



Survivorship for the Primary Care Physician

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 **THE OHIO STATE UNIVERSITY**
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Educational Objectives

- Define Cancer Survivorship and Summarize Prevalence and Characteristics of Cancer Survivors in the United States
- Review Four Key Tenets of Survivorship Care
- Summarize Recommendations for Recurrence Screening for Breast, Prostate, Colon and Melanoma

Educational Objectives Con't

- Summarize Guideline Based Recommendations for Management of Following:
 - Fear of Recurrence
 - Anxiety/Depression
 - Cancer Related Fatigue
 - Bone Health
 - Vasomotor Symptoms
 - Aromatase Inhibitor Induced Arthralgias
 - Peripheral Neuropathy

Question 1

- In the United States, there are currently _____ cancer survivors.
 - A. 12 million
 - B. 15 million
 - C. 18 million
 - D. 20 million
 - E. 22 million

Question 2

Which of the following results in highest risk of bone loss?

- A) Aromatase Inhibitor Therapy
- B) Chemotherapy-induced Ovarian Failure
- C) Combined Aromatase Inhibitor Therapy and Ovarian Suppression
- D) Menopause

Question 3

• Routine lab monitoring is recommended for recurrence screening for which of the following malignancies?

- A. Colon
- B. Prostate
- C. Breast Cancer
- D. Melanoma
- E. A & B
- F. All of the Above

Question 4

- Which of the following best approximates the prevalence of any mood disorder among cancer survivors?
 - A. 5%
 - B. 10%
 - C. 15%
 - D. 20%
 - E. 25%

Question 5

All of the following are reasonable supportive care for hot flashes EXCEPT

- A. Acupuncture
- B. Black Cohosh 20mg BID
- C. Oxybutynin 2.5 to 5mg PO BID
- D. Venlafaxine 37.5 to 75mg daily
- E. Vitamin E 800 IU daily



Overview

Definition of a Survivor

“Anyone who has been diagnosed with cancer from the time of diagnosis through the balance of his or her life”

Adapted from the National Coalition for Cancer Survivorship

Cancer Survivors By Site

Top 5 Men

- Prostate
- Colon & Rectum
- Melanoma
- Bladder
- Non-Hodgkin's Lymphoma

Top 5 Women

- Breast
- Uterine
- Colon & Rectum
- Thyroid
- Melanoma

Miller KD, Nogueira L, Mariotto AB, et al: Cancer treatment and survivorship statistics, 2019. CA: a cancer journal for clinicians 69:363-385, 2019

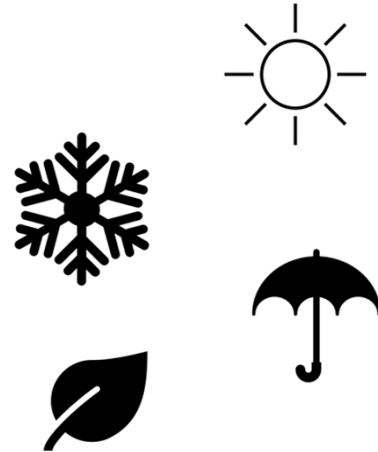
Statistics

- 18.1 million cancer survivors in the United States
- Number of cancer survivors is expected to increase to 22.5 million by 2032 (24.4% increase) and 26.0 million by 2040
- Cancer survivors surviving greater than 5 years to increase to 16.3 million over the next 10 years
- In 2022:
 - 69% of survivors live \geq 5 years after diagnosis
 - 47% of survivors live \geq 10 years after diagnosis
 - 18% of survivors live \geq 20 years after diagnosis

<https://cancercontrol.cancer.gov/ocs/statistics#graphs>

Phases of Survivorship Care

- Early-Stage (Curative)
 - Acute
 - Enhanced
 - Long-Term
- Advanced or Metastatic Stage
 - Control Disease
 - Prolong Life
- End-Stage
 - End of Life Care



1. Survivorship OoC: Survivorship Terms, National Cancer Institute Division of Cancer Control and Population Sciences, 2022



Tenets of Survivorship

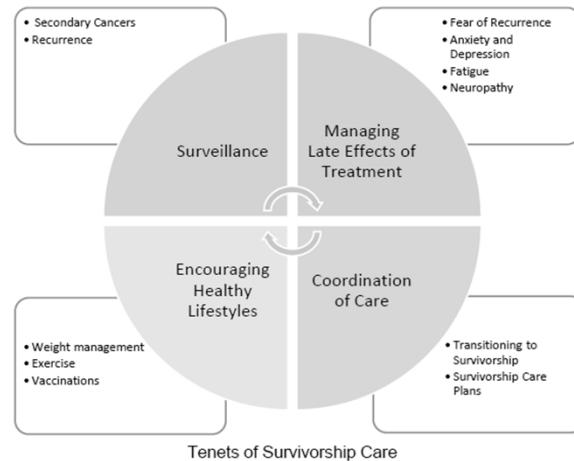
“From Cancer Patient to Cancer Survivor: Lost in Transition”

- No Standards of Care for Cancer Survivors
- Insufficient Communication between Cancer Specialists and Primary Care Providers
- Focus on Surveillance
- Need for Cancer Survivorship Research

McCabe MS, Bhatia S, Oeffinger KC, et al: American Society of Clinical Oncology statement: achieving high-quality cancer survivorship care. *Journal of Clinical Oncology* 31:631, 2013

Four Tenets of Survivorship Care

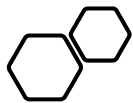
1. Surveillance
2. Prevention
(Encouraging Healthy Lifestyles)
3. Assessment and Treatment of Long Term and Late Effects
4. Coordination of care



Sanft, Tara, et al. "NCCN Guidelines Insights: Survivorship, Version 2.2019: Featured Updates to the NCCN Guidelines." *Journal of the National Comprehensive Cancer Network* 17.7 (2019): 784-794.

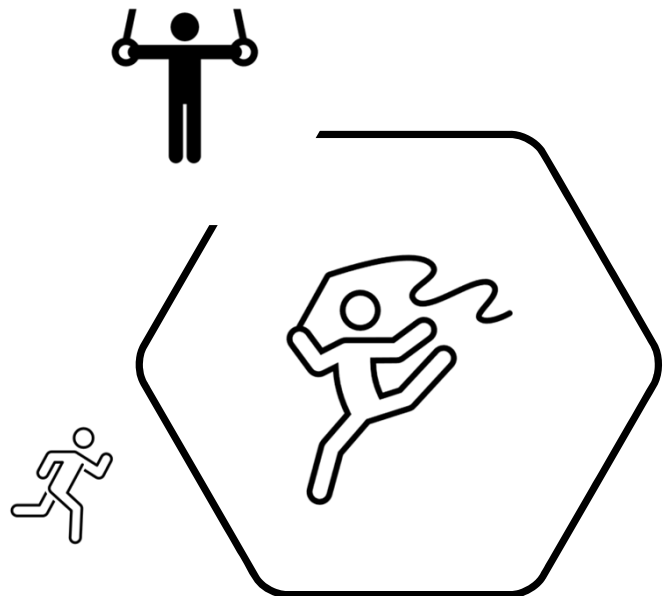
Surveillance

- Higher Rates of Cancer Compared to the General Population
- 18% of All Cancers (2009-2013) were a Second Primary
- Risk of Second Cancer Differs by Type
- 8.1% of Survivors will Develop a Subsequent Cancer
- Screening for Recurrence and Secondary Malignancies



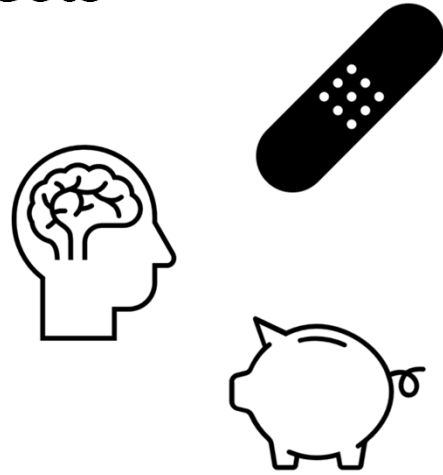
Prevention

- Promoting Healthy Lifestyles
- Avoiding Toxic Exposures
- Immunizations
- Risk Reduction
- Routine Follow-up with PCP



Late and Long-Term Effects

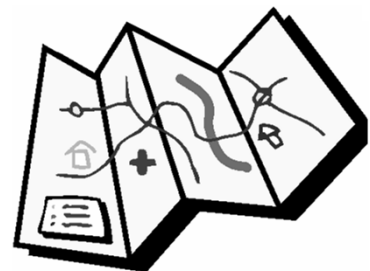
- Multitude of Potential Adverse Effects from Cancer and Treatment
- Appropriate Referrals
- Appropriate Treatment
- Financial and Employment Burdens



<https://www.cancercenter.com/-/media/ctca/images/others/blogs/2017/03-march/03-blog-fatigue-l.jpg>

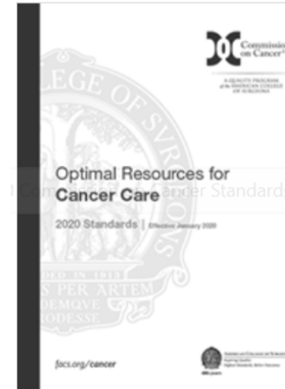
Coordination of Care

- Best Outcomes for Patients Co-Managed by Oncologist and PCP
- Survivorship Care Plans and Treatment Summaries



Commission on Cancer (COC) Standard 4.8

- “Focuses on development of a survivorship program to ensure that the needs of a cancer survivor are being met”
- Lead by Survivorship Program Coordinator
- Develop Survivorship Team
- Minimum of 3 Program Services



Examples of Services Offered At the James

- Survivorship Clinic
- Care and Aging Resiliency Clinic (CARE)
- Living Well with Advanced Breast Cancer Clinic (LWABC)
- Adolescent and Young Adult Program
- H.O.P.E. Program and Support Groups
- Women’s Intimacy and Sexual Health Program (WISH)
- Hope’s Boutique



Screening

Surveillance for Breast Cancer Recurrence

- **History and Physical**
 - Year 1 to 3: Every 3 to 6 months
 - Year 4 to 5: Every 6 to 12 months
 - Beyond Year 5: Annually
- **Mammogram**
 - Previously Received Lumpectomy: Bilateral mammograms
 - Previously Received Unilateral Mastectomy: Unilateral mammogram
 - Previously Received Bilateral Mastectomy: No routine breast imaging
- **Labs Testing**
 - Not recommended
- **Imaging**
 - Not recommended

Runowicz, Carolyn D., et al. "American cancer society/American society of clinical oncology breast cancer survivorship care guideline." *CA: a cancer journal for clinicians* 66.1 (2016): 43-73.

Surveillance for Prostate Cancer Recurrence

- 5 Risk Groups (Very Low, Low, Intermediate, High, Very High)
- Active Surveillance (Very Low Risk and Most Patients with Low Risk)
 - PSA (\leq every 6 months)
 - DRE, Repeat Prostate Biopsy or mpMRI (\leq 12 months)

NCCN Guidelines Version 4.2022 Prostate Cancer

Surveillance for Prostate Cancer Recurrence

- Those on Initial Definitive Therapy
 - PSA every 6-12 months for 5 years than annually
 - DRE annually (may be omitted if PSA undetectable)
- N1 on ADT or localized on observation
 - Physical Exam and PSA every 3-6 months
 - Imaging if symptoms or rising PSA

NCCN Guidelines Version 4.2022 Prostate Cancer

Surveillance for Colon Cancer Recurrence Stage I

- Repeat colonoscopy 1 year after surgery.
- If advanced adenoma repeat in 1 year
- Repeat in 3 years than 5 years otherwise

NCCN Guidelines Version 1.2022 Colon Cancer

Surveillance for Colon Cancer Recurrence Stage II and III

Years 1-2

- H&P every 3-6 months
- CEA every 3-6 months
- CT CAP every 6-12 months
- Colonoscopy in 1 year.
 - If advanced adenoma repeat in 1 year
 - repeat in 3 years than 5 years otherwise

Years 3-5

- H&P every 6 months
- CEA every 6 months
- CT CAP every 6-12 months

NCCN Guidelines Version 1.2022 Colon Cancer

Surveillance for Melanoma Recurrence Stage 0

- H&P at least annually
- Routine labs and imaging are NOT recommended

NCCN Guidelines Version 3.2022 Melanoma: Cutaneous

Surveillance for Melanoma Recurrence Stage IA-IIA

- H&P every 6-12 months for 5 years then annually
- Routine labs and imaging are NOT recommended

NCCN Guidelines Version 3.2022 Melanoma: Cutaneous

Surveillance for Melanoma Recurrence Stage IIB-IV

- Years 1-2
 - H&P every 3-6 months
 - Imaging every 3-12 months
- Years 3-5
 - H&P annually
 - Imaging every 6-12 months
- Routine imaging is NOT recommended after 3-5 years*

NCCN Guidelines Version 3.2022 Melanoma: Cutaneous

Recommended Surveillance Tests

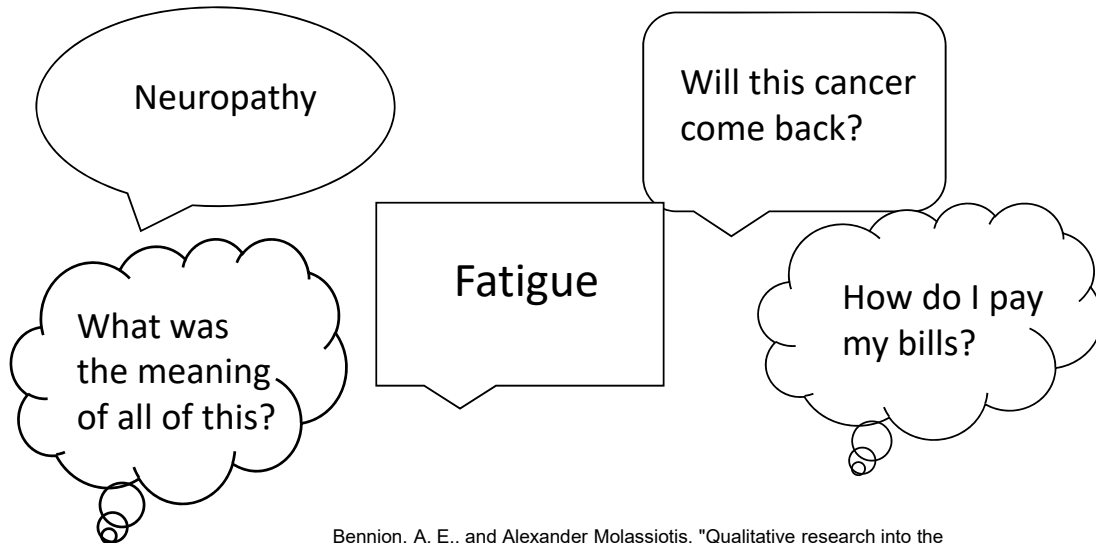
- Breast
 - H&P, Mammogram
- Colorectal
 - H&P, CEA, CT CAP*
- Prostate
 - H&P, PSA
- Melanoma
 - Self-Exam, H&P, CT*, MRI*, PET*

Andersen, Barbara L., et al.
"Screening, assessment, and care of anxiety and depressive symptoms in adults with cancer: an American Society of Clinical Oncology guideline adaptation." *Journal of Clinical Oncology* 32.15 (2014): 1605.



Monitoring and Managing Late Effects

Potential Needs of Survivors



Bennion, A. E., and Alexander Molassiotis. "Qualitative research into the symptom experiences of adult cancer patients after treatments: a systematic review and meta-synthesis." *Supportive Care in Cancer* 21.1 (2013): 9-25.

Fear of Cancer Recurrence (FCR)

- Prevalence
 - Mild to Moderate: 49%
 - Severe: 7%
- Definition
 - Fear, worry, or concern relating to the possibility that cancer will come back or progress (Ozakinci et al. 2016)
- One of the Most Prevalent Unmet Needs
 - 30% Surveyed Report This as a Significant Unmet Need (Armes et al. 2009)

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FCR Presentations

- Mild
 - Occasional Thoughts of Cancer
 - Presence of External Triggers
 - Typically Lasts a Few Days
 - Usually Improves Over Time
- Moderate-Severe
 - Frequent Thoughts of Cancer (≥ 1 per Week)
 - No Trigger
 - Inability to Control Thoughts
 - Significant Stress Related to These Thoughts

Butow, Phyllis, et al.
 "Fear of cancer recurrence: a practical guide for clinicians." *Oncology (Williston Park)* 32.1 (2018): 32-38.

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Management of FCR

- Respond to emotional cues from patient/family
- Verbally ask the patient about FCR at key follow-ups.
- Reinforce that FCR is common, normal and even helpful to some degree
- Convey that severe FCR needs to be managed
- Emphasize the importance of talking about FCR will reduce stigma and patient denial of anxiety (Butow et al., 2018)

Butow, Phyllis, et al. "Fear of cancer recurrence: a practical guide for clinicians." *Oncology (Williston Park)* 32.1 (2018): 32-38.

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Risk Reduction and Management

- Recommended Surveillance Tests
- Referral to Survivorship Clinic
- Referral to Support Group
- Referral to Mental Health Services
- Smoking Cessation
- Exercise Recommendations
- Sleep Hygiene
- Healthful Eating/Dietitian Referral



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Distress in Cancer

- “Distress is a multifactorial unpleasant experience of a psychological (ie, cognitive, behavioral, emotional), social, spiritual, and/or physical nature that may interfere with one’s ability to cope effectively with cancer, its physical symptoms, and its treatment. Distress extends along a continuum, ranging from common normal feelings of vulnerability, sadness, and fears to problems that can become disabling, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis.”

National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: distress management. 2022. https://www.nccn.org/professionals/physician_gls/pdf/distress.pdf (accessed May 17, 2022)

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Prevalence

- All Survivors
 - Depression: 13%
 - Anxiety: 10-18%
 - Adjustment Disorder: 19.4%
 - Any Mood Disorder: 20.7%
- >5 years post-treatment
 - Anxiety and Depression: 21%
- Anxiety is most common long-term mental health issue for survivors



1. Andersen, Barbara L., et al. "Screening, assessment, and care of anxiety and depressive symptoms in adults with cancer: an American Society of Clinical Oncology guideline adaptation." *Journal of Clinical Oncology* 32.15 (2014): 1605.

2. Emery, Jon, et al. "Management of common clinical problems experienced by survivors of cancer." *The Lancet* 399.10334 (2022): 1537-1550.

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Screening Options

Anxiety

- NCCN Distress Thermometer
- GAD-7
- Beck Anxiety Inventory
- Generalized Anxiety Disorder Questionnaire

Depression

- NCCN Distress Thermometer
- PHQ-2/PHQ-9
- Geriatric Depression Scale (GDS)
- Hamilton Rating Scale for Depression
- Beck Depression Inventory

Stepped Model for Treatment Delivery

- Educate and Destigmatize Mood Disorders
- Low-Intensity
 - Peer Support Groups
 - Physical Activity Programs
 - Guided Self-Help Programs
- High-Intensity
 - Individual or Group CBT
 - Supportive-Expressive Psychotherapies
- Collaborative

Bone Health Recommendations

- Women can lose up to 30% of bone mass within first 5 years of menopause.
- Cancer treatment related bone loss is more severe and faster than postmenopausal related bone loss
- Screening Guidelines
 - ASCO: ≥ 1 risk factor should be offered BMD testing¹
 - NCCN: Women on aromatase inhibitor or ovarian failure – bone monitoring at baseline and periodically going forward²

1) Shapiro, Charles L., et al. "Management of osteoporosis in survivors of adult cancers with nonmetastatic disease: ASCO clinical practice guideline." *Journal of Clinical Oncology* 37.31 (2019): 2916-2946.

2) National Comprehensive Cancer Network. (2020). Breast cancer (version 4.2020). Retrieved from https://www.nccn.org/professionals_gls/pdf/breast.pdf. Accessed May 22, 2020.

Management of Fatigue

- Prevalence is between 28 and 91%
- Common Causes Include Chemotherapy, Radiation, and Surgery
- Differential: Anemia, Thyroid Dysfunction, Cardiac Dysfunction, Mood Disorders, Sleep Disorders, Pain
- Several Scales have been Validated
 - Brief Fatigue Inventory
 - Cancer-Related Fatigue Distress Scale

Schmitz KH, Courneya KS, Matthews C, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. *Med Sci Sports Exerc.* 2010 Jul;42(7):1409-26.

Schmitz, et al. Exercise Is Medicine in Oncology: Engaging Clinicians to Help Patients Move Through Cancer. *CA CANCER J CLIN* 2019;0:1–17

Benefits of Exercise

- Best Treatment Data is for Exercise
 - Aerobic Exercise
 - Resistance Exercise
 - American College of Sports Medicine Recommends 150 minutes per week of Moderate Exercise
- Can Help in Multiple Domains
 - Fatigue
 - Mood
 - Quality of Life

Hot Flash Management

- | | |
|---|--|
| <ul style="list-style-type: none"> • Pharmacologic <ul style="list-style-type: none"> • Venlafaxine 37.5 to 75mg daily (Preferred) • Gabapentin 300mg TID* (Preferred) • Pregabalin 75 to 150mg daily • Citalopram 10 to 20mg daily • Paroxetine 10 to 20mg daily** • Oxybutynin 2.5 to 5mg BID | <ul style="list-style-type: none"> • Non-Pharmacologic <ul style="list-style-type: none"> • Acupuncture • Cognitive Behavioral Therapy • Non-Prescription <ul style="list-style-type: none"> • Vitamin E 800 IU daily • Magnesium Oxide 400mg BID* |
|---|--|

Carpenter JS, StornioloAM, Johns S et al. Randomized double blind placebo controlled cross over trials of venlafaxine for hot flashes after breast cancer. Oncologist 2007; 12: 124-135.

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Survivorship: Cognitive Function, Version 2.2020.National Comprehensive Cancer Network. Available at https://www.nccn.org/professionals/physician_gls/pdf/survivorship.pdf

Management of Aromatase Inhibitor (AI) Induced Arthralgia

- 50% of Postmenopausal Women on AI Therapy Report Arthralgias and Myalgias
- 20% Discontinue AI therapy due to their Musculoskeletal Symptoms
- Switching AI can lead to Tolerance in up to 40% of Women
- Exercise and Acupuncture Have Demonstrated in Randomized Trials a Significant Reduction in Pain and Interference

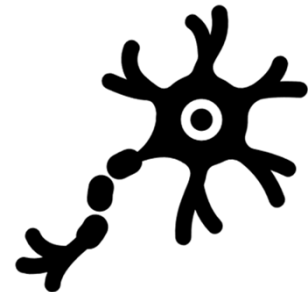
Irwin, Melinda L., et al. "Randomized exercise trial of aromatase inhibitor–induced arthralgia in breast cancer survivors." *Journal of Clinical Oncology* 33.10 (2015): 1104.

Crew, Katherine D., et al. "Randomized, blinded, sham-controlled trial of acupuncture for the management of aromatase inhibitor–associated joint symptoms in women with early-stage breast cancer." *Journal of Clinical Oncology* 28.7 (2010): 1154-1160.

Peripheral Neuropathy

Definition: Nerve related pain, numbness, tingling, swelling, cold sensitivity and/or muscle weakness or cramps

- Overall prevalence from 19% to over 85%, dependent upon the treatment received
- May lead to permanent symptoms and disability in up to 40% of cancer survivors



NCI Dictionary of Cancer Terms. <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/peripheral-neuropathy>. 2019.

Zajackowska, R., et al. *International Journal of Molecular Science*. 2018.

Park S, PhD, et al. *CA: A Cancer Journal For Clinicians*. 2013.

Peripheral Neuropathy

- Causative agents
 - Chemotherapy-induced (CIPN):
 - Platinum-based antineoplastic agents (70-100%)
 - Vinca alkaloids
 - Epothilones such as ixabepilone (60-65%)
 - Taxanes (11-87%)
 - Proteasome inhibitors such as bortezomib
 - Immunomodulatory drugs such as thalidomide (20-60%)
 - Radiation therapy induced
 - Mechanism not well understood
 - May be related to vascular injury, radiation fibrosis and nerve compression locally

Zajaczkowska R, et al. International Journal of Molecular Sciences. 2019.
 Kerckhove N, et al. Frontiers in Pharmacology. 2017.
 Delanin, S, Lefaix, J, and Pradat P. Radiotherapy and Oncology. 2012.

Peripheral Neuropathy

- Treatment Options
 - Protection and Consider the Impact on Quality of Life
 - B6 100mg daily
 - B12 1000mcg daily
 - Anticonvulsants – Gabapentin, Pregabalin
 - TCAs – Nortriptyline, Amitriptyline
 - SNRIs – **Duloxetine**, Venlafaxine
 - Acupuncture and other Complimentary Therapy options
 - Physical Activity and Sensitization Exercises



https://www.researchgate.net/profile/Sudhakar_Tummala2/publication/51438332/figure/fig1/AS:601585084280841@1520440469223/Symptoms-of-chemotherapy-induced-peripheral-neuropathy-Adapted-from-Simpson-DA.png

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Summary

- More Patients are Surviving Beyond Their Initial Diagnosis of Cancer with the Number of Survivors Expected to Continue to Increase Substantially in the Coming Years
- Routine Care of Cancer Survivors Includes Screening for Recurrence and Second Malignancy, Risk Reduction and Optimization of Healthy Behaviors, Managing Late and Long-term Side Effects and Usually Entails more Complex Care Coordination
- Cancer Survivors are at Increased Risk of a Second Cancer and Screening Recommendations for Recurrence Varies
- Anxiety, Depression and Fear of Recurrence Remain Very Common and Many Survivors Describe this as an Unmet Need