicine (ACOEM) Practice Guidelines to a New York version of the Medical Treatment Guidelines (MTG). In this capacity, the MAC provided valuable input and made recommendations to help guide the final version of these Guidelines. With full consensus reached on many topics, and a careful review of any dissenting opinions on others, the Board established the final product.

Joseph Canovas, Esq.
Special Counsel
New York State AFL-CIO

Kenneth B. Chapman, MD
Director Pain Medicine, SIUH Northwell Health Systems
Assistant Clinical Professor, NYU Langone Medical Center
Adjunct Assistant Professor, Hofstra Medical School

Lev Ginsburg, Esq.
Senior Director of Government Affairs
The Business Council of New York State

Robert Goldberg, DO
Attending Physician – Department of Rehabilitation, Beth Israel Hospital and Medical Center of NYC
Professor of Physical Medicine and Rehabilitation and Health Policy
Clinical Associate Professor of Rehabilitation Medicine, New York Medical College
Clinical Professor of Rehabilitation Medicine, Philadelphia College of Osteopathic Medicine
Member Council on Medical Education of the American Medical Association

David Kamelhar, MD, FACP, FCCP
Clinical Professor of Medicine
Department of Pulmonary, Critical Care and Sleep Medicine
NYU School of Medicine

Joseph Pachman, MD, PhD, MBA, MPH
Licensed Psychologist and Physician
Board Certified in Occupational Medicine
Fellow in ACOEM
Vice President and National Medical Director, Liberty Mutual

Elaine Sobol-Berger, MD, JD
Former Medical Director and Senior Policy Advisor,
New York State Workers' Compensation Board

Jaime Szeinuk, MD

Attending Physician, Occupational and Environmental Medicine of Long Island
Assistant Professor, Department of Occupational Medicine, Epidemiology and Prevention
Northwell Health

James A. Tacci, MD, JD, MPH
Medical Director and Executive Medical Policy Director,
New York State Workers' Compensation Board
(At the time of drafting: Attending Physician, Associate Professor, and Medical Director, University of Rochester Medical Center)

Edward C. Tanner, MD,
Chair, Department of Orthopaedics at Rochester General Hospital
Past President, New York State Society of Orthopaedic Surgeons (NYSSOS)
Member, American Academy of Orthopaedic Surgeons (AAOS)
Member, American Association of Hip and Knee Surgeons (AAHKS)

Contributors to ACOEM Occupational Interstitial Lung Disease Guideline

Editor-in-Chief:
Kurt T. Hegmann, MD, MPH, FACOEM, FACP

Assistant Editors:
Jeremy J. Biggs, MD, MSPH
Matthew A. Hughes, MD, MPH, FACOEM

Evidence-based Practice Interstitial Lung Disease Panel Chairs:
Francesca K. Litow, MD, MPH, FACOEM
Edward Lee Petsonk, MD, CM, FACP

Evidence-based Practice Interstitial Lung Disease Panel Members:
Bruce K. Bohnker, MD, MPH, FACOEM
Carl A. Brodkin, MD, MPH, FACOEM
Clayton T. Cowl, MD, MS, FACOEM
Tee L. Guidotti, MD, MPH, FACOEM
Philip Harber, MD, MPH, FACOEM

Panel members represent several disciplines including: occupational medicine, internal medicine, preventive medicine, pulmonary medicine, toxicology, epidemiology, and aerospace medicine.

Panel Consultant:
Mary C. Townsend, DrPH

Managing Editors:
Production: Marianne Dreger, MA
Research: Julie A. Ording, MPH

Research Conducted By:
Jeremy J. Biggs, MD, MSPH
Matthew A. Hughes, MD, MPH, FACOEM
Matthew S. Thiese, PhD, MSPH
Ulrike Ott, PhD, MSPH

Atim C. Effiong, MPH
Leslie M. Cepeda-Echeverria
Tessa Langley
Deborah G. Passey, MS
William Caughey, MS
Kylee Fon Tokita, BS
Riann Robbins, BS
Alzina Koric, MPP
Jeremiah L. Dortch, BS

Specialty Society and Society Representative Listing
ACOEM acknowledges the following organizations and their representatives who served as reviewers of the Occupational Interstitial Lung Disease Guideline. Their contributions are greatly appreciated. By listing the following individuals or organizations, it does not infer that these individuals or organizations support or endorse the Occupational Interstitial Lung Disease Guideline developed by ACOEM.

American College of Chest Physicians
Stephen A. Mette, MD, FCCP, FACP

Other External Reviewers:
Stephen Frangos, MD, MPH, FACOEM
Charles Yarborough, MD, MPH, FACOEM

Table of Contents

A. GENERAL GUIDELINE PRINCIPLES

The principles summarized in this section are key to the intended application of the New York State Medical Treatment Guidelines (MTG) and are applicable to all Workers' Compensation Medical Treatment Guidelines.

A.1 Medical Care

Medical care and treatment required as a result of a work-related injury should be focused on restoring functional ability required to meet the patient's daily and work activities with a focus on a return to work, while striving to restore the patient's health to its pre-injury status in so far as is feasible.

A.2 Rendering Of Medical Services

Any medical provider rendering services to a workers' compensation patient must utilize the Treatment Guidelines as provided for with respect to all work-related injuries and/or illnesses.

A.3 Positive Patient Response

Positive results are defined primarily as functional gains which can be objectively measured. Objective functional gains include, but are not limited to, positional tolerances, range of motion, strength, endurance, activities of daily living (ADL), cognition, psychological behavior, and efficiency/velocity measures which can be quantified. Subjective reports of pain and function may be considered and given relative weight when the pain has anatomic and physiologic correlation in proportion to the injury.

A.4 Re-Evaluate Treatment

If a given treatment or modality is not producing positive results within a well-defined timeframe, the provider should either modify or discontinue the treatment regime. The provider should evaluate the efficacy of the treatment or modality 2 to 3 weeks after the initial visit and 3 to 4 weeks thereafter. These timeframes may be slightly longer in the context of conditions that are inherently mental health issues, and shorter for other non-musculoskeletal medical conditions (e.g. pulmonary, dermatologic etc.). Recognition that treatment failure is at times attributable to an incorrect diagnosis a failure to respond should prompt the clinician to reconsider the diagnosis in the event of an unexpected poor response to an otherwise rational intervention.

A.5 Education

Education of the patient and family, as well as the employer, insurer, policy makers and the community should be a primary emphasis in the treatment of work-related injury or illness. Practitioners should develop

and implement effective educational strategies and skills. An education-based paradigm should always start with communication providing reassuring information to the patient. No treatment plan is complete without addressing issues of individual and/or group patient education as a means of facilitating self-management of symptoms and prevention of future injury.

Time Frames

A.6 Acuity

Acute, Subacute and Chronic are generally defined as timeframes for disease stages:

- Acute – Less than one month
- Subacute - One to three month, and
- Chronic - greater than three months.

A.7 Initial Evaluation

Initial evaluation refers to the acute timeframe following an injury and is not used to define when a given physician first evaluates an injured worker (initial encounter) in an office or clinical setting.

A.8 Diagnostic Time Frames

Diagnostic time frames for conducting diagnostic testing commence on the date of injury. Clinical judgment may substantiate the need to accelerate or decelerate the time frames discussed in this document.

A.9 Treatment Time Frames

Treatment time frames for specific interventions commence once treatments have been initiated, not on the date of injury. It is recognized that treatment duration may be impacted by disease process and severity, patient compliance, as well as availability of services. Clinical judgment may substantiate the need to accelerate or decelerate the time frames discussed in this document.

A.10 Delayed Recovery

For those patients who fail to make expected progress 6-12 weeks after an injury and whose subjective symptoms do not correlate with objective signs and tests, reexamination in order to confirm the accuracy of the diagnosis and re-evaluation of the treatment program should be performed. When addressing a clinical issue that is not inherently a mental health issue, assessment for potential barriers to recovery (yellow flags/psychological issues) should be ongoing throughout the care of the patient. At 6-12 weeks, alternate treatment programs, including formal psychological or psychosocial evaluation should be considered. Clinicians

must be vigilant for any pre-existing mental health issues or subsequent, consequential mental health issues that may be impacting recovery. For issues that are clearly and inherently mental health issues from the outset (i.e. when it is evident that there is an underlying, work-related, mental health disorder as part of the claim at issue), referral to a mental health provider can and should occur much sooner. Referrals to mental health providers for the evaluation and management of delayed recovery do not indicate or require the establishment of a psychiatric or psychological condition. The evaluation and management of delayed recovery does not require the establishment of a psychiatric or psychological claim.

Treatment Approaches

A.11 Active Interventions

Active interventions emphasizing patient responsibility, such as therapeutic exercise and/or functional treatment, are generally emphasized over passive modalities, especially as treatment progresses. Generally, passive and palliative interventions are viewed as a means to facilitate progress in an active rehabilitation program with concomitant attainment of objective functional gains.

A.12 Active Therapeutic Exercise Program

Active therapeutic exercise program goals should incorporate patient strength, endurance, flexibility, range of motion, sensory integration, coordination, cognition and behavior (when at issue) and education as clinically indicated. This includes functional application in vocational or community settings.

A.13 Diagnostic Imaging And Testing Procedures

Clinical information obtained by history taking and physical examination should be the basis for selection of imaging procedures and interpretation of results. All diagnostic procedures have characteristic specificities and sensitivities for various diagnoses. Usually, selection of one procedure over others depends upon various factors, which may include: relative diagnostic value; risk/benefit profile of the procedure; availability of technology; a patient's tolerance; and/or the treating practitioner's familiarity with the procedure.

When a diagnostic procedure, in conjunction with clinical information, provides sufficient information to establish an accurate diagnosis, a second diagnostic procedure is not required. However, a subsequent diagnostic procedure including a repeat of the original (same) procedure can be performed, when the specialty physician (e.g. physiatrist, sports medicine physician or other appropriate specialist) radiologist or surgeon documents that the initial study was of inadequate quality to make a diagnosis. Therefore, in such circumstances, a repeat or complementary diagnostic procedure is permissible under the MTG.

It is recognized that repeat imaging studies and other tests may be warranted by the clinical course and/or to follow the progress of treatment in some cases. It may be of value to repeat diagnostic procedures (e.g., imaging studies) during the course of care to reassess or stage the pathology when there is progression of symptoms or findings, prior to surgical interventions and/or therapeutic injections when clinically indicated, and post-operatively to follow the healing process. Regarding serial imaging, (including x-rays, but particularly CT scans), it must be recognized that repeat procedures result in an increase in cumulative radiation dose and associated risks.

A given diagnostic imaging procedure may provide the same or distinctive information as obtained by other procedures. Therefore, prudent choice of procedures(s) for a single diagnostic procedure, a complementary procedure in combination with other procedures(s), or a proper sequential order in multiple procedures will ensure maximum diagnostic accuracy, minimize the likelihood of adverse effect on patients, and promote efficiency by avoiding duplication or redundancy.

A.14 Surgical Interventions

Consideration of surgery should be within the context of expected functional outcome. The concept of "cure" with respect to surgical treatment by itself is generally a misnomer. All operative interventions must be based upon positive correlation of clinical findings, clinical course and imaging and other diagnostic tests. A comprehensive assimilation of these factors must lead to a specific diagnosis with positive identification of pathologic condition(s). For surgery to be performed to treat pain, there must be clear correlation between the pain symptoms and objective evidence of its cause. In all cases, shared decision making with the patient is advised. The patient should be given the opportunity to understand the pros and cons of surgery, potential for rehabilitation as an alternative where applicable, evidence-based outcomes, and specific surgical experience.

A.15 Pre-Authorization

All diagnostic imaging, testing procedures, non-surgical and surgical therapeutic procedures, and other therapeutics within the criteria of the Medical Treatment Guidelines and based on a correct application of the Medical Treatment Guidelines are considered authorized, with the exception of the procedures listed in section 324.3(1)(a) of Title 12 NYCRR. These are not included on the list of pre-authorized procedures. Providers who want to perform one of these procedures must request pre-authorization from the carrier before performing the procedure.

Second or subsequent procedures (the repeat performance of a surgical procedure due to failure of, or incomplete success from the same surgical procedure performed earlier, if the Medical Treatment Guidelines do not specifically address multiple procedures) also require pre-authorization.

A.16 Psychological/Psychiatric Evaluations

In select patients, mental health evaluations are essential to make, secure or confirm a diagnosis. Of course, the extent and duration of evaluations and/or interventions by mental health professionals may vary, particularly based on whether: the underlying clinical issue in the claim is inherently a mental health issue; or there is a mental health issue that is secondary or consequential to the medical injury or illness that is at issue in the claim in question; or there is a pre-existing, unrelated mental health issue that has been made worse by, or is impeding the recovery from (or both) the medical injury or illness that is at issue in the claim in question.

Tests of psychological function or psychometric testing, when indicated, can be a valuable component of the psychological evaluation in identifying associated psychological, personality and psychosocial issues. Although these instruments may suggest a diagnosis, neither screening nor psychometric tests are capable of making a diagnosis. The diagnosis should only be made after careful analysis of all available data, including from a thorough history and clinical interview.

A professional fluent in the primary language of the patient is strongly preferred. When such a provider is not available, services of a professional language interpreter must be provided.

Frequency: When assessing for a pre-existing, unrelated mental health issue that has been made worse by, or is impeding the recovery from (or both) a work-related, medical injury or illness, then a one-time visit for initial psychiatric/psychological encounter should be sufficient, as care would normally be continued by the prior treating provider. If psychometric testing is indicated by findings in the initial encounter, time for such testing should not exceed an additional three hours of professional time. For conditions in which a mental health issue is a central part of the initial claim, or in which there is a mental health issue that is secondary or consequential to the work-related, medical injury or illness, that is part of the claim in question, then more extensive diagnostic and therapeutic interventions may be clinically indicated, and are discussed in detail in the Medical Treatment Guidelines for such mental health conditions.

A.17 Personality/Psychological/Psychosocial Intervention

Following psychosocial evaluation, when intervention is recommended, such intervention should be implemented as soon as possible. This can be used alone or in conjunction with other treatment modalities. For all psychological/psychiatric interventions, there must be an assessment and treatment plan with measurable behavioral goals, time frames and specific interventions planned**.**

- Time to produce effect: two to eight weeks.
- Optimum duration: six weeks to three months.
- Maximum duration: three to six months.
- Counseling is not intended to delay but rather to enhance functional recovery.

For PTSD Psychological Intervention:

- Optimum duration three to six months.
- Maximum duration: nine to twelve months.

For select patients, longer supervision and treatment may be required, and if further treatment is indicated, documentation of the nature of the psychological factors, as well as projecting a realistic functional prognosis, should be provided by the authorized treating practitioner every four weeks during the first six months of treatment. For treatment expected to last six to twelve months, such documentation should be provided every four to eight weeks. For long-term treatment beyond twelve months, such documentation should be provided every eight to twelve weeks. All parties should strive for ongoing and continuous communications, in order to facilitate seamless, continuous and uninterrupted treatment.

A.18 Functional Capacity Evaluation (FCE)

Functional capacity evaluation is a comprehensive or more restricted evaluation of the various aspects of function as they relate to the patient's ability to return to work. Areas such as endurance, lifting (dynamic and static), postural tolerance, specific range-of-motion, coordination and strength, worker habits, employability, as well as psychosocial, cognitive, and sensory perceptual aspects of competitive employment may be evaluated. Components of this evaluation may include: (a) musculoskeletal screen; (b) cardiovascular profile/aerobic capacity; (c) coordination; (d) lift/carrying analysis; (e) job-specific activity tolerance; (f) maximum voluntary effort; (g) pain assessment/psychological screening; (h) non-material and material handling activities; (i) cognitive and behavioral; (j) visual; and (k) sensory perceptual factors.

In most cases, the question of whether a patient can return to work can be answered without an FCE.

An FCE may be considered at time of MMI, following reasonable prior attempts to return to full duty throughout course of treatment, when the treating physician is unable to make a clear determination on work status on case closure. An FCE is not indicated early during a treatment regime for any reason including one to support a therapeutic plan.

When an FCE is being used to determine return to a specific job site, the treating physician is responsible for understanding and considering the job duties. FCEs cannot be used in isolation to determine work restrictions. The authorized treating physician must interpret the FCE in light of the individual patient's presentation and medical and personal perceptions. FCEs should not be used as the sole criteria to diagnose malingering.

A.19 Return To Work

For purposes of these guidelines, return to work is defined as any work or duty that the patient is able to perform safely. It may not be the patient's regular work. Ascertaining a return to work status is part of medical care, and should be included in the treatment and rehabilitation plan. It is normally addressed at every outpatient visit. A description of the patient's status and task limitations is part of any treatment plan and should provide the basis for restriction of work activities when warranted. Early return to work should be a prime goal in treating occupational injuries. The emphasis within these guidelines is to move patients along a continuum of care and return to work, since the prognosis of returning an injured worker to work drops progressively the longer the worker has been out of work.

A.20 Job Site Evaluation

The treating physician may communicate with the employer or employer's designee, either in person, by video conference, or by telephone, to obtain information regarding the individual or specific demands of the patient's pre-injury job. This may include a description of the exertional demands of the job, the need for repetitive activities, load lifting, static or awkward postures, environmental exposures, psychological stressors and other factors that would pose a barrier to re-entry, risk of re-injury or disrupt convalescence. When returning to work at the patient's previous job tasks or setting is not feasible, given the clinically determined restrictions on the patient's activities, inquiry should be made about modified duty work settings that align with, the patient's condition in view of proposed work activities/demands in modified duty jobs. It should be noted, that under certain circumstances, more than one job site evaluation may be indicated.

Ideally, the physician would gain the most information from an on-site inspection of the job settings and activities; but it is recognized that this may not be feasible in most cases. If job videos/CDs/DVDs are available

from the employer, these can contribute valuable information, as can video conferences, conducted from the worksite and ideally workstation or work area.

Frequency: one or two contacts

- 1st contact: Patient is in a functional state where the patient can perform some work.
- 2nd contact: Patient has advanced to state where the patient is capable of enhanced functional demands in a work environment.

The physician shall document the conversation.

Other

A.21 Guideline Recommendations And Medical Evidence

The Workers' Compensation Board and its Medical Advisory Committee have not independently evaluated or vetted the scientific medical literature used in support of the guidelines, but have relied on the methodology used by the developers of various guidelines utilized and referenced in these Guidelines.

A.22 Experimental/Investigational Treatment

Medical treatment that is experimental/investigational and not approved for any purpose, application or indication by the FDA is not permitted under these Guidelines.

A.23 Injured Workers As Patients

In these Guidelines, injured workers are referred to as patients recognizing that in certain circumstances there is no doctor-patient relationship.

A.24 Scope Of Practice

These Guidelines do not address scope of practice or change the scope of practice.

Occupational Interstitial Lung Disease

Effective date will coincide with the launch of OnBoard: Limited Release

B. Occupational Interstitial Lung Disease Guideline

B.1 Overview

Occupational lung disease is often classified into several different categories, of which Interstitial Lung Diseases (ILD) is one of the main categories and work-related asthma is another (Work related asthma is addressed in the NY Occupational Asthma/Work Related Asthma Medical Treatment Guideline).

This guideline is intended as an evidence-based approach to the diagnosis and treatment of Occupational Interstitial Lung Diseases (ILD). The guideline covers inorganic dust-related diseases (e.g., silicosis, asbestosis, and coal workers' pneumoconiosis (CWP)), and the immunologically mediated diseases such as chronic beryllium disease (CBD) or hypersensitivity pneumonitis (HP). Occupational exposure history, presentation, and diagnostic and screening test results form the foundation for diagnosis and treatment plans.

ILDs are a heterogeneous group of more than 100 diseases that inflame and/or scar the lung parenchyma and which are classified together because of similar clinical, roentgenographic, physiologic, and/or pathologic features. ILD describes disorders affecting the lung interstitium. Acute injury to the interstitium is manifested mostly by edema and inflammation, while chronic injury is characterized by fibrosis, the end stage of chronic inflammation. ILD sometimes referred to as "pulmonary fibrosis" or "interstitial fibrosis" is a group of chronic, generally irreversible conditions manifested by a vigorous immune and/or inflammatory response and exuberant fibroblast activity that results in excessive collagen deposition

B.2 Introduction

Occupationally related ILD fall into four often clinically overlapping categories:

- Pneumoconiosis
- Hypersensitivity Pneumonitis (HP)
- Other Granulomatous Diseases
- Toxic Inhalation Injury

ILD associated with pneumoconioses and autoimmune processes tends to progress through stages, ultimately reaching a similar "end stage" condition. This condition is characterized by:

- restrictive disease
- pulmonary hypertension
- cor pulmonale
- congestive heart failure
- lung infections due to loss of host defense mechanisms

ILD, as it advances, is often associated with a chronic dry cough, which may require suppression particularly when it interferes with sleep.

Table 1: Most Common ILD Conditions, Etiologic Agents, Latency

ILD is a large category of disease; the list of conditions below is not all inclusive of all work-related ILD.

All listed exposures may have increased risk of occupational ILDs where there is sufficient frequency, intensity and duration of exposures.

Category	Condition/Examples	Occupational Exposure (Etiologic Agent)	Latency (Time of exposure to onset of symptoms)
Pneumoconiosis (Three most common)	Silicosis	Crystalline silica	Years to decades
	Asbestosis	Asbestos Minerals	Decades
	Coal Workers	Coal Mine Dust, Graphite	Decades
Hypersensitivity Pneumonitis (Organic Respirable Dusts/Low Molecular Weight) Sensitizing Chemicals	Farmers Lung Bird Fanciers Lung	Animal proteins, plant proteins, bacteria, fungi, and paints, foam, PVC fumes, diisocyanates.	Defined as acute, subacute and chronic. As early as hours in acute.
Other Granulomatous Diseases	Berylliosis Hard Metal Disease (Cobalt, Tin)	Beryllium, Cobalt Tin. Hard Metal	Years to decades
Toxic Inhalation Injury	Irritant inhalation injury(diffuse alveolar related to nitrogen oxide) ex. Nitrogen Dioxide, Ozone, Phosgene or ionizing radiation (Gases	ex. Nitrogen Dioxide, Ozone, Phosgene or ionizing radiation (Gases	Hours

Table 2: Industrial Exposure

Category	Industry	Occupational Activities
Pneumoconiosis (Three most common) Silicosis	Mining, oil and gas, construction, foundry, pottery, manufacturing Sandblasting, foundry workers, tunnel diggers, ceramic workers	Drilling, mining, excavating, abrasive blasting, grinding, cutting
Pneumoconiosis: Asbestosis	Power plant, foundry, demolition, ship building, brake and clutch linings, asbestos cement, asbestos textile, fireproofing, insulation	Removal of, disturbing old asbestos-containing construction materials (e.g., insulation), insulation application, brake and clutch work,
Pneumoconiosis: Coal Workers	Mining, electricity generation and storage, metals	Coal mining/ handling, battery manufacture, pencil making
Hypersensitivity Pneumonitis	Wood and food products, animal rearing, farming, painting, chemicals manufacturing	Cleaning, water sprays, shredding,
Other Granulomatous Diseases	Nuclear, aircraft, tools, electronics	Machining, grinding, smelting, metal product manufacturing
Toxic Inhalation Injury	Chemical production, manufacturing, Transportation	Generally acute exposure in the course of accidents or other disasters

B.3 Key Concepts

B.3.a Latency

Latency can be defined as the time interval between initial exposure and onset of symptoms/clinical diagnosis. The concept of latency is important in occupational ILD as most of the occupational ILDs have a long latency time.

B.3.b Relationship between Latency and Exposure (See Tables 1 and 2)

B.3.c Comorbidities

As per the International Agency for Research on Cancer (IARC), asbestos exposure is associated with an increased risk for lung cancer (with far greater risk, or interaction, with cigarette smoking), mesothelioma (involving pleural or peritoneal serosal membranes), laryngeal and ovarian cancer. Other studies show that asbestos may be associated with increases in cancers in other sites such as pharyngeal, stomach, colon, and kidney cancers. Asbestos exposure has also been associated with risk for airway disease.

- CWP is associated with an elevated risk of autoimmune disorders, principally rheumatoid arthritis (aka, “Caplan’s syndrome”). Thus, workers with CWP may have associated autoimmune disorders and develop systemic clinical manifestations. CWP has also been associated with risk for airway disease.
- Silicosis also increases risk for lung cancer, pulmonary tuberculosis, autoimmune disease, renal disease, and airways diseases. There is also an interaction of increased lung cancer and cigarette smoking, although not as strong as that one for asbestos exposure.

B.4 Conditions

B.4.a Silicosis

Exposure to sufficient respirable silica leads to silicosis, an irreversible disease which is associated with a variety of systemic and pulmonary conditions. Patients with silicosis or silica exposure have an increased risk for lung cancer. The IARC reclassified silica as a Group I substance (“carcinogenic to humans”) in October 1996.

Silicosis is still the most common occupational disease worldwide and at least 1.7 million U.S. workers are exposed to respirable crystalline silica.

B.4.a.i Etiologic Agent

Silicosis results from exposure to crystalline silicon dioxide. Exposure to silica in other forms such as glass and other amorphous forms of silica has not been associated with silicosis. However, crystalline silica is present in sand. Silica exposure occurs in a variety of industries and occupations, including construction, sandblasting, and mining.

B.4.a.ii Condition Considerations

Exposure to silica can result in one of three different disease patterns: chronic silicosis, subacute/accelerated silicosis and acute silicosis. The most common form is chronic silicosis, which is usually seen after more than ten years of exposure. Subacute silicosis results from shorter, heavier exposures, usually after two to five years of latency. Acute silicosis is often seen following intense exposure to fine silica-containing dust over a several month period.

Chronic silicosis may progress to massive, accreted fibrotic zones in the lung (“conglomerative silicosis”) that result in:

- respiratory failure,
- pulmonary hypertension,
- cor pulmonale with right heart failure.

Patients with silicosis also have increased risk for:

- Chronic bronchitis, defined by chronic sputum production, with or without obstructive impairment in pulmonary function tests,
- Exposure to silica at levels below those associated with simple silicosis has been associated with chronic airflow limitation and/or mucus hypersecretion and/or pathologic emphysema,
- lung cancer,
- pulmonary tuberculosis,
- autoimmune disease,
- renal disease.

B.4.a.iii Latency

Silicosis typically becomes clinically apparent over a period of years, exceptions are rare but include accelerated silicosis.

B.4.a.iv Diagnosis

The diagnosis of silicosis is typically made clinically, based on occupational history of sufficient exposure with appropriate latency, objective radiographic evidence (chest radiograph and/or high resolution CT), assessment of pulmonary function and consideration of alternative differential diagnoses.

B.4.b Asbestosis

B.4.b.i Condition Considerations

Exposure to asbestos can result in one of several different disease patterns. Asbestosis refers to the diffuse type of pulmonary fibrosis that results from inhaling asbestos fibers. Pleural thickening, in the form of discreet pleural plaques (calcified or uncalcified) is the most common manifestation of asbestos exposure. Diffuse pleural thickening, rounded atelectasis and non-malignant asbestos-related pleural effusion are other manifestations of pleural disease caused by asbestos exposure.

B.4.b.ii Comorbidities

Common with asbestos-related disease. Asbestos exposure is associated with an increased risk for:

- Lung cancer (with far greater risk, or interaction, with cigarette smoking).
- Mesothelioma (involving pleural or peritoneal serosal membranes).
- Laryngeal and ovarian cancer.

Individuals with asbestosis experience variable rates of disease progression, ranging from mild to severe respiratory impairment. Asbestosis symptoms and radiographic findings are worsened by cigarette smoking history and other exposures such as diesel fuel fumes.

B.4.b.iii Latency
The symptoms of asbestosis can take decades after exposure to show up.

B.4.b.iv Diagnosis
The diagnosis of asbestosis and other asbestos-related diseases is typically made clinically, based on occupational history of sufficient exposure with appropriate latency, objective radiographic evidence (chest radiograph and/or HRCT), assessment of pulmonary function, and consideration of alternative differential diagnoses.

B.4.c Coal Workers' Pneumoconiosis (CWP)

Coal dust is a mixture of carbon and complex organic materials and minerals, including variable amounts of silica and silicates.

B.4.c.i Condition Considerations
- CWP Is a distinct disease, distinguishable pathologically from silicosis, although the two may occur together particularly in miners who drilled or cut through rock.
- CWP differs histologically from silicosis in the morphology of the lesion.
- Coal workers' pneumoconiosis (CWP) is often associated with bronchitis and some degree of airways obstruction.
- CWP may progress to large intrathoracic fibrotic masses, usually visible on chest x-rays in the upper and mid lung fields ("progressive massive fibrosis"), which are associated with severe respiratory impairment.

B.4.c.ii Comorbidities CWP is associated with an elevated risk of:
- Autoimmune disorders, principally rheumatoid arthritis (aka, "Caplan's syndrome").
- Workers with CWP may have associated autoimmune disorders and develop systemic clinical manifestations.

B.4.c.iii Latency
- CWP Pneumoconiosis typically becomes clinically apparent over a period of decades.
- Exceptions are rare but include CWP associated with high exposure levels.

B.4.c.iv Diagnosis
The diagnosis of CWP is typically made clinically, based on occupational history of sufficient exposure with appropriate latency, objective radiographic evidence (chest radiograph and/or HRCT), assessment of pulmonary function, and consideration of alternative differential diagnoses

B.4.d Hypersensitivity Pneumonitis (HP)

Hypersensitivity Pneumonitis (HP), also known as extrinsic allergic alveolitis, can be caused by inhalation of organic dust with antigenic properties or exposure to low-molecular weight sensitizing chemicals.

B.4.d.i Condition Considerations

HP Is a large family of disorders of immune response often associated with granulomatous pathological changes. HPs tend to be highly specific to occupation or environmental settings.

Inhaled causative agents include:

- Animal proteins
- Plant proteins
- Bacteria
- Fungi
- Diisocyanates.
- Paints
- Trimellitic anhydride
- Epoxy resins
- “Bordeaux mixture” (a pesticide made from copper sulfate used in vineyards)

These dusts arise from:

- Renovation of buildings (especially demolition or exposing damp interior walls), exposure to contaminated water or persistently wet spaces (humidifiers, hot tubs, saunas, and unventilated showers)
- Handling birds
- Occasionally from sensitization to other animals (such as farmer’s lung)
- Insects (such as miller’s lung, the antigen to which is a wheat weevil protein)
- Amoebae (humidifier lung)
- Pesticide powder (pyrethrum HP)
- Spores of a thermophilic actinomycete bacteria resulting in furrier’s lung
- Animal-derived dusts
- Grain dusts
- Mold spores

HP often begins with wheezing and airways obstruction. Untreated and unmanaged, it may progress to respiratory insufficiency and profound impairment. Pigeon breeders’ lung famously is associated with clubbing, unlike most hypersensitivity pneumonitides.

B.4.d.ii Latency

- In HP, sensitization may occur in the first few weeks after beginning exposure, in others it may be delayed for months or years.
- The acute, predominant airways symptoms of HP develop in a sensitized individual over days to weeks and may progress over weeks to interstitial inflammation and ultimately to fibrosis.
- Rarely also hyperacute or sudden in onset, similar to some eosinophilic pneumonias or some drug-induced pneumonitis.

B.4.d.iii Differential Diagnosis

HP should be included in a differential diagnosis of an acute influenza-like or febrile disorder in a patient with a history of exposure to inhaled antigens. However, it may also suggest rheumatological or autoimmune lung disease and infection (mycoplasma, Legionella spp., or diffuse mycosis) as a cause of interstitial disease, the latter especially in a host with a compromised immune system. A history of exposure to birds should also raise the possibility of other diseases including psittacosis.

While there are no well-established risk factors for development of HP, personal and familial susceptibility may play a role.

B.4.e Other Granulomatous Diseases

ILD caused by chronic immune and foreign-body responses to antigens in the lung, which may be metal dusts and, therefore, also considered pneumoconioses.

B.4.e.i Prominent examples include:

- Beryllium (Beryllium Disease)
- Cobalt in cemented tungsten carbide (Hard Metal Disease)
- Work-related Sarcoidosis

B.4.e.ii Condition Considerations

The clinical manifestations of hard metal disease are overall similar to other pneumoconioses. The pathology findings of hard metal disease are that of a giant cell interstitial pneumonia. The interstitial fibrosis is accompanied by activated macrophages that fill alveoli and is part of a dysfunctional foreign body reaction.

Chronic beryllium disease is a systemic granulomatous inflammatory disorder that is very similar to sarcoidosis. The tissue response is mediated by immune mechanisms and may not localize to an area of dust accumulation. This may manifest in systemic, body-wise disease manifestations, although less frequently than in sarcoidosis.

B.4.e.iii Latency

These disorders are uncommon, problems develop at different exposure levels in different people. It can be decades before these disorders become clinically apparent and the clinical presentations are variable.

B.4.e.iv Condition Considerations

- This condition usually results from irritant inhalation injury (e.g., diffuse alveolar injury related to nitrogen oxides).
- Diffuse interstitial fibrosis should be distinguished from more common idiopathic interstitial fibrosis either of the “usual interstitial pneumonia” or the “nonspecific interstitial pneumonia” types.
- Extensive fibrosis, which may occur following recovery from diffuse alveolar damage by toxic inhalation, is refractory to direct management.
- Advanced forms of all of the occupational ILDs may have a similar clinical presentation to diffuse interstitial fibrosis.

B.4.f Toxic Inhalation Injury

ILD due to toxic inhalation injury is generally the result of severe lung injury after an acute exposure to high concentration of noxious gases, fumes or mists.

B.5 History Taking and Physical Examination

Occupational exposure history, presentation, and diagnostic screening test results form the foundation for diagnosis and treatment plans.

B.5.a History of Present Illness

The History of Present Illness (HPI) should document:

- Occupational and non-occupational pulmonary exposures.
- Occupation: current/past and types of work activities (such as: construction, demolition, mining, manufacturing, drilling). See table below for examples.
- Time spent at each job, including jobs held years to decades in the past.

Industry	Mining, oil and gas, construction, foundry, pottery, manufacturing	Power plant, foundry, demolition	Mining, electricity generation and storage, metals	Wood and food products, animal rearing, farming	Nuclear, aircraft, tools, electronics

Occupational Activities	Drilling, mining, excavating, abrasive blasting, grinding, cutting	Removal of old asbestos-containing construction materials (e.g., insulation)	Coal mining/ handling, battery manufacture, pencil making	Cleaning, water sprays, shredding	Machining, grinding, smelting, metal product manufacturing

Exposures to:

- Dusts: organic dusts (fungi, bacteria, plant and animal proteins) and inorganic mineral dusts (silica, asbestosis, coal).
- Metals (Beryllium (old light bulbs, aerospace), tin, cobalt).
- Toxic and inflammatory fumes, gas, vapors, aerosols.
- History of exposure should include non-occupational exposures to these agents with a description of exposure, duration of exposure, and intensity of exposure.
- Intensity of exposure: ideally with environmental measurements (industrial hygiene data) or at least a qualitative description of intensity of exposure, e.g., daily, weekly, monthly, yearly, etc.
- Include questions detailing the individual's responsibilities and exposure (e.g. did you work in the office, etc.).

Symptoms:

- Symptoms and when symptoms began
- Including complaints of:
  - Throat tightness
  - Shortness of breath
  - Difficulty with inspiration or expiration
  - Harsh sounds
  - Cough
  - Sputum production

Duration, onset and frequency of symptoms.

- Symptom development including:
  - Aggravation and alleviation of symptoms in relationship to work environment
  - Changes in work environment
  - Changes in symptoms in relation to days worked and not worked
  - Progression of symptoms
- Pulmonary imaging and testing.
- Previous treatments.
- Relationship to work: This includes a statement of the probability that the illness, or injury is work-related.
- Ability to perform job duties and activities of daily living.

B.5.b Past History

- Past medical history including but not limited to prior pulmonary exposures and treatments (include prone to bronchitis, pneumonia).
- Review of systems includes, but is not limited to, symptoms of rheumatologic, neurologic, endocrine, neoplastic, and other systemic diseases.
- Detailed smoking history (including marijuana, vaping, etc.).
- Detailed medication history including use of Amiodarone, chemotherapeutic agents, and nitrofurantoin.
- Vocational and recreational pursuits.
- Prior imaging studies.
- Past surgical history.
- Allergy history.

B.5.c Physical Examination

An occupational pulmonary physical examination should include the following elements:

- Vital signs, including measured respiratory rate, O2 saturation.
- Overall functional abilities, including ease of movement, walking and changing positions, dressing and undressing while assessing signs and symptoms of dyspnea.
- Assessment of respiratory status (e.g., rate, depth, use of accessory muscles, nasal flaring).
- Inspection for stigmata of pulmonary disease as well as potential etiologies including:
  - Mucous membrane abnormalities
  - Nasal polyps/swelling/discharge
  - Clubbing (asbestosis, idiopathic pulmonary fibrosis, some hypersensitivity pneumonitides)
  - Anterior-posterior diameter
  - Scoliosis
  - Kyphosis

- Palpation for:
  - Chest wall abnormalities
  - Adenopathy and neck masses

- Percussion for resonance to identify:
  - Aeration
  - Diaphragm level
  - Suggestion for fluid interface or consolidation

- Auscultation for:
  - Inspiration to expiration ratio
  - Adventitious breath sounds (crackles, wheeze (often a secondary manifestation of HP and a primary manifestation of eosinophilic pneumonia) rales, rhonchi)

- Pleural rubs, as well as timing, location and persistence of lung findings

- Cardiac examination with attention to findings of cor pulmonale and heart failure.

- Dermal examination for signs of disease, i.e., erythema nodosum (sarcoidosis).

B.5.d Diagnostic Approach

The diagnoses of occupational ILD typically is made clinically, based on occupational history of sufficient exposure with appropriate latency, objective radiographic evidence (chest radiograph and/or HRCT), assessment of pulmonary function (including consistent changes in ventilatory capacity, static lung volumes or gas-exchange), and consideration of alternative differential diagnoses.

In a worker with a typical clinical picture (including exposure history, latency, and radiographic presentation), lung biopsy is rarely needed to provide a diagnosis of occupational ILD. Pathologic examination of lung tissue may at times be required in settings where clinical or radiographic features are inconclusive or atypical.

Recommended: Follow-Up Diagnostic Tests
Periodic medical follow up, including pulmonary function tests and imaging studies in the medical evaluation of pulmonary occupational disease.

B.6 Diagnostic Testing

B.6.a Spirometry

Spirometry is a useful initial test of lung function. Spirometry provides physiologic evidence for occupational ILD and differentiates between obstructive and restrictive lung patterns of lung function. Spirometry should be performed on all patients as a key component in the diagnosis and monitoring of occupational interstitial lung disease. However, ILD is not defined by spirometry. Abnormal spirometry results should lead to further testing including confirmation by lung volume testing according to ATS accepted recommendations or referral to a specialist.

Ideally, the modern diagnostic evaluation of pulmonary occupational disease should include measurements of lung volumes and diffusing capacity. As per clinical necessity, further analysis of gas exchange physiology, cardiopulmonary exercise testing and/or six-minute walk test should be used to supplement the diagnostic and therapeutic evaluations of occupational lung disease.

Technique – Diagnostic spirometry testing:

- Should be performed using recommended equipment and procedures by an appropriately trained technician.
- Should be performed in accordance with the most recent recommendations or requirements of American Thoracic Society, as well as Occupational Safety and Health Administration (OSHA), NIOSH, and Mine Safety and Health Administration (MSHA).
- When diagnostic spirometry is abnormal, testing should first be repeated on another occasion, if possible, to ensure that a worker was maximally inhaling, blasting out hard, and exhaling fully during the test.
- If results remain abnormal, short term reversibility of the spirometry results should be assessed, most often by repeating the spirometry testing after the individual has undergone a standardized short-acting bronchodilator inhalation protocol.
- Once a satisfactory test has been recorded for the worker, diagnostic interpretation may compare his/her largest results with normal ranges derived from appropriate similar populations.

Interpretation – There are several steps in the interpretation of spirometry testing performed as part of the evaluation of workers at risk of occupational ILD. First, the interpreter must review and comment on test quality and determine whether acceptability criteria are met. If the test is considered adequate for interpretation, then adjust for age, height, gender and race/ethnicity using appropriate reference tables for normal or predicted values.

For patients who have previously completed spirometry, changes in test results are evaluated over time.

Spirometry for Occupational Interstitial Lung Disease Diagnosis and Monitoring

B.6.a.i Spirometry

<u>Recommended</u> in the diagnostic work-up and monitoring of individuals with occupationally related interstitial lung diseases.

Indications – Diagnostic: Patients with history and/or chest radiography consistent with ILD and workplace exposure consistent with plausible etiologies (e.g., worker complaining of chronic or intermittent cough, shortness of breath, or decreased physical abilities). Spirometry should generally be postponed if there has been recent surgery, respiratory infections, or recent cardiac problems.

Indications – Monitoring/Surveillance: Periodic spirometry (yearly) with longitudinal evaluation of loss of pulmonary function is recommended for workers in occupations with exposures that are either known or thought to be associated

with development of occupational lung disease. Longitudinal evaluation is accomplished by tracking FEV1 loss over a period of time, since the FEV1 is the most repeatable lung function parameter. Such evaluation should be calculated when spirometry tests are of adequate technical quality. In general, a loss of FEV1 in excess of 50 ml/year is considered a loss of pulmonary function in excess of the aging effect. The American College of Occupational Medicine (ACOEM), the American Thoracic Society (ATS) and the National Institute of Occupational Safety and Health (NISOH) all have different proposed methodologies to calculate the loss of pulmonary function and determine if such loss is above the expected age-related loss of pulmonary function. Computerized software is available to calculate trends over time, such as NIOSH's Spirola.

Evidence for Use of Spirometry

B.6.b Static (Full) Lung Volumes

Measurement of static lung volumes, including Total Lung Capacity (TLC), Functional Residual Capacity (FRC) and Residual Volume (RV), is indicated to complement the information obtained on a spirometry test when further clarification of diagnosis is indicated.

The finding of a reduced FVC on spirometry could be due to several disease processes. In order to fully clarify a reduced FVC on spirometry, measurement of static lung volumes is required to confirm the diagnosis of a true restrictive disorder, i.e., a reduced TLC below lower limits of normal.

Static lung volumes can be used in obstructive diseases as well to assess the existence of air trapping, for example in emphysema or asthma. In these conditions, the TLC is increased as is the RV/TLC ratio.

Measurement of static lung volumes can be accomplished by inert gas dilution or body plethysmography.

Recommended – in the assessment of Occupational ILD to clarify a reduced FVC on spirometry, especially when the FEV1/FVC ratio is normal.

Indications – Static lung volumes are recommended in the assessment of Occupational ILD to clarify a reduced FVC on spirometry, especially when the FEV1/FVC ratio is normal.

B.6.c Measurement of Oxygenation

Measurement of oxygenation can be accomplished by non-invasive oximetry or by arterial blood gas sampling.

Non-invasive oximetry measures oxyhemoglobin or oxygen saturation of the hemoglobin. It is a simple method commonly used in the outpatient setting.
Arterial blood gas is helpful in accurately measuring the partial pressure and saturation of oxygen and allows the calculation of alveolar-arterial oxygen gradient.

Recommended – Non-invasive oximetry measurements of oxygenation (pulse oximetry) in the evaluation and management of Occupational ILD.

Recommended- Arterial blood gas measurements in select patients where accurately measuring the partial pressure and saturation of oxygen and calculation of alveolar-arterial oxygen gradient is indicated.

Indications – Measurements of oxygenation are recommended in the assessment of Occupational ILD.

B.6.d Chest Radiographs

Evaluation of pulmonary occupational disease should include imaging studies. At minimum, a chest radiograph PA and Lateral should be part of the diagnostic work-up. It is preferable that chest radiographs should be interpreted according to the International Labor Organization Classification for Pneumoconiosis.

Radiographs provide structural anatomic information about the lung parenchyma and pleura that informs the differential diagnosis of occupational ILD and also provides information about the extent of involvement and progression of disease. However, although radiographs may assist in the diagnosis of occupational lung diseases, they are less sensitive and specific than CT/ HRCT.

Radiographs should be interpreted by a physician with ***appropriate training, experience, and skills*** in interpretation of radiographs for diagnosis of ILD and occupational lung disease. To document the patterns and severity of radiographic appearances of pneumoconiosis, radiographs are preferably interpreted according to the International Labour Organization (ILO) classification[80] by readers who have "B" reader certification for this classification system or individuals with appropriate training and skills. The Board recognizes that other standard-setting organizations require “B” reader qualifications for interpretation of radiographs in certain situations.

Evidence for Use of Chest Radiographs

B.6.d.i Posterior-Anterior (PA) and Lateral Chest Radiographs

Recommended for the diagnosis of occupational interstitial lung disease.

Performed –Physicians who interpret chest radiographs for diagnosis of occupational lung disease should have appropriate training, experience, and skills and have "B" reader certification for the ILO classification system or individuals with appropriate training and skills.

B.6.e High Resolution Computed Tomography (HRCT) Scans /Computed Tomography (CT)

HRCT/CT should be considered in the evaluation of occupational ILD, when additional diagnostics are required based on clinical findings (including spirometry and chest X-Ray). Readers of HRCT/CT scans for occupational lung disease should have appropriate training and experience. It is recommended that a specialized thoracic radiologist review the chest CT scan.

B.6.e.i HRCT/CT

Recommended - in the evaluation of occupational ILD to confirm or exclude the diagnosis of ILD

Indications/Technique: HRCT/CT may be helpful in confirming or excluding a diagnosis of occupational ILD.

- When indicated HRCT/CT of the chest should include lung, mediastinal and high-resolution windows.
- HRCT/CT is generally performed in the supine position, but prone imaging may be of use in certain circumstances, for example, confirmation that subtle peripheral and/or basilar findings represent interstitial abnormality.
- Inspiratory/expiratory imaging is particularly useful when considering air trapping with associated with HP.

Recommended - in the diagnostic work up of pneumoconiosis and other pulmonary occupational diseases especially in those lung diseases that result in increased risk for lung cancer, as this imaging study not only has diagnostic value but can be used as a screening test for early detection of lung cancer

Evidence for the Use of HRCT

B.6.f Magnetic Resonance Imaging (MRI) of the Chest

Not Recommended - as a primary diagnostic tool for occupational ILD.

B.6.g PET/CT Scans of the Chest

Recommended - in select cases in the evaluation of cancer associated with ILD (lung cancer and mesothelioma) and certain other comorbid conditions.

B.6.h Carbon Monoxide Diffusing Capacity (DL_{co})

DL_{co} (Diffusing capacity of the lungs) is a test that measures the movement of gas from the lungs (alveoli/ air spaces) to blood flowing in the pulmonary capillaries. DL_{co} is typically used to describe the single breath diffusing capacity test which measures this diffusion. In this test the patient inhales a known amount of CO and the difference between what is inhaled and the CO measured in the exhaled gas is measured as the diffusing capacity (for a gas) of the lungs into blood. The test indirectly assesses the ability of the lungs to transfer oxygen to blood through the use of a calibrated test gas, CO.

Using appropriate methods for the test and adjustments for the results the test can be used to assess lung function and the presence of several lung diseases including ILD. The test should be performed according to the ATS/ERS statement published in 2017. This statement includes the methods and adjustments that must be made to obtain a valid test. https://protect2.fireeye.com/url?k=a4914a5d-f8b5bc3c-a493b368-0cc47a6d17e02ee7efddf3f04a65&u=https://www.thoracic.org/statements/resources/pft/DLCO.pdf

Further:

- At least two DL_{co} tests should be performed and the average reported.
- The two measurements for the DL_{co} should agree within 10%.
- It is important to obtain smoking status as cigarette smoking may cause measurable baseline levels of CO causing an increased back-pressure and carboxyhemoglobin.
- It is important to have available the patient's hemoglobin, as anemia will lower the measured diffusion. Equations for correction of anemia are available.

B.6.h.i Carbon Monoxide Diffusing Capacity (DL_{co})

Recommended - for use in diagnosing occupational lung disease.

Indications – DL_{CO} may be used to help in diagnosing gas exchange abnormalities in patients with lung disease.

Advantages and Limitations – DL_{CO} may be affected by different diseases and exposures (Table 3). These **must** be considered when interpreting the test results.

Evidence for the Use of DL_{co}

Table 3. Diseases /Conditions Associated with Alterations in DLCO

Diseases/Conditions that Decrease DL_{CO}
• Reduced effort or respiratory muscle weakness • Thoracic deformity preventing full inflation • Anemia • Pulmonary emboli • Hb binding changes (e.g., HbCO, increased Fl, O_2) • Valsalva maneuver • Lung resection • Emphysema • Interstitial lung disease (e.g., IPF, sarcoidosis) • Chronic beryllium disease (CBD) • Pulmonary edema • Pulmonary vasculitis • Pulmonary hypertension

Adapted from MacIntyre N, Crapo R, Viegi G. Stadardization of the single-breath determination of carbon monoxide uptake in the lung. *Eur Respir J*. 2005;26:720-35. Additional source: Pappas GP, Newman LS. Early pulmonary physiologic abnormalities in beryllium disease. *Am Rev Respir Dis*. 1993;148:661-6.

B.6.i Biological Sampling

B.6.i.i Invasive Procedures

Including, but not limited to, bronchoscopy, bronchoalveolar lavage analysis and lung biopsy **<u>are not routinely required</u>** to diagnose occupational lung disease, but should be included as part of the diagnostic armamentarium when clinically indicated and/or necessary to confirm or exclude a specific diagnosis. Often specific CT findings are considered diagnostic in certain conditions.

B.6.i.ii Sputum Samples and Bronchoalveolar Lavage (BAL)

If there is insufficient objective clinical evidence obtained from physical examination, chest radiographs and spirometry, additional testing including biological sampling may be indicated to confirm the diagnosis of occupational ILD.

B.6.i.ii.a Sputum Sample (both induced and spontaneous)

<u>Recommended</u> - in select patients as an aid for the diagnosis of occupational lung disease.

Indication/Technique - If insufficient clinical objective evidence is obtained from physical examination, chest radiographs and spirometry, additional testing including sputum sampling may be indicated to confirm the diagnosis of

occupational ILD. Sputum sampling may support the diagnosis of occupation lung disease but is not required given the availability of modern testing (i.e. HRCT). Sampling is done by having the patient cough to attempt to produce the sputum from deep within the lungs. It is recommended that each sample be at least 15mL to help increase the sensitivity of the sample.

B.6.i.ii.b Bronchoalveolar Lavage

Recommended - in select patients as an aid for the diagnosis of occupational lung disease.

Indications/Technique – To assist in the diagnosis of occupationally-related interstitial lung disease. BAL may support the diagnosis but is not required given the availability of modern testing (i.e. HRCT).

BAL should be performed according to the ATS guidelines on performance of BAL for ILD.

B.6.i.iii Bronchoscopy and/or Lung Biopsy

Recommended - in very select patients to confirm or exclude diagnosis in specific cases

Evidence for the Use of Bronchial Alveolar Lavage (BAL) and Sputum

B.7 Management of Occupational Interstitial Lung Disease

Management of workers diagnosed with occupational ILD is aimed at preventing further loss of lung function by decreasing inflammation and preventing the progression of lung scarring.

- Avoid additional provocative exposure to protect from disease progression.
  - Exposure assessment for workers diagnosed with occupational ILD to determine whether a worker might return to a specific job/exposure including use of PPE.
  - Avoid source of the problem.
  - Stop smoking and avoid passive smoke exposure.
  - Avoid airway irritants such fragrances, solvents and dust.

- Pharmacological treatment.
  - Follow established guidelines for treatment of ILD.
  - Bronchodilators, inhaled corticosteroids, cytotoxic drugs or immunotherapy.

- Monitor Progress
  - Periodic medical follow-up, including PFTs and imaging studies for pulmonary ILD
  - Six-minute walk test as a means to monitor response to treatment or progression of disease

- Minimize and manage potential complications of ILD
  - Immunization against pneumococcal pneumonia and influenza
  - Monitor for acute flare-up
  - Aggressive management of respiratory infections with a low threshold for hospitalization
  - Specific management of co-morbidities (including potential opportunistic infections, cancer)
  - Supportive (supplemental) oxygenation if desaturation is documented during exertion or sleep
  - Management of cardiac complications (e.g. pulmonary hypertension, right-sided heart failure, CHF).

- Screen for lung cancer

- Pulmonary Rehabilitation to improve functional capacity
  - Alternate efficient breathing methods
  - Evaluate and maximize home environment to save exertional energy
  - Maintain caloric intake

B.7.a Lung Transplantation

Recommended - In advanced or rapidly progressive cases, evaluation for lung transplantation should be performed.

B.7.b Pharmacological Treatment

Recommended – the goal of pharmacologic treatment for occupational ILD primarily addresses symptoms and limitations, it cannot reduce fibrosis. Recommendations for the pharmacological treatment of ILD should follow those of ATS or similarly recognized guideline issuing organizations.

Workers with clinical findings consistent with a given type of occupational ILD should be referred to a physician with training and experience in medical management of that condition.

B.7.c Exposure Assessment

Recommended - that an exposure assessment be completed for workers diagnosed with occupational interstitial lung disease.

Exposure Assessment for Workers with Occupational ILD - Exposure data from industrial hygiene surveys and Safety Data Sheets (formerly

known as Material Safety Data Sheets) and other sources such as area or personal monitoring data should be reviewed and considered for each worker diagnosed with occupational ILD.

Rationale for Recommendations - Exposure assessment data are necessary to determine past and present exposures to specific agents, to ascertain the degree of respiratory hazards that exist, and to identify appropriate personal protective equipment to reduce exposure.

The ability of a worker to use appropriate personal protective equipment to protect from further exposure is dependent upon pulmonary function and the physical demands of the job. Generally speaking, workers with severe to very severe respiratory impairment may not have sufficient inspiratory capacity to work while wearing respirators that increase the work of breathing (such as half-or full-face filtering respirators), and likewise may not be able to perform the functions of an occupation requiring moderate physical activity.

B.7.d 6-Minute Walk Test (6MWT)

The 6-minute walk test is a prognostic tool used for monitoring individuals to assess performance/functional ability over time. The test measures the distance a patient can walk on a flat, hard surface in a period of 6 minutes.

Recommended - in individuals with interstitial lung disease as a means to monitor response to treatment or progression of the disease.

Indication/Technique – To measure the response to medical interventions in patients with moderate to severe lung disease. It may also be used as a measure of functional status of patients as well as a predictor of morbidity and mortality.

Absolute contraindications for the 6MWT include:

1. History of unstable angina.
2. Heart attack within the previous month.

Relative contraindications for the 6MWT include:

1. Resting tachycardia (>120 beats/minute).
2. Uncontrolled hypertension.

Reasons for immediately stopping the test are chest pain, intolerable dyspnea, leg cramps, staggering, excessive diaphoresis, and pale or ashen appearance.

Evidence for the Use of the 6-Minute Walk Test

Appendix 1: The ILO Classification

The ILO Classification depends on 22 standard reference radiographs that are used to formally identify and characterize pneumoconiosis and related pulmonary abnormalities arising from occupational exposure. These reference radiographs demonstrate a variety of types and severities of lung abnormalities that frequently arise from occupational dust exposure. Proper use of the classification involves a visual comparison of the test subject's x-ray film side-by-side with the standards. The test subject is assigned the classification pertaining to the standard radiograph or radiographs to which it is most similar in appearance. Ie. Category 0/0, 1/1, 2/2 or 3/3; and the types p/p, q/q, r/r, s/s, t/t or u/u where applicable. The person undertaking the classification, typically a physician formally trained in the use of the ILO Classification, completes a data entry sheet where they record their classifications of each of the various abnormalities. In addition, ancillary information on the quality of the radiograph and the presence of other medical findings is noted. The ILO classification system has been shown to be related to the amount and composition of dust retained in the lung.

Appendix 2: Evidence Tables

Evidence for the Use of Spirometry

Townsend, MC. J Occup Environ Med, 2005; 47: 1307-16 https://www.cdc.gov/niosh/topics/spirometry/spirola-software.html

Author/ Year	Score (0-11)	N	Test Used	Comparison Test	Population	Length of Follow-up	Outcome measures	Results	Conclusion	Comments
Occupational Interstitial Lung Disease										
Miller 1994	7.0	2611	Spirometry	Chest radiography History	Insulators working pre 1970s with asbestos exposure	None	Radiography Smoking status FEV_1, FVC, FEV_1/FVC	Non-smokers with asbestos exposure: 172/515 (33%) had abnormal FVC. 31/515 (6%) had reduced FEV_1/FVC. Smokers: 971/2096 (46%) had abnormal FVC, 518/2096 (25%) with reduced FEV_1/FVC.	"That reduced FVC and reduced FEV_1/FVC are both more frequent in insulators who have smoked (compared with NS insulators or smokers in the general population) suggests an interaction between asbestos and smoking in producing both these physiologic abnormalities."	Eighty-seven percent of participants had 30+ years exposure to insulation. Diagnosis of asbestosis made with chest radiography only. No baseline data on other exposures or disease. Data suggest spirometry is sensitive to radiographic findings in workers exposed to asbestos. Sensitivity increased in workers with smoking history.
Wang 1999	7.0	130	Spirometry	Chest radiography DL_{CO}	Male Chinese refractory plant workers	None	Radiography FEV_1 FEV_1/FVC ratio	Radiographic hyperinflation was related to silicosis diagnosis. Relationship between radiographic hyperinflation was stronger than silicosis when looking at decreased spirometry values ($p < 0.05$).	"[T]he findings indicate that emphysema associated with silicosis is likely to be responsible for the pulmonary obstruction and decreased diffusing capacity."	Authors had access to environmental readings on dust exposure. "Controls" younger and still working while majority of "cases" were retired. Evaluated smoking in regression analysis. Data suggest silicosis causes decrease in FVC, FEV_1, FEV_1/FVC that correlates with chest radiograph findings. Emphysema common in silicosis patients.

Kilburn 1994	6.5	2,662	Spirometry TLC	Chest radiography	1,146 men with asbestosis and 1,146 age-matched exposed to asbestos without a diagnosis of asbestosis, 320 unexposed controls	None	Chest radiography Spirometry values Smoking status Symptoms	Never smoked: Controls compared to exposed group had no significant change in FVC, FEV_1, FEF25-75. Controls compared to asbestosis group had significant difference in all parameters ($p < 0.004$).	"Asbestos exposure reduced flows and produced air trapping after 20 years in workers who never smoked. Smoking increases these abnormalities."	Case-control study design. Occupational exposure measured by interview. Used smoking as stratification. Data suggest spirometry values may be used in diagnosing and screening for asbestosis in conjunction with chest radiography.
Barnhart 1988	6.5	40	TLC Spirometry	Chest radiography DL_{CO} P(A-a)O2	Cases referred to occupational medicine because of concern with asbestosis	None	Chest radiography TLC FEV_1 FVC DL_{CO} P(A-a)O2	Group 1 (interstitial fibrosis and COPD) had no case of restriction on TLC. There was decreased FEV_1 ($p<0.001$) compared to Group 2 which had only interstitial fibrosis on chest radiography.	"[I]n patients with asbestos exposure, radiographic fibrosis, and COPD, the TLC is an insensitive test for indicating functional effect of asbestos-induced fibrosis. In the setting of airflow obstruction, caution should be used in excluding adverse respiratory effect due to asbestos exposure through the use of TLC."	Much of data collected by retrospective chart review. Two readers read chest radiographs. Asbestos exposure done by patient interview. Data suggest TLC is an insensitive measure of lung restriction due to asbestos exposure in patients who also have COPD. Multiple measures should be taken into consideration in diagnosis of asbestosis.
Leung 2005	6.5	1,576	Spirometry	Chest radiography	Cases referred to the statutory Pneumoconiosis Medical Board for assessment	None	FVC FEV_1/FVC (FER)	55.6% had normal spirometry; 7.6% had reduced FVC with normal FER; 8.4% had reduced FVC and FER. On regression analysis: age, smoking, history of TB, size of lung nodules and PMF were independent predictors of airflow obstruction.	"In an occupational compensation setting, disease indices and history of tuberculosis are independent predictors of both airflow obstruction and reduced capacity for silicotic patients."	Patients diagnosed with silicosis if they had nodules scored as >1/0 in ILO classification system. A record review study. Data suggest patients with radiographic evidence of silicosis may have decreased lung function, but that more than half have normal values on spirometry.
Rosenman 2010	6.0	526	Spirometry	Chest radiography	"Confirmed" silicosis patients either by chest	None	Radiography FVC, FEV_1, FEV_1/FVC ratio	Obstruction on spirometry:	"Both obstructive and restrictive patterns were observed regardless of	Obtained chest radiography and spirometry values by medical record review.

					radiography or biopsy or both			17.3% of non-smokers (NS) 26.5% of smokers (S) Restriction: 30.1% NS, 28.1% S Mixed: 22.4% NS, 25.7% S	smoking status with a low profusion category of simple silicosis."	Smoking status obtained by interview of worker or next of kin or medical record review. Data suggest both restrictive and obstructive results may occur in workers with silicosis on spirometry. Less than half of workers diagnosed with silicosis had abnormal spirometry.
Brodkin 1993 Cohort validation study of respiratory questionnaire	6.0	812	Spirometry	1) Chest radiography 2) Respiratory symptoms questionnaire (ATS-DLD-78A)	Men enrolled in Beta-Carotene and Retinol Efficacy Trial (RCT) with history of asbestos exposure for prevention of lung cancer	None	Radiography FVC FEV_1 FEV_1/FVC Self-report symptoms	OR for restrictive ventilator impairment: Cough 0.91 (p = NS), phlegm 0.83 (p = NS), wheezing 2.18 (p <0.01), [smoking ever/never] 0.85 (p = NS), parenchymal small opacities 1.41 (p <0.001), pleural thickening 1.06 (p = NS).	"These results support the validity of the ATS questionnaire as an epidemiological tool and emphasize the importance of clinical history in assessing respiratory status."	Data suggest report of wheezing, dyspnea have strongest association with ventilatory defects. Reported a significant correlation of radiographic findings with ventilatory defects.
Kilburn 1985	6.0	257	Spirometry	Chest radiography DL_{CO} Symptoms	Male shipyard workers	None	Radiography FVC, FEV_1, FeF_{25-27}, FEF_{75-85} DL_{CO} Symptoms	14/43 (33%) nonsmokers had 1/1 radiographs with normal spirometry values. Current and ex-smokers had a downward trend in same values.	"These shipyard workers had minimal to moderate asbestosis with much pleural disease and little functional impairment when compared to a smoking-specific reference population."	Used PA and lateral chest radiographs with 3 different B readers to diagnosis asbestosis in shipyard workers. Included smoking as a variable. Data suggest earlier asbestosis does not cause a significant drop in FEV_1, FVC in older shipyard workers.
Non-Occupational Interstitial Lung Disease										
Aaron 1999	5.5	1,831	Spirometry	Helium dilution Plethysmograph	Uncertain	None	TLC VC FEV_1 FVC FEV_1/FVC	Sensitivity: 193/225 (86%); Specificity: 1,329/1606 (83%); PPV: 193/470 (41%); NPV: 1,329/1,361 (97.6%)	"[T]he accuracy with which spirometric measurement of FVC and expiratory flow rates can diagnose the presence of a restrictive impairment. Patients whose FVC fall above the 95% CI of	Uncertain what type of patients included in study. Does not appear to have any occupationally-related cases. Data suggest spirometry is useful in ruling out a restrictive lung disease diagnosis.

									the predicted value are very unlikely to have a restrictive impairment, and in these patients… measurement of lung volumes can be avoided."	
Boros 2004	4.0	1,173	Spirometry	Whole body plethysmo-graphy	Mean age 44.3 – with HP (74), sarcoidosis (568), pulmonary fibrosis (194), connective tissue disease (51), and pneumoconiosis (23)	None	TLC VC	882/1,173 (75.2%) both indices were above (LLN), 267/1,173 (22.8%) TLC was markedly reduced, 209/1,173 (17.8%) VC reduced ($p < 0.01$), 185/1,173 (15.8%) had both indices reduced.	"Our results indicate that the spirometric measurement of VC is not enough for the detection of restriction, and may result in missing the diagnosis of diminished lung volume in almost 10% of patients. Thus in order to assess lung function reliably in ILD patients, the measurement of TLC seems to be essential."	How each patient was originally diagnosed not described. Small number of pneumoconiosis patients. No separation of results based on diagnosis. Making this study difficult to assess in terms of occupational lung disease. Data suggest that in generalized ILD patients both VC and TLC is useful.
Other										
Sircar 2007	4.5	1,730	Spirometry	None	Coal miners	12 years	FEV_1 Death	Odds ratios: Compared to below 30ml/year loss. 1.39 (0.99-1.97) 60ml/year to 90ml/year 1.90 (1.32-2.76) more than 90ml/year loss of FEV_1.	"Risk of death increases in individuals with rates of decline above about 60ml/year and is statistically significant with declines of 90ml or more. These results should be useful to healthcare providers in assessing lung function declines observed in individuals."	A retrospective review of cross-sectional studies. Cause of death determined by death certificates. Data suggest serial FEV_1 in coal miners with lung disease may aid in the management of the disease. If there is a loss of over 90ml/year then the risk of death increases.

Evidence for Use of Chest Radiographs

Author/ Year	Score (0-11)	N	Test Used	Comparison Test	Population	Length of Follow-up	Outcome Measures	Results	Conclusion	Comments
Sun 2008	9.5	90	Chest x-ray	HRCT	Mine-machine manufacturing workers in China involved in sand casting	None	Radiography classifications	Of 30 employees without silicosis on x-ray, 8 (26%) had evidence of silicosis on HRCT.	"HRCT is not currently accepted as a diagnostic tool for the detection of pneumoconiosis…HRCT scans should be considered for the better and earlier diagnosis of pneumoconiosis."	Both x-ray and HRCT scan readers blinded to diagnosis status. All patients male. No background information given such as smoking status or other exposures. Data suggest HRCT will detect evidence of silicosis earlier than x-ray.
Paris 2004	9.5	706	PA chest x-ray	High resolution CT, basilar crackles, age, cumulative exposure index to asbestos fibers, Total Lung Capacity	Retired asymptomatic workers with documented asbestos exposures. Average age 65.2, 89% male.	None	ILO classification Plethysmography CEI Clinical examination	Compared to HRCT scan as gold standard: Small irregular opacities in x-ray: Sn: 46% Sp: 80%. Pleural abnormalities: Sn: 66% Sp: 47%. Basilar crackles: Sn: 46% Sp: 76%. Low TLC: Sn: 27% Sp: 85% CEI: Sn: 95% Sp: 18%	"Our findings confirm that HRCT can detect early-stage asbestosis in people who have been highly exposed to asbestos whose X-ray can be considered normal… Moreover, HRCT screening does not seem warranted for people with low occupational exposure (CEI <25 fibers/ml x years)…"	All participants had no known asbestos related disease. X-rays and HRCT scans read by 3 independent readers blinded to patient status. Data suggest a combination of clinical exam, exposure history and testing increases both sensitivity and specificity in diagnosing asbestosis.
Vallyathan 1996	8.0	430	PA X-ray	Autopsy results	Coal miners in West Virginia exposed to medium to high rank bituminous coal	None	Pathology X-ray readings	298/430 (69%) of films were classified as >0/1 (41%) classified as 2/1 or greater.	"Overall the study showed good agreement between the predicted probabilities and observed responses of a profusion category >/= 0/1 for pathologic CWP lesions. However, the study also showed that CXR were insensitive for detecting minimal CWP lesions, and were unreliable indicators in	X-rays were PA and read by 3 different readers. Average age of death 68, but no data on cause of death. Data suggest that PA x-rays may assist in diagnosis of CWP but will often miss smaller lesions less than 3-5mm in diameter.

									the presence of concomitant pulmonary pathology."	
Wain 1984	8.0	50	PA X-rays only	Autopsy results	Patients with plaques on autopsy from a Veterans hospital. Controls.	None	X-ray findings Autopsy results	Prevalence of pleural plaques on autopsy 5.8%. 7/25 (28%) of autopsy-confirmed cases had evidence of plaques on x-ray. None of controls had evidence of plaques on x-ray.	"It is clear that an accurate occupational history is essential for the recognition of relationships between asbestos and pleural plaques, carcinoma, and asbestos body counts."	Occupational/exposure history obtained through chart review. X-rays PA only. All male veterans. Data suggest PA x-rays have high specificity but low sensitivity for detection of pleural plaques in patients exposed to asbestos.
Kipen 1987	7.0	138	PA X-ray	Autopsy results	Asbestos insulation workers who died from lung cancer	None	X-ray findings Autopsy pathology	All 138 cases had histologic evidence of parenchymal fibrosis. 10/138 (10%) negative for any fibrosis on x-ray.	"Discrepancies in the results of radiological and pathological examination for interstitial fibrosis were present in 18% of those heavily exposed insulators… These findings indicate the primacy of the history of asbestos exposure, irrespective of the presence of absence of non-malignant x-ray changes (asbestosis)…"	Consensus of 3 x-ray readers taken. No mention of blinding done. Data suggest that a negative x-ray does not rule out moderate to severe interstitial fibrosis in workers exposed to asbestos.
Ruckley 1984	7.0	261	X-ray	Lung tissue	Male coal miners	Years	ILO classification Emphysema Death	45% of men with no opacity on x-ray had simple pneumoconiosis. In x-rays with p type opacities 89% had simple pneumoconiosis. In x-rays with q or r irregularities 61% had simple pneumoconiosis. Intra-observer variation was small, inter-observer variation evident. Lungs with no x-ray opacities had fewer foci that were small and rarely palpable.	"This study has shown that the composition of dust retained in the lung, as well as its amount, makes an important contribution to the radiographic appearances of pneumoconiosis."	Study used lung tissue to confirm dust burden and emphysema diagnosis. No good baseline data on participants such as smoking status/years exposed. Data suggest certain level of dust burden must be met before x-ray opacities are seen. Certain types of opacities signify different types of dust exposure in coal miners; 45% of lungs with simple pneumoconiosis had normal chest x-ray.

Rossiter 1972	7.0	98	X-ray	Lung tissue	Coal miners in England	Years	ILO classification of x-rays Lung dust Dust particle make up	Correlation between pneumoconiosis score and lung dust content was r = 0.90. Iron and other mineral contents of coal is important in disease status.	"For the main, homogenous group of 98 miners, the correlation between the simple pneumoconiosis score and the coal and other mineral contents was 0.9."	Used one of the lungs to determine dust burden. Data suggest the higher the amount of dust in lungs the more opacities seen on chest x-ray.
Fernie 1987	7.0	71	X-ray	Lung biopsy	Coal miners	None	X-ray ILO classification Lung dissection results	Lungs classified as category O may contain several pinhead fibrotic lesions up to >3mm in diameter. Subjects with predominately p opacities contained more macules and pinhead fibrotic nodules than those of subjects presenting q or r opacities.	"[T]he results of this study and others make increasingly clear the complexity of the relation between what is seen on a chest radiograph and what is present in the lungs of coalworkers, and emphasize the fundamental importance of the character of the dust lesions and the composition of the dust itself."	This study same sample of patients as Ruckley 1984. One sagittal slice of lung tissue of each lung examined pathologically for nodules and fibrosis. No history given for total occupational exposure or smoking status. Data suggest that x-rays may assist in the diagnosis of CWP, but that normal x-rays do not rule out lung nodules.
Lopes 2008	6.5	53	X-ray	HRCT Spirometry Helium Dilution DL_{CO}	Workers exposed to silica - mainly sandblasters and stone cutters	None	X-ray CT scans Spirometry Helium dilution DL_{CO}	Small opacities: concordance between radiographs and CT scans was 56.8%. For large opacities, concordance was 70.5%.	"In the early detection of silicosis and the identification of progressive massive fibrosis, HRCT scans are superior to x-rays."	Nonsmoking male workers with diagnosis of silicosis. Minimal baseline characteristics given. Data suggest HRCT finds more abnormalities compared to PA chest x-ray in workers with silicosis.
Bourgkard 1998	6.5	240	X-ray	Symptom questionnaire. Chest CT scans. Dust exposures. Spirometry	Coal workers 1. Exposed with x-ray findings at baseline 2. Exposed without x-ray findings 3. Less exposed without x-ray findings	4 years	X-rays CT scans Spirometry Symptoms	Exposed group with x-ray findings: 24/78 (31%) had worsened x-rays at 4 years, 10/78 (13%) had developed CWP. Exposed group with normal x-rays: 6/78 (8%) had worsened x-rays. Less exposed group with normal x-rays: 1/78 had worsened x-rays.	"[W]orsening x-ray findings and pneumoconiosis were more often observed in coal miners with micronodules on lung CT scans, wheezing, low values of MMEF and FEF25%, and high dust exposure at the first examination."	Included 2 control groups, one with similar exposure with normal x-rays and another with limited exposure and normal x-rays. Data suggest young coal workers with findings on x-rays may continue to develop CWP. Suggests that workers with ILO classification findings of 0/1 or 1/0 have vigorous interventions to lesson coal dust exposure. Also suggests CT scan may be useful in evaluation of workers with x-ray findings.

Musk 1981	6.0	87	X-ray	Spirometry Pulmonary function test with closed circuit helium dilution Plethysmo-graphy Exercise test Symptom Questionnaire	Coal miners	9 years	ILO classification	Men with r opacities had a reduction in lung compliance over men with q opacities.	"[T]he different radiographic abnormalities of simple pneumoconiosis reflex underlying structural differences which, at the extremes, range from very small to largish nodules of accumulated dust and from diffuse focal emphysema to diffuse fibrosis."	Full occupational history and smoking history was included. Data suggest chest radiographs with opacities may indicate pulmonary fibrosis.
Brodkin 1993	6.0	816	X-ray	Spirometry Symptoms-Questionnaire in asbestos workers	Various workers exposed to asbestos	None	FVC FEV_1 Pre and post bronchodilator response x-ray ILO classification Symptoms	324/816 (40%) had unremarkable chest x-ray. 219/816 (27%) had pleural abnormalities 100/816 (12%) had parenchymal abnormalities 169/816 had both Parenchymal small opacities on x-ray increased odds of restrictive ventilator pattern by OR 1.41 (1.32-1.52) (p <0.001). No significant findings on x-ray and obstructive ventilator pattern	"[R]espiratory symptoms of cough, sputum, wheeze, and dyspnea are associated with a significantly lower ventilator capacity in asbestos-exposed populations. Wheeze and dyspnea appear to be especially significant predictors of ventilator impairment, independent of smoking…These findings also underscore the continued importance of utilizing clinical history to assess respiratory status."	Participants part of CARET study. Used PA x-rays, 2 readers looking at x-rays. 17% of participants were smokers. Data suggest questionnaires are helpful in determining respiratory illness in asbestos workers. X-ray findings were correlated with restrictive findings on spirometry, but there was no correlation between x-ray findings and obstructive findings on spirometry.
Larson 2012	5.0	6475	PA Chest x-ray	Spirometry Some had HRCT scans (363/6476)	Citizens of Libby, MT who were participating in a community screening program	None	FVC FEV_1 X-ray ILO category	Participants with HRCT scan 3% had parenchymal abnormalities not seen on x-rays. 77% (5003/6476) had normal spirometry. No trends between prevalence of abnormal spirometry with surrogate of amphibole exposure.	"[I]n this cohort of community screening participants, LPT is statistically associated with restrictive spirometry."	Chest x-rays evaluated by 2 or 3 B-readers. Study's main focus to evaluate if localized pleural thickening (LPT) associated with abnormal spirometry. Data suggest LPT is associated with mainly restrictive spirometry in a community based study in asbestosis exposure.

Collins 1988	5.0	895	X-ray	Symptom questionnaire, Work history and smoking questionnaires	Coal miners	None	X-ray ILO classification Symptoms Spirometry	Men with small opacities who were smokers 2 or 3 times more likely to report breathlessness, cough and sputum. Dust exposure increased changes of reporting same symptoms. Both age and dust exposure related inversely to lung function.	"[T]he presence and profusion of small irregular opacities should be taken into consideration when assessing the severity of coal workers' simple pneumoconiosis."	Included detailed occupational exposure history, including dust samples. They also included smoking. Data suggest the small irregular opacities seen on x-ray also correlate with decreased lung function in coal workers.
Cockcroft 1983	5.0	124	X-ray	Physical exam	Coal miners	Years	Smoking Age Underground exposure	Increasing age associated with increasing irregularity of small opacities (p <0.001). Smoking associated with increasing irregularity of small opacities (p <0.01).	"Our findings suggest that irregular opacities are related to underground exposure and should probably be considered to be part of simple coal workers' pneumoconiosis."	Included detailed occupational exposure history, and smoking status. Data suggest the irregular opacities may signify CWP with or without small regular opacities irrespective of age and smoking status.
Hurley 1982	4.5	2,600	X-ray	Symptoms, dust exposure	Coal miners	10 years	Classification Dust exposure	Men who worked longer hours in coalmining had higher prevalence of coal worker pneumoconiosis. Little evidence that exposures to quartz dust influenced the chances of developing CWP.	"The radiological signs…can therefore be regarded as an indirect measure of increased risks of reduced breathing capacity, disability, and excess mortality."	Included detailed occupational exposure history, including dust samples. Data suggest that overall coal dust exposure burden results in greater findings on x-ray, but higher exposure to quartz in this cohort did not seem to have an effect on development of CWP classified by x-ray.
Amandus 1976	4.0	6,166	X-ray	Spirometry Symptoms	Coal miners	None	X-ray findings Symptoms Spirometry	Smoking, age, and years underground contributed significantly to prevalence of irregular lesions.	"This study shows that there is a statistical association between cigarette smoking and the presence of irregular opacities. The results also suggest that other factors such as bronchitis, age, and exposure to coal dust are involved in the development of these lesions."	Included smoking status. No other confirmatory test other than symptoms and some spirometry values. Data suggest that smoking, age, and years underground are associated with irregular opacities in underground coal miners.

Evidence for the Use of HRCT

Author/ Year	Score (0-11)	N	Test Used	Comparison Test	Population	Length of Follow-up	Outcome Measures	Results	Conclusion	Comments
Collins 1993	10.0	21	High resolution CT scan	Chest radiography Spirometry Arterial blood gases Physical history	Coal miners	None	Radiography Spirometry	Of 9 patients who had negative chest radiography, 4 had evidence of nodules on HRCT scan consistent with CWP. Only miners with a history of smoking had airflow limitations.	"For detecting evidence of coal dust accumulation in lung parenchyma and identifying focal emphysema, HRCT was more sensitive than standard chest radiography. However, despite earlier detection of parenchymal abnormalities, abnormal pulmonary function attributable to coal dust could not be identified."	Small sample size. Each radiograph PA and read by 2 blinded B readers. Each HRCT scan read by 2 blinded radiologists. Excluded miners with evidence of airflow obstruction on spirometry. Data suggest HRCT scans are more sensitive than chest radiography in detecting nodules in miners. This earlier detection does not correlate well to functional limitations.
Newman 1994	9.5	40	High resolution CT scan	Chest radiography Lung biopsy	Various workers exposed to beryllium and either positive of BeLT surveillance testing or had symptoms and chest radiography consistent with beryllium disease	None	Radiography Biopsy	15/28 (54%) of biopsy confirmed cases had abnormal chest radiographs. 25/28 (89%) of biopsy confirmed cases had abnormal HRCT scans 10/13 (77%) of the normal chest radiographs and abnormal HRCT scans.	"Thin-section CT was more sensitive than chest radiography in detection of beryllium disease, but the diagnosis was missed in up to 25% of cases with histologic proof."	All cases had biopsy confirmed beryllium disease and positive BeLT immunological testing. Two groups: 1) workers without symptoms but had positive BeLT immunological testing on surveillance; and 2) workers with symptoms and positive chest radiographs. Data suggest HRCT is more sensitive in detecting lung pathology in beryllium disease, but it still missed up to 25% of cases.
Gamsu 1995	9.5	30	High resolution CT scan	Biopsy Chest radiograph (in 25/30)	Workers exposed to asbestos in shipyards or construction; 6 lungs came from autopsy	None	Radiography Biopsy	Pathology normal in 5/30 (15%) of cases. HRCT negative in 14/30 (48%) and positive in 16/30 (52%). When two findings were needed to diagnose the Specificity went from 60% to 100%, Sensitivity went from 88% to 78%.	"[H]igh-resolution CT detection of asbestosis, a combination of the cumulative number of different findings and an assessment of the extent and severity of the abnormalities could be complimentary. We also conclude that asbestosis can be present histopathologically with normal or near normal high-resolution CT scan.	The 6 lung samples did not have pleura present and little to no clinical data available. Baseline data sparse. CT Scans and pathologists blinded. Data suggest HRCT scans are both sensitive and specific in the diagnosed of asbestosis.
Gevenois 1994	8.0	83	High resolution CT	Chest radiography CT	Patients involved in medicolegal evaluations	None	Radiography	2/9 (22%) of the patients with negative chest radiography had a positive CT scan.	"[T]hese data point out the limited value of CR, graded according to the ILO classification to evaluate low grade CWP in exposed workers, especially when the opacities described on CR are	Two different readers on both chest radiography and HRCT. No baseline data noted. Data suggest HRCT is more sensitive in detecting micronodules in silicosis than chest radiography.

									irregular. In this study, we confirmed that CCT and HRCT are more sensitive than CR to detect silicosis."	
Lynch 1995	8.0	63	High resolution CT scan	Open lung biopsy	Various	None	Radiography Pathology	HRCT was able to distinguish between HP and IPF in 90% of cases if they were definite, 60% if diagnosis was probable.	"[H]igh resolution CT features can be used to distinguish IPF from HP in most but not all cases. Desquamative interstitial pneumonia cannot reliably be distinguished from acute or subacute HP."	Retrospective review of CT scans and biopsy results. Two thoracic radiologists read CTs in blinded fashion. Baseline data lacking, no mention of pack-year smoking history. Data suggest HRCT scans are helpful in diagnosing HP but biopsy is still more accurate.
Ziora 2005	7.5	20	High resolution CT	FEV_1, FVC, DCO	Patients diagnosed with HP	None	FEV_1, FVC, DCO	All patients had a diminished DCO. 19/20 (95%) had FVC and FEV_1 <70% predicted and FEV_1/FVC >/= 75%.	"[W]e have found a relatively strong correlation between nodules and examined spirometric and diffusion parameters, which suggests that the presence of intraluminal granulation tissue in bronchioles and adjacent aveoli may impair the ventilatory and diffusion capacity in HP patients."	Small numbers. All had HRCT findings on exam. Data suggest a restrictive pattern on spirometry and diminished DCO are present in patients with HP.
Huuskonen 2001	7.5	651	High resolution CT	Chest radiography	Workers exposed to asbestos fibers	None	Radiography	85/602 (14%) had a diagnosis of asbestosis. Chest radiography with ILO Sn: 51%, Sp: 89%. HRCT Sn: 70%.	"The examined HRCT scoring method proved to be a simple, reliable, and reproducible method for classifying lung fibrosis and diagnosing asbestosis also in large populations with occupational disease, and it would be possible to use it as a part of an international classification."	Good baseline data given. Three different radiologists read the images. Data suggest HRCT is more sensitive in the diagnosis of asbestosis compared to chest radiography.
Eterovic 1993	7.0	35	High resolution CT scan	Chest radiography Biopsy PFTs with DL_{CO}	Workers in asbestos cement plant and controls	None	Radiography PFT results	HRCT had a higher probability score in advanced asbestosis patients then in early asbestosis. (p=0.013) Chest radiography had more advance ILO scores as asbestosis disease advanced.	"[A]lthough HRCT is evidently a more sensitive technique than conventional computed tomography or chest radiography for an early radiological diagnosis or asbestosis, its qualitative analysis may seem less sensitive than some simple lung function tests."	No baseline smoking status data presented. Smaller numbers. HRCT scanning was done both in prone and supine positions. Data suggest HRCT, chest radiography and PFTs all contribute to the diagnosis of asbestosis in both early and more advanced disease.
Mosiewicz 2004	6.5	64	High resolution CT scan	Chest radiography	Iron foundry workers with silicosis	None	Radiography	HRCT and radiography were 88%-94% consistent when the findings were nodules. HRCT scan detected	"Results of [HRCT] correlate well with results of conventional radiography in the assessment of nodular changes in silicosis of iron foundry workers. [HRCT]	No mention of smoking or other types of exposures. No co-morbidities noted. Data suggest HRCT scans are more sensitive in detecting smaller nodules

								nodules in 45%-75% of patients with negative chest radiography for intralobular nodules and peripheral subpleural nodules.	enables significantly more frequent detection of nodular changes of small sizes, especially those localized under the pleura."	and nodules in the subpleural space.
Aberle 1988	6.0	63	High resolution CT scan	CT scan Chest radiography PA and Lateral Spirometry	Workers diagnosed with clinical asbestosis and controls	None	Radiography Spirometry	In workers, HRCT showed more Curvilinear subpleural lines compared to controls.	"HRCT can complement the clinical and radiologic assessment of subjects who have had asbestos exposure."	Lack of baseline characteristics such as smoking status. No mention of other exposures or health conditions. Data suggest HRCT more sensitive than CT or chest radiography in detecting subpleural lines and position may affect outcomes.
Hanak 2008	4.5	69	High resolution CT scan	Some patients had spirometry and some physical exams	Patients with a diagnosis of HP	Up to 9 years	CT scan-fibrosis All-cause mortality	26/69 (38%) were classified as fibrotic. 11/26 (42%) of fibrotic group died. 1/43 (2%) of non-fibrotic died.	"CT findings of parenchymal fibrosis are associated with reduced survival in patients with HP and may serve as a useful prognostic indicator."	Retrospective medical record review from Jan 1997 to Dec 2002. Death data collected December 2006. Good background data. Data suggest fibrosis seen on HRCT is similar to biopsy in that it is indicative of a higher mortality rate.
Lynch 1988	4.0	260	High resolution CT scan	None	Asbestos exposed workers with inconclusive chest x-rays for asbestos related lung disease	None	CT scans	27 of 260 workers had focal lung masses for a total 43 lesions.	"Careful interpretation of CT and high-resolution CT features and close surveillance can obviate the need for biopsy in the majority of instances."	All workers exposed to asbestos in construction or shipyards. All at least 10 years since exposure. Some had IV contrast. CT scans not directly compared to any other diagnostic tool so a comparison is not able to be drawn. No biopsies done.
Han 2000	4.0	85	High resolution CT	Clinical history in 53/85, Spirometry in 53/85	Welders in shipyards or assembly plants who had alleged lung abnormalities	None	CT scan	79% of welders were smokers. 54/85 (64%) welders had positive findings on HRCT. 6/43 (14%) of smokers had similar findings.	"Poorly-defined centrilobular micronodules and branching linear structures were the thin-section CT findings most frequently seen in patients with arc-welder's pneumoconiosis."	Lack of baseline data. Two different radiologists read images. Data suggest there are findings on HRCT in workers with clinical signs or symptoms relate to welding.
OTHER										
Topcu 2000	5.0	26	High resolution CT	Chest radiography	Workers already diagnosed with asbestosis	None	CT scan	24/26 (92%) had evidence of asbestosis on HRCT. 9/26 had apical pleural thickening. 7/26 had apical honeycombing.	"We suggest that the HRCT protocol for examining asbestos-exposed individuals with pleural plaques on chest X-rays should include the whole thorax, since the asbestos-related pathologies	Small numbers. Did not really compare findings in light of diagnosing asbestosis. Other exposures not well explained. Discussed tobacco use. Data suggest HRCT scans should include the apices if pleural plaques

									may involve all parts of the lung."	are seen on chest radiographs.

Evidence for the Use of DL_{co}

Author/ Year	Score (0-11)	N	Test Used	Comparison Test	Population	Length of Follow-up	Outcome Measures	Results	Conclusion	Comments
Eterovic 1993	7.0	35	Single breath DL_{CO}	Biopsy Chest radiographs HRCT- prone and supine Spirometry Stress testing on bicycle ergometer	Workers of chrysotile asbestos cement factory	None	DL_{CO} Biopsy results	14/15 (93%) with advanced asbestosis had reduced DLCO.	"[A] biphasic mid-expiratory flow rate and change in DLCO (initial increase followed by a decrease) in non-smoking subjects may be the earliest functional abnormality indicative of future interstitial asbestosis."	Uncertain where 13 control subjects came from. No mention if controls had biopsy or not. Data suggest changes in DLCO may be useful in diagnosis of asbestos related disease.
Dujic 1992	7.0	14	Single breath DL_{CO}	HRCT PA and LAT chest radiography Spirometry	Asbestos cement workers, average age of 42	9 years	DL_{CO} (Dm and Vc) FVC FEV_1 ILO scores	DLCO increased ($p<0.0005$) but remained in normal range. HRCT showed pleural thickening in 6 employees.	"Lung function test were suggested to be more sensitive than chest radiographs in detection of early asbestosis."	Participants asymptomatic at start of study and had normal spirometry and chest radiographs. Exposed to predominately chrysotile asbestos; 11 non-smokers, 3 smokers. No controls. Small sample size. Data suggest decreases in DLCO may be monitored in employees exposed to asbestos before symptoms occur to help identify earlier onset disease.
Abejie 2010	6.5	454	Single breath DL_{CO}	PA chest radiography Spirometry	Chrysotile exposed workers compared to electronic workers as controls	None	DL_{CO} FVC FEV_1/FVC ILO classification	Chest radiograph: 36% emphysema, 31% asbestosis, 15% both. When employees with asbestosis on chest radiograph excluded, employees exposed to asbestos had lower DL_{CO} and FVC vs. controls. Employees with chest radiographs consistent with asbestosis had lower DL_{CO} and FVC values vs.	"…our study showed that asbestos exposure with or without radiographic asbestosis is significantly associated with reduced DLCO and restrictive lung impairment. However, asbestos exposure was not significantly associated with reduced FEV_1/FVC.	Controls were younger, smoked less. Data suggest DLCO and FVC are lower in employees both exposed to asbestos and with findings on chest radiography consistent with asbestosis.

								asbestos exposed subjects only (p <0.05).		
Non-Occupational Lung Diseases										
Orens 1995	7.0	25	HRCT DL_{CO}	Lung biopsy Chest radiograph Spirometry Exercise testing	Idiopathic Pulmonary Fibrosis patients	None	Biopsy HRCT DL_{CO}	3/25 (12%) had negative HRCT; 4/25 (16%) had negative chest radiographs. DL_{CO} in 21 abnormal HRCT was 46.1% of predicted, in the 4 normal HRCT was 65.7% predicted.	"In our patient population, physiologic testing was more sensitive than HRCT in detecting mild abnormalities in patients with idiopathic pulmonary fibrosis proved by biopsy specimen."	Main focus of study was HRCT scan. DL_{CO} had lower values with an abnormal HRCT. No occupational exposures.
Sette 2004	7.0	82	Single breath DL_{CO}	HRCT Chest radiography Exercise testing Spirometry	Asbestos cement workers Chrysotile miners	None	Images Gas exchange values	16/82 (20%) had normal pulmonary gas exchange values.	"[D]ual semiquantitative and qualitative thin-section CT classification of lung parenchymal abnormalities can be used successfully to estimate the individual likelihood of pulmonary gas exchange impairment."	Gas exchange impairment was defined as DL_{CO} <70% predicted.
Boros 2010	6.0	830	Single breath DL_{CO}	Chest x-ray Spirometry Whole body plethysmography Static lung compliance	Patients with sarcoidosis	None	DL_{CO} values	772/830 had normal lung volumes. 75% had parenchymal involvement on chest x-ray. 123/830 (14.8%) had low DL_{CO} values.	"Static lung compliance and DL_{CO} concern different aspects of respiratory pathophysiology."	ERS reference values used for DL_{CO}. No occupational lung disease.

Evidence for the Use of Bronchial Alveolar Lavage (BAL) and Sputum

Author/ Year	Score (0-11)	N	Test Used	Comparison Test	Population	Length of Follow-up	Outcome Measures	Results	Conclusion	Comments
BAL										
Teschler 1996	7.5	135	BAL	Sputum tissue samples	Workers exposed to asbestos dust: Group 1 classified as high exposure, Group 2 as medium, Group 3 as	None	Asbestos bodies (light microscopy, at 400x) in BAL and sputum in all subjects. Lung tissue in 21 subjects.	33% of subjection in group 1, 68% in group 2; 45% in group 3 had ABs in BAL but not Sputum. Open lung biopsy had ABs in all samples. Samples with less than 1,000 ABs/cm3 had no Abs in sputum samples.	"…many subjects with positive BAL fluid analysis had negative sputum results. These findings suggest that BAL is the superior of the two methods for assessing lung AB content."	Tissue samples done only on 21 subjects. Data suggest BAL is more sensitive than Sputum in detecting FBs in subjects. No correlation is made between FBs and disease burden.

					occasional exposure					
Vathesatogkit 2004	7.0	60	BAL	Chest radiography HRCT scan Spirometry DL_{CO}	Utility workers and controls	None	Asbestos bodies (light microscopy, at 40x) Respiratory symptoms Chest radiographs HRCT scans Spirometry DL_{CO}	AB found in 10/30 subjects (33%) and 0/30 controls. AB positive subjects had reduced FEV_1 and diffusion capacity ($p < 0.05$). HRCT scans showed higher prevalence of parenchymal disease ($p < 0.05$).	"In asbestos-exposed subjects, the presence of AB in BAL cytospin slides should be viewed as a clinically important finding, and their HRCT scans should be reviewed carefully for evidence of interstitial lung disease."	Two blinded pathologist read slides for AB. Data suggest detection of Asbestos bodies in utility workers represents an indicator of exposure, but not necessarily related to asbestos diseases.
Corhay 1990	4.5	121	BAL	Chest radiography Spirometry DL_{CO}	Steel workers and controls (white collar workers)	5 year repeat BAL in 7 subjects. Others, none.	Asbestos bodies (light microscopy, at 200x)	Chest radiographs normal in 65 steel workers. ABs found in 38/65 (58.5%) of steel workers and 6% of controls. Smoking habits and presence of COPD did not influence AB counts.	"This study shows that steel workers may be subject to a nontrivial exposure to asbestos in an industrial plan environment."	Not compared to tissue samples. No sputum samples taken. Data suggest steel workers may be exposed to asbestos as part of their job.
Karjalainen 1994	4.0	156	BAL	Exposure data	Exposed workers	None	Asbestos bodies (light microscopy, at 200x)	Concentration of >\= AB/ml found in 85% exposed to asbestos, and 7% of those not likely exposed. Patients with asbestosis (n = 9) showed higher average concentrations of AB (median 13) than patients with pleural disease only (median 2.4).	"…the correlation between AB concentration and exposure history was greater than in earlier studies on workers exposed to chrysotile."	No other biological testing done other than BAL. Broke analyses down by type of job. Data suggest higher concentrations of ABs seem to correlate with higher exposure and more significant disease but the correlation is not linear.
Sputum										
Alexopoulos 2011	7.0	39	Induced Sputum	Broncho-alveolar lavage Chest radiography Spirometry ECG	Romanian brake factory workers without pneumo-coniosis	None	Total number and vitality of cells Number of dust cells Iron laden macrophages Asbestos bodies (AB)	In the six workers who reported using PPE none had asbestos bodies in IS or BALF. 14/39 (36%) had AB in BALF. Of those 7/14 (50%) has AB in IS.	IS "usefulness for screening of workers should be further evaluated because the inflammatory response in our study lacks specificity since it might have been induced [by] asbestos, dust and smoking."	At least 15 years of exposure to asbestos at >5 fibers per mL. Chest radiographs </= 1/0 ILO classification by two physicians. BAL performed in right middle lobe. Sputum induction done by inhaling saline then asked to cough. Study suggests IS may be helpful in proving insight for both

										inhalation of dusts and inflammatory processes in lung.
McLarty 1980	6.0	674	Sputum	Chest radiography Spirometry Smoking status	Exposed workers in insulation	10 years	Ferruginous bodies Chest radiography Spirometry	Workers with ferruginous bodies and irregular small opacities was correlated ($p<0.001$). Workers with ferruginous bodies and restriction on spirometry was correlated ($p<0.02$).	"Clinically, the presence of ferruginous bodies in the sputum was found to be significantly related to radiographic findings of interstitial pulmonary and pleural fibrosis and to spirometric findings of restrictive lung disease."	Both spontaneous and aerosol-induced sputum specimens used. Data suggest sputum samples not only show asbestos exposure, but may be correlated with radiological changes and spirometry findings.
Paris 2002	4.5	223	Sputum	Exposure data	Exposed workers, brake and textile	None	Asbestos body (light microscopy, at 160x) Exposure data	118/223 (53%) sputum samples.	"It is clear that a negative mineralogical sputum examination cannot therefore, exclude the reality of even high occupational exposure."	No other diagnostic tests used. Data suggest a negative result on sputum cannot exclude asbestos exposure.
Sulotto 1997	4.0	142	Sputum	Spirometry Chest radiography	Exposed workers in textile	Up to 5 years	Ferruginous bodies (light microscopy, at 400x) Spirometry	Asbestos-related diseases were present in 58% of subjects. ABs were found in 94 smears (21%) and in at least 1 specimen in 44.4% of subjects.	"…our study confirms the utility of obtaining several specimens from each subject in order to increase the probability of asbestos body identification."	Collection of sputum samples for 3 weeks or less. Minimum amount of specimens was 2. Data suggest multiple sputum samples beneficial up to 4 in identifying FBs in sputum in exposed workers.

Evidence for the Use of the 6-Minute Walk Test

Author/Year	Score (0-11)	N	Test Used	Comparison Test	Population	Length of Follow-up	Outcome Measures	Results	Conclusion	Comments
Du Bois 2011	5.0	822	6-minute walk test	Spirometry	Patients with confirmed IPF	None	FVC, DL_{CO}, resting alveolar-arterial oxygen gradient ($AaPO_2$), UC San Diego Shortness of Breath Questionnaire (UCSD SOBQ), St.	Distance walked during the 6MWT was correlated with FVC, DL_{CO}, Resting $AaPo_2$, UCSD SOBQ,	"[O]ur results demonstrate that the 6MWT is a reliable, valid, and responsive measure of exercise tolerance in patients with IPF, and that a decline in 6MWD of 24-	Data obtained during a drug study. Large sample size. All with IPF. Minimal clinical difference of 24-45 meters. Data suggest 6 minute walk test useful in determining

							George's Respiratory Questionnaire (SGRQ).	and SGRQ (p <0.001).	45 m represents a small but clinically important difference."	exercise tolerance and risk for mortality.
Pimenta 2010	5.0	60	6-minute walk test	Whole-body plethysmo-graphy DLco	Patients from an ILD clinic; healthy controls	None	VS, DLco, Dyspnea score, O2 Saturations	Mean distance: ILD patients 430 meters; Controls: 602 meters. SpO2 Median desaturation distance ratio: ILD patients: 10 Controls: 2.5	"Desaturation distance ratio is a promising concept and a more reliable physiologic tool to assess pulmonary diseases characterized by involvement of the alveolar-capillary membrane, such as interstitial lung diseases."	Mean age 60 for ILD patients from a tertiary referral clinic. Data suggest combination of distance and desaturations during 6MWT helps to diagnose ILD patients. Data seems weak for diagnosis of ILD as it doesn't compare to other lung disorders, nor control for other conditions.
Alhamad 2010	4.5	59	6-minute walk test	Spirometry	Patients with diagnosed pulmonary sarcoidosis.	None. Retrospective study.	6-minute walking distance and lowest oxygen saturation (DSP). Forced expiratory volume (FEV), (FEV_1), total lung capacity (TLC), and defined product of 6Used predicted values based on age and gender.	Distance walked on 6MWT had significant relationship with FEV_1 and FVC (p <0.001), TLC (p = 0.003), final Borg Score (p = 0.028), and PaO_2 (p = 0.005).	"[E]xercise intolerance among patients with pulmonary sarcoidosis manifests as shorter distances walked during the 6MWT. We have identified several factors that contribute to reductions in 6MWD, including gender, pulmonary function parameters dyspnea score, and PaO_2."	Retrospective record review. All had sarcoidosis. Data suggest DSP may be helpful in determining functional status in patients with sarcoidosis.
Modryka mien 2010	4.0	58	6-minute walk test	Echocardio-graphy, distance saturation product (DSP), and pulse oximetry (SPO_2)	Patients with pulmonary arterial hypertension (PAH) and pre-transplant diagnosis of IPF	Retrospective review of data.	Right-ventricle systolic pressure (RVSP), 6MWT distance, FVC, mean oxygen concentration requirement (FIO2), cardiac output, (SPO_2) at rest.	Sensitivity and specificity were: RVSP (72% and 66%), 6MWD (45% and 67%), DSP (64% and 57%), and SPO_2 (44% and 76%).	"[N]oninvasive diagnostic tests applied to patients with IPF perform poorly in detecting PAH."	Retrospective records review. Patients with IPF with/without PAH. Data suggest pulmonary arterial hypertension may affect 6MWD in patients with IPF
Flaherty 2006	4.0	197	6- minute walk test	FVC DL_{CO} SaO2	Patients with idiopathic pulmonary fibrosis, no obvious occupational exposures.	6 months for testing, years for mortality.	FVC, FVC %, DLco, 6MWT	Categorical baseline walk distance was a weak predictor of mortality for the entire cohort (p = 0.038) Baseline desaturation SaO2 </= 88% had a mean survival time of 3.21 years vs.	"[T]his study highlights that desaturation at baseline increases the risk of subsequent mortality; baseline walk distance is a good predictor of subsequent walk distance but does not reliably predict risk of subsequent mortality…"	6 minute walk test stopped when SaO2 was <86%. No oxygen allowed during testing. Retrospective study design. Mortality appears to be all cause mortality. Data suggest in patients with IPF, desaturations at baseline, not 6MWD is a better predictor of subsequent mortality.

								6.83 years (p = 0.006)		

Appendix 3: Low-Quality / Supplementary Studies

The following low-quality/supplementary studies were reviewed by the Evidence-based Practice Interstitial Lung Disease Panel to be all inclusive, but were not relied upon for purpose of developing this document's guidance because they were not of high quality due to one or more errors (e.g., lack of defined methodology, incomplete database searches, selective use of the studies and inadequate or incorrect interpretation of the studies' results, etc.), which may render the conclusions invalid. ACOEM's Methodology requires that only moderate- to high-quality literature be used in making recommendations.[196]

SPIROMETRY

Author/ Year	Score (0-11)	N	Test Used	Comparison Test	Population	Length of Follow up	Outcome Measures	Results	Conclusion	Comments
Ng 1987	NA	81	Spirometry	Chest radiography	Granite workers	10 years	FEV_1, FVC, radiography, exposure data	Workers classified as having simple silicosis had a FVC of 4% below predicted. Complicated silicosis had FVC 13% below predicted.	"The progression of simple silicosis is thus accompanied by appreciable declines in lung function and is strongly affected by previous levels of exposure to dust."	No additional exposures considered. Smoking evaluated. Data suggest spirometry values decline with progression of silicosis as seen on chest radiographs and may be used in monitoring programs.
Cowie 1998	NA	242	Spirometry	Chest radiography DCO	Gold miners in South Africa	4.5 years	FEV_1, FVC FEV_1/FVC DCO	FEV_1 loss over 4.5 years was average of 37ml/year in workers without evidence of silicosis and 125ml/year for worst cases (p = 0.000001). FVC: 15ml/year vs. 116 ml/year. DCO 0.54 vs. 1.37	"[T]his study of a sample of a cohort of older gold miners reexamined 4.5 years…has shown a substantial loss of lung function attributable to the presence and degree of silicosis."	No additional exposures considered. Evaluated at smoking and age in data analysis. Data suggest spirometry and carbon monoxide diffusion decrease with time in workers with silicosis more than workers without silicosis.
Wang 2006	NA	1,884	Spirometry	None	Coal mine workers	>10 years	FEV_1	Individuals with short-term declines found to be 3-18 times more likely to have long-term declines	"Our findings provide guidance for interpreting periodic spirometry results from individuals exposed to respiratory hazards."	Not a true diagnostic study, no comparison test, no real diagnosis given.
Hankinson 1986	NA	NA	Spirometry	None	Healthy volunteers for normal values	None	FVC FEV_1 FEV_1/FVC	None	"This paper is a brief guide for those in the medical profession attempting to establish or improve their medical surveillance programs for occupational respiratory diseases."	Study is for background information, not comparing spirometry to any other diagnostic test. Had set of healthy volunteers to get "normalized" values.
Hankingson 1993	NA	NA								See Hankinson 1986 for details

Wang 2005	NA	449	Spirometry	Symptoms	Newly hired Chinese underground coal miners	3 years	FVC FEV_1 FEV_1/FVC	FEV_1 slope averaged -39ml/year in miners; 160ml/year in referents	"Dust and smoking affect lung function in young, newly hired Chinese coal miners. FEV_1 change over the first three years of employment in non-linear."	No comparison test used. Baseline differences between miners and referents significant in many areas.
Beeckman 2001	NA	634	Spirometry	Symptoms, mortality, illnesses	Coal miners	18 years	FVC FEV_1 Mortality Diagnosis	Higher proportion of coal miners with symptoms than coal miners without ($p < 0.05$). CS group had more symptoms of respiratory illness than RF group. CS had more deaths from cardiovascular disease or nonmalignant respirator disease.	"The results of this study document the potential consequence of rapid declines in lung function, and emphasize the importance of recognition and effective interventions for individuals who experience accelerated losses of FEV_1."	Several different diagnoses included, most were COPD diagnoses. Diagnoses determined by either asking miner or family member. Cause of death taken from death certificate.

CHEST RADIOGRAPHS

Author/ Year	Score (0-11)	N	Test used	Comparison Test	Population	Length of Follow up	Outcome measures	Results	Conclusion	Comments
Attfield 1995	3.5	3,194	X-ray	Symptoms Employment status	Coal Miners	None	X-ray findings Employment status	53% were current miners, 47% ex-miners. (14% left for health reasons) CWP was 7-9%.	"[T]he results described here indicate that the present coal mining work force is still at risk of developing CWP over a life time's work."	Included detailed occupational exposure history, and smoking status and dust exposure levels.

BRONCHIAL ALVEOLAR LAVAGE AND SPUTUM

Author/ Year	Score (0-11)	N	Test Used	Comparison Test	Population	Length of Follow-up	Outcome Measures	Results	Conclusion	Comments
Christman 1991	3.5	86	BAL	Symptoms	Granite workers Controls	Up to 5 years	Dust (silica) particles in BALF and in collected macrophages using polarized light microscopy.	Control subjects averaged 4.35% of macrophages with particles. Granite workers had up to 50% with particles. The difference was significant ($p<0.0001$)	"With further understanding, BAL may become a more useful tool for the evaluation of workers with occupational exposure to dusty trades."	Participants not necessarily diagnosed with any specific disease. Other possible exposures not defined. Data suggest BALF may aid in detecting dust exposure in granite workers.
Dodson 1993	NA	5	BAL	None	Foundry workers	None	Ferruginous bodies (200x and 400x)	Ferruginous bodies were seen by electron microscopy and light microscopy.	"Our present study of lavage samples from foundry workers confirmed the presence of classical ferruginous bodies as reported in previous studies of tissue samples…"	Small numbers, no comparison test.

Havarneanu 2008	NA	112	Sputum	None	39 workers occupationally exposed to asbestos fibers; 72 controls.	None	Asbestos bodies, Ferruginous bodies in sputum	29/39 (74%) exposed had asbestos bodies. 6/72 (8%) controls had asbestos bodies.	"The presence in sputum of asbestos bodies represents an important indicator for occupational exposure to respirable particles."	No comparison test. Smoking exposure evaluated. Data suggest trend towards more asbestos bodies in sputum of occupationally exposed workers over matched controls.

6-MINUTE WALK TEST

Author/ Year	Score (0-11)	N	Test Used	Comparison Test	Population	Length of Follow-up	Outcome Measures	Results	Conclusion	Comments
Buch 2007	3.5	163	6-minute walk test	Spirometry	Patients with interstitial lung disease secondary to systemic sclerosis (SSc).	No follow-up.	FVC, single breath diffusing capacity (DL_{CO}), Borg Dyspnoea Index	No correlation found between 6MWT, pulmonary function, and Borg Dyspnea Index.	"[T]he lack of criterion validity and the poor correlation with gas-exchange measurements raises important questions on the overall suitability of this test in SSc-ILD."	Data from a drug study. Patients with Systemic Sclerosis Interstitial Lung Disease. No normative values for age, gender, ethnicity used. Data suggest 6 minute walk test not effective predictor of dyspnea in these patients.
Chetta 2001	2.5	40	6- minute walk test	Spirometry Body plethysmo-graphy. Carbon monoxide transfer capacity. Oximitry	Interstitial lung disease patients with history of breathlessness	None	Walk Distance, Age, Breathlessness, FVC, SpO2	Mean walk distance 487 m. 24/40 (60%) had >2% fall in oxygen saturation.	"[O]ur study confirms that the 6MWT is a simple and inexpensive test that can provide a global evaluation of sub-maximal exercise capacity in ILD patients. Furthermore, we demonstrate that in these patients walk distance and oxygen desaturation during walk, but not breathlessness perception after walk, can be predicted by resting lung function."	Used second walk test to allow for learning effect. Different causes of ILD were included including sarcoidosis, idiopathic, etc. Patients had the disease from 1-19 years. No comparison diagnostic study included. Data suggest 6MWT may be used in ILD patients.
OTHER										
Gibbons 2001	NA	79	6- minute walk distance	Age Height Gender	Healthy participants to develop reference values for 6 minute walk distance.	None	6MWD	Best 6MWD average 698 meters. Distance inversely related to age (p <.001). Distance directly related to height (p <0.001). Distance	"Selection of appropriate predicted 6MWD values for interpretation of performance should be guided by subject age and degree of test familiarization provided."	Distance used for test was 20 meters. This is different than ATS recommended 30 meters. Normative values needed based on age, height, and gender.

					Age range 20-80 years.			related to gender (p <0.0002)		
Enright 1998	NA	290	6-minute walk distance	Age, gender, height, weight, spirometry, Oxygen saturation, degree of dyspnea (Borg scale) Pulse rate.	Healthy participants to develop reference values for 6 minute walk distance. Aged 40-80.	None	6MWD	Median distance walked: Men 576 m; qomen 494 m. Age, weight and height also influenced distance.	"These reference equations may be used to compute the percentage predicted 6MWD for individual adult patients performing the test for the first time, when using the standardized protocol."	Distance used for test was 100 feet. This is different than ATS recommended 30 meters. They excluded BMI >35 kg/m2 and FEV_1 <70%. Reference values are valid only for first time performing the 6MWT.
Troosters 1999	NA	51	6- minute walk distance	Age Height Sex Weight	Healthy elderly volunteers.	None	6MWD	Distance averaged 631 m. Males had 84m more than females on average (p <0.001). There was a correlation with age and height (p <0.01)	"[T]he six minute walking distance can be predicted adequately using a clinically useful model in healthy elderly subjects. Its variability is explained largely by age, sex, height and weight. Results of the six minute walking distance may be interpreted more adequately if expressed as a percentage of the predicted value."	Performed in 50m long hallway. Patients encouraged every 30 seconds. Study proposes a formula for normative values in 6MWD and states that a % of predicted is a more accurate result than absolute distance.
Jenkins 2010	NA	349	6- minute walk distance	Repeated 6-minute walk distance maximum of 4 weeks after first.	Patients with COPD, interstitial lung disease (ILD), bronchiectasis and asthma before starting a pulmonary rehabilitation	None	6MWD	6MWD increased in patients on second test. (p <0.001) with at least 80% of patients in each cohort.	"Respiratory diagnosis influences the magnitude of the learning effect for the 6MWT. The findings support the recommendation of a practice 6MWT at baseline assessment in order to provide an accurate measure of the effects of rehabilitation on 6MWD."	Retrospective study. Appears to be a learning effect for 6MWD after first test, but not after second.
Garin 2009	NA	128	6- minute walk distance	Mortality	Patients with scleroderma and or idiopathic pulmonary fibrosis	Uncertain	6MWD Dyspnea Lower extremity pain Pain	No significant difference between scleroderma patients and IPF. Lower extremity pain was primary limitation to walk distance for 15-20% of subjects.	"Pain limitations confound the utility of the 6MWT, particularly in SSc patients without both ILD and PH… 6MWT distance is not always reflective of the same physiological process."	Retrospective record review. In patients with systemic scleroderma pain and other factors may limit walk distance more than dyspnea.
Baughman 2007	NA	142	6-minute walk distance	Spirometry, St. George Respiratory Questionnaire Fatigue assessment scale, Dyspnea score	Sarcoidosis patients, 130/142 (92%) had extra-pulmonary manifestation	6 weeks	6MWD	73/142 had distance <400 m; 32/142 had distance <300 m.	"6MWD was reduced in the majority of sarcoidosis patients. Several factors were associated with a reduced 6MWD, including FVC, oxygen saturation with exercise, and self-reported respiratory health."	Participants were patients referred to tertiary sarcoidosis clinic. Most had extrapulmonary illnesses. FVC % predicted was 82% (17-

										151%) FEV_1 76% (16-155%)

Appendix 4: References

1. Raghu G, Collard H, Egan J, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med*. 2011;183:788-824.
2. Ryu JH, Daniels CE, Hartman TE, Yi ES. Diagnosis of interstitial lung diseases. *Mayo Clin Proc*. 2007;82(8):976-86.
3. King TE, Jr. Clinical advances in the diagnosis and therapy of the interstitial lung diseases. *Am J Respir Crit Care Med*. 2005;172(3):268-79.
4. Bates DV, Gotsch AR, Brooks S, Landrigan PJ, Hankinson JL, Merchant JA. Prevention of occupational lung disease. Task Force on Research and Education for the Prevention and Control of Respiratory Diseases. *Chest*. 1992;102(3 Suppl):257S-76S.
5. American Thoracic Society, European Respiratory Society. American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. *Am J Respir Crit Care Med*. 2002;165(2):277-304.
6. Petsonk EL, Rose C, Cohen R. Coal mine dust lung disease. New lessons from old exposure. *Am J Respir Crit Care Med*. 2013;187(11):1178-85.
7. Boros PW, Franczuk M, Wesolowski S. Value of spirometry in detecting volume restriction in interstitial lung disease patients. Spirometry in interstitial lung diseases. *Respiration*. 2004;71(4):374-9.
8. Stansbury RC, Beeckman-Wagner LA, Wang ML, Hogg JP, Petsonk EL. Rapid decline in lung function in coal miners: evidence of disease in small airways. *Am J Ind Med*. 2013;56(9):1107-12.
9. Allen B, Garland B. Patient's page. Interstitial lung disease. *South Med J*. 2007;100(6):619.
10. Olson A, Schwarz, M, Roman J. Interstitial lung disease. In: Schraufnagel D, ed. *Breathing in America: Diseases, Progress, and Hope*: American Thoracic Society; 2010:99-108.
11. Wells A, Hirani N, and on behalf of the British Thoracic Society Interstitial Lung Disease Guideline Group, a subgroup of the British Thoracic Society Standards of Care Committee, in collaboration with the Thoracic Society of Australia, and New Zealand and the Irish Thoracic Society. Interstitial lung disease guideline: the British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society. *Thorax*. 2008;63(Suppl V):v1-58.
12. Glenn D. Current issues surrounding silica. *Professional Safety*. 2008;53(2):37-46.
13. Schenker MB, ed. Respiratory health hazards in agriculture. American Thoracic Society Consensus Report. *Am J Respir Crit Care Med*. 1998;158(suppl 4):S1-76.
14. Cummings KJ, Deubner DC, Day GA, et al. Enhanced preventive programme at a beryllium oxide ceramics facility reduces beryllium sensitisation among new workers. *Occup Environ Med*. 2007;64(2):134-40.
15. Infante PF, Newman LS. Beryllium exposure and chronic beryllium disease. *Lancet*. 2004;363(9407):415-6.
16. Silver K, Kukulka G, Gorniewicz J, Rayman K, Sharp R. Genetic susceptibility testing for beryllium: worker knowledge, beliefs, and attitudes. *Am J Ind Med*. 2011;54(7):521-32.
17. Thomas CA, Bailey RL, Kent MS, Deubner DC, Kreiss K, Schuler CR. Efficacy of a program to prevent beryllium sensitization among new employees at a copper-beryllium alloy processing facility. *Public Health Rep*. 2009;124 (Suppl 1):112-24.
18. Steenland K, Brown D. Mortality study of gold miners exposed to silica and nonasbestiform amphibole minerals: an update with 14 more years of follow-up. *Am J Ind Med*. 1995;27(2):217-29.
19. American Thoracic Society. Adverse effects of crystalline silica exposure. *Am J Respir Crit Care Med*. 1997;155:761-5.
20. Brodkin CA, Barnhart S, Checkoway H, Balmes J, Omenn GS, Rosenstock L. Longitudinal pattern of reported respiratory symptoms and accelerated ventilatory loss in asbestos-exposed workers. *Chest*. 1996;109(1):120-6.
21. Straif K, Benbrahim-Tallaa L, Baan R, et al. A review of human carcinogens-Part C: metals, arsenic, dusts, and fibres. *Lancet Oncology*. 2009;10(5):453-4.
22. American Thoracic Society. Diagnosis and initial management of nonmalignant diseases related to asbestos. *Am J Respir Crit Care Med*. 2004;170:691-715.
23. Caplan A. Correlation of radiological category with lung pathology in coal-workers' pneumoconiosis. *Br J Ind Med*. 1962;19171-9.
24. Patel AM, Ryu JH, Reed CE. Hypersensitivity pneumonitis: current concepts and future questions. *J Allergy Clin Immunol*. 2001;108(5):661-70.
25. Lison D, Lauwerys R, Demedts M, Nemery B. Experimental research into the pathogenesis of cobalt/hard metal lung disease. *Eur Respir J*. 1996;9(5):1024-8.
26. Naqvi AH, Hunt A, Burnett BR, Abraham JL. Pathologic spectrum and lung dust burden in giant cell interstitial pneumonia (hard metal disease/cobalt pneumonitis): review of 100 cases. *Arch Environ Occup Health*. 2008;63(2):51-70.

27. Choi JW, Lee KS, Chung MP, Han J, Chung MJ, Park JS. Giant cell interstitial pneumonia: high-resolution CT and pathologic findings in four adult patients. *AJR Am J Roentgenol*. 2005;184(1):268-72.
28. Rosenman KD, Reilly MJ, Henneberger PK. Estimating the total number of newly-recognized silicosis cases in the United States. *Am J Ind Med*. 2003;44(2):141-7.
29. Mazurek J, Wood J. Asbestosis-Related Years of Potential Life Lost Before Age 65 Years -- United States, 1968-2005. *MMWR*. 2008;57(49):1321-5.
30. Mazurek J, Laney A, Wood J. Coal Workers' Pneumoconiosis-Related Years of Potential Life Lost Before Age 65 Years -- United States, 1968-2006. *MMWR*. 2009;58(50):1412-6.
31. Loomis D. Basic protections are still lacking. *Occup Environ Med*. 2010;67(6):361.
32. Cummings KJ, Nakano M, Omae K, et al. Indium lung disease. *Chest*. 2012;141(6):1512-21.
33. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. Publication Number 2002-129 -- NIOSH Hazard Review: Health Effects of Occupational Exposure to Respirable Crystalline Silica. Available at: http://www.cdc.gov/niosh/docs/2002-129/. 2002 (April).
34. Hueper W. Section IV. Human exposure to asbestos: community studies. Occupational and nonoccupational exposures to asbestos. *Annals New York Academy of Sciences*. 1965;184-95.
35. Wolff H, Vehmas T, Oksa P, Rantanen J, Vainio H. Asbestos, asbestosis, and cancer: Helsinki Criteria update 2014: Recommendations. Consensus Report. *Scand J Work Environ Health*. 2014;Online-first article.
36. Agency for Toxic Substances and Disease Registry. What Is Asbestos? . 2008. Retrieved December 22, 2014 from: http://www.atsdr.cdc.gov/asbestos/more_about_asbestos/what_is_asbestos.
37. Agency for Toxic Substances and Disease Registry. Toxicological Profile for Asbestos. 2001. Retrieved December 22, 2014 from: http://www.atsdr.cdc.gov/toxprofiles/tp61.pdf.
38. World Health Organization. *International Programme on Chemical Safety. Environmental Health Criteria 53. Asbestos and Other Natural Mineral Fibers*. Geneva; 1986.
39. Mayer AS, Hamzeh N, Maier LA. Sarcoidosis and chronic beryllium disease: similarities and differences. *Semin Respir Crit Care Med*. 2014;35(3):316-29.
40. Hypersensitivity Pneumonitis Update (Review). Diffuse Lung Disease & Interstitial Lung Disease, Society Journal 1. Available at: http://pulmccm.org/2012/review-articles/hypersensitivity-pneumonitis-2012-update-review-chest/. 2012.
41. U.S. Department of Health and Human Services, National Institute for Occupational Safety and Health, Division of Respiratory Disease Studies. Work-related Lung Disease Surveillance Report 1999. DHHS (NIOSH) Number 2000-105. Available at: http://www.cdc.gov/niosh/docs/2000-105/pdfs/2000-105.pdf. 1999.
42. Mapel DW, Coultas DB, James DS, Hunt WC, Stidley CA, Gilliland FD. Ethnic differences in the prevalence of nonmalignant respiratory disease among uranium miners. *Am J Public Health*. 1997;87(5):833-8.
43. Cowl CT. Occupational asthma: review of assessment, treatment, and compensation. *Chest*. 2011;139(3):674-81.
44. Blanc P, Balmes J. History and physical examination. In: Harber P, Schenker M, J B, eds. *Occupational and Environmental Respiratory Diseases*. St. Louis, MO: Mosby; 1995:28-38.
45. Bickley L, Szilagyi P, Bates B. *Bates' Guide to Physical Examination and History Taking*: Lippincott Williams & Wilkins; 2009.
46. LeBlond R, Brown D, DeGowin R. *DeGowin's Diagnostic Examination, Ninth Edition*: McGraw-Hill Professional; 2008.
47. Wang ML, Avashia BH, Petsonk EL. Interpreting periodic lung function tests in individuals: the relationship between 1- to 5-year and long-term FEV1 changes. *Chest*. 2006;130(2):493-9.
48. Beeckman LA, Wang ML, Petsonk EL, Wagner GR. Rapid declines in FEV1 and subsequent respiratory symptoms, illnesses, and mortality in coal miners in the United States. *Am J Respir Crit Care Med*. 2001;163(3 Pt 1):633-9.
49. Miller MR, Crapo R, Hankinson J, et al. General considerations for lung function testing. *Eur Respir J*. 2005;26(1):153-61.
50. Townsend M, Occupational and Environmental Lung Disorders Committee. Spirometry in the occupational health setting - 2011 update. *JOEM*. 2011;53(5):569-84.
51. U.S. Department of Labor, Occupational Safety and Health Administration. OSHA Publication No. 3637-2013. Spirometry Testing in Occupational Health Programs. Best Practices for Healthcare Professionals. Available at: https://www.osha.gov/Publications/OSHA3637.pdf. 2013.
52. Leung CC, Chang KC, Law WS, et al. Determinants of spirometric abnormalities among silicotic patients in Hong Kong. *Occup Med (Lond)*. 2005;55(6):490-3.
53. Townsend MC. Evaluating pulmonary function change over time in the occupational setting. *J Occup Environ Med*. 2005;47(12):1307-16.
54. Hankinson JL. Pulmonary function testing in the screening of workers: guidelines for instrumentation, performance, and interpretation. *J Occup Med*. 1986;28(10):1081-92.
55. Hankinson JL, Bang KM. Acceptability and reproducibility criteria of the American Thoracic Society as observed in a sample of the general population. *Am Rev Respir Dis*. 1991;143(3):516-21.

56. Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. *Eur Respir J*. 2005;26(5):948-68.
57. Rondinelli R. *AMA Guides to the Evaluation of Permanent Impairment, Sixth Edition*. Chicago, IL: American Medical Association; 2007.
58. Redlich CA, Tarlo SM, Hankinson JL, et al. Official American Thoracic Society technical standards: spirometry in the occupational setting. *Am J Respir Crit Care Med*. 2014;189(8):983-93.
59. Wang X, Yano E. Pulmonary dysfunction in silica-exposed workers: a relationship to radiographic signs of silicosis and emphysema. *Am J Ind Med*. 1999;36(2):299-306.
60. Miller A, Lilis R, Godbold J, Chan E, Wu X, Selikoff IJ. Spirometric impairments in long-term insulators. Relationships to duration of exposure, smoking, and radiographic abnormalities. *Chest*. 1994;105(1):175-82.
61. Kilburn KH, Warshaw RH. Airways obstruction from asbestos exposure. Effects of asbestosis and smoking. *Chest*. 1994;106(4):1061-70.
62. Barnhart S, Hudson LD, Mason SE, Pierson DJ, Rosenstock L. Total lung capacity. An insensitive measure of impairment in patients with asbestosis and chronic obstructive pulmonary disease? *Chest*. 1988;93(2):299-302.
63. Rosenman KD, Reilly MJ, Gardiner J. Results of spirometry among individuals in a silicosis registry. *J Occup Environ Med*. 2010;52(12):1173-8.
64. Brodkin CA, Barnhart S, Anderson G, Checkoway H, Omenn GS, Rosenstock L. Correlation between respiratory symptoms and pulmonary function in asbestos-exposed workers. *Am Rev Respir Dis*. 1993;148(1):32-7.
65. Kilburn KH, Warshaw R, Thornton JC. Asbestosis, pulmonary symptoms and functional impairment in shipyard workers. *Chest*. 1985;88(2):254-9.
66. Aaron SD, Dales RE, Cardinal P. How accurate is spirometry at predicting restrictive pulmonary impairment? *Chest*. 1999;115(3):869-73.
67. Sircar K, Hnizdo E, Petsonk E, Attfield M. Decline in lung function and mortality: implications for medical monitoring. *Occup Environ Med*. 2007;64(7):461-6.
68. Ng TP, Chan SL, Lam KP. Radiological progression and lung function in silicosis: a ten year follow up study. *Br Med J (Clin Res Ed)*. 1987;295(6591):164-8.
69. Cowie RL. The influence of silicosis on deteriorating lung function in gold miners. *Chest*. 1998;113(2):340-3.
70. Hankinson JL, Wagner GR. Medical screening using periodic spirometry for detection of chronic lung disease. *Occup Med*. 1993;8(2):353-61.
71. Wang ML, Wu ZE, Du QG, et al. A prospective cohort study among new Chinese coal miners: the early pattern of lung function change. *Occup Environ Med*. 2005;62(11):800-5.
72. Hourihane DO, Lessof L, Richardson PC. Hyaline and calcified pleural plaques as an index of exposure to asbestos. *Br Med J*. 1966;1(5495):1069-74.
73. Ruckley VA, Fernie JM, Chapman JS, et al. Comparison of radiographic appearances with associated pathology and lung dust content in a group of coalworkers. *Br J Ind Med*. 1984;41(4):459-67.
74. Musk AW, Cotes JE, Bevan C, Campbell MJ. Relationship between type of simple coalworkers' pneumoconiosis and lung function. A nine-year follow-up study of subjects with small rounded opacities. *Br J Ind Med*. 1981;38(4):313-20.
75. Fernie JM, Ruckley VA. Coalworkers' pneumoconiosis: correlation between opacity profusion and number and type of dust lesions with special reference to opacity type. *Br J Ind Med*. 1987;44(4):273-7.
76. Uragoda CG. Graphite pneumoconiosis and its declining prevalence in Sri Lanka. *J Trop Med Hyg*. 1989;92(6):422-4.
77. Rossiter CE. Relation between content and composition of coalworkers' lungs and radiological appearances. *Br J Ind Med*. 1972;29(1):31-44.
78. Kim KI, Kim CW, Lee MK, et al. Imaging of occupational lung disease. *Radiographics*. 2001;21(6):1371-91.
79. Epler GR. Clinical overview of occupational lung disease. *Radiol Clin North Am*. 1992;30(6):1121-33.
80. International Labour Office. *Guidelines for the use of the ILO International Classification of Radiographs of Pneumoconioses, Revised edition 2011*. Geneva: International Labour Office; 2011.
81. Cockcroft A, Lyons JP, Andersson N, Saunders MJ. Prevalence and relation to underground exposure of radiological irregular opacities in South Wales coal workers with pneumoconiosis. *Br J Ind Med*. 1983;40(2):169-72.
82. Attfield M, Morring K. An investigation into the relationship between coal workers' pneumoconiosis and dust exposure in U.S. coal miners. *Am Ind Hyg Assoc*. 1992;53:486-92.
83. Attfield MD, Seixas NS. Prevalence of pneumoconiosis and its relationship to dust exposure in a cohort of U.S. bituminous coal miners and ex-miners. *Am J Ind Med*. 1995;27(1):137-51.
84. Stark P, Jacobson F, Shaffer K. Standard imaging in silicosis and coal worker's pneumoconiosis. *Radiol Clin North Am*. 1992;30(6):1147-54.
85. Gefter WB, Conant EF. Issues and controversies in the plain-film diagnosis of asbestos-related disorders in the chest. *J Thorac Imaging*. 1988;3(4):11-28.

86. Lopes A, Mogami R, Capone D, Tessarollo B, Lopes De Melo P, Jansen J. High-resolution computed tomography in silicosis: correlation with chest radiography and pulmonary function tests. *J Bras Pneumol*. 2008;34(5):264-72.
87. American College of Radiology (ACR), Society for Pediatric Radiology (SPR). ACR–SPR Practice Guideline for the Performance of Chest Radiography. Available at: http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/Chest_Radiography.pdf. 2011.
88. Kipen HM, Lilis R, Suzuki Y, Valciukas JA, Selikoff IJ. Pulmonary fibrosis in asbestos insulation workers with lung cancer: a radiological and histopathological evaluation. *Br J Ind Med*. 1987;44(2):96-100.
89. Laney AS, Attfield MD. Coal workers' pneumoconiosis and progressive massive fibrosis are increasingly more prevalent among workers in small underground coal mines in the United States. *Occup Environ Med*. 2010;67(6):428-31.
90. Paris C, Benichou J, Raffaelli C, et al. Factors associated with early-stage pulmonary fibrosis as determined by high-resolution computed tomography among persons occupationally exposed to asbestos. *Scand J Work Environ Health*. 2004;30(3):206-14.
91. Wain SL, Roggli VL, Foster WL, Jr. Parietal pleural plaques, asbestos bodies, and neoplasia. A clinical, pathologic, and roentgenographic correlation of 25 consecutive cases. *Chest*. 1984;86(5):707-13.
92. Vallyathan V, Brower PS, Green FH, Attfield MD. Radiographic and pathologic correlation of coal workers' pneumoconiosis. *Am J Respir Crit Care Med*. 1996;154(3 Pt 1):741-8.
93. Hurley JF, Burns J, Copland L, Dodgson J, Jacobsen M. Coalworkers' simple pneumoconiosis and exposure to dust at 10 British coalmines. *Br J Ind Med*. 1982;39(2):120-7.
94. Bourgkard E, Bernadac P, Chau N, Bertrand JP, Teculescu D, Pham QT. Can the evolution to pneumoconiosis be suspected in coal miners? A longitudinal study. *Am J Respir Crit Care Med*. 1998;158(2):504-9.
95. Amandus HE, Lapp NL, Jacobson G, Reger RB. Significance of irregular small opacities in radiographs of coalminers in the USA. *Br J Ind Med*. 1976;33(1):13-7.
96. Sun J, Weng D, Jin C, et al. The value of high resolution computed tomography in the diagnostics of small opacities and complications of silicosis in mine machinery manufacturing workers, compared to radiography. *J Occup Health*. 2008;50(5):400-5.
97. Larson TC, Lewin M, Gottschall EB, Antao VC, Kapil V, Rose CS. Associations between radiographic findings and spirometry in a community exposed to Libby amphibole. *Occup Environ Med*. 2012;69(5):361-6.
98. Collins HP, Dick JA, Bennett JG, et al. Irregularly shaped small shadows on chest radiographs, dust exposure, and lung function in coalworkers' pneumoconiosis. *Br J Ind Med*. 1988;45(1):43-55.
99. Gevenois PA, Pichot E, Dargent F, Dedeire S, Vande Weyer R, De Vuyst P. Low grade coal worker's pneumoconiosis. Comparison of CT and chest radiography. *Acta Radiol*. 1994;35(4):351-6.
100. Huuskonen O, Kivisaari L, Zitting A, Taskinen K, Tossavainen A, Vehmas T. High-resolution computed tomography classification of lung fibrosis for patients with asbestos-related disease. *Scand J Work Environ Health*. 2001;27(2):106-12.
101. Hanak V, Golbin JM, Hartman TE, Ryu JH. High-resolution CT findings of parenchymal fibrosis correlate with prognosis in hypersensitivity pneumonitis. *Chest*. 2008;134(1):133-8.
102. Gamsu G, Salmon CJ, Warnock ML, Blanc PD. CT quantification of interstitial fibrosis in patients with asbestosis: a comparison of two methods. *AJR Am J Roentgenol*. 1995;164(1):63-8.
103. Eterovic D, Dujic Z, Tocilj J, Capkun V. High resolution pulmonary computed tomography scans quantified by analysis of density distribution: application to asbestosis. *Br J Ind Med*. 1993;50(6):514-9.
104. Newman LS, Buschman DL, Newell JD, Jr., Lynch DA. Beryllium disease: assessment with CT. *Radiology*. 1994;190(3):835-40.
105. Mosiewicz J, Myslinski W, Zlomaniec G, Czabak-Garbacz R, Krupski W, Dzida G. Diagnostic value of high resolution computed tomography in the assessment of nodular changes in pneumoconiosis in foundry workers in Lublin. *Ann Agric Environ Med*. 2004;11(2):279-84.
106. Collins LC, Willing S, Bretz R, Harty M, Lane E, Anderson WH. High-resolution CT in simple coal workers' pneumoconiosis. Lack of correlation with pulmonary function tests and arterial blood gas values. *Chest*. 1993;104(4):1156-62.
107. Aberle DR, Gamsu G, Ray CS, Feuerstein IM. Asbestos-related pleural and parenchymal fibrosis: detection with high-resolution CT. *Radiology*. 1988;166(3):729-34.
108. Bergin CJ, Castellino RA, Blank N, Moses L. Specificity of high-resolution CT findings in pulmonary asbestosis: do patients scanned for other indications have similar findings? *AJR Am J Roentgenol*. 1994;163(3):551-5.
109. Akira M, Yokoyama K, Yamamoto S, et al. Early asbestosis: evaluation with high-resolution CT. *Radiology*. 1991;178(2):409-16.
110. Afeltra A, Zennaro D, Garzia P, et al. Prevalence of interstitial lung involvement in patients with connective tissue diseases assessed with high-resolution computed tomography. *Scand J Rheumatol*. 2006;35(5):388-94.
111. Topcu F, Bayram H, Simsek M, et al. High-resolution computed tomography in cases with environmental exposure to asbestos in Turkey. *Respiration*. 2000;67:139-45.

112. Han D, Goo JM, Im JG, Lee KS, Paek DM, Park SH. Thin-section CT findings of arc-welders' pneumoconiosis. *Korean J Radiol*. 2000;1(2):79-83.
113. Lynch DA, Newell JD, Logan PM, King TE, Jr., Muller NL. Can CT distinguish hypersensitivity pneumonitis from idiopathic pulmonary fibrosis? *AJR Am J Roentgenol*. 1995;165(4):807-11.
114. Ziora D, Jastrzebski D, Lubina M, Wojdala A, Kozielski J. High-resolution computed tomography in hypersensitivity pneumonitis - correlation with pulmonary function. *Ann Agric Environ Med*. 2005;12(1):31-4.
115. Lynch DA, Gamsu G, Ray CS, Aberle DR. Asbestos-related focal lung masses: manifestations on conventional and high-resolution CT scans. *Radiology*. 1988;169(3):603-7.
116. Punjabi NM, Shade D, Patel AM, Wise RA. Measurement variability in single-breath diffusing capacity of the lung. *Chest*. 2003;123(4):1082-9.
117. Gaensler EA, Smith AA. Attachment for automated single breath diffusing capacity measurement. *Chest*. 1973;63(2):136-45.
118. Hughes JM, Pride NB. Examination of the carbon monoxide diffusing capacity (DL(CO)) in relation to its KCO and VA components. *Am J Respir Crit Care Med*. 2012;186(2):132-9.
119. Macintyre N, Crapo RO, Viegi G, et al. Standardisation of the single-breath determination of carbon monoxide uptake in the lung. *Eur Respir J*. 2005;26(4):720-35.
120. Johnson DC. Importance of adjusting carbon monoxide diffusing capacity (DLCO) and carbon monoxide transfer coefficient (KCO) for alveolar volume. *Respir Med*. 2000;94(1):28-37.
121. Frey TM, Crapo RO, Jensen RL, Elliott CG. Diurnal variation of the diffusing capacity of the lung: is it real? *Am Rev Respir Dis*. 1987;136(6):1381-4.
122. American Thoracic Society. Single-breath carbon monoxide diffusing capacity (transfer factor). Recommendations for a standard technique - 1995 update. *Am J Respir Crit Care Med*. 1995;152:2185-98.
123. Kaminsky DA, Whitman T, Callas PW. DLCO versus DLCO/VA as predictors of pulmonary gas exchange. *Respir Med*. 2007;101(5):989-94.
124. Dujic Z, Tocilj J, Boschi S, Saric M, Eterovic D. Biphasic lung diffusing capacity: detection of early asbestos induced changes in lung function. *Br J Ind Med*. 1992;49(4):260-7.
125. Abejie BA, Wang X, Kales SN, Christiani DC. Patterns of pulmonary dysfunction in asbestos workers: a cross-sectional study. *J Occup Med Toxicol*. 2010;512.
126. Orens JB, Kazerooni EA, Martinez FJ, et al. The sensitivity of high-resolution CT in detecting idiopathic pulmonary fibrosis proved by open lung biopsy. A prospective study. *Chest*. 1995;108(1):109-15.
127. Sette A, Neder JA, Nery LE, et al. Thin-section CT abnormalities and pulmonary gas exchange impairment in workers exposed to asbestos. *Radiology*. 2004;232(1):66-74.
128. Boros PW, Enright PL, Quanjer PH, Borsboom GJ, Wesolowski SP, Hyatt RE. Impaired lung compliance and DL,CO but no restrictive ventilatory defect in sarcoidosis. *Eur Respir J*. 2010;36(6):1315-22.
129. Dodson RF, O'Sullivan M, Corn CJ, Garcia JG, Stocks JM, Griffith DE. Analysis of ferruginous bodies in bronchoalveolar lavage from foundry workers. *Br J Ind Med*. 1993;50(11):1032-8.
130. Vathesatogkit P, Harkin TJ, Addrizzo-Harris DJ, Bodkin M, Crane M, Rom WN. Clinical correlation of asbestos bodies in BAL fluid. *Chest*. 2004;126(3):966-71.
131. Christman JW, Emerson RJ, Hemenway DR, Graham WG, Davis GS. Effects of work exposure, retirement, and smoking on bronchoalveolar lavage measurements of lung dust in Vermont granite workers. *Am Rev Respir Dis*. 1991;144(6):1307-13.
132. Meyer KC, Raghu G, Baughman RP, et al. An official American Thoracic Society clinical practice guideline: the clinical utility of bronchoalveolar lavage cellular analysis in interstitial lung disease. *Am J Respir Crit Care Med*. 2012;185(9):1004-14.
133. Teschler H, Thompson AB, Dollenkamp R, Konietzko N, Costabel U. Relevance of asbestos bodies in sputum. *Eur Respir J*. 1996;9(4):680-6.
134. Havarneanu D, Alexandrescu I, Popa D. The risk assessment in occupational exposure to asbestos dusts through sputum cytologic examination. *J Prev Med*. 2008;16(3-4):46-53.
135. Alexopoulos EC, Bouros D, Dimadi M, Serbescu A, Bakoyannis G, Kokkinis FP. Comparative analysis of induced sputum and bronchoalveolar lavage fluid (BALF) profile in asbestos exposed workers. *J Occup Med Toxicol*. 2011;623.
136. Pairon JC, Martinon L, Iwatsubo Y, et al. Retention of asbestos bodies in the lungs of welders. *Am J Ind Med*. 1994;25(6):793-804.
137. Corhay JL, Delavignette JP, Bury T, Saint-Remy P, Radermecker MF. Occult exposure to asbestos in steel workers revealed by bronchoalveolar lavage. *Arch Environ Health*. 1990;45(5):278-82.
138. De Vuyst P, Karjalainen A, Dumortier P, et al. Guidelines for mineral fibre analyses in biological samples: report of the ERS Working Group. European Respiratory Society. *Eur Respir J*. 1998;11(6):1416-26.
139. McLarty JW, Greenberg SD, Hurst GA, et al. The clinical significance of ferruginous bodies in sputa. *J Occup Med*. 1980;22(2):92-6.
140. Paris C, Galateau-Salle F, Creveuil C, et al. Asbestos bodies in the sputum of asbestos workers: correlation with occupational exposure. *Eur Respir J*. 2002;20(5):1167-73.

141. Sulotto F, Capellaro E, Chiesa A, Villari S, Bontempi S, Scansetti G. Relationship between asbestos bodies in sputum and the number of specimens. *Scand J Work Environ Health*. 1997;23(1):48-53.
142. Modin BE, Greenberg SD, Buffler PA, Lockhart JA, Seitzman LH, Awe RJ. Asbestos bodies in a general hospital/clinic population. *Acta Cytol*. 1982;26(5):667-77.
143. Karjalainen A, Anttila S, Mantyla T, Taskinen E, Kyyronen P, Tukiainen P. Asbestos bodies in bronchoalveolar lavage fluid in relation to occupational history. *Am J Ind Med*. 1994;26(5):645-54.
144. Sharma S, Pane J, Verma K. Effect of prednisolone treatment in chronic silicosis. *Am Rev Respir Dis*. 1991;143 (4 Pt 1):814-21.
145. Goodman G, Kaplan P, Stachura I, et al. Acute silicosis responding to corticosteroid therapy. *Chest*. 1992;101(2):366-70.
146. Wood DE, Eapen GA, Ettinger DS, et al. Lung cancer screening. *J Natl Compr Canc Netw*. 2012;10(2):240-65.
147. Ochmann U, Jorres RA, Nowak D. Long-term efficacy of pulmonary rehabilitation: a state-of-the-art review. *J Cardiopulm Rehabil Prev*. 2012;32(3):117-26.
148. Ochmann U, Kotschy-Lang N, Raab W, Kellberger J, Nowak D, Jorres RA. Long-term efficacy of pulmonary rehabilitation in patients with occupational respiratory diseases. *Respiration*. 2012;84(5):396-405.
149. Nicolson C, Phillips B, Denehy L. A survey of pulmonary rehabilitation programs in Australia and their associated maintenance programs and support groups. *National Cardiothoracic Group 9th Biennial Conference*. Melbourne, Australia: e-AJP; 2005:S22.
150. Department of Labor, Employment Standards Administration. Regulations Implementing the Federal Coal Mine Health and Safety Act of 1969, as Amended. *Federal Register*. 2000;65(245).
151. Muhm JM. Medical surveillance for respirator users. *J Occup Environ Med*. 1999;41(11):989-94.
152. American Thoracic Society. ATS Statement: Guidelines for the Six-Minute Walk Test. *Am J Respir Crit Care Med*. 2002;166:111-7.
153. Alhamad EH, Shaik SA, Idrees MM, Alanezi MO, Isnani AC. Outcome measures of the 6 minute walk test: relationships with physiologic and computed tomography findings in patients with sarcoidosis. *BMC Pulm Med*. 2010;1042.
154. Buch MH, Denton CP, Furst DE, et al. Submaximal exercise testing in the assessment of interstitial lung disease secondary to systemic sclerosis: reproducibility and correlations of the 6-min walk test. *Ann Rheum Dis*. 2007;66(2):169-73.
155. Mao J, Zhang J, Zhou S, et al. Updated assessment of the six-minute walk test as predictor of acute radiation-induced pneumonitis. *Int J Radiat Oncol Biol Phys*. 2007;67(3):759-67.
156. Modrykamien AM, Gudavalli R, McCarthy K, Parambil J. Echocardiography, 6-minute walk distance, and distance-saturation product as predictors of pulmonary arterial hypertension in idiopathic pulmonary fibrosis. *Respir Care*. 2010;55(5):584-8.
157. Gibbons WJ, Fruchter N, Sloan S, Levy RD. Reference values for a multiple repetition 6-minute walk test in healthy adults older than 20 years. *J Cardiopulm Rehabil*. 2001;21(2):87-93.
158. Solway S, Brooks D, Lacasse Y, Thomas S. A qualitative systematic overview of the measurement properties of functional walk tests used in the cardiorespiratory domain. *Chest*. 2001;119(1):256-70.
159. Wilsher M, Good N, Hopkins R, et al. The six-minute walk test using forehead oximetry is reliable in the assessment of scleroderma lung disease. *Respirology*. 2012;17(4):647-52.
160. Baughman RP, Sparkman BK, Lower EE. Six-minute walk test and health status assessment in sarcoidosis. *Chest*. 2007;132(1):207-13.
161. Chetta A, Aiello M, Foresi A, et al. Relationship between outcome measures of six-minute walk test and baseline lung function in patients with interstitial lung disease. *Sarcoidosis Vasc Diffuse Lung Dis*. 2001;18(2):170-5.
162. Flaherty KR, Andrei AC, Murray S, et al. Idiopathic pulmonary fibrosis: prognostic value of changes in physiology and six-minute-walk test. *Am J Respir Crit Care Med*. 2006;174(7):803-9.
163. Xaubet A, Serrano-Mollar A, Ancochea J. Pirfenidone for the treatment of idiopathic pulmonary fibrosis. *Expert Opin Pharmacother*. 2014;15(2):275-81.
164. Florian J, Rubin A, Mattiello R, Fontoura FF, Camargo Jde J, Teixeira PJ. Impact of pulmonary rehabilitation on quality of life and functional capacity in patients on waiting lists for lung transplantation. *J Bras Pneumol*. 2013;39(3):349-56.
165. Watanabe F, Taniguchi H, Sakamoto K, et al. Quadriceps weakness contributes to exercise capacity in nonspecific interstitial pneumonia. *Respir Med*. 2013;107(4):622-8.
166. Rammaert B, Leroy S, Cavestri B, Wallaert B, Grosbois JM. Home-based pulmonary rehabilitation in idiopathic pulmonary fibrosis. *Rev Mal Respir*. 2011;28(7):e52-7.
167. Heresi GA, Dweik RA. Strengths and limitations of the six-minute-walk test: a model biomarker study in idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med*. 2011;183(9):1122-4.
168. du Bois RM, Weycker D, Albera C, et al. Six-minute-walk test in idiopathic pulmonary fibrosis: test validation and minimal clinically important difference. *Am J Respir Crit Care Med*. 2011;183(9):1231-7.

169. Swigris JJ, Olson AL, Shlobin OA, Ahmad S, Brown KK, Nathan SD. Heart rate recovery after six-minute walk test predicts pulmonary hypertension in patients with idiopathic pulmonary fibrosis. *Respirology*. 2011;16(3):439-45.
170. Coelho AC, Knorst MM, Gazzana MB, Barreto SS. Predictors of physical and mental health-related quality of life in patients with interstitial lung disease: a multifactorial analysis. *J Bras Pneumol*. 2010;36(5):562-70.
171. Jenkins S, Cecins NM. Six-minute walk test in pulmonary rehabilitation: do all patients need a practice test? *Respirology*. 2010;15(8):1192-6.
172. Caminati A, Harari S. IPF: New insight in diagnosis and prognosis. *Respir Med*. 2010;104 Suppl 1S2-10.
173. Holland AE, Hill CJ, Conron M, Munro P, McDonald CF. Small changes in six-minute walk distance are important in diffuse parenchymal lung disease. *Respir Med*. 2009;103(10):1430-5.
174. Rasekaba T, Lee AL, Naughton MT, Williams TJ, Holland AE. The six-minute walk test: a useful metric for the cardiopulmonary patient. *Intern Med J*. 2009;39(8):495-501.
175. Lederer DJ, Arcasoy SM, Wilt JS, D'Ovidio F, Sonett JR, Kawut SM. Six-minute-walk distance predicts waiting list survival in idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med*. 2006;174(6):659-64.
176. Eaton T, Young P, Milne D, Wells AU. Six-minute walk, maximal exercise tests: reproducibility in fibrotic interstitial pneumonia. *Am J Respir Crit Care Med*. 2005;171(10):1150-7.
177. Leuchte HH, Neurohr C, Baumgartner R, et al. Brain natriuretic peptide and exercise capacity in lung fibrosis and pulmonary hypertension. *Am J Respir Crit Care Med*. 2004;170(4):360-5.
178. Kadikar A, Maurer J, Kesten S. The six-minute walk test: a guide to assessment for lung transplantation. *J Heart Lung Transplant*. 1997;16(3):313-9.
179. Doyle TJ, Washko GR, Fernandez IE, et al. Interstitial lung abnormalities and reduced exercise capacity. *Am J Respir Crit Care Med*. 2012;185(7):756-62.
180. Ochmann U, Kotschy-Lang N, Raab W, Kellberger J, Nowak D, Jorres RA. Is an individual prediction of maximal work rate by 6-minute walk distance and further measurements reliable in male patients with different lung diseases? *Respiration*. 2013;86(5):384-92.
181. Favre MN, Roche F, Januel B, et al. Exercise test and evaluation of exertional dyspnoea in former coal miners. *Rev Mal Respir*. 2002;19(3):315-22.
182. Stevens D, Elpern E, Sharma K, Szidon P, Ankin M, Kesten S. Comparison of hallway and treadmill six-minute walk tests. *Am J Respir Crit Care Med*. 1999;160(5 Pt 1):1540-3.
183. Chuang ML, Lin IF, Wasserman K. The body weight-walking distance product as related to lung function, anaerobic threshold and peak VO2 in COPD patients. *Respir Med*. 2001;95(7):618-26.
184. Carter R, Holiday DB, Nwasuruba C, Stocks J, Grothues C, Tiep B. 6-minute walk work for assessment of functional capacity in patients with COPD. *Chest*. 2003;123(5):1408-15.
185. Enright PL. The six-minute walk test. *Respir Care*. 2003;48(8):783-5.
186. Troosters T, Gosselink R, Decramer M. Six minute walking distance in healthy elderly subjects. *Eur Respir J*. 1999;14(2):270-4.
187. Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. *Am J Respir Crit Care Med*. 1998;158(5 Pt 1):1384-7.
188. Poh H, Eastwood PR, Cecins NM, Ho KT, Jenkins SC. Six-minute walk distance in healthy Singaporean adults cannot be predicted using reference equations derived from Caucasian populations. *Respirology*. 2006;11(2):211-6.
189. Pinto-Plata VM, Cote C, Cabral H, Taylor J, Celli BR. The 6-min walk distance: change over time and value as a predictor of survival in severe COPD. *Eur Respir J*. 2004;23(1):28-33.
190. Redelmeier DA, Bayoumi AM, Goldstein RS, Guyatt GH. Interpreting small differences in functional status: the Six Minute Walk test in chronic lung disease patients. *Am J Respir Crit Care Med*. 1997;155(4):1278-82.
191. Cote CG, Casanova C, Marin JM, et al. Validation and comparison of reference equations for the 6-min walk distance test. *Eur Respir J*. 2008;31(3):571-8.
192. Karpman C, DePew Z, LeBrasseur N, Novotny P, Benzo R. Determinants of gait speed in COPD. *Chest*. 2014;146(1):104-10.
193. Pimenta SP, Rocha RB, Baldi BG, Kawassaki Ade M, Kairalla RA, Carvalho CR. Desaturation - distance ratio: a new concept for a functional assessment of interstitial lung diseases. *Clinics (Sao Paulo)*. 2010;65(9):841-6.
194. Garin MC, Highland KB, Silver RM, Strange C. Limitations to the 6-minute walk test in interstitial lung disease and pulmonary hypertension in scleroderma. *J Rheumatol*. 2009;36(2):330-6.
195. International Labour Office. *International classification of radiographs of pneumoconiosis 1980. Occupational Safety and Health Series 22*. Geneva: ILO; 1980.
196. Harris JS, Sinnott PL, Holland JP, et al. Methodology to update the practice recommendations in the American College of Occupational and Environmental Medicine's Occupational Medicine Practice Guidelines, second edition. *J Occup Environ Med*. 2008;50(3):282-95.