2024 Breast Cancer Congress

with Updates from the 2023 SABCS

Friday, February 2, 2024
1:45 PM – 2:45 PM CST

Issues with Sexuality and Sexual Function in Patients with Breast Cancer

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Session Learning Objectives

- Identify issues faced by breast cancer patients regarding sexual function and sexuality.
- Describe treatment options for sexual dysfunction that are available for patients with breast cancer.

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Sexual health concerns are prevalent in breast cancer survivors

43

Percentage of women in the US reporting sexual dysfunction

73

Percentage of breast cancer survivors reporting sexual dysfunction

19.3

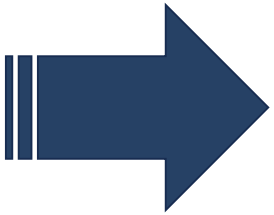
Average female sexual function index (FSFI) score among breast cancer survivors

**Scores < 26.5 indicate female sexual dysfunction

Based on metanalysis of 15 studies: Jing et al, *Supportive Care in Cancer*, 2019

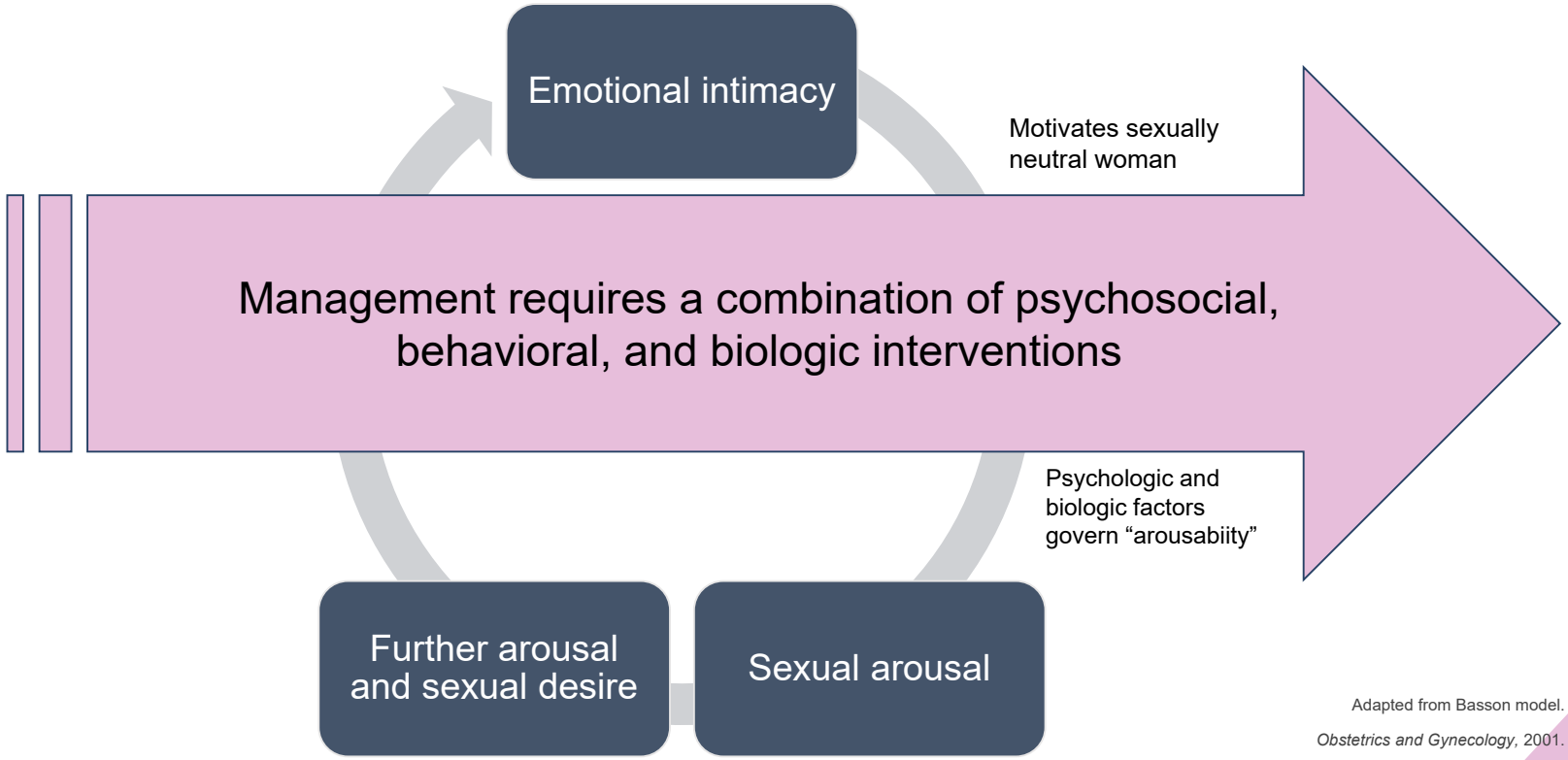
Sexual health concerns are prevalent in breast cancer survivors

Diagnosis
Breast surgery
Chemotherapy
Chest wall radiation
Estrogen deprivation therapy



Emotional distress
Partner stress
Poor body image
Low libido
Dyspareunia
Vaginal dryness

Breast cancer experience impacts all aspects of sexual response cycle



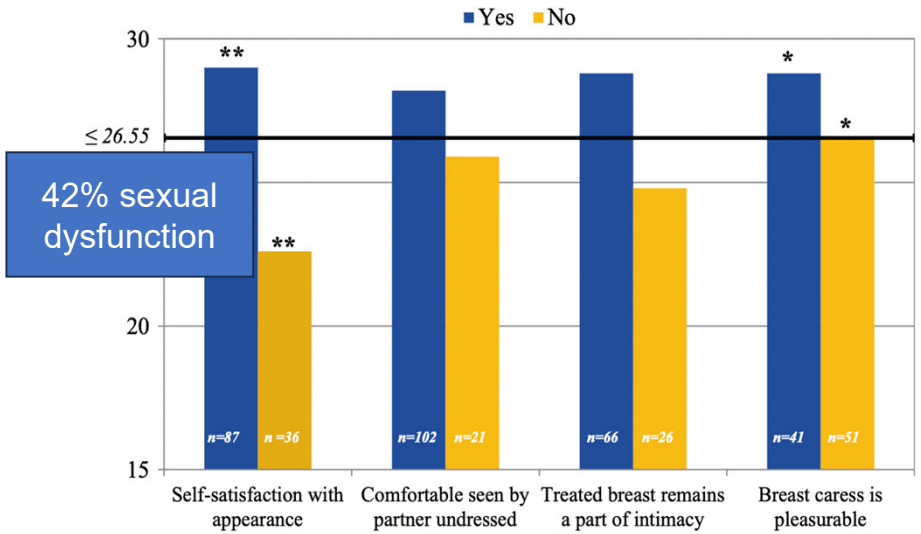
Adapted from Basson model.

Obstetrics and Gynecology, 2001.

Breast surgery modality impacts elements of sexual health

My chest plays a role in intimacy and sex	BCS	MRM	MRM with recon
Before surgery	83%	87%	93%
After surgery	73%	59%	76%
Breast appearance satisfaction	80%	NA	65%

Sexual dysfunction rates by median FSFI stratified by being satisfied with breast appearance after surgery



42% sexual dysfunction

Impact on intimacy should be discussed during surgical shared decision-making discussions

Gass et al, *Annals of Surgical Oncology*, 2017.

Impact of endocrine therapy: more than just vaginal dryness

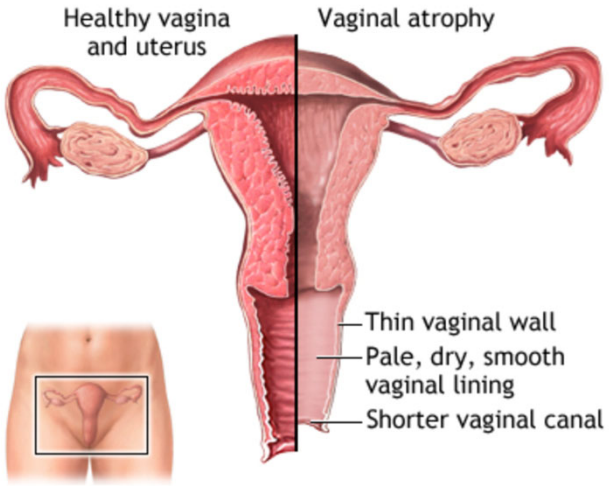


Photo: MedlinePlus.

Type of endocrine therapy matters –SOFT/TEXT trial analysis

	Tamoxifen alone	Tamoxifen + OFS	Exemestane + OFS
Decreased libido	43.2%	42.2%	45.6%
Dyspareunia	24.1%	27.3%	31.6%
Dryness	42.4%	49.2%	53.7%

Francis PA et al, *NEJM*, 2018

Despite high prevalence, only ~30% of breast cancer survivors report discussing sexual health issues with their oncologist

- 80-90% reporting willingness and desire to have this discussion

WHY?

Flynn et al, Psychooncology, 2012

Barriers to discussion:

Patient

- Discomfort discussing sexual health/fear of making provider uncomfortable
- Perception of demographic discordance with provider
- Feeling of lack of patient-centered communication
- Belief that sexual dysfunction is untreatable

Provider

- Lack of time during patient visits
- Discomfort/fear of making patient uncomfortable
- Lack of knowledge of treatment options
- Lack of access to timely or coordinated care
- Biases

Wiggens et al, J Psychosoc Oncol, 2007; Marwick et al, JAMA, 1999; DeSimone et al, American Journal of Clinical Oncology, 2014

Sexual health concerns need early and repeated monitoring

- **Screening tools**
  - NCCN distress thermometer: domains include concerns around sexual health, appearance changes, relationships
  - NCCN survivorship survey: "Do you have any concerns regarding your sexual function, sexual activity, sexual relationships, or sex life?"
- **Patient-reported outcome measures**
  - Female sexual function index
  - Brief sexual symptom checklist
  - PROMIS Sexual function and satisfaction measure

BRIEF SEXUAL SYMPTOM CHECKLIST FOR WOMEN[a,b]

Please answer the following questions about your overall sexual function:
1. Are you satisfied with your sexual function?

__ Yes __No
If no, please continue.

2. How long have you been dissatisfied with your sexual function?

3a. The problem(s) with your sexual function is:
(mark one or more)

__1 Problem with little or no interest in sex
__2 Problem with decreased genital sensation (feeling)
__3 Problem with decreased vaginal lubrication (dryness)
__4 Problem reaching orgasm
__5 Problem with pain during sex
__6 Other:

3b. Which problem is most bothersome? (circle)
1 2 3 4 5 6

4. Would you like to talk about it with your doctor?
__Yes __No

Hatzichristou D, Rosen RC, Derogatis LR, et al. Recommendations for the clinical evaluation of men and women with sexual dysfunction. J Sex Med 2010;7:337-348.

NCCN Guidelines® for Distress Management ((Version 1.2024) and Survivorship (v1.2023). © 2024 National Comprehensive Cancer Network, Inc. Available at: NCCN.org.

Tips for direct discussion:

- “I’d like to review how you are doing with regard to sex and intimacy, would that be okay?”
- “Many patients who have been through this treatment frequently find themselves facing changes in sexual function. What has your experience been like?”
- “Can you tell me about the impact cancer has had on sexuality or intimacy for you?”
- “A common complaint is pain during intercourse. Is that happening for you?”

→ Specific suggestions or referrals for more intense therapy

Bober, JCO, 2012; Dizon et al, Oncologist, 2014

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I didn't even want to try [to have an orgasm]; this is just like, let's not even [try]…because it is so much work and pressure on you to enjoy sex when it's painful…

-Female early stage BC survivor

Pressure, "giving up", avoidance

Fear (not relaxation), distracting negative thoughts → loss of focus and pleasure

You are scared and you are wondering, is it going to be like this forever? Then before you know it, you are out of it [the mood] and you are never going to have pleasure.

-Young female early stage BC survivor

Reese JB, Porter LS, Casale KE, et al. (2016). *Health Psych, 35*, 1085-96

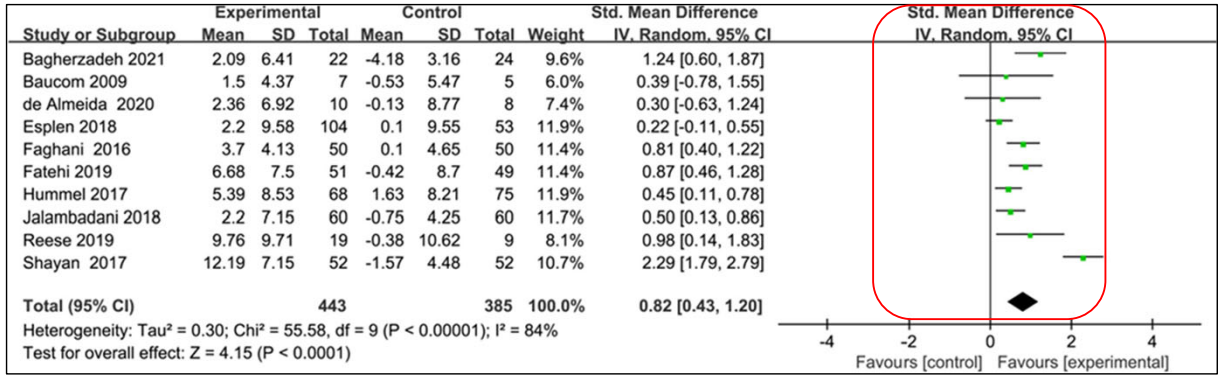
Impact of Thoughts on Sex and Intimacy

Couple Relationship

- Joint coping efforts
- Communication difficulties
- Partner unsure how to respond
- Loss of spontaneity
- Getting “out of the habit”
- Patient/caregiver roles

Psychosocial Interventions

- Education, skills training, counseling
- Mix of RCTs and quasi-experimental designs, mostly smaller studies although changing
- Different formats (in-person, online, telephone, combination), approaches (CBT, mindfulness)
- Feasible, well-received
- Recent systematic reviews find significant effects for sexual function, satisfaction, distress



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Bagherzadeh 2021	2.09	6.41	22	-4.18	3.16	24	9.6%	1.24 [0.60, 1.87]
Baucom 2009	1.5	4.37	7	-0.53	5.47	5	6.0%	0.39 [-0.78, 1.55]
de Almeida 2020	2.36	6.92	10	-0.13	8.77	8	7.4%	0.30 [-0.63, 1.24]
Esplen 2018	2.2	9.58	104	0.1	9.55	53	11.9%	0.22 [-0.11, 0.55]
Faghani 2016	3.7	4.13	50	0.1	4.65	50	11.4%	0.81 [0.40, 1.22]
Fatehi 2019	6.68	7.5	51	-0.42	8.7	49	11.4%	0.87 [0.46, 1.28]
Hummel 2017	5.39	8.53	68	1.63	8.21	75	11.9%	0.45 [0.11, 0.78]
Jalambadani 2018	2.2	7.15	60	-0.75	4.25	60	11.7%	0.50 [0.13, 0.86]
Reese 2019	9.76	9.71	19	-0.38	10.62	9	8.1%	0.98 [0.14, 1.83]
Shayan 2017	12.19	7.15	52	-1.57	4.48	52	10.7%	2.29 [1.79, 2.79]
Total (95% CI)			**443**			**385**	**100.0%**	**0.82 [0.43, 1.20]**

Heterogeneity: Tau² = 0.30; Chi² = 55.58, df = 9 (P < 0.00001); I² = 84%
Test for overall effect: Z = 4.15 (P < 0.0001)

Xu J, Xue B, Qiao J et al. (2022). *JCN,* https://doi.org/10.1111/jocn.16194

What is Mindfulness?

- Paying attention, on purpose, non-judgmentally to present moment experiences
- Skill

During intimacy → focusing on the sensations without expectations or judgment

Slide Content Adapted from Lauren Zimmaro, PhD

Mindfulness for Sexual Problems

Authors (Year)	Population	Study Design	Intervention Description	Sexual Function Measure(s)	Improvement in Sexual Function Outcome?	Improvement in Sexual Distress Outcome?
Bagherzadeh et al., 2021	n=52 (breast cancer)	RCT + qualitative	MBSR	FSFI	Yes	n/a
Chang et al., 2022	n=51 (breast cancer)	RCT	MBSR	FSFI	Yes	n/a
Kemerer et al., 2023	n=68 couples (prostate cancer)	RCT: 3 groups	Abbrev MBSR for Couples	FSDS-R; IIEF/IIEF-MSM + FSFI	Yes	Yes
Paterson, 2015	n=91 (breast cancer)	RCT	MBSR-BC	FSDS	n/a	No
Huberty et al., 2019	n=128 (myeloproliferative neoplasm)	RCT: 4 group with cross-over design	10% Happier app and Calm app	PROMIS Sexual Function	Yes	n/a
Rahmani et al., 2014	n=36 (breast cancer)	RCT: 3 groups	MBSR	QLQ-BR23 sexual functioning	Yes	n/a
Brotto et al., 2012	n=31 (cervical or endometrial cancer)	RCT/quasi-randomized	psychoeducation (later called "PED")	FSFI + FSDS	Yes	Yes
Bober et al., 2020	n=20 (breast cancer)	Single-arm pre-post trial	SHARE-OS	FSFI	Yes	n/a
Bober et al., 2017	n=46 (ovarian cancer)	Single-arm trial/baseline 'run-in' control phase	SHARE	FSFI	Yes	n/a
Brotto et al., 2017	n=61 (gyn or colorectal)	Single-arm pre-post trial	Psychoeducational Intervention for Sexual	FSFI/IIEF + FSDS	Yes	Yes
Brotto et al., 2008	n=22 (gyn cancer)	Single-arm pre-post trial	PED	FSFI + FSDS + SFQ + Physiological Sexual response	Yes	Yes
Sears et al. 2022	n=30 (breast cancer)	Single-arm pre-post trial	"MBCT for Sexuality"	SIDI interview + FSFI	Yes	Yes
Bossio et al., 2021	n=14 couples (prostate cancer)	Single-arm pre-post trial	IMPPACT	FSFI/IIEF	Yes	n/a

Systematic Review
TOTAL reports included
(n = 13 studies)

- *RCTs: n=7*
- *Single-arm pre/post trials: n=6*
- *6 in breast cancer*

Improvements in sexual function found in 5 of 6 studies in breast cancer

Zimmaro, L.A., Lepore, S.J., Reese, J.B. (2022, November). Abstract presented at the 8th Conference of the Scientific Network on Female Sexual Health and Cancer, November 17-18, New Haven, CT.

Sexual Changes and Challenges – LGBTQ Breast Cancer Survivors

…The aromatase inhibitors have done a number on me. I don't get turned on as easily, I don't have orgasms as easily. Vaginal dryness is a big issue… I was always happiest being very femme [feminine] in bed, and now it's hard to feel like I still have that curvy, femme appeal. My chest is numb some places, over sensitive in others. (Female, lesbian)

I do not think I would have chosen this [no reconstruction] had I not had the experience of living in the gay world, dated women, been open to difference. (Human, bisexual).

Brown, M.T. & McElroy, J.A. (2017). *Women Health, 58,* 403-418.

Case control study in 85 LBW post-treatment for breast cancer and 85 age- and partner-matched controls; gender identity not reported

Table 2. *Comparison of Sexual Functioning by Case-Control Status*

	Cases ($n = 85$)	Noncancer Control ($n = 85$)	Mean Difference (95% CI)	p-Value
Sexual frequency[a]				
N	85	84		
Range	0 to 208.0	0 to 208.0		
Median (IQR)	12.0 (2.0, 36.0)	36.0 (2.0, 52.0)		
Mean ± *SD*	24.3 ± 37.5	47.9 ± 59.4		
Log sexual frequency				
N	85	84	−0.51 (−0.92, −0.10)	0.02*
Range	0 to 5.3	0 to 5.3		
Median (IQR)	2.6 (1.1, 3.6)	3.6 (1.1, 4.0)		
Mean ± *SD*	2.3 ± 1.5	2.9 ± 1.7		
FSFI score				
N	59	70	−1.93 (−4.08, 0.21)	0.08
Range	7.2 to 34.9	11.6 to 33.6		
Median (IQR)	25.2 (17.7, 30.7)	27.2 (22.9, 30.2)		
Mean ± *SD*	24.0 ± 7.2	26.0 ± 5.3		
FSFI (*N* (%))				
Normal function	28 (47.5)	39 (55.7)		0.31
Risk of dysfunction	31 (52.5)	31 (44.3)	1.44 (0.72, 2.90)[†]	
FSFI desire subscale				
N	85	84	−1.34 (−1.94, −0.75)	<0.01**
Range	2.0 to 10.0	2.0 to 10.0		
Median (IQR)	4.0 (2.0, 6.0)	6.0 (4.0, 7.5)		
Mean ± *SD*	4.3 ± 2.0	5.7 ± 2.2		
FSFI arousal subscale				
N	61	69	−1.57 (−3.23, 0.09)	0.07
Range	4.0 to 20.0	4.0 to 20.0		
Median (IQR)	14.0 (9.0, 18.0)	16.0 (12.0, 18.0)		
Mean ± *SD*	13.2 ± 5.3	14.9 ± 4.5		
FSFI lubrication subscale				
N	56	67	1.77 (0.25, 3.29)	0.03*
Range	4.0 to 20.0	8.0 to 14.0		
Median (IQR)	14.0 (8.0, 20.0)	12.0 (11.0, 12.0)		
Mean ± *SD*	13.2 ± 6.0	11.6 ± 1.1		
FSFI orgasm subscale				
N	58	70	−1.45 (−2.76, −0.13)	0.04*
Range	3.0 to 15.0	3.0 to 15.0		
Median (IQR)	12.5 (8.0, 15.0)	14.0 (11.0, 15.0)		
Mean ± *SD*	11.1 ± 4.1	12.6 ± 3.2		

Boehmer, U., Ozonoff, A., Timm, A. et al. (2014). *J Sex Res, 51*, 681-89.

LGBTQ Breast Cancer Survivors

- Comparison with heterosexual survivors
  - Effects on sexual function similar
  - Loss of breast sensation and associated arousal similar
  - Opting for no breast reconstruction more common
  - Possibly fewer sexual identity/ body image concerns
  - Effects dependent on individual values, roles, other factors

Boehmer, U. & Freund, L.R. (2007). *Plastic & Recon Surg, 119,* 464-472.
Brown, M.T. & McElroy, J.A. (2017). *Women Health, 58,* 403-418.
Kamen, C., Pratt-Chapman, M.L., & Quinn, G.P. (2020). *Curr Sex Health Rep, 12*, 320-328.

Sexual Changes and Challenges – Trans Patients

I found out who I really am. That I am transgender. I tried implants and had them removed. I got fitted for prosthetics and wore those a while, then realized I didn't want breasts. (Transgender looking to transition, now lesbian but will be straight after transition)

… the surgery… was the final step in my quest to find myself comfortable on the gender spectrum … I feel like I now have a body that fits me. (Genderqueer, queer)

Brown, M.T. & McElroy, J.A. (2017). *Women Health, 58,* 403-418.

Trans Patients

- Little known about sexual function in trans survivors
  - Review in 2021[1] found 7 studies examining HRQOL
  - None examined sexual function in detail
- Gender affirming mastectomy helpful for trans men with breast cancer[2]
- More research needed

1 Pratt-Chapman, M.L., Alpert, A.B., Castillo, D.A. (2021). *BMC Systematic Reviews, 10.*
2 Brown, M.T. & McElroy, J.A. (2017). *Women Health, 58,* 403-418.

Considerations for Sexual Rehabilitation

- Treatment of vaginal symptoms same regardless of sexual orientation
- Possibly less reliance on ability to engage in penetrative intercourse (don't assume → ask about practice/need for help)
- Acceptance/comfort with using vaginal lubricants
- May be better able to adapt to body changes, sexual issues (can still be highly bothersome)

Kamen, C., Pratt-Chapman, M.L., & Quinn, G.P. (2020). *Curr Sex Health Rep, 12*, 320-328;
Reese, J.B., Zimmaro, L.A., McIlhenny, S., et al. (2022). *Front Psychol, 10, doi: 10.3389/fpsyg.2022.864893.*
Austria, M.D., Lynch, K., Le, T. et al. (2021). *J Sex Med, 18,* 2020-2027.

Before offering suggestions for rehabilitation…

Do you know your patient's sexual orientation and gender status?

Gay/bisexual people whose sexual orientation is known to provider → more likely to discuss sexual problems[1]

SGM patients generally willing to disclose[2]

1 Flynn, K.E., Whicker, D., Lin, L., et al. (2019). *J Gen Int Med, 34,* 2505-2511.
2 Fish, J., Williamson, I., & Brown, J. (2019). BMC Cancer, 678.

It is important to know the sexual orientation of my patients to provide the best care	
Strongly disagree	12 (8.1)
Disagree	39 (26.2)
Neutral	34 (22.8)
Agree	50 (33.6)
Strongly agree	9 (6.0)
Do not know or prefer not to answer	3 (2.0)
Missing	2 (1.3)

Survey of 149 oncologists

40%

66% for gender status

Schabath, M.B., Blackburn, C.A., Sutter, M.E., et al. (2019). *J Clin Oncol, 37*, 547-558.

Take Home Messages

- Sexual function/identity problems common, distressing, diverse
- Patients differ in priorities, needs for help
- Important not to assume patient is heterosexual or engages in a certain type of sexual activity
- More research needed on efficacy of sexual rehabilitation, more training for providers to improve comfort in discussing sexual issues

Further Resources

- Provider Resources
  - National LGBT Cancer Network Cultural Competency Training (cancer-network.org)
    - Cancer-network.org/welcoming-spaces
- Patient Resources
  - Escape AYA
    - https://www.escapeayac.org/resources
  - Queering Cancer
    - https://queeringcancer.ca/
  - Prostate Cancer Foundation (pcf.org)
    - https://www.pcf.org/c/for-gay-and-bisexual-men-what-you-need-to-know-about-treatment-for-localized-prostate-cancer/

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Who We Are

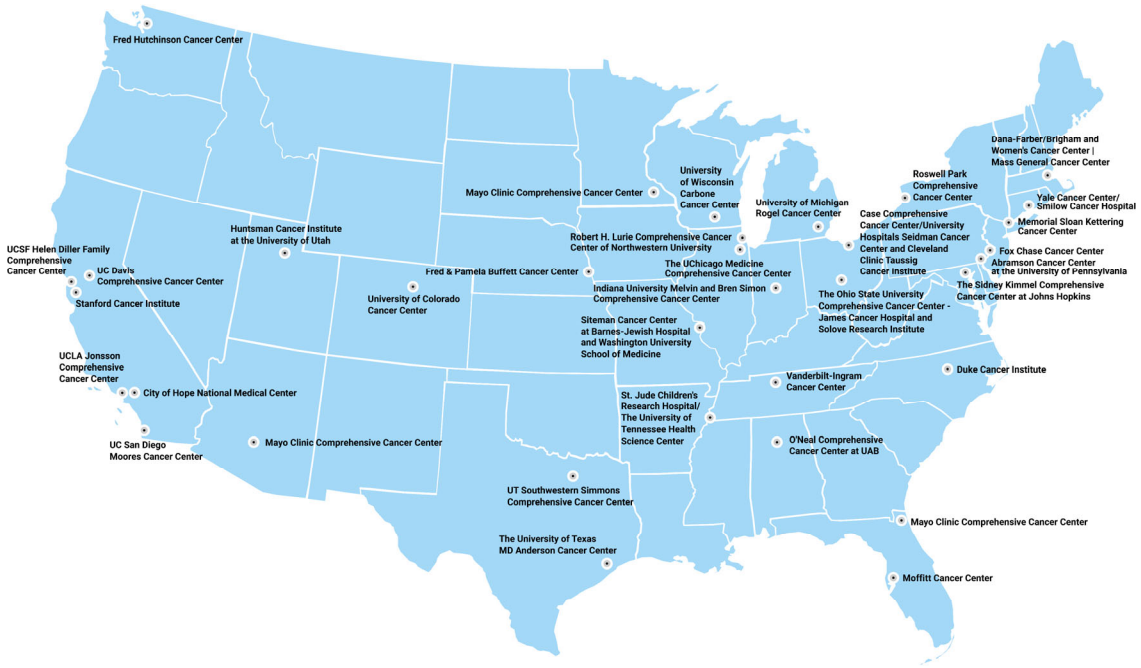
An alliance of leading cancer centers devoted to patient care, research, and education

Our Mission

To improve and facilitate quality, effective, equitable, and accessible cancer care so all patients can live better lives

Our Vision

To define and advance high-quality, high-value, patient-centered cancer care globally



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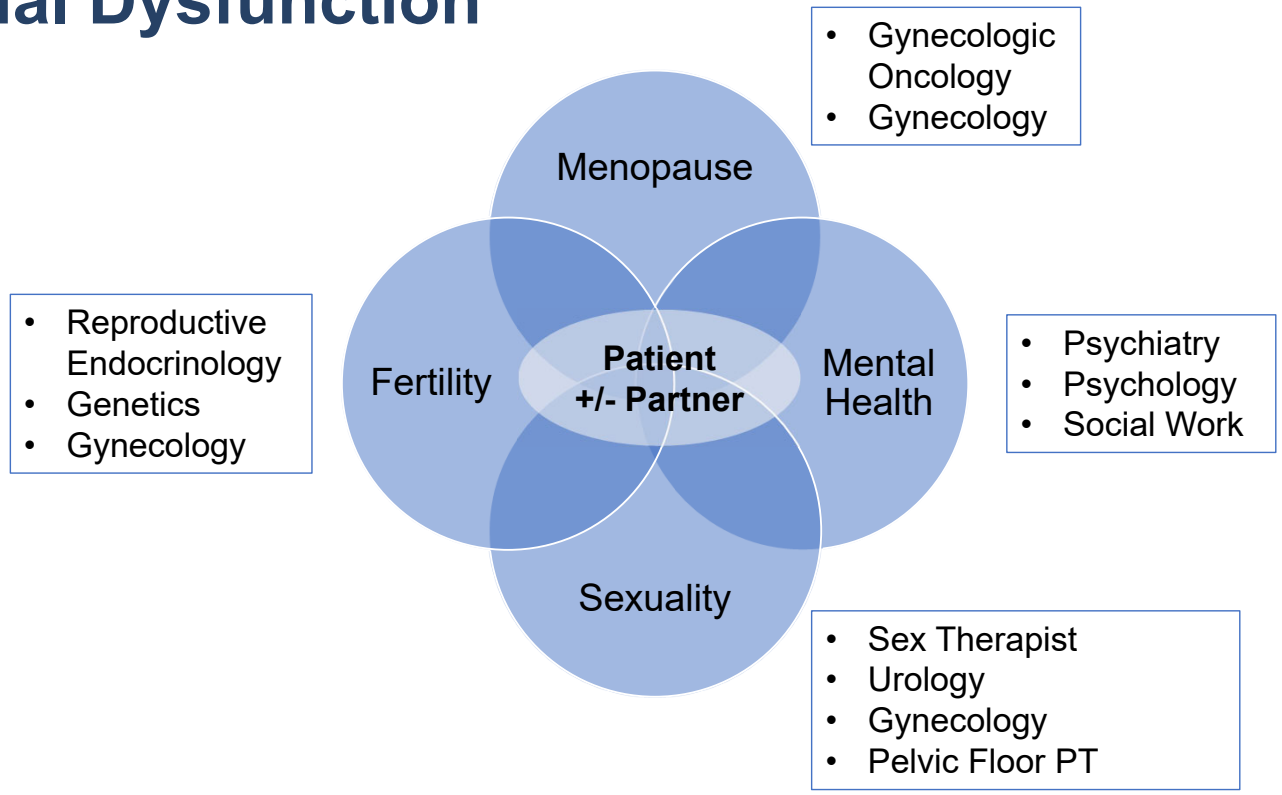
Assessing Sexual Function is Guideline-Driven

NCCN Guidelines for Survivorship: Sexual Function (Version 1.2023)

- Ask about sexual function at regular intervals
- Discuss treatment-associated infertility and refer to fertility specialist if indicated
- Consider use of a screening tool:
  - Brief Sexual Symptom Checklist for Women
  - Sexual Health Inventory for Men
- Refer to sexual health specialist, if survivor is interested
- Appropriate referrals for:
  - Psychotherapy
  - Sexual/couples counseling
  - Gynecologic care
  - Urology care
  - Sexual health specialist, if available
  - Sex therapist, if available
- Re-evaluate at regular intervals

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Survivorship. (Version 1.2023). © 2023 National Comprehensive Cancer Network, Inc. Available at: NCCN.org.

Interdisciplinary Approach to Management of Sexual Dysfunction



Management of Sexual Dysfunction

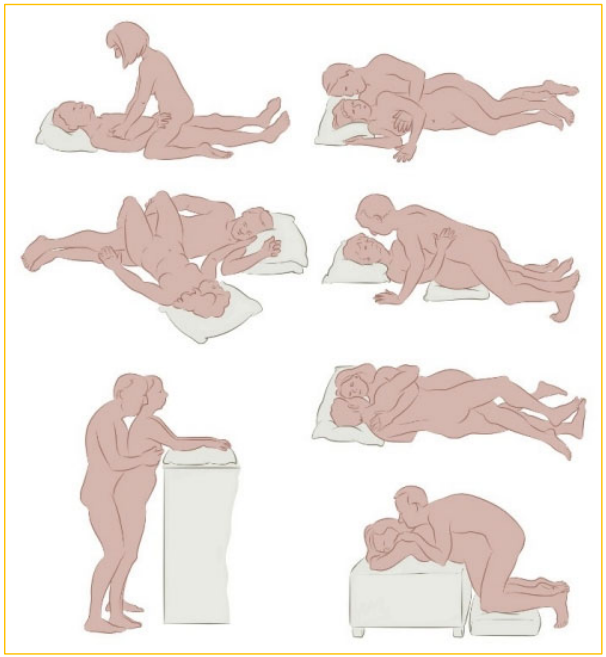
Treatment	Examples
Education	Discuss side effects before initiating cancer therapy
Validation and Support	Assess and treat side effects during cancer therapy
Psychological Interventions	Cognitive behavioral therapy Mindfulness-based therapy Sex therapy
Non-pharmacologic therapies	Lubricants Moisturizers Vaginal dilators Medical devices Pelvic floor physical therapy
Pharmacologic therapies	Herbal remedies Hormonal preparations SSRI/SNRI Anti-depressants PDE5 inhibitors
Community Referrals	Behavioral health Urologist, menopause provider Sex therapist or sexual health counselor Survivorship program Integrative medicine

Psychological Interventions

- Issues related to grief and loss
- Anxiety and negative patterns of thinking
- Ways to cope with dating and communicating about sexuality and intimacy with current or potential partners
- Relational issues/conflicts that can affect sexuality and intimacy
- Facilitate communication between partners
- Develop relaxation skills useful in achieving more satisfying sexual encounters
- Partner engagement
- Embracing a “new normal”

Behavioral Interventions

- Lifestyle modifications
- Positioning during intercourse
- Kegel exercises
- Pelvic floor PT
- Experimentation and exploration



American Cancer Society: Sex and the Woman with Cancer.
https://www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/fertility-and-sexual-side-effects/sexuality-for-women-with-cancer/problems.html

Medical Interventions for Women

Lubricants

Vaginal Moisturizers

Medications

Vaginal Dilators

Sexual Devices

Menopausal Hormone Therapy (MHT)

- Can be safely used in women with many cancer types:
  - Hematologic
  - Colorectal
  - Cervical
  - Vulvar/vaginal
- Low-dose vaginal estrogen for localized symptoms
- Systemic HT for vasomotor symptoms, bone health, cognition, etc.

Kuhle CL, Kapoor E, Sood R, Thielen JM, Jatoi A, Faubion SS. Menopausal hormone therapy in cancer survivors: A narrative review of the literature. *Maturitas*. 2016;92:86-96.

Special Population: Breast Cancer

Considerations:

- Large prevalence of survivors
- Early-stage breast cancer survivorship is common
- Women are living longer with metastatic disease
- Treatment is multi-modal
- Hormone therapy often contraindicated

Special Population: Breast Cancer

Breast cancer treatment has sexual consequences:

- **Breast surgery**
  - Pain, scarring, altered sensation, asymmetry
  - Breast and reconstruction/flap sites (abdomen, thighs)
  - Lymphedema
  - Difficulty with sexual positioning, flexibility and comfort
  - Body image changes
- **Radiation therapy**
  - Pain, scarring, skin changes
  - Fatigue
- **Chemotherapy**
  - Chemotherapy-induced menopause
  - Side effects, immunosuppression
- **Endocrine therapy**
  - Hormonal side effects (vasomotor symptoms, genitourinary symptoms)
  - Joint pain

Special Population: Breast Cancer

Management of sexual consequences:

- Shared decision-making and patient education
- Psychotherapy and emotional support
- Nutrition support, physical therapy, management of side effects
- Systemic MHT is not recommended
- Non-hormonal therapies for genitourinary symptoms: moisturizers, lubricants, vibrators, vaginal dilators, pelvic floor physical therapy (PT), lidocaine
- Local hormonal therapies for genitourinary symptoms: vaginal estrogen and DHEA are likely safe, but may increase systemic estradiol levels slightly/transiently; vaginal testosterone off-label use is controversial (must discuss with med onc team)
- Vaginal CO2 laser therapy – investigational
- Non-hormonal therapies for systemic symptoms: herbal remedies, SSRIs/SNRIs

Faubion SS, Larkin LC, Stuenkel CA, Bachmann GA, Chism LA, Kagan R, et al. Management of genitourinary syndrome of menopause in women with or at high risk for breast cancer: consensus recommendations from The North American Menopause Society and The International Society for the Study of Women's Sexual Health. Menopause: The Journal of The North American Menopause Society. June 2018. Vol. 25 No. 6, pp. 594-595.

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Liotta M, Escobar PF. Hormone replacement after breast cancer: is it safe? Clin ObstetGynecol 2011;54:1739.

Sokol ER, Karram MM. Use of a novel fractionalCO2 laser for the treatment of genitourinary syndrome of menopause: 1-year outcomes. Menopause 2017;24:810–4.

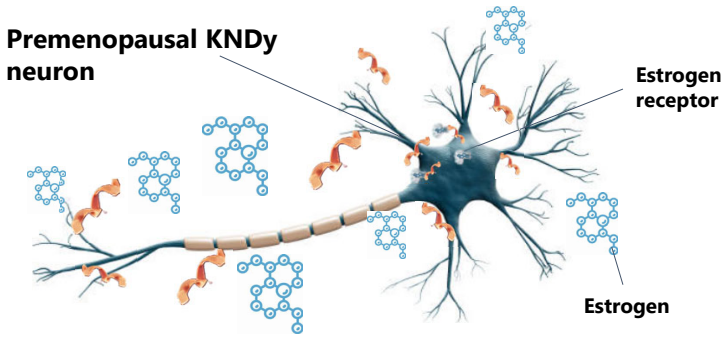
Menopause symptoms
Systemic/Hot flashes
Neurokinin Receptor Antagonists:Therapeutic Rationale

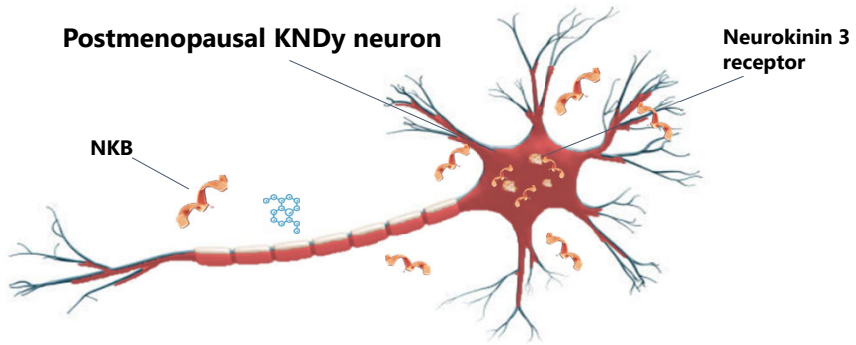
Thermoregulatory Homeostasis

1. KNDy neurons contribute to body temperature control inside the thermoregulatory center in the hypothalamus
2. KNDy neurons are inhibited by estrogen and stimulated by NKB

During the Transition to Menopause

3. Declining estrogen in menopause leads to uninhibited NKB-mediated stimulation of KNDy neurons
4. Heat dissipation effectors are triggered from the thermoregulatory center, experienced as VMS





KNDy, kisspeptin, neurokinin B, dynorphin A; NKB, neurokinin B

Menown SJ and Tello JA. Adv Ther. 2021;38(10):5025-5045. 2. Padilla SL, et al. Cell Rep. 2018;24(2):271-277. 3. Krajewski-Hall SJ, et al. Temperature. 2018;5(1):56-69 Safety of Fezolinetant for Vasomotor Symptoms Associated With Menopause: A Randomized Controlled Trial.Neal-Perry G, Cano A, Lederman S, Nappi RE, Santoro N, Wolfman W, English M, Franklin C, Valluri U, Ottery FD. Obstet Gynecol. 2023 Apr 1;141(4):737-747. doi: 10.1097/AOG.0000000000005114. Epub 2023 Mar 9. PMID: 36897180

A phase 2b, randomized, placebo-controlled, double-blind, dose-ranging study of the neurokinin 3 receptor antagonist fezolinetant for vasomotor symptoms associated with menopause.Fraser GL, Lederman S, Waldbaum A, Kroll R, Santoro N, Lee M, Skillern L, Ramael S. Menopause. 2020 Apr;27(4):382-392. doi: 10.1097/GME.0000000000001510.

Menopause symptoms

Urinary tract symptoms (including pelvic floor disorders)

- Systemic hormone therapy does not improve urinary incontinence and may increase the incidence of stress urinary incontinence.
- Low-dose vaginal estrogen therapy may provide benefit for urinary symptoms, including prevention of recurrent urinary tract infections, overactive bladder, and urge incontinence.
- Hormone therapy does not have FDA approval for any urinary health indication.

Sturdee DW, Panay N; International Menopause Society Writing Group. Recommendations for the management of postmenopausalvaginal atrophy. Climacteric. 2010;13:509–22.

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Melisko ME, Goldman ME, Hwang J, et al. Vaginal Testosterone Cream vs Estradiol Vaginal Ring for Vaginal Dryness or Decreased Libido in Women Receiving Aromatase Inhibitors for Early-Stage Breast Cancer: A Randomized Clinical Trial. JAMA Oncol. 2017;3(3):313–319. doi:10.1001/jamaoncol.2016.3904

Management of genitourinary syndrome of menopause in female cancer patients: a focus on vaginal hormonal therapy. Katie K. Crean-Tate, MD; Stephanie S. Faubion, MD; Holly J. Pederson, MD; Jennifer A. Vencill, PhD, LP; Pelin Batur, MD, NCMP, CCD. https://doi.org/10.1016/j.ajog.2019.08.043

Menopause symptoms
Sexual function

- Both systemic hormone therapy and low-dose vaginal estrogen therapy (ET) increase lubrication, blood flow, and sensation of vaginal tissues.
- Systemic hormone therapy generally does not improve sexual function, sexual interest, arousal, or orgasmic response independent of its effect on genitourinary syndrome of menopause (GSM).
- If sexual function or libido are concerns in women with menopause symptoms, transdermal ET may be preferable over oral ET because of minimal effect on sex hormone-binding globulin and free testosterone levels.
- Low-dose vaginal ET improves sexual function in postmenopausal women with GSM.
- Non-estrogen FDA-approved alternatives for dyspareunia include ospemifene and intravaginal dehydroepiandrosterone.

Carter J, Stabile C, Seidel B, Baser RE, Goldfarb S, Goldfrank DJ. Vaginal and sexual health treatment strategies within a female sexual medicine program for cancer patients and survivors. J Cancer Surviv 2017;11:274–83.

DeSimone M, Spriggs E, Gass JS, Carson SA, Krychman ML, Dizon DS. Sexual dysfunction in female cancer survivors.AmJ Clin Oncol 2014;37:101–6.

Faubion SS, Kuhle CL, Shuster LT, Rocca WA. Long-term health consequences of premature or early menopause and considerations for management. Climacteric 2015;18:483–91.

Graziottin A. Menopause and sexuality:key issues in premature menopause and beyond. Ann N Y Acad Sci 2010;1205: 254–61.

Falk SJ, Dizon DS. Sexual dysfunction in women with cancer. Fertil Steril 2013;100: 916–21.

Conclusions

- For women who initiate hormone therapy more than 10 or 20 years from menopause onset or when aged 60 years or older, the benefit-risk ratio appears less favorable than for younger women because of greater absolute risks of coronary heart disease, stroke, venous thromboembolism, and dementia.

- For genitourinary syndrome of menopause symptoms not relieved with nonhormone therapies, low-dose vaginal estrogen therapy or other government-approved therapies (e.g., vaginal dehydroepiandrosterone or oral ospemifene) are recommended.

Labrie F, Archer DF, Koltun W, et al. Efficacy of intravaginal dehydroepiandrosterone (DHEA) on moderate to severe dyspareunia and vaginal dryness, symptoms of vulvovaginal atrophy, and of the genitourinary syndrome of menopause. Menopause 2018;25:1339–53.

Bygdeman M, Swahn ML. Replens versus dienoestrol cream in the symptomatic treatment of vaginal atrophy in postmenopausal women. Maturitas 1996;23:259–63.

Willhite LA, O'Connell MB. Urogenital atrophy: prevention and treatment. Pharmacotherapy 2001;21:464–80.

Menopausal symptoms
Special Population: Breast Cancer

- Systemic hormone therapy is generally not advised for survivors of breast cancer, although hormone therapy use may be considered in women with severe vasomotor symptoms unresponsive to nonhormone options, with shared decision-making in conjunction with their oncologists. (Level III)

- For survivors of breast cancer with the genitourinary syndrome of menopause, low-dose vaginal estrogen therapy (ET) or dehydroepiandrosterone may be considered in consultation with their oncologists if bothersome symptoms persist after a trial of nonhormone therapy. There is increased concern with low-dose vaginal ET for women on aromatase inhibitors. (Level III)

- Regular breast cancer surveillance is advised for all postmenopausal women per current breast cancer screening guidelines, including those who use hormone therapy. (Level I)

Raggio GA, Butryn ML, Arigo D, Mikorski R, Palmer SC. Prevalence and correlates of sexual morbidity in long-term breast cancer survivors. Psychol Health 2014;29:632–50.
Ponzone R, Biglia N, Jacomuzzi ME, Maggiorotto F, Mariani L, Sismondi P. Vaginal oestrogen therapy after breast cancer: is it safe? Eur J Cancer 2005;41:2673–81.
O'Meara ES, Rossing MA, Daling JR, Elmore JG, Barlow WE, Weiss NS. Hormone replacement therapy after a diagnosis of breastcancer in relation to recurrence and mortality. J Natl Cancer Inst 2001;93:754–62.
Le Ray I, Dell'Aniello S, Bonnetain F, Azoulay L, Suissa S. Local estrogen therapy and risk of breast cancer recurrence among hormone-treated patients: a nested Case control study. Breast Cancer Res Treat 2012;135:603–9.
Kwan K, Ward C, Marsden J. Is there a role or hormone replacement therapy after breast cancer? J Br Menopause Soc 2005;11:140–4

Vaginal Estrogens in Breast Cancer Survivors

- 49,237 Females 40-79yo with newly diagnosed breast cancer in Scotland (2010-2017) and Wales (2000-2016) who were followed until 2020 for breast cancer-specific mortality.
- “In vaginal estrogen therapy users compared with HRT nonusers, there was no evidence of higher risk of breast cancer-specific mortality in the pooled fully adjusted model (HR, 0.77; 95% CI, 0.63-0.94).”
- Conclusion: “Results of this study showed no evidence of increased early breast cancer-specific mortality in patients who used vaginal estrogen therapy compared with patients who did not use HRT. This finding may provide some reassurance to prescribing clinicians and support the guidelines suggesting that vaginal estrogen therapy can be considered in patients with breast cancer and genitourinary symptoms.”

McVicker L, Labeit AM, Coupland CAC, Hughes C, McMenamin U, McIntosh SA, Murchie P, Cardwell CR. Vaginal Estrogen Therapy Use and Survival in Females With Breast Cancer. JAMA Oncol. 2024 Jan 1;10 (1): 103-108. doi: 10.1001/jamaoncol.2023.4508. PMID: 37917089; PMC10623297.

Special Population: The Single Patient

Considerations:

- Lack of support system/caregiver
- Fear of rejection
- Dating and disclosure
- Fear of sex with a new partner (sexual function, embarrassment)
- Fertility and family planning concerns
- Self-esteem and body image
- Feeling of being “damaged”
- Shifting priorities
- Life expectancy

Special Population: Previvors

Considerations:

- Young, otherwise healthy patients
- Emotional challenge of decision-making
- Survivor's guilt
- Surgical menopause → abrupt hormone changes
- Unable to care for young children during recovery

Alexandre M, Black J, Whicker M, Minkin MJ, Ratner E. The management of sexuality, intimacy, and menopause symptoms (SIMS) after prophylactic bilateral salpingo-oophorectomy: How to maintain sexual health in "previvors". *Maturitas*. 2017. 105; 46-51.

Summary

- Asking about intimacy is guideline-driven
- Cancer diagnosis and treatment can have lasting impacts on sexuality
- Symptoms are multifactorial:
  - Anatomic changes
  - Hormonal changes
  - Emotional changes
- Approach to treatment has to be multifactorial
- Education and symptom acknowledgement are of most importance
- It can get better!
- Many resources available for patients and providers

Resources for Patients

- American Cancer Society

  www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/fertility-and-sexual-side-effects/sexuality-for-women-with-cancer.html

  https://www.cancer.org/treatment/treatments-and-side- effects/physical-side-effects/fertility-and-sexual-side-effects/sexuality-for-men-with-cancer.html

- The Scientific Network on Female Sexual Health and Cancer (www.cancersexnetwork.org)
- American Association of Sexuality Educators, Counselors and Therapists (www.aasect.org)
- North American Menopause Society www.menopause.org/
- Foundation for Women's Cancer www.wcn.org/
- BreastCancer.org www.breastcancer.org/tips/intimacy

National Comprehensive Cancer Network®

NCCN Member Institutions

Who We Are

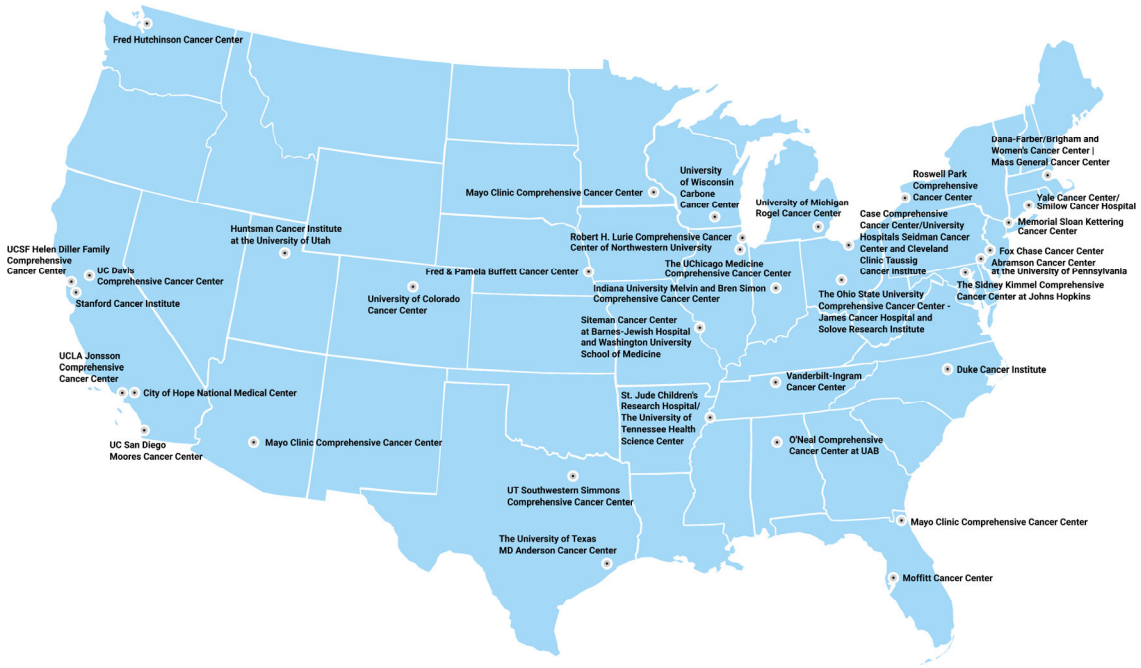
An alliance of leading cancer centers devoted to patient care, research, and education

Our Mission

To improve and facilitate quality, effective, equitable, and accessible cancer care so all patients can live better lives

Our Vision

To define and advance high-quality, high-value, patient-centered cancer care globally



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