

Cancer and Cancer Treatment Fatigue

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Disclaimer and Disclosures

Disclaimer

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Disclosure

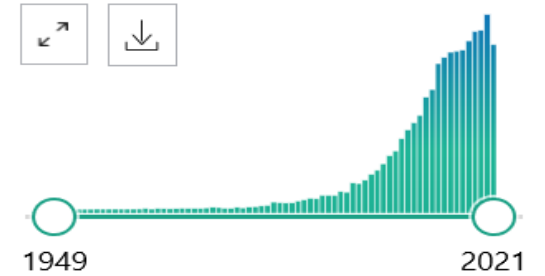
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Objectives of Presentation

- **State of the Science**
 - **Historical perspective**
 - **Epidemiology of cancer-related fatigue (CRF)**
 - **Definition of CRF**
- **Measures to evaluate CRF**
- **Phenotypic risk factors for CRF**
- **Mechanisms underlying CRF**

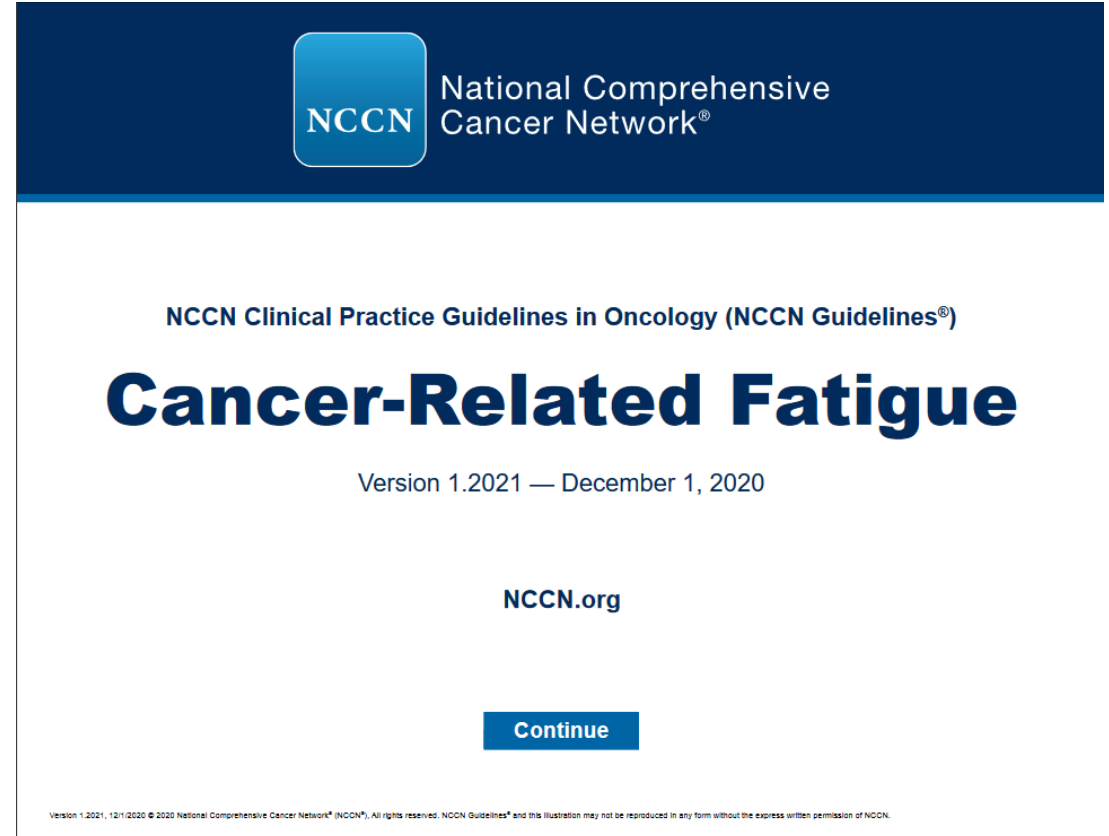
Historical Perspective

- Research on CRF began in ~1993
 - 23,984 references in PubMed
- Research was based on patients' reports of the occurrence of this symptom
- Initial studies focused on measurement
 - Oncology Nursing Society supported early research on CRF
 - Model to study fatigue was based on the theoretical perspectives from pain research – **multidimensional symptom**



Epidemiology of CRF

- Most common symptom in cancer patients
- 80% of patients who receive chemotherapy and radiation therapy
- >75% in patients with metastatic disease
- Prevalence rate in survivors is unknown (~29%)
- **During COVID-19 - ~42%**



NCCN National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Cancer-Related Fatigue

Version 1.2021 — December 1, 2020

NCCN.org

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Definition of CRF

A distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning. Compared with the fatigue experienced by healthy individuals, CRF is more severe, more distressing, and less likely to be relieved by rest.



www.bjfm.co.uk

ICD-10-CM Code R53.0

Neoplastic (malignant) related fatigue

https://www.nccn.org/professionals/physician_gls/pdf/fatigue.pdf

Measures to Evaluate CRF

- Brief Fatigue Inventory – **severity** – 9 items
- Daily Fatigue Cancer Scale – **severity** – 3 items
- EORTC QLQ-C30 – **severity** – 1 item
- EORTC QLQ-FA12 – **physical, emotional, cognitive** – 12 items
- Fatigue Questionnaire – **severity** – 11 items
- Visual Analogue Fatigue Scale – **severity** – 18 items
- Fatigue Symptom Inventory – **severity, frequency, diurnal variation, interference** – 14 items
- Functional Assessment of Cancer Therapy – Fatigue – **physical, social/family, emotional, functional** – 41 or 13 items
- Multidimensional Fatigue Inventory – **general, physical, reduced activity, reduced motivation** – 20 items
- Multidimensional Fatigue Symptom Inventory – **general, physical, mental, emotional, vigor** – 83 or 30 items
- Piper Fatigue Score-12 – **sensory, behavioral/severity, affective meaning, cognitive/ mood** – 12 items
- PROMIS CAT – **fatigue, sleep disturbance, sleep impairment** – Up to 20 items
- Schwartz Cancer Fatigue Scale Revised – **physical and perceptual** – 6 items

Phenotypic Risk Factors

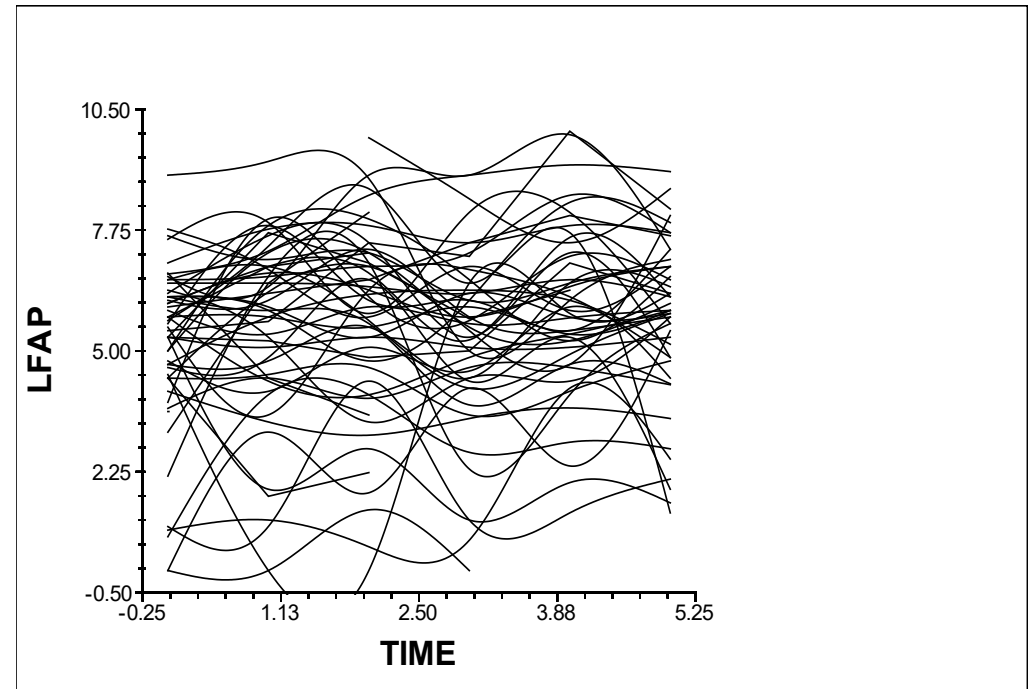
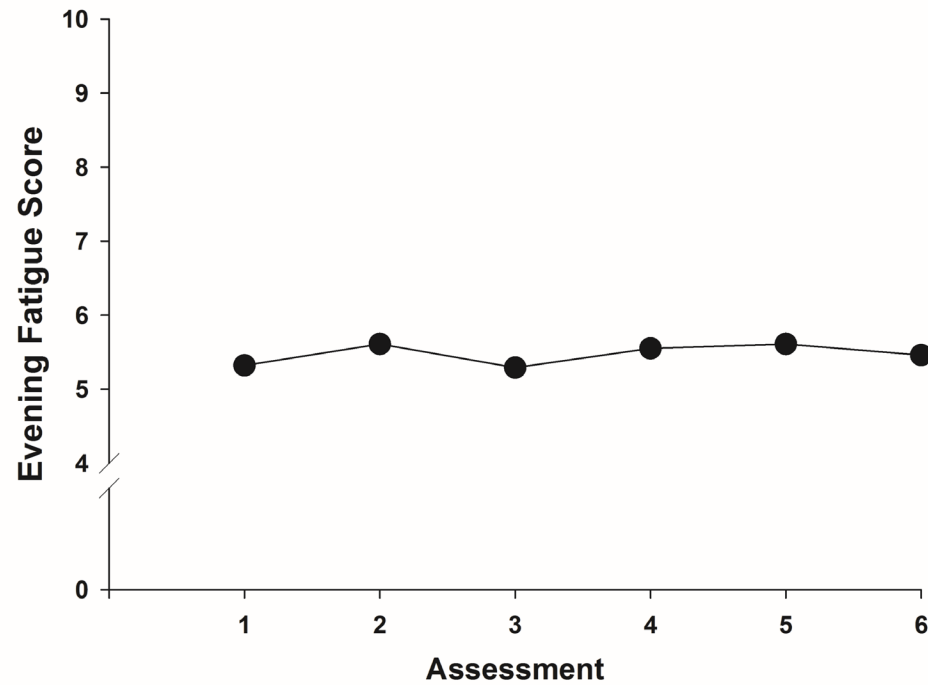
Risk Factors

- Female gender
- Younger age
- Higher level of comorbidity
- Decreased level of physical activity
- Higher levels of co-occurring symptoms
 - Depression
 - Sleep disturbance
 - Cognitive dysfunction
- Higher levels of stress
 - General stress
 - Cancer-specific stress
 - Cumulative life stress

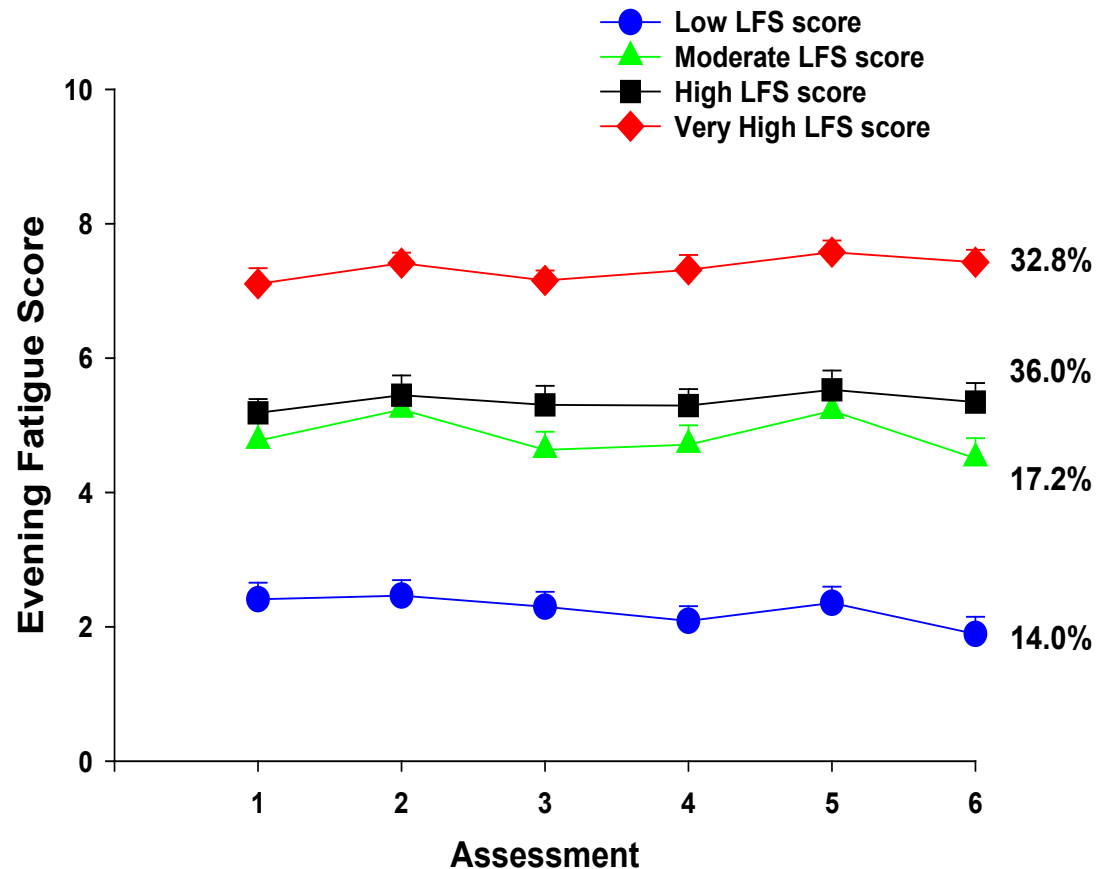
Methodologic Considerations

- Lack of consistent findings regarding
 - Social determinants of health
 - Disease and treatment characteristics
- Appropriate comparison group ????
 - Case controls
 - Use of clinically meaningful cutoff scores to dichotomize samples of oncology patients
- Focus on mean fatigue scores
 - Lack of evaluation in inter-individual variability in fatigue severity
 - Lack of studies on diurnal variations in fatigue severity

Inter-individual Variability in Evening Fatigue

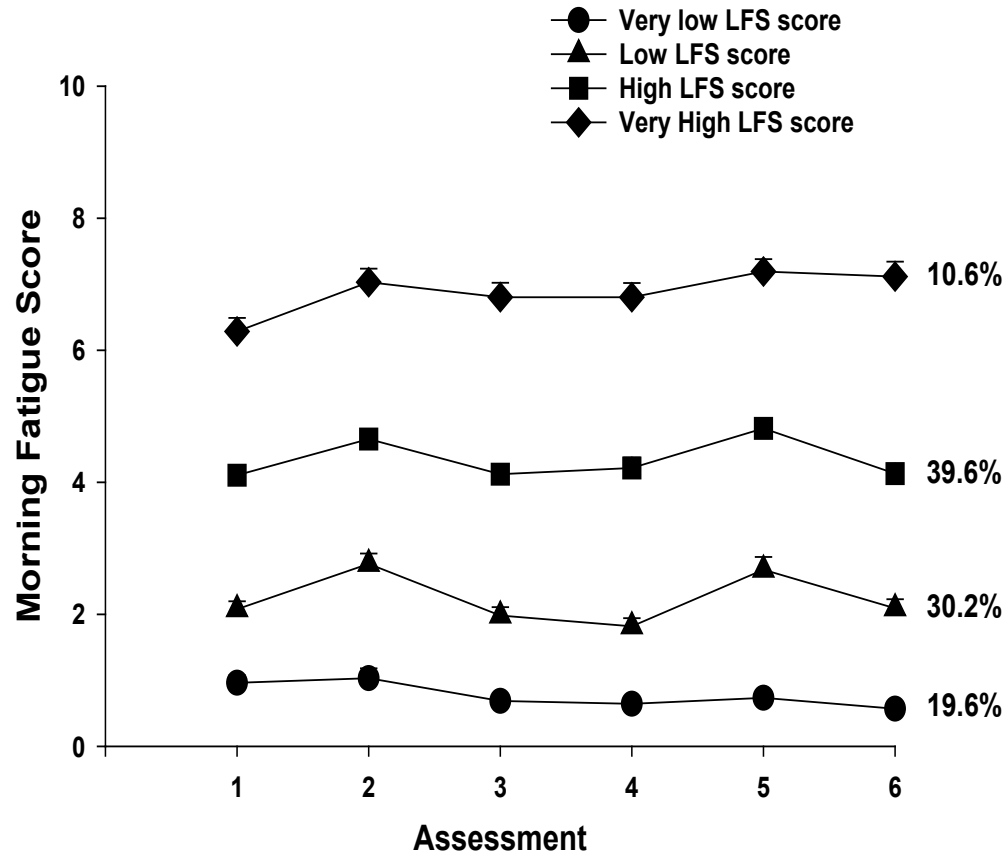


Latent Profile Analysis of Evening Fatigue



- Younger age
- Higher education
- Being female
- Being White
- **Having child care responsibilities**
- Lower functional status
- Higher comorbidity
- Diagnosis of depression
- Higher levels of stress
- Higher levels of sleep disturbance

Latent Profile Analysis of Morning Fatigue

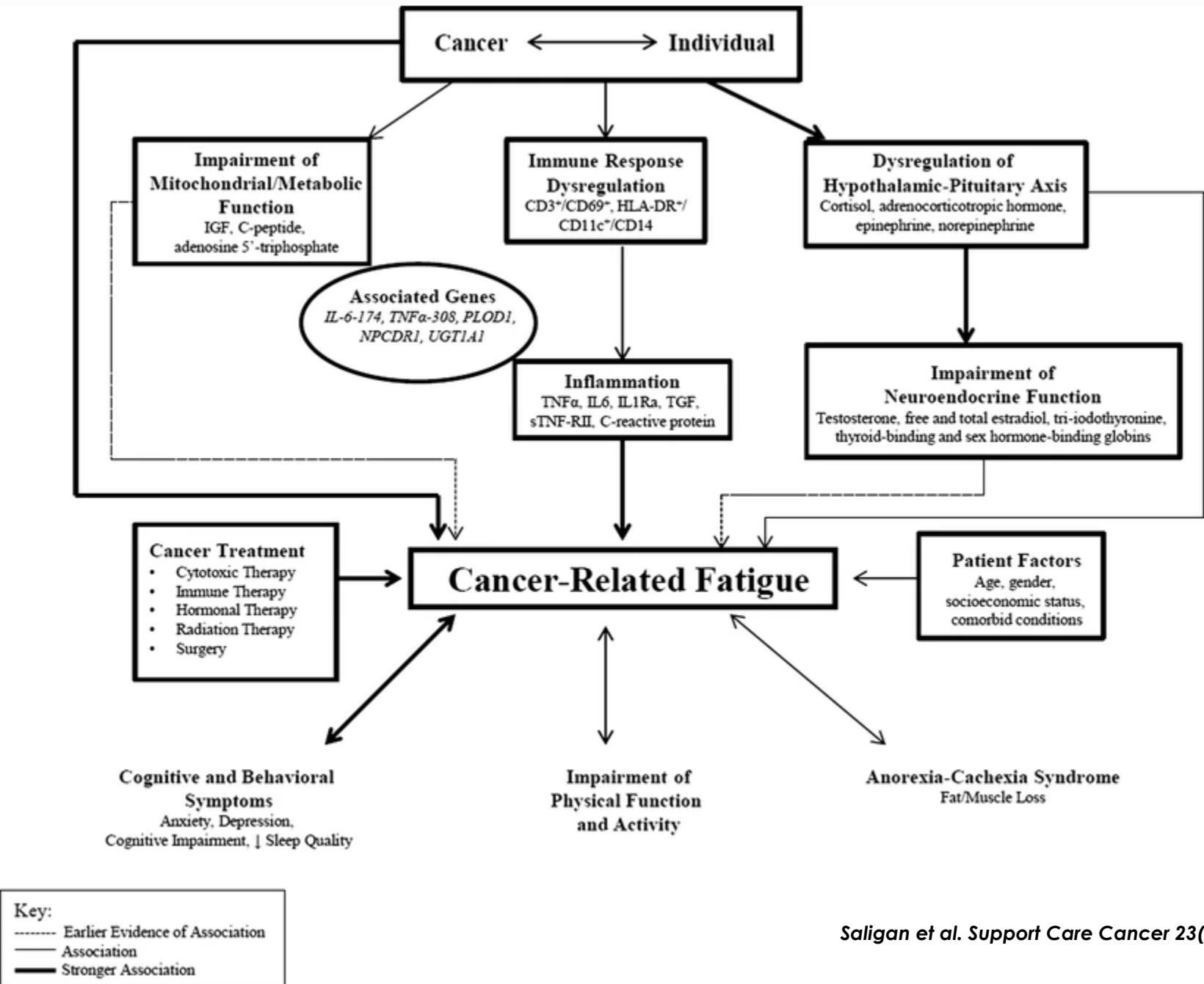


- Younger age
- Being female
- **Not married/partnered**
- **Living alone**
- **Having a higher income**
- **Being unemployed**
- **Higher BMI**
- Lower functional status
- Higher comorbidity
- Diagnosis of depression
- Higher levels of stress
- Higher levels of sleep disturbance

Purple indicates different from PM fatigue

Perturbed KEGG Pathways (FWER <.05)

Number	Pathway Name	AM Fatigue	PM Fatigue
04145	Phagosome	X	X
04144	Endocytosis	X	X
04062	Chemokine signaling	X	X
04612	Antigen processing and presentation	X	X
04060	Cytokine-cytokine receptor interaction	X	X
04672	Intestinal immune network for IgA production	X	X
04695	Th17 cell differentiation	X	X
04010	MAPK signaling	X	X
04962	Relaxin signaling pathway	X	
05320	Autoimmune thyroid disease	X	
04921	Oxytocin signaling pathway	X	
03320	PPAR signaling pathway	X	
04080	Neuroactive receptor ligand interaction pathway	X	
04726	Serotonergic synapse	X	
05145	Toxoplasmosis		X
04072	Phospholipase D signaling pathway		X
04015	RAP 1 signaling pathway		X
01523	Antifolate resistance		X



SUMMARY

- **Fatigue is a common problem across the continuum of cancer care**
 - Significant impact on all aspects of quality of life
- **Lack of consensus on measurement**
 - Single versus multiple dimensions
 - Diurnal variations in fatigue
 - Correlations with objective measures of physical and cognitive function
- **Extremely complex phenotype**
 - Phenotypic risk factors warrant additional evaluation
 - Relationships between fatigue and stress (general, disease specific, cumulative life stress)
 - Relationship between stress and multiple co-occurring symptoms
- **Extremely complex mechanism**
- **Can a biosignature for CRF be created to predict high risk patients?**

Acknowledgements

- **National Cancer Institute**
- **American Cancer Society**
- **Members of Symptom Management Research Group**
- **All of the patients who participated in our studies**