Survivorship in Hematological Malignancies

The Long Road

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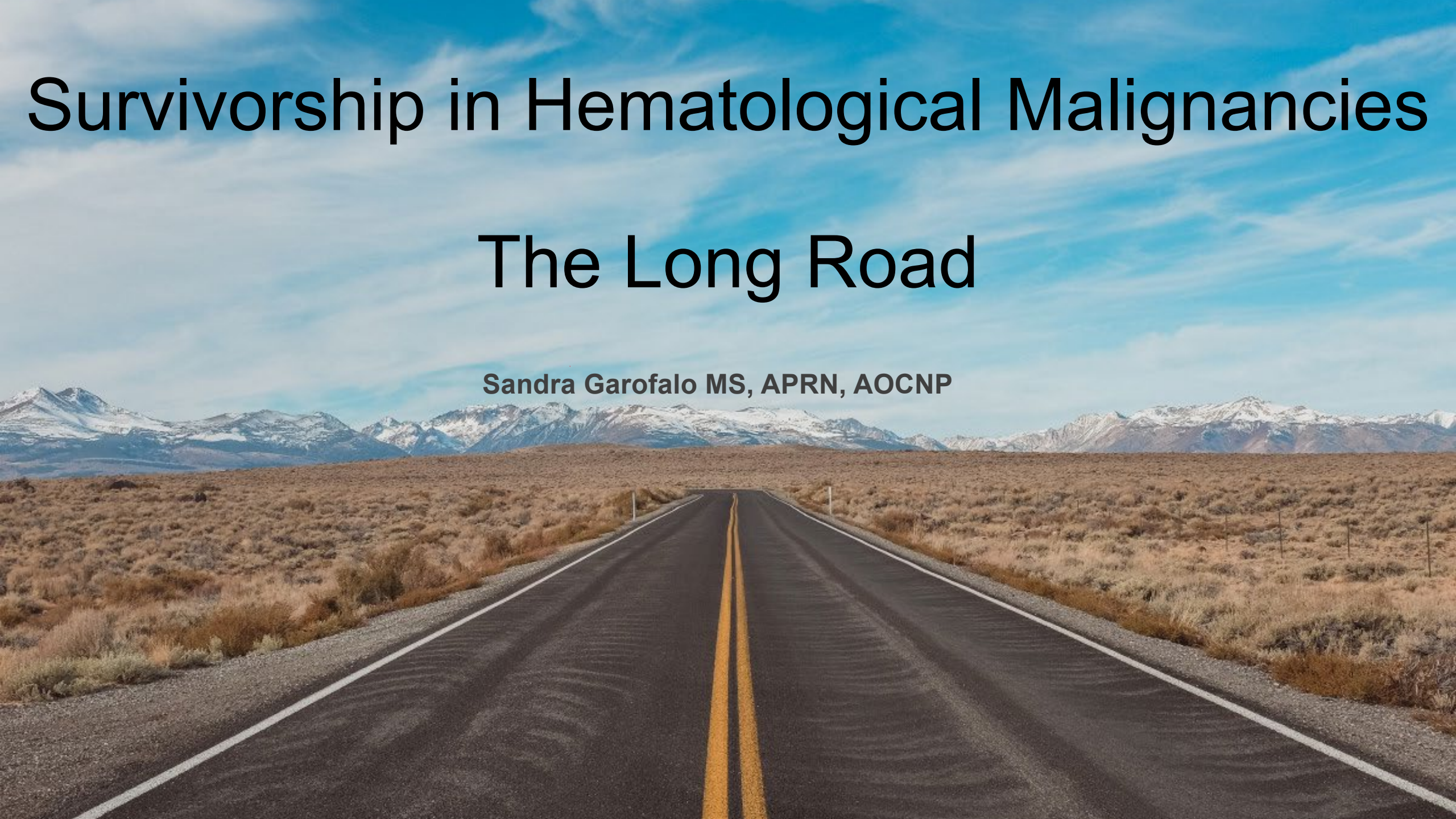

Disclosures:

N/A

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Learning Objectives

- Define survivorship and it's phases
- Recognize historical changes in long term survivorship
- Outline National Comprehensive Cancer Network (NCCN) guidelines for survivorship care
- Identify impact of adverse affects on survivors
- Describe social, emotional and physical challenges of cancer survivors and etiology
- List interventions for challenges that survivors face

Objective: Focus on Neuropathy

- Describe neuropathy and impact on quality of life
- List Neurotoxic agents
- Recognize risk factors for neuropathy
- Identify American Society of Clinical Oncology (ASCO) recommendations for the prevention and treatment of neuropathy
- Discuss Interventions
- Formulate plan for treatment of neuropathy in affected patients

Survivorship begins at diagnosis

As of January 2022, it is estimated that there are 18.1 million cancer survivors in the United States. This represents approximately 5.4% of the population.

Over the next decade, the number of people who have lived 5 or more years after their cancer diagnosis is projected to increase approximately 30%, to 16.3 million.

The number of cancer survivors is projected to increase by 24.4%, to 22.5 million, by 2032.

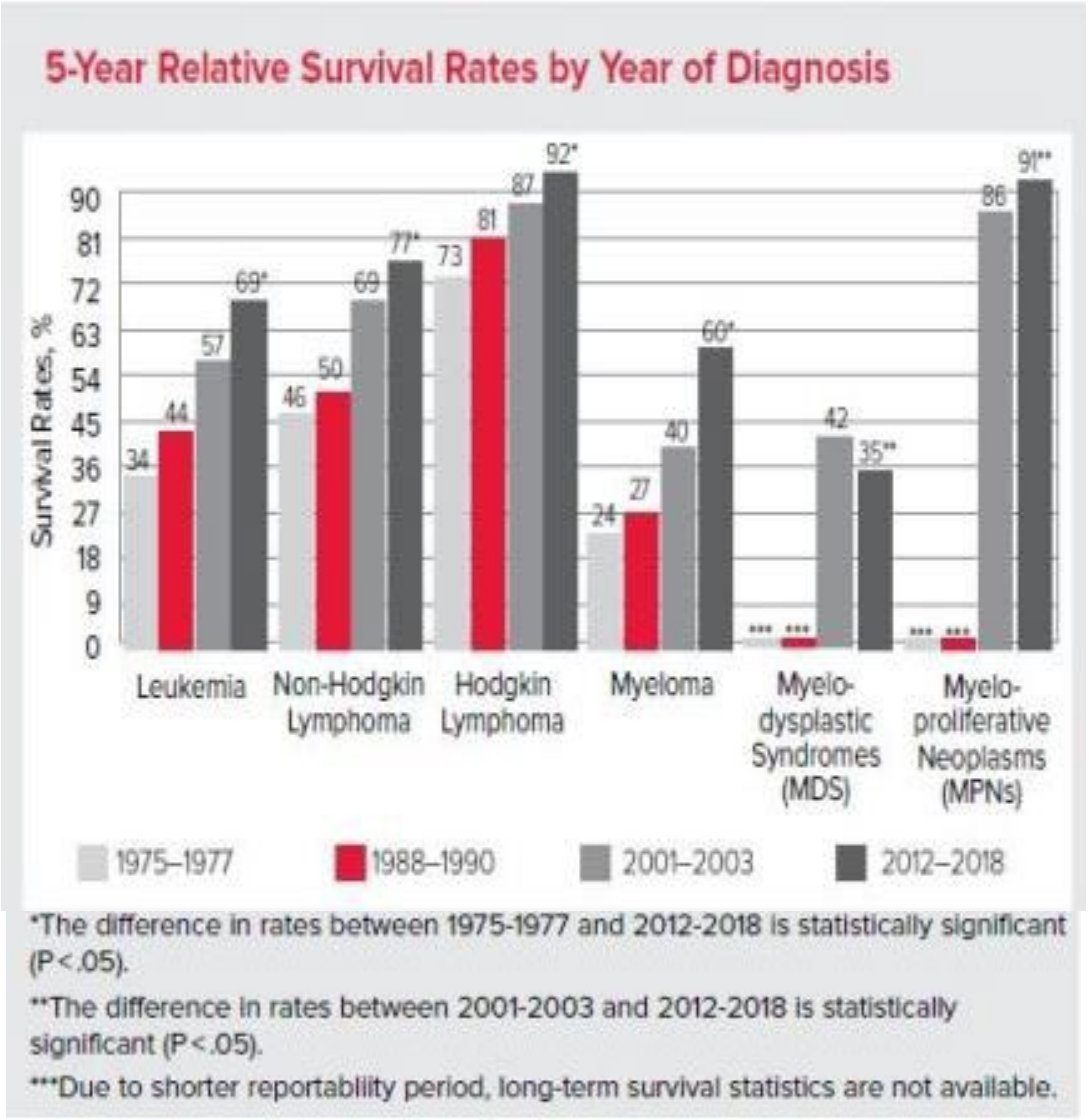
Division of Cancer Control and Population Sciences (DCCPS). (n.d.). https://cancercontrol.cancer.gov/

Phases of Survivorship

	Time of Diagnosis Acute Survivorship	End of Initial Treatment Extended Survivorship	End of Initial Assessment Permanent Survivorship
Focus	Cancer Treatment	Immediate effects of cancer and treatment	Long term effects of cancer and treatment
Duration	Several weeks	Several months	Several years

Physical, social and emotional challenges exist through all phases of treatment

Long term Survivors- How has it changed?



- Rate increase is statistically significant for each disease type.
- Leukemia survival rate has nearly doubled. (34% to 69%)
- Multiple Myeloma rate has more than doubled, nearly 2.5 times more than earliest data. (24% to 60%)
- MDS and MPN data was not collected prior to 2001.
- Examples of MPNs are polycythemia vera, essential thrombocytosis and myelofibrosis

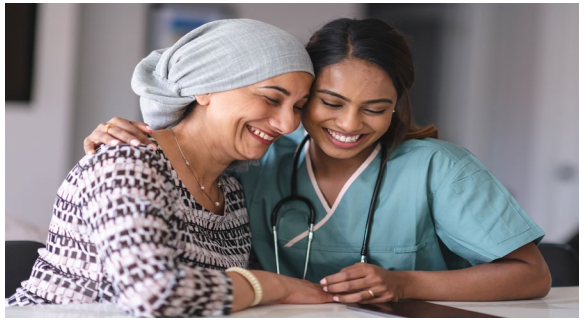
SEER (Surveillance, Epidemiology, and End Results) Cancer Statistics Review, 1975-1977. National Cancer Institute; 2020

NCCN Guidelines

- Screening for recurrence, progression or additional cancers
- Monitoring long-term effects of cancer and treatment
- Health Maintenance and management
- Coordination of Care, referral to specialists
- Support and Education in survivorship

Denlinger CS, Sanft T, Moslehi JJ, et al. NCCN Guidelines Insights: Survivorship, Version 2.2020. *J Natl Compr Canc Netw*. 2020;18(8):1016-1023. doi:10.6004/jnccn.2020.0037

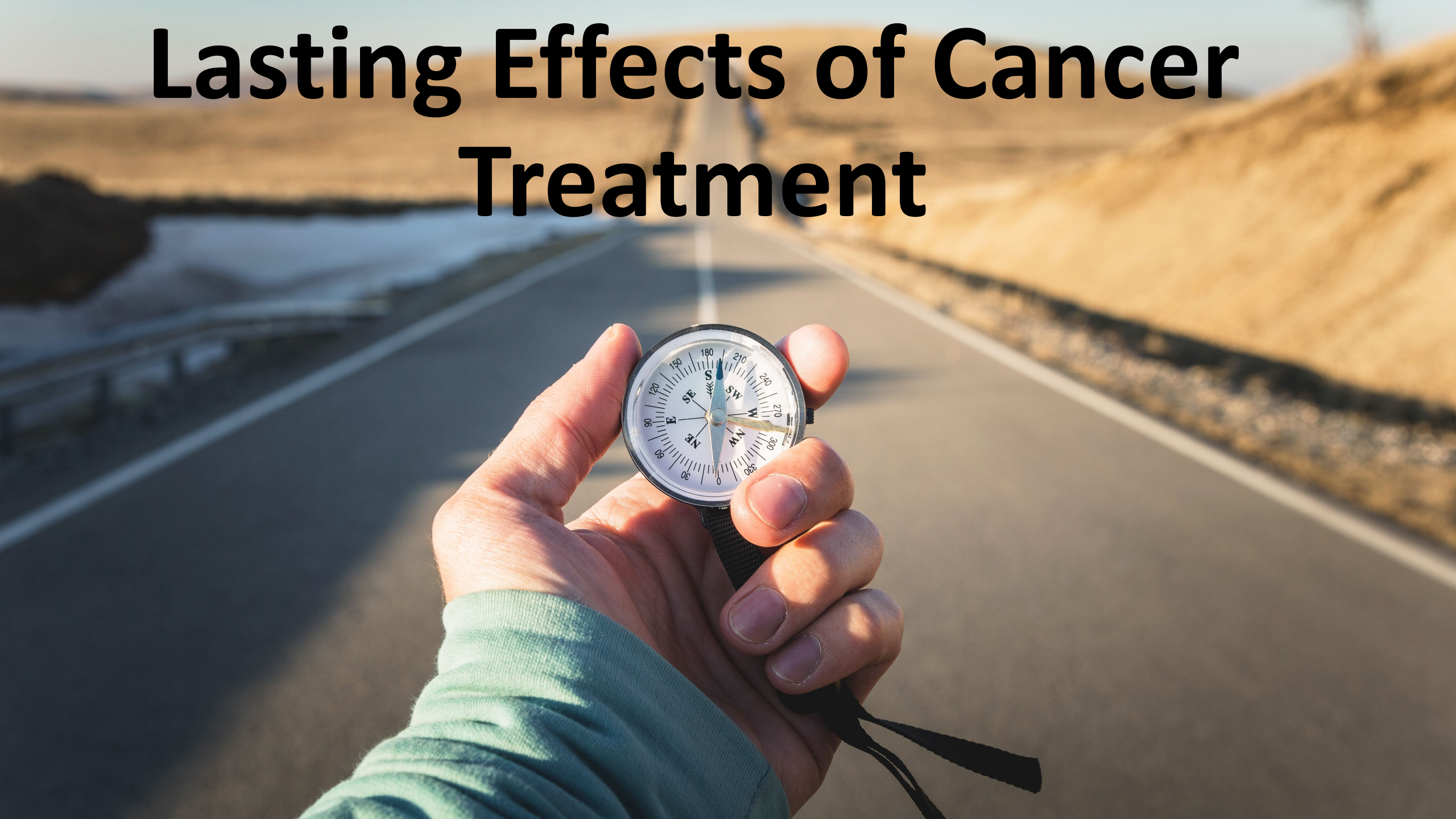
Nursing Care Plans



- Survivorship care plans are recommended by The Institute of Medicine
- Oncology Nursing Society conducted extensive literature review of the use and outcomes of care plans
  - Evidence and evaluation of the effectiveness of survivorship care plans in hematology care plans is lacking especially in comparison to those of solid tumors
  - **Nurses** have expertise in health promotion, information, support, resource provision and can develop and disseminate survivorship care plans to facilitate communication and action between patient and medical team.
  - Current evidence shows benefit to well structured care plan in survivorship

Taylor K, Monterosso L. Survivorship Care Plans and Treatment Summaries in Adult Patients With Hematologic Cancer: An Integrative Literature Review. *Oncol Nurs Forum*. 2015 May;42(3):283-91.

Lasting Effects of Cancer Treatment



Impact of Lasting Side Effects

- Greatest Impact on Quality of life per patient report 9
  - Fatigue 42.9%
  - Chemotherapy induced peripheral neuropathy 27.4%
  - Pain 12.4%
  - Sexual dysfunction and/or infertility 9.6%
- Disparities in adverse effects
  - Children and young adults (<1 yr – 39 yrs) have higher risk of severe and long term side effects 8
  - Women have a 34% high rate of severe adverse effects of cancer treatment 14
    - Higher compliance to treatment?
    - More likely to report symptoms?
    - Difference in metabolism?

Social and Emotional Challenges and Causes

Anxiety	• fear of progression and recurrence
Depression	• fatigue, isolation, lasting side effects
Fatigue	• Common side effect of medications
Insomnia	• steroid use, anxiety, depression
Financial toxicity	• cost of medical care, medications, chemotherapy
Loss of employment	• due to physical disabilities, side effects, frequency of treatment and/or distance from treatment
Loss of "pre-cancer" identity	• role changes due to illness, co-morbities and physical changes in appearance

Interventions

Anxiety	Counseling, support groups, frequent screening and clinic contact
Depression	Yoga, art therapy, physical therapy
Fatigue	Psychiatry referral for medications
Insomnia	Check labs for anemia, hypothyroidism, vitamin deficiency
Financial toxicity	Sleep hygiene, medications
Loss of employment	Social work consult
Loss of "pre-cancer" identity	Patient advocacy for financial resources
	Side effect management

Physical challenges of Survivorship

Cardiotoxicity

- Athracyclines (doxorubicin), BTK inhibitors (zanubrutinib, ibrutinib)

Endocrine dysfunction

- Thyroid dysfunction from Tyrosine kinase inhibitors (dastatinib) , hyperglycemia from steroid use

Decreased bone density

- Chronic steroids use, anti-resorptive therapy (denosumab for multiple myeloma)

Pulmonary dysfunction

- Cyclophosphamide, busulfan, fludarabine, methotrexate

Physical challenges of Survivorship

Kidney dysfunction

- Disease state (multiple myeloma), chemotherapy toxicity, comorbid conditions

Fatigue

- Common side effect of neoplastic agents, nutritional deficiency, depression, insommnia

Infertility and sexual dysfunction

- Chemo toxicity, barrier methods and birth control for long term therapies

Malnutrition

- Anorexia, dysgeusia, comorbid conditions

Interventions

- Cardiotoxicity
- Endocrine dysfunction
- Bone density
- Pulmonary function
- Fatigue
- Kidney dysfunction
- Infertility/Sexual dysfunction
- Malnutrition

Cardiology referral, cardiac rehab

Monitor TSH, glucose

Chest CT, pulmonology, medications

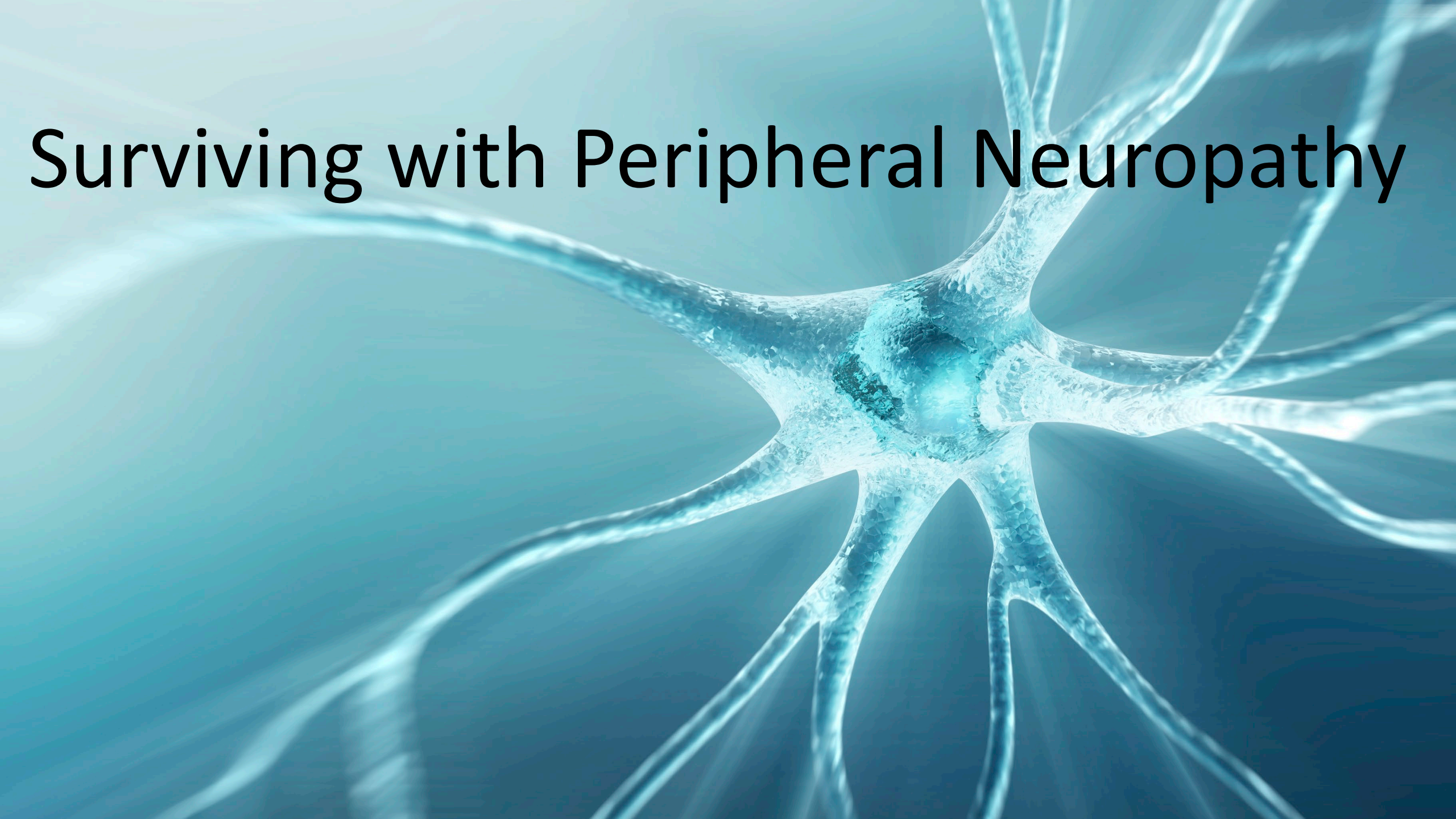
Nephrology, monitor creatinine, control hypertension

Check vitamin D, B12, iron

Fertility clinic (prior to treatment), sex therapist

Dietician consult, medications

Surviving with Peripheral Neuropathy



Chemotherapy Induced Peripheral Neuropathy

Classes of Neurotoxic agents

- Platinum-based (Carboplatin)
- Vinca alkaloids (Vinblastine)
- Epothilones (ixabepilone)
- Taxanes (docetaxel)
- proteasome inhibitors (bortezomib)
- Immunomodulatory drugs (lenalidomide)

Primary Neurotoxic Agents

- Oxaliplatin 85-96%
- Paclitaxel 61-92%
- Cisplatin 12-85%
- Bortezomib 47% (decreased with subcutaneous injection vs intravenous)
- Vincristine 20%

Mezzanotte JN, Grimm M, Shinde NV, et al. Updates in the Treatment of Chemotherapy-Induced Peripheral Neuropathy. *Curr Treat Options Oncol*. 2022;23(1):29-42. doi:10.1007/s11864-021-00926-0

Impact of CIPN

- **Risk Factors**
  - Previous chemotherapy with neurotoxic agents
  - diabetes,
  - existing neuropathy
  - cardiovascular medications (beta blockers)
  - older age
  - obesity
  - Smoking and alcohol use

Frequency of CIPN in patient that receive neurotoxic chemotherapy

- 30-40% of patients will develop acute CIPN
- 30% of patients will have chronic and permanent CIPN

Effect on quality of life

- 78% of patients reported that CIPN had a significant effect on their quality of life
- Higher incidence of pain, depression, anxiety, insomnia, falls and sexual dysfunction

Battaglini E, Goldstein D, Grimison P, McCullough S, Mendoza-Jones P, Park SB. Chemotherapy-Induced Peripheral Neurotoxicity in Cancer Survivors: Predictors of Long-Term Patient Outcomes. J Natl Compr Canc Netw. 2021 Jul 28;19(7):821-828. doi: 10.6004/jnccn.2021.7026. PMID: 34340206.

Colvin LA. Chemotherapy-induced peripheral neuropathy: where are we now?. *Pain*. 2019;160 Suppl 1(Suppl 1):S1-S10. doi:10.1097/j.pain.0000000000001540

American Society of Clinical Oncology (ASCO) Guidelines

Not recommended- risk outweighs potential benefit

No recommendation- low evidence of efficacy

*some evidence of efficacy-needs more research for recommendation

Recommended-evidence to support its use with low evidence of risk

Recommendations for Prevention

- **No recommendation** –low efficacy– more than 25 agents evaluated
  - Ex. Gabapentin, metformin, amitriptyline, venlafaxine, b12, cannabinoids, duloxetine

***More research needed**

- Acupuncture
- Cryotherapy
- Compression therapy
- Exercise therapy
- Ganglioside-monosialic acid- intravenous or subcutaneous injection -plays a vital role in neurogenesis, nerve development, differentiation and repair after injury

- **Recommended- Prevention**
  - Dose reduction or delay during treatment
  - Recognize increased risk

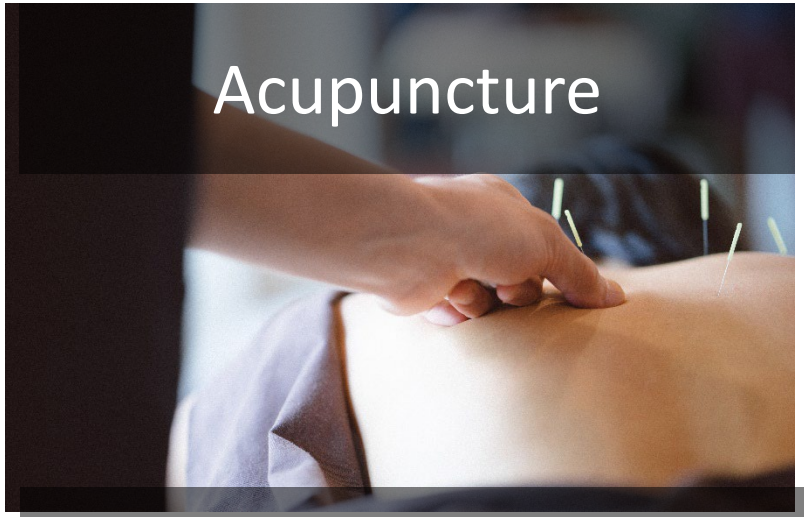
Loprinzi CL, Lacchetti C, Bleeker J, et al. Prevention and Management of Chemotherapy-Induced Peripheral Neuropathy in Survivors of Adult Cancers: ASCO Guideline Update. *J Clin Oncol*. 2020;38(28):3325-3348. doi:10.1200/JCO.20.01399

Recommendations for Treatment

- **Not recommended**
  - acetyl-L-carnitine (advertised as nerve booster, weight loss supplement)
  - Risk of bleeding and no strong evidence that it is helpful.
  - Some studies showed worsened CIPN after 2 years.
- **No recommendation**
  - Gabapentin/pregabalin
  - Topical gel treatment containing baclofen, amitriptyline HCL, plus/minus ketamine
  - Tricyclic antidepressants
  - Oral cannabinoids
- ***More research needed**
  - Exercise therapy
  - Acupuncture
  - Scrambler therapy (electric skin stimulation)
- **Recommended**
  - Duloxetine- limited benefits/ Venlafaxine also tested with lower efficacy

Loprinzi CL, Lacchetti C, Bleeker J, et al. Prevention and Management of Chemotherapy-Induced Peripheral Neuropathy in Survivors of Adult Cancers: ASCO Guideline Update. *J Clin Oncol*. 2020;38(28):3325-3348. doi:10.1200/JCO.20.01399

Beyond the Prescription Pad



- Acupuncture 10
  - Shown to be anti-inflammatory but mechanisms are hypothesized
  - Low risk of harm, regulated by FDA but not approved treatment
  - Insurance coverage is rare
- Exercise therapy 6
  - Overall showed significant improvement in quality of life, not always a reduction in CIPN
  - Highest efficacy are those that increase balance and strength
  - Sensorimotor and mind-body exercises (Physical therapy, yoga, tai chi, Pilates)
  - Ensure exercises are safe for individual
  - Offer resources specific for oncology patients (hospital, Little Red Door, etc..)
- Scrambler therapy 2 (Not transcutaneous electrical nerve stimulator TENS)
  - Stimulates nerves on dermatome mapping- replace painful signals with non-painful ones
  - Pulsation simulates human nerve pattern
  - 60% of patients reported a 50% reduction in pain

Summary

- People are surviving longer with hematological malignancies
- Nurses and survivorship plans are essential in management
- Long term effects include physical, social and emotional issues
- Fatigue and CIPN have biggest impact on quality of life
- Duloxetine is only recommended therapy by ASCO
- More research is needed on alternative therapies for neuropathy
- Alternative therapies require time and education
    - No quick fixes, no magic pill

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