Fatigue
Fatigue

☐ **Rationale**

This guideline is adapted for inter-professional primary care providers working in various settings in Fraser Health, British Columbia and the Fraser Valley Cancer Center and any other clinical setting to which a user may see the guidelines as applicable.

☐ **Scope**

This guideline provides recommendations for the assessment and symptom management of adult patients (age 19 years and older) that are living with advanced life threatening illness and experiencing the symptom of fatigue. This guideline does not address disease specific approaches in the management of weakness.

Fatigue is one of the most common symptoms in advanced cancer and is nearly universal in the terminal stages of illness.\(^1\) Fatigue is reported from 36% to 78% in studies of cancer patients at various stages of their disease.\(^2\)

☐ **Definition of Terms**

Fatigue is defined as “a subjective perception and/or experience related to disease, emotional state and/or treatment. Fatigue is a multidimensional symptom involving physical, emotional, social and spiritual well-being and affecting quality of life.”\(^3\) The words asthenia and fatigue are often used interchangeably by health professionals.\(^2, 4, 5\) Patients and families often use a number of words interchangeably to describe weakness; drowsiness, tiredness, fatigue, lethargy, reduced alertness.\(^6\)

☐ **Standard of Care**

1. Assessment
2. Diagnosis
3. Education
4. Treatment: Nonpharmacological
5. Treatment: Pharmacological
**Recommendation 1**  
**Assessment of Fatigue**

Ongoing comprehensive assessment is the foundation of effective management of fatigue, including interview, physical assessment, medication review, medical and surgical review, sleep patterns, psychosocial review, review of physical environment and appropriate diagnostics. Assessment must determine the cause, effectiveness and impact on quality of life for the patient and their family\(^{(2)}\) (see Table 1).

*Table 1: Fatigue Assessment using Acronym O, P, Q, R, S, T, U and V*

<table>
<thead>
<tr>
<th><strong>Onset</strong></th>
<th>When did it begin? How long does it last? How often does it occur?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Provoking / Palliating</strong></td>
<td>What brings it on? What makes it better? What makes it worse?</td>
</tr>
<tr>
<td><strong>Quality</strong></td>
<td>What does it feel like? How are you sleeping? How is your appetite? Have you lost weight?</td>
</tr>
<tr>
<td><strong>Region / Radiation</strong></td>
<td>Is this an overall feeling or is it localized?</td>
</tr>
<tr>
<td><strong>Severity</strong></td>
<td>What is the intensity of this symptom (On a scale of 0 to 10 with 0 being none and 10 being worst possible)? Right Now? At Best? At Worst? On Average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom?</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>What medications and treatments are you currently using? How effective are these? Do you have any side effects from the medications and treatments? What medications/treatments have you used in the past?</td>
</tr>
<tr>
<td><strong>Understanding / Impact on You</strong></td>
<td>What do you believe is causing this symptom? How is this symptom affecting you and/or your family?</td>
</tr>
<tr>
<td><strong>Values</strong></td>
<td>What is your goal for this symptom? What is your comfort goal or acceptable level for this symptom (On a scale of 0 to 10 with 0 being none and 10 being worst possible)? Are there any other views or feelings about this symptom that are important to you or your family?</td>
</tr>
</tbody>
</table>

* Physical Assessment (as appropriate for symptom)
**Recommendation 1** *Assessment of Fatigue continued...*

**Physical Examination**[^2, 7, 8]

<table>
<thead>
<tr>
<th>Region</th>
<th>Look for</th>
<th>Suggests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head</td>
<td>Coarse hair</td>
<td>Hypothyroid</td>
</tr>
<tr>
<td></td>
<td>Thinning of lateral third of eyebrows</td>
<td>Hypothyroid</td>
</tr>
<tr>
<td></td>
<td>Lid lag</td>
<td>Hypothyroid</td>
</tr>
<tr>
<td>Eyes</td>
<td>Miosis</td>
<td>Opioid overdose</td>
</tr>
<tr>
<td></td>
<td>Conjunctival pallor</td>
<td>Anemia</td>
</tr>
<tr>
<td>Mouth</td>
<td>Cheliosis, reddened shiny tongue</td>
<td>Vitamin deficiencies</td>
</tr>
<tr>
<td>Abdomen</td>
<td>Palpable bladder</td>
<td>Spinal cord compression</td>
</tr>
<tr>
<td>Extremities</td>
<td>Asterixsis</td>
<td>Hepatic or renal insufficiency</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypokalemia</td>
</tr>
<tr>
<td>Back</td>
<td>Tenderness to percussion over vertebrae</td>
<td>Spinal cord compression</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Proximal myopathy</td>
<td>Eaton-Lambert or other myopathic syndrome</td>
</tr>
<tr>
<td></td>
<td>Absent deep tendon reflexes (DTRs) that reappear after 10 seconds of maximal voluntary contraction</td>
<td>Eaton-Lambert syndrome</td>
</tr>
<tr>
<td></td>
<td>Prolonged relaxation time of DTRs</td>
<td>Hypothyroid</td>
</tr>
<tr>
<td></td>
<td>Hyperactive DTRs</td>
<td>Acute cord compression</td>
</tr>
<tr>
<td></td>
<td>Spasticity, sensory loss, extensor plantar</td>
<td>Acute cord compression</td>
</tr>
</tbody>
</table>

**Laboratory studies**

Hemoglobin, WBC count, serum sodium, potassium, calcium, magnesium, blood glucose, serum urea, creatinine, liver enzymes, triiodothyronine, thyroxine, drug levels (phenytoin, digoxin).[^1]

**Recommendation 2** *Diagnosis*

Identifying the underlying etiology of weakness is essential in determining the interventions required.

Use an objective scale, such as the Palliative Performance Scale (PPS) or the performance status scale of the Eastern Co-operative Oncology Group (ECOG)[^2](see Appendix A). The diagnosis of fatigue is based on the patient’s report of the symptom.[^5] It is important to document therapeutic outcome in both subjective and objective perspectives in palliative care of cancer patients.[^9]
**Recommendation 2** Diagnosis continued...

**Causes of Fatigue:**

- Fatigue usually has **multiple causes**.\(^1,2,5,8,10-12\)
- **Tumour related:**
  - Altered metabolism.\(^2\)
  - Cancer cachexia – wasting affects both skeletal and cardiac muscle.\(^2,4-6,11\)
  - Cancer-induced cytokines and other substances.\(^2,4\)
  - Paraneoplastic syndromes – Eaton-Lambert and other myopathies.\(^2,4,6,7\)
  - Spinal cord compression.\(^2,6\)
  - Tumour burden.\(^2,6\)
- **Treatment related:**
  - Chemotherapy.\(^4,6-8,12\)
  - Radiation therapy.\(^4,6-8,12\)
  - Surgery.\(^4\)
  - Biotherapy.\(^12\)
- **Non cancer related:**
  - Autonomic failure – postural hypotension, occasional syncope, fixed heart rate and gastrointestinal symptoms (nausea, anorexia, constipation or diarrhea).\(^7,11,13\)
  - Cardiopulmonary disorders.\(^1,2,4,5,7-9,12\)
- **Reversible causes:**
  - Anemia.\(^2,4,11,12\)
  - Bed rest.\(^1,2,4,6,7,11,12\)
  - Bleeding.
  - Depression\(^4-7,12,13\) or anxiety.\(^4,5,12\)
  - Dehydration.\(^2,4,6,7,13\)
  - Drugs – opioids, antidepressants, phenothiazines\(^2,4-7,12,13\) beta blockers\(^12\) phenytoin, levothyroxine.
  - Endocrine imbalances – hypothyroid, hypoadrenalism (most often due to rapid withdrawal of corticosteroid medication).\(^8,12\) diabetes mellitus\(^4\) and Addison's disease.\(^4-6\)
  - Hypercapnia or hypoxia\(^1,2,4-7,13\)
Fatigue

Recommendation 2  Diagnosis continued...

- Reversible causes continued:
  - Insufficient sleep. (1, 2, 4-8, 12, 13)
  - Metabolic disturbances – hypercalcemia, hypokalemia (4) and hyponatremia. (1, 2, 4-8)
  - Occult or chronic sepsis. (5-7)
  - Poor nutrition. (1, 5, 8, 12, 13)
  - Unrelieved symptoms – pain, diarrhea, nausea and vomiting. (2)

Recommendation 3  Education

- Patients and family will focus on the symptom rather than its underlying cause. Often this complaint is viewed as the patient has “given up” or is “not fighting”. Education must center on what is and is not correctable or beyond the patient’s control (14) and giving the patient “permission to rest”. (13) Work with patients and family caregivers to improve assessment of fatigue and identify management strategies. (2, 4, 6, 8, 13, 15)
- Help patient plan periods of rest and periods of activity to maximize the energy the patient has available for things that are really important to him/her. (2, 4-6, 8, 12, 15)
- Help the patient to delegate tasks that he/she is no longer able to perform and arrange for assistance where necessary. (2)
- When fatigue is mild, encourage moderate physical activity to preserve muscle function. As weakness progresses, use physical aids (walkers, grab bars) to help preserve mobility. (16) Rehabilitation goals need to be carefully weighed when the patient has a short life expectancy to assure that the benefits of treatment outweigh the burdens. (2, 4, 5)

Recommendation 4  Treatment: Nonpharmacological

Anemia – refrain from transfusion unless the patient is severely symptomatic and the patient is capable of benefiting from an increased red cell mass (ECOG of 3 or better). (9)

Depression/anxiety disorders – counseling. (12, 16) Patient mobility may help combat depression. (1) Massage and aromatherapy have been found to offer some relief for depression related fatigue. (13) Consider attention restoring activities (exposure to natural environment, music). (12, 14)

Dehydration – give fluids orally (4) or parenterally (I.V. or hypodermoclysis). (2)
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Recommendation 4  Treatment: Nonpharmacological continued...

Hypercalcemia – give hydration.\(^{(2, 6)}\)

Hypokalemia – for severe hypokalemia (potassium less than 2.8 mEq per litre) give potassium rich foods (citrus juice, tomatoes, bananas).\(^{(4)}\)

Hyponatremia – fluid restriction is frequently undesirable for patients and onerous for caregivers.\(^{(7, 13)}\)

Poor nutrition – nutritional counseling\(^{(6, 12)}\) although in late stages eating becomes more important for pleasure and comfort than nutrition.\(^{(2, 4, 8, 15)}\)

Prolonged immobilization – physiotherapy.\(^{(7, 12)}\) Exercise has been shown to have the strongest evidence of benefit.\(^{(11)}\) Daily stretching or isometric muscle contractions can help maintain muscle strength.\(^{(5, 7, 14)}\)

Sleep disturbances – sleep therapy\(^{(12, 13)}\) such as stimulus control (avoiding caffeine and stimulants, going to bed when sleepy), sleep consolidation strategies (avoiding long naps, limiting time in bed) strategies to reduce cognitive-emotional arousal and cognitive-behavioural interventions (relaxation training).\(^{(2)}\)

Recommendation 5  Treatment: Pharmacological

Anorexia/cachexia – give dexamethasone 4 mg PO daily and multivitamins.\(^{(2, 5, 7, 14)}\)

Depression – consider psychostimulants. See Fraser Health Hospice Palliative Care Symptom Guideline for Depression.

Endocrine imbalance – give replacement therapy (thyroid hormone or restart corticosteroids if recently withdrawn).\(^{(2)}\)

Hypercalcemia – see Fraser Health Hospice Palliative Care Symptom Guideline for Hypercalcemia.

Hypokalemia – change loop diuretic to potassium sparing diuretic (spironolactone 100 mg daily) for a few days and recheck serum potassium. Correct hypokalemia with potassium supplement.\(^{(2)}\)

Insomnia – give sedative or hypnotic medication.\(^{(2)}\)

Sepsis – give antibiotics and antipyretics where appropriate.\(^{(2)}\)
Fatigue

References

Information was compiled using the CINAHL, Medline (1996 to April 2006) and Cochrane DSR, ACP Journal Club, DARE and CCTR databases, limiting to reviews/systematic reviews, clinical trials, case studies and guidelines/protocols using fatigue/weakness/asthenia terms in conjunction with palliative/hospice/end of life/dying. Palliative care textbooks mentioned in generated articles were hand searched. Articles not written in English were excluded.


Approved by: Hospice Palliative Care, Clinical Practice Committee, November 24, 2006
# Palliative Performance Scale (PPSv2) – version 2

<table>
<thead>
<tr>
<th>PPS Level</th>
<th>Ambulation</th>
<th>Activity &amp; Evidence of Disease</th>
<th>Self-Care</th>
<th>Intake</th>
<th>Conscious Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>Full</td>
<td>Normal activity &amp; work</td>
<td>Full</td>
<td>Normal</td>
<td>Full</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No evidence of disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>90%</td>
<td>Full</td>
<td>Normal activity &amp; work</td>
<td>Full</td>
<td>Normal</td>
<td>Full</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Some evidence of disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>80%</td>
<td>Full</td>
<td>Normal activity with Effort</td>
<td>Full</td>
<td>Normal or reduced</td>
<td>Full</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Some evidence of disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70%</td>
<td>Reduced</td>
<td>Unable Normal Job/Work</td>
<td>Occasional assistance necessary</td>
<td>Normal or reduced</td>
<td>Full</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Significant disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60%</td>
<td>Reduced</td>
<td>Unable hobby/house work</td>
<td>Considerable assistance required</td>
<td>Normal or reduced</td>
<td>Full or Confusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Significant disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50%</td>
<td>Mainly Sit/Lie</td>
<td>Unable to do any work</td>
<td>Considerable assistance required</td>
<td>Normal or reduced</td>
<td>Full or Confusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Extensive disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40%</td>
<td>Mainly in Bed</td>
<td>Unable to do most activity</td>
<td>Mainly assistance</td>
<td>Normal or reduced</td>
<td>Full or Drowsy +/- Confusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Extensive disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30%</td>
<td>Totally Bed Bound</td>
<td>Unable to do any activity</td>
<td>Total Care</td>
<td>Normal or reduced</td>
<td>Full or Drowsy +/- Confusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Extensive disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20%</td>
<td>Totally Bed Bound</td>
<td>Unable to do any activity</td>
<td>Total Care</td>
<td>Minimal to sips</td>
<td>Full or Drowsy +/- Confusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Extensive disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10%</td>
<td>Totally Bed Bound</td>
<td>Unable to do any activity</td>
<td>Total Care</td>
<td>Mouth care only</td>
<td>Drowsy or Coma +/- Confusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Extensive disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0%</td>
<td>Death</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

## Instructions for Use of PPS (see also definition of terms)

1. PPS scores are determined by reading horizontally at each level to find a ‘best fit’ for the patient which is then assigned as the PPS% score.

2. Begin at the left column and read downwards until the appropriate ambulation level is reached, then read across to the next column and downwards again until the activity/evidence of disease is located. These steps are repeated until all five columns are covered before assigning the actual PPS for that patient. In this way, ‘leftward’ columns (columns to the left of any specific column) are ‘stronger’ determinants and generally take precedence over others.

Example 1: A patient who spends the majority of the day sitting or lying down due to fatigue from advanced disease and requires considerable assistance to walk even for short distances but who is otherwise fully conscious level with good intake would be scored at PPS 50%.
Example 2: A patient who has become paralyzed and quadriplegic requiring total care would be PPS 30%. Although this patient may be placed in a wheelchair (and perhaps seem initially to be at 50%), the score is 30% because he or she would be otherwise totally bed bound due to the disease or complication if it were not for caregivers providing total care including lift/transfer. The patient may have normal intake and full conscious level.

Example 3: However, if the patient in example 2 was paraplegic and bed bound but still able to do some self-care such as feed themselves, then the PPS would be higher at 40 or 50% since he or she is not ‘total care.’

3. PPS scores are in 10% increments only. Sometimes, there are several columns easily placed at one level but one or two which seem better at a higher or lower level. One then needs to make a ‘best fit’ decision. Choosing a ‘half-fit’ value of PPS 45%, for example, is not correct. The combination of clinical judgment and ‘leftward precedence’ is used to determine whether 40% or 50% is the more accurate score for that patient.

4. PPS may be used for several purposes. First, it is an excellent communication tool for quickly describing a patient’s current functional level. Second, it may have value in criteria for workload assessment or other measurements and comparisons. Finally, it appears to have prognostic value.

**Definition of Terms for PPS**

As noted below, some of the terms have similar meanings with the differences being more readily apparent as one reads horizontally across each row to find an overall ‘best fit’ using all five columns.

**1. Ambulation**

The items ‘mainly sit/lie,’ ‘mainly in bed,’ and ‘totally bed bound’ are clearly similar. The subtle differences are related to items in the self-care column. For example, ‘totally bed bound’ at PPS 30% is due to either profound weakness or paralysis such that the patient not only can’t get out of bed but is also unable to do any self-care. The difference between ‘sit/lie’ and ‘bed’ is proportionate to the amount of time the patient is able to sit up vs need to lie down.

‘Reduced ambulation’ is located at the PPS 70% and PPS 60% level. By using the adjacent column, the reduction of ambulation is tied to inability to carry out their normal job, work occupation or some hobbies or housework activities. The person is still able to walk and transfer on their own but at PPS 60% needs occasional assistance.
2. Activity & Extent of disease

‘Some,’ ‘significant,’ and ‘extensive’ disease refer to physical and investigative evidence which shows degrees of progression. For example in breast cancer, a local recurrence would imply ‘some’ disease, one or two metastases in the lung or bone would imply ‘significant’ disease, whereas multiple metastases in lung, bone, liver, brain, hypercalcemia or other major complications would be ‘extensive’ disease. The extent may also refer to progression of disease despite active treatments. Using PPS in AIDS, ‘some’ may mean the shift from HIV to AIDS, ‘significant’ implies progression in physical decline, new or difficult symptoms and laboratory findings with low counts. ‘Extensive’ refers to one or more serious complications with or without continuation of active antiretrovirals, antibiotics, etc.

The above extent of disease is also judged in context with the ability to maintain one’s work and hobbies or activities. Decline in activity may mean the person still plays golf but reduces from playing 18 holes to 9 holes, or just a par 3, or to backyard putting. People who enjoy walking will gradually reduce the distance covered, although they may continue trying, sometimes even close to death (eg. trying to walk the halls).

3. Self-Care

‘Occasional assistance’ means that most of the time patients are able to transfer out of bed, walk, wash, toilet and eat by their own means, but that on occasion (perhaps once daily or a few times weekly) they require minor assistance.

‘Considerable assistance’ means that regularly every day the patient needs help, usually by one person, to do some of the activities noted above. For example, the person needs help to get to the bathroom but is then able to brush his or her teeth or wash at least hands and face. Food will often need to be cut into edible sizes but the patient is then able to eat of his or her own accord.

‘Mainly assistance’ is a further extension of ‘considerable.’ Using the above example, the patient now needs help getting up but also needs assistance washing his face and shaving, but can usually eat with minimal or no help. This may fluctuate according to fatigue during the day.

‘Total care’ means that the patient is completely unable to eat without help, toilet or do any self-care. Depending on the clinical situation, the patient may or may not be able to chew and swallow food once prepared and fed to him or her.

4. Intake

Changes in intake are quite obvious with ‘normal intake’ referring to the person’s usual eating habits while healthy. ‘Reduced’ means any reduction from that and is highly variable according to the unique individual circumstances. ‘Minimal’ refers to very small amounts, usually pureed or liquid, which are well below nutritional sustenance.
5. Conscious Level

‘Full consciousness’ implies full alertness and orientation with good cognitive abilities in various domains of thinking, memory, etc. ‘Confusion’ is used to denote presence of either delirium or dementia and is a reduced level of consciousness. It may be mild, moderate or severe with multiple possible etiologies. ‘Drowsiness’ implies either fatigue, drug side effects, delirium or closeness to death and is sometimes included in the term stupor. ‘Coma’ in this context is the absence of response to verbal or physical stimuli; some reflexes may or may not remain. The depth of coma may fluctuate throughout a 24 hour period.
Appendix B

Fatigue

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**ECOG Performance Status***(17)**

<table>
<thead>
<tr>
<th>Grade</th>
<th>ECOG</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all pre-disease performance without restriction.</td>
</tr>
<tr>
<td>1</td>
<td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all self care but unable to carry out any work activities. Up and about more than 50% of waking hours.</td>
</tr>
<tr>
<td>3</td>
<td>Capable of only limited self care, confined to bed or chair more than 50% of waking hours.</td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled. Cannot carry on any self care. Totally confined to bed or chair.</td>
</tr>
<tr>
<td>5</td>
<td>Dead.</td>
</tr>
</tbody>
</table>

The Eastern Cooperative Oncology Group, Robert Comis M.D., Group Chair.