

Sexual Health in Female Cancer Survivors

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knowledge changing life



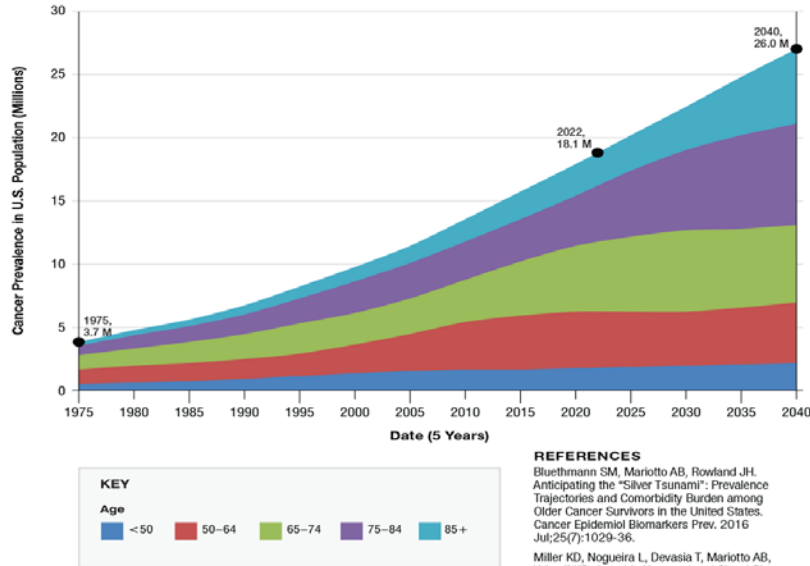
Objectives

1. Scope of the sexual health problem in cancer survivors
2. Barriers to treatment
3. Screening tools
4. Effects of cancer treatment on sexual health
5. Interventions
6. Case reports
7. Importance of communication and cooperation

What is the scope?

Survivorship matters

Cancer prevalence and projections in
U.S. Population from 1975-2040



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Bluthmann SM, Mariotto AB, Rowland JH. Anticipating the "Silver Tsunami": Prevalence Trajectories and Comorbidity Burden among Older Cancer Survivors in the United States. *Cancer Epidemiol Biomarkers Prev*. 2016 Jul;25(7):1029-36.

Miller KD, Nogueira L, Devasia T, Mariotto AB, Yabroff KR, Jemal A, Kramer J and Siegel RL. Cancer Treatment and Survivorship Statistics. *CA A Cancer J Clin*. 2022.

- As of January 2022, there are 4.1 million women living with breast cancer in the USA.
- Since 2004, the incidence of invasive breast cancer is slowly rising by 0.5% per year.

Scope of the Problem

- Cancer treatment can affect Sexual Health in many different ways
- Sexual dysfunction is one of the most common long-term side effects of cancer treatment ⁽⁴⁾
- Sexual dysfunction usually does not self-resolved ⁽³⁾
- Sexual Health problems tend to worsen if not addressed ⁽²⁾



For example:

- **Surgery:** loss of body parts or body integrity
- **Radiation therapy:** Loss of skin sensitivity, lymphedema
- **Chemotherapy:** Fatigue, Neuropathy, Ovarian suppression
- **Hormonal therapy:** Loss of libido, menopausal symptoms

Scope of the Problem

- Prevalence of sexual dysfunction in the USA is approximately **40%**.
- It can rise to **90%** in gynecological cancer survivors and affects **50-80%** of prostate cancer survivors. (7,8,9)
- In the AYA population, **52%** of female survivors and **32%** of male survivors are reporting sexual dysfunction (6)
- **25%** of female survivors of hematopoietic stem cell transplantation report cGVHD changes at the vulva/vagina (10)
- Among patients with advanced cancer, **57%** of women and **68%** of men rated sexual quality of life as an important factor (11)

90% of cancer survivors report that their sexual health concerns were insufficiently addressed (12)

Scope of the Problem

VICAN study: 5 years after cancer diagnosis

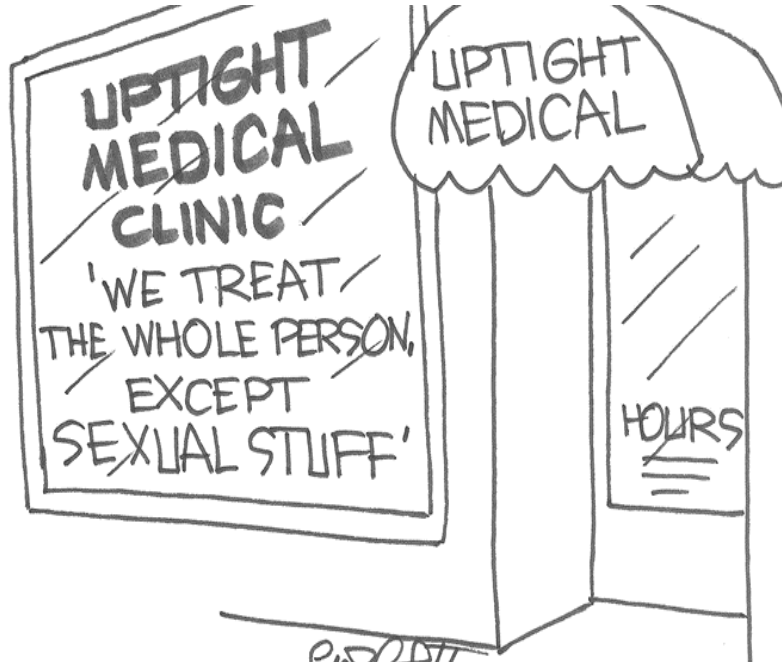
- **30.8%** severe deterioration of sexual health,
- **26.5%** moderate,
- **31.5%** weak,
- **11.5%** stable sexual health ⁽¹³⁾

Cohort study on premenopausal BCS

- **52%** reported having at least 2 sexual functions problems
- 5 and 10 years after breast cancer diagnosis sexual dysfunction remained significant in **26%** and **19%** ⁽¹⁴⁾

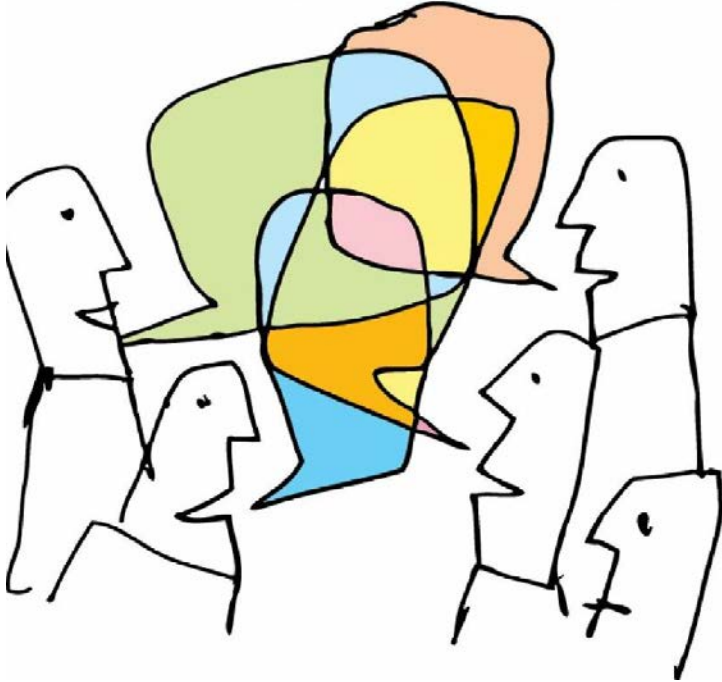
What are the barriers?

Barriers for Providers



- Lack of appropriate training
- Embarrassment
- Time pressure
- Knowledge about treatment options
- Lack of insurance coverage
- Scarcity of resources

Barriers for Patients

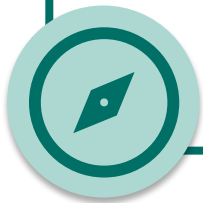


- Embarrassment
- Other symptoms are easier to describe and mention
- Feeling rushed
- Gender, culture, age of provider
- Misconception: If the provider is not talking about sexual health, there might not be any treatment and symptoms need to be accepted and endured ⁽¹²⁾

Guidelines

NCCN guidelines

- There should be a provider-initiated discussion about sexual concerns
- Sexual Health concerns should be evaluated prior to, during, and after treatment



ASCO guidelines from 2017

- Psychosocial and/or psychosexual counseling should be offered to all patients with cancer
- Medical and treatable contributing factors should be identified and addressed first

How to screen?

Screening Question

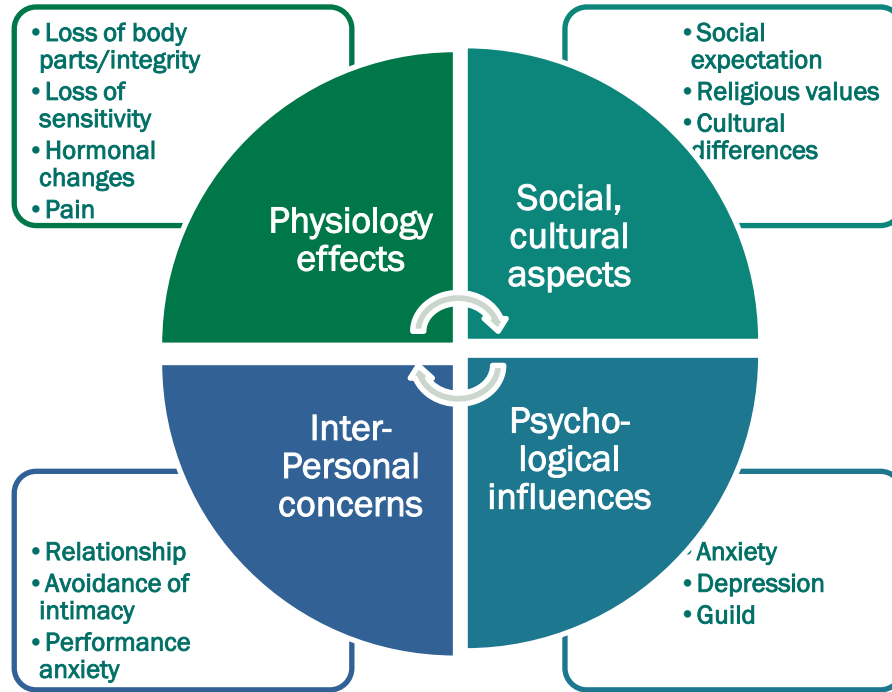


Screening Tools

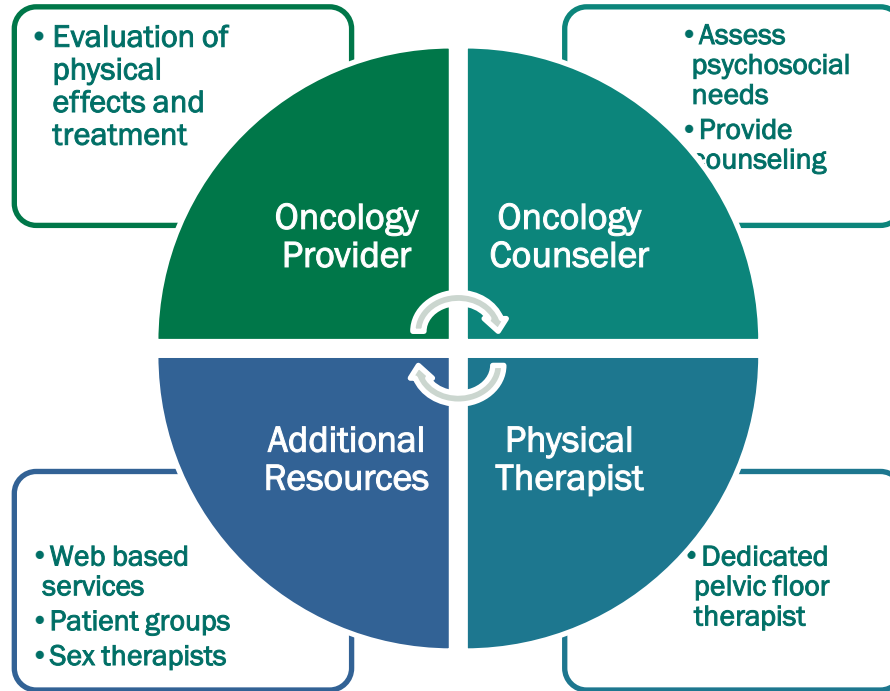
- Screening tools should be comprehensive in order to screen for all domains of sexual dysfunction according to DSM-5.
 - Desire, Arousal, Orgasm, Pain, Distress
- A review from 2013 mentioned 3 most comprehensive screening tools in breast cancer patients ⁽¹⁵⁾
 - Arizona Sexual Experience scale (ASES): 5 items
 - Female Sexual Function Index (FSFI): 19 items (reflects upon sexual activity over last month)
 - Sexual Problem Scale (SPS): 9 items
- There are many other screening tests as sexual questionnaires in QOL measures ⁽³³⁾

Effects of Cancer Treatment

Sexual Health Dysfunction is Multifactorial

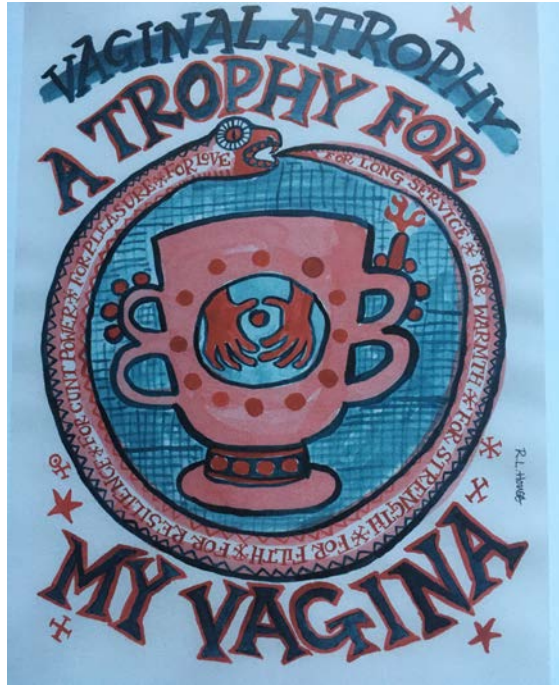


Multidisciplinary Team



GSM (Assessment and Treatment)

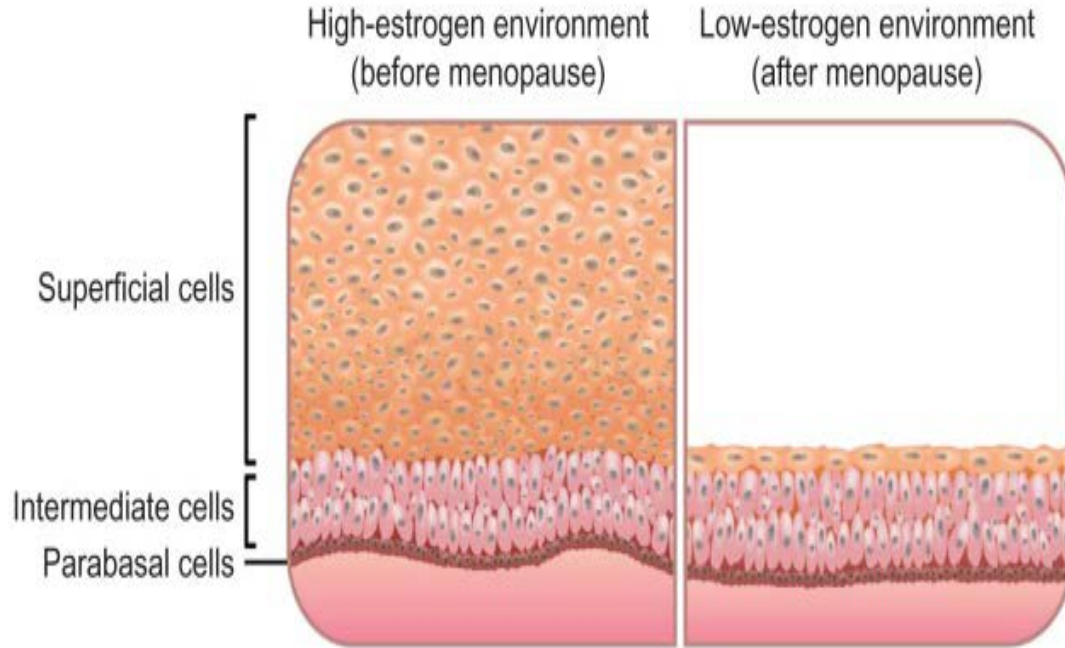
Genitourinary Symptoms of Menopause (GSM)



Lack of estrogen leads to:

- pH changes in the vagina
- Loss of elasticity
- Reduced blood supply
- Thinning of the vaginal mucosa
- Petechial bleeding in the mucosa
- Subjective symptoms:
 - Dryness,
 - Burning,
 - Dyspareunia,
 - Itching,
 - Bleeding (16,19)

Assessment of GSM



- Vaginal maturation index/Vaginal atrophy score (VAS):
 - pH
 - elasticity
 - moisture
 - wall thickness
 - epithelial integrity
- Most bothersome symptom (16)

Non-Hormonal Treatment Options for GSM

- Vaginal lubricants (variety of products: water, oil, latex-based)
- Vaginal moisturizers (variety of products, e.g., coconut oil, Hyaluronic acid, Vit E vaginal sup.)
- Physical therapy (increase of control of pelvic muscle and relaxation, increase in blood flow)
- Vaginal dilator therapy: massages of painful areas, increase elasticity, relaxation training
- Aqueous 4% lidocaine prior to penetration ⁽¹⁶⁾

CO2 Laser Treatment for GSM

Causing micro-abrasions in vaginal mucosa to stimulate new blood vessels and collagen increase

3-4 treatments every 4-6 weeks, maintenance yearly, side effects are dryness and burning

Potential constraints:

- FDA approved but not covered by insurance. Initial treatment is around \$1800, maintenance around \$500
- Paucity of long-term data and safety

Sham procedure: showed benefit of treatment over placebo ⁽¹⁷⁾

VeLVET trial: comparing local estrogen to CO2 treatment: no difference in effect on GSM, urinary and sexual function ⁽¹⁸⁾

Pelvic Floor Muscle Therapy (PFMT) for GSM

PFMT can increase blood flow to the vagina/vulva area, improve relaxation and strength of PFM and vulvovaginal elasticity (20)

- Feasibility trial of PFMT in gynecological cancer survivors showed a high acceptance rate of treatment and 90% of patients reported improved outcome (21)
- Meta-analysis of 5 RCT and 2 retrospective cohort studies showed moderate level evidence that PFMT was beneficial for sexual function in gynecological cancer survivors (22)

Hormonal Treatment of GSM

Local Hormonal Treatment for GSM

- Most local estrogen preparation will not lead to increased postmenopausal levels of estrogen (<20 pg/ml)
- Multiple studies demonstrated no increased risk of developing breast or endometrial cancer in non-breast cancer patients
- The exact threshold of “safe” estrogen levels in breast cancer survivors is not known ⁽¹⁶⁾
- ACOG recommendations for local estrogen:
 - The decision should be based on the risk of recurrence, HR type, and severity of GSM symptoms,
 - Non-hormonal approaches should be used first
 - Should be considered in conjunction with the oncologist

NAMS and ISSWSH Recommendations

Factors to consider prior to prescribing vaginal hormones in breast cancer patients

	More desirable candidates	Less desirable candidates
Stage of disease	Stage 0—2, or metastatic with limited life expectancy	Stage 3, or metastatic with extended life expectancy
Grade of disease	Low—intermediate grade	High grade
Lymph node involvement	No	Yes
Hormone receptor status	Negative	Positive
Endocrine therapy	Tamoxifen	Aromatase inhibitors
Risk of recurrence	Low	High
Time since diagnosis	Remote	Recent
Symptom severity	Severe	Mild
Nonhormone therapies	Failed	Effective
Effect on quality of life	Severe	Mild

Adapted from NAMS/ISSWSH Consensus Recommendations.²⁴

Local Estrogen Therapy for GSM

4 µg estradiol preparations
(Imvexxy)

*Daily for 2 weeks, then
twice weekly*

7.5 µg estradiol ring (Estring)

1 ring every 3 months

10 µg tablets (creams can differ
more in dosage) (Vagifem)

*Daily for 2 weeks, then
twice weekly*

Local DHEA Therapy for GSM

- Goal of Aromatase Inhibitor (AI) treatment is to keep estradiol levels at a minimum. Even local estrogen could affect this goal.
- Vaginal DHEA preparations showed low levels of estradiol/estrone levels, well in the postmenopausal range of <5 pg/ml
- In women on AI therapy no change in estrogen levels was observed
- Testosterone levels increased slightly, androgen effect on breast cancer cells is controversial but could be protective
- Prasterone (Intrarosa) daily inserts (preferred therapy on AI) (off label for estrogen sensitive cancers) ⁽²⁵⁾

Local Testosterone Therapy

- Testosterone is used for GSM due to the richness of testosterone receptors in the vagina/vulva
- Treatment with compounded testosterone over 12 weeks showed improvement in GSM over placebo
- Few studies showed improvement of GSM in breast cancer patients under AI therapy
- Studies failed to report fully systemic androgen and estradiol levels. Therefore, local testosterone is not recommended for breast cancer survivors ⁽¹⁶⁾

Systemic Hormonal Treatment in BCS

HABITS trial: women 5 years after breast cancer diagnosis and bothersome postmenopausal symptoms were randomized to HRT vs placebo

The trial was stopped early after an HR of 3.3 for breast cancer recurrence over a median follow-up of 2.1 years ⁽²⁵⁾

Summary

Systemic HRT is not recommended for ER+ breast cancer survivors at any time ⁽²⁶⁾

Selective Estrogen Receptor Modulator

Ospemifene

- FDA approved for treatment of GSM in postmenopausal women
- Preclinical studies have shown anti-estrogenic effect on breast cells, but less potent than Tamoxifen or Raloxifene
- Not approved to use in breast cancer survivors or patients with high breast cancer risk
- Side effects: hot flashes and increased thromboembolic risk as other SERMs ⁽²⁷⁾

Psychosocial Effects on Sexual Health



- Decreased Libido
- Changes in body image
- Changes in self-esteem
- Avoidance of intimacy
- Partner communication and expectations
- Depression
- Anxiety ⁽²⁸⁾

FSIAD or HSDD

Female Sexual Interest/Arousal Disorder (FSIAD)

FSIAD affects about 6-13% of women in the age range of 20-70 years

Can increase with surgical or medical-induced menopause ⁽²⁹⁾

Best addressed with a *multi-disciplinary team*



- Cognitive behavior therapy
- Mindfulness
- Body awareness exercises
- Medical treatment
- Sex therapy ⁽²⁸⁾

Treatment of FSIAD with Supplements

- During arousal the endothelial Nitric Oxide Synthase (eNOS) is activated, converting Arginine and Citrulline into nitric oxide (NO)
- NO can lead to
 - Vasodilation
 - Increased lubrication
 - Relaxation of smooth muscles
- A systemic review looked at 5 RCT and 2 non-randomized trials with 6 of the seven studies reporting significant improvement in the FSFI
- Typical supplements: ArgininMax, Stronvivo, Ristela, effect after 4 weeks of treatment (30)

Pharmacological Treatment of FSIAD

Pharmacological treatment of FSIAD is based on the serotonin inhibitory pathways and dopaminergic/noradrenaline excitatory effects

Flibanserin (Addyi) reduces serotonin inhibition, FDA-approved 2015

- 100 mg daily
- Black box warning of alcohol consumption and hypotension was removed in 2019
- Often cost prohibiting ⁽³¹⁾

Bremelanotide (Vyleesi) is a melanocortin agonist, FDA approved 2020

- Auto-injector 45 min prior to a sexual encounter
- Common side effects nausea (39%), flushing (20%), and headaches (11%)
- No more than 1 dose in 24 h, no more than 8 doses per month ⁽³²⁾

Case Reports

Case Report 1

65 year old woman

- Stage IIA IDC left breast in 2012 , ER/PR +, Her2+, treated with lumpectomy , chemotherapy , RT and adjuvant Trastuzumab and AI therapy. Bilateral mastectomies in 2013
- Second L breast IDC in 2/2022 ER/PR+, Her2- Oncotype 34, wide excision, received TC and RT and now awaiting anti-estrogen therapy
- Throughout the anti-estrogen therapy after her first breast cancer, she suffered from severe vestibulodynia and dyspareunia and could only endure it with a combination of
 - Local estriol cream 0.5mg in a combination of DHEA 3x/week
 - Testosterone cream 2% 3x/week
 - Triple pain cream (Amitriptyline 2%, Gabapentin 6%, Baclofen 2% in the mornings
- She had multiple warnings from her PCP and gynecologist.

Case Report 2

- Transgender man, 38 years old
- Had BSO in 2013, bilateral mastectomies in 2017 and developed a breast cancer on his left chest wall in 2022, pT1b,N0, G3 ER/PR+, Her2-, Androgen receptor-positive
- He was on subcutaneous Testosterone treatment since 2011
- BRCA 1 positive
- Received TC x4 and started on Anastrozole
- What is the risk of Testosterone?

Thank you



Appendix

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Additional Resources

- <http://www.cancersexnetwork.org>
- <http://www.menopause.org>
- <https://www.isswsh.org>
- <https://lgbtcancer.org>
- www.cancercare.org/diagnosis/breast_cancer
- <https://sstarnet.org>

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