A qualitative exploration of South African men's perceived effects of Androgen Deprivation Therapy (ADT) as a treatment for advanced prostate cancer

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Abstract

Objective: We undertake qualitative research with men treated in a Pretoria, South Africa Oncology clinic to address men's self-reported experiences on Androgen Deprivation Therapy (ADT).

Methods: Analyses rely upon 22 men's responses to open-ended questions during interviews. These men were 63-78 years of age, and almost all married (three widowed), had children and were no longer engaged in paid work.

Results: In addressing questions about the anticipated and experienced positive and broader side effects of ADT, men referred to its treatment for prostate cancer, with several generally specifying health or life. Patients also referred to a variety of more specific effects such as pain, nausea, difficulties urinating, gaining weight, low energy and sleep disruptions that appeared to reflect a mixture of influences of prostate cancer, ADT and oncological treatment. In addressing a question about the effects of ADT on romantic/sex life, 16 of 19 married men referred to deleterious impacts on their sex lives. With respect to perceived family, work or broader social life impacts, some men noted others' worries and social support.

Conclusion: Findings are situated within discussions of existing research on ADT largely from North American or European samples, and broader views of testosterone and male social behavior.

Key words: prostate cancer, androgen deprivation therapy, castration, sexual behavior, erectile dysfunction, aging

Introduction

Androgen Deprivation Therapy (ADT) is employed for advanced or high-risk prostate cancer diagnosis, with the aim of effectively removing the fuel (androgen) for continued or accelerated prostate cancer growth. Evidence suggests ADT has little effect on survival for men with less-advanced and more localized cancer [1]. However, in some circumstances such as its use in combination with radiation therapy in high-grade cancer it may confer survival benefits [2]. Along with surgical removal of the prostate and radiation or chemotherapy targeting cancer, ADT has developed as a primary clinical tool for managing prostate cancer [3]. A study of men 75 years of age and older found no differences in survival between men on ADT and radical prostatectomy, though men on ADT had more serious adverse effects such as bone fractures [4].

However, the decreased testosterone resulting from ADT may influence a variety of androgen-related characteristics. Observational studies of older men on ADT have pointed to negative consequences for bone maintenance, muscle loss, increased risk of gynecomastia, increased anemia, decreased energy, diminished sexual desire and erectile function, and hot flashes, among other effects [5-13]. More specifically, in a review of ADT and male sexual function, drawing on animal models and human clinical trials, deleterious impacts of ADT on sexual function were noted [14]. The percentage of men not engaging in sexual behavior increased after ADT [15], while ADT increased erectile dysfunction compared to brachytherapy alone [16]. Among older hypogonadal men, the administration of exogenous testosterone has impacts on sexual desire, erectile function and sexual activity [17,18], implicating the relevance of testosterone in male sexual function.

Drawing upon this ADT background, the aim of the present research is to report experiences of men in South Africa treated with ADT to share their perceived effects of the treatment. In

contrast to observational or randomized trials, little qualitative research based on open-ended questions has been conducted to identify patients' perspectives on ADT treatment (see [19]). In a sample of 12 Canadian men interviewed about perceived effects of their ADT, several themes emerged such as contrasts between expectations and reality of treatment in addition to impacts on sexual function and relationships [20]. In a sample of 21 men with metastatic prostate cancer interviewed at a London teaching hospital, the primary adverse effects of ADT reported by patients were hot flashes, gynecomastia, cognitive decline, and diminished sexual function [21]. Three Canadian men interviewed about their ADT experience and exercise drew connections to music and routines [22]. Yet as more men live longer lives, and in which ADT may be a relevant treatment for high-risk prostate cancer, it becomes important to hear what patients say about the perceived risks and benefits, including ones that might not be captured in close-ended clinical outcomes. The perceived effects of ADT, including with respect to sexual function, must be placed in sociocultural and clinical context, another argument for hearing what men report about their ADT experiences based on open-ended questions.

ADT in South Africa

Research suggests relatively high rates of prostate cancer in South Africa compared with lower income countries and populations in sub-Saharan Africa [23,24]. Several key population factors influence the prevalence and profile of South African patients receiving ADT. With more men leading longer lives [25] and often in states of energetic surplus (e.g., overweight, diabetic), these conditions can favor prostate growths for which ADT is indicated [26]. Approximately 7% of South Africans are 60 years of age or older, which is higher than other countries in sub-Saharan Africa. By 2025, approximately 10.5% of South Africans are expected to be 60 years of

age or older. The HIV/AIDS epidemic has had a significant population impact, with nearly 20% of adults HIV positive, though now regularly able to manage their HIV status with antiretroviral therapy. A high percentage of the South African population, including in urban areas, is overweight or obese [27]. Among men aged 50 and older, estimates are that 28% of men are overweight and another 38% obese. This increases the risk of non-communicable diseases such as high-risk prostate cancer [28], in addition to other comorbidities such as erectile dysfunction [29].

South Africa does not have a national program of Prostate Specific Antigen (PSA) screening for prostate cancer. Nor is there a structured national effort for community education on prostate cancer. Patients in the middle class and above who have access to private medical services make up 16.4% of a population of 55 million [30]. The patients on medical aid may have access to information on prostate cancer and choose to voluntarily go for screening. The majority of the population, more than 47 million, are served by state hospitals such as Steve Biko Academic Hospital (also the venue at which participants in the present study were recruited).

Sex differences in mortality are pronounced in South Africa, giving rise to a female-biased sex ratio at advancing ages. Family relationships can be variable, from a spectrum of lifelong monogamous marriages to more fluid mating relationships [31]. The institution of marriage is also declining, but offset by high non-marital cohabitation [32,33]. This can also shape the availability of social support from family and friends, with a major concern being low social capital among aging men [34]. Older, single men in poorer health are less likely to be sexually active [35]. Pointing to potential racial differences in healthcare experiences, Black South African prostate cancer patients tend to present with more advanced prostate cancer and higher PSA levels than Whites [36]. Put simply, as South African men increasingly live longer lives

with potential challenges to their health and social lives, they may also face life-stage relevant health, family and well-being concerns that shape their experiences on ADT.

Materials and Methods

Research was undertaken with men treated with ADT in an urban Oncology clinic in Pretoria, South Africa. This Oncology clinic is at one of the leading public medical facilities (Steve Biko Academic Hospital) in sub-Saharan Africa at which patients visit for assessment and treatment of prostate cancer. This is one of the three tertiary academic hospitals, which serves as a referral center for primary and secondary hospitals in three of the country's nine provinces: Gauteng, Mpumalanga, and North West. The clinic thus draws patients from not just Pretoria but the broader region in South Africa, with patients of varied racial/tribal and socioeconomic backgrounds. Eligible participants were required to be living in South Africa, on ADT, and 60 years of age or older. Subject recruitment took place between June 2019 and March 2020.

Eligible participants visiting a weekly Oncology clinic for ADT treatment and follow-up were presented with study materials. After informed consent was obtained, men participated in a semi-structured interview conducted in a private space in the Department of Urology, at Steve Biko Academic Hospital, affiliated with the University of Pretoria. Demographic items included age, relationship status, number and ages of children, race, work status, education, income and living arrangements. Open-ended questions touched on duration and treatment with ADT and a standardized battery that yields the empirical core of this study: What did you expect the effects of ADT to be? What have been the positive effects of ADT? What side effects or concerns have you experienced from ADT? How has ADT affected your family life? How has ADT affected

your romantic/sex life? How has ADT affected your work or broader social life? The selection of these open-ended questions drew upon purported effects of ADT on patient samples from Europe and North America (see [37]) in concert with an interdisciplinary approach to testosterone and aging men [38].

Responses to open-ended questions were recorded and transcribed. Interviews were conducted in either English or Afrikaans, with Afrikaans responses translated to English. All interviews were conducted by Franco Meintjes, who is fluent in both English and Afrikaans. Peter Gray also participated in the initial five interviews. Analysis of responses primarily entailed clustering by questions (e.g., What did you expect the effects of ADT to be?), with illustrative quotations identified. Ethical reviews took place at UNLV (deemed Exempt by Biomedical IRB, protocol #140254-02) and approved by the Research Ethics Committee of the Faculty of Health Sciences, University of Pretoria, Reference number: 75/2019.

Results

Twenty-two men between 63-78 years of age participated in an interview concerning their experiences on ADT. Other key sociodemographic variables of the sample are presented in Table 1, with one individual's educational data not provided. No men reported work with the exception of one man who was a paid cleric. All married men live with a wife, and additionally nine live with children, though these tend to be older-age children. The typical income reported is a South African social grant (government pension) of 1780 South African Rand or approximately 100 US Dollars.

Table 1. Sociodemographic Profile of South African Male Sample

Variable	Number	Percentage
Marital Status		
Married	19	86.4%
Widowed	3	13.6%
Have Children		
Yes	18	81.8%
No	4	18.2%
Ethnicity		
Black	17	77.3%
White	5	22.7%
Educational Attainment		
Some primary	8	38.1%
Secondary	9	42.9%
Tertiary	2	9.5%
Postgraduate school	2	9.5%

Approximately half of respondents had been on ADT less than a year. With the exception of two men on ADT since 2011 (so 8-9 years prior to interview), all other patients had been on ADT four years or less. Symptoms and other care for prostate cancer preceded ADT, with ADT treatment in this Oncology clinic considered tertiary care for which previous caregivers provided referrals. Patients noted that checkups in the Oncology clinic were often at three-month intervals, which might entail receiving Goserelin (Zoladex™) injections. The prevailing ADT practice at the clinic and for participants is bilateral orchiectomy (removal of both testes: physical castration) rather than chemical castration (e.g., administration of GnRH agonists such as Goserelin or Leuprorelin). Many patients had other treatments besides ADT requiring hospital visits (e.g., antihypertensives, chemotherapy, ARVs for HIV).

The remainder of this Results section clusters patients' responses according to the central open-ended questions to which they responded. Not all patients responded substantively to all questions, yielding variable numbers of responses and depth for specific questions.

What did you expect the effects of ADT to be?

A majority of patients expected effects of ADT. While seven indicated they expected "nothing" from ADT and another did not know what the effects would be, most other responses were couched in terms of prostate cancer improvements, health and/or life. Five men indicated they expected improvements to their prostate cancer experience. This might include improved PSA level and reduced pain, for example. As one respondent conveyed the diagnosis, with a vague allusion to health and life, "The doctor told me I have good news and bad news. The good news is you have 8-10 years left, the bad news is you have advanced prostate cancer that has spread throughout your body. That shocked me but I am handling it and getting treatment." Another patient stated, "I wanted health" as an anticipated effect of ADT. Still another patient noted hot flashes as a specific anticipated effect of ADT.

Two men spoke explicitly of potential effects of ADT on their lifespan. One patient stated, "They just told me if they take out the balls I live a little bit longer. The first Doctor told me the disease won't give me long, maybe a year then I would be dead. After they took out the balls they promised me a bit longer time." Another patient related an exchange with his wife about whether to undergo ADT, identifying tradeoffs between life and caregiving with a sex life: "The life comes first. The sex come after. Go and do that operation. That's why, that's why I came back. I've talked with my wife. You can take my balls off." Another patient reported a conversation about the impact of ADT on his sexual function: "The doctor said I won't control this thing anymore. [Refers to penis] They just said they need to take out the balls."

What have been the positive effects of ADT?

Patients identified an array of positive effects of ADT. These included a general recognition of better/good condition (four times), increased weight (twice), decreased PSA level (twice), and living longer (once). Three patients also identified improved urination and/or defecation. As a more detailed characterization of positive effects, intermixed with ambivalence, one man stated, ""Well…the only thing, when I am passing water, it's improving there, but what you call it, the only thing I'll tell is this … I'm not satisfied, my sexual what you call is not working, but physically I am alright. I can do sport, do anything. I can because I'm playing what you call it, golf. Most of the time I don't take the golf cart, I use just to walk, more or less 6 km the whole course. I can do that and walk physically I am just fine. At times, I just get, what you call, my knees and legs, on the knees I have pains sometimes and then sometimes only very what you call, on the kidneys, it's not very strong, slight pains."

What side effects or concerns have you experienced from ADT?

Patients referred to a variety of effects or concerns associated with ADT. Their responses sometimes intertwined effects of prostate cancer, other treatments for the cancer besides ADT such as radiation- or chemotherapy, and ADT itself, making it difficult to discern which perceived effects might trace to ADT. Moreover, the course (e.g., duration, presentation, comorbidities, other medications) of patient treatment varied, further complicating any potential for identifying perceived effects of ADT on men's experiences. Men sometimes alluded to symptoms or concerns more tied to other aspects of treatment besides ADT, with the following responses including men's inferences about the source of these symptoms.

Respondents reported urinary problems (e.g., little urine or hot, burning urination), defecation problems (e.g., diarrhea), bladder infections (which some men related to use of catheters), nausea (which, as one man noted, might be related to other treatments such as chemotherapy), weight loss (with loss of appetite, perhaps more tied to other treatments besides ADT), cramps (perhaps directly due to prostate cancer itself rather than ADT), low energy, sleep disruption (in part related to pain management and use of catheters), breast growth, memory problems, and either feeling good or bad. One man, discussing the effects of Zoladex, a hormonal modulator of prostate cancer, noted, "Side effects I think it is the Zoladex. Zoladex has so many side effects. Manhood, you don't feel nothing there. [Points toward groin] You don't even think of anything. There is nothing you can do if you take Zoladex, this treatment. And my breasts, I think are growing slowly."

How has ADT affected your family life?

About half of respondents reported that ADT has not affected their family lives. As one patient put it, "My family, they are not affected. They just say, 'thanks God, this man is back again in his life.' Because I was begging God—take me. Why you still do me in this way? Take serious people. Mandela. They have many degrees. I have no degree. I'm not educated. I'm just learned. Why don't you take me? God says, 'no it's not your time.'"

Among the remainder of respondents, effects on family life varied rather than pointed to a common or universal effect. Several noted emotional impacts of the men's prostate cancer diagnosis and treatment on family: one man said that family were shocked at first but are now supportive. Others noted that family were worried or understanding. More tangible effects were

also reported, with one man noting that family sometimes had to carry him given his physical limitations, and another recognizing that improved mobility with ADT required less family attention. Lastly, one man stated, “Hmm, my wife needs to work harder and I do less. But no, not really.”

How has ADT affected your romantic/sex life?

Nearly all (16 of 19) partnered men responding to this question indicated that their sex lives were impacted by ADT. Of the three partnered men who said there were no effects of ADT, one said that at his advanced age he was already not sexually active before treatment, and two others had erectile dysfunction prior to treatment, meaning that there was not an effect due to ADT. Three widowers expressed that they were not sexually active. Two of these men did not seem to be actively pursuing attempts to find a mate. However, the third widower described the negative impacts of his sexual incapacity in a relationship with another woman: “No that lady she left, that woman she left me, so I’m staying all by myself. She left…it don’t get cured. Immediately after getting this Zoladex, it’s become poorer and poorer, very poor. And then from there everything was…she decided to go away.”

Thirteen partnered men reported that they were not sexually active, with 10 partnered men explicitly referencing an inability to maintain an erection. One man stated, “My dick does not stand up anymore.” As another patient put it, “It’s [his penis, unable to maintain an erection] half past six. Doing half past six. Doesn’t work anymore. But my wife, she accept that. It’s OK. That sex that is gone now. No more sex.” Still another man put it succinctly: “We do not have sex. I can’t get erections.”

Three men reported conversations with their wives about the relevance of men's and their wives' ages as a factor in discerning these potential consequences. One exchange suggested that if the man were 30, he would want a sex life, but instead in his 70s he could give up that sex life for treatment. As another patient explained, "My wife supported me. I told myself, 'she's still young.' I told her, my wife, 'you see, this problem. I see you are still young. You will need sex. So I say give OK you can go…" [in other words, he's talking about giving his wife permission to seek sex elsewhere.] She say, no, no, no, no. I'm not going anywhere.' I say OK. I'm asking you. Satisfied!? And I will never look after you if…because I can't [makes a sound of intercourse]." Another man stood out for not discussing the cause of his sexual incapacity with his wife: "Can I be honest with you? I have not told my wife I am getting the surgery. She doesn't know why I can't have sex anymore."

How has ADT affected your work or broader social life?

A majority (15/19) of respondents to this question stated that ADT had not affected work or broader social life. Few men work, given their age, which likely helps account for this pattern. Men at these ages may also have narrower social lives than younger versions of themselves, perhaps also helping contribute to few perceived effects on broader social life. As illustrations, one man stated, "I wasn't really a guy for social life, but if I go to places I fit in I don't have any problems." Another patient responded, "I still have all my friends, they have accepted it and supports me very well. They always ask how it is going with me."

That said, one respondent who identified an effect of ADT connected that to not attending church anymore. Two others reported less activity due to pain (which might be more related to prostate

cancer itself than ADT) and having less energy. As one man put it, “It has affected my work life because I have less energy. I can’t do everything I did before the surgery. It also has affected my social life because I do not associate with some of the people anymore for fear of having to disclose my condition.” This man was not alone in expressing a wish to limit knowledge of ADT with the concern it might impact how others perceived him. As another patient put it, “It’s a secret. My secret. Because if I can tell everyone in the street hey you know I don’t have any more balls they will make it ehh a joke.”

One other patient related how ADT influences his self-perception when with others: “I’m not feeling happy all the time, that it disturbs my, what you call it, disturbs me, they look down at me because I can’t. I start despise myself when I’m among female friends. You can see them talk and everything and immediately that thing comes up in my mind. I feel small.”

Discussion

Perhaps the most compelling pattern to emerge from men’s responses to questions about their ADT experience is the negative impact on sexual function. Sixteen of 19 married men reported such impacts, with many also referencing problems with erectile function. A few married men and one single man connected sexual function problems with relationship concerns, such as an inability to sexually satisfy a partner. Men also reported effects of ADT on sexual function beyond those that might be anticipated for older men with comorbid health concerns. The negative impacts of ADT on sexual behavior and erectile dysfunction are consistent with previous work on samples from Europe and North America [14].

Men reported a broader array of symptoms and effects associated with ADT, including weight gain, lowered PSA levels and low energy. Some of these effects are consistent with clinical research on ADT [5-13]. However, many responses by participants appeared to mix effects of prostate cancer, other treatments and ADT, making it difficult to isolate perceived effects stemming from ADT itself. This make an argument for the value of a prospective study of ADT to better pinpoint effects of ADT longitudinally, including the timing of effects after initiation of ADT. The mixing of these symptoms as reported by men may also suggests that the experience of ADT so much overlaps that of prostate cancer and other treatments that these are intertwined in how men conceptualize them.

Some men's responses indicate tradeoffs between health and sexual function. Several men highlighted anticipated effects of ADT on their very survival, but at expense to sexual function. These observations are broadly consistent with clinical research on the benefits and risks of augmented testosterone [39-41], in addition to evolutionary life history models [42-44] of the pleiotropic (multiple) effects of testosterone in vertebrates generally. Several men also pointed to the importance of age in the meaning of impacts of ADT on sexual function. The negative impacts of ADT on sexual function could be better sustained at these later-life ages than if they had occurred earlier in adult life, with the importance of sexual behavior less central at these older ages. That observation aligns with other research pointing to declines in sexual behavior, sexual desire and erectile function with advancing age [45-47].

Even when asked about effects of ADT on family life, no patients specifically mentioned concerns over children or grandchildren (e.g., wanting to stay alive to maintain relationships with grandchildren). Few men commented on broader impacts on social life (e.g., outside of family) either. Given other research suggesting that as men age, they may shift into more generative

roles (e.g., caring for descendant kin or contributing to community) [48-50], the lack of attention to such concerns expressed by men here warrants further attention. The little overt attention to such broader social concerns could be due to varied reasons such as communication styles (e.g., holding such concerns but not expressing them) or diminished weighting of those concerns relative to oneself and a marital partner (given that most effects referred to the patient himself and his wife).

The ages at which men have been subject to ADT here, primarily by physical castration, warrant comparisons with other studies conducted among males of varied ages. Nonhuman animal research on rhesus monkeys [51] and domestic dogs [52], for example, reveals that secondary sexual characteristics and adult status-seeking and sexual behavior may be diminished if castration occurs prior to puberty. Some human research points to the same (e.g., the male voice does not deepen if boys are castrated prior to puberty) [53,54]. A focus on human castration among men recently castrated (e.g., mostly in the past year) in their 60s and 70s, then, amounts to investigating the impact not just post-pubertally but after a long adult life in which men have grown accustomed to their bodies functioning certain ways. Studies of rhesus monkeys, common marmosets and men castrated at earlier adult ages indicate that some males were able to maintain sexual function and behavior, indicating some inertia (rather than driven by circulating testosterone) in male sexual behavior [51, 53-55]. By contrast, men subject to ADT at these later ages may have less physiological capacity for sexual behavior, and may (in light of other points concerning male aging) place less value on the maintenance of sexual function compared to younger ages.

Although few overt patterns in this study indicate differences in South African men's experiences on ADT compared with samples in Europe or North America, the practice of ADT

in South Africa does differ in several ways. One is that physical rather than chemical castration is the primary type of ADT employed in this South African setting. Physical castration is cheaper and requires less regular monitoring, two key reasons why it is employed over chemical castration. The options for ADT available at Steve Biko Academic Hospital include 3 monthly injection (Zoladex) and once-off surgical castration (bilateral orchidectomy) with or without daily oral treatment (Androcur). The cost to the state of the daily or 3 monthly treatments, as well as to the patients to travel to the hospital to fetch their monthly treatment or get their 3-monthly injection, surpass the cost of a single surgical intervention under local anaesthesia and guarantees compliance. Physical castration, by eliminating potential patient non-compliance, also reduces the risk for bladder outlet obstruction symptoms and spinal cord compression, which itself can serve as a devastating complication of metastatic prostate cancer, resulting in paralysis from the waist down and urinary and fecal incontinence.

Another consideration is the practice and time course of a prostate cancer diagnosis and treatment for it. The steps to the diagnosis and treatment of prostate cancer at Steve Biko Academic Hospital include a clinical suspicion of cancer typically based on symptoms, followed by a digital rectal examination and serum PSA levels. The time required for these steps, including available scheduling and the logistics of transporting the patient by hospital or public means, can be substantial (e.g. an average of 4.5 months from making an appointment until obtaining results from a prostate biopsy). In the early stages prostate cancer is asymptomatic; however, most patients by the time the they present, they are symptomatic already with locally advanced and possibly with distant metastases, at which point the most appropriate treatment is ADT. The logistical difficulties with getting patients to the academic hospital persist into the treatment period. The delays in diagnosis are such that by the time that treatment can be initiated

the cancer is even further advanced and thus definitive management is often the ideal option from the perspective of maximum oncological control.

This study is subject to limitations. One-time interviews of men preclude a more exact longitudinal approach to identifying the effects of ADT. In a few interviews, a participants' son or wife (who had helped take a patient to the Hospital) was also present and serving as an intermediary during an interview. The lack of close-ended interview questions about specific domains such as hot flashes, energy, social competition and grandfathering means that quantifying the prevalence or magnitude of such impacts is not feasible, and leaves open questions about how to interpret absence of evidence (e.g., of grandfathering). Cultural and communication issues (e.g., conversing with a young adult White South African [FM] and a middle-aged White American [PG]) could be more closely evaluated to determine whether men (like in this predominantly Black South African sample) differentially share impacts depending upon the background of the interviewer.

Conclusion

The present study extends existing research in several key ways. To our knowledge, this is the first qualitative study of men's experiences on ADT in sub-Saharan Africa. The key empirical pattern observed is the decrease in sexual behavior, often linked to problems with erectile function. This observation is consistent with findings from other samples internationally. Men also reported a variety of other symptoms and effects of ADT such as increased weight and having less energy. While few men reported impacts of ADT on their broader social lives, those

involving family were more variable. Findings are relevant to broader discussions of the role of testosterone, including decreases through castration at specific life stages, on male behavior.

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