

SEXUALITY AND INTIMACY AFTER CANCER

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Lifespan Cancer Institute Rhode Island Hospital • The Miriam Hospital Newport Hospital Delivering health with care?







- Understand the incidence and significance of sexual health in patients diagnosed with cancer
- Understand the relationship between intimacy and intercourse for women and men
- Understand what providers can do to address sexual health issues in their patients with cancer



SEXUAL DYSFUNCTION IS A LONG-TERM ISSUE

- Impacted population:
 >12 million cancer survivors
- Livestrong 2010 Survey (n=3129)
 - Predominantly white (90%) and female (60%)
 - Educated (54% with bachelor's or graduate degree)
 - Majority diagnosed before 40 years
 - Most prevalent- breast, colorectal, lung





THE LIVESTRONG 2010 SURVEY



- Sexual functioning and satisfaction ranked THIRD most frequently reported physical concern
 - Reported as a lot in 29%
 - Reported as a little in 37%
 - Of those reporting, less than half received medical care
- Survivors expressed significant emotional concerns related to sexual health (% rated as a lot/a little):
 - Sadness and depression (9/36)
 - Personal appearance (14/39)
 - Stigma (6/31)
 - Personal relationships (15/56)



SEX IS NOT CONFINED TO PENILE-VAGINAL INTERCOURSE

- Intimacy
- Sensuality
- Body image
- Arousal
- Desire
- Climax
- Satisfaction





SEXUAL PROBLEMS Sexual health is impacted regardless of cancer type:

INCIDENCE OF

- Across all cancers $\rightarrow 60\%^1$ in women; up to $80\%^2$ in men
 - Breast cancer: up to 90%²
 - Gynaecologic cancer: 78.4%¹
 - Non-Hodgkins Lymphoma (Up to 64% in women, 49% in men)³
 - Prostate cancer (40-82% with localised disease)^{4,5}
 - Rectal cancer
 (70-80%⁶ in men; 30-45%⁷ in women)
 - HSCT recipients (51% in men, 66% in women)⁸

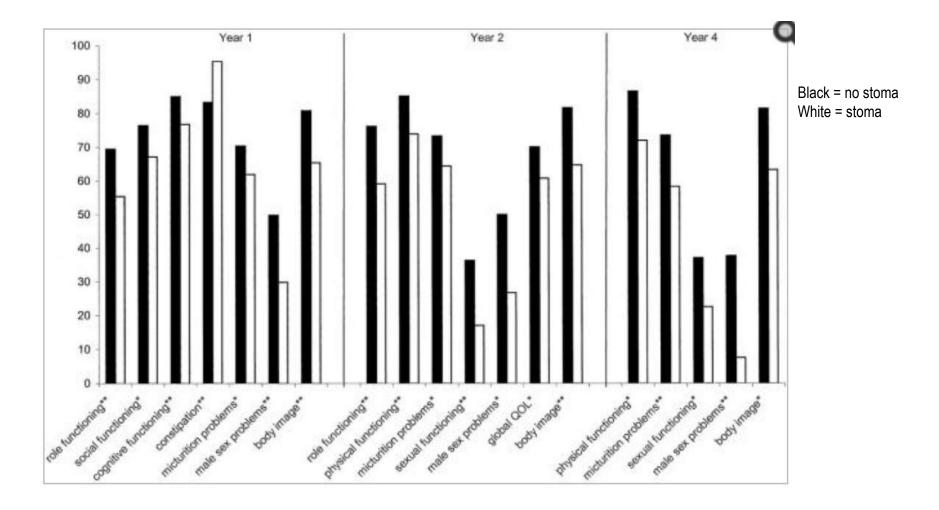
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SPECIAL ISSUES: STOMAS





SPECIAL ISSUES: MUCOSAL GVHD



- Common complication after transplantation
- Seen acutely, but can be a chronic issue
 - For women¹:
 - Impacts 25 to 49% of women after allo transplant
 - Median onset 7-10 months, but can develop much later
 - Must do a pelvic exam to diagnose!
 - For men²:
 - Genital skin changes reported by at least 20% when asked
 - Erectile dysfunction present in 65%
 - Sexual discontent reported by 60%



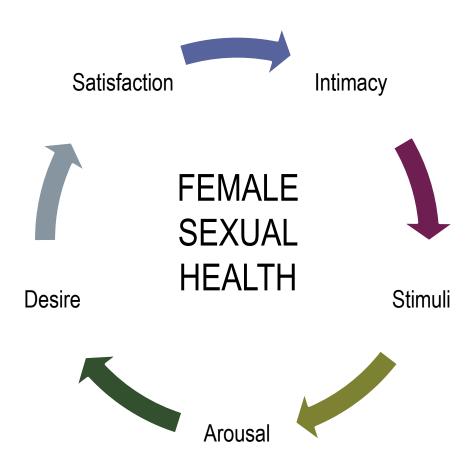
FEMALE SEXUAL HEALTH AFTER CANCER





BASSON MODEL OF FEMALE SEXUAL HEALTH







BREAST SPECIFIC SENSUALITY

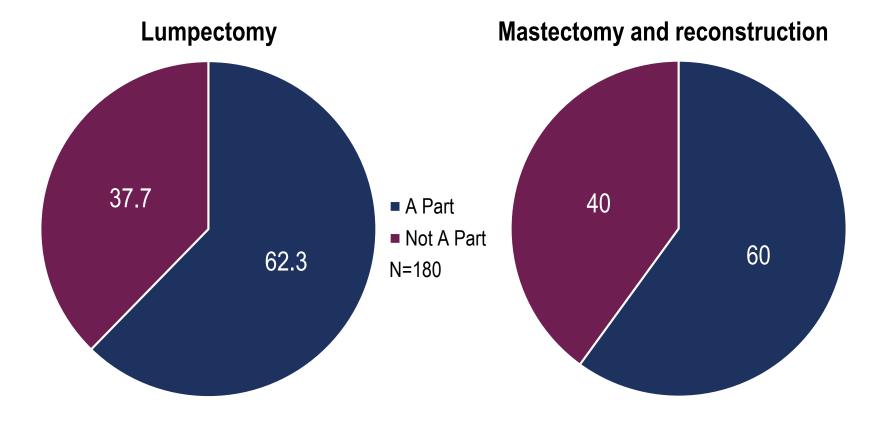


	BCS	MRM	MRM with Recon
Before surgery, chest play was part of my sexuality (n=262)	83%	95%	93%
Chest play is a part of my sexuality after surgery (n= 253)	74%	47%	77%
I am satisfied with my surgical outcome	80%	48%	67%



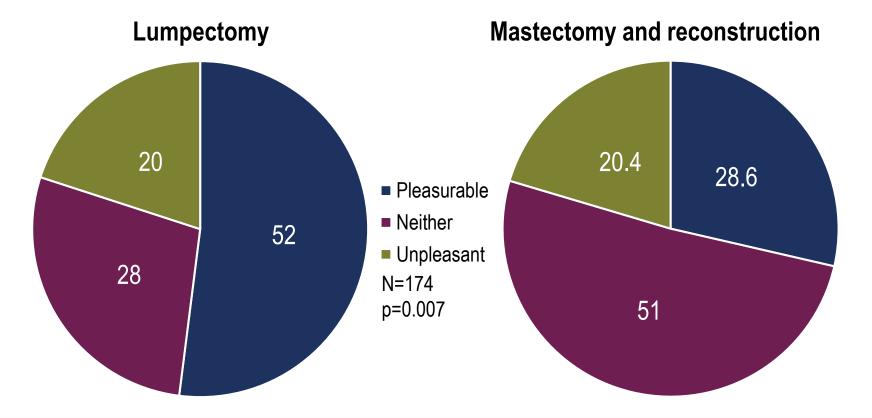
BREAST SPECIFIC SENSUALITY







BREAST SPECIFIC SENSUALITY





APPROACH TO TREATMENT



- Vaginal Health
 - Address Genitourinary Symptoms of Menopause (GSM)
 - Vulvar and vaginal moisturisers
 - Vaginal laser therapy
 - Hormonal treatment
- Sexual Health
 - Address ways to make sexual activities more pleasurable
 - Lubricants, Lidocaine, Dilators
 - Address desire



TREATMENT FOR GSM





NON-HORMONAL THERAPY: VAGINAL MOISTURISERS



- Part of routine gynaecologic health
- Benefit for sexual comfort
- Many types:
 - Polycarbophil-based
 - Loprinzi, 1997¹: RCT *vs.* placebo → Significant improvement in dyspareunia in 60% (40% with placebo)
 - Vitamin E
 - Natural oils (coconut, olive)
 - Apply externally only
 - Parabens free²



NON-HORMONAL THERAPY: VAGINAL LASER THERAPY



- Fractional microablative CO2 laser therapy x3
- Salvatore, et al.:
 - Patients: 77 postmenopausal women with vulvovaginal atrophy (VVA)
 - Intervention: 3 treatments over 12 weeks
 - Comparator: None
 - Outcomes with treatment compared to baseline:
 - Significant improvement in function at 12 weeks (measured by FSFI)
 - 17 of 20 women regained a normal sexual life at 12 weeks
 - Significant improvement in physical and mental domains in quality of life (measured using SF-12)



VAGINAL LASER THERAPY AFTER BREAST CANCER



- Pieralli A, *et al.*, 2016:
 - Patients: 50 women with dyspareunia associated with an oncologic menopause
 - Intervention: CO2 laser therapy
 - Comparator: None
 - Outcomes:
 - Significant improvement in dyspareunia (by Visual Analogue Scale)
 - Significant improvement in vulvovaginal atrophic symptoms (by Vaginal Health Index)
 - Satisfaction persisted at 11 months follow-up for 52% of patients
- Promising technology
 - No randomised trials
 - No data for women on ongoing anti-oestrogen therapy

HORMONE THERAPY AFTER CANCER



- Vaginal oestrogen appears to be safe, especially if not breast cancer
 - Multiple small studies
 - RE: BREAST CANCER: No **association** between vaginal oestrogen and outcomes
 - LeRay, 2012: Women who relapsed (n=917) vs. Women who remained without evidence of disease (n=8885)
 - Concomitant vaginal oestrogen and Endocrine tx: RR 0.78, 95% CI 0.48-1.25
 - Sequential: RR 0.97, 95% CI 0.22-4.18



ACOG CLINICAL OPINION



- Nonhormonal approaches are the first-line choices during or after treatment for breast cancer
- For women with ER+ breast cancer experiencing urogenital symptoms, vaginal oestrogen should be reserved for those patients who do not benefit from nonhormonal remedies
 - This decision must be coordinated between the oncologist and other providers
 - It must be preceded by an informed decision-making and consent process
- Data **do not show** an increased risk of cancer recurrence among women currently undergoing treatment for breast cancer or those with a personal history of breast cancer who use vaginal oestrogen to relieve urogenital symptoms



ORAL HT AND CANCER: A SUMMARY



- Oral HT can be given in women with cancer, not considered hormonally driven
 - Routinely done after ovarian, endometrial, cervical cancer
- Oral HT, however, may not be safe after HR+ breast cancer



ORAL HT AND BREAST CANCER



- HABITS (HT after breast cancer: Is it Safe)
 - Design: Open-label RCT
 - Patients: Stage 0-2 breast cancer, <4 nodes involved (n= 497)
 - Tamoxifen adjuvant treatment OK, but not an AI
 - Intervention: HT (2-years)
 - Choice determined by local practice
 - Sequential E-P combination preferred for women with an intact uterus
 - Medium-potency E for women s/p hysterectomy
 - Comparison: Best symptomatic management without hormones

Characteristic	HT arm	Non-HT arm
Patients with follow-up, n	221	221
Follow-up in years, median (range)	4.1 (0.01-7.8)	4.0 (0.2-7.7)
Time in years between primary treatment and randomisation, median (range)	2.1 (0.1-23.2)	2.2 (0.1-26.5)
Age in years, mean (range)	55.6 (42-75)	54.8 (38-74)
Node positive, n (%)	44 (19.7)	42 (18.8)
Hormone receptor positive,n (%)	139 (62.3)	122 (54.5)
Hormone receptor status unknown,n (%)	64 (28.7)	75 (33.5)
Breast preserved,n (%)	127 (57.0)	126 (56.3)
On HT before diagnosis,n (%)	115 (51.6)	115 (51.3)
On adjuvant tamoxifen at randomisation,n (%)	75 (33.6)	75 (33.5)
Follow-up clinic visits for breast cancer, median	6	6



221 women followed according to ITT.218 records checked in 2005/200611 women never exposed to HT

First events of breast cancer:

Local recurrence n=17 Ipsilateral axilla n=1 Contralateral cancer n=11 Distant metastases n=10 Breast cancer death n=0 Total breast cancer events n=39 Death by other causes n=3 221 women followed according to ITT.220 records checked in 2005/200639 women exposed to HT

First events of breast cancer: Local recurrence n=4 Ipsilateral axilla n=1 Contralateral cancer n=4 Distant metastases n=8 Breast cancer death n=0 Total breast cancer events n=17 Death by other causes n=0



ESMO

HR (95%CI) of a new breast cancer event with HT

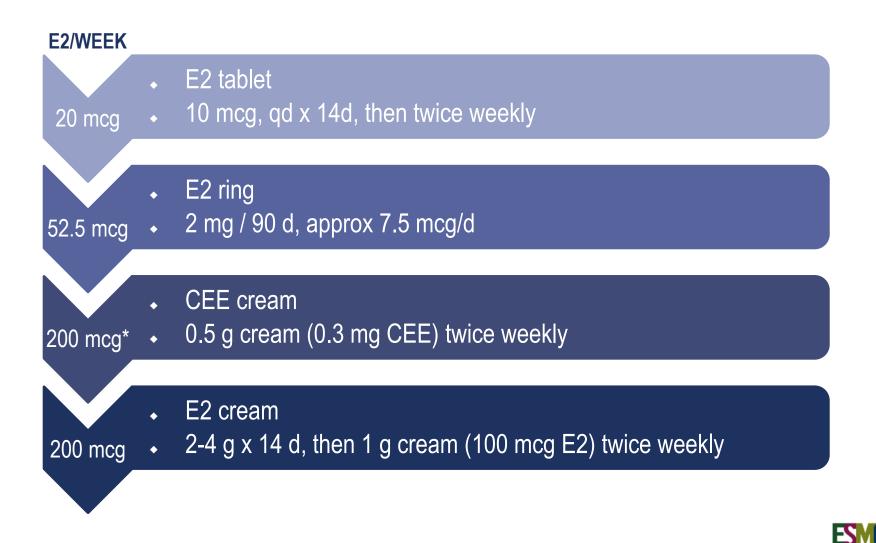
Characteristic	No. of events (No. of women in subset)	HR (95% CI)
All women	56 (442)	2.4 (1.3–4.2)
All women, adjusted	52 (416)	2.2 (1.0–5.1)
Hormone receptor positive	37 (268)	2.6 (1.3–5.4)
Hormone receptor negative	19 (174)	1.8 (0.7–4.8)
Tamoxifen	18 (153)	4.7 (1.4–16.2)
No tamoxifen	38 (289)	1.9 (1.0–3.6)
HT before diagnosis	26 (230)	2.3 (1.0–5.3)
No HT before diagnosis	26 (186)	2.2 (1.0–5.1)
Node negative	30 (282)	2.4 (1.1 –5.4)
Node positive	18 (110)	2.3 (0.8–6.4)



The Bottom Line: For women with breast cancer, compared to no HT, HT (x2y) results in:

- A significantly increased risk of a breast cancer event (HR 2.4, 95%CI 1.3-4.2)
- 5-year cumulative incidence was 22 *versus* 8%
- Significance of risk seems limited to HR+ breast cancer
- Unknown impact on mortality (no deaths recorded)
- Study **underpowered** to assess different preparations of HRT
 - E2 alone compared to continuous combined regimen: HR 1.4 (95%CI 0.55-3.3)

VAGINAL OESTROGEN THERAPY: PREPARATIONS



*0.5 g CEE cream is approximately bioequivalent to 1 g estradiol cream.

WHAT ABOUT...



Ospemifene?

- What is it? A Vaginal SERM
- FDA Indication: The treatment of moderate to severe dyspareunia (secondary to vulvovaginal atrophy)

cancer; therefore, it should not be used in women with known or suspected breast cancer or with a history of breast cancer.



WHAT ABOUT...



Estriol

- Brief-acting oestrogen
- Studies date back to 1987
- Available as 0.005% estriol gel (50 mcg of estriol)
- Typical use: Daily x3 week, then BIW x12
- Cano, 2012: Compared to placebo in postmenopausal women (NO HISTORY of cancer), significantly improved dryness and global symptoms



VAGINAL DEHYDROEPIANDROSTERONE?



- ASCO 2014: Barton DL, et al.
 - RCT (Alliance N10C1)
 - Women with breast or gynaecologic cancer (n=441)
 - Vaginal DHEA (3.25 v 6.5 mg) versus placebo
 - Results:
 - All 3 arms had improvement in symptoms
 - At 12 weeks, DHEA improved sexual satisfaction significantly
 - » Effect size based on FSFI: +0.3-0.6
 - Side effects with DHEA: voice change, headache

TREATING FOR SEXUAL COMFORT





VAGINAL LUBRICANTS



- Two varieties:
 - Water-based
 - Silicone-based
- Limited comparative studies
 - Double-blind trial comparing these in >2400 women¹
 - No difference in pleasure or satisfaction found
 - For penile-anal intercourse: Preference towards water-based lubricant (versus none at all)

NATURAL OILS AS A LUBRICANT?



- Coconut and olive oil commonly used, instead of lubricants
- OVERCOME study (n= 25):
 - Pelvic Floor Relaxation Exercises (by PT at W0, W4)
 - Polycarbophil-based vaginal moisturiser
 - Olive Oil during sex
 - Results:
 - Max benefit = 12 weeks
 - PFR Exercises helpful in 93%, Vaginal moisturiser in 88%, Olive Oil in 73%



TOPICAL LIDOCAINE FOR VESTIBULAR TENDERNESS

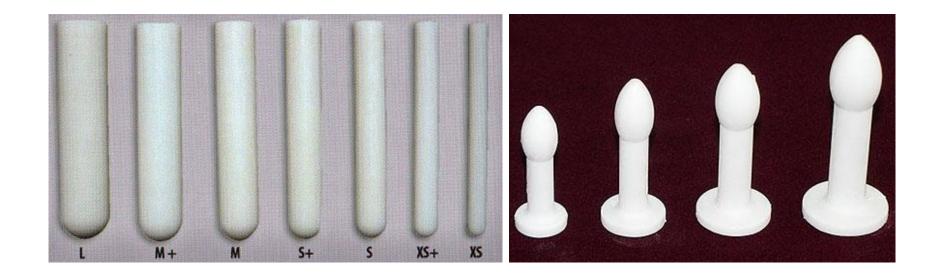


- RCT: 46 breast cancer survivors (median pain with penetration score 8 out of 10)
- Method:
 - Saline or 4% aqueous lidocaine to vulvar vestibule (3m before penetration)
 - 1-month blinded then open-label (all patients) for 2-months
 - Measurement: twice-weekly tampon insertion or intercourse
 - Place on cotton swab, hold at vestibule for 30s
- Results with lidocaine:
 - At one month had less pain (median score 1 vs. 5)
 - After open-label: 90% comfortable penetration
 - 17/20 who were abstinent at entry resumed penetrative intercourse



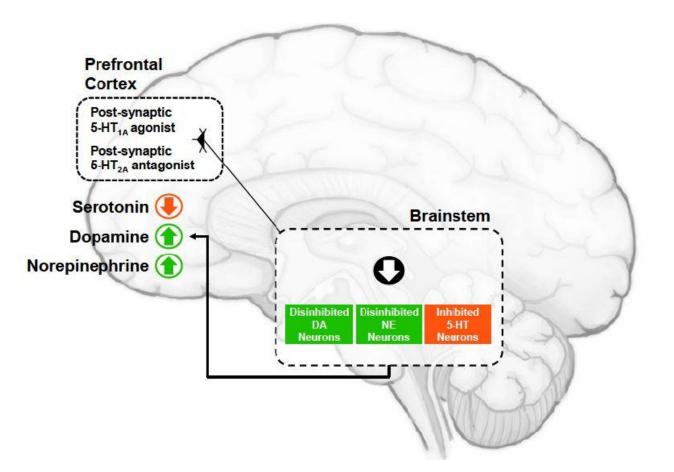
VAGINAL DILATORS FOR VAGINISMUS







FLIBANSERIN FOR DESIRE?



FLIBANSERIN: RESPONDER ANALYSIS



Percent responders in the pivotal Phase 3 studies by anchoring the efficacy endpoints to the Patient Global Impression of Improvement (PGI) – FDA analysis

	Study 71			Study 75*			Study 147		
Endpoints	FLI 100 mg	Placebo	Trt. Diff	FLI 100 mg	Placebo	Trt. Diff	FLI 100 mg	Placebo	Trt. Diff
SSEs (standardised)	41%	29%	12%	43%	33%	10%	44%	34%	10%
FSFI desire domain	55%	40%	15%	54%	40%	14%	58%	48%	10%
FSDS-R Item 13	55%	43%	12%	49%	40%	9%	62%	49%	13%

*Excluded two sites

Flibansering FDA Briefing Document. BRUDAC and DSaRM Advisory Committee. June 4, 2015.

http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM449088.pdf Accessed Jun 2017



PDE-5 INHIBITORS?



- No data in this population
- Women without cancer: No more effective than placebo¹
- Cochrane systematic review in 2007:
 - Only data available for men with ED after prostate cancer
 - Poor quality clinical trials

TESTOSTERONE TO IMPROVE SEXUAL HEALTH?





- Effective in women **without** cancer
 - Postmenopausal women: It improves interest and satisfaction in sex¹
 - Women with HSDD: It is associated with an average increase of 4.4 sexual encounters per 4 weeks²

- OR (benefit): 2.4

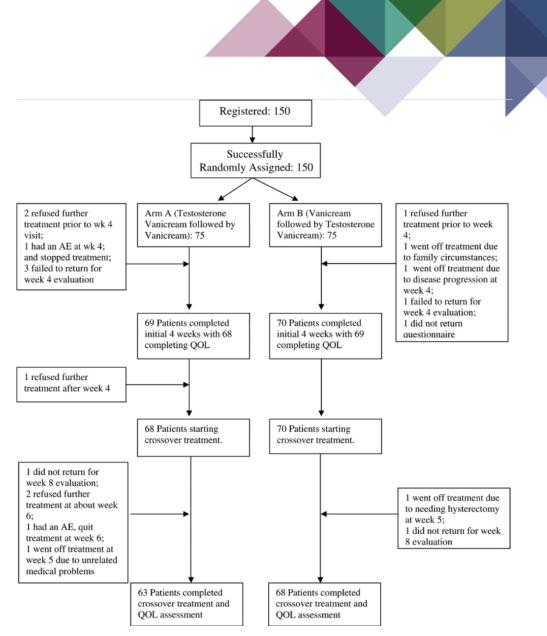
 Women s/p TAH-BSO: It increased frequency of activity (p=0.03) and pleasure-orgasm (p=0.03)³



NC02C3

- Patients: 150 postmenopausal women, NED
- Intervention: 2% testosterone in Vanicream
- Comparator: Vanicream plus placebo
- Outcome: Improvement in sexual desire or libido

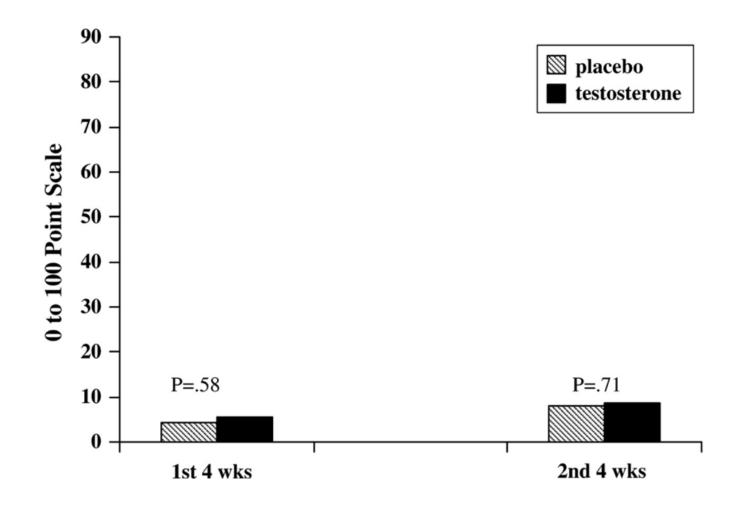
Trial design: Randomised Phase 3 trial with cross-over



FSM

NC02C3







Barton DL, et al., Randomized Controlled Trial to Evaluate Transdermal Testosterone in Female Cancer Survivors With Decreased Libido; North Central Cancer Treatment Group Protocol N02C3J Natl Cancer Inst 2007;99(9):659-61. by permission of Oxford University Press

TESTOSTERONE FOR WOMEN?



- One RCT \rightarrow No benefit when administered as a cream
- In general, not recommended
- Caveats:
 - Cream application doesn't work, but what about other types (e.g., transdermal)
 - Most patients on NC02C3 had breast cancer (generalisability?)



TREATING GENITAL GVHD



• Women:

- Dilator therapy to prevent stenosis
- If erosions/ulcers present \rightarrow Topical steroids
 - Clobetasol propionate 0.05% (once daily at bedtime)
 - If no response \rightarrow Topical cyclosporine or Tacrolimus ointment 0.01%
- No erosions/ulcers (incl. once healed) \rightarrow Topical oestrogen
- For stenosis:
 - Agglutination or scars may require lysing
 - Dilators coated with steroids



MALE SEXUAL HEALTH: MORE THAN ERECTILE DYSFUNCTION





MOST COMMON FORMS OF SEXUAL DYSFUNCTION



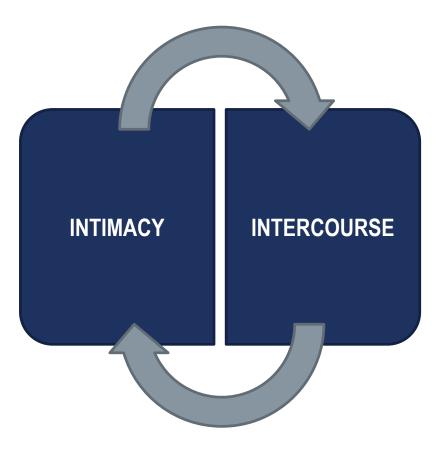
- Erectile dysfunction (ED)
- Others:
 - Sexual bother
 - Orgasm/Ejaculatory disorder
 - Reduction in penile length



MALE SEXUAL HEALTH IS TYPICALLY SIMPLIFIED



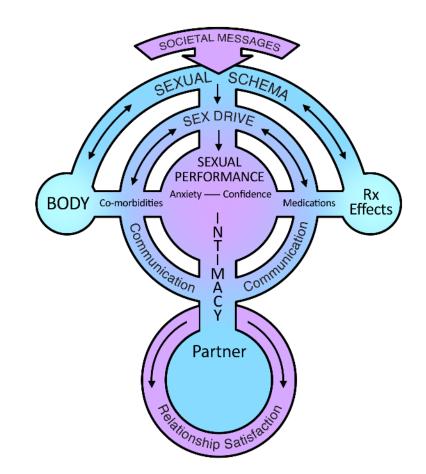
Male sexual health







KATZ-DIZON MODEL FOR MEN AFTER CANCER





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MALE THERAPEUTICS





PDE-5 INHIBITORS FOR ED



- Sildenafil, Tadalafil, Vardenafil
- Most data from men with prostate cancer
- Bottom Line: Compared to placebo, these agents:
 - Are effective after radical prostatectomy with positive benefits in¹:
 - Erectile function
 - Successful vaginal penetration
 - Successful intercourse
 - Have a positive impact after radiation therapy including in²:
 - Erection frequency
 - Firmness of erections
 - Maintenance of erections

PDE-5 INHIBITORS: DOES DOSING MATTER ?



- Tadalafil RCT: 20 mg on-demand vs. 5 mg daily
- Patients: 52 men with prostate cancer treated with RT
- Results:
 - Both treatments effective, no differences seen
 - Positive scores for global efficacy: 86% versus 95% (p=0.27)
 - Daily dosing associated with better compliance (86 versus 100%)
 - Also associated with trend towards fewer side effects

PDE-5 INHIBITORS: DOES TIMING MATTER ?



REACTT trial: 20 mg on-demand vs. 5 mg daily Tadalafil vs. placebo

- Blinded Trial (BT) period \rightarrow 9 months followed by
- Drug Free Washout (DFW) period \rightarrow 6 weeks followed by
- Open-Label treatment (OLT) of 3 months
- Patients: 422 men with prostate cancer treated with nerve-sparing prostatectomy
- Results (On-demand and daily *vs.* placebo)
 - Back to baseline erectile function:
 - End of BT: 11 and 22% vs. 8%
 - Following DFW: No difference
 - After OLT: All arms showed near doubling of "back to baseline" reports
- Take home point: Early initiation helps with treatment-related ED

PDE-5 INHIBITORS: DOES TIMING MATTER ?



- What about if taken prophylactically?
- RTC of sildenafil vs placebo (started 3 days before treatment and then daily for 6 months):
 - Patients: 279 men, localised prostate cancer to undergo RT
 - Outcomes (sildenafil vs. placebo):
 - Mild to no ED at 12 months reported by 73 vs. 50% (p=.024)
 - Functional erections at 24 months: 82 vs. 56% (p=.045)



PILLS ARE NOT ENOUGH



- Include the partner!
- Address expectations
- Exercise the penis: Nightly stretch
- Healthy (Healthier) Lifestyles is important
- Stress Reduction
- Erections are not needed for:
 - Intimacy
 - Orgasm
 - Climax



RELATIONSHIPS SUFFER WHEN MEN HAVE SEXUAL DYSFUNCTION

- For men with prostate cancer, ED is associated with:
 - Withdrawal from partner
 - Overall reduction in intimate encounters
 - Lowered rate of sexual contact
- Why?



FOR MEN WHO DO NOT RESPOND TO PDE5 INHIBITORS:

- Address expectations:
 - Neural injury may take up to 4 years to heal
 - Scarring may be a more permanent issue
- Beyond oral medications:
 - Penile injection therapy (To corpus cavernosum)
 - Intraurethral suppositories
 - Vacuum pumps
 - Penis Prosthetic Devices
 - Any of these need a urological or men's health specialist
- Don't abandon:
 - Re-challenge every 2-3 months



YOUR ROLE IN THE SEXUAL HEALTH OF YOUR PATIENTS



WHY CLINICIANS DON'T TALK ABOUT IT

- We're too busy (you should bring it up)
- You're single
- You're too old
- You have metastatic disease
- You survived cancer!
- I don't want to go there







THE ROLE OF THE CLINICIAN



- Normalise sexual health as a valid concern
 - Take a sexual history
 - Incorporate into the review of systems At initial visit and during all follow-up
 - Refer!



APPROACHING SEXUAL HEALTH

I'd like to review how you are doing as it relates to both sexuality and intimacy. Would that be ok?

Some women complain that sex

and intimacy are different now.

In fact, it's pretty common. How

has your experience been?

Are you (and your partner) having problems being intimate?

PERMISSION

Invites patient to enter into a discussion about sexual health

A common complaint is pain during intercourse. Is this something that is happening with you?

LIMITED INFORMATION

Normalizes that issues related to sexual health are common

If you have some trouble with vaginal dryness, it may help to use a lubricant before and during sex

SPECIFIC SUGGESTIONS

Offer advice that can be actionable and easy to incorporate if possible

It sounds like you might benefit from seeing an expert in sexual health. Can I suggest a referral?

INTENSIVE THERAPY

If one is not comfortable with issues brought up or does not know what to advise, offer expert consultation locally (if possible) or refer to educational resources



EDUCATION IS KEY



- Explore sexual health is a concept beyond intercourse.
- Re-examine what it means to be "sexual"
- Normalise their experience
- Encourage communication between partners

RECOGNISE IN YOURSELF:

- Your own personal comfort zone
- Your own sexual self-schema



EMPHASISE THE TINCTURE OF TIME

- Re-defining sex after cancer is a process
- Pleasure is the goal, not performance
- Sexual homework:
 - Intimacy exercises
 - Communication exercises
 - Mandatory dates
 - Re-introducing sexual activities beyond penetrative intercourse



IT'S NOT ALL ABOUT INTERCOURSE

- Perz J, et al.: Views on sexual satisfaction were highly variable among patients, partners, and their clinicians
 - Clinicians tend to emphasise the importance of performance
 - Patients and partners expressed more nuanced view:
 - Intimacy as important and as satisfying as penetrative intercourse
 - Alternative forms of sexual expression were satisfying
 - Patients and partners want to navigate any physical impediments





- **Communication** side effects, symptoms
- **Consultation** seek help and advice proactively
- **Compromise** e.g., alternatives to intercourse
- **Clarity** define patient's needs in addition to acknowledging his/her partner's



AFTER CANCER...

Everyone deserves a sex life including:

- The young adult
- The older patient
- Patients in relationships
- Patients without a partner
- LGBTQ patients
- Patients with advanced or metastatic disease
- The oncologist







CANCER IS A SOCIAL DISEASE

Your patient with cancer includes his or her partner







QUESTIONS?





THANK YOU!



