The Psychological and Sexual Impact of Androgen Deprivation Therapy on Prostate Cancer Patients and Their Partners: Defining the Problem and Developing Interventions

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General Background

With increased awareness of prostate cancer (PCa) and modern screening, men are increasingly diagnosed and treated for the disease when they are largely asymptomatic. As such, any long term suffering they experience will more likely be from the side effects of the treatments than from the disease itself.

Approximately half of all men who are treated for PCa will be on Androgen Deprivation Therapy (ADT) at some time during their treatment.
Primary indications for ADT

- Neoadjuvant; i.e., short-term before radiation therapy.
- Adjuvant; i.e., long-term with prostatectomy or radiation therapy.
- Biochemical recurrence and metastatic disease.

Prevalence of ADT

~600,000 men in North America are on ADT at any one time. Minimally 40,000 of those men start on long term ADT each year.

Despite moves toward active surveillance and intermittent ADT use, leading to a slight decline in ADT use overall (Krahn et al. 2011), earlier detection results in PCa patients starting on ADT at a younger average age than in previous years. Some PCa patients may now be on ADT for 20+ years.

Krahn M. et al. 2011 Androgen deprivation therapy in prostate cancer: are rising concerns leading to falling use? BJU Int. 2011 [Epub ahead of print]
Learning Objectives

1. To know what are the common psychological and social side effects of ADT when used to treat prostate cancer.

2. To know the various interventions that can mitigate the psychological impact of ADT on prostate cancer patients—including ways to help prostate cancer couples maintain intimacy and a strong dyad in the face of reduced libido.

3. To understand the roles (and needs) of the partners of prostate cancer patients on ADT and why caring for the partners can benefit the patients.

Common forms of ADT in Canada

1. *Chemical Castration*
   - estrogen (oral and parenteral forms)
   - luteinizing hormone releasing hormone agonist (LH-RHa); e.g., leuprolide, goserelin
   - anti-androgen monotherapy; e.g., flutamide, bicalutimide.

2. *Orchidectomy*

3. *Combined Androgen Blockade* in various forms; e.g., leuprolide & bicalutimide

Long term ADT = “castration” although it is typically euphemized to “hormonal therapy”.
Hormonal therapy

- Both MDs and patients tend to avoid the word “castration” because of the stigma associated with that term.

- In North America, Europe, Australia, Japan, ADT is usually in the form of depot injections of an LH-RH agonist (e.g., Zoladex, Eligard, Lupron).

- These are expensive drugs, with an increasingly long list of side effects that can affect the quality of life and/or survival of prostate cancer patients, such as…

<table>
<thead>
<tr>
<th>Side Effects</th>
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<tbody>
<tr>
<td>Erectile dysfunction</td>
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<td>Osteoporosis</td>
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<td>Hot flashes</td>
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<td>Loss of sexual interest</td>
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<td>Genital shrinkage</td>
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<td>Gynecomastia</td>
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<td>Impaired memory and attention</td>
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<td>Weight gain/body fat redistribution</td>
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<td>Loss of muscle mass</td>
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<td>Anemia</td>
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<td>- cardiovascular disease</td>
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<tr>
<td>Increased emotionality and tearfulness</td>
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<td>Distress at loss of identifiers of masculinity (e.g., loss of body hair)</td>
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Psychosocial side effects of ADT

Side effects identified as particularly challenging—as summarized in Elliott et al. 2010—are:

1. body feminization
2. changes in sexual performance
3. cognitive and affective symptoms
4. relationship changes
5. fatigue, sleep disturbance, and depression.


1. feminization of the body

• Loss of body hair
• Loss of muscle mass (~4%)
• Increase in weight (~10%) largely as cutaneous body fat in the abdomen and thighs
• Some gynecomastia (and mastalgia) depending on the drugs used

Altered or reduced body odour? Likely… and could have serious social/sexual implications, but remains completely uninvestigated.
On alopecia and gynecomastia…

Patients vary greatly on how they interpret such physical side effects. Indeed...

…it is often assumed that hair loss is a trivial matter of little consequence, but that gynecomastia may be devastating. However, it can be the other way around. Patients are often more bothered by the physical discomfort of mastalgia than the cosmetic issue of gynecomastia.

I know of no validated questionnaire or survey instrument that can be used to predict who will find such bodily changes most and least distressing.

2. sexual side effects

With long term ADT there is:

• Testicular and penile shrinkage
• Impotence (in >80%)
• Reduced libido (in >80%)

More than 50% of men treated for localized prostate cancer by surgery, radiation therapy, or brachytherapy have residual erectile dysfunction (ED). Only about 1/3 find Viagra or other phosphodiesterase inhibitors (PDE-5i) fully effective.

The low libido issue is discussed more below.
3. cognitive and affective symptoms

Depression—commonly reported, but not well documented in controlled studies; hard to separate from the grief of having failed primary treatment.

Cognitive effects—“verbal memory…[is]…significantly worse in patients on ADT” (Beer et al., 2006). As an aside, there is evidence that this can be reduced or reversed with transdermal estradiol, but this has not yet been replicated in larger studies.

Note: there is some evidence that the intensity of both side effects may be in part age dependent.

Other psychological changes are not so rigorously defined.

ADT and depression

Depression is often associated with low testosterone. In PCa patients it may be linked as well to anxiety associated with disease progression.

DiBlasio et al. reported “a three-fold increase…between rates of pre-ADT psychiatric illness and development of de novo illness [after starting ADT]” (9% vs. 29%). Most common was depression, reported in 56% of those patients.

More on cognition and mood…

“Significant changes in self-rated mood such as increased depression, tension, anxiety, fatigue and irritability were evident during [ADT] treatment.”

ADT “…may result in some adverse changes in cognition and mood. However, many but not all [my emphasis] of these changes can return to baseline after cessation of ADT.”


More on cognitive effects of ADT

“ADT patients evidenced a significant decline in spatial reasoning, spatial abilities and working memory during treatment… compared with baseline.”

*Both physicians and patients (plus their partners) should be aware of how this may manifest itself in everyday life.*

The bottom line on cognitive decline:

“Between 47% and 69% of men on ADT … [experience a decline]… in at least one cognitive area, most commonly in visuospatial abilities and executive functioning.” ADT “is linked to subtle but significant cognitive declines in men with prostate cancer.”

“The authors believe that clinicians should… inform and monitor patients for this possible side effect of treatment.”


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Emotionality

- Changes in emotionality have been repeatedly reported for androgen-deprived prostate cancer patients (as well as male-to-female transsexuals) …most conspicuously as an increase in tearfulness.

- In our society women may cry, but “real men don’t cry.”

- Increased tearfulness can thus be embarrassing to men on ADT.
The American Cancer Society claims that…
“Men who no longer have their testicles or who are on hormone therapy drugs often feel like ‘less of a man.’ This is a myth. Manhood does not depend on hormones, but on a lifetime of being male.”

From: Sexuality and Cancer: For the man who has cancer and his partner. American Cancer Society, 2009.

This presumption, that the male gender is first socially constructed and then invariable, sounds reassuring. However…

… many studies have shown that the psychological consequences of impotence alone are severe and exacerbated by the common male response to illness and disease—to suffer stoically and silently. Additional cognitive, affective, depressive, and emasculating side effects of ADT don’t help.

Overall, ADT typically leaves patients impotent and depressed…and, as shown in many studies in the last two decades, with seriously reduced quality of life.
ADT often challenges men’s core identity, leaving many…feeling like they are at the border of masculinity: not fully masculine nor feminine, but undefined; i.e. in a liminal gender space (Navon & Morag, 2004).


“Whenever I saw my body, I wondered, ‘Who am I? A woman? A man? It’s a very confusing situation. I believe I’m neither one thing nor another; that’s the only way I can think about myself without becoming confused. To tell the truth, at first, every time I looked at myself [in the mirror] I became depressed.”

Navon L & A Morag (2003) Advanced prostate cancer patients’ ways of coping with the hormonal therapy’s effect on body sexuality and spousal ties. Qualitative Health Research, 13:1378-1392.

Similar quotes from prostate cancer patients’ reactions to ADT can be found in six qualitative studies published by research groups in the last eight years…from Israel, Australia, England, USA and Canada.
4. relationship changes

Faced with such changes in their lives, many men:

→ withdraw their affection from, and physical contact with, their partners.
→ are embarrassed by the changes they’ve experienced and are reluctant to discuss them with their partners.

… which leads to depression & frustration in their partners.

**Cost to the partner**

Studies going back to 1994 show that the psychological distress on the partners of prostate cancer patients is even greater than that on the patients themselves. Withdrawal of intimacy in general—not necessarily loss of coital sex—seems to be the biggest problem.


**The communication problem**

Critical factors explaining a spouse’s greater distress include “the discordance in communication between partners, with the spouse needing to openly discuss disease-related feelings and problems, and the husband needing to minimize the effects of the disease, with little desire to have open discussions about charged issues.”

Loss of intimacy harms both the patient and the partner

Women may “perceive [a] lack of emotional mutuality or reciprocity…[as]…emotional abandonment and their own deficiencies in interpersonal sensitivity, which leads to feelings of isolation and social inadequacy, and thus poorer mental health.”

Distress in the partners correlates with distress in patients. Namely there is “evidence of partner effects, at least for women. That is, women’s distress predict[s] men’s physical health, over and above the men’s distress, …age, and cancer stage.” (Kim et al., 2008)

5. fatigue, sleep disturbance & depression

• Sleep disturbance can be associated with insomnia leading to daytime fatigue. [Anemia doesn’t help.]
• Insomnia itself can result from nocturnal hot flashes.

The trio of symptoms—depression, insomnia and fatigue—are common in many cancer patients. [Insomnia in patients can disturb their partners’ sleep.]

When ADT is administered for disease progression after failed primary treatments, and a curative treatment is no longer an option, psychological distress manifested by this trio is not surprising.
Learning Objectives

Covered so far:
• The common psychological and social side effects of ADT when used to treat prostate cancer.
• The roles (and needs) of the partners of prostate cancer patients on ADT and why caring for the partners can benefit the patients.

Still to cover:
• Interventions that can mitigate the psychological impact of ADT—including ways to help prostate cancer couples maintain intimacy and a strong dyad in the face of reduced libido.

What can be done for these patients and their partners?

Goal: To explore options that go beyond standard treatments for ED, which are too often ineffective or unacceptable for many patients… particularly those on ADT.

• Since the side effects impact both the patients and their partners, addressing these side effects is an issue for couples, not just individual patients.
• Since the physical and psychological side effects interact, they need to be addressed concurrently.
Managing ADT’s psychological side effects

- SSRIs or other anti-depressants plus exercise can help with mood.
- SNRIs, such as Venlafaxine (i.e., Effexor), help with hot flashes.
- The single, best documented intervention for most ADT’s nonsexual side effects is EXERCISE.
- Transdermal estradiol can help with mental acuity plus menopausal symptoms (e.g., hot flashes, osteoporosis, and possibly libido). [However it increases gynecomastia.]

A note on exercise

Nine studies have been published on exercise as an intervention for managing ADT’s side effects. Collectively they show:
- Muscle strength and endurance: positive benefit
- Cardiovascular fitness: mixed results
- Weight control: no benefit
- Fatigue, depression: mostly positive results

Do not advise your patients to exercise to avoid weight gain on ADT; it will do no good. Instead it sets the patients up for failure, which can add to their depression.
But back to the impact of ADT on sexual function and interest…

What do we know?

- ~50% of PCa couples stop using ED treatments within a year, even when the treatment works and the patient is not on ADT. [This affirms that there is more to a good sex life than just erections.]
- Loss of a sex life is the most distressing long term side effect of PCa treatments for patients. Loss of intimacy of both a sexual and nonsexual nature is a loss for both patients and partners.
- Loss of libido is little solace for the distress to a couple caused by ED.
- Approximately half of all couples on ADT experience some erosion of spousal relations!
Depressed libido

- Most men on ADT experience nearly complete loss of sexual interest and the ability to have orgasms.
- ~15% however still report being sexually active at some level—and are capable of having orgasms even without erections.

So who are these sexually active men?
- Key factors are likely to be: age, general health status and motivation.
- Voluntarily castrated males (e.g., male-to-female transsexuals) are not uniformly asexual.

Culture influences the sexuality of androgen-deprived males

Historically not all castrated men were celibate nor sexually inactive. Eunuchs in Roman antiquity, early Islamic societies, and during the Castrati period in Europe were known to be sexual, desired as partners, and even considered lascivious. Eunuchs married women in both Chinese dynasties and the Ottoman Empire.

The amount and type of sexual activity of modern day castrated males varies greatly. For example…

• < 7% of voluntarily castrated sex offenders (a procedure permitted in ~14 US states) become recidivists; a group highly motivated to be asexual.

• Many castrated male-to-female transsexuals, in contrast, are known to be sexually active and work in the sex trade.

• In an internet survey of voluntarily castrated, modern day self-identified eunuchs in the western world, only 4% considered themselves asexual (N <350).

• Modern day eunuchs in India, the Hijra, are active in the sex trade. Some also marry.

Sexuality with impotence and low libido

So, how is this possible?
Approaches for sexual recovery

1. ED treatments—(the phallocentric or “male approach”).
   • Goal: to recover previous capability for penetrative sex.
   • This is what most men want and what is regularly offered patients. But... if ED treatments are not 100% effective they can exacerbate a patient’s sense of loss, making things worse not better.

2. Accepting non-penetrative sexual practices—(the non-phallocentric or “female approach”).
   • This is acceptable for some men, but still a loss if penile-vaginal sex remains the man’s “gold standard” for sex.

3. “Renegotiated” or novel sexuality (see below).
Alternative sexual practices

A third approach is the use of a mechanical sex aid which is an alternative to both 1) imperfect ED treatments and 2) the acceptance of non-penetrative sex.

Option #3, however, is rarely presented to patients in ED treatment programs nor actively explored by PCa couples for it is neither a strategy for sexual recovery (#1) nor acceptance of non-coital sex (#2), but rather an acceptance of a new sexuality.

Note: Couples that discuss novel sex play may be able to maintain and even rebuild intimacy of both a sexual and non-sexual nature.

Renegotiating sexuality

In the medicalized language of Gray & Klotz (2004) option #3 includes the use of a “belted prosthetic phallus” which does not depend on penile erections, yet allows for insertive-receptive coital sex. In street language this is a strap-on dildo.


Some physiological considerations…

Sex with a strap-on dildo allows for natural full body contact, a natural embrace, and normal hip movements. Such movements are difficult, if not impossible, with incomplete (or “hinged”) erections, as typically occurs for patients using ED treatments that are not 100% effective.

In the Warkentin et al. case study, the patient on ADT reported that his partner held his penis with her hand during dildo-vaginal copulation and mutual orgasms were achieved. This can be partially explained by the fact that a penis that is wet, warm, and tactiley stimulated does not care where it is. Note: it was his movements that determined the penile stimulatory rhythm.

The rubber hand illusion

This hand is my hand. Activation of the premotor cortex during the rubber hand illusion. In the illusion, normal individuals experience an artificial limb (rubber hand) as if it were part of their own body.


Experimental set-up to induce illusory ownership of an artificial body (left panel). The participant could see the mannequin's body from the perspective of the mannequin's head (right panel).

When ED treatments aren’t perfect…

Consider, for example, the Vacuum Erection Device (VED):

In “Saving Your Sex Life” Mulhall (2008) says that “the most significant disadvantage of the device is that it generates a non-cosmetic erection…[i.e.]...one that does not appear pink.” A bigger problem is the hinge effect due to the fact that the root of the penis is inside the body and can not be engorged with blood with a VED. The result is that the penis acts as if it is hinged at the body wall. The hinge effect does not occur with a belted prosthetic phallus.

• With imperfect ED treatments the penis may be enlarged, firm, but will not be truly erect. This makes maintaining coitus difficult.

• Having to adjust posture to remain in copulo distracts from the naturalness of coital sex and inhibits orgasm.

• Many couples give up on the VED and other ED treatments that aren’t 100% effective, yet never know why they just didn’t work for them.

• An ED treatment that is not fully effective but only partially effective can do more harm than good. It can erode a patient’s confidence in his sense of virility and masculine capability.
Response of the partner

• The “strap-on option” is now being cautiously offered by counselors in Halifax, Toronto and Calgary to some couples who are dealing with impotence.

• Some of those couples willing to try it, found it gratifying.

• For a couple willing to explore this option, such sex play may rebuild intimacy even if one or both fail to achieve orgasm.

• More research is necessary to find out for whom this “end run” around ED treatments is acceptable and effective.

Walker and Robinson (2010) pointed out that couples often assume “sex to be impossible after commencing ADT”. However they also confirmed that “some couples are able to enjoy satisfying sex, despite castrate levels of testosterone...”. Furthermore they suggested that “the couples who continued to struggle to adjust…[to ADT]…may have faired better if they had known how other couples are able to maintain satisfying sex while the man is androgen-deprived.”

Introducing sexual aids

Patients and partners need explicit instruction about options for alternative sexual practices. It is not good enough to hint at the idea of alternative practices, nor present ideas to one partner and not to the other.

Partners need information presented to them together as they both need to be onboard for trying new sexual activities/aids…and to make sure nothing gets lost in translation.

The counseling challenges here include: 1) encouraging both partners to be willing to explore new ideas as a couple and 2) giving the couple detailed information in an acceptable way.

On orgasms without erections

Stimulation to orgasm for impotent patients with low libido typically requires extra tactile stimulation (and, of course, recognition that orgasms are possible without erections or penile coitus).

With ED, penile stimulation will need to be longer and firmer to reach orgasm. It is harder to stimulate cutaneous nerves in the penis if it is flaccid. But if there is no option for erection, then to adequately but safely stimulate those nerves without abrading the skin of the penis, a lubricant (e.g., Astroglide, K-Y Silk, or a similar product) is essential.

But do the patients know all that?
### Lubrication: essential for masturbation & sex toy use in this population

**Relevant questions:**

- Are both partners familiar and comfortable with commercial lubricants?
- Have they used them before?
- Do they understand the need for lubricants?
- Do they know the names of reliable products, which ones are best for males, for females, for vaginal insertive use, where to buy them, etc.?

### More on sex with a strap-on prosthesis

- Growing in popularity in the lesbian community.
- Effective because of multi-sensory stimulation and integration—i.e., the couple’s embrace, body orientations, head positions, hip movements, etc. are virtually identical to normal penile-vaginal intercourse.
- It can be used effectively with either the male or female on top and can build confidence since there is no risk of loss of erection and little risk of premature dildo-vaginal separation.
- Either the patient or his partner can wear the prosthesis.
More on presenting options to couples

The idea of starting with the least invasive and working toward the most invasive treatments in a stepwise fashion means that failures become cumulative. After a man has tried two or three ED treatments that have failed, his morale (his masculinity) is often compromised and his enthusiasm for exploring further is diminished.

Solution: Present more than one option at a time. Explore with the patients and partners, singularly and together, ways to eroticize mechanical and pharmaceutical sex aids, and ways to combine them.

General points about eroticization

- In virtually every case where sex aids are found to truly benefit a couple eroticization is at the core.

- Effective eroticization means associating the new object/aid or technique with the sexual pleasure that the partner can provide. This is true whether we are dealing with something as simple as a little blue pill or as complex as intercavernous injections.

- The arousal for one partner that is linked to the aid can feed back on the other partner and elevate their level of arousal for both (as has been reported for strap-on use).
Learning Objectives

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3. To understand the roles (and needs) of the partners of prostate cancer patients on ADT and why caring for the partners can benefit the patients.

Critical psychosocial issues

The willingness for couples to explore novel sex practices may be influenced by the following:

• Previous experience with such sex play.
• Intimacy and spousal dynamics before treatment.
• Comfort and commitment of both individuals to discussing options.
• The setting in which these ideas are presented to them (i.e., in a doctor’s office, in a sexual function clinic, or at a non-clinical sex workshop)…

are all in need of investigation.
Who needs help most?

Not all PCa couples need psychological support nor could the health care system ever afford support for all. Those who are sexually active or have problematic dynamics at the start of ADT appear to be in the most need…and also the populations that can be most helped.

Manne et al. (2011) showed that partners with higher cancer-specific distress, lower marital satisfaction, and lower intimacy improved with a five session couples’ therapy program. However those who weren’t so distressed at the outset were worse off after the intervention!


Selecting patients and partners to be offered psychological support

We need ways to sort out patients and their partners ahead of time, into who are in most need of, and who can benefit most from, some counseling/education intervention.

Simple survey instruments, such as the Dyadic Adjustment Scale and the Brief Index of Sexual Function, probably can do the job. These could be be administered by an nurse/assistant in about ten minutes to patients about to start ADT and their partners.
On-going research

Canadian Institutes of Health Research Project

Who needs help most and what is the best way to help them? Developing and evaluating a preemptive educational intervention to reduce the psychological distress of ADT on prostate cancer patients and their partners

PI: Richard Wassersug—Halifax, Nova Scotia
Co-I: John Robinson—Calgary, Alberta

Status: Enrollment now closed and data analysis underway.

Educational intervention study

Overall goals:

• To develop ways to help patients on ADT and their partners maintain a good quality of life.

• To establish which PCa couples benefit most from supportive educational interventions.

• To determine if this educational intervention is effective if given preemptively.
Consent and Baseline Questionnaire

Randomization
Stratified by sexual activity

Immediate Intervention
Guide & Workshop
Immediately...
Questionnaires every 3 months for 12 months

Delayed Intervention
Guide & Workshop @ 6 months
Questionnaires every 3 months for 12 months
Outcome measures

- EPIC — Expanded Prostate Cancer Index Composite
- DAS — Dyadic Adjustment Scale
- PAIR — Personal Assessment of Intimacy in Relationships
- BISF-M/W — Brief Index of Sexual Function for Men and Women
- Knowledge of Hormone Therapy Side Effects
BISF: Yes, I have been sexually active in the past month

Preliminary results

Small sample size, thus underpowered, but…

Data to date suggest that:

• Early and comprehensive information on ADT appears to help couples adjust to ADT.
• Information is particularly helpful to the couples who are sexually active prior to starting on ADT.

Current status:

A full scale Randomized Control Trial of this simple educational intervention is underway in Calgary.
Key conclusions

1. ADT psychologically burdens PCa patients and often their partners even more so.

3. Patients who are sexually active at the start of ADT are in the most need of help.

4. Both the patient and the partner should be assessed before starting ADT and both should be offered some psychological support if needed.

5. A preemptive educational intervention can help.

6. Orgasmic sex is possible for some PCa patients on ADT and knowing about this possibility can help couples, even if they don’t explore such options.

As a last point, it is not enough to ask a couple whether they think they might need psychological support to deal with the impact of ADT. In your office, a couple may elect to present themselves as a co-supportive team. If the patient says he is doing fine, his partner may then feel obliged to say the same.

However, if you ask them individually you may find that one or both of the individuals needs additional support, but was reluctant to admit that to you in front of their partner.
THANK YOU!