Addressing the Problems of Cancer Survivors: Where Are We?

Paul B. Jacobsen, Ph.D.
Moffitt Cancer Center and Research Institute
University of South Florida
Tampa, Florida

Cancer Survivorship: Pathways to Health After Treatment
June 17, 2004
Addressing the Problems of Cancer Survivors: Where Are We?

• Provide a framework for summarizing accomplishments and identifying challenges and opportunities in addressing problems of cancer survivors

• Illustrate this approach using a common and distressing problem experienced by cancer survivors
What Do We Know About These Problems?

- How are we defining the problem?
- How are we measuring the problem?
- How are we studying occurrence of the problem?
  - Content and timing of assessments
  - Sampling strategy
What Do We Know About These Problems?

• What have we learned about occurrence of the problem?
  – Prevalence
  – Characteristics
  – Course
  – Risk factors
  – Mechanisms
What Do We Know About These Problems?

• How are we studying management of the problem?
  – Types of interventions
  – Types of research designs
  – Samples recruited
  – Timing of the intervention
What Do We Know About These Problems?

• What have we learned about management of the problem?
  – Intervention efficacy
  – Moderators of intervention efficacy
  – Mediators of intervention efficacy
  – “Real world” effectiveness of intervention
  – Cost and cost-effectiveness of intervention
What Do We Know About These Problems?

- What do we need to accomplish to better address the problem?
# Chief Concerns Following Transplantation

<table>
<thead>
<tr>
<th>Concern</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fears of disease recurrence</td>
<td>77%</td>
</tr>
<tr>
<td>Energy level</td>
<td>57%</td>
</tr>
<tr>
<td>Difficulty remembering/concentrating</td>
<td>43%</td>
</tr>
<tr>
<td>Feeling tense or anxious</td>
<td>42%</td>
</tr>
<tr>
<td>Difficulties with medical insurance</td>
<td>41%</td>
</tr>
<tr>
<td>Returning to “normal”</td>
<td>40%</td>
</tr>
<tr>
<td>Sexual functioning</td>
<td>40%</td>
</tr>
<tr>
<td>Achieving life goals</td>
<td>39%</td>
</tr>
<tr>
<td>Poor sleep</td>
<td>39%</td>
</tr>
<tr>
<td>Feeling depressed</td>
<td>37%</td>
</tr>
</tbody>
</table>

Andrykowski et al., Bone Marrow Transpl 1999;24:1121-1129
MEDLINE Citations for “Neoplasms” AND “Fatigue”

- 1966-2004: 919 citations
- 1966-1993: 195 citations (21%)
- 1994-2004: 724 citations (79%)
- 1966-2004 Breast Ca: 117 citations (13%)
- 1966-2004 Age 0-18: 98 citations (11%)
Defining the Problem

- Lack of consensus regarding the definition and conceptualization of fatigue in cancer patients
Measuring the Problem

• Lack of assessment tools consistent with a multidimensional conceptualization of fatigue
### Examples of Multidimensional Measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>Dimensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brief Fatigue Inventory</td>
<td>severity, interference</td>
</tr>
<tr>
<td>Cancer Fatigue Scale</td>
<td>physical, cognitive, affective</td>
</tr>
<tr>
<td>Multidimensional Fatigue Inventory</td>
<td>general, physical, mental, reduced activity, reduced motivation</td>
</tr>
<tr>
<td>Piper Fatigue Scale (rev.)</td>
<td>behavioral/severity, sensory, affective meaning, cognitive/mood</td>
</tr>
<tr>
<td>Schwartz Cancer Fatigue Scale (rev.)</td>
<td>physical, perceptual</td>
</tr>
</tbody>
</table>
Multidimensional Approach

Fatigue Symptom Inventory

- Severity
- Duration
- Interference with quality of life

Hann et al., Qual Life Res 1998;7:301-10
Multidimensional Approach

Multidimensional Fatigue Symptom Inventory

- Physical
- Emotional
- Mental

Stein et al., Cancer Practice 1998;6:143-152; J Pain Symptom Manage 2004;27:14-23
Occurrence of the Problem

Methodological Limitations of Early Research

• Use of unidimensional measures
• Use of cross-sectional research designs
• Sampling of participants with broad range of time since tx completion
• Inclusion of different disease types in too few numbers to permit valid comparisons
• Inclusion of different treatment types in too few numbers to permit valid comparisons
• Failure to distinguish patients according to current disease status
• Absence of noncancer comparison group
Fatigue in Breast Cancer Survivors

Preliminary Studies

*Aim*: Determine whether women previously treated for breast cancer and with no current clinical evidence of disease were experiencing greater fatigue than women with no history of cancer

Sample 1: High dose chemotherapy
Sample 2: Standard dose chemotherapy
Sample 3: Radiotherapy
# Disease and Treatment Characteristics

<table>
<thead>
<tr>
<th>Disease stage</th>
<th>BMT (N=43)</th>
<th>ACT (N=61)</th>
<th>PRT (N=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0/1</td>
<td>0%</td>
<td>25%</td>
<td>78%</td>
</tr>
<tr>
<td>2</td>
<td>30%</td>
<td>64%</td>
<td>20%</td>
</tr>
<tr>
<td>3</td>
<td>30%</td>
<td>8%</td>
<td>2%</td>
</tr>
<tr>
<td>4</td>
<td>40%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Mos. from dx (M, SD)</td>
<td>40 (25)</td>
<td>22 (7)</td>
<td>23 (20)</td>
</tr>
<tr>
<td>Mos. from tx (M, SD)</td>
<td>20 (16)</td>
<td>16 (7)</td>
<td>22 (14)</td>
</tr>
</tbody>
</table>
# Fatigue Among BMT Survivors

<table>
<thead>
<tr>
<th></th>
<th>BMT M (SD)</th>
<th>Comparison M (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>POMS-F</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue severity*</td>
<td>9.6 (8.1)</td>
<td>6.3 (6.1)</td>
</tr>
<tr>
<td><strong>FSI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration*</td>
<td>4.0 (2.3)</td>
<td>3.0 (2.3)</td>
</tr>
<tr>
<td>Interference with QoL**</td>
<td>2.7 (2.6)</td>
<td>1.5 (1.5)</td>
</tr>
<tr>
<td><strong>MFSI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental symptoms*</td>
<td>5.0 (5.5)</td>
<td>3.0 (2.7)</td>
</tr>
<tr>
<td>Emotional symptoms</td>
<td>4.9 (5.3)</td>
<td>3.7 (3.8)</td>
</tr>
<tr>
<td>Physical symptoms*</td>
<td>4.0 (4.2)</td>
<td>2.3 (2.8)</td>
</tr>
</tbody>
</table>

*p ≤ .05, ** ≤ .01

Hann et al., Supportive Care Cancer 1997;5:44-52
Fatigue Among ACT Survivors

<table>
<thead>
<tr>
<th></th>
<th>ACT M (SD)</th>
<th>Comparison M (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>POMS-F</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue severity**</td>
<td>8.2 (6.7)</td>
<td>5.3 (5.2)</td>
</tr>
<tr>
<td><strong>FSI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration</td>
<td>3.7 (2.5)</td>
<td>3.1 (2.5)</td>
</tr>
<tr>
<td>Interference with QoL*</td>
<td>2.0 (2.0)</td>
<td>1.3 (1.6)</td>
</tr>
<tr>
<td><strong>MFSI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental symptoms**</td>
<td>5.0 (5.1)</td>
<td>2.9 (3.0)</td>
</tr>
<tr>
<td>Emotional symptoms</td>
<td>4.5 (4.8)</td>
<td>3.4 (4.4)</td>
</tr>
<tr>
<td>Physical symptoms**</td>
<td>4.1 (4.6)</td>
<td>2.0 (2.6)</td>
</tr>
</tbody>
</table>

*p < .05, ** < .01

Broeckel et al., J Clin Oncol 1998;16:1689-96
### Fatigue Among PRT Survivors

<table>
<thead>
<tr>
<th></th>
<th>PRT GROUP</th>
<th>Comparison GROUP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M (SD)</td>
<td>M (SD)</td>
</tr>
<tr>
<td><strong>POMS-F</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue severity</td>
<td>7.4 (8.1)</td>
<td>6.6 (5.8)</td>
</tr>
<tr>
<td><strong>FSI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration</td>
<td>3.2 (2.8)</td>
<td>3.0 (2.2)</td>
</tr>
<tr>
<td>Interference with QoL</td>
<td>1.4 (2.1)</td>
<td>1.4 (1.5)</td>
</tr>
<tr>
<td><strong>MFSI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental symptoms</td>
<td>3.4 (3.6)</td>
<td>3.6 (3.3)</td>
</tr>
<tr>
<td>Emotional symptoms</td>
<td>2.9 (3.7)</td>
<td>3.7 (4.3)</td>
</tr>
<tr>
<td>Physical symptoms</td>
<td>3.6 (4.4)</td>
<td>3.1 (3.8)</td>
</tr>
</tbody>
</table>

*p< .05, **< .01

Hann et al., J Clin Psychol Med Settings 1998;5:19-33
Fatigue in Breast Cancer Survivors

• Limitations
  Lack of randomization to treatment conditions
  Use of cross-sectional research designs
Problems with Identifying Prevalence

- Lack of consensus for defining “clinically significant” fatigue
- Reports of prevalence are wide-ranging due, in part, to differences across studies in measures used and criteria applied
- Explore use of clinical syndrome approach as one means of standardizing definition and assessment of clinically significant fatigue
Proposed Criteria for Clinical Syndrome of Cancer-Related Fatigue

A. Six or more of the following present every day or nearly every day during same 2-week period in the past month and at least one is significant fatigue (A1).

1. Significant fatigue, diminished energy, or increased need to rest disproportionate to recent change in activity level
2. Generalized weakness, limb heaviness
3. Diminished concentration, attention
4. Decreased motivation, interest in activities
5. Insomnia, hypersomnia
6. Sleep unrefreshing, nonrestorative
7. Struggle to overcome inactivity
8. Marked emotional reactivity (sadness, frustration, irritability) to fatigue
9. Difficulty completing daily tasks attributed to fatigue
10. Short-term memory problems
11. Postexertional malaise lasting several hours

Cella et al., Oncology 1998;12:369-377
Proposed Criteria for Clinical Syndrome of Cancer-Related Fatigue (cont’d)

B. Symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning

C. Evidence from history, physical examination, or laboratory findings that symptoms are a consequence of cancer or cancer therapy

D. Symptoms are not primarily a consequence of comorbid psychiatric disorders such as major depression, somatization or somatoform disorder, or delirium

Cella et al., Oncology 1998;12:369-377
# Clinical Syndrome Approach

## Participants (N = 51)

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>48 years (s.d. = 9; range = 23 - 63)</td>
</tr>
<tr>
<td>Gender</td>
<td>female (75%), male (25%)</td>
</tr>
<tr>
<td>Transplant</td>
<td>autologous (76%), allogeneic (24%)</td>
</tr>
<tr>
<td>Diagnoses</td>
<td>breast (61%), myeloma (14%), leukemia (13%), lymphoma (10%), other (2%)</td>
</tr>
<tr>
<td>BMT stay</td>
<td>23 days (s.d. = 10; range = 16 - 77)</td>
</tr>
<tr>
<td>Time elapsed</td>
<td>6.9 months (s.d. = 1.1; range = 5-11)</td>
</tr>
</tbody>
</table>

Sadler et al., Journal of Pain & Symptom Management 2002;23:406-413
<table>
<thead>
<tr>
<th>Condition</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two weeks of fatigue in past month (A1)</td>
<td>22</td>
<td>43%</td>
</tr>
<tr>
<td>5 or more additional symptoms (A1 + 5)</td>
<td>13</td>
<td>25%</td>
</tr>
<tr>
<td>Significant distress or impairment (B)</td>
<td>12</td>
<td>23%</td>
</tr>
<tr>
<td>Consequence of cancer or treatment (C)</td>
<td>12</td>
<td>23%</td>
</tr>
<tr>
<td>Not due to co-morbid psychiatric disorder (D)</td>
<td>11</td>
<td>21%</td>
</tr>
<tr>
<td>Criteria met for clinical syndrome</td>
<td>11</td>
<td>21%</td>
</tr>
</tbody>
</table>

Sadler et al., Journal of Pain & Symptom Management 2002;23:406-413
### Clinical Syndrome Approach

<table>
<thead>
<tr>
<th></th>
<th>Criteria met</th>
<th>Criteria not met</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M (SD)</td>
<td>M (SD)</td>
</tr>
<tr>
<td><strong>FSI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current fatigue*</td>
<td>4.8 (3.2)</td>
<td>2.6 (2.7)</td>
</tr>
<tr>
<td>Average fatigue*</td>
<td>4.8 (2.4)</td>
<td>3.1 (2.4)</td>
</tr>
<tr>
<td>Most fatigue**</td>
<td>7.5 (1.9)</td>
<td>4.5 (2.9)</td>
</tr>
<tr>
<td>Least fatigue*</td>
<td>3.3 (2.2)</td>
<td>1.7 (1.8)</td>
</tr>
<tr>
<td>No. of days fatigued***</td>
<td>5.8 (1.4)</td>
<td>3.5 (2.8)</td>
</tr>
<tr>
<td><strong>SF-36</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitality**</td>
<td>35.0 (18.8)</td>
<td>57.9 (23.2)</td>
</tr>
<tr>
<td>Role-Physical*</td>
<td>25.0 (35.4)</td>
<td>54.4 (43.1)</td>
</tr>
<tr>
<td>Role-Emotional**</td>
<td>45.5 (37.3)</td>
<td>80.8 (36.1)</td>
</tr>
</tbody>
</table>

*p < 0.05, ** < 0.01, ***p < .001

Sadler et al., Journal of Pain & Symptom Management 2002;23:406-413
## Risk Factors – Demographic Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of studies</th>
<th>None</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>12</td>
<td>6</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Education</td>
<td>9</td>
<td>6</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Gender</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
## Risk Factors – Clinical Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of studies</th>
<th>Relationship</th>
<th>None</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time since tx completion</td>
<td>14</td>
<td></td>
<td>13</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Stage at dx</td>
<td>7</td>
<td></td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cancer dx</td>
<td>4</td>
<td></td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>No. chemo cycles</td>
<td>3</td>
<td></td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Note: (lung) indicates lung cancer.
## Risk Factors – Clinical Variables

### Breast Cancer Studies

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of studies</th>
<th>None</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Surgery type</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Possible Causes of Fatigue Following Treatment Completion

- Anemia
- Physical inactivity / deconditioning

Diagram:
- Physical
- Inactivity
- Deconditioning
Effects of Exercise Training on QoL

Participants
Postmenopausal women (ages 50-69) with early stage breast cancer, who had completed treatment an average of 14 months previously

Design
15 week randomized clinical trial

Interventions
Exercise sessions (15 to 35 mins) on cycle ergometers 3x/wk for 15 weeks (N = 24)
No exercise (N= 28)

Effects of Exercise Training on QoL

Primary Outcomes
- Cardiopulmonary function (peak oxygen consumption)
- Overall quality of life (FACT-B)

Secondary Outcomes
- Fatigue (FACT-FS)
- Additional indices of cardiopulmonary function

### Effects of Exercise Training on QoL

<table>
<thead>
<tr>
<th>Outcome</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Outcomes</strong></td>
<td></td>
</tr>
<tr>
<td>Peak oxygen consumption (L/min)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Overall quality of life (0-140)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Secondary Outcomes</strong></td>
<td></td>
</tr>
<tr>
<td>Fatigue (0-52)</td>
<td>.006</td>
</tr>
<tr>
<td>Peak power output (W)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

## Correlations Between Changes in Cardiopulmonary Function and Fatigue


<table>
<thead>
<tr>
<th>Variables</th>
<th>Peak Oxygen Consumption</th>
<th>Peak Power Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>-.41**</td>
<td>-.54**</td>
</tr>
</tbody>
</table>

* * p < .05, ** p < .01

Mediational Role of Cardiopulmonary Function

Exercise → Peak Power Output → Fatigue

Possible Causes of Fatigue Following Treatment Completion

• Anemia
• Physical inactivity / deconditioning
• Depression
Etiologic Role of Depression

- Is depression a cause or an effect of fatigue?
Stress Management Training for Chemotherapy Patients

Aim:

To compare the clinical effectiveness and economic efficiency of two methods of delivering stress management training

Jacobsen et al., J Clin Oncol 2002; 20:2851-2862

Supported by: NCI R01 CA70875; ACS PBR-99
Stress Management Training for Chemotherapy Patients

Consists of instruction in
– Deep breathing
– Progressive muscle relaxation + guided imagery
– Use of coping self-statements

Two versions
– Professionally-administered (via face-to-face meeting)
– Patient self-administered (via brochure, audiotape, and videotape)
Study Design

Recruitment, Baseline Evaluation

Randomized to Intervention

Self-Administered Intervention + Usual Care

Professionally-Administered Intervention + Usual Care

Usual Care Only

Outcome Evaluations Before Cycles 2,3,4
Stress Management for Chemotherapy Patients

Participants (N = 382)

Age: 26 to 88 years (M = 56)
Gender: female 76%
Race: white 90%
Education: attended college 63%
ECOG: 0 55%, 1 39%, 2 5%, 3 1%
Dx: breast 58%, lung 21%, ovarian 5%, other 14%
CUS-D (Depression)

Change from Baseline

Pre Cycle 2  Pre Cycle 3  Pre Cycle 4

Usual Care Only
Self Administered Stress Management
Professionally Administered Stress Management
SF-36 Vitality (Energy)

Change from Baseline

Pre Cycle 2  Pre Cycle 3  Pre Cycle 4

Usual Care Only
Self Administered Stress Management
Professionally Administered Stress Management
Possible Causes of Fatigue Following Treatment Completion

- Anemia
- Physical inactivity / deconditioning
- Depression
- CNS toxicity
Possible Causes of Fatigue Following Treatment Completion

CNS toxicity

- Cognitive Impairment
- Cognitive Complaints
- Fatigue
Possible Interpretations of Findings

• Fatigue is unrelated to CNS toxicity as evidenced by the lack of relationship with objective measures of cognitive functioning
• Lack of relationship of fatigue with objective measures of cognitive functioning may reflect use of cross-sectional research designs
Possible Causes of Fatigue Following Treatment Completion

- Anemia
- Physical inactivity / deconditioning
- Depression
- CNS toxicity
- Altered immune function
Possible Causes of Fatigue Following Treatment Completion

Cancer and/or its treatment

Increase in proinflammatory cytokines

Sickness behavior
(fatigue, somnolence, decreased activity, depressed mood, cognitive disturbance)
Possible Causes of Fatigue Following Treatment Completion

- Anemia
- Physical inactivity / deconditioning
- Depression
- CNS toxicity
- Altered immune function
- Altered endocrine function
Possible Causes of Fatigue Following Treatment Completion

- Treatment-induced estrogen changes
- Discontinuation or contraindication of ERT
  
  → More severe menopausal symptoms
  
  → Heightened fatigue
## Correlates of Fatigue Severity

<table>
<thead>
<tr>
<th>Fatigue (POMS-F)</th>
<th>Menopausal Symptoms (MSC)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total number 0.55*</td>
</tr>
<tr>
<td></td>
<td>Vasomotor symptoms 0.39*</td>
</tr>
</tbody>
</table>

*p≤.01

Broeckel et al., J Clin Oncol 1998;16:1689-1696
## Paroxetine for Hot Flashes in Women with Breast Cancer

<table>
<thead>
<tr>
<th></th>
<th>Pre-Tx M (SD)</th>
<th>Post-Tx M (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hot flash severity (HFQ)**</td>
<td>3.6 (0.5)</td>
<td>2.1 (1.3)</td>
</tr>
<tr>
<td>Depressive symptoms (CES-D)**</td>
<td>25.7 (15.0)</td>
<td>10.8 (10.8)</td>
</tr>
<tr>
<td>Fatigue severity (MFSI)*</td>
<td>35.7 (24.7)</td>
<td>20.2 (29.4)</td>
</tr>
<tr>
<td>Sleep quality (PSI)**</td>
<td>1.9 (0.7)</td>
<td>0.8 (0.6)</td>
</tr>
</tbody>
</table>

*p< 0.01, **< 0.001

Weitzner et al., J Pain Symptom Manage, 2002;23:337-345.
Defining and Measuring the Problem

Accomplishments

• Multidimensional conceptualizations of fatigue
• Creation and validation of self-report measures
Defining and Measuring the Problem

Challenges/Opportunities

- Lack of consensus on dimensional structure of fatigue
- Lack of consensus on optimal assessment approach
- Difficulty distinguishing fatigue from related constructs
- Lack of consensus on defining “clinically significant” fatigue
Occurrence of the Problem

Accomplishments

• Characterization of fatigue in subgroups of survivors defined in terms of both type of cancer and previous cancer treatment

• Understanding of the impact of fatigue on quality of life
Occurrence of the Problem

Challenges/Opportunities

• Limited understanding of the course of fatigue in cancer survivors
• Limited understanding of how fatigue in cancer survivors differs from fatigue in people without cancer
• Limited understanding of the prevalence of “clinically significant” fatigue in cancer survivors
Risk Factors

Accomplishments

• Demonstration that certain treatment characteristics are unlikely to be risk factors (e.g., type of surgery and tamoxifen use in early stage breast cancer survivors)
Risk Factors

Challenges/Opportunities

• Few well replicated findings regarding risk factors
• Limited understanding of the role of physical status characteristics as risk factors (e.g., co-morbidity, BMI)
• Role of genetic factors remains to be explored
Mechanisms

Accomplishments

• Accumulating evidence of the contributory role of:
  physical inactivity and physical deconditioning
  depression and psychological distress
  other poorly menopausal symptoms
• Preliminary evidence of the contributory role of
  cytokine activity
Mechanisms

Challenges/Opportunities

• Clarification of why certain patients and not others show posttreatment elevations in cytokine activity
• Identifying treatment implications of cytokine research
• Clarification of the contributory role of CNS toxicity
• Evaluation of other possible biological mechanisms (e.g., thyroid function)
Management

Accomplishments

• Accumulating evidence of the role of exercise and physical activity interventions in relieving fatigue and the mediating role of changes in cardiopulmonary fitness

• Preliminary evidence of the role of stress management interventions in relieving fatigue
Management

Challenges/Opportunities

• Replication, extension, and dissemination of findings regarding beneficial effects of exercise and stress management

• Evaluation of promising pharmacological agents
  - Anti-depressants
  - Wake-promoting agents
  - Anti-inflammatory agents

• Design studies in which fatigue is the primary outcome
Management

Challenges/Opportunities

• Develop intervention strategies aimed at preventing the persistence or development of fatigue in the posttreatment period