Multidisciplinary Management of Cancer-Related Fatigue
Speaker Disclosure

• Grant/Sponsorship Support: Astellas, AZ
• Honorarium/Consulting Fees/Speaker Fees: Astellas, Janssen, Roche, AZ, Sanofi-Aventis, Ipsen, Merck
Objectives

- Review common causes of cancer related fatigue and how to assess
- Discuss treatment options for fatigue based on the domains that might contribute
- Discuss a new patient fatigue management program under development for patients and caregivers
Objectives

01 What is it?
Describe the prevalence and impact of cancer-related fatigue (CRF)

02 How to assess?
Discuss appropriate screening and assessment of CRF

03 How to treat?
Recommend or refer to physical activity, psychosocial, sleep, spiritual, and nutrition-based interventions that can help reduce CRF

04 Who can help?
Recognize the role of a multidisciplinary team approach in managing CRF and tailoring interventions to the needs of the individual patient
Cancer-Related Fatigue: What is it? Why is it important to my practice and my patients?
What Is Cancer-Related Fatigue (CRF)?

“A distressing, persistent, subjective sense of tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning”

What Is the Difference Between Normal and Cancer-Related Fatigue?

- Longer lasting, unrelieved by rest
- May be associated with poor memory and concentration
- Possible loss of enjoyment of previously valued activities or interactions

Alberta Health Service (AHS) patient guide to cancer related fatigue, 2017.
What Is the Prevalence of CRF?

- Reporting prevalence will vary depending on time point and approach/instrument used to assess CRF
  - May be present at initial diagnosis
  - Often increases with treatment

Common and persistent

59-100%

What Is the Impact of CRF?

**Patients**
- May affect all activities of daily living and quality of life
- Impact on other symptoms associated with cancer and its treatment
- May reduce adherence with cancer treatment

**Informal Caregivers**
- Anxiety and distress over loved one’s symptoms
- Exhaustion and burnout
- Frequent absenteeism or need to take leave of absence to provide care
- Frustration with healthcare professionals (HCPs)

**Healthcare System**
- Costs (direct/indirect) of more frequent visits
- Patient-directed concerns regarding side effect management

What Are the Causes of CRF?

- Cancer; the disease process itself
- Cancer treatments
- Physical symptoms (e.g., pain, nausea)
- Psychological symptoms (e.g., pain, anxiety, depression)
- Sleep problems
- Lack of physical activity and exercise
- Nutrition problems
- Other medical or comorbid conditions (e.g., anemia)
- Other medications

Multidisciplinary Approach in CRF

Psychological/Social Factors

Biological/Physical Factors

Behavioural Factors

Oncologist (Medical, Surgical)
Psychologist/ Psychosocial Oncology
Oncology Nurse
Spiritual Health Practitioner
Family Physician
Sleep Specialist
Geriatrician
Physiotherapist/ Kinesiologist/ Rehabilitation
Pharmacist
Dietitian
Family Physician
Psychiatrist

Cancer-Related Fatigue

Biological/Physical Factors

Behavioural Factors

Psychological/Social Factors
# Screening for CRF

## Guideline Recommendations

<table>
<thead>
<tr>
<th>Screen for presence of CRF:</th>
<th>Use a valid scale for level of severity:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Initial diagnosis</td>
<td>• Numeric rating scale (0-10), such as the Edmonton Symptom Assessment System (ESAS)</td>
</tr>
<tr>
<td>• Periodically throughout treatment</td>
<td>• Semi-quantitative tool, such as fatigue pictogram</td>
</tr>
<tr>
<td>• Post-treatment follow-up visits</td>
<td></td>
</tr>
<tr>
<td>• As clinically indicated changes in disease status or treatment</td>
<td></td>
</tr>
</tbody>
</table>

# Fatigue Severity

The Edmonton Symptom Assessment System (ESAS-R) is a tool used to assess fatigue severity.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Score Range</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Pain</td>
<td>0-10</td>
<td>Worst Possible Pain</td>
</tr>
<tr>
<td>No Tiredness</td>
<td>0-10</td>
<td>Worst Possible Tiredness</td>
</tr>
<tr>
<td>No Drowsiness</td>
<td>0-10</td>
<td>Worst Possible Drowsiness</td>
</tr>
<tr>
<td>No Nausea</td>
<td>0-10</td>
<td>Worst Possible Nausea</td>
</tr>
<tr>
<td>No Lack of Appetite</td>
<td>0-10</td>
<td>Worst Possible Lack of Appetite</td>
</tr>
<tr>
<td>No Shortness of Breath</td>
<td>0-10</td>
<td>Worst Possible Shortness of Breath</td>
</tr>
<tr>
<td>No Depression</td>
<td>0-10</td>
<td>Worst Possible Depression</td>
</tr>
<tr>
<td>No Anxiety</td>
<td>0-10</td>
<td>Worst Possible Anxiety</td>
</tr>
<tr>
<td>Best Wellbeing</td>
<td>0-10</td>
<td>Worst Possible Wellbeing</td>
</tr>
<tr>
<td>Other Problem</td>
<td>0-10</td>
<td>Worst Possible Other Problem</td>
</tr>
</tbody>
</table>

- **MILD fatigue (score 1-3)**
- **MODERATE fatigue (score 4-6)**
- **SEVERE fatigue (score 7-10)**
Individualized Approach

- Interventions should be individualized/adapted based on:
  - Causes and contributors of CRF
  - Disease status, stage of cancer treatment
  - Age, function, physical limitations
  - Patient preferences

Non-Pharmacological Interventions

Based on assessment and preferences, specific interventions can be selected:

- Physical activity and exercise
- Psychosocial/psychological strategies
- Optimizing sleep quality and continuity
- Spiritual practices
- Nutrition-based interventions

How can physical activity and exercise help reduce CRF?
Physical Activity/Exercise Interventions Are Safe, Feasible, and Effective

- Strongest evidence for treating CRF
  - Numerous RCTs, systematic reviews, and meta-analyses

**Recent Systematic Review** (Mustian et al, 2017)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>No. of effect sizes</th>
<th>WES</th>
<th>SE</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>127</td>
<td>0.33</td>
<td>0.05</td>
<td>(0.24-0.43)</td>
</tr>
<tr>
<td>Pharmaceutical</td>
<td>14</td>
<td>0.09</td>
<td>0.05</td>
<td>(0.00-0.19)</td>
</tr>
<tr>
<td>Exercise + psychological</td>
<td>10</td>
<td>0.26</td>
<td>0.07</td>
<td>(0.13-0.38)</td>
</tr>
<tr>
<td>Psychological</td>
<td>34</td>
<td>0.27</td>
<td>0.05</td>
<td>(0.21-0.33)</td>
</tr>
<tr>
<td>Exercise</td>
<td>69</td>
<td>0.30</td>
<td>0.03</td>
<td>(0.25-0.36)</td>
</tr>
</tbody>
</table>

CI, confidence interval; RCT, randomized controlled trial.
SE, standard error; WES, weighted effect size.

Avoid Inactivity/Sedentary Behaviour

For most patients with cancer:

- **Any type of physical activity** at moderate levels of intensity (e.g., walking, yoga) will likely contribute to decreasing CRF
  - Some physical activity is always better than none!
  - More physical activity is generally better than less
  - Start easy and progress slowly
  - Group-based exercise may be especially effective

How can psychosocial/psychological strategies help reduce CRF?
Fatigue-Specific Psychological Interventions Are Effective

- Numerous RCTs and systematic reviews show psychoeducation (self-care, coping strategies, energy/activity management) and/or cognitive-behavioural therapy (CBT) for fatigue are effective.

**Recent Systematic Review** (Bennett et al, 2016)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of studies</th>
<th>Number of participants</th>
<th>Effect size SMD (95% CI)</th>
<th>Test for overall effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>General fatigue</td>
<td>12</td>
<td>1680</td>
<td>-0.27 (-0.51 to -0.04)</td>
<td>Z=2.27 (p=0.02)</td>
</tr>
<tr>
<td>Fatigue intensity</td>
<td>8</td>
<td>1524</td>
<td>-0.28 (-0.51 to -0.04)</td>
<td>Z=2.34 (p=0.02)</td>
</tr>
<tr>
<td>Fatigue distress</td>
<td>3</td>
<td>622</td>
<td>-0.57 (-1.09 to -0.05)</td>
<td>Z=2.17 (p=0.03)</td>
</tr>
<tr>
<td>Fatigue interference</td>
<td>4</td>
<td>439</td>
<td>-0.35 (-0.54 to -0.16)</td>
<td>Z=3.67 (p=0.0002)</td>
</tr>
</tbody>
</table>

SMD, standard mean difference.
### Basic Information to Include When Educating Patients on CRF

**All patients likely to benefit from routine education on fatigue**

<table>
<thead>
<tr>
<th>Topic</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference between normal and cancer-related fatigue</td>
<td></td>
</tr>
<tr>
<td>Causes/contributing factors of fatigue</td>
<td></td>
</tr>
<tr>
<td>Fatigue patterns/fluctuations; may normally disappear over time</td>
<td></td>
</tr>
<tr>
<td>Use of treatment log/diary to monitor fatigue levels/patterns</td>
<td></td>
</tr>
<tr>
<td>Tips on self-management, energy balancing, and coping strategies</td>
<td></td>
</tr>
<tr>
<td>Signs/symptoms of worsening fatigue to report to healthcare team</td>
<td></td>
</tr>
<tr>
<td>Information on local support groups or online resources</td>
<td></td>
</tr>
</tbody>
</table>

How can optimizing sleep quality and continuity help reduce CRF?
CBT-I is effective in improving sleep outcomes and may reduce CRF

- Cognitive-behavioural therapy for insomnia (CBT-I): multicomponent intervention including stimulus control, sleep restriction, cognitive restructuring, and sleep hygiene

RCT; N=242 breast cancer patients with insomnia (Savard et al, 2016)

Graph: Multidimensional Fatigue Inventory (MFI)

- Control
- VCBT-I
- PCBT-I

F=3.96, p=0.02

FU3, 3-month follow-up; FU6, 6-month follow-up; FU12, 12-month follow-up.

PCBT-I, professionally administered CBT-I; RCT, randomized controlled trial.

Tx, treatment; VCBT-I, video-based CBT-I.

Components of CBT-I

- **Stimulus control**
  - By modifying maladaptive sleep behaviours, aims to re-associate the bed/bedroom with sleep and resynchronize the sleep-wake cycle

- **Sleep restriction**
  - Aims to limit the time spent in bed to actual sleep time, promoting a more consolidated and efficient/deep sleep

- **Cognitive restructuring**
  - Aims to revise maladaptive beliefs and attitudes about sleep that interfere with one’s ability to sleep at night

- **Sleep hygiene**
  - Aims to change some behaviours/environmental factors that may have a negative impact on sleep
How can spiritual practices help reduce CRF?
Practices That Enhance Spiritual Well-Being Likely Beneficial for CRF

- Spiritual practices include meditation, spiritual self-reflection, prayer, spiritual communities, compassion to others, and more
- Growing body of evidence suggests that mind-body therapies, including meditation, yoga, and tai chi/qigong improve CRF, mood, and overall quality of life
- Mindfulness-based stress reduction (MBSR)
  - Structured group program combining meditation practices
  - Designed to cultivate increasing levels of mindfulness in daily life, focusing on non-judgmental awareness and acceptance
  - Increasing evidence for efficacy in improving CRF

How can nutrition-based interventions help reduce CRF?
Nutritional Interventions for CRF

• Limited data on nutritional interventions alone to modify CRF

Emerging studies:

**Prospective observational study, N=285 cancer patients**

• Low protein intake associated with higher risk of CRF

**Cross-sectional pilot study, N=40 cancer survivors**

• Participants with no or mild CRF consumed more fish, whole grains, and vegetables than those with moderate or severe CRF

**Pilot randomized trial, N=30 cancer survivors**

• Fatigue Reduction Diet (a diet rich in fruit, vegetables, whole grains, and omega-3 fatty acid–rich foods for 3 months) improved CRF

What about pharmacological interventions for CRF?
Pharmacological Interventions Not Recommended for CRF

Insufficient evidence at the present time to support use of pharmacotherapy (corticosteroids, methylphenidate, modafinil), supplements or herbal medicines for CRF

Patient Personalized Action Plans

- **Part 1: Decision Aid** – tool to discuss treatment options with your patients and their caregivers
- Once decision is made, refer to appropriate HCP for intervention selected; can be accessed by contacting the respective departments of most cancer centres

- **Part 2: Management Guide** with general tips/strategies per intervention
  - Includes daily/weekly tracker to assess progress
  - List of additional resources on [www.MyCancerFatigue.ca](http://www.MyCancerFatigue.ca)
CRF Program: HCP and Patient Resources

• Part B: Material for Patients and Caregivers
  – Patient Pamphlet and Decision Aid
  – Personalized action plan diary
<table>
<thead>
<tr>
<th>Energy Levels</th>
<th>Sunday</th>
<th>Monday</th>
<th>Tuesday</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MORNING</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>AFTERNOON</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>EVENING</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer Treatment</td>
<td>Dinner date with husband</td>
<td>Hospital appt 8 am</td>
<td>Chemo</td>
</tr>
<tr>
<td>Priority Activities</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strategies To Improve Cancer Fatigue</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical Activity</strong></td>
</tr>
<tr>
<td><strong>Psychological Wellness</strong></td>
</tr>
<tr>
<td><strong>Sleep</strong></td>
</tr>
<tr>
<td><strong>Spiritual Well Being</strong></td>
</tr>
<tr>
<td><strong>Nutrition</strong></td>
</tr>
</tbody>
</table>

**NOTES:** Dr. said mild anemia | Too tired to do house chores | | |
How would you feel?

• If your physician said you should go exercise and you’ll feel less fatigued, would that be sufficient to do something? Do you need more concrete direction?

• What if she said to you that you needed to sleep better and you would be less tired? Would you feel frustrated?
## Walking Program

Start **week 1** with 3 days per week. Continue with at **least 3 walking sessions** during each week. Aim to walk at least five days a week.

<table>
<thead>
<tr>
<th>Week</th>
<th>Warm-up (Walk slowly)</th>
<th>Activity (Brisk walking)</th>
<th>Cool-down (Walk slowly)</th>
<th>Total Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5 minutes</td>
<td>5 minutes</td>
<td>5 minutes</td>
<td>15 minutes</td>
</tr>
<tr>
<td>2</td>
<td>5 minutes</td>
<td>7 minutes</td>
<td>5 minutes</td>
<td>17 minutes</td>
</tr>
<tr>
<td>3</td>
<td>5 minutes</td>
<td>9 minutes</td>
<td>5 minutes</td>
<td>19 minutes</td>
</tr>
<tr>
<td>4</td>
<td>5 minutes</td>
<td>11 minutes</td>
<td>5 minutes</td>
<td>21 minutes</td>
</tr>
<tr>
<td>5</td>
<td>5 minutes</td>
<td>13 minutes</td>
<td>5 minutes</td>
<td>23 minutes</td>
</tr>
<tr>
<td>6</td>
<td>5 minutes</td>
<td>15 minutes</td>
<td>5 minutes</td>
<td>25 minutes</td>
</tr>
<tr>
<td>7</td>
<td>5 minutes</td>
<td>18 minutes</td>
<td>5 minutes</td>
<td>28 minutes</td>
</tr>
<tr>
<td>8</td>
<td>5 minutes</td>
<td>20 minutes</td>
<td>5 minutes</td>
<td>30 minutes</td>
</tr>
<tr>
<td>9</td>
<td>5 minutes</td>
<td>23 minutes</td>
<td>5 minutes</td>
<td>33 minutes</td>
</tr>
<tr>
<td>10</td>
<td>5 minutes</td>
<td>26 minutes</td>
<td>5 minutes</td>
<td>36 minutes</td>
</tr>
<tr>
<td><strong>11</strong></td>
<td>5 minutes</td>
<td>28 minutes</td>
<td>5 minutes</td>
<td>38 minutes</td>
</tr>
<tr>
<td>12</td>
<td>5 minutes</td>
<td>30 minutes</td>
<td>5 minutes</td>
<td>40 minutes</td>
</tr>
</tbody>
</table>

Continue program indefinitely, and keep updating your healthcare team.

This program can be very useful for people during treatment. You may experience cycles of fatigue while receiving cancer treatment. Fatigue will increase shortly after you receive chemotherapy, and decrease the further away from chemo you get. This program can be **RESET** with every round of chemo, starting back at week 1. This can help you build strength and recover from fatigue once treatment is complete.
Tips on How to Sleep Better

Stimulus control and sleep restriction are the most effective sleep strategies.

**Stimulus Control:** consists of a set of instructions to change poor sleep habits, such as spending too much time in bed and not having a regular sleep schedule. A stimulus is something that brings on a response. The goal of this method is to reassociate the bed and bedroom with sleep and to put your sleep-wake cycle back in sync.

<table>
<thead>
<tr>
<th><strong>Go to bed only when sleepy (as opposed to feeling fatigued)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fatigue</strong>&lt;br&gt;lack of energy to do activities, such as after intense exercising or busy day at work</td>
</tr>
<tr>
<td><strong>Sleepiness</strong>&lt;br&gt;can’t control an urge to close eyes/lie down, yawning, nodding, heavy eyelids, watery eyes, etc.</td>
</tr>
</tbody>
</table>

- Use the bed and bedroom only for sleeping and having sex (do not read, eat, watch TV, or do anything else in bed)
- If you can’t fall asleep (or go back to sleep) during the night (within ~20 to 30 minutes), leave the bedroom (go into another room and do something relaxing) and return to bed only when sleepy again
- Maintain a regular sleep schedule (same bedtime and wake-up time), even on weekends and after a poor night’s sleep
- Avoid daytime napping. If you need a nap, keep it short (less than an hour) and before 3 p.m.
What have patients said?

• Feedback from our focus groups in program development

  – “I tried to find information on fatigue and it was all over the place – there was no one single point I could go to for advice”

  – “Fatigue was probably the most difficult symptom for me to manage and I didn’t really feel like anyone could help”

  – “I felt guilty because I was so tired I couldn’t care for my family and I wish I had known what to do”
### Key Messages

1. **CRF is common, distressing, and persistent**

2. **There are various causes/contributors of CRF, including biological, behavioural, and psychosocial risk factors**

3. **It is important to screen/assess for CRF throughout the disease trajectory with ongoing monitoring and follow-up**

4. **Non-pharmacological interventions, including physical activity, psychosocial, sleep, spiritual, and nutrition-based strategies, have been shown to reduce CRF and improve overall quality of life**

5. **A multimodal strategy combining targeted and individualized interventions should be implemented**