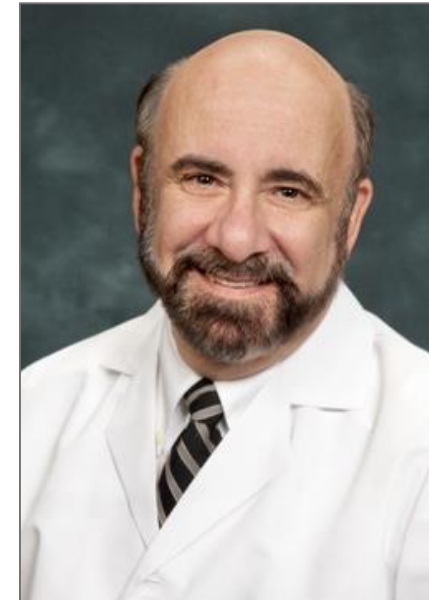


Fatigue and Transplant: New Insights

Celebrating a Second Chance at Life
Survivorship Symposium

July 11-17, 2020



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Fatigue and Transplant New Insights

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Transplant
Related
Fatigue

New Insights.



Learning Objectives:

1. Understand the effects of fatigue on quality of life following a transplant.
2. Understand what are the causes of fatigue.
3. Understand the possible treatments for fatigue.
4. Understand what you, the patient, can do to decrease the effects of Fatigue.

Tired versus Fatigue

Tired

- Weariness
- Lack of energy
- Decreased endurance
- Bored
- Doing too much but you bounce back
- Relieved by rest
- Generally temporary

Fatigue

- Less energy
- Less alert
- Trouble concentrating
- Socially isolating
- Not related to activities
- Not improved by rest
- Impaired sleep pattern
- Long lasting
- Difficult to treat

What is Cancer Fatigue?

Definition:

“a distressing persistent, sense of physical, emotional and/or cognitive tiredness or exhaustion that is not proportional to recent activity and interferes with usual functioning.”

Fatigue: Findings and Patient Complaints

I feel so ...

- Weak
- Tired all the time - every part of body is tired.
- I wake up tired.
- Need to rest all the time.

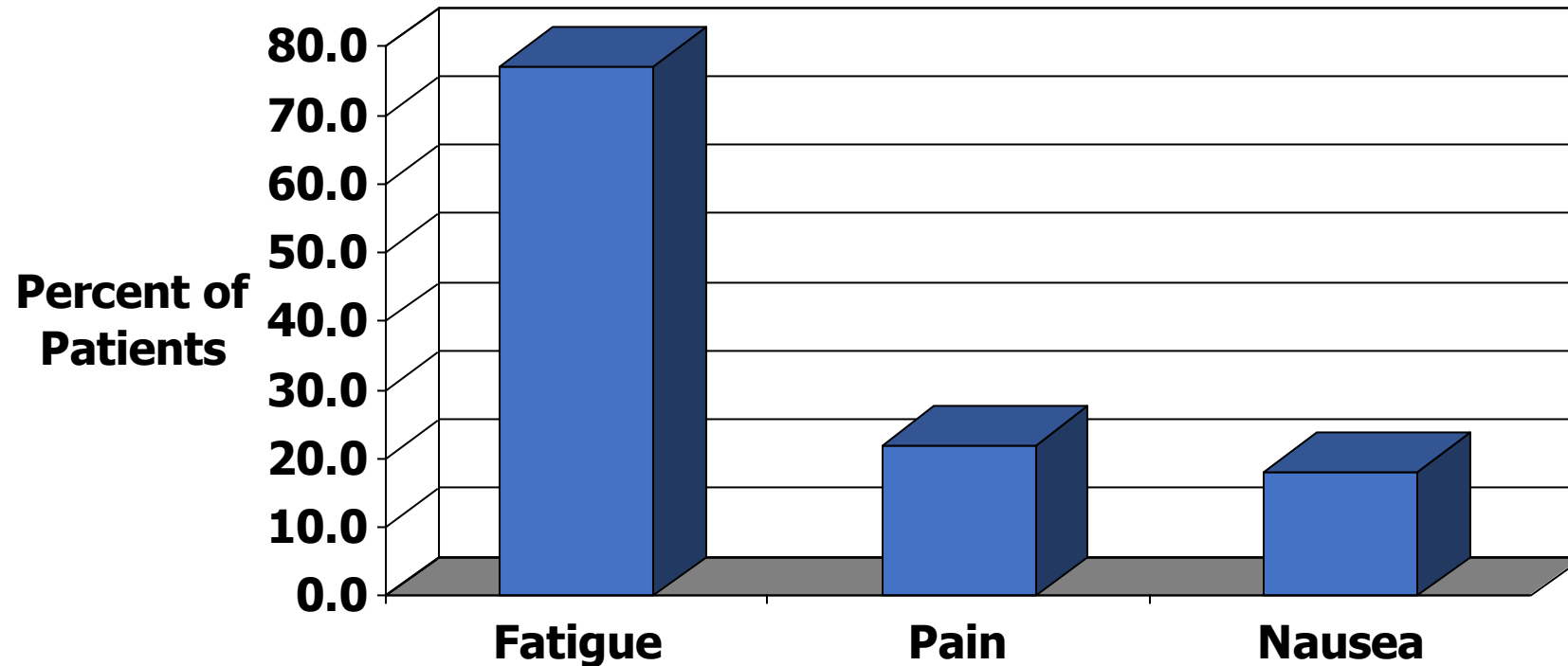
I now ...

- Lack motivation.
- Interest in others.
- Have trouble sleeping at night.
- Am too tired to think clearly.

I used to...

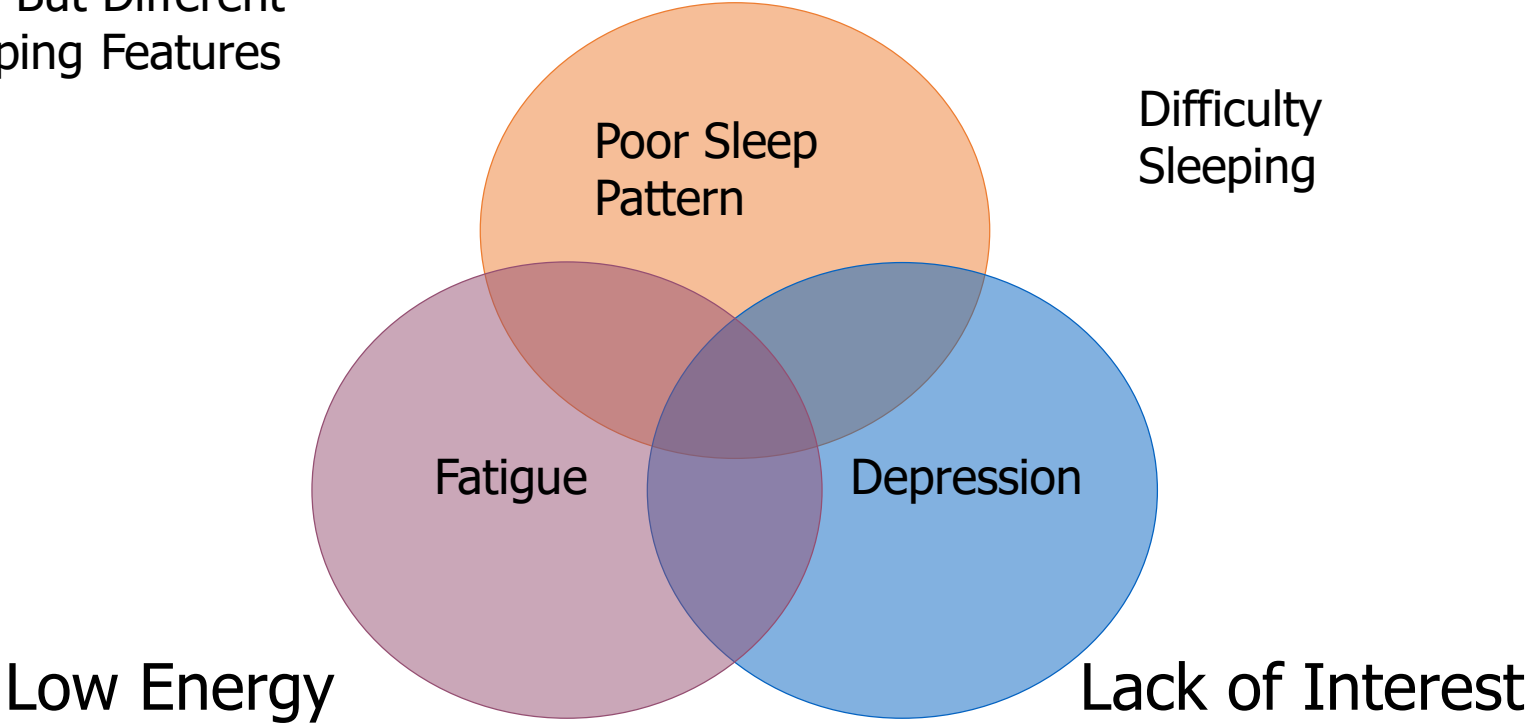
- Work.
- Have lots of interests.
- Socialize frequently.
- Interested in sexual relations.

Fatigue -The Most Common Symptom Associated with Cancer Survivorship.



Fatigue – Multifactorial

Similar But Different-
Overlapping Features

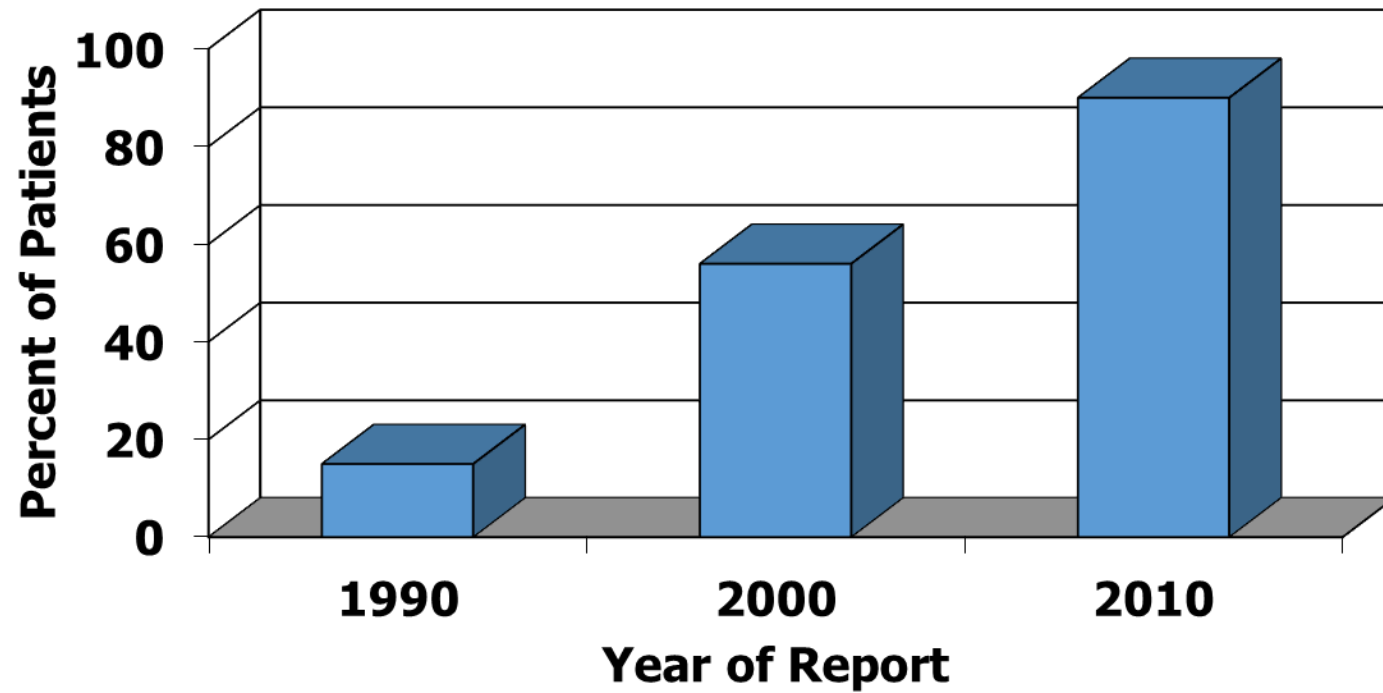


Conceptually Different

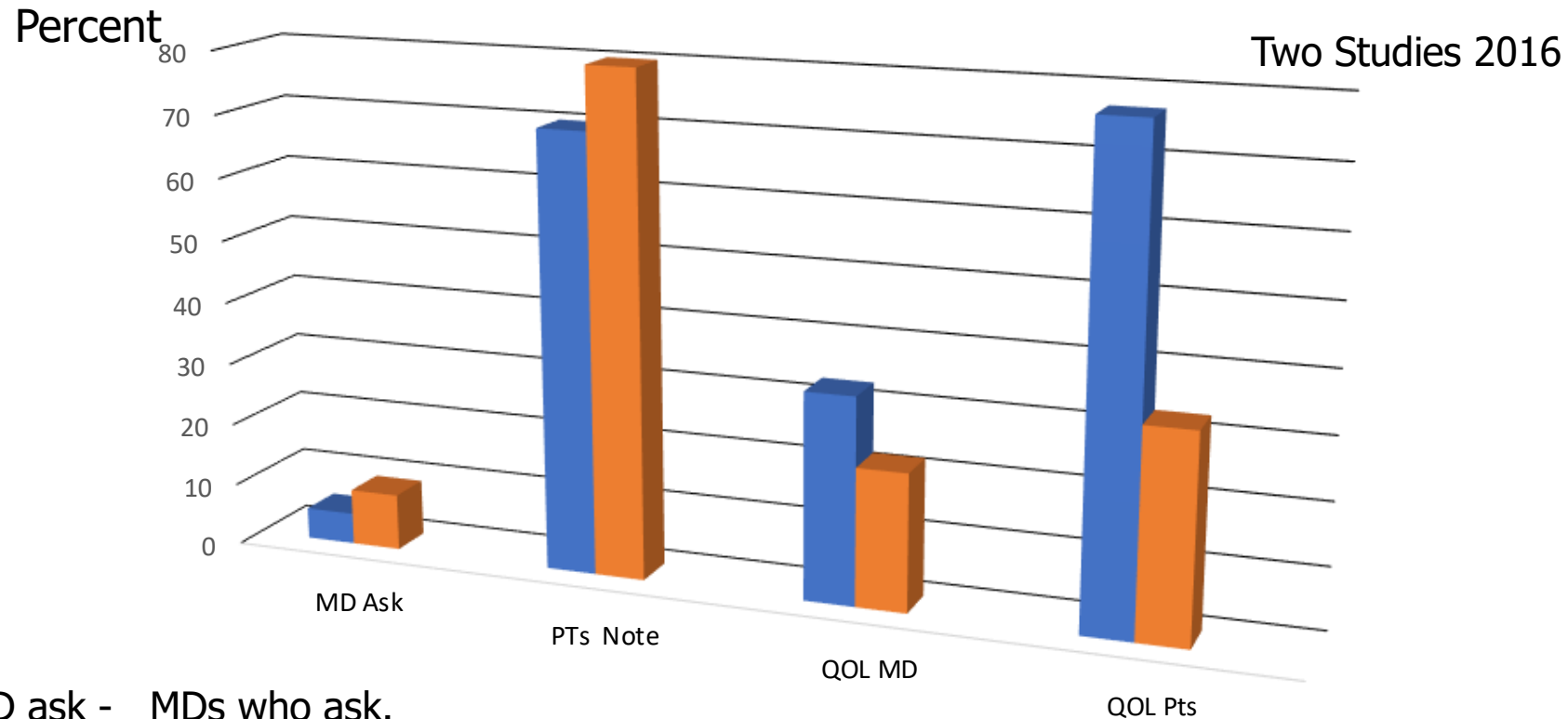
Fatigue – Studies in Transplant Patients

- Age related - Fatigue Increased in patients over the age of 60
- More frequent in females
- Correlated with sleep disturbances – poor sleep patterns
- More frequent following total body irradiation
- May not improve with time
- Correlated with pre–transplant symptoms and treatments

Physicians Don't Ask, Patients Don't Tell



Fatigue – Do You Tell the Doctor ?



MD ask - MDs who ask.

PTs Note - Patients - fatigue when asked.

QOL MD – MD note impaired QOL.

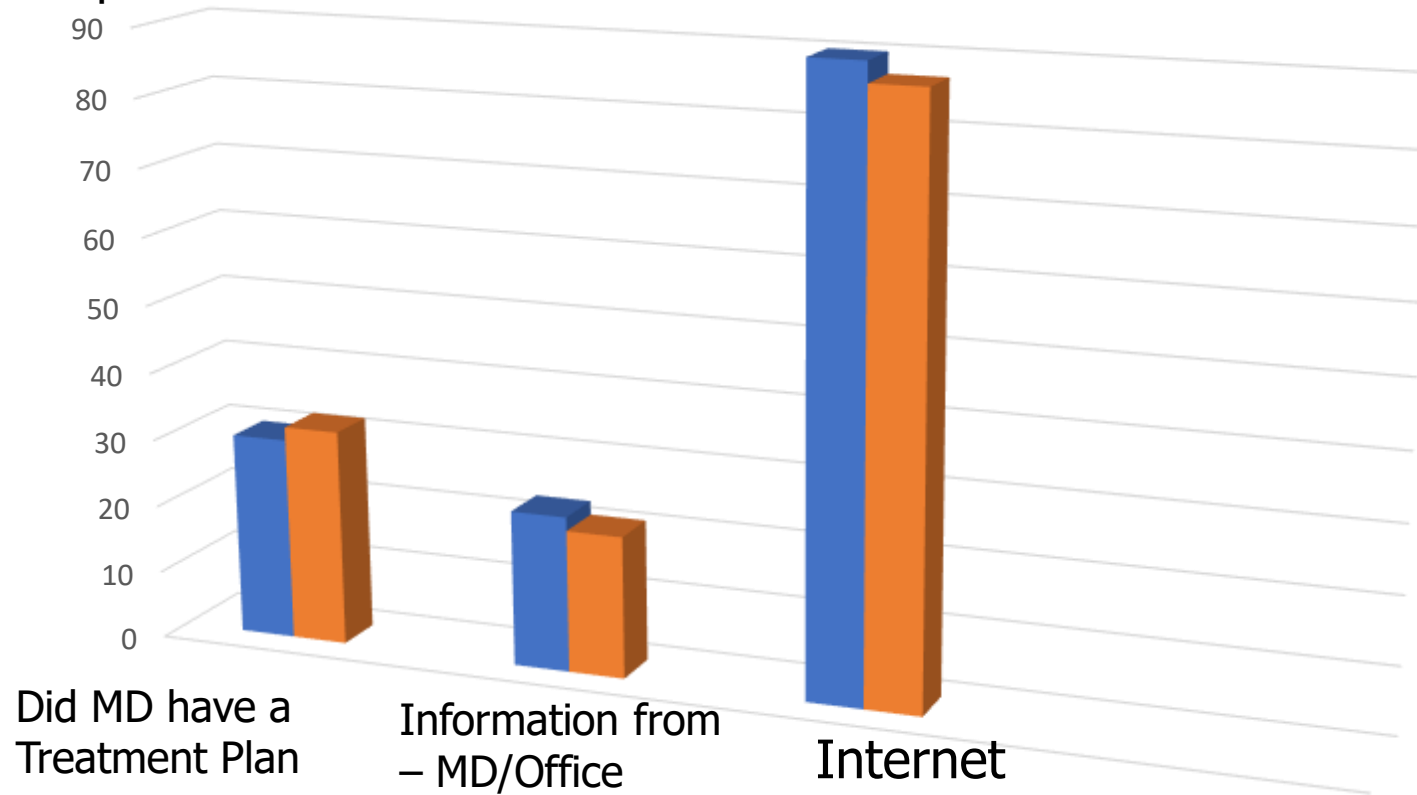
QOL PTs - Patient noted impairment of QOL

Why Patients Don't Ask about Fatigue

- Fear – a sign of relapse?
- Doctor does not know how to treat fatigue.
- More important things to discuss.
- Not enough time to discuss.
- It's my fault – I'm just not doing enough.
- Want to help/please the physician – I'M OK.

Patients - Source of Information on Fatigue

Percent of Patients
-2 Groups



Why Physicians Don't Ask?

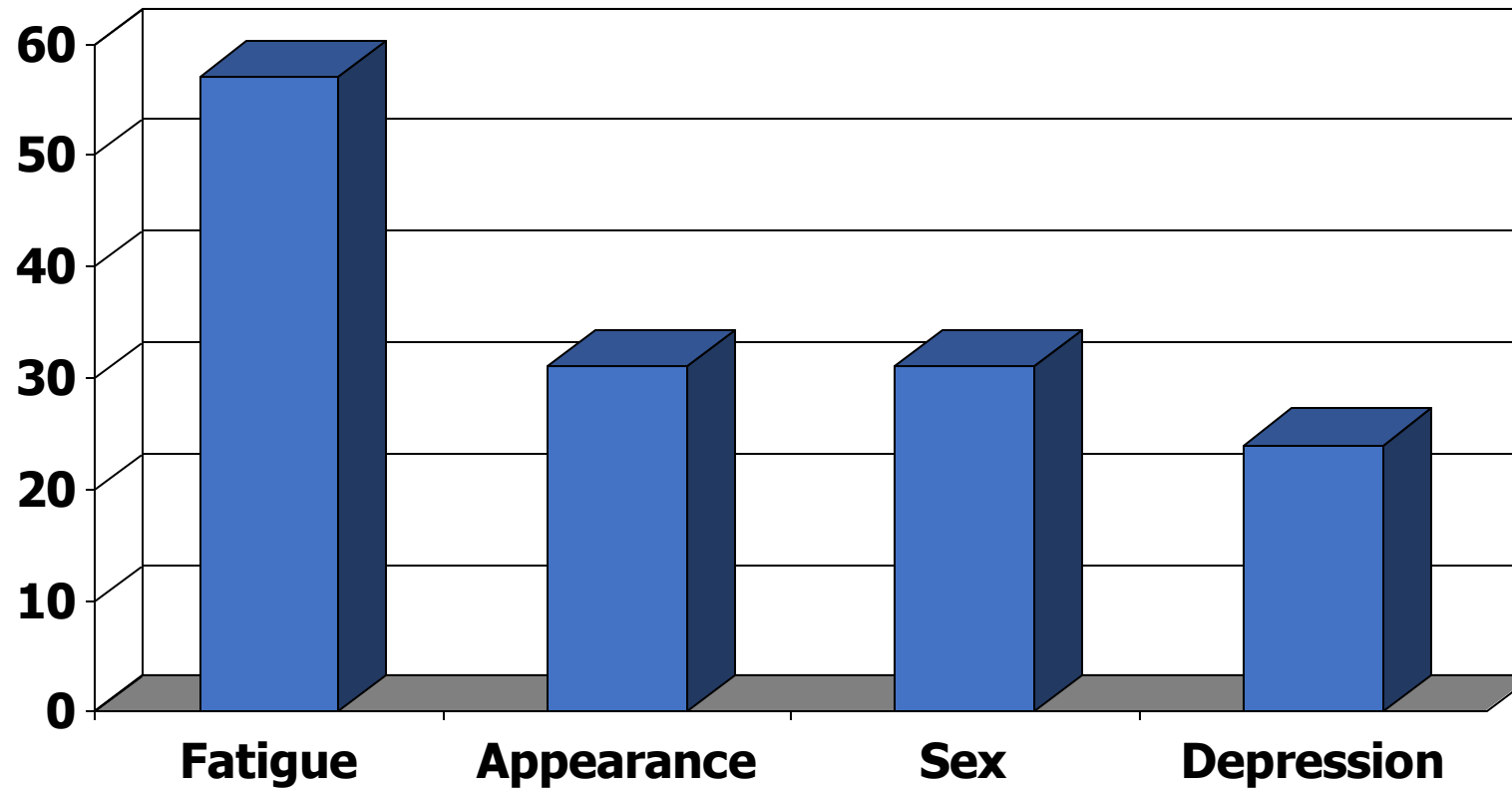
- It's not a big problem.
- More important issues to discuss.
- Can't fix it.
- Not enough time to discuss.
- I'm tired all the time too.
- Lack of accepted diagnostic criteria – restricted drugs, no simple solutions.

Fatigue Pre-Transplant Studies in Patients Who Developed Fatigue after Transplant.

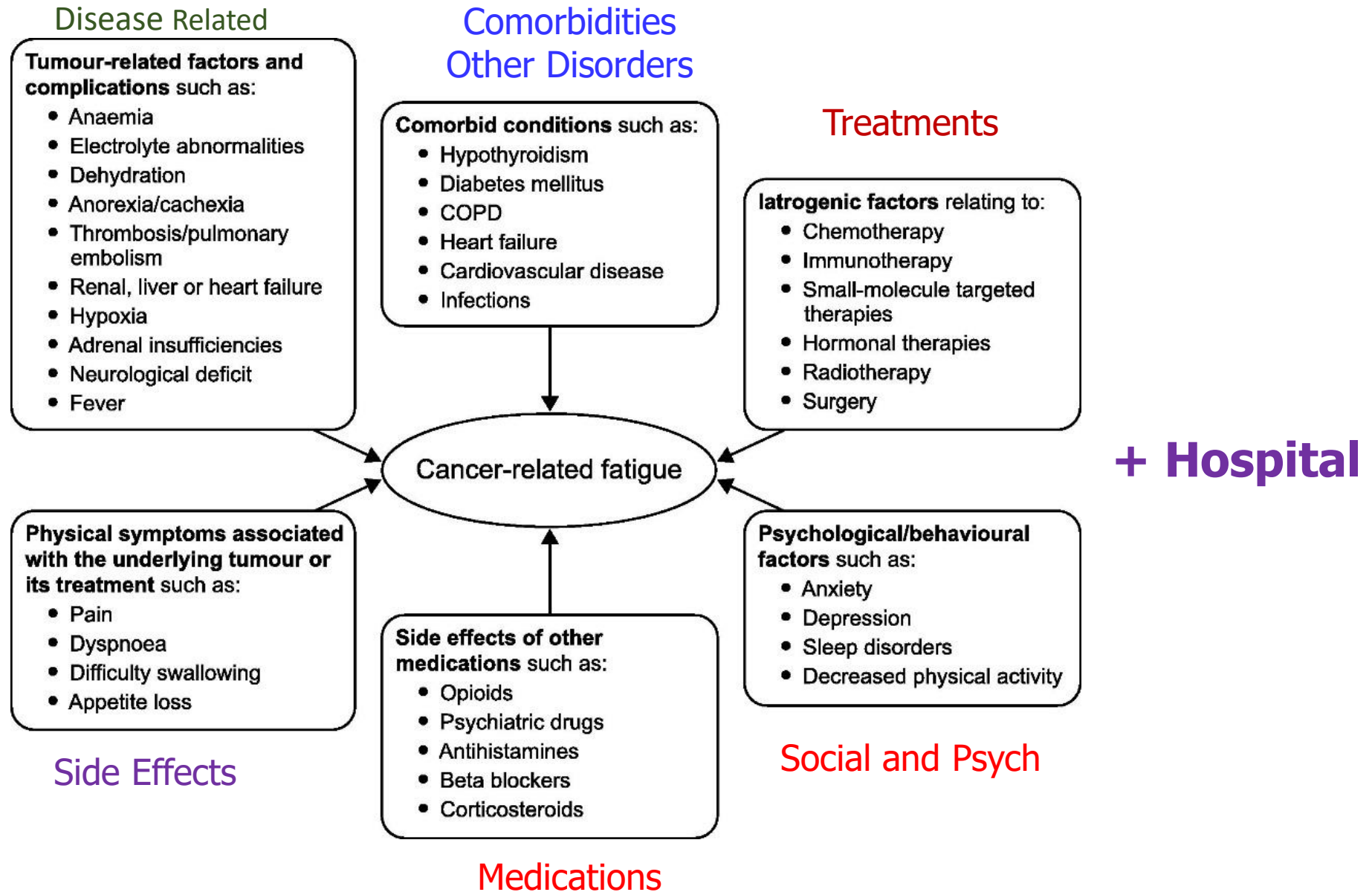
- Age related - Greater than 60 years higher pre and post transplant
- Baseline Quality of Life
- Females more than Males
- Emotional Support - Resources , Family, Spouse, Children
- Correlated with Disturbances in Sleep. Poor sleep pattern
- Income – negative – Higher income more likely to note fatigue

Can Address Prior to Starting the Transplant.

Quality of Life Concerns in Transplant Survivors > 1 Year



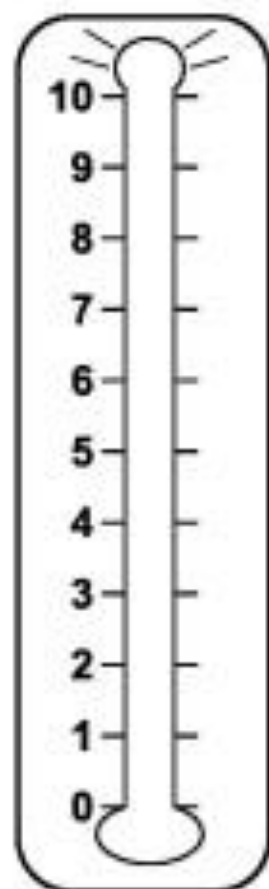
Causes of Fatigue



SCREENING TOOLS FOR MEASURING DISTRESS

Instructions: First please circle the number (0-10) that best describes how much distress you have been experiencing in the past week including today.

Extreme distress



No distress

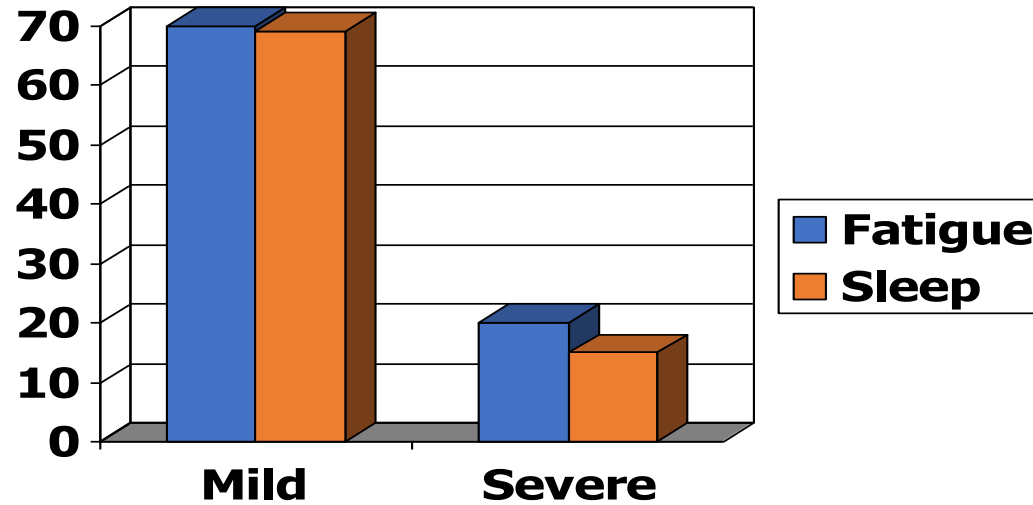
Second, please indicate if any of the following has been a problem for you in the past week including today. Be sure to check YES or NO for each.

- | YES | NO | <u>Practical Problems</u> | YES | NO | <u>Physical Problems</u> |
|--------------------------|--------------------------|--------------------------------------|--------------------------|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> | Child care | <input type="checkbox"/> | <input type="checkbox"/> | Appearance |
| <input type="checkbox"/> | <input type="checkbox"/> | Housing | <input type="checkbox"/> | <input type="checkbox"/> | Bathing/dressing |
| <input type="checkbox"/> | <input type="checkbox"/> | Insurance/financial | <input type="checkbox"/> | <input type="checkbox"/> | Breathing |
| <input type="checkbox"/> | <input type="checkbox"/> | Transportation | <input type="checkbox"/> | <input type="checkbox"/> | Changes in urination |
| <input type="checkbox"/> | <input type="checkbox"/> | Work/school | <input type="checkbox"/> | <input type="checkbox"/> | Constipation |
| <input type="checkbox"/> | <input type="checkbox"/> | Treatment decisions | <input type="checkbox"/> | <input type="checkbox"/> | Diarrhea |
| | | | <input type="checkbox"/> | <input type="checkbox"/> | Eating |
| | | | <input type="checkbox"/> | <input type="checkbox"/> | Fatigue |
| | | | <input type="checkbox"/> | <input type="checkbox"/> | Feeling swollen |
| <input type="checkbox"/> | <input type="checkbox"/> | <u>Family Problems</u> | <input type="checkbox"/> | <input type="checkbox"/> | Fevers |
| <input type="checkbox"/> | <input type="checkbox"/> | Dealing with children | <input type="checkbox"/> | <input type="checkbox"/> | Getting around |
| <input type="checkbox"/> | <input type="checkbox"/> | Dealing with partner | <input type="checkbox"/> | <input type="checkbox"/> | Indigestion |
| <input type="checkbox"/> | <input type="checkbox"/> | Ability to have children | <input type="checkbox"/> | <input type="checkbox"/> | Memory/concentration |
| <input type="checkbox"/> | <input type="checkbox"/> | Family health issues | <input type="checkbox"/> | <input type="checkbox"/> | Mouth sores |
| | | | <input type="checkbox"/> | <input type="checkbox"/> | Nausea |
| | | | <input type="checkbox"/> | <input type="checkbox"/> | Nose dry/congested |
| <input type="checkbox"/> | <input type="checkbox"/> | <u>Emotional Problems</u> | <input type="checkbox"/> | <input type="checkbox"/> | Pain |
| <input type="checkbox"/> | <input type="checkbox"/> | Depression | <input type="checkbox"/> | <input type="checkbox"/> | Sexual |
| <input type="checkbox"/> | <input type="checkbox"/> | Fears | <input type="checkbox"/> | <input type="checkbox"/> | Skin dry/itchy |
| <input type="checkbox"/> | <input type="checkbox"/> | Nervousness | <input type="checkbox"/> | <input type="checkbox"/> | Sleep |
| <input type="checkbox"/> | <input type="checkbox"/> | Sadness | <input type="checkbox"/> | <input type="checkbox"/> | Substance abuse |
| <input type="checkbox"/> | <input type="checkbox"/> | Worry | <input type="checkbox"/> | <input type="checkbox"/> | Tingling in hands/feet |
| <input type="checkbox"/> | <input type="checkbox"/> | Loss of interest in usual activities | | | |
| <input type="checkbox"/> | <input type="checkbox"/> | <u>Spiritual/religious concerns</u> | | | |

Other Problems: _____

Sleep Disturbances Related to Fatigue

Percent Reporting



Cancer Related Fatigue Positive Feedback Cycle

- Fatigue > less physically active → deconditioning → loss of muscle mass > increased weakness.
- Fatigue - naps > trouble with nighttime sleeping → daytime fatigue.
- Fatigue > less enjoyable activities - becomes more depressed – lonely.
- Medications > Antiemetics, opioids, pain meds.
- Cancer and treatment - can cause fatigue through neurohormonal mechanisms - side effects.

But, The Big Picture Why Does it Happen?



Disorders with Fatigue

Common Features and Similar Causes

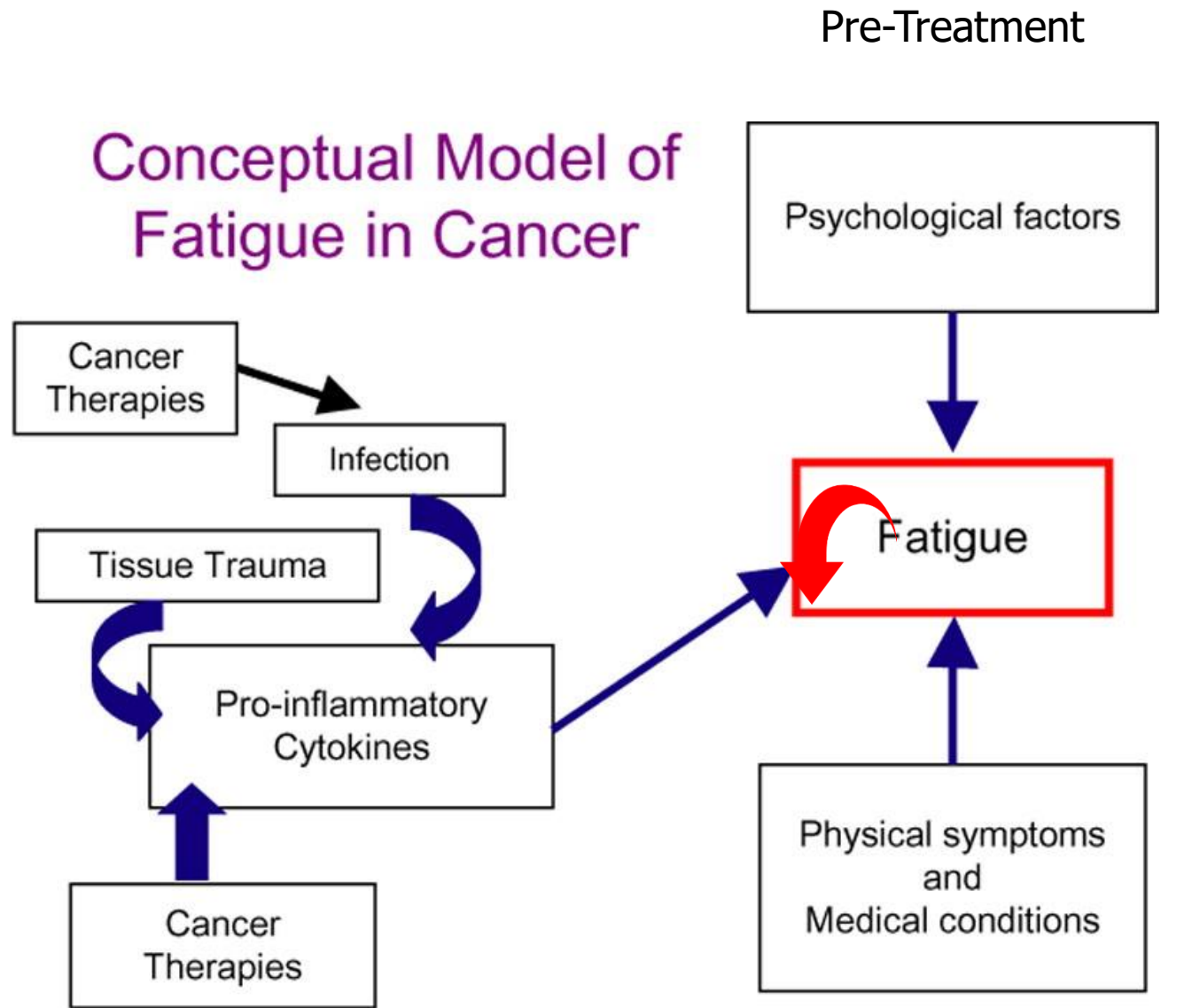
- Aging – Aging is associated with fatigue. But aging is not linear- studies hard to compare.
- Frailty – Cancer associated cachexia - Loss of muscle mass. Falls increase.
- Multiple Sclerosis - Target cytokines & inflammation 3-6 , 12 months.
- Myasthenia gravis.
- Post Stroke Fatigue.
- Heart Failure.
- Blood Disorders - Myeloid Neoplasms.*

Cancer- Transplant Related Fatigue

- Cancer – cancer treatments *
- Effects of treatment – anemia –low white counts, low platelets.
- Infection - end organ effects.
- Decreased appetite- poor nutrition, weight loss.
- Electrolyte abnormalities.
- Medication side effects
- Concurrent symptoms- pain, nausea, diarrhea, dyspnea
- Impaired sleep
- Inactivity- loss of muscle mass
- Psychological distress – depression- anxiety- financial

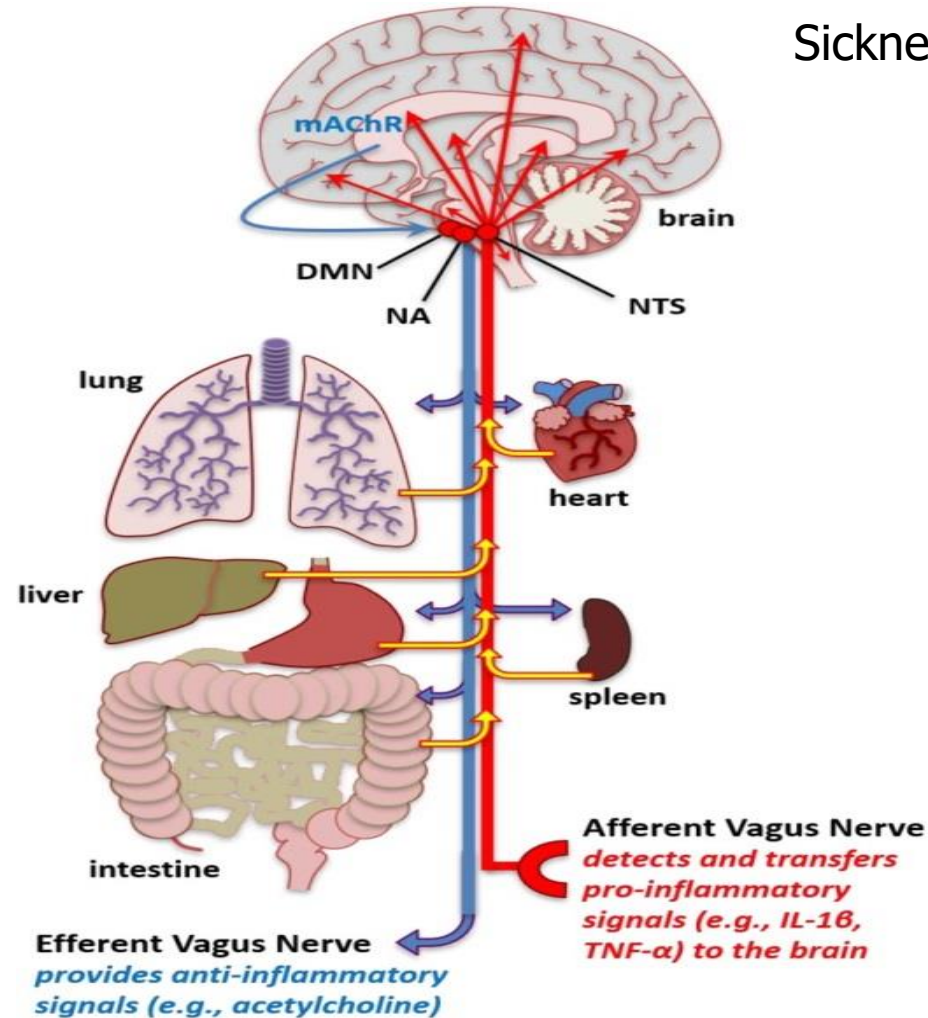
Pro-inflammatory cytokine mediated effects. *

Conceptual Model of Fatigue in Cancer



Pre and Post Treatment Effects.

New Concepts in Fatigue – Inflammation from End Organ Sends Signals to the Brain



Sickness Behavior – Brain Interprets it all.

Similar to Heart failure.

Cirrhosis.

Neurological Disorders – MS.

“Sickness Behavior” Signals to the Brain

- Fatigue.
- Disturbed Sleep – decreased or increased – impaired sleep pattern.
- Depression.
- Decreased appetite.

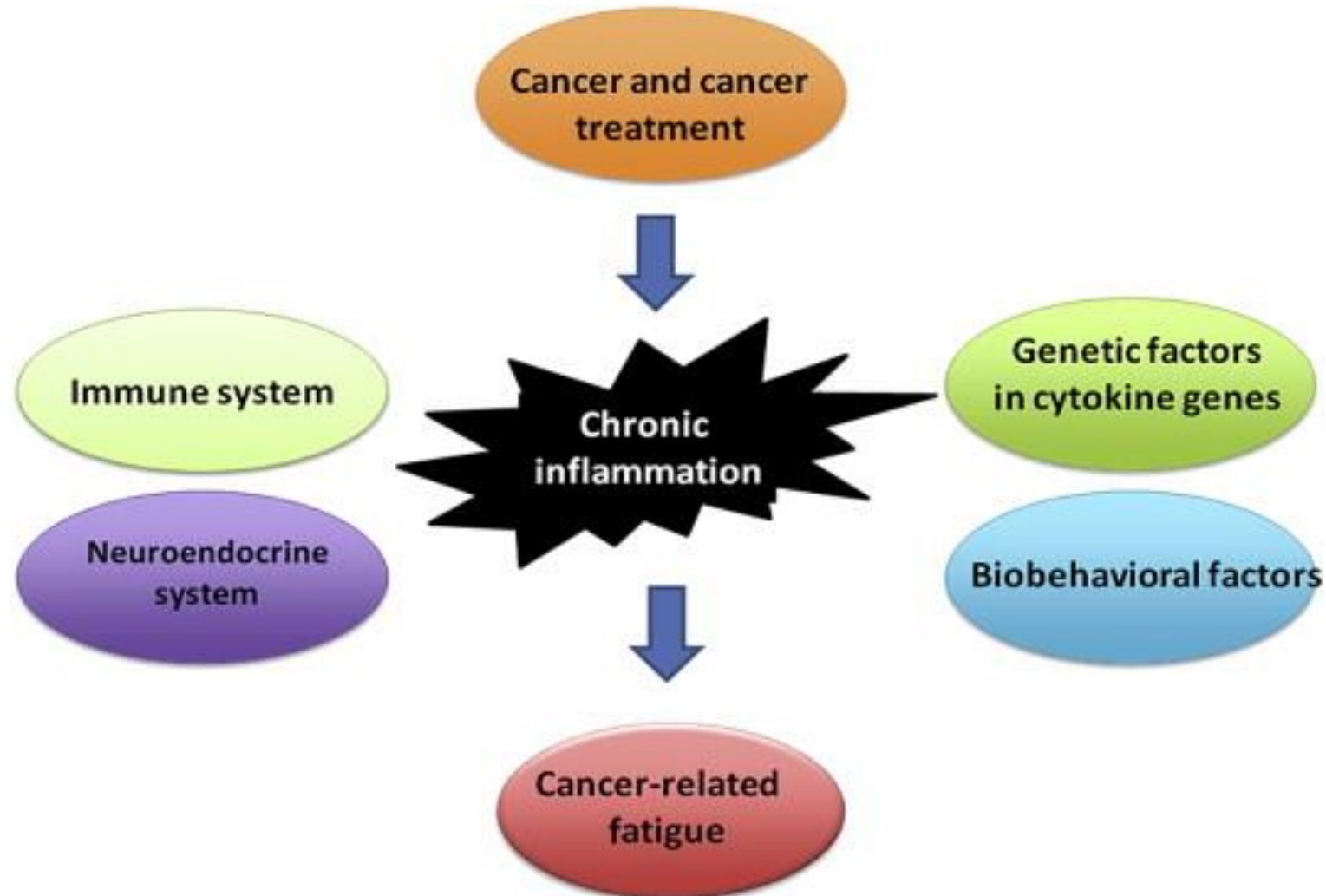
Cause of Fatigue- Current Theories

- Activation of pro-inflammatory cytokines.
- Signals to the brain to promote “Sickness Behavior” = fatigue, disturbed sleep, depression.
- Increased Expression of inflammatory related genes.
- Abnormalities of energy metabolism- impaired muscle function. Muscles require increased energy needs.
- Fatigue – maybe patient, cytokine, cancer and treatment specific.

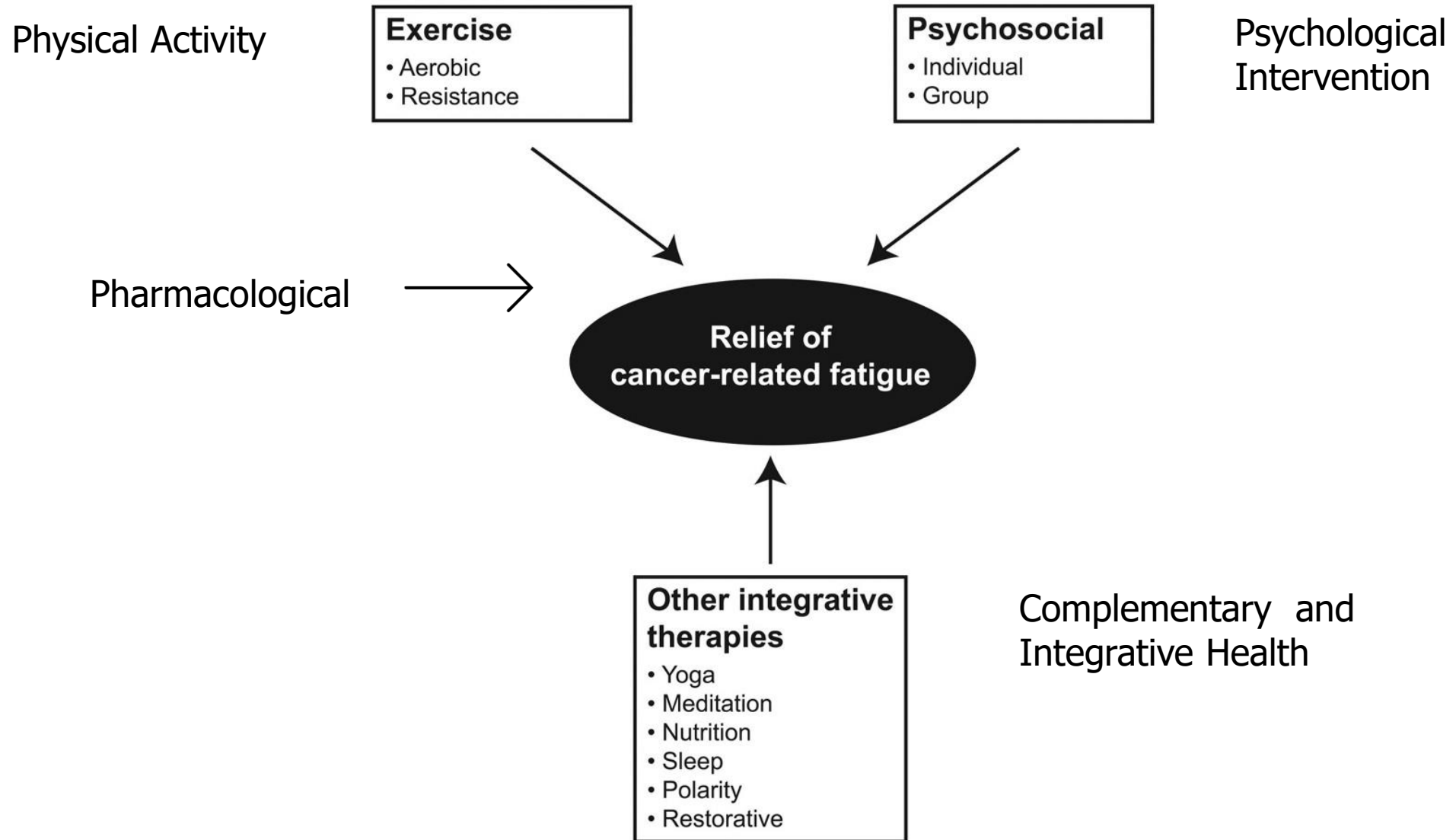
Fatigue and Transplantation

- Fatigue can occur early or late after transplant.
- Fatigue impairs quality of life.
- Increased incidence in graft versus host disease.
- Fatigue in both allogeneic and autologous stem cell transplants.
- Age related >60 years
- May last for years
- New scoring system FACT-F

Cancer Transplant Related Fatigue Multifactorial



Treatments



Positive Studies with Baseline Fatigue

Exercise:

- Physical deconditioning
- Strength training helpful
- Targeted physical therapy
- Combined with cognitive behavioral therapy
- Aerobic and Non aerobic - both better
- Every other day > 10 minutes
- Supervised better

Exercise - Mechanisms of Action

- Optimize function of multiple systems
- Changes muscle biochemistry
- Delays muscle fatigue
- Decreases perception of fatigue and shortness of breath
- Decreased depression and anxiety
- Cognitive behavior changes

Exercise: When to Begin?

- Study started exercise on admission- prior to transplant
- Randomized 1:1 Individual Exercise Program to Day +100
- Aerobic 30 min, 5 days a week – 40-60% max heart rate –light to moderate intensity
- Patients in the exercise group noted less fatigue and increased cognitive function and “improved “ quality of life at day +100. In hospital supervised exercise is possible.

Cognitive Behavior Therapy: CBT-Strategies

- Targeted physical therapy.
- Change in illness related cognition- adaptive strategies (wheel chair, lifts, O₂, carts, walking). Help yourself.
- Motivation.
- Maintain social contacts.
- Don't set patients up to fail!
- Need to plan your day.

“Reality leaves a lot to the imagination.”

[John Lennon](#)

Mind and Body Practices to Reduce Fatigue – Non Physical Interventions

- Non Physical Activities to Reduce Fatigue
- Evaluated multiple trials – 4975 patients
- Mindfulness and Relaxation Reduced Fatigue Severity.
- Mindfulness - Supportive therapy
 - Defined as bringing one's complete attention to the present moment-to-moment experience in an accepting way.
 - This can help people become more aware of their automatic reactions to situations in life so that they can then choose to respond more effectively.
 - Focus patients' awareness to the present moment can help them experience less distress.

Alertness Enhancing Agents

Psycho-stimulants

- Antidepressants – but not all – unclear benefit
- Caffeine –limited benefit
- Stimulants
- Methylphenidate/dexamethylphenidate – Ritalin
 - Short acting vs long acting.
 - Addictive potential
 - Intermittent Dosing - use prior to activities/exercise/family events
 - AM or early afternoon
 - Studies suggest benefit
 - Side effects - dose is patient specific
 - Controlled substance

Alertness Enhancing Agents

Excessive sleepiness, narcolepsy-sleep apnea, Shift-work disorders, “Non Stimulants”

- Less highs and lows - less jittery - longer lasting
- Less addictive potential
- Insomnia an issue
- New field of research- not approved for CRF
 - Provigil (Modafinil)
 - Nuvigil (Armodafinil)
 - Once a day - less dependence?
 - Side effect profile - still an issue - dosing unclear
 - Long benefit unclear

Alternative Treatments

- Complementary & alternative Medicine
- Yoga
- Acupuncture
- Relation therapy
- Sleep hygiene
- Diet

Fatigue

**New instruments to measure.
Better studies to come.**

- Energy
- Mood
- Intellectual capacity
- Family life
- Sexual relationships
- Professional life
- Leisure activity
- QOL

Fatigue Scoring System - NCCN

Score

- 0 No symptoms
- 1-3 Mild
- 4-6 Moderate
- 6-9 Severe
- 10 Worst

Proposed ICD-10 Criteria for Cancer Related Fatigue

1. Significant fatigue, diminished energy, or increased need to rest disproportionate to any recent change in activity level
2. Complaints of generalized weakness or limb heaviness
3. Diminished concentration or attention
4. Decreased motivation or interest to engage in usual activities
5. Insomnia or hypersomnia
6. Experience of sleep as unrefreshing or nonrestorative
7. Perceived need to struggle to overcome inactivity
8. Marked emotional reactivity (e.g. sadness, frustration, or irritability) to feeling fatigued
9. Difficulty completing daily tasks attributed to feeling fatigued
10. Perceived problems with short-term memory
11. Post exertional malaise lasting several hours

- **Standards of care in cancer-related fatigue management:**
 - Use a multidisciplinary approach.
 - Educate and train health professionals in fatigue management.
 - Include fatigue in clinical health outcome studies and institutional continuous quality improvement projects.
 - Medical care contracts should include reimbursement and pay for treatments.
 - Disability insurance should include coverage for the continuing effects of fatigue.
 - Rehabilitation should begin with the diagnosis.

Importance of ICD codes

- Proposed ICD-10 Criteria for Cancer Related Fatigue.
- ICD codes help in prescribing medications.
- ICD codes help with disability.
- ICD codes in obtaining services and payments.

Fatigue – Preventive Strategies

- Schedule the day
- Plan activities
- Medication timing - Review medications
 - Avoid taking steroids in the evening
 - Avoid diuretics at night
 - Avoid day time sedation
- Difficult to catch up on loss of sleep
- Sleep Hygiene – need to plan
- Diet
- Hospitals are no place to sleep

What I do.



No one answer
One size fits all – No
Multiple approaches in each patient

Fatigue – What Should Patients Do?

- Talk to your health care provider.
- Ask for help.
- Discuss medications if fatigue continues.
- Structured exercise is better.
- Review sleep patterns – sleep hygiene.
- It takes time and planning.

Summary

- Cancer related fatigue is common.
 - 70-100% of patients on any kind of treatment experience fatigue.
- Lasts months to years after treatment ends – may be delayed in onset.
- Patient perceptions of fatigue
 - most distressing symptom
 - worse than pain or N/V
- Under-reported
- Under-diagnosed
- Under-treated
- **QOL- Need to ASK**

Sir William Osler, 1849-1919.
Died of influenza in the influenza pandemic 1918-1919
at the age of 70 in Oxford, England

The Father of Modern Medicine.

“The practice of medicine is an art, not a trade; a calling from your heart and your head.

Least we forget amid the racket of practice, few of us have the chance to warm both our hearts and hands at the fire of life, for our work is not an easy task...we must not forget to listen to our patients. ”



Questions?



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