Sidney Kimmel Cancer Center
Jefferson Health® | NCI – designated

Until every cancer is cured

Maximizing Breast Cancer Survivorship: A Focus on Partnership

Ana Maria Lopez, MD, MPH, MACP
Professor and Vice Chair, Medical Oncology
Chief of Cancer Services, Jefferson Health New Jersey
Sidney Kimmel Cancer Center, NCI Designated
Thomas Jefferson University

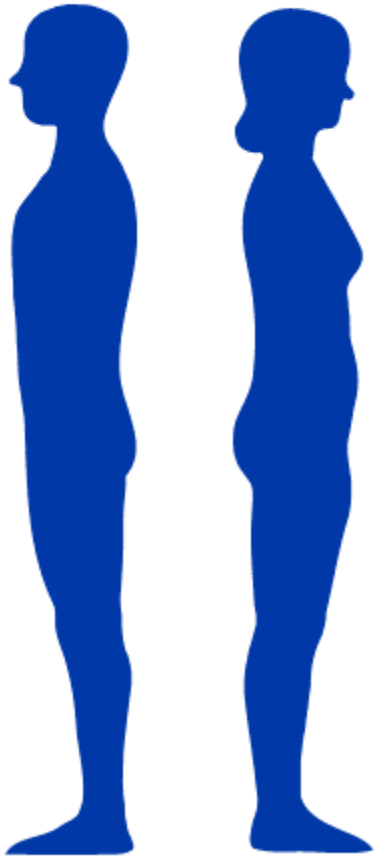
Towards a primary care-oncology partnership

Why?

Let’s look at the landscape

Estimated New Cancer Cases* in the US in 2019

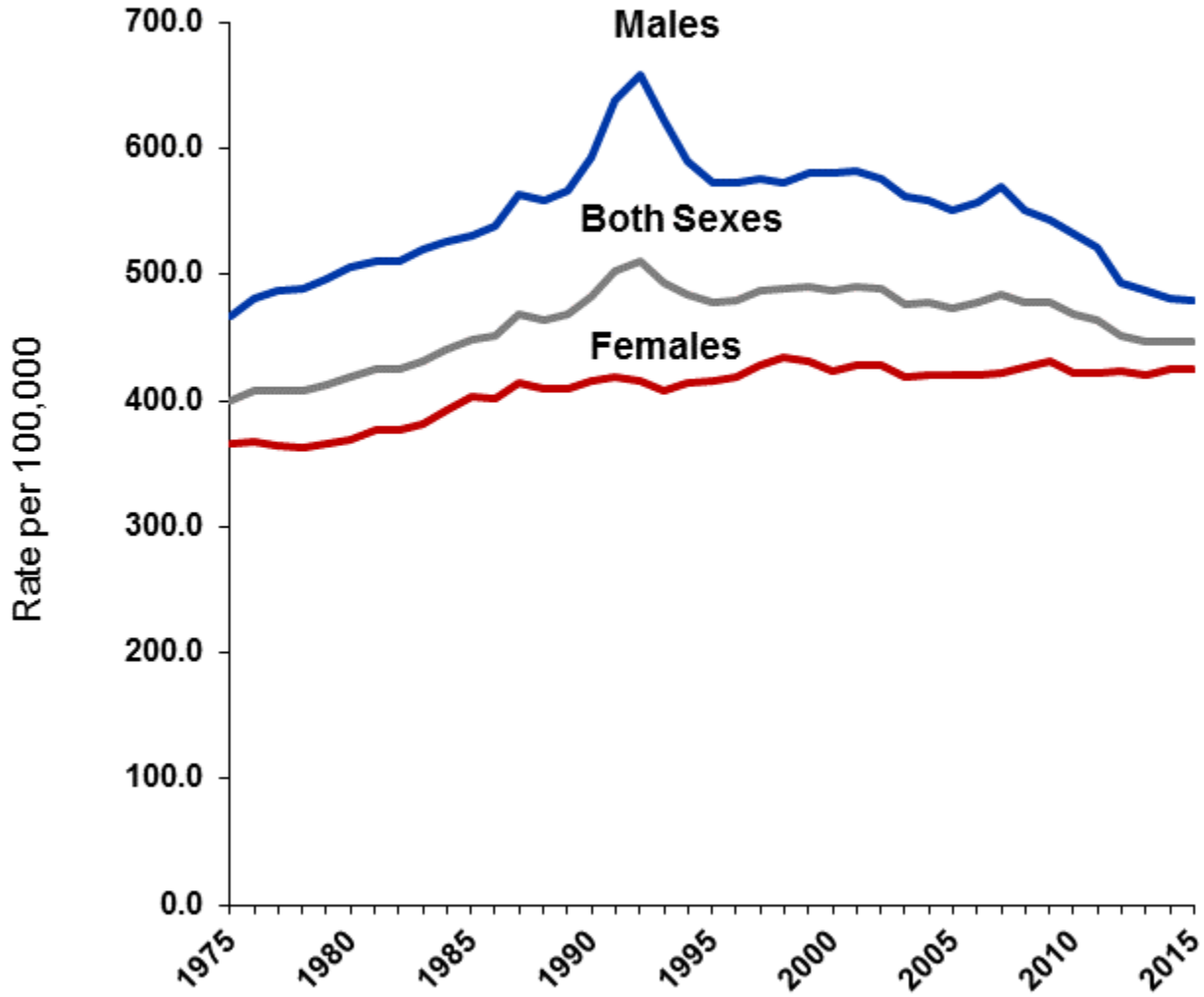
Males 870,970	
Prostate	20%
Lung & bronchus	13%
Colon & rectum	9%
Urinary bladder	7%
Melanoma of skin	7%
Kidney & renal pelvis	5%
Non-Hodgkin lymphoma	5%
Oral cavity & pharynx	4%
Leukemia	4%
Pancreas	3%
All other sites	22%



Females 891,480	
30%	Breast
13%	Lung & bronchus
7%	Colon & rectum
7%	Uterine corpus
5%	Melanoma of skin
4%	Thyroid
4%	Non-Hodgkin lymphoma
3%	Kidney & renal pelvis
3%	Pancreas
3%	Leukemia
21%	All other sites

*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

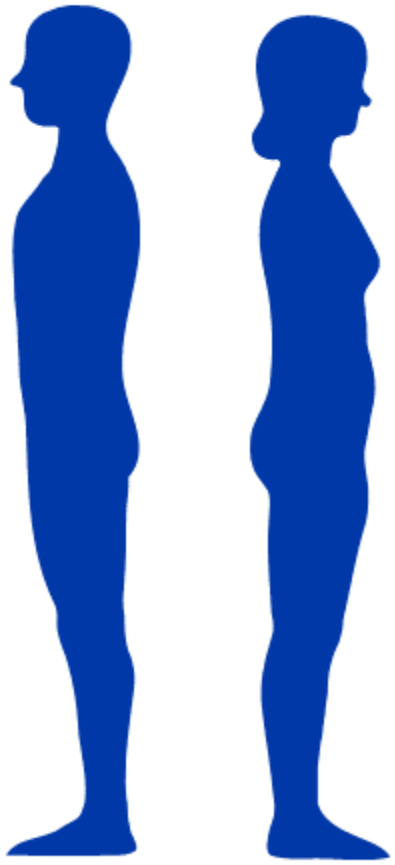
Trends in Cancer Incidence Rates*, US, 1975-2015



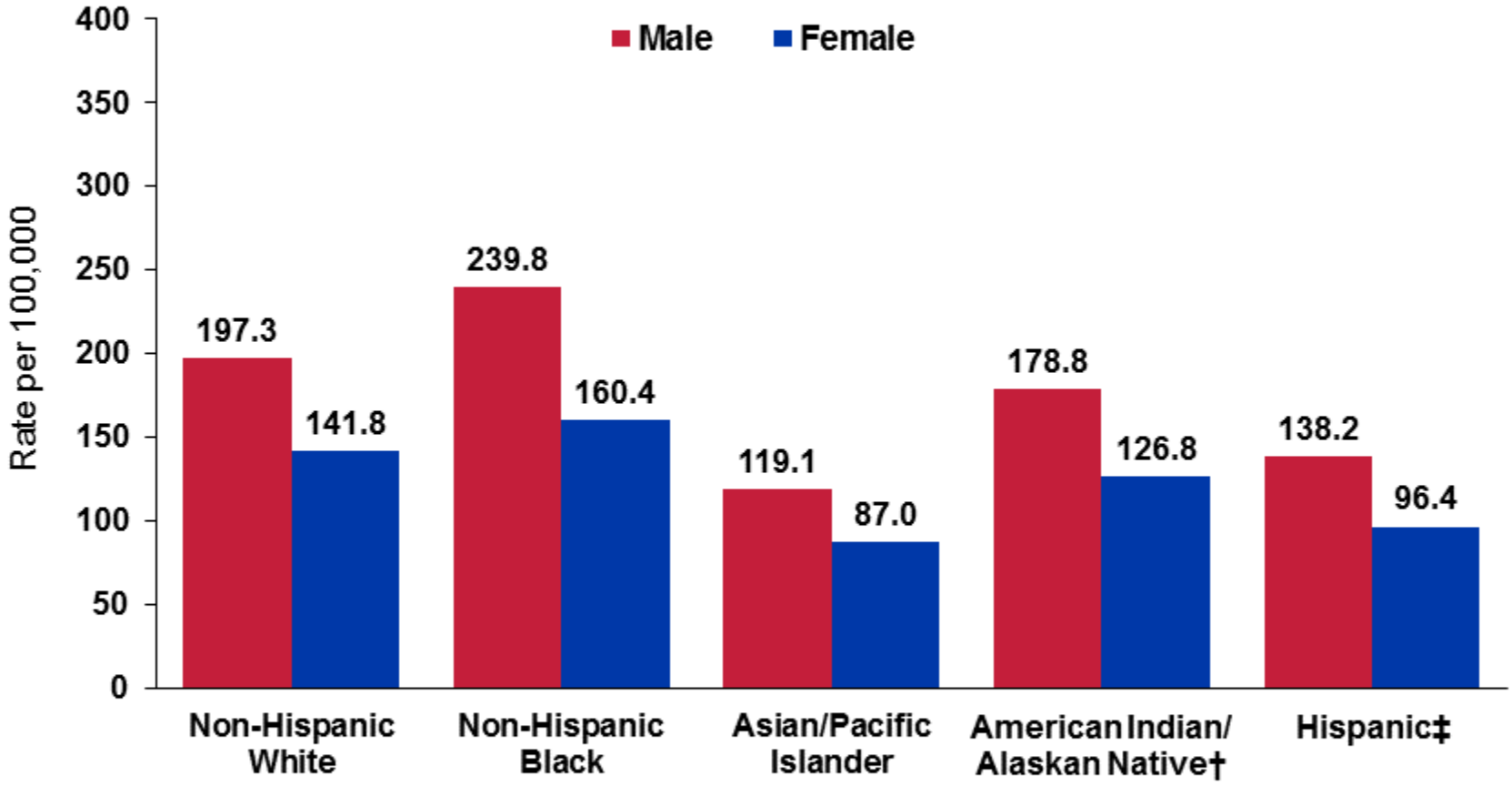
*Age-adjusted to the 2000 US standard population and adjusted for delays in reporting.
Source: Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute, 2018.

Estimated Cancer Deaths in the US in 2019

Males 321,670		Females 285,210	
Lung & bronchus	24%	23%	Lung & bronchus
Prostate	10%	15%	Breast
Colon & rectum	9%	8%	Colon & rectum
Pancreas	7%	8%	Pancreas
Liver & intrahepatic bile duct	7%	5%	Ovary
Leukemia	4%	4%	Uterine corpus
Esophagus	4%	4%	Liver & intrahepatic bile duct
Urinary bladder	4%	3%	Leukemia
Non-Hodgkin lymphoma	4%	3%	Non-Hodgkin lymphoma
Brain & other nervous system	3%	3%	Brain & other nervous system
All other sites	25%	24%	All other sites

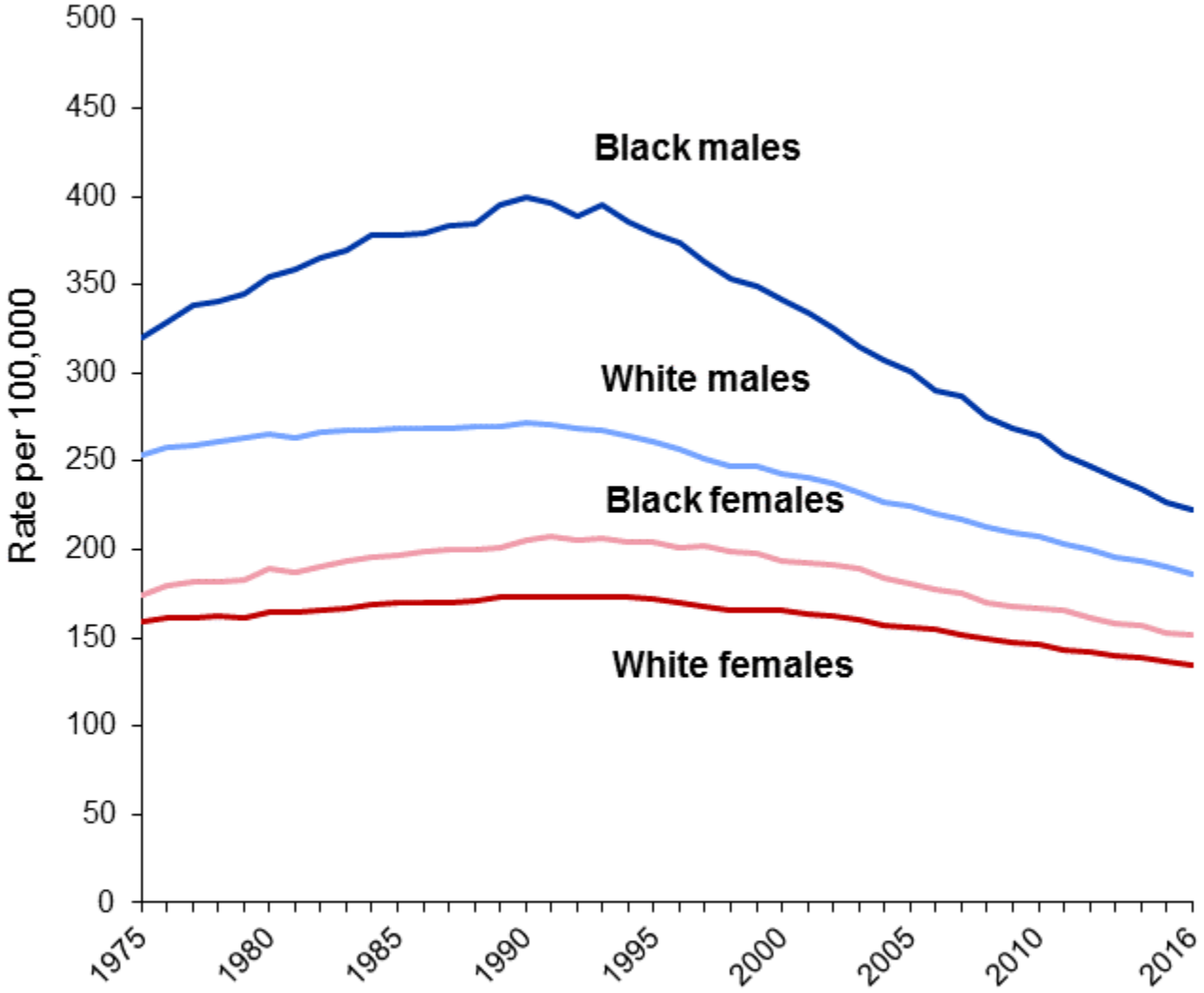


Cancer Death Rates* by Race and Ethnicity, US, 2012-2016



*Per 100,000, age-adjusted to the 2000 US standard population. †Data based on Indian Health Service Contract Health Service Delivery Area counties.
‡Persons of Hispanic origin may be of any race.
Sources: National Center for Health Statistics, Centers for Disease Control and Prevention, 2018.

Trends in Cancer Death Rates* by Sex and Race, US, 1975-2016



*Age-adjusted to the 2000 US standard population.
Source: National Center for Health Statistics, Centers for Disease Control and Prevention, 2018.

As a society, we are in a “New Normal” in thinking about the care of the cancer survivor

What's different about the cancer survivor?

- Cancer survivorship begins at the time of diagnosis
- Short-term cancer diagnosis/treatment sequelae
  - Symptom management
  - Risk of relapse
- Long-term cancer diagnosis/treatment sequelae
  - Organ toxicities
  - Risk for second cancers
  - Risk of relapse

Why consider primary care-oncology partnership?

- Strong primary care is the foundation for better health outcomes and reduced costs
- Can facilitate continuity through the transitions in care

- And
  - Growing numbers of cancer survivors
  - More than half of patients with a cancer diagnosis will be alive 5+ years!

Care of the cancer survivor

- Is it oncology?
- Is it general adult primary care?
- Is it both?

- Getting to shared care models: integrated survivorship care

Patients value primary care

- Turn to primary care physician with whom they've had a relationship to discuss:
  - Diagnosis
  - Treatment options
  - Side effect management

D. Brandenberg et al. Scand J Prim Health Care: 2014)

Primary care efficacy

Cochrane review: standard follow-up surveillance-primary care physician or subspec

- Breast cancer (stage I, II, or III) survivors
- Treatment by subspecialist: enhanced radiology/labs (CXR, scans, tumor markers)
- No difference in overall survival, disease-free survival, or quality of life
- Patient satisfaction was higher among patients treated by a primary care physician
- No difference in recommended surveillance testing

Benefits of primary care: improved outcomes

- Receive greater high value cancer screening
- Improved patient experience
  - Improved physician communication

Levine DM, Landon BE, Linder JA. Quality and Experience of Outpatient Care in the United States for Adults With
or Without Primary Care. *JAMA Intern Med*. Published online January 28, 2019. doi:10.1001/jamainternmed.2018.6716

Additional benefits of primary care

- Offer continuity of care which can help
  - Address physical, psychological, and social needs
  - Address the needs of co-survivors
  - Address screening for late effects of therapy
    - Cardiotoxicity
    - Osteoporosis
  - Address health and wellness
  - Early detection of secondary cancers
  - Offer reassurance, communication in a familiar setting

What would be/should be the focus of the partnership?

- Screening
- Survivorship
- Other?

What is needed for integrated survivorship care?

https://www.guysandstthomas.nhs.uk/news-and-events/events/2017-events/june/20

Breast Cancer: Significance

- Most common cancer in women, globally
- 1 in 8 women in the US
- 300,000 new cases annually
- Increase in early disease

Incidence

- 129 per 100,000 for non-Hispanic whites
- 126 per 100,000 for non-Hispanic blacks
- 100 per 100,000 for Native American
- 92 per 100,000 for Hispanics
- 91 per 100,000 for Asians

Mortality

- Mortality rates have been declining
- The current annual mortality rates:
  - 21 per 100,000 for non-Hispanic whites
  - 30 per 100,000 for non-Hispanic blacks
  - 14 per 100,000 for Native Americans
  - 14 per 100,000 for Hispanics
  - 11 per 100,000 for Asians

Screening for recurrence

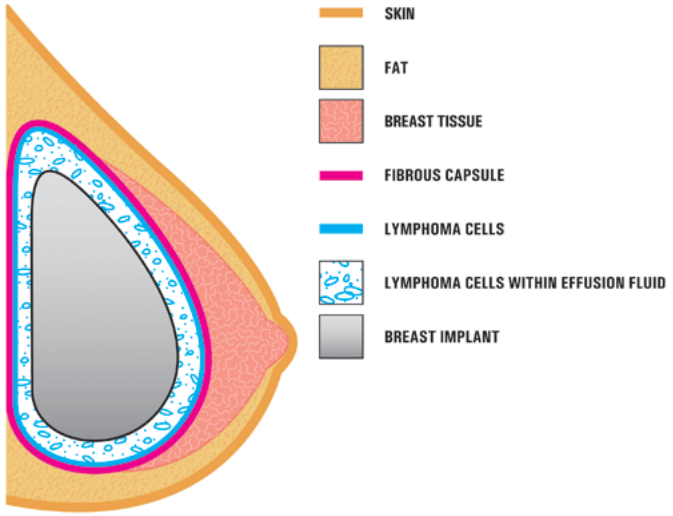
- Guidelines published by the American Cancer Society/American Society of Clinical Oncology
- H/P: q 3-6 months x 3 y posttreatment, q 6-12 months x 2 y, then annually
- Educate patients about the signs and symptoms of local recurrence.

Radiologic surveillance

- Annual mammography of both breasts or the remaining breast
- Annual MRI should be performed only in patients at high risk of recurrence
- Risk factors for recurrence include a calculated lifetime risk of more than 20%, a strong family history of breast or ovarian cancer, and a personal history of Hodgkin disease.

What about implants?

- Risk for anaplastic large B-cell lymphoma
- Greater for textured implants/expanders
- Develops in the scar tissue and fluid near the implant
- Symptoms: swelling and pain near implant
- No diff: saline or silicone
- Dutch study quantified risk
  - 1 in 35,000 for women age 50
  - 1 in 12,000 at age 70
  - 1 in 7,000 at age 75



Prevention through genetic detection

- BRCA 1/2 and more…
  - Lifetime risk
    - BRCA 1/2: 50 -55%
    - PALB2: 35%
    - CHEK2: 25%
    - ATM: 15%
    - Polygenetic risk score (313 gen loci): 30% (HR+) and 4% (TNBC)

Hereditary breast cancer

- Risk factors:
  - breast cancer before 50 yo
  - triple-negative cancer types (estrogen receptor negative, progesterone receptor negative, and human epidermal growth factor negative)
  - strong family history of breast or ovarian cancer
  - Male breast cancer
- Genetic counseling referral is indicated if there is a hereditary component

Cancer screening

- Continue screening for cervical, colon, lung, and ovarian cancers according to published guidelines.
- In the absence of a genetic syndrome, there is no indication for enhanced screening for these other cancers

Treatment Sequelae

Symptoms related to low estrogen

- Due to:
  - chemotherapy-induced ovarian failure or antiestrogen hormonal therapy
- Can lead to hot flashes, dyspareunia, vaginal dryness, and urogenital atrophy

Hot flashes

- Prevalence varies in breast cancer survivors
- May be as high as 50% -70% in premenopausal survivors treated with tamoxifen
- Because of the risk of recurrence: oral estrogens contraindicated
  - Concern about topical estrogen preparations because some have been shown to increase serum estradiol levels.
- Treatment of hot flashes in breast cancer survivors begins with lifestyle modifications (e.g., dressing in layers, using a fan, sipping cool drinks).
- Pharmacologic treatment: selective serotonin reuptake inhibitors, the serotonin-norepinephrine reuptake inhibitor venlafaxine (Effexor), and gabapentin (Neurontin) are preferred medications

Vaginal dryness

- Guidelines suggest the use of vaginal lubricants for sexual intercourse and vaginal moisturizers for general comfort.
- In addition, there is evidence that pH-balanced vaginal gel is effective for vaginal symptoms and a lidocaine compress applied to the vulvar vestibule is effective for dyspareunia

Cardiotoxicity

- Multiple aspects of breast cancer treatment may contribute to a higher risk of cardiovascular disease in survivors:
  - Induced menopause, use of hormonal treatments, and use of certain chemotherapies such as anthracycline-type drugs (e.g., doxorubicin [Adriamycin]) and trastuzumab [Herceptin])
  - Current doses and techniques of radiation therapy for breast cancer do not appear to increase cardiovascular toxicity.

Cardiotoxicity

- Breast cancer survivors should continue to receive regular age-appropriate cardiovascular risk screening and risk factor reduction according to guidelines.
- Patients should be encouraged to report potential cardiac symptoms, such as shortness of breath or unexplained fatigue.
- If symptoms are present, appropriate workup and cardiology referral should be initiated.

Cardiotoxicity

- No well-established recommendations on screening for cardiotoxicity in breast cancer survivors
- Echocardiography should be considered six to 12 months after breast cancer treatment in asymptomatic patients at high risk of cardiotoxicity:
  - those who received high-dose anthracycline chemotherapy, trastuzumab or low-dose anthracyclines in combination with cardiac risk factors or radiation therapy with the heart in the treatment field, or high-dose radiation with the heart in the treatment field).

Cognitive impairment

- Cognitive impairment is common during and after breast cancer treatment
  - May affect the patient's daily functioning
- Cognitive impairment, measured by a variety of neuropsychiatric tests, is most pronounced in survivors who received systemic chemotherapy
  - 39% of these patients reporting cognitive difficulty up to five years after diagnosis.
  - Verbal memory and psychomotor function are particularly affected.

Cognitive impairment

- Ask about cognitive impairment after breast cancer treatment
- Refer affected patients for neuropsychiatric testing
- There is evidence that cognitive rehabilitation therapy, consisting of exercises to improve verbal and visual memory and speed of processing information, is effective
  - in group and individual settings.
- Stimulants, mindfulness-based stress reduction, and cognitive behavior therapy not effective

Bone density

- Breast cancer survivors, including those who are premenopausal, are at increased risk of osteoporotic fractures.
- Rapid and profound bone loss may occur as a result of chemotherapy-induced ovarian failure or ovarian suppression from adjuvant therapies such as aromatase inhibitors.

Bone density

- Who is at risk?
  - Women who have chemotherapy-induced premature menopause
  - Women who are premenopausal and were treated with tamoxifen or a gonadotropin-releasing hormone agonist
  - Women who were treated with an aromatase inhibitor
- Follow-up
  - DEXA at baseline and then every 1-2 years

Bone density

- Strategies to limit bone loss:
  - weight-bearing exercise
  - limited alcohol intake
  - not smoking
  - adequate intake of dietary calcium and vitamin D

Bone density

- Zoledronic acid (Reclast) or denosumab (Prolia): recommended for the prevention of bone loss in patients receiving aromatase inhibitor therapy.
  - If zoledronic acid is chosen, it should be given for 3-5 years.
  - The optimal duration of denosumab therapy is unclear, but durations of up to 24 months have been studied.
  - Of note, the use of bisphosphonates may be associated with a lower risk of metastatic disease in patients with early breast cancer.
- Not recommended:
  - Teriparatide (Forteo), a parathyroid hormone agonist
  - Selective estrogen receptor modulators

Lymphedema

Occurrences vary widely, depending on the type of treatment and the criteria used to diagnose lymphedema:

- Rates of lymphedema are as much as double in women who undergo radiotherapy
- Increased in women who are obese, w/advanced cancer at diagnosis
- Greater incidence in patients receiving axillary lymph node dissection vs. sentinel node biopsy
  - Women who undergo axillary node dissection, the cumulative incidence of lymphedema is 41% at 10 years.

Lymphedema

- New cases of lymphedema may emerge months or years after treatment
- Cumulative incidence: rises over 5Y of follow-up
- Not all cases of lymphedema are clinically significant:
  - e.g. incidence lymphedema 5Y posttreatment: 94% (increased arm circumference of 2 cm or more)
  - 43% of these patients had signs and symptoms of limb heaviness or swelling

Lymphedema

Approach:

- Weight management, as appropriate
- Refer to lymphedema therapy: massage/self-administered manual lymphatic drainage, ongoing skin care, and use of compression garments
- Complex decongestive therapy has been shown to decrease arm volume, increase quality of life, improve range of motion and strength in the affected arm, and not cause or worsen lymphedema.

Lymphedema

Risks:

- Breast cancer–related lymphedema: doubles risk of developing cellulitis or lymphangitis in age-based controls
- Cellulitis may further damage lymphatic drainage, worsening lymphedema
- It is therefore imperative to diagnose and treat infections promptly

Chronic pain

- Chronic pain after breast cancer treatment is a well-described phenomenon

Chronic pain

- Most common: postmastectomy pain syndrome (PMPS),
  - Lasts ~3 months
  - Arm, axilla, chest wall, scar, or shoulder, or may present as phantom breast pain.
  - Neuropathic: burning, stinging, or like an electric shock.
    - Little or no role for chronic opioid use in patients with PMPS
  - Incidence: 20% to 50%
    - Chemotherapy inconsistent effect
      - May be confounded by stage or patient age
    - Radiation therapy increases the risk of persistent pain

Chronic pain

- Axillary node dissection: higher rate of persistent pain than SLN alone
  - Due to damage to the intercostobrachial nerve with ALND
- Lower age: risk factor for persistent pain
  - Possibly because younger women may have more severe disease
- Pain may also be a result of peripheral neuropathy related to use of chemotherapy in breast cancer treatment.

Chronic pain

- Additional risk factors for the development of chronic pain after breast cancer treatment
  - Presence of preoperative breast pain (from breast cancer itself or prior treatments)
  - Unrelated preexisting pain syndrome: headache or back pain
  - Aggressive postoperative pain control has been demonstrated to reduce the risk of persistent pain.

Chronic pain

- Psychological factors: predictors
  - Anxiety, catastrophizing, disturbed sleep, and tendency toward somatization - predict the presence of ongoing pain at 3y
  - Depression incidence of chronic pain at 9 months was decreased by approximately one-half in patients who were psychologically resilient before breast cancer treatment

Chronic pain

- Assess patients for persistent pain *beyond* the expected time of healing and for neuropathy
- Preferred treatments: acetaminophen, nonsteroidal anti-inflammatory drugs, physical activity, and occupational therapy as indicated.
- PT/OT after breast surgery:
  - Focus on preserving ROM and strength in the ipsilateral arm
  - Effective in treating postoperative pain
  - Refer early

Health related QOL

- Nearly 50% of breast cancer survivors (BCS) experience anxiety and/or depression in the first year after diagnosis

Health related QOL

- Body image may be negatively affected by surgeries, weight gain, changes in physical conditioning, and changes in sexual functioning
  - Younger women are particularly affected by declines in body image

Health related QOL

- One year after treatment:
  - BCS have significantly lower scores than the general population in the domains of emotional state, social functioning, fatigue, insomnia, and body image.
  - have ongoing breast cancer–specific symptoms (e.g., arm and breast symptoms)
  - quality-of-life difficulties (may persist at 10 years): cognitive function, social issues, and fatigue

Health related QOL

- Screen for depression and anxiety
- Ask about body image and social support
  - Group interventions, guided imagery, physical activity: lessen body image concerns and increase quality of life
  - Breast reconstruction, breast prosthesis, wigs…may help body image

What could integrated survivorship care look like?

Thank you!

anamaria.lopez@jefferson.edu

Sidney Kimmel Cancer Center
Jefferson Health® | NCI – designated

Until every cancer is cured