

# Androgen Deprivation Therapy for Prostate Cancer: Recommendations to Improve Patient and Partner Quality of Life

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## ABSTRACT

**Introduction.** Because of improved prostate cancer detection, more patients begin androgen deprivation therapy (ADT) earlier and remain on it longer than before. Patients now may be androgen deprived for over a decade, even when they are otherwise free of cancer symptoms.

**Aim.** An ADT Survivorship Working Group was formed to develop and evaluate interventions to limit the physiological and emotional trauma patients and their partners experience from this treatment.

**Methods.** The multidisciplinary Working Group met for 2 days to define the challenges couples face when patients commence ADT. A writing sub-group was formed. It compiled the meeting's proceedings, reviewed the literature and, in consultation with the other members of the working group, wrote the manuscript.

**Main Outcome Measures.** Expert opinion of the side effects of ADT that affect the quality of life (QOL) of patients and their partners and the recommendations for managing ADT to optimize QOL were based on the best available literature, clinical experience, and widespread internal discussions among Working Group members.

**Results.** Side effects identified as particularly challenging include: (i) body feminization; (ii) changes in sexual performance; (iii) relationship changes; (iv) cognitive and affective symptoms; and (v) fatigue, sleep disturbance, and depression. Recommendations for managing ADT include providing information about ADT side effects before administration of ADT, and, where appropriate, providing referrals for psychosocial support. Sexual rehabilitation principles for persons with chronic illness may prove useful. Psychological interventions for sexual sequelae need to be offered and individualized to patients, regardless of their age or partnership. Support should also be offered to partners.

**Conclusions.** Our hope is that this plan will serve as a guide for optimizing how ADT is carried out and improve the lives of androgen-deprived men and their intimate partners. **Elliott S, Latini DM, Walker LM, Wassersug R, Robinson JW, and the ADT Survivorship Working Group ASWG. Androgen deprivation therapy for prostate cancer: Recommendations to improve patient and partner quality of life. J Sex Med \*\*;\*\*\*:\*\*-\*\*.**

**Key Words.** Prostate Cancer; Androgen Deprivation; Hormonal Therapy; Sexual Dysfunction; LH–RH Agonists; Couples

## Introduction

<sup>1</sup>The ADT Survivorship Working Group members are: Sylvie Aubin, Andrea Beck, Jack Clark, Joyce Davison, Kristine Donovan, Stacy Elliott, Karen Fergus, Anne Katz, David Latini, Andrew Matthew, Rose Matousek, Debbie McLeod, Gail Newth, John Oliffe, John Robinson, Natalie Rosen, Bejoy Thomas, Lauren Walker, and Richard Wassersug.

An estimated 600,000 men undergo androgen deprivation therapy (ADT) in North America per year [1] as either primary, neoadjuvant, adjuvant, or palliative treatment for prostate cancer (PCa). ADT—primarily in the form of depot

injections of luteinizing hormone-releasing hormone (LH-RH) agonists, such as leuprolide, goserelin, and triptorelin—is also being used increasingly with younger men as a result of improved PCa detection from prostate-specific antigen (PSA) testing. Because of ADT, many men can live out their lives free of PCa symptoms [2]. However, they experience substantial physiological and psychological treatment sequelae.

Castrate levels of testosterone are associated with numerous physiological side effects that together form a constellation of symptoms now recognized as androgen deprivation syndrome [3]. Symptoms include fatigue, weight gain, loss of muscle mass, loss of body hair, vasomotor (hot) flushing, sexual dysfunction, testicular atrophy and/or penile volume loss, depression, mood swings, and decrements in cognitive functioning [4–8]. ADT also results in significantly increased risks of osteoporosis, heart disease, obesity, and diabetes [9]. These symptoms result in declines in quality of life (QOL), manifested in physical, social, and sexual functioning [10–13].

The psychological, social, and sexual side effects of ADT also significantly affect the intimate partners of patients [14–21]. Recent studies indicate that partners often experience more distress than the patients themselves [19,20]. An Institute of Medicine report, *From Cancer Patient to Survivor: Lost in Transition* [22], calls for implementation and evaluation of care plans addressing cancer survivors' needs across a broad spectrum, from ongoing medical care to psychosocial concerns. Building on the Institute of Medicine reports, we review here the unique symptoms experienced by patients on ADT, particularly those of a sexual, psychological and psychosocial nature, as well as their impact on men's lives and the lives of their intimate partners. We further suggest strategies that urology, oncology, and supportive-care professionals can employ to help improve the lives of patients and their partners. This article is intended as a foundation to help researchers identify gaps in the literature and proposes procedures for assisting patients and their partners to adapt to ADT-related challenges, including suggestions for the patient-referral process.

## Method

A multidisciplinary Working Group met for 2 days in spring 2008 to define the challenges couples face when a patient commences ADT. The team included a sexual medicine specialist, several PhD-

level clinical and counseling psychologists (who specialize in oncology), and PhD-level nurses and researchers. Of the 21 professionals who attended the Working Group, all have published in the peer-reviewed literature on the psychosocial or sexuality issues facing cancer patients.

## Aims

The first aim of the clinicians and researchers of the Working Group was to identify and categorize challenges that affect PCa patients undergoing ADT, as well as the burden of ADT on their partners. The problems in each of these areas were explored, and areas for future research were identified. The group then drafted a "Survivorship Management Plan" to improve the quality and availability of resources to help patients and their partners adjust to ADT, as the long-term goal of the group is to inform ADT patients and their partners, as well as healthcare professionals, about resources available to address the physical and psychosocial challenges they face.

## Results

The group identified the following concerns: body feminization, sexual changes, relationship changes, cognitive and affective symptoms, fatigue, sleep disturbance and depression. Suggestions made for side-effect management are highlighted in Table 1.

### Body Feminization

Physical changes induced by ADT affect a patient's body image and can lead to a self-perceived decline in masculine presentation [23,24]. Physical changes include gynecomastia and mastodynia (i.e., breast tenderness/pain); the extent of each varies according to the agent used to achieve androgen deprivation. Gynecomastia can be particularly distressing for men who have a strong sense of masculinity [25]. In the extreme, unwanted breast growth can be managed by mastectomy or liposuction, as well as preventively to some degree through radiation treatments [7,26–28]. However, gynecomastia is more commonly managed by camouflaging and/or binding, which can, unfortunately, promote social isolation and reluctance to participate publicly in physical exercise [29]. It has recently been reported that selective estrogen receptor modulator (SERM) tamoxifen is effective for treating bicalutamide-induced gynecomastia [30] for men using antian-

**Table 1** Some strategies for managing major psychosocial and sexual side effects of ADT

Side effects of ADT	Possible management strategies
Body feminization	
Gynecomastia and mastodynia	Preventive management through radiation treatment Binding/camouflage Selective estrogen receptor modulators (e.g., tamoxifen) Mastectomy/liposuction Sexualization or autoeroticization of breasts
Weight gain and loss of muscle mass	Increased physical activity
Hot flashes	SSRIs (e.g., venlafaxine, transdermal estradiol) Diaphragmatic breathing/paced respiration Pharmacological and physical ED treatments
Genital shrinkage	
Sexual changes	
Erectile dysfunction	Standard pharmacological and physical ED treatments Redefinition or reframing of sexual activities (e.g., nonpenetrative sexual activity)
Loss of sexual desire	Bupropion Special effort to enhance displays of physical affection Counseling to recruit past sexual fantasies and explore expanding erogenous zones (e.g., new breast sensitivity)
Delayed or absent orgasm	Use of lubricants to permit increased stimulation without skin irritation Vibrator or sex toys
Changes in reception to touch	Increased effort and alteration of habitual sexual experiences Increased sexual communication
Infertility	Sperm banking
Relationship changes	Counseling to aid couple's adjustment Increased effort toward emotion and physical connectedness Patient and partner education about potential relational consequences/challenges before starting ADT
Cognitive and affective symptoms	Standard management strategies for cognitive changes in the elderly
Fatigue, sleep disturbance, and depression	Standard treatment for depression, including use of antidepressant medication and psychotherapy (e.g., cognitive-behavioral therapy or interpersonal therapy) Standard treatment for sleep disturbance in oncology, including medication and cognitive-behavioral therapy

ADT = androgen-deprivation therapy; SSRIs = selective serotonin reuptake inhibitors.

drogens to achieve androgen suppression. However, tamoxifen and other SERMs may exacerbate estrogen deficiency—the primary cause of many side effects of androgen deprivation—particularly where the androgen deprivation is achieved by either surgical castration or LH-RH agonists [31,32].

For many (if not most) men, the presence of breasts is a stark reminder of the loss of physical fitness and masculinity [33]. Other individuals are less bothered and able to adapt to or ignore gynecomastia. In the extreme, some men may even auto-eroticize their new breasts [25]. No studies have investigated predictors of gynecomastia distress in advance of ADT; therefore, it is impossible to know who might benefit from prophylactic interventions.

Weight gain, altered fat distribution, loss of muscle mass, physical weakness, and loss of body hair on the torso and extremities are all visible daily reminders to a man on ADT of the loss of male physical attributes. In addition, hot flashes provoked by ADT are uncomfortable and disruptive and can be embarrassing, as they are most commonly associated with menopausal women.

The loss of testicular volume and penile length [34] can also affect a man's sense of maleness and sexual self-esteem. Increased abdominal girth secondary to weight gain can further reduce visibility of the penis for the patient. How common and serious a problem this is for men on ADT remains largely uninvestigated. However, anecdotal evidence suggests that this inability to see the penis results in many ADT patients having reduced accuracy when aiming their urine stream and eventually electing to sit while voiding, which may further diminish the individual's sense of masculinity. Penile length and width can be maintained to some degree by penile rehabilitation methods that encourage erections, which, in turn, increase tissue oxygenation and promote a healthy elastin/fibrinogen ratio [35]. Erection-enhancement methods include intracavernosal injections, vacuum therapy, or the regular use of phosphodiesterase 5 inhibitors (PDE5i) such as Cialis<sup>®</sup>, Levitra<sup>®</sup>, or Viagra<sup>®</sup> [36]. The effectiveness of these treatments has not been rigorously assessed for patients on ADT, but PDE5i are known to work poorly in low-testosterone environments [37,38]. In addition, low serum testosterone levels are a

recognized etiology of venous leak in the animal model [39] and appear to be a cause of erectile dysfunction (ED) in PCa patients [40]. Overall, studies looking at the awareness of and motivation for engaging in penile health and preventive measures specifically for ADT patients are lacking.

Although the American Cancer Society asserts in its widely distributed publication on sexuality for men with cancer that genital size and sexual function do not define manhood, and that maleness is thus not lost after ADT [41], some men on ADT disagree [42]. Healthcare professionals should not assume that bold reassurances that the sense of masculinity will be preserved in spite of ADT will ring true for all or most ADT patients. Men treated with radical prostatectomy without concomitant ADT report substantial changes in self-confidence, secondary to iatrogenic ED [43–47]. For many men on ADT, loss of strength and physical capacity can subvert feelings of male dominance or “male hierarchy,” thereby further creating a feeling of demasculinization [47–49]. Some patients experience an erosion or dislocation of gender identity (referred to as *liminality* in the sociological literature) because of the feminizing changes brought on by such severe hormonal manipulation. All told, ADT genuinely challenges a man’s sense of masculinity [48,50]. Yet some men are able to accept a modified definition of manhood. A few perceive themselves as existing in an alternative gender space and openly define themselves as eunuchs, following the formal definition of a genetic male without functional testicles [45,50–52]. Given the pejorative nature of that label [53], this may simply reflect self-deprecation (e.g., Fergus et al. [45]). Alternatively, it may reflect an honest acceptance of emasculation, which may be beneficial for some patients, as the more common strategy of denial has been shown to be psychologically detrimental in the long run [42,54].

### Sexual Changes

A large body of literature shows that both patients and their partners are negatively affected by ED as a consequence of primary PCa treatments, and that resolving ED can improve their QOL [16,55–61]. PCa patients treated with radical prostatectomy, external radiation, or brachytherapy, have poignantly described the negative impact of ED on their sense of masculinity and self-esteem [43]. Men treated with ADT bear a double burden: not only do they experience diminished erectile func-

tion, but they also struggle with reduced or absent libido. Clinicians in the Working Group noted that the loss of the internal drive to seek sexual stimuli, sexual arousal, or satisfaction (i.e., orgasmic attainment) is often described by couples as the single most disconcerting sexual side effect of ADT. In addition, some patients report being especially distressed by fewer sexual fantasies and sexual dreams, and a decreased sexual response to visual and tactile cues; however, for other patients and/or their partners, decreased libido can come as a relief. For many patients and their partners, though, these changes are distressing, especially when unexpected. Although most patients may be capable of intellectually understanding the changes to come described by healthcare professionals, fewer seem able to anticipate the severity and implications of these side effects until they have actually experienced them firsthand. Therefore, well-intentioned warnings that libido may be affected underplay the impact of such wide-reaching side effects on QOL.

A common but naïve presumption is that a reduced libido caused by ADT negates a patient’s concern about ED [62]. Although diminishing libido may, in fact, reduce sexual frustration in some patients, it can increase it in others. In either case, the overall loss of sexuality and intimacy will continue to burden the couple [63–65].

Knowing that the androgen status cannot be improved, patients may still be interested in treatments for loss of desire, such as cognitive-behavioral therapy or nonhormonal alternatives [66]. Partners of men with ED from other etiologies are often motivated to encourage ED treatment [67]; the same may be true for men on ADT for PCa, but we have insufficient data to speculate. Evidence suggests that bupropion may be useful as a treatment for low sexual desire in women; however, it has yet to be evaluated as a treatment for men on ADT [68].

The Working Group reached a consensus that patients’ lack of preparation for, and appreciation of, such side effects likely results in regret, anger, or depression associated with the decision to initiate ADT (cf. Templeton and Coates [69]). It was hypothesized that patients care about this disconnection with libido, as well as declining erectile and orgasmic capacity, because it is integral to the sense of self and masculinity, and therefore place in the world [23,48,70–72]. Significant literature supports the pervasive effect of loss of libido on patients’ sense of masculinity, quality of intimate relationships, and QOL [29,46,48,71,73].

Erectile function, while not solely dependent on serum testosterone levels, is usually affected in ~85% of the population on ADT [74]. For many men, it is important to restore a functional erection to allow penetrative activities, as patients may continue to engage in sexual experiences for the benefit of their sexual partner, despite their lack of libido [67]. The Working Group also acknowledged the importance to most men of being able to attain an erection, even if not used for coital sex. In a society that equates masculinity with virility, the capacity for erections also bolsters self-esteem and confidence [70,72,75]. This desire for the return of erection, for “return to normalcy,” for solo or partnered sexual practices should be validated and respected [76–78]. Even when erectile recovery is not an issue for the patient, rehabilitation of the musculature of the pelvic floor and penile rehabilitation should be offered, as the former can help with urinary continence [79–81].

Studies in men with ED from mixed etiologies have shown that psychological distress increases with severity of ED [82] and that men who respond to ED treatment report clinically significant improvements in QOL, as do their partners [55,83–87]. The same assumption may be applied to men on ADT, as they, too, suffer from ED. Anecdotally, the Working Group noted that daily or even as-needed use of PDE5i that improves morning [88] or spontaneous daytime penile fullness (not necessarily linked to a particular sexual objective) has been noted by many PCa patients as “an acknowledgement of the brain–genitalia connection,” and therefore felt to be a step toward normalization, as well as life and manhood affirming. Return of morning and sexual erections in hypogonadal men treated with testosterone replacement therapy has also had the same effect on self-confidence [89]. Future studies could help to determine whether the severity of ED correlates as well with distress in men with lack of libido secondary to ADT.

Unfortunately, for many men with PCa, erectile aids are not effective, and up to 50% of patients who report success with these methods stop using them within 1 year [74]. An implicit assumption in ED-focused treatment programs is that sexual satisfaction for men depends solely on the ability to achieve erections (as demonstrated in several studies that singularly equate sexual health with erectile function [90]). The Working Group felt that this definition is overly simplistic and may, in the long term, be a disservice to both the patient and his partner.

Frustration and disappointment during sexual encounters can further reduce a patient’s motivation to engage in sex. Delayed orgasm or inability to attain orgasm is a common complaint among patients on ADT, as it is in many hypogonadal men [91], and men on ADT can experience both lower penile vibratory thresholds and decreasing penile sensitivity [92]. If orgasm is further complicated by incontinence (climacturia), this can even be more distressing for both partners [93,94].

In addition, primary PCa treatments (e.g., radical prostatectomy, external-beam radiation, brachytherapy) eliminate most, if not all, ejaculate. For nonsurgical patients on ADT who can still attain orgasm, ejaculatory volume will continually diminish and eventually disappear. As testicular function and spermatogenesis cease, infertility results. Healthcare professionals should discuss options for accommodating post-ADT infertility (e.g., sperm-banking) with patients of all ages rather than only young patients [95,96]. The Working Group noted that this primary side effect of diminished ejaculate volume and subsequent sterility with ADT is largely ignored in the urological and popular literature, perhaps because of the often advanced age of patients or because of the association, historically at least, of ADT with advanced disease. A recent report on PCa patients’ understanding of medical terminology suggests that clinicians need to do more to directly inform patients of these effects [97].

Lack of genital arousal and penile insensitivity either from aging or hypogonadism add to frustration and disappointment [98]; Hypogonadal alterations in libido and mood may also contribute to the lack of response to sexual touch in erogenous areas. Removal of the prostate and possibly ADT itself may also result in diminished pelvic arousal previously associated with prostate engorgement and contraction. Nonpenile sources of genital erotic play may potentially be negatively affected. Partner sexual experiences may therefore require more effort, communication, and alteration.

### *Relationship Changes*

For many men, reduced quality of sexual relationship(s) can result in a withdrawal of both emotional and physical intimacy [19,20]. Patients’ embarrassment and reluctance to talk can also lead to significant partner distress [65]. In general, partners of PCa patients report even more distress than patients themselves [19,99–101]. It has been observed that partners often want to talk about the changes associated with ADT; however, patients

tend to minimize these issues [102]. Although denial appears to be a common coping mechanism, Roesch et al. [54] found this strategy to be detrimental to PCa patients in the long term (see Wootten et al. [103] for more extensive discussion of coping strategies for PCa patients not on long-term ADT). Evidence shows that spousal coping strategies and spousal distress affect patient adjustment and QOL [59,104]. Conflicting coping methods exacerbate the problem. Discordance in communication results in isolation for the patient, the partner, or both [29,73]. Research suggests that an overall loss of relational intimacy can be even more destructive than the loss of coital sex [19,20].

Although it is commonly assumed that an active sex life is impossible to maintain with castrate levels of testosterone, this is neither historically accurate nor confirmed in various populations with genetic males who are not PCa patients but are androgen-deprived [105,106]. However, it is also common for patients and partners to lose hope of satisfying sexual encounters. Sexual encounters may become associated with significant performance anxiety and a feeling of failure, leading to increased self-doubt, relational tension, frustration, and irritation in both the patient and partner. Couples may also notice a decrease in general physical affection as their sexual activities become less frequent. With ADT, sexual experiences require more effort and determination than was previously needed. Patients and partners can easily become discouraged and withdraw from sexual contact with their partner.

Against those odds, some PCa couples experiencing such sequelae nevertheless remain interested in maintaining a physically intimate relationship. Several factors—e.g., age, comorbidity, current level of sexual activity, length of relationship, partner's age and health status—may all be important. Except for age and health status for the couples, how the ability of ADT patients and their partners to remain sexually active is affected by these variables remains largely uninvestigated.

Couples who strive to remain sexually intimate must make a concerted effort to stay emotionally and physically connected in new and redefined ways [107,108]. For example, a couple can use sex-therapy techniques to learn how to recruit erotic memories and possibly new kinds of satisfying physical sensations. Other couples may adapt by discovering pleasure in nonpenetrative sexual activities with or without orgasm, incorporating areas outside the genitals and scrotum as erog-

enous, and incorporating sexual aids (e.g., Warkentin et al. [109]; Wassersug [42]). Because of the depressed libido of the patient, the partner may elect to take the leading role in initiating sex play. Accepting role-reversal in terms of who initiates sexual activity requires good communication between the partners. Some couples may find it beneficial to seek professional counseling to assist in these adaptive processes [110,111].

Aside from changes associated with the patient's sexual performance, some partners may feel less attracted to their partner while he is on ADT; or, alternately, partners may begin to doubt their own attractiveness by personalizing the dampened sexual drive noted in their androgen-deprived mates [107]. These changes can provoke a new dynamic that is hard for the partner to integrate sexually, regardless of the love or compassion he/she may feel. Furthermore, it can be psychologically challenging for the partner to switch from lover to caretaker and caretaker to lover, especially if he/she also holds new or increased responsibility for sexual initiation and/or a role-reversal challenge. When these changes run contrary to prescribed cultural and social gender roles, challenges become even more evident. It may be helpful for couples to be informed of these potential consequences, prior to experiencing them, to increase early identification of such challenges.

#### *Cognitive and Affective Symptoms*

Older cancer patients show poorer mental health than age-matched controls [112]. PCa patients on ADT often report experiencing emotional lability, including tearfulness, increased irritability, and anger [64]. Navon and Morag [29,48] report that patients experience decreased motivation and excitement in all areas of their lives. Hopelessness and discouragement can result from decreased physical and sexual ability, as well as from changes to intimate relationships. For some patients, ADT signifies a progression of disease in which hopes to cure PCa are dashed; and the focus moves toward disease management.

Results from research as to how ADT affects cognitive ability have been mixed. Whereas some studies document changes in visual-spatial processing, attention, and verbal memory problems [113–116], other studies have not [117–118]. Without a clear idea who is most likely to experience cognitive problems on ADT, and what problems they are most likely to experience, it is difficult to propose or test interventions. However, interventions for cognitive decline from other

causes may be appropriate for ADT patients with such symptoms, although little research has been done to investigate this in the context of ADT.

#### *Fatigue, Sleep Disturbance, and Depression*

PCa patients commonly list fatigue as one of the most bothersome side effects of ADT [63,119–121]. Aside from fatigue associated with hypogonadism per se, insomnia correlates significantly with fatigue [122], with higher fatigue associated with greater insomnia [123]. Sleep disturbance is reported by approximately one-third of all patients who have had a radical prostatectomy, and ADT has been identified as a specific risk factor for sleep disturbance in these patients [124].

The physiological mechanism by which ADT causes sleep disturbance is not clear, and fatigue and poor sleep quality cannot be easily separated from other psychological factors. Fatigue, depression, and insomnia form a symptom cluster in cancer patients in general [125], and it is hard to separate cause from effect. Hot flashes, however, have been specifically linked to insomnia and disrupted sleep in breast cancer patients and, not surprisingly, in men on ADT as well [124]. Hot flashes have also been shown to contribute to depression in the elderly in general [126] and in PCa patients on ADT in particular [127].

In the event that patients present with depression and/or sleep disturbance, standard treatments can be used. Antidepressant medications and/or psychotherapy (e.g., cognitive-behavioral therapy or interpersonal therapy) have a strong empirical base for the treatment of depression [128] and medications and/or cognitive-behavioral therapy can be used for the treatment of sleep disturbances [129].

The literature on depression in men on ADT is enormous but equivocal (e.g., Kunkel et al. [14]). Although depression is often associated with low levels of serum testosterone [130], that association is not strong for younger men on ADT [131]. Some researchers [3,132] argue that depression in ADT patients over 65 is primarily caused by age and comorbidities; however, this does not explain the presence of depression in younger patients on ADT, who are diagnosed because of the increased use of PSA screening. Seidman et al. [133] have recently found in a blinded study that testosterone can help alleviate depressive symptoms in middle-aged men with dysthymia. In contrast, Savard et al. [127] concluded that depression in ADT patients is directly associated with PCa treatments and their side effects rather than testosterone defi-

ciency. Notably, though, in the latter study, patients were older, with a mean age of 73 years [127]. Regardless of whether depression is attributable to treatment side effects or testosterone deficiency, it is evident that ADT patients experience elevated rates of depression and would likely benefit from prophylactic assessment and treatment.

Research is needed to track both sleep disturbance and depression to clarify the relationship of these psychological domains to each other and to hot flashes. Depression per se is a well-recognized cause of decreased desire and ED. Changes in mood, sleep patterns, and other QOL domains affect not just patients, but also their intimate partners [134]. The mechanisms for this can be direct, for example, when hot flashes disrupt the sleep of a patient, who then inadvertently interrupts the sleep of his partner. They can also be indirect, for example, an emotionally withdrawn patient can cause his partner to feel isolated [73,135,136]. Clinicians in the Working Group noted that many couples stop sharing a bed when a patient commences ADT. All this can lead to the patient's partner feeling isolated [65] and potentially undergoing his/her own mood alterations.

#### *Recommendations for Care Management for Men on ADT*

Proposed care management options to be considered by healthcare professionals are detailed below (see Table 2 for highlights). Some recommendations are evidence based; others, for which we could not find evidence in the literature, are based on the consensus opinion generated within the group.

1. *Responsible and accurate preparation for couples, prior to administering ADT.* Rather than simply providing patients with a list of potential side effects, clinicians should discuss the anticipated effect of potential changes [96,137,138]. Whenever possible, partners should be included in the treatment decision, as they can be significantly affected by treatment side effects [108]. Research is needed to evaluate the most effective way to deliver information on ADT side effects to patients and their partners.

Patient care management ought to be viewed from the perspective of ADT as a syndrome of interacting and compounding symptoms, as opposed to a series of independent symptoms [108]. Some treatments aimed at a specific symptom exacerbate other symptoms. For

**Table 2** Key components for psychosocial management of patients commencing ADT

1. Responsible and accurate preparation for ADT, involving:
  - Discussion of anticipated effect of ADT
  - Inclusion, whenever possible, of partners, in treatment decision/preparation
  - Presentation of ADT as a syndrome of interacting and compounding symptoms
2. Medical optimization to minimize side effects:
  - Consideration of parenteral estrogen add-back
3. Referral to appropriate psychosocial resources:
  - Counseling to assist couples in adjusting to changes in sexual function
  - Screening to identify men who may be at high risk for psychological morbidity (e.g., gay, young, single, those with a history of relationship discord, and/or mental health problems)
4. Adherence to principles of sexual rehabilitation for person with chronic illness:
  - Assistance to couples in discussing options for maintaining sexual intimacy
  - Maximization of remaining physiological capacities
  - Encouragement of persistence and an attitude of exploration and optimism
  - Addressing concerns about stigmatization in seeking help
5. Individualization of medical and psychological intervention for sexual sequelae:
  - Active encouragement of counseling for individuals and couples who value their sexuality
  - Informing patients and partners of on-line, as well as in-person, resources
  - Informing all patients, regardless of current sexual activity, about the benefits of maintaining penile health
  - Build in resilience by having patients and partners develop strategies to manage the disappointment from treatment failure

ADT = androgen-deprivation therapy.

example, treatments for hot flashes may have other adverse effects. Medroxyprogesterone acetate, for instance, which has been shown to have good efficacy in a recent double-blind, randomized trial [139], may negatively affect cognitive functions [140]; while selective serotonin reuptake inhibitors, which have been found to be effective at reducing hot flashes, may further decrease libido and one's ability to achieve orgasm [141]. Other treatments for hot flashes have yet to be investigated in men on ADT, including relaxation techniques such as paced respiration (shown to be effective for menopause-induced hot flashes) [142].

Growing evidence suggests that exercise, which helps to maintain bone strength, muscle mass, and normal weight for patients on ADT, can also reduce fatigue, leading to improvements in mood, motivation, and sexual functioning [143–145] (Murphy R, Dechman G, Wassersug R. The role of exercise in managing the adverse effects of androgen deprivation therapy in men with prostate cancer, unpublished data, 2009).

There is growing acknowledgement of the impact that health literacy has on patient health-related QOL and other outcomes [146]. Given the documented low health literacy of some PCa patients [147,148], it is clear that information provided to PCa survivors and their partners should be at the appropriate reading level and possibly in multiple formats to ensure adequate understanding. Teach-back techniques, in which the information recipient explains the material back to the provider, can help ensure understanding.

2. *Medical optimization of ADT to minimize side effects.* Patients should not only be informed about medical techniques available for managing the side effects of ADT, but, where possible, ADT should be optimized to reduce its side effects. For example, parenteral estrogen therapy, provided by transdermal estradiol patches or gel, rather than through the use of LH-RH agonists, shows promise [149] and may help preserve libido [32]. The use of non-oral estradiol rather than, or in addition to, LH-RH agonists may have protective benefits, as estrogen reduces hot flashes [150], as well as protects against osteoporotic [151] and cardiovascular symptoms [31,152–155]. There is some evidence of cognitive improvement with estrogenic therapy [156], but others have failed to find improvements following the addition of short-term estradiol to combined androgen blockade in older men with PCa (cf. Matousek and Sherwin [118]).

3. *Referral to appropriate psychosocial resources* [157–160]. Both patients and partners may grieve over changes to the patients' physique (e.g., body feminization) and function (e.g., ED, low libido, fatigue). Regret and anger over the decision to undergo treatment are also common. Physicians prescribing ADT need to be aware that the declining quality of intimate relationships, as well as cognitive and affective changes in the patient, can be traumatic to the patient's partner, even if minor or unacknowledged by the patient. As the challenges that ADT patients experience are secondary to cancer treatment, they may go



unidentified. It is important that healthcare professionals screen for signs of grief and loss in both patients and partners, which are common and can be intense and prolonged. Healthcare professionals should be aware of these potential responses and recommend counseling resources where necessary.

Unless a multidisciplinary team already exists within a cancer or urological service, the patient and his partner should receive a referral to an appropriate clinical psychologist, counselor, sex therapist, or sexual medicine specialist for complex sexual and relationship issues. Furthermore, healthcare professionals should be aware that several groups of men may be at high risk of distress (e.g., young men, gay men, single men, men in relationships that are already distressed, men with a mental health and/or addiction history, men who are not members of the host cultural population) and keep the specific needs of these populations in mind when treating patients.

4. *Use the same sexual rehabilitation principles as for any person with chronic illness or disability.* A desire to maintain sexual function needs to be assessed through forthright discussion between patients, their partners, and their healthcare providers before starting ADT [137]. As in any sexual rehabilitation program, healthcare professionals should remember to: (i) maximize the remaining physiological capacities of the total body and stabilize mood and behavior; (ii) adapt to the residual limitations by using specialized therapies and medications; and (iii) persist in rehabilitation efforts with an exploratory and open mind as well as an optimistic and hopeful attitude [161]. However, men on ADT are at a disadvantage, as their biological libido and sexual motivation are muted. If one assumes there is a desire to maintain sexual intimacy, men on ADT may need to learn to recruit intact sensory and erogenous pathways in positive, affirming ways. This should be attended to before adding medical interventions to be most effective. This can be done alone or with partners, but unpartnered men or men in same-sex relationships may need special encouragement to seek assistance [162]. In couple relationships, both the patient and his partner are significantly affected, and both need to be included in a therapeutic intervention.

It is important to assure patients and their partners that attendance at a therapeutic or educational session is not a judgment or critique of their past or present relationship, but rather a strategy

for dealing with the unwanted side effects of ADT. Couples can also be taught how to evaluate the impact of ADT-related changes on their relationship and sexual experiences.

5. *Individualized medical and psychological intervention for sexual sequelae.* Treatment for low sexual desire in testosterone-suppressed men may require professional therapy. Some sexual-therapy techniques can invoke awareness of sexual fantasies, relying on their potential to trigger sexual desire and arousal [163]. Moreover, cognitive reframing or redefining of the sexual experience, such as focusing on the positive aspects and rewards of the experience, and mindfulness techniques, are additional techniques that may be helpful for men on ADT and their partners [107].

Treatment guidelines recommend psychosexual counseling and patient education for patients with sexual dysfunction, but patients do not widely use such services [44,164,165]. Recent work has shown that even brief psychosocial interventions delivered either in person or across the Internet can improve satisfaction with ED treatment and erectile functioning [160,166–168]. Thus, it is important for healthcare professionals to actively encourage counseling for patients who value their sexuality [96].

Patients should also be informed that treatment methods aimed at maintaining erections may help prevent penile volume loss [36]. In patients who had satisfactory erections (unassisted or with erection enhancement aids) before starting ADT, introduction or continuation of erection aids should be prescribed concurrent with ADT [169]. Patients should be educated about maintaining penile health to aid in reducing penile volume loss/length and improving continence and erectile function, especially if they are sexually active and may not remain on ADT indefinitely. Any medical intervention for ED should include frank discussion with the patient and his partner about the possibility of treatment failure and the likelihood that alternative strategies, including more invasive ED interventions, may be warranted.

Men should also be warned that producing an erection through artificial means, such as an intracavernosal injection, does not automatically result in sexual arousal. In fact, the disconnect between an artificial erection from intracavernosal injections when sexual desire is low or absent can be disconcerting for some men on ADT. Because the action of oral PDE5i is dependent on the nitric-oxide pathway primarily generated by release of

nitric oxide at the remaining terminal nerve endings, patients should be informed of the importance of physical and mental sexual arousal to not only trigger the mechanism but also maximize the effect of the drugs. In addition, other information about the appropriate use of ED treatments should be provided (e.g., penile rehabilitation with vacuum devices and constriction bands; intraurethral pellet of prostaglandin; PDE5i optimization, especially higher dosing; and the contraindication of concomitant or nitrate use [170]).

Successful treatment of a patient who has difficulty attaining orgasm often requires experimentation and open-mindedness regarding the use of sexual aids, such as intracavernosal injections, or vibrators, masturbatory aids (i.e., Fleshlight) or penetrative aids to induce orgasm [42,109]. Experimentation with other sources of stimulation (i.e., new breast sensitivity, perineal/perianal stimulation), and mental adaptation to an altered masculine role may also be beneficial. On a practical note, men should be instructed that more vigorous, prolonged stimulation will be required to achieve orgasm with a flaccid penis, and that water-based, bottled lubricants can help protect the skin from potential irritations that can result from such stimulation.

## Conclusion

Approximately half of all men treated for PCa will be offered ADT at some time during their treatment. As a consequence of improved PCa detection and treatment, patients are starting ADT earlier than before; and many are remaining on it longer, some for over a decade, even when they are otherwise free of cancer symptoms. For the rest of their lives, these patients and their partners will have to adapt to its side effects.

Although ADT may delay the onset or reappearance of cancer symptoms, life without testosterone can be profoundly challenging. The Working Group recommends that physicians, when prescribing ADT, fully inform men of all the challenges that they may face; this means not only listing the potential side effects but also noting the consequences that may potentially follow from these side effects and ways that these may affect their lives and intimate relationships. The effects on patients' partners should be recognized, and help should be offered to them as well, whether or not the patient wishes help. The ADT Survivorship Working Group used the best available evidence and its collective experience to develop

recommendations for care management. Our hope is that this plan will serve as a guide for optimizing how ADT is carried out and improve the QOL of androgen-deprived men and their intimate partners.

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