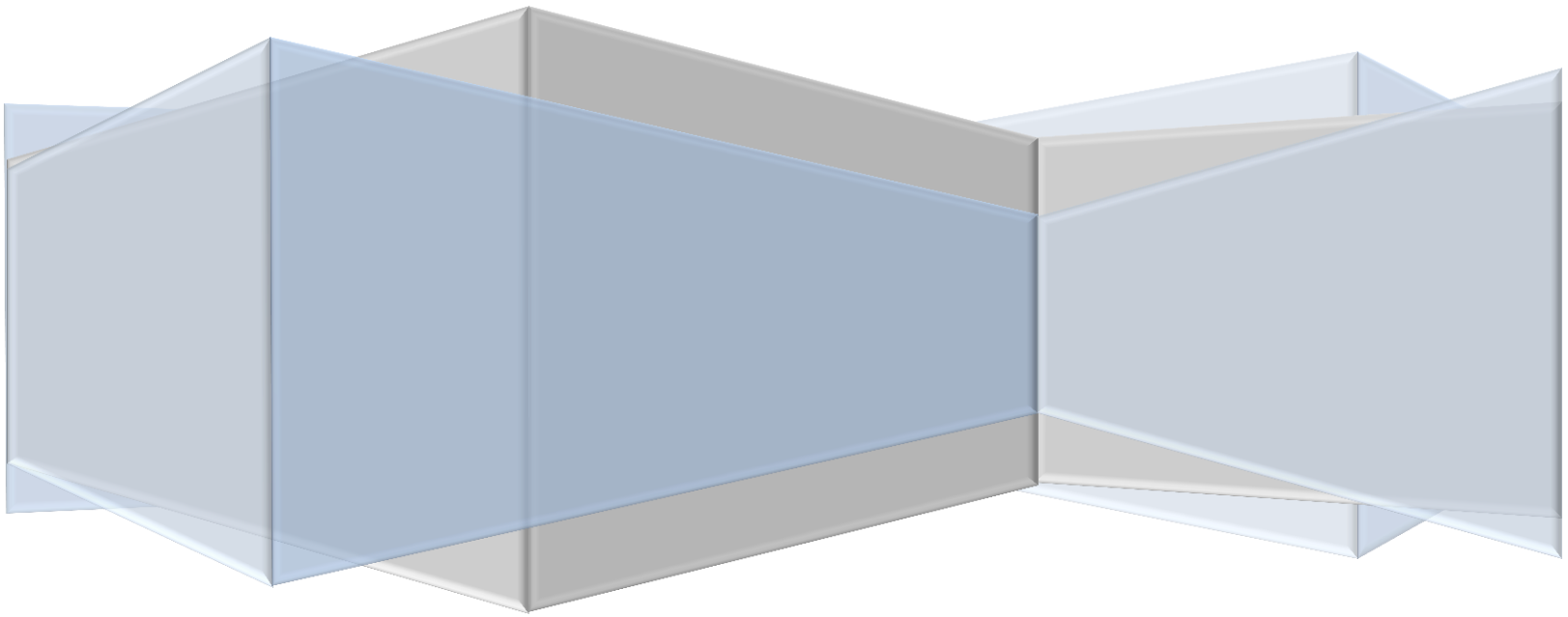
Pulmonary Fibrosis Foundation™

PFF Patient Registry Protocol

Version 1.0 date 21 Jan 2016



Contents

SYNOPSIS

The Pulmonary Fibrosis Foundation Patient Registry will collect data on at least 2,000 patients at approximately 40 clinical sites in the US. The Pulmonary Fibrosis Foundation Patient Registry will collect data on at least 2,000 patients at approximately 40 clinical sites in the US. The Registry is targeting enrollment of approximately 60% of the 2,000 ILD participants to have IPF. The aim of the Registry is to create a cohort of well-characterized patients with interstitial lung disease (ILD) for participation in retrospective and prospective research Patients who meet inclusion and exclusion criteria and are being treated at a Registry site can be asked to participate. Patients will be required to read and sign an IRB-approved informed consent document prior to any Registry activity taking place.

At the time of informed consent, participants will be asked to indicate if they are interested in being contacted by Registry site personnel for potential participation in future clinical trials and/or studies. Participants who opt out will not be contacted for future studies.
No clinical procedures, testing, or diagnostics will be required by virtue of Registry participation. Participants will permit Registry staff to abstract clinical data obtained as part of routine clinical care in the diagnosis and treatment of ILD. These data will be entered into a web-based, electronic data capture (EDC) by the Registry staff to at regular intervals. Some of these data will be retrospective, having been collected prior to consenting for the Registry. Computed tomography (CT) images collected for diagnosis and / or treatment will be de-identified at the Registry site and uploaded to a secure server that is a 21 CRF Part 11, GCP, and HIPAA compliant online imaging repository.

Participants will be asked to complete patient reported outcome (PRO) surveys related to ILD symptoms and quality of life at the time of enrollment and during clinical follow-up visits (Appendix A – PRO Questionnaires). Participants who are not seen for clinical follow-up within 12 months will be contacted by telephone or mail by Registry site personnel to complete the PRO assessment.

The University of Michigan Statistical Analysis of Biomedical and Educational Research (SABER) unit will serve as the Registry Data Coordinating Center and will manage data entered into a web based, CFR 21 Part 11 compliant electronic data capture (EDC) system by the Registry sites.

BACKGROUND & SIGNIFICANCE

Background

Interstitial lung diseases (ILD) describe a diverse group of conditions where, in general, the lung tissue becomes thickened, stiff, and scarred. The medical terminology used to describe this scar tissue is fibrosis, or in the lung – pulmonary fibrosis (PF).

Significance

As defined by the National Committee on Vital and Health Statistics, a medical or public health registry is "an organized system for the collection, storage, retrieval, analysis, and dissemination of information on individual persons who have either a particular disease, a condition that predisposes to the occurrence of a health-related event, or prior exposure to substances (or circumstances) known or suspected to cause adverse health effects."
While a number of single-center or state-wide registries of ILD currently exist, their value is limited by the lack of geographical coverage, a focus restricted to one of the many types of ILD, and/or data related only to a single institution's treatment patterns. There remains a need for a large, multi-center registry that will provide researchers and clinicians access to accurate, validated, standardized, well-characterized patient data. Analysis of these data may allow comparisons of the impact of biomarkers, genetic and environmental factors, and differing care patterns or treatment regimens across the spectrum of ILDs causing pulmonary fibrosis.

OBJECTIVES & SPECIFIC AIMS

Objective

The objective of this project is the development of a Pulmonary Fibrosis Foundation (PFF) Patient Registry that includes PFF Care Center Network (CCN) sites.

Specific Aims

This registry will accomplish the following specific aims.

1. Create a cohort of well-characterized patients with interstitial lung disease (ILD) for participation in retrospective and prospective research.

2. Collect clinically obtained data to support research in improving quality of life and outcomes of patients with ILD.

3. Collect data on the differing patterns of clinical care for patients with ILD to support research into the impact of those patterns on outcomes (including quality of life, mortality, safety profiles and others).

4. Collect baseline and longitudinal patient reported outcome (PRO) surveys for ILD research.

5. Improve awareness of and facilitate enrollment into clinical trials and research studies.

6. Gather data on healthcare utilization to be combined with clinical data in support of ILD research.

RESEARCH DESIGN AND METHODS

The PFF Patient Registry will collect data on at least 2,000 patients at approximately 40 clinical sites in the US. The Registry is targeting enrollment of approximately 60% of the 2,000 participants to have IPF. Additional patients and sites may be added depending on available funding for the Registry.
Patients will be followed from the time to consent through the lifetime of the Registry or the patient, unless the patient chooses to withdraw from the Registry.

Inclusion / Exclusion Criteria

To be eligible to participate in the registry, patients must meet all of the following inclusion and none of the exclusion criteria:

Inclusion Criteria

1. 18 years old or older

2. Understand and sign the informed consent document

3. ILD Diagnosis must be made / confirmed at a participating Registry center.

    a. The diagnostic evaluation must include, at a minimum, a medical history, physical examination, pulmonary function testing and a computerized tomography (CT) scan of the chest.

    b. If patients exhibit another pulmonary disease (such as emphysema or asthma), the primary disease must be ILD.

4. Anticipated additional follow up at the Registry center within one year.

Exclusion Criteria

1. Diagnosed with:

    a. Sarcoid

    b. Lymphangioleiomyomatosis (LAM)

    c. Pulmonary alveolar proteinosis (PAP)

    d. Cystic fibrosis (CF)

    e. Amyloidosis

Enrollment

Once the subject's written informed consent is obtained, the Registry personnel will assign a unique identifier that will be used to link patient data during participation in the PFF Patient Registry.

Collection of Subject Information

Participants will be asked to complete four (4) PRO surveys (Appendix A) at baseline and during clinic visits that occur at the enrolling Registry site during the period of the Registry. Participants will be informed that they may choose to not answer any questions.

At 6-month intervals from the time of enrollment, Registry site personnel will abstract specified data from the participant's medical record and enter these data to the DCC web based EDC system.

Data Elements

1. Demographics (e.g., birthdate, gender, marital status, state of residence)
2. Medical and family history information
3. Diagnostic information
4. Pulmonary function test results
5. Hospitalizations
6. Pulmonary rehabilitation utilization
7. Transplant status
8. Medication usage
9. Patient-reported outcomes
    a. Rand Short Form-6D (7 items)
    b. Leicester Cough Questionnaire (19 items)
    c. University of California San Diego Shortness of Breath Questionnaire (24 items)
    d. Fatigue Severity Scale (9 items)
10. Medical event and mortality data

Registry Activities (Schedule of Assessments)

Assessment	**Enrollment**[4]	**6- month Reporting Period Collection by Site**	**Early Termination**
Review patient eligibility (inclusion/exclusion criteria)	**X**		
Informed consent and medical release[2]	**X**		
Demographic data	**X**		
Date of ILD diagnosis and diagnostic process	**X**		
Treatment and medical history	**X**		
Smoking history	**X**		
Height	**X**		
Weight	**X**	**X**	**X**
ILD disease status, including pulmonary function and walk test results	**X**	**X**	**X**
Current treatment(s)	**X**	**X**	**X**
Patient Report Outcomes Questionnaires[3]	**X**	**X**	**X**
CT image upload	**X**	**X**	**X**
Significant medical events		**X**	**X**
Patient vital status		**X**	**X**
Reason for early termination			**X**

[1]Patients will be treated according to their physician's standard practice and discretion. No alterations to a patient's clinic schedule are expected as a result of participation in the Registry. Data from patient medical records will be abstracted and entered into the Registry every 6 months from the enrollment date.

[2]Written informed consent must be obtained prior to any Registry procedures.

[3]PRO questionnaires will be performed at enrollment and at each patient visit to the clinic and may be completed by telephone or mail if participant does not return to the Registry clinic within a 12 month period.

[4]Data should be entered into the database by the site staff within two weeks of consent.

STATISTICAL CONSIDERATIONS AND REGISTRY REPORTING

Because this registry is not hypothesis-driven, formal prospective calculations of sample sizes are not provided. However, we will periodically assess variation in ILD management, clinical events, and patient-reported outcomes to evaluate temporal changes concurrent with registry participation.

The analysis of registry data will lead to aggregated reports summarizing the epidemiology of ILD, as well as disease, treatment and outcomes. These reports will include a public annual data report, a center-specific report that is provided to CCN directors and center-level quality improvement data. Assessments will be made on general population characteristics, frequency of missing data elements, and such general elements as necessary to establish quality control of the data being entered into the registry. Prior to analysis and reporting, a statistical analysis plan (SAP) will be created by the DCC and approved by a committee consisting of CCN investigators and PFF personnel.

FUTURE STUDIES AND ANALYSES

Potential future research areas of interest include detailed ILD care patterns and related outcomes, trends in healthcare utilization, and predictors of patient-reported and clinical outcomes. By consenting to registry participation, subjects consent to existing, de-identified data to be used for these research purposes, without requirement of additional informed consent. Some of these data may have been collected by the clinical site prior to the provision of consent.

Access to the Registry data for research purposes not listed above shall be granted only upon the provision of documentation of IRB approval.
Contact of Registry participants for potential research studies or clinical trials will only be done through the enrolling site and only for subjects who consent for this contact. No identifiable information will be provided to sources outside of a participant's enrolling Registry site and the Registry Data Coordinating Center.

DATA TRANSMISSION, STORAGE AND CONFIDENTIALITY

Data will be transferred to the Registry Data Coordinating Center through a secure, electronic DCC Registry data collection system, OpenClinica or as an electronic data transfer via an encrypted secure sockets layer (SSL) protocol. Data transferred may include protected health information (PHI) (e.g. date of birth). This PHI will not be shared outside the enrolling center and the Registry Data Coordinating Center and will be removed or converted (e.g. changed to age) prior to distribution to researchers.

Centralized registry data security includes password-protected login to the EDC system, and access provided only to PFF or Registry Data Coordinating Center personnel authorized as part of the Registry. Data integrity is ensured by handling in accordance with CFR 21 Part 11 requirements.

Sites will be provided regular reports including details of their enrollment numbers, overall data collection statistics, and other information related to the activity at their site. Site reports will not include information about enrollment or activity at other participating sites.

The Registry Data Coordinating Center and staff of the PFF will periodically review reports on study enrollment and data collection statistics for the Registry overall, including site-by-site comparisons.

ADVERSE EVENTS

This is not a treatment protocol and no adverse event reporting is solicited. Spontaneously reported adverse events will be handled in accordance with applicable federal, state and local regulations. Local IRBs will be informed of any adverse event that takes place as a result of participation in this registry (e.g., HIPAA violations, or activity that threatens the confidentiality of the registry participants.)

ETHICAL CONSIDERATIONS

Institutional Review Board

All Registry documents will be approved by the Registry site's local Institutional Review Board (IRB) before any Registry activities take place.

Informed Consent

All patients must provide written informed consent. The informed consent process and document must be approved by the Registry site's IRB.
Participants will receive a copy of the informed consent form at the time of signing.

Participants will be informed that they may cease to participate in the Registry at any time. However all data collected up until the point of time consent is withdrawn will remain in the registry.

Risks of Participation

This is an observational study involving no more than minimal risk. Participation in the PFF Patient Registry does involve the potential risks of a breach of confidentiality of the medical record information and associated privacy of the participants. These risks will be clearly explained in the Registry consent document.

COSTS AND PAYMENTS

All costs associated with the implementation and maintenance of the PFF Patient Registry shall be supported by the PFF. Registry subjects or their health care providers will incur no costs. Participating sites will be compensated by the PFF for effort related to the Registry. PFF Patient Registry subjects will not be paid for their participation in the research registry.

APPENDIX A: PATIENT REPORTED OUTCOME QUESTIONNAIRES

Rand Short Form-6D

Your Health and Well-Being

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. ***Thank you for completing this survey!***

For each of the following questions, please mark an ☒ in the one box that best describes your answer.

1. The following questions are about activities you might do during a typical day. Does <u>your health now limit you</u> in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	☐1	☐2	☐3
b Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐1	☐2	☐3
c Bathing or dressing yourself	☐1	☐2	☐3

2. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Were limited in the kind of work or other activities	☐1	☐2	☐3	☐4	☐5

3. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Accomplished less than you would like	☐1	☐2	☐3	☐4	☐5

4. How much bodily pain have you had during the past 4 weeks?

None	Very mild	Mild	Moderate	Severe	Very Severe
☐1	☐2	☐3	☐4	☐5	☐6

5. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐1	☐2	☐3	☐4	☐5

6. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Have you been very nervous?	☐1	☐2	☐3	☐4	☐5
b Did you have a lot of energy?	☐1	☐2	☐3	☐4	☐5
c Have you felt downhearted and depressed?	☐1	☐2	☐3	☐4	☐5

7. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐1	☐2	☐3	☐4	☐5

THANK YOU FOR COMPLETING THESE QUESTIONS!

Leicester Cough Questionnaire

This questionnaire is designed to assess the impact of cough on various aspects of your life. Read each question carefully and answer by CIRCLING the response that best applies to you. Please answer ALL questions, as honestly as you can.

1. In the last 2 weeks, have you had chest or stomach pains as a result of your cough?

1	2	3	4	5	6	7
All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time

2. In the last 2 weeks, have you been bothered by sputum (phlegm) production when you cough?

1	2	3	4	5	6	7
Every time	Most times	Several times	Some times	Occasionally	Rarely	Never

3. In the last 2 weeks, have you been tired because of your cough?

1	2	3	4	5	6	7
All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time

4. In the last 2 weeks, have you felt in control of your cough?

1	2	3	4	5	6	7
None of the time	Hardly any of the time	A little of the time	Some of the time	A good bit of the time	Most of the time	All of the time

5. How often during the last 2 weeks have you felt embarrassed by your coughing?

1	2	3	4	5	6	7
All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time

6. In the last 2 weeks, my cough has made me feel anxious

1	2	3	4	5	6	7
All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time

7. In the last 2 weeks, my cough has interfered with my job, or other daily tasks

1	2	3	4	5	6	7
All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time

8. In the last 2 weeks, I felt that my cough interfered with the overall enjoyment of my life

1	2	3	4	5	6	7
All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time

9. In the last 2 weeks, exposure to paints or fumes has made me cough

1	2	3	4	5	6	7
All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time

10. In the last 2 weeks, has your cough disturbed your sleep?

1	2	3	4	5	6	7
All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time

11. In the last 2 weeks, how many times a day have you had coughing bouts?

1 All of the time (continuously)	2 Most times during the day	3 Several times during the day	4 Some times during the day	5 Occasionally through the day	6 Rarely	7 None

12. In the last 2 weeks, my cough has made me feel frustrated

1	2	3	4	5	6	7
All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time

13. In the last 2 weeks, my cough has made me feel fed up

1	2	3	4	5	6	7
All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time

14. In the last 2 weeks, have you suffered from a hoarse voice as a result of your cough?

1	2	3	4	5	6	7
All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time

15. In the last 2 weeks, have you had a lot of energy?

1	2	3	4	5	6	7
None of the time	Hardly any of the time	A little of the time	Some of the time	A good bit of the time	Most of the time	All of the time

16. In the last 2 weeks, have you worried that your cough may indicate serious illness?

1	2	3	4	5	6	7
All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time

17. In the last 2 weeks, have you been concerned that other people think something is wrong with you, because of your cough?

1	2	3	4	5	6	7
All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time

18. In the last 2 weeks, my cough has interrupted conversation or telephone calls

1	2	3	4	5	6	7
Every time	Most times	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time

19. In the last 2 weeks, I feel that my cough has annoyed my partner, family or friends

1	2	3	4	5	6	7
Every time I cough	Most times when I cough	Several times when I cough	Some times when I cough	Occasionally when I cough	Rarely	Never

Thank you for completing this questionnaire.

University of California San Diego Shortness of Breath Questionnaire

UCSD MEDICAL CENTER
PULMONARY REHABILITATION PROGRAM
SHORTNESS-OF-BREATH QUESTIONNAIRE

Please rate the breathlessness you experience when you do, or if you were to do, each of the following tasks. **Do not skip any items**. If you've never performed a task or no longer perform it, give your best estimate of the breathlessness you would experience while doing that activity. Please review the two sample questions below before turning the page to begin the questionnaire.

When I do, or if I were to do, the following tasks, I would rate my breathlessness as:

0	None at all
1	
2	
3	
4	Severe
5	Maximal or unable to do because of breathlessness

1. Brushing teeth ..... **0 1 2 ③ 4 5**

Harry has felt moderately short of breath during the past week while brushing his teeth and so circles a three for this activity.

2. Mowing the lawn ..... **0 1 2 3 4 ⑤**

Anne has never mowed the lawn before but estimates that she would have been too breathless to do this activity during the past week. She circles a five for this activity.

When I do, or if I were to do, the following tasks, I would rate my breathlessness as:

0	None at all
1	
2	
3	
4	Severe
5	Maximal or unable to do because of breathlessness

1.	At rest	0	1	2	3	4	5
2.	Walking on a level at your own pace	0	1	2	3	4	5
3.	Walking on a level with others your age	0	1	2	3	4	5
4.	Walking up a hill	0	1	2	3	4	5
5	Walking up stairs	0	1	2	3	4	5
6.	While eating	0	1	2	3	4	5
7.	Standing up from a chair	0	1	2	3	4	5
8.	Brushing teeth	0	1	2	3	4	5
9.	Shaving and/or brushing hair	0	1	2	3	4	5
10.	Showering/bathing	0	1	2	3	4	5
11.	Dressing	0	1	2	3	4	5
12.	Picking up and straightening	0	1	2	3	4	5

When I do, or if I were to do, the following tasks, I would rate my breathlessness as:

0	None at all
1	
2	
3	
4	Severe
5	Maximal or unable to do because of breathlessness

13.	Doing dishes	0	1	2	3	4	5
14.	Sweeping /vacuuming	0	1	2	3	4	5
15.	Making bed	0	1	2	3	4	5
16.	Shopping	0	1	2	3	4	5
17.	Doing laundry	0	1	2	3	4	5
18.	Washing car	0	1	2	3	4	5
19.	Mowing lawn	0	1	2	3	4	5
20.	Watering lawn	0	1	2	3	4	5
21.	Sexual activities	0	1	2	3	4	5

How much do these limit you in your daily life?

22.	Shortness of breath	0	1	2	3	4	5
23.	Fear of "hurting myself" by overexerting	0	1	2	3	4	5
24.	Fear of shortness of breath	0	1	2	3	4	5

Fatigue Severity Scale

Fatigue Severity Scale

The FSS questionnaire contains nine statements that attempt to explore severity of fatigue symptoms. Read each statement and circle a number from 1 to 7, depending on how appropriate they felt the statement applied to them over the preceding week. A low value indicates that the statement is not very appropriate whereas a high value indicates agreement (1 disagree, 7 agree).

FSS Questionnaire							
During the past week, I have found that:	**Score**						
1. My motivation is lower when I am fatigued.	1	2	3	4	5	6	7
2. Exercise brings on my fatigue.	1	2	3	4	5	6	7
3. I am easily fatigued.	1	2	3	4	5	6	7
4. Fatigue interferes with my physical functioning.	1	2	3	4	5	6	7
5. Fatigue causes frequent problems for me.	1	2	3	4	5	6	7
6. My fatigue prevents sustained physical functioning.	1	2	3	4	5	6	7
7. Fatigue interferes with carrying out certain duties and responsibilities.	1	2	3	4	5	6	7
8. Fatigue is among my three most disabling symptoms.	1	2	3	4	5	6	7
9. Fatigue interferes with my work, family, or social life.	1	2	3	4	5	6	7

The scoring is done by calculating the average response to the questions (adding up all the answers and dividing by nine).