Care of the Cancer Survivor Kimberly S. Peairs, MD Johns Hopkins School of Medicine July 27, 2015 No Disclosure or Conflicts Disclosure • Dr. Kimberly Peairs has no conflict of interest, financial agreement, or working affiliation with any group or organization. Learning Objectives • Understand the therapeutic exposures and potential late effects from cancer treatment;

• Distinguish differences in cancer survivorship outcomes by

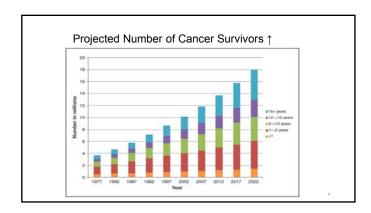
· Understand the neurocognitive and psychosocial effects of

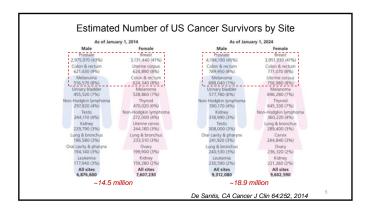
 Gain knowledge of referrals to appropriate community resources in patients who are transitioning from active care to

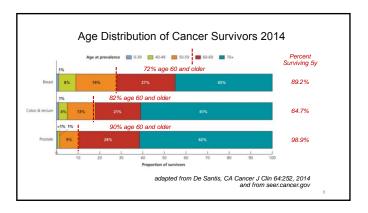
gender, ethnicity, and socio-economic status;

cancer treatment on survivors;

life beyond cancer survivorship care.







Hurdles in Caring for Cancer Survivors!



Cancer survivors are diverse!!!

- Some cancers rarely seen in primary care, so can't have enough expertise
- Inadequate information about the previous cancer and/or its treatment
- Lack of knowledge and confidence about survivorship care
- Patient lack of confidence in PCP knowledge
- Competing demands on PCP time
- Numerous specialists leading to gaps in communication/coordination
- Duffy Land, 2006; Kadan-Lottick, 2002; Mao 2009; Del Guidice 2009; Bober, 2009; Kantsiper 2009; Potosky 2011 Shortage!

Essential Components of	Survivorship	Care
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- · Prevention of recurrent & new cancers, and of other late effects
- Surveillance
 - · Cancer spread, recurrence, or second cancers
 - Assessment of medical and psychosocial late effects
- Intervention for consequences of cancer and its treatment
 - Medical problems (e.g., lymphedema, sexual dysfunction); symptoms (e.g., pain, fatigue); psychological distress (survivors, caregivers); employment, insurance, and disability
- Coordination between specialists and primary care providers to ensure that all of the survivor's health needs are met.

Cancer Patient to Cancer Survivor: Lost in Transition (IOM 2005)

Risk-stratified Model of Survivorship Care

- Survivors differ by:
 - Risk of recurrence
 - Risk of ongoing and late toxicities of therapy
 - Ongoing therapiesComorbid conditions

 - Psychosocial needs
 - · Risk of second primary cancers
 - Genetic predisposition
 - Lifestyle
- Content and intensity of survivorship care should differ based on different needs of different survivors

McCabe Seminars in Oncology 2013 Oeffinger ASCO Educational Book 2014

Models of Primary Care in Survivorship

- "Oncogeneralist"
 Continuity care in cancer center
 Consultative care in cancer center
- Primary care providers with cancer center relationship
- Primary care providers without close cancer center relationship

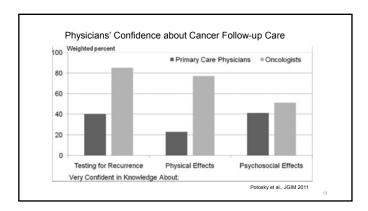
Nekhlyudov. The Oncologist. 2014

Shared-Care Model

- Cancer care domain
 - Short/mid-term surveillance
 - · Acute/short term complications
 - Screening for 2nd cancers
- · Primary care domain
 - Preventive services (diabetes, heart disease, osteoporosis, vaccinations, ...)
 • Screening for 2nd cancers

 - Long-term surveillance (if necessary)
 Long-term complications (if applicable)

Preferred Model for Care of Cancer Survivor: the Physicians' Preferences 100 ■ Primary Care Physicians ■ Oncologists 80 60 40 20 Shared Model Oncologist-led PCP-led MD Specialty Nurses or PA Clinic Clinic Top Ranked Model Option Potosky et al., JGIM 2011



Delivery of Survivorship Care by Primary Care Physicians: The Patient's Perspective

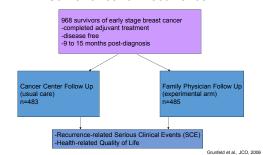
Breast cancer survivors' rating of PCP-related survivorship care: > Strongly endorsed:
General Care (78%), Psychosocial support (73%), health promotion (73%)

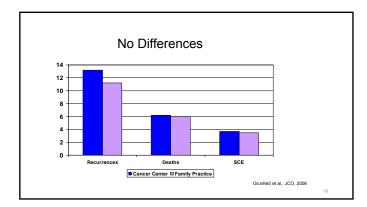
➤ Less knowledgeable:
• Cancer follow-up (50%), late effects of cancer therapies (59%), treating symptoms related to cancer (41%)

>Only 28% felt PCPs and oncologists communicated

Mao J. et al., J Clin Oncol 2009

Surveillance for Recurrence





Cancer Survivorship Education

- Acknowledge cancer survivorship needs
- Understand "best evidence" and/or "best practices" in the following aspects of cancer survivorship care:
 (a) cancer screening and surveillance

 - (b) late effects monitoring and co-morbidities

 - (c) psychosocial wellbeing and care (d) prevention and health promotion.

QUESTION

A patient presents to you as her new PCP. She is 37 yo with history of Wilms Tumor dx at age 5. She was treated with vincristine, cytoxan, adriamycin, as well as radiation to the lungs and left chest and abdomen.

She of the following is she at higher risk compared to non-cancer patient?

- A. Bladder cancer
- B. Colorectal cancer
- C. Aortic valve disease
- D. Basal cell carcinoma E. All of the above

Henderson TO et al. Secondary Gastrointestinal Cancer in Childhood Cancer Survivors: A Cohort Study. Annals Intern Med 2012: 196: 757-766.
Nottage, N. et al. Secondary Cohoreati Carcinoma silter Childhood Cancer. J Clin Checkl 2017; 30: 255-2558
Wall To et al. Resident-Petated Marie Childhood Cancer. A Report from the Childhood Cancer Survivor Study. JNCI 2012; 104: 1240-1250.

Late Effects of Cancer Treatment

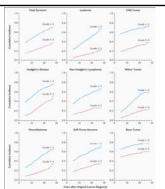
- Childhood Cancer Survivor Study

 - Retrospective cohort study
 Adults diagnosed with childhood cancer 1970-1986 vs. non-cancer siblings
- Oeffinger, et al. (NEJM, 2006)

 - 10K survivors vs. 3K siblings
 Severity score for chronic health conditions
 - CHF, second malignancy, joint replacement, cognitive dysfunction, CAD, CVA, renal failure, hearing or vision loss and ovarian failure (grade 3 or 4)

 - 5x more common among survivors than siblings

Cumulative Incidence of Chronic Health Conditions in Adult Survivors of Pediatric Cancer



Risk of Secondary Cancers

- Chemotherapy
 - Early to late risk of leukemias, solid tumors
 - Increased risk with higher drug doses, longer treatment time, and higher dose intensity.
- Radiation therapy
 Most are not seen for at least 10 years after radiation.
 Dose of radiation
 Area treated

 - Age at treatment
 Chemotherapy

http://www.cancer.org/acs/groups/cid/documents/webcontent/002043-pdf.pdf

Secondary Cancers Table 2 Subsequent Solid Tumors After Treatment for Adut-Onset Cancer First Primary Cancer Second Solid Tumors for Mitchin Increased Risks Have Been Interest Been

Screening For Secondary Malignancies

• Consensus based guidelines (mostly based on children's literature) –

www. survivorshipquidelines.org

www.nccn.org

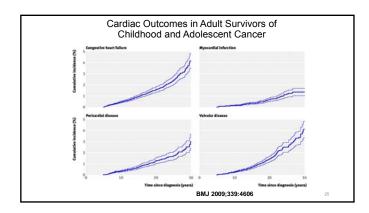
- Early screening than general population based on risk
- Patients and physicians to be vigilant about symptoms!!!

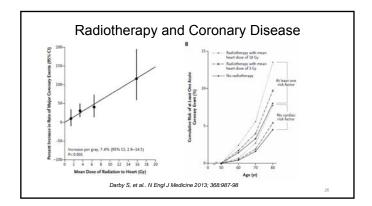
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Cardiac Outcomes in Adult Survivors of Childhood and Adolescent Cancer

	Survivors	Siblings
Heart failure	1.7%	0.2%
Myocardial infarction	0.7%	0.2%
Pericardial disease	1.3%	0.3%
Valvular abnormalities	1.6%	0.5%

BMJ 2009;339:4606





Potential Cardiac Late-Effects of Chemotherapy

• Anthracyclines

- Late heart failure may present as non-ischemic CM
 May begin to present in adults 5 yr after treatment
 Risk increased if:
 <18 or >65 ylo when treated
 Underlying CAD or HTN
 Radiation treatment
 High dose
 Combination chemotherapy (+ trastuzumab)

 Trastuzumach

Trastuzumab

- Cardiac events up to 4.1%
 Risks: Older age and underlying cardiac dysfunction

Is Cardiac Screening Recommended?

- Van der Pal, et al. J Clin Oncol 2012
 - · Most common cardiac event for childhood survivors was CHF
 - 1 in 8 developed severe heart disease after 30 years
 - Highest risk if anthracyclines + radiation
- Screening is recommended for childhood cancer survivors
 - Periodic assessment of LVEF
 - · www.survivorshipguidelines.org

· Adult guidelines...

- Risk factor modification!
 BP control, cholesterol management, tobacco cessation
 Diabetes and weight control...

QUESTION- Breast Cancer

60 year old woman with invasive ductal carcinoma of the breast dx in 2008. Treated with breast conserving surgery, radiation and completed 5 years of tamoxifen. Her oncologist feels that she can be followed by PCP alone. What surveillance do you recommend?

- A. Yearly mammogram
- B. Yearly breast MRI
- C. Blood work, including blood count and chemistries
- D. CA-15-3 tumor marker
- E. All of the above

Side Effects from Breast Cancer Treatment

Early effects (0-6 months)

- Cytopenias
- Fatigue
- Alopecia
- Pain (musculoskeletal)
- Cancer Induced Peripheral Neuropathy (CIPN)
- Neurocognitive dysfunction

Chronic/Late effects (6 months to lifetime)

- Cardiomyopathy
- Chemo-Induced Peripheral Neuropathy
- Neurocognitive dysfunction
- Psychosocial impact
- Second cancers
- Early Menopause (bone health and cardiovascular disease)
- Fertility

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Common Issues After **Breast Cancer Therapy**

Problems/Symptoms	Who should be involved?			
(adapted from Hayes, NEJM 2007)	Cancer specialist	PCP	GYN	
Bone health	x	х	х	
Cardiovascular Health	x	х		
Cognitive function	x	х		
Neuropathy	x	х		
Depression, Fatigue	x	х	х	
Cancer Surveillance & Screening	x	х	х	
Hot flashes	x	х	х	
Lymphedema	x			
Musculoskeletal, Bone Health	x	х	x	
Sexual function	x	х	x	
Weight gain	х	х		

Breast Cancer	Treatment Symp	toms/Side	Effects:
Comm	non Behavioral S	ymptoms	

- Sleep disturbance
- Depression
- Cognitive impairment
- Fatigue

Bower J. J Clin Oncol 2008

Breast Cancer Treatment Symptoms/Side Effects: Fatigue

- · Likely multifactorial; Establish severity
- Treatment options
 Nonpharmacologic
 Psychosocial
 Exercise
 Sleep Therapy
 Acupuncture

 - Pharmacologic
 Antidepressants
 Stimulants? (studies in pts. with advanced ca)

Escalante CP. J Gen Intern Med 2009.

Breast Cancer Treatment Symptoms/Side Effects of Endocrine Therapy

Tamoxifen

- Selective estrogen receptor modulator
- Effective for hormone receptor + cancer
- Slight increased risk of Venous Thromboembolism
- Slight increase risk for Endometrial Cancer
- · Increase in Hot Flashes
- Metabolized by cytochrome P450 enzyme, CYP2D6
 - · Drug interaction

Breast Cancer Treatment Symptoms/Side Effects: **Endocrine Therapy**

Aromatase inhibitors (anastrozole, letrozole, exemestane)

- Used if hormone receptor + cancer
- Blocks conversion of androgens to estrogen
- · Only used in postmenopausal women

Side effects:

- Hot Flashes
- · Vaginal dryness
- · Arthralgias and myalgias
- Transient LFT elevation (Al's)
- · Osteopenia or osteoporosis (Al's)

Breast Cancer Treatment Symptoms/Side Effects: Menopausal Symptoms

Vasomotor symptoms most common

- 20% of breast cancer pts consider stopping endocrine therapy because of symptoms.
- · Treatment:
 - Venlafaxine 37.5 mg or 75 mg QD*
 - Citalapram 20mg*
 - Paroxetine 7.5mg QD (strong CYPD2 inhibitor)
 - Gabapentin 300 mg TID*
 - Pregabalin*
- Clonidine* (many side effects)
 *Non-FDA indication

-	-
	LZ

Breast Cancer Treatment Symptoms/Side Effects: Bone Loss

- Tamoxifen preserves bone density in post menopausal
- Tamoxifen increases bone loss in pre menopausal
- Al cause increase bone loss in post menopausal
- GnRH causes bone loss
- Treatment:

 - Calcium, vitamin D
 Weight bearing exercise
 Stop tobacco, etoh
 Bisphosphonates; utilize Fracture Risk Assessment (FRAX)
 - Zoledronic acid 4mg q6months reduced bone loss if on GnRH +tamoxifen or Al (Gnant et al, 2007)

Dexa Scan Monitoring in Women with Cancer

- Women >65
- Women 60-64 y/o with one of the following:
 - FHx of osteoporosis
 - -Low body weight
 - Prior non-traumatic fracture
 - Other osteoporosis risk factors (steroids, smoking)
- · Postmenopausal women on aromatase inhibitor
- Premenopausal women who develop treatment related premature menopause

Pant, S, Shapiro, CL. Drugs 2008; 68:2591 Hillner, BE, Ingle, JN et al. J Clin Oncol 2003:2042

Prostate: Common Survivorship Challenges Following Therapy

- · Cancer recurrence or secondary malignancies
- Psychological distress of patient and/or care provider
- Sexual dysfunction (impotence)
- Bladder dysfunction (incontinence)
- Bowel dysfunction
- Fatigue
- Bone health
- Cardiovascular risk / metabolic syndrome from androgen deprivation therapy

Prostate Cancer Treatment Related Impotence • After prostatectomy: 60% reported no erections within one year after treatment, about 40-50% of men who undergo nerve-sparing prostatectomy will have returned to their pre-treatment function • After XRT: 45-55% reported Erectile Dysfunction (less for brachytherapy) little improvement over time • See JHMI web site for detailed treatment options. http://urology.jhu.edu/erectileDysfunction/erectile_dysfunctions_Rehab_php Prostate Cancer Treatment Related Incontinence • After prostatectomy: 20-30% wore pads for urinary incontinence • After XRT: 45% reported urinary incontinence • the use of pads decreases to 10% after several years · See JHMI web site for detailed treatment options. http://urology.jhu.edu/incontinence/urge_incontinence.php (for Urge incontinence) http://urology.jhu.edu/incontinence/stress incontinence.php (for Stress incontinence) Data source: Prostate Cancer Foundation http://www.pcf.org/site/c.leJRIROrEpH/b.5814053/k.1572/Urinary_Dysfunction.htm Prostate Cancer Treatment Related Bowel Dysfunction

- After prostatectomy: very rare (2-3%)
- After XRT:
 - After 2 yrs, about 10-20% of men reported having persistent diarrhea
 - Rectal bleeding increased steadily from 5% immediately after treatment to 25% after 2 yrs. (Rates lower with intensity modulated RT (IMRT)
 - After brachytherapy, bowel dysfunction rates are lower and stabilize at around 10%.

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Prostate Cancer Therapy Related Bone Health Androgen Deprivation Therapy (ADT) • Increased risk of osteoporosis, vertebral and hip fractures, even after discontinuation • Increased risk of pelvic fracture (small) • Recommend screening bone density for men on initiation of ADT or in men with prior treatment with ADT GI malignancies: Common Survivorship Challenges During/Following therapy Cancer recurrence · Second primary cancer following radiation Psychological distress · Pelvic insufficiency fractures · Genitourinary dysfunction · Bowel dysfunction, stoma stigmata Fatigue • Peripheral neuropathy (Oxaliplatin) Colorectal Cancer Treatment Related Genitourinary Dysfunction • Increased risk of urinary and sexual dysfunction with pelvic dissection

Ureteral injury during surgery <8%
After Radiation and Surgery
39% GU dysfunction
40% sexual dysfunction

• Treatment: Pelvic floor rehab

damage

• Risk factors: Preop incontinence, female gender, stoma, nerve

Colorectal Cancer Treatment Related Bowel Dysfunction

- Common after surgery, surgery and radiation, ostomy takedown
 13-50% chronic diarrhea
 50-90% urgency
 10-00% incompleted.

 - 40-60% incontinence40-80% clustering
- Treatment: Therapeutic choices, pelvic floor rehab, undergarment pads, bulking agents/fiber, anti-diarrheals, diet

JCO 2007; 25 and Ann Surg 2007; 246

	1 year	2 year	3 year	4 year	5 year
Dysphagia	1.46 (1.24-1.70)	1.15 (0.96-1.38)	0.78 (0.62-0.98)	0.80 (0.61-1.06)	0.59 (0.33-1.03)
Weight loss	1.30 (1.09-1.57)	1.40 (1.13-1.74)	1.31 (1.01-1.71)	1.14 (0.81-1.60)	1.35 (0.69-2.64)
Esophageal stricture	3.84 (2.48-5.94)	5.38 (3.38-8.57)	5.58 (3.22-9.66)	3.43 (1.79-6.56)	2.46 (0.70-8.67)
Gastrostomy tube	0.66 (0.53-0.82)	0.37 (0.28-0.48)	0.30 (0.21-0.44)	0.30 (0.18-0.48)	0.17 (0.06-0.43)
Airway obstruction	1.90 (1.58-2.28)	2.48 (2.01-3.05)	2.67 (2.08-3.42)	3.03 (2.25-4.09)	3.25 (1.83-5.75)
Tracheostomy tube	1.46 (1.15-1.86)	1.38 (1.03-1.84)	1.03 (0.72-1.48)	1.21 (0.77-1.88)	0.40 (0.14-1.11)
Pneumonia	1.75 (1.40-2.18)	2.49 (1.94-3.21)	1.86 (1.36-2.57)	3.41 (2.35-4.94)	5.17 (2.51-10.65)

Question

Exercise has NOT been shown in studies to reduce cancer specific mortality for which tumor types?

- A. Breast cancer
- B. Prostate cancer
- C. Colorectal cancer
- D. Ovarian cancer
- E. All of the above
- F. None of the above

Physical Activity and Cancer Ballard-Barbash et al. Physical Activity. Biomarkers, and Disease Outcomes in Cancer Survivors: A Systematic Review. JNCI, 2012, 104.815-840. Review Inclusion oriteria: RCT's or observational studies of physical activity and cancer specifical-activity mortality recurrence Mostly observational studies (n = 27) Over half in breast cancer All except one published since 2000 Breast Cancer: No studies found increasing mortality with increasing exercise Decreases in breast cancer specific mortality range from 13 to 51% Almost ½ of studies reported significant 'dose response' Benefits from both pre- and post-diagnosis physical activity Physical Activity and Cancer Colorectal cancer: Physical activity after cancer diagnosis may reduce cancer specific mortality (45-61%), and death from all causes (23 to 61%) One study examined in the same coloret exercise before and after diagnosis Prostate cancer: Prostate cancer: Physical activity after diagnosis associated with reduced cancer specific all cause

Exercise What is Recommended?

- 2.5 hours (150min) of moderate-intensity aerobic activity weekly <u>and</u>
- 2 or more days of week of muscle-strengthening activities of major muscle groups
- 10 minutes at a time works!
- · Individualize the pace

mortality

Ovarian cancer:

Test for trend positive (+ dose response)

No significant associations between pre-dx activity and mortality, but
 Suggestion of some benefit for young women (18-30) with early stage disease
 Borderline significant reduction in all cause mortality for non-obese women (BMI <= 30)

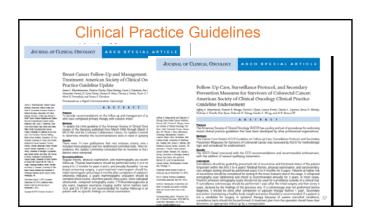
www.cdc.gov/physicalactivity/everyone/guidelines/adults.html

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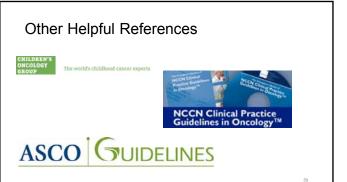
Nutrition for Cancer Survivors • Maintain healthy weight • Minimum of 5 servings fruit + veg. / day Whole grains (avoid refined foods) Lean protein · Low-fat dairy Variety of foods · Limit alcohol consumption • Food is best source of vitamins and minerals NCCN.com **Nutritional Supplements?** · Vitamin D • Primary source is sunshine • Recommended daily intake 600-800 i.u./day* Calcium • Encourage dietary sources • Soy? – dietary sources • Green tea? · Others? www.cancer.org/Treatment/SurvivorshipDuringandAfterTreatment/Nutrition Treatment Summary & Survivorship Care Plan • Healthcare provider contact information Basic disease characteristics · Basic treatment summary · Need for ongoing treatment • Schedule of visits, cancer surveillance, other tests Who is responsible When/How often · Possible late- and long-term effects · Lifestyle and psychosocial issues

ASCO Treatment Summary and Care Plan Original Contribution American Society of Clinical Oncology Clinical Expert Statement on Cancer Survivorship Care Planning By Debands K. Meyer. PhD. Larina Nebblyndor, MD. MPH, Claire F. Suyder, PhD. Janette K. Merrill, MS, Dana S. Wellin, MCC, and Lawrence N. Shubata, MD University of North Cambus, Chapt His, NC; Harvand Madica Shood and Harvard Vanguard Modical Associates, Dana Farber Cancer Institute, Boston, MA, Johns Hopkins School of Medicine, Bultimore, MD, and American Society of Clinical Oncology, Alexandria, VA Consensus conference of multiple stakeholders: - Medical, surgical, and radiation oncologists - Oncology nurses - Primary care providers - Patient navigators - Social workers - Cancer survivors - Oncology practice administrators - Insurers

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ASCO Trei		y and Survivorship Care	Plan	Lindsted based on a		Self on 9.27.13 and the 4900 t	and and in Committee
Patient Name:	General II	Parient 000:					
Patient shone:		Faseir oce:			cer surveillance or	other recommended relate	
	Care Broudders (to	scholing Names, Institutio	with the same of t	Coordinating Provider		What/When	How Often
Primary Care Provider:	Care Process	county manual common	NO.				
Surgeon:							
Radiation Oncologist:							
Medical Oscologist:							
Other Providers:				Please continue to see your primary			
COM PROME				age, including cancer screening test			ntion of your provider:
	Treatmen	nt Summary		Anything that represents a			
Oragnosis				Anything that represents a pensistent symptom;			
Cancer Type/Location/Histology Subtype: Diagnosis Date (year):			Anything you are worried at	bout that might be	related to the cancer coming	g back.	
Stage: Ct Ct Ct Ct Chot applicable	ie			Possible late- and long term effects	that someone with	h this type of cancer and trea	tment may experience:
		etmant					
Surgery - Nes		Surgery Date(s) (year):		Cancer survivors may experience is: please speak with your doctors or n			
Surgical procedure/location/lindings:				☐ Physical Functioning	☐ Insurance	☐ 5chool/Work	Ofinancial advice or assistance
	Body area treated:		f Date (year):	☐ Memory or concentration loss	□ Parenting	☐ Fertility	☐ Sexual functioning
Systemic Therapy (chemotherapy, hormo	nal therapy, other	G □ Yes □No		□ Other			
Names of Agents Used			End Dates (year)				
				A number of lifestyle/behaviors can			
				developing another cancer. Discuss	these recommend		me:
				☐Tobacco use/cresation		☐ Diet	
				□Alcohol use		☐Sun screen u	
Persistent symptoms or side effects at co-	mpletion of treatm	ment: @ No @ Yes (enter f)	petid :	☐Weight management (loss/gain)		☐Physical activ	ity
		http://wv	vw.asco.org/practic	e-research/cancer-surv	ivorship		56







Other Helpful References

- National Coalition on Cancer Survivorship http://www.canceradvocacy.org/
- Cancer Related Fatigue: The Approach and Treatment http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2763160/
- Surveillance of demographic characteristics and health behaviors among adult cancer survivors http://www.ncbi.nlm.nih.gov/pubmed/22258477
- Nutrition for Cancer Survivors-National Comprehensive Cancer Network http://nccn.com/component/content/article/66-physical/129-nutrition-for-cancer-survivors.html
- Nutritional Supplements-American Cancer Society www.cancer.org/Treatment/SurvivorshipDuringandAfterTreatment/Nutrition
- Exercise Recommendations-Centers for Disease Control and Prevention www.cdc.gov/physicalactivity/everyone/guidelines/adults.htm
- The Johns Hopkins Breast Cancer Survivorship Program http://www.hopkinsmedicine.org/breast_cancer_survivor_care

