



UTAH SOCIETY OF
HEALTH-SYSTEM PHARMACISTS

Presented by: Rebecca Martin, Pharm.D.
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**Life after cancer:
The battle is won, but the war is not over**

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Disclosure

Relevant Financial Conflicts of Interest

- CE Presenter, Rebecca Martin
 - Huntsman Cancer Institute
 - No financial relationships to disclose
- CE Mentor, Steve Kirkegaard
 - Huntsman Cancer Institute
 - No financial relationships to disclose
- CE Mentor, Dr. Anna Beck
 - Huntsman Cancer Institute
 - No financial relationships to disclose
- Off Label Uses of Medications
 - Vitamin E, B12 and B6, alpha lipoic acid



Pharmacist Learning Objectives

1. Describe common complications of life after cancer
2. Identify limitations of current literature and data of supportive care plans
3. Discuss gaps of current supportive care plan structures
4. Identify resources for management of cancer survivorship complications



Technician Learning Objectives

1. Describe common complications of life after cancer
2. Recall medications that have evidence for psychologic treatment in cancer survivors
3. Recall medications that have evidence for sexual dysfunction in cancer survivors



Cancer Survivorship

Fitzhugh Mullan, from his essay
Seasons of Survival: Reflections of a Physician with Cancer
New England Journal of Medicine, July 1985



What is Cancer Survivorship?

- *“Considered a survival from the time of diagnosis, through the balance of his or her life.”*
– NCCN Guidelines
- *“Living with, through and beyond a cancer diagnosis”*
– NCCS
- *“Having no signs of cancer after finishing treatment”*
– Cancer.net
- *“The health and life of a person with cancer post treatment until the end of life”*
– NCI



Statistics

- Survivors increased from 3 million in 1971 to 15 million in 2016
- Predicted to reach 20.3 million survivors by 2026
- Due to rising cancer incidence rates, earlier detection and better treatment



Statistics

- Approximately 1 in 5 adults, 65 years of age or older are cancer survivors
- Almost 70% of survivors finished treatment at least 5 years ago
- 44% of survivors finished treatment 10 years ago
- 20% have survived 20 years or longer
- Only 5% of cancer survivors are younger than 40 years of age



Etiology of Cancer Survivorship

Cancer Type	5 Year Survival Rate
Prostate Cancer	98.2%
Thyroid Cancer	98.1%
Testicular Cancer	95.3%
Melanoma	91.8%
Breast Cancer	89.7%
Pediatric ALL*	85.1%
Bladder Cancer	76.8%
Kidney Cancer	74.5%

*ALL = Acute Lymphoblastic Leukemia



Etiology of Cancer Survivorship

- Types of new survivors
 - Living with active cancer
 - Immunotherapy
 - Oral chemotherapy
 - CAR-T cell therapy
 - Adults of childhood cancers
- FDA approvals of new chemotherapy
 - 11/2016- 10/2017:
 - 18 new chemotherapies and 13 new uses of cancer therapies



Complications of Cancer Survivorship

- Physical and mental changes to body
- Financial burdens
- Risk for secondary malignancy
- Lost to follow up and need for supportive care plans (SCPs)
- Gap between health care systems
- Exposed to poorer health outcomes due to lack of post-cancer care and rehabilitation
- Risk of experiencing adverse physical, physiological and social symptoms



Timeline of Cancer Survivorship Management

1985	1986	1991	2005	2012
"Seasons of Survival" NEJM	Foundation of NCCS	The Cancer Survivorship Movement	Cancer Care Trajectory	Commission on Cancer
3 phases: Acute, Extended, Permanent	Survivor from day of diagnosis through end of life	Organizations emerging due to informed health-care consumers	From Cancer Patient to Cancer Survivor: Lost in Transition	SCP added to program accreditation standards



NCCN Guidelines, Cancer Survivorship, 1.2018

Timeline of Cancer Survivorship Management

2013	2015	2015	} 2018
NCCN	Commission on Cancer	ASCO	
First clinical practice guidelines for survivorship	Go-live with SCPs for accreditation standards	Survivorship curriculum publication	



NCCN Guidelines, Cancer Survivorship, 1.2018

Survivorship Initiatives

- Young-adult cancer survivors and seeking follow-up
- Exercise during chemotherapy and survival
- Web-based interventions
- Therapeutic sexual aids
- Mental health and late-cancer effects



ASCO Cancer Survivorship Symposium 018

Survivorship Initiatives

Research Initiatives:

- Existing research provides little evidence that SCP's improve health outcomes and healthcare delivery
 - Heterogeneity in study designs
 - Low likelihood that SCP delivery alone would influence distal outcomes
 - Subjectivity of outcomes when measuring patient quality-of-life



ASCO Cancer Survivorship Symposium 018

What is a Supportive Care Plan?



- A "road-map" for post-treatment healthcare
- A personalized treatment summary, including information on:
 - Possible late and long-term effects
 - Information on signs of recurrence
 - Guidelines for follow-up care
 - Identification of providers who will be following the patient
 - Recommendations for healthy living
 - Identification of supportive care resources



NCCN Guidelines, Cancer Survivorship, 1.2018

What is a Supportive Care Program?

- To provide:
 - Emotional, physical, and spiritual support
- Goal to impart:
 - Knowledge and understanding of problem during diagnosis, treatment and follow-up
- Provide tools to patients and families:
 - For self-management and comprehension of problems that may arise
- Communication:
 - From oncologist to the physician taking over care, including an SCP



NCCN Guidelines, Cancer Survivorship, 1.2018

Models of Survivorship Care Programs

- Oncology specialist models
- Multidisciplinary clinics
- Treatment-specific or disease site-specific clinics
- General survivorship clinics
- Consultative survivorship clinics
- Integrated survivorship clinics
- Community generalist models
- Shared care models (with and without transitions)

No standard of care exists



Ishklyev et al., Lancet 1, 2017

Systematic Review

A Systematic Review of the Impact of Cancer Survivorship Care Plans on Health Outcomes and Health Care Delivery

Design	- 1,399 SCP Studies screened, 24 meeting inclusion - 13 randomized, 11 non-randomized
Methods	- Inclusion: published in English, involved delivery of SCP to survivors diagnosed with cancer and/or their health providers, and evaluated patient-reported outcomes, health care use, or disease outcomes in relation to SCP delivery
Results	- Randomized: Negative for most commonly assessed outcomes - Non-randomized: Descriptive information on satisfaction with care and reactions to SCP's - Positive findings in single studies in other outcomes (amount of information received, satisfaction with care, physician implementation of recommended care)
Conclusion	- Existing research provides little evidence that SCP's improve health outcomes and health care delivery - Possible explanations: - Heterogeneity in study designs - Low likelihood that SCP delivery alone would influence outcomes



Jacobsen et al., Journal of Clinical Oncology, 8, 2018

Non-Randomized Studies

11 studies evaluated	
Locations	USA, Netherlands, Canada, Australia,
Cancer Type(s)	Lung, Breast, Childhood Cancers, Colorectal, Hodgkin Lymphoma, Leukemia
# patients (range)	10 - 4021
Age (years) (range)	22.4-59; not reported
Delivery of SCP's	In person, website, mail



Jacobsen et al., Journal of Clinical Oncology, 8, 2018

Randomized Studies

13 studies evaluated	
Locations	USA, Netherlands, Canada, Australia,
Cancer Type(s)	Breast, Gynecological, Prostate, Mixed, Colorectal, Endometrial
# patients (range)	41 - 968
Age (years) (range)	40.1 - 67.7
Delivery of SCP's	In person with oncologist, in person with nurse, sent to SCP, mailed to patient, in person, website



Jacobsen et al., Journal of Clinical Oncology, 8, 2018

Description of information in SCP's

- Treatment summary only
- Information on health care
- Surveillance recommendations
- Health lifestyle advice
- Health promotional advice
- Effects on social and sexual life
- Psychosocial recommendations
- Risk-based screening recommendations
- Unmet needs
- Recommended screening guidelines and health maintenance
- Specific cancer-related adverse effects
- Recommended follow-up care only
- Discussion of late toxicities and effects
- Cardiomyopathy screening recommendations
- Information on short and long term effects
- Signs of recurrence and second cancers
- Rehabilitation resources



Jacobsen et al., Journal of Clinical Oncology, 8, 2018

Outcomes measured in SCP's

- Post-treatment effects
- Receipt of survivorship care
- Evaluation of SCP by survivor
- Satisfaction with care
- Communication with physician
- Quality of life
- Unmet needs
- Psychological distress
- Knowledge
- Worry and concern
- Reaction to SCP
- Communication preferences
- Cancer-specific distress
- Continuity and coordination of care
- Adherence to follow-up guidelines
- Health care use
- Total costs and QALY's
- Preferences for future care



Jacobsen et al., Journal of Clinical Oncology, 8, 2018

Systematic Review: Measures not commonly used for assessment

- Supportive care plan and program structure
- Survival and quality-adjusted life-years
- Functional status
- Social support services
- Nutritional support
- Rehabilitation services
- Fertility preservation
- Appropriate use of resources
- Costs
- Advancement of health equity

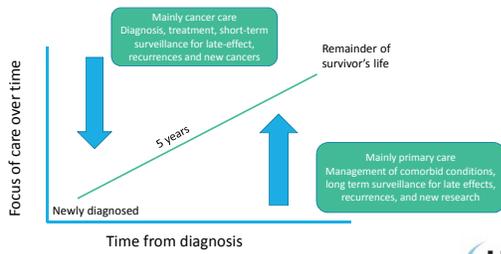


Challenges of Supportive Care Program's

- Fragmentation of care delivery
- PCP's feeling like they are out of the loop
- Shortage of PCP's
- Disparities in access
- Lack of role clarity about who can most effectively deliver which aspects of care
- Lack of education of PCP's on cancer survivorship
- Time needed to prepare an SCP
- Out-of-pocket expenses
- No reimbursement
- Paucity of data regarding the association of SCP and improved outcomes



Bridging the Gap



Models of Survivorship Care Programs

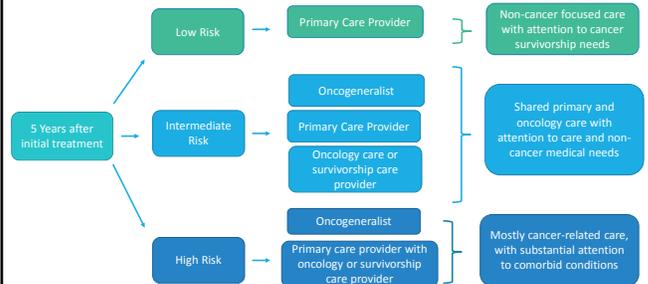
- Multitude of structures studied in the past
- 8 key program models discussed within ASCO guidelines
- Common theme throughout: no discussion of pharmacist utilization or interventions



How can we as pharmacists help bridge the gap ?



Risk-Stratification Model



Risk Stratification Model

Low Risk

- Surgery only
- Non-alkylating chemotherapy
- No radiotherapy
- Low risk of recurrence
- Mild or no persistent toxicity of therapy

Intermediate Risk

- Low or moderate-dose alkylating agent
- Low or moderate-dose radiotherapy
- Auto stem cell transplant
- Moderate risk of recurrence
- Moderate persistent toxicity of treatment

High Risk

- High-dose alkylating agents
- High-dose radiotherapy
- Allogenic stem cell transplant
- High risk of recurrence
- Multi-organ persistent toxicity of therapy

Baskiyev et al. Lancet 1, 2017

Misconceptions About Life After Cancer

- Broad consensus exists that most cancer survivors adapt well after completing their cancer treatment
- 15-40% of survivors have prominent psychosocial needs
- Most common psychological issues after cancer:
 - Anxiety
 - Depression
 - Post Traumatic Stress Disorder
 - Fear of recurrence
 - Survivor guilt
 - Spiritual or existential concerns
 - Sleep disorders
 - Nutrition and weight management

"It's not over, when it's over"

- Altered body image
- Sexual dysfunction
- Social isolation
- Lymphedema
- Lack of employment or insurance
- Financial burdens
- Chemotherapy-induced peripheral neuropathy
- Lack of support
- Supplemental use
- Immunization and infections
- Anthracycline-Induced Cardiac Toxicity
- Pain
- Fatigue

Baskiyev et al. Lancet 1, 2017

Gaps in SCP Communication

- Counseling on new disease states secondary to cancer treatment
- Complications from chemotherapy, radiation and/or surgery
- Peripheral neuropathy, secondary malignancies, diabetes, heart failure, sexual dysfunction, anxiety, depression and PTSD
- Healthy lifestyle modifications
 - Weight loss or weight gain
 - Smoking cessation
- Signs and symptoms of secondary malignancies or new primary

*PTSD: Post-Traumatic Stress Disorder

Baskiyev et al. Lancet 1, 2017

Medication Reconciliation

- Average cancer patient acquires anywhere from 2-5 comorbidities throughout treatment
- Patient seeing multiple physicians prescribing multiple medications
 - Oncologist, primary care provider, psychiatrist, gynecologist, cardiologist, endocrinologist, dermatologist, etc.
- Therapy duplication
- Polypharmacy – average 9.5 medications per cancer patient
- High risk of drug interactions
 - Chemotherapy, hormone therapy, biological agents, supportive therapies

Baskiyev et al. J Oncol Pharm Pract. 9, 2009

Chemotherapy-Induced Peripheral Neuropathy (CIPN)

- Weakness, numbness, burning and pain in hands in feet due to nerve damage
 - Cold sensitivity
- Common culprits
 - Platinums (cisplatin, carboplatin, oxaliplatin)
 - Taxanes (paclitaxel, docetaxel)
 - Vinca alkaloids (vinblastine, vincristine)
 - Bortezomib
 - Thalidomide
- Mechanism: alter aspects of peripheral nerve and immune cell function → causing sustained neuropathy and pain

Kim et al. Curr Opin Anaesthesiol. 2017 Oct

Chemotherapy-Induced Peripheral Neuropathy (CIPN)

- Risk of CIPN increases with each subsequent cycle
- Often can persist as a chronic pain syndrome
- Associated with decreased quality of life
- Prevention:
 - Vitamin E, B12 or acupuncture
- Treatment:
 - Duloxetine – mainstay of therapy
 - Gabapentin
 - Pregabalin
 - Alpha lipoic acid
 - Vitamin B6

Kim et al. Curr Opin Anaesthesiol. 2017 Oct

Secondary Malignancies

- Signs and symptoms
 - Unexplained weight loss over weeks-months
 - Poor appetite
 - Weakness
 - Fatigue
 - Bone pain
 - Feeling of "fullness"
 - Cough or hoarseness that does not go away
 - Change in bowel movements
 - Swollen, firm or non-tender lymph nodes




Rheingold et al. Holland-Frei Cancer Medicine, 6th Edition

Secondary Malignancies

Radiation Exposure

- Within or at the margin of radiated field
- ~ 10 years after exposure
 - Up to 34 years later
- Bone and soft-tissue sarcomas
- Skin, brain, thyroid and breast cancers




Rheingold et al. Holland-Frei Cancer Medicine, 6th Edition

Secondary Malignancies

Chemotherapy Exposure

<ul style="list-style-type: none"> • Topoisomerase inhibitors <ul style="list-style-type: none"> • Irinotecan • Topotecan • Alkylating agents <ul style="list-style-type: none"> • Cyclophosphamide • Ifosfamide • Cisplatin • Carboplatin • Busulfan • Melphalan • Procarbazine 	<ul style="list-style-type: none"> • AML*, ALL**, and MDS*** • 5-24 fold increased risk • ~4-7 years after exposure
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*AML = Acute Myeloid Leukemia
**ALL = Acute Lymphoblastic Leukemia
***MDS = Myelodysplastic Syndrome



Rheingold et al. Holland-Frei Cancer Medicine, 6th Edition

Secondary Malignancies

Cancers with Higher Risk

- Breast Cancer
- Prostate Cancer
- Testicular Cancer
- Colorectal Cancer
- Endometrial Cancer
- Skin Cancer




Rheingold et al. Holland-Frei Cancer Medicine, 6th Edition

Sexual Dysfunction

Men	Women
<ul style="list-style-type: none"> • Prostate, testicular, bladder, colon, rectal cancers, graft-versus host disease (GVHD) • Manifestation: <ul style="list-style-type: none"> • Erectile dysfunction • Pain 	<ul style="list-style-type: none"> • Ovarian, endometrial, cervical, breast, GVHD • Manifestation <ul style="list-style-type: none"> • Menopause • Vulvodynia • Vaginismus • Vaginal fibrosis • Bleeding



D'Amico et al. Am J Clin Oncol 2014

Causes of Sexual Dysfunction

- Men and Women:
 - Radiation to pelvis
 - Malignancies affecting continence and bowel function
 - Psychological issues
 - Surgeries
 - Oophorectomy, hysterectomy, salpingectomy
 - ED: colon, rectal, prostate or penile surgery
 - Lymph node removal



D'Amico et al. Am J Clin Oncol 2014

Causes of Sexual Dysfunction

- Chemotherapy
- Breast Cancer:
 - Estrogen Receptor (ER) or Progesterone Receptor (PR) positive
 - SERM (Selective Estrogen Receptor Modulators): Tamoxifen
 - Aromatase Inhibitors: Anastrozole, Letrozole, Exemestane
- Prostate Cancer:
 - Androgen Deprivation Therapies (ADT)



NCCN Guidelines, Survivorship 1.2018

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Sexual Dysfunction in Women with Cancer

- Recent Discussions
 - Largest barrier to treatment is ourselves
 - Why are we not talking about sexual dysfunction?
- Patient surveys:
 - Estimates of the incidence of sexual dysfunction range from 30% to 100% among female cancer patients
 - Recent global survey: 14% of US respondents reported being asked about their sexual health or concerns in last 3 years



DeSimone et al. Am J Clin Oncol 2014

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Management of Sexual Dysfunction in Women

- Cancers with physiological changes: pain or discomfort
 - Topical vaginal therapies
 - Ospemifene (ospemifene)*
 - Zestra (testosterone)*
 - DHEA (prasterone)*
 - Addyi (flibanserin)
 - Orillisa (elagolix)
 - Pelvic physical therapy

* Avoid in hormone-sensitive cancers



Taylor et al. NEJM May 2017; Ivaskoff et al. Human Reproductive Update. 21.4, 500-516. 5.2015, NCCN Survivorship 1.2018

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Management of Anxiety, Depression and Distress

- First line treatment
 - SSRI's (sertraline, citalopram, fluoxetine)
 - SNRI's (venlafaxine, duloxetine)
 - Benzodiazepine (acute anxiety) (lorazepam, diazepam)
 - Counseling
- Recent literature of psychological management in cancer patients and survivors

Avoid SSRI's in hormone-sensitive cancer, physiological sexual dysfunction



Ivaskoff et al. Human Reproductive Update. 21.4, 500-516. 5.2015, NCCN Survivorship 1.2018

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Management of Anxiety, Depression and Distress

- Lack of desire, libido or intimacy
 - Androgens
 - Bupropion (Wellbutrin)
 - Bupirone (Buspar)
 - Flibanserin (Addyi)

* Avoid SSRI's in hormone-sensitive cancer, physiological sexual dysfunction



Ivaskoff et al. Human Reproductive Update. 21.4, 500-516. 5.2015, NCCN Survivorship 1.2018

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Anthracycline-Induced Cardiotoxicity

- Generation of free radicals through mitochondrial redox cycling in cardiomyocyte
- Results in left ventricular dysfunction and congestive heart failure
- Anthracyclines:
 - Daunorubicin, doxorubicin, epirubicin, idarubicin, mitoxantrone, valrubicin
- Lifetime cumulative dose:
 - > 550 mg/m² (doxorubicin equivalents)
 - 5% risk
- Commonly used for:
 - Breast cancer, leukemia's, small cell lung cancer, ovarian



Jacobsen et al. Journal of Clinical Oncology. 8.2018
<https://www.jco.org/content/36/8/1043-1048.full.pdf>
 10.1200/JCO.2017.36.8.1043
 DOI: 10.1200/JCO.2017.36.8.1043

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Cancer Survivorship Resources

- National Comprehensive Cancer Network (NCCN)
- American Society of Clinical Oncology (ASCO)
- Diagnostic and Statistical Manual of Mental Disorders (DSM-5)
- Center for Disease Control and Prevention (CDC)
- Livestrong Foundation
- National Coalition of Cancer Survivorship
- National Cancer Survivorship Resource Center – American Cancer Society



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The Future of Supportive Care Plan's

1. Bridging gap between oncologist and provider taking over care
2. Expansion on education to primary care providers
3. Ensuring follow up recommendations and screening parameters are being acted upon
4. Expansion of patient education on comorbidities and future expectations



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Halpern et al. *Lancet* 1, 2017

Summary

- Conflicting literature exists on supportive care plans and programs
- Transition from oncologist to PCP should include more in-depth conversations with the patient
- Future studies needed with consistent variables to measure outcomes
- Initiatives to start conversations with patients on sexual health and psychological challenges are needed
- Pharmacists represent large asset to the care of cancer survivors both in and outside of supportive care clinics



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Pharmacist and Technician: Question #1

Which of the following are common complications of life after cancer?

- A. Sexual, psychosocial or psychological dysfunction
- B. Financial burdens
- C. PTSD
- D. Loss to follow up
- E. All of the above



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Pharmacist: Question #2

What is a limitation of current supportive care plan literature?

- A. Small numbers of patients that meet inclusion
- B. Mostly retrospective literature
- C. Subjective evaluation of patient quality of life
- D. Inconsistency in design
- E. Both C & D



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Pharmacist: Question #3

Which of the following are gaps in current supportive care plan structures?

- A. Lack of trust of PCP's by patients
- B. Disparities in access
- C. Paucity of data regarding the association of SCP and improved outcomes
- D. Shortage of providers
- E. All of the above



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Pharmacist: Question #4

What resources may you turn to for management of cancer survivorship complications?

- A. ASCO and NCCN guidelines
- B. DSM-5
- C. CDC
- D. National Coalition of Cancer Survivorship
- E. All of the above



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Technician: Question #1

Which of the following medications is not recommended in ASCO or NCCN guidelines for women with sexual dysfunction secondary to cancer therapy?

- A. Addyi
- B. Zestra
- C. Ospemifene
- D. Orilisa
- E. None of the above



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Technician: Question #2

Which of the following medications could be indicated for lack of desire or intimacy in women?

- A. Bupropion
- B. Metoprolol
- C. Albuterol
- D. Prednisone
- E. None of the above



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Complexities of Cancer Survivorship

- Anthracycline-Induced Cardiac Toxicity
- Anxiety
- Depression
- Distress
- PTSD*
- Cognitive Function
- Lymphedema
- Fatigue
- Hormone-Related Symptoms
- Pain
- Sexual Function
- Sleep Disorders
- Nutrition and Weight Management
- Supplement Use
- Immunization and Infections

*Post-traumatic Stress Disorder

NCCN Guidelines, Cancer Survivorship, 1.2018



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Management of Sexual Dysfunction in Women

- Every patient should be screened for overall sexual function and satisfaction
- Diagnosis should be established when there are physical issues
- Education should be provided on changes to expect prior to treatment initiation
- Psychosocial and psychosexual counseling should be offered to women with cancer
- Current evidence does not support one type of counseling over the other
- Group therapy or group therapy with exercise
- Couples counseling logical distress
- Multidisciplinary approach indicated due to multitude of contributing factors



The ASCO Post, 3, 2018

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Shared Care Model

- Oeffinger and McCabe
 - Describes the need for risk stratification strategies to differentiate between cancer survivors who should be transitioned into oncology-based, primary care-based or shared-care long term care models
- Study 1 <https://www.ncbi.nlm.nih.gov/pubmed/21731511>
- Study 2 <https://www.ncbi.nlm.nih.gov/pubmed/26245952>
- Challenges with this type
- PUT BACK IN TABLE COMPARING THE TWO STUDIES & THEIR OUTCOMES



Nebkhyudov et al. Lancet 3, 2017

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Consultative or Oncogeneralist Model

- Oeffinger and McCabe
 - Describes the need for risk stratification strategies to differentiate between cancer survivors who should be transitioned into oncology-based, primary care-based or shared-care long term care models
- Study 1 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5145775/>
- Study 2: <https://www.ncbi.nlm.nih.gov/pubmed/26278341>

Challenges with this type
PUT BACK IN TABLE COMPARING THE TWO - PROS N CONS



Haskhyedov et al. Lancet 1, 2017 67

Efforts to Improve Evaluation

P.LI.SS.IT.

P Permission	L Limited Information	S Specific Suggestions	I Intensive Therapy
Invite the patient to enter into a discussion about sexual health	Explain normal sexual functioning	Give specific and easy information that can help with sexual relations	Suggest referral to a sexual specialist



Desimone et al. Am J Clin Oncol 2014 68

Efforts to Improve Evaluation

- Female Sexual Function Index (FSFI):
 - 19 items that cover 6 domains in female sexuality:
 - Desire, arousal, lubrication, orgasm, satisfaction, and pain
 - For women not actively engaged in sexual activity
 - Does not take into consideration certain psychological issues that are relevant in women with cancer
- Brief Sexual Symptom Checklist for Women (SSFF-A): 3 domains in women
 - 1) Libido
 - 2) Sexual activity
 - 3) Sexual satisfaction



Desimone et al. Am J Clin Oncol 2014 69

Efforts to Improve Evaluation

- 2015, Bartula and Sherman
 - Adaptation of the FSFI in women with breast cancer (FSFI-BC)
 - Adds cancer and distress subscales
 - Favorable psychometric properties
 - Acceptable for use in this population, irrespective of whether or not women were currently sexually active.
 - Utilization in women with other types of cancers is an open question



Desimone et al. Am J Clin Oncol 2014 70

