Patient Preference and Adherence

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ORIGINAL RESEARCH

Patients' Preferences for Attributes of Oral vs Injectable Androgen Deprivation Therapy in Prostate Cancer: A Discrete Choice Experiment

Sean P Collins[1], Agnes Hong[2], Brett Hauber[2], Scott C Flanders[3], Oliver Will[4], Martine C Maculaitis[4], Sergio C Gatoulis[2], Marty Chakoian[5], Jared Thorley[6]

[1]Department of Radiation Medicine, Georgetown University; MedStar Georgetown University Hospital, Washington, DC, USA; [2]Pfizer Inc., New York, NY, USA; [3]Sumitomo Pharma America, Inc., Cambridge, MA, USA; [4]Oracle Life Sciences, Austin, TX, USA; [5]UsTOO in Seattle Prostate Cancer Support Group, Seattle, WA, USA; [6]Intermountain Healthcare, Murray, UT, USA

Correspondence: Sean P Collins, Department of Radiation Oncology, University of South Florida, 3 Tampa General Circle, Tampa, FL, 33606, Tel +1 (813) 844-8910, Email sbrtsean@gmail.com

Purpose: Patient involvement in treatment decisions improves outcomes, but data on patients' perspectives of medical androgen deprivation therapy (ADT) options for prostate cancer are limited. This study quantified the impact of multiple attributes of currently available oral and injectable ADTs on patient treatment choice.

Patients and Methods: From February to July 2022, US males aged >40 years with localized or advanced prostate cancer completed a cross-sectional survey, including a discrete choice experiment (DCE), to assess preferences for ADT attributes. In each DCE task, participants were asked to choose between two hypothetical ADT treatment profiles defined by administration mode, testosterone surge after initiation, cardiovascular risk, impact on sexual interest, time to testosterone recovery after discontinuation, and out-of-pocket cost. Hierarchical Bayesian models generated preference weights, which were used to estimate attribute relative importance (RI). RIs were compared by five subgroups (cancer stage, race/ethnicity, cardiovascular comorbidities, age, and ADT experience) with two-sample t-tests.

Results: A total of 304 participants in the US were included in analyses (median age: 65.0 years). Holding out-of-pocket cost constant, mode of administration, and impact on sexual interest were most important, followed by risk of cardiovascular events. Across all subgroups, on average respondents preferred a once-daily ADT pill over less frequent intramuscular or subcutaneous injections. This preference was significantly stronger among respondents with advanced prostate cancer, those with cardiovascular comorbidities, and among racial/ethnic minorities. Treatment preferences did not differ between ADT-experienced and ADT-naïve respondents.

Conclusion: On average, patients preferred to treat prostate cancer by taking a once-daily ADT pill at home rather than receiving less frequent injections. Shared decision-making between healthcare providers and patients, including discussing the benefits, risks, and administration burden of available ADT options, should be encouraged to ensure that patients receive the prostate cancer treatment that is best suited for their care and needs.

Plain language summary: Androgen deprivation therapy (ADT) lowers testosterone levels in patients with advanced prostate cancer to stop the spread of cancer. There are a few available ADT options, and each option has different features. These features include the way that the medicine is taken (for example, a pill taken by mouth every day at home or an injection received every 3–4 months at a doctor's office), as well as the medicine's side effects, costs, and its impact on a person's interest in sexual activity.

Researchers wanted to see which features of ADT were most important to patients and whether patients with different characteristics (such as age or if they had received ADT in the past) had different preferences. Researchers asked 304 patients a series of questions. In each question, patients chose between two hypothetical (meaning not real) ADT options with different features. Researchers found that, in general, patients preferred to take a pill by mouth once a day at home, rather than an injection every 3–4 months at a doctor's office. This preference was stronger for patients with advanced prostate cancer, patients who were non-White, and patients who had heart or blood vessel problems. Patients who had received ADT in the past had similar preferences to patients

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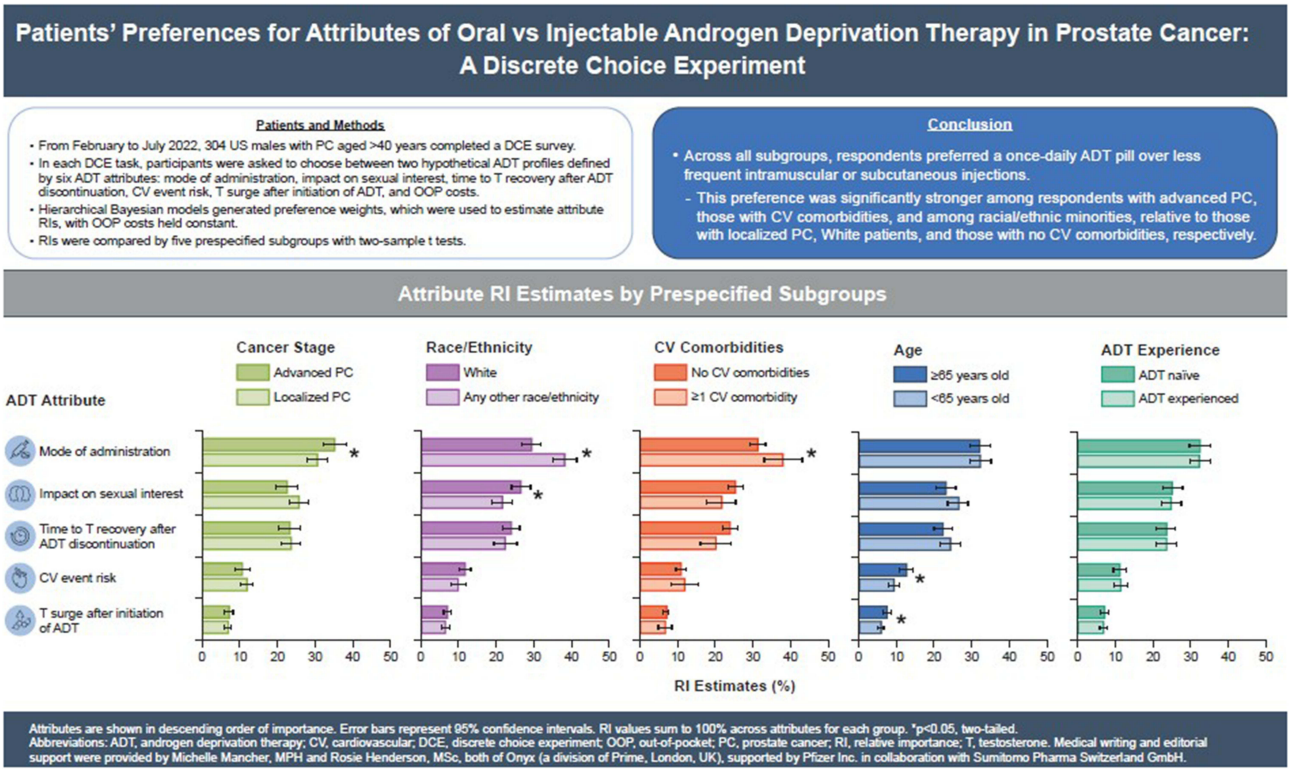
Graphical Abstract



who had never received ADT. These results can help doctors learn about the types of treatments that patients with different characteristics may prefer. Doctors and patients should discuss the features of available ADT options to find the right one for each patient.

Keywords: mode of administration, patient preferences, shared decision-making, gonadotropin-releasing hormone agonists, gonadotropin-releasing hormone antagonists, testosterone recovery

Introduction

Prostate cancer (PC) is the most commonly occurring cancer among males in the United States (US).[1] In 2025, there will be an estimated 313,780 cases of PC diagnosed in the US, which represents approximately 30% of all new cancer cases in males and 15% of new cancer cases overall.[1] Androgen deprivation therapy (ADT) with chemical or surgical castration is the recommended standard of care for advanced PC, which includes unfavorable localized cancer, high-risk biochemically recurrent disease, and metastatic disease.[2] Medical ADT with gonadotropin-releasing hormone (GnRH) receptor agonists or antagonists inhibits the growth of PC by reducing testosterone levels to achieve chemical castration.[3]

Currently available GnRH receptor agonists and antagonists differ in key attributes, such as a testosterone surge at treatment initiation, time to testosterone recovery after discontinuation, potential cardiovascular risk, mode of administration, impact on sexual function, and out-of-pocket (OOP) costs. GnRH receptor agonists (eg, leuprolide) cause a testosterone surge at treatment initiation, which can delay chemical castration and necessitate the concomitant use of a first-generation antiandrogen medication (eg, bicalutamide).[2] In addition, after treatment cessation with GnRH receptor agonists, patients often experience a prolonged time to testosterone recovery and chronically low testosterone levels,

which can lead to poorer health and quality of life outcomes, and negatively impact patients' libido.[4,5] In contrast, GnRH receptor antagonists do not result in a testosterone surge, which allows for chemical castration to be more rapidly achieved;[3] GnRH receptor antagonists have been associated with faster testosterone recovery after treatment discontinuation.[6]

ADT is potentially associated with increased risk for adverse cardiovascular events in patients with PC.[7] Some evidence suggests that this risk may be lower with GnRH receptor antagonists compared with agonists.[6,8,9] According to a meta-analysis of 11 randomized trials, GnRH receptor antagonists may be associated with fewer cardiovascular events than GnRH receptor agonists; however, the available evidence is not definitive.[10]

Prior to 2020, medical ADT in the form of GnRH receptor agonists and the single GnRH antagonist option (degarelix) had been available primarily as intramuscular or subcutaneous injectable formulations, which required up to monthly administration for patients.[11–13] Relugolix, a daily oral GnRH antagonist, was approved by the US Food and Drug Administration to treat adults with advanced PC in December 2020.[14] Unlike injectable ADTs, which must be administered at a physician's office, an oral ADT can be taken at home, which offers a potentially less burdensome option for patients.

To facilitate shared decision-making between patients and physicians, it is important to understand how patients with PC weigh the potential benefits, risks, and other attributes when considering ADT. Accordingly, the current study aimed to quantify the preferences of US patients with PC for attributes that differentiate currently available medical ADT options and to estimate the relative importance (RI) of each attribute to treatment choice. Additionally, subgroup analyses assessed whether patient preferences and attribute importance differed by cancer stage, race/ethnicity, cardiovascular comorbidities, age, and ADT experience.

Materials and Methods

Study Design and Population

An online cross-sectional survey including a discrete choice experiment (DCE) was developed to elicit patient preferences for hypothetical ADT options among US patients with localized or advanced PC. Participants were recruited via a healthcare research panel (Kantar Profiles). US males aged >40 years who had healthcare coverage for the past 3 years and self-reported being diagnosed with PC were eligible to participate. Individuals who self-reported a physician diagnosis of any other type of cancer (aside from PC), Alzheimer's disease, or dementia; those who did not know or recall whether their PC had been treated with ADT; those enrolled in any clinical trial; or those who were unable to answer the study questionnaire independently (ie, required assistance from a caregiver) were ineligible to participate. Recruitment quotas were set to ensure an approximately even split (~150 participants each) of ADT-experienced (ie, those who reported current or prior ADT use) and ADT-naïve participants. The study complies with the Declaration of Helsinki and was determined by the Sterling institutional review board (IRB) to be exempt from ethical review on October 28, 2021, based on a category 2 exemption (research involving educational tests, surveys, interviews, or observation) of the US Department of Health and Human Service's policy 45 C.F.R. §46.104(d) (Sterling IRB; Atlanta, Georgia, US; IRB Protocol #: 9398-MMaculaitis), and all participants provided their informed consent electronically.

DCE Development and Administration

A targeted literature search helped inform the six ADT attributes that were selected for inclusion in the DCE, and these attributes reflected the differences in currently available ADT options reported from clinical trials and observational or real-world studies (Table 1). The first attribute, mode of administration, was described in terms of the formulation, frequency, and location of treatment administration to fully capture the distinctions among currently available ADTs.[3,11] The second attribute was evaluated to distinguish between ADTs that do or do not necessitate an additional medication to mitigate the consequences of a testosterone surge and corresponding clinical flare during ADT initiation.[2,6] The third attribute reflected the potential differences in the risk of cardiovascular events associated with currently available ADTs, as observed in the Phase 3 HERO trial (NCT03085095), which assessed the efficacy and safety of relugolix compared with leuprolide in patients with advanced PC.[6] Finally, attributes that represented differences in the degree of impact that

Table 1 Discrete Choice Experiment Attributes and Levels

Attribute	Description	Levels
Mode of administration	How the medication is taken	Injected under the skin of the abdomen once a month at a doctor's office[13]
		Injected into the muscle of the arm, thigh, or buttock once every 3–4 months at a doctor's office[12]
		Injected into the muscle of the arm, thigh, or buttock once every 6 months at a doctor's office[12]
		Pill taken daily at home[14]
Testosterone surge after initiation	Additional medication is needed to prevent a testosterone surge from occurring	Additional medication (pill) needed to prevent a testosterone surge, taken daily for approximately 3 weeks to prevent a testosterone surge from occurring[2]
		The treatment does not cause a testosterone surge, so no additional medication is needed[6]
Cardiovascular event risk	X out of 100 patients (X%) taking the treatment have a heart event (such as heart attack or stroke)	3 out of 100 patients (3%)[6]
		6 out of 100 patients (6%)[6]
Impact on sexual interest	Decreases interest in sex	Decreases interest in sex very much[15]
		Decreases interest in sex moderately[16]
		Decreases interest in sex a little[17]
Time to testosterone recovery after discontinuation	3 months after stopping treatment, X out of 100 patients (X%) will return to normal testosterone levels, meaning a reduction in treatment-related side effects, like hot flashes, fatigue, and sexual problems	3 out of 100 patients (3%)[6]
		16 out of 100 patients (16%)[15]
		54 out of 100 patients (54%)[6]
OOP cost[a]	Total out-of-pocket cost for treatment, including all doses, is $X/month	$5 per month
		$75 per month
		$200 per month
		$350 per month

Notes: [a]The levels of this attribute were not obtained from the literature; however, they were evaluated in the cognitive interviews. From Hauber, B., Hong, A., Hunsche, E. et al. Patient Preferences for Attributes of Androgen Deprivation Therapies in Prostate Cancer: A Discrete Choice Experiment with Latent Class Analysis. *Adv Ther* **41**, 3934–3950 (2024). https://doi.org/10.1007/s12325-024-02955-1. Minor adaptations under http://creativecommons.org/licenses/by-nc/4.0/.

ADTs may have on patients' sexual interest,[15–17] as well as the rate of recovery to normal testosterone levels following treatment cessation,[6,15] were also studied. Though these attributes are clinically related, in pretest interviews, participants considered them to be separate attributes. Lastly, the DCE included an attribute to represent the varying levels of OOP costs associated with ADTs.

The final DCE contained a series of 11 choice tasks, which each presented two hypothetical ADT profiles with varying levels of each attribute and asked participants to indicate which one they preferred (Figure S1). The hypothetical profiles were combinations of attribute levels determined by an experimental design and not intended to reflect any individual ADT option that is currently available. In addition to the DCE, the survey included questions to characterize the study sample. These questions assessed sociodemographic characteristics (eg, age, race/ethnicity, and education), clinical characteristics (eg, comorbidities and time since diagnosis), and treatment history (eg, prior procedures and treatments received for PC).

The current study was conducted in two stages: a qualitative and a quantitative phase. To pretest the final survey instrument, 45-minute structured cognitive interviews were conducted via telephone among 12 participants who met all study eligibility criteria. The cognitive interviews were used to verify that the survey questions were clear, understandable, and accurately interpreted, and that the set of attributes in the DCE provided sufficient detail about the hypothetical treatment options for participants to make an informed choice. The quantitative phase involved the administration of the online survey to all participants from February 17, 2022, to July 25, 2022.

Study Outcomes

The key outcomes of the survey were: (1) a set of preference weights for each participant in the sample to capture the impact of each attribute level on ADT preference; (2) an average RI estimate for each attribute to capture the impact of each attribute on treatment choice; and (3) individual attribute-level preference weights and average RI estimates for the following five subgroup pairs: cancer stage (localized vs advanced), race/ethnicity (White vs any other race/ethnicity), cardiovascular comorbidities (≥1 cardiovascular comorbidity vs no cardiovascular comorbidities), age (<65 years vs ≥65 years), and ADT experience (ADT-experienced vs ADT-naïve). Cancer stage, age, and cardiovascular comorbidity subgroups were analyzed to understand whether participants who are more likely to be in poorer health due to advanced age, have more aggressive disease, or have comorbidities have different preferences compared with (or vs) participants who are younger, have more favorable prognosis, or have fewer complications. The race/ethnicity subgroup was analyzed to understand whether the treatment preferences of racial minorities differed from the majority White population. Finally, the ADT-experienced subgroup was analyzed to understand whether participants who had previous experience with an injectable ADT option differed in their preferences from participants who had not received ADT previously.

Statistical Analysis

The study aimed to collect survey responses from at least 300 participants. Participant characteristics were summarized using means and standard deviations (SDs) for continuous data; median and range were additionally reported for patient age. Categorical data were presented as frequencies and percentages.

Hierarchical Bayesian models were used to analyze the DCE data and generate a preference weight for each attribute level for each participant in the sample.[18,19] Mean preference weights for each attribute level were then computed for the full sample. The difference between the mean preference weights for any two levels of a given attribute provides an estimate of the change in preference associated with a change in the levels of that attribute. Larger differences signify that the change between those two attribute levels is more strongly preferred. Attribute levels were effects coded and the preference weight for each attribute was estimated relative to the mean effect of the attribute. To calculate the statistical significance of the difference in mean preference weight estimates, one level of each attribute was designated as the reference, and each level within that attribute was compared with the respective reference level; p-values of <0.05, two-tailed, indicate a statistically significant difference between each attribute level and the reference level. Mean preference weights were estimated for the total participant sample and for each subgroup.

Attribute RI estimates were calculated for each participant in the sample by dividing the range of preference weights for each attribute (the participant's preference weight of the most preferred level minus the participant's preference weight of the least preferred level) by the sum of the ranges of all attributes and then standardizing to sum to 100% across all attributes. Average RI estimates for the sample are calculated as the mean of the participant-level RI estimates. RI reflects how much variation in treatment choice is explained by a given attribute, on average, among participants; higher RI values indicate a greater influence on treatment choice. OOP costs were held constant when estimating RI, as preferences regarding this attribute are largely influenced by personal factors (eg, insurance status) and may vary over time.[20] Average attribute RI estimates were compared using two-sample t-tests; average RI estimates and 95% confidence intervals were calculated. P-values <0.05, two-tailed, were considered statistically significant.

Data from the DCE choice tasks were analyzed using Sawtooth Lighthouse Studio v9.8 (Sawtooth Software, Inc., 2020). Descriptive analyses were performed using IBM SPSS v28.0.[21]

Results

Participant Characteristics

A total of 304 eligible participants with a median age of 65 years responded to the survey and were included in the analyses (Table 2). Most respondents self-identified as White, in a committed relationship/married, and retired. Mean (SD) time since diagnosis was 5.4 (4.8) years, and the most frequently reported diagnosed comorbidities were high blood pressure and high cholesterol. Approximately half of the respondents were ADT-naïve and half planned to be sexually active.

Patient characteristics were largely balanced between subgroup pairs with some exceptions (Table 2; Table S1). In the cancer stage subgroups, respondents with localized PC (n=168) more often were college-educated, ADT-naïve, and planned to be sexually active, but were less often on Medicare or retired, compared with respondents with advanced PC (n=115). In the race/ethnicity subgroups, White respondents (n=198) more often were on Medicare, in a committed relationship, college-educated, and employed vs respondents of any other race/ethnicity (n=106). Those of any other race/ethnicity were more often on Medicaid/MediCal and more often reported being diagnosed with diabetes vs White respondents.

In the cardiovascular comorbidities subgroups, respondents with ≥1 cardiovascular comorbidity (n=46) more often were older, retired, and on Medicare, but less frequently planned to be sexually active vs those with no cardiovascular comorbidities (n=258). Respondents with ≥1 cardiovascular comorbidity more frequently reported being diagnosed with high blood pressure and diabetes; they also had a longer mean time since PC diagnosis and more often had received chemotherapy compared with those with no cardiovascular comorbidities. In the age subgroups, respondents aged ≥65 years (n=161) more frequently reported having received radiation and had a longer time since PC diagnosis compared with respondents aged <65 years (n=143). Those aged <65 years more often self-identified as Black/African American vs respondents aged ≥65 years.

Sociodemographic characteristics did not differ by ADT experience. ADT-naïve respondents (n=155) less often reported receiving antiandrogens or androgen receptor pathway inhibitors, compared with ADT-experienced respondents (n=149). ADT-naïve respondents also had a significantly shorter time since diagnosis vs ADT-experienced respondents.

ADT Treatment Preferences

Among respondents in the full sample, decreasing OOP costs, changing from an injectable option to a once-daily oral mode of administration, and reducing impact on sexual interest were more influential to the treatment preferences vs reducing cardiovascular event risk, avoiding the need to take a pill to mitigate the consequences of a testosterone surge after ADT initiation, or a faster time to testosterone recovery after treatment discontinuation (Figure 1). On average, respondents were willing to accept an increase in the impact on sexual interest from "moderately" to "very much" (difference in mean preference weights [Δ]: −0.01−[−1.05]=1.04) in exchange for changing the mode of administration from an injection once every 3–4 months to a once-daily pill (Δ: 1.06–[–0.18]=1.24; Table S2). In addition, for changing the mode of administration from a subcutaneous injection once a month at a doctor's office to a once-daily pill, respondents were willing to accept a testosterone surge that required additional medication, a reduction in cardiovascular risk of 3 percentage points, and a 51 percentage-point reduction in the probability of achieving normal testosterone after 3 months.

A once-daily pill was significantly more preferred over each injectable alternative across all prespecified subgroup analyses including: age (Table S3), ADT experience (Table S4), cancer stage (Table S5), race/ethnicity (Table S6), and cardiovascular comorbidities (Table S7). All other within-attribute changes in levels were also statistically significant, with the exception of a 51 percentage-point reduction in the probability of testosterone recovery within 3 months after treatment discontinuation, in which there were no differences among the total patient sample (Table S2), those >65 years of age (Table S3), and in both ADT-experienced and ADT-naïve subgroups (Table S4).

Table 2 Patient Characteristics

Variables	Total Sample (n=304)	Cancer Stage[a]		Race/Ethnicity		CV Comorbidities		Age		ADT Experience	
		Localized PC (n=168)	Advanced PC (n=115)	White Only (n=198)	Any Other Race/ Ethnicity (n=106)	≥1 CV Comorbidity (n=46)	No CV Comorbidities (n=258)	<65 Years (n=143)	≥65 Years (n=161)	ADT-Experienced (n=149)	ADT-Naïve (n=155)
Race/ethnicity, n (%)											
White (only)	198 (65.1)	112 (66.7)	68 (59.1)	198 (100.0)	0 (0.0)[b]	27 (58.7)	171 (66.3)	87 (60.8)	111 (68.9)	100 (67.1)	98 (63.2)
Black/African American	51 (16.8)	30 (17.9)	18 (15.7)	0 (0.0)*	51 (48.1)*	10 (21.7)	41 (15.9)	32 (22.4)*	19 (11.8)*	29 (19.5)	22 (14.2)
Hispanic/Latino	21 (6.9)	9 (5.4)	12 (10.4)	0 (0.0)*	21 (19.8)*	5 (10.9)	16 (6.2)	7 (4.9)	14 (8.7)	8 (5.4)	13 (8.4)
Age, n (%)											
≥65 years, n (%)	161 (52.9)	81 (48.2)	66 (57.4)	111 (56.1)	50 (47.2)	40 (87.0)*	121 (46.9)*	0 (0.0)	161 (100.0)[b]	76 (51.0)	85 (54.8)
Median (range)	65 (41–82)	64 (41–82)*	66 (45–79)*	66 (41–82)	64 (47–79)	68 (48–82)*	64 (41–81)*	60 (41–64)	68 (65–82)	65 (45–82)	65 (41–81)
Insurance type, n (%)[c]											
Individual/family insurance plans	160 (52.6)	97 (57.7)	54 (47.0)	103 (52.0)	57 (53.8)	13 (28.3)*	147 (57.0)*	124 (86.7)*	36 (22.4)*	75 (50.3)	85 (54.8)
Medicare	151 (49.7)	72 (42.9)*	65 (56.5)*	107 (54.0)*	44 (41.5)*	36 (78.3)*	115 (44.6)*	9 (6.3)*	142 (88.2)*	81 (54.4)	70 (45.2)
Medicaid/MediCal	20 (6.6)	8 (4.8)	11 (9.6)	7 (3.5)*	13 (12.3)*	4 (8.7)	16 (6.2)	11 (7.7)	9 (5.6)	8 (5.4)	12 (7.7)
Comorbidities, n (%)[c]											
High blood pressure	136 (44.7)	80 (47.6)	47 (40.9)	86 (43.4)	50 (47.2)	30 (65.2)*	106 (41.1)*	51 (35.7)*	85 (52.8)*	60 (40.3)	76 (49.0)
High cholesterol	119 (39.1)	70 (41.7)	40 (34.8)	78 (39.4)	41 (38.7)	21 (45.7)	98 (38.0)	44 (30.8)*	75 (46.6)*	51 (34.2)	68 (43.9)
Diabetes	49 (16.1)	25 (14.9)	21 (18.3)	25 (12.6)*	24 (22.6)*	13 (28.3)*	36 (14.0)*	15 (10.5)*	34 (21.1)*	22 (14.8)	27 (17.4)
CV comorbidities[d]	46 (15.1)	23 (13.7)	22 (19.1)	27 (13.6)	19 (17.9)	46 (100.0)	0 (0.0)[b]	6 (4.2)*	40 (24.8)*	21 (14.1)	25 (16.1)
Sexually active, n (%)											
Plan to be sexually active	152 (50.0)	106 (63.1)*	34 (29.6)*	107 (54.0)	45 (42.5)	14 (30.4)*	138 (53.5)*	95 (66.4)*	57 (35.4)*	69 (46.3)	83 (53.5)
Time since diagnosis (years)[e]											
Mean (SD)	5.4 (4.8)	5.1 (5.1)	5.5 (4.3)	5.8 (5.3)	4.7 (3.5)	7.8 (8.0)*	5.0 (3.8)*	4.1 (3.1)*	6.5 (5.7)*	6.0 (5.3)*	4.8 (4.2)*
ADT experience, n (%)											
ADT-naïve	155 (51.0)	97 (57.7)*	51 (44.3)*	98 (49.5)	57 (53.8)	25 (54.3)	130 (50.4)	70 (49.0)	85 (52.8)	0 (0.0)	155 (100.0)[b]

Notes: * indicates p<0.05, two-tailed, for pairwise comparison. [a]Patients were asked "Which of the following best describes your cancer currently?" Localized PC was defined as a response of "cancer is in prostate only" on this item. Advanced PC was defined as a response of "Cancer has spread to lymph nodes" and/or a response of "Cancer has spread to bones and/or other organs" on this item. Patients with responses of "Don't recall/not sure" (n=21) on this item were excluded from the "Cancer stage" subgroup comparison. [b]Pairwise comparison could not be conducted for this variable, as it is the grouping variable. [c]Patients could select >1 response option. [d]Includes self-reported diagnosis of ≥1 of the following: congestive heart failure, heart disease, myocardial infarction, and/or stroke. [e]Data on this variable were excluded for n=5 patients (n=3 did not recall year of diagnosis and n=2 provided illogical response for year of diagnosis).

Abbreviations: ADT, androgen deprivation therapy; CV, cardiovascular; PC, prostate cancer; SD, standard deviation.

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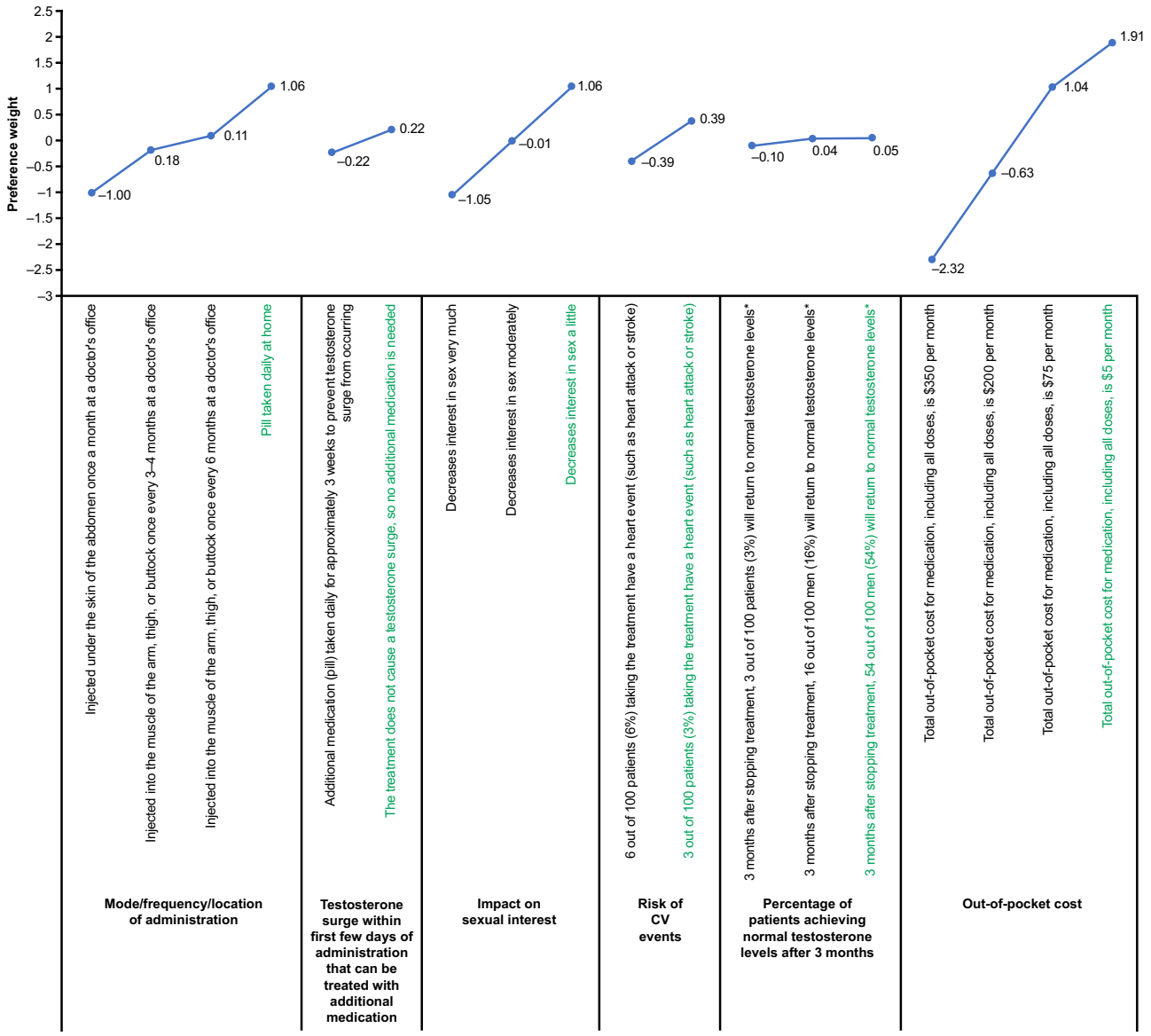

Figure 1 Attribute-level preference weights.

Notes: Attributes are shown in the order in which they were presented to respondents in the DCE tasks. The change in preference associated with a change in the levels of each attribute is represented by the vertical distance between the preference weights for any 2 levels of that attribute. Larger differences between preference weights indicate that the change between those two levels is perceived by patients as relatively more influential to overall preference. The reference level for each attribute is indicated with green text.

Abbreviations: CV, cardiovascular; DCE, discrete choice experiment.

Attribute RI

When OOP costs were held constant, mode of administration had the highest average RI, followed by impact on sexual interest and time to testosterone recovery after ADT discontinuation (Figure 2). The average RI of a change in mode of administration was 1.3–4.5 times higher than the average RI of each of the other four attributes. Impact on sexual interest had the next highest average RI and was perceived by respondents as being similar in importance to a change in the mode of administration. Risk of cardiovascular events and testosterone surge after initiation of ADT had average RIs of 11.4% and 7.2%, respectively.

In general, attribute RIs were similarly rank-ordered in the subgroup analyses, with mode of administration being the most important attribute across all subgroups (Figure S2-S6). However, there were some statistically significant differences in RI estimates between subgroups. For example, a change in mode of administration had a higher average

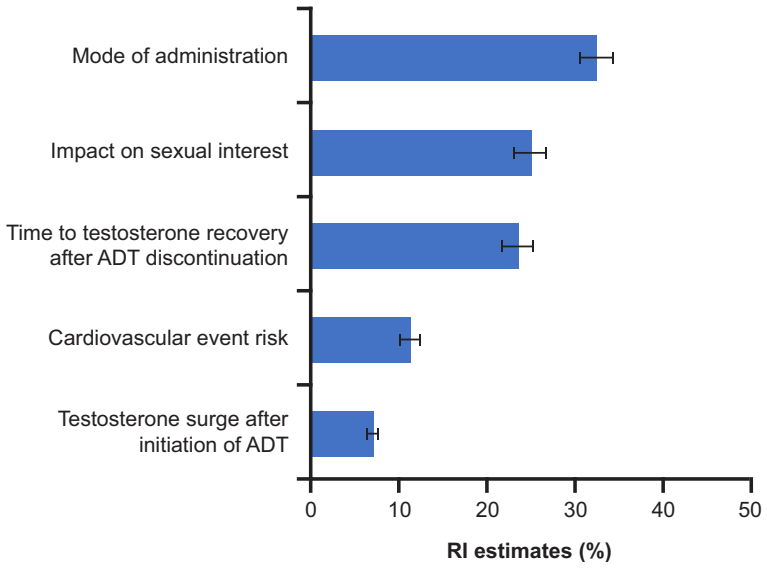

Figure 2 Average attribute relative importance estimates.
Notes: Attributes are shown in descending order of average importance. Error bars represent 95% confidence intervals. Relative importance values sum to 100% across attributes.
Abbreviations: ADT, androgen deprivation therapy; RI, relative importance.

RI among respondents with advanced PC compared with those with localized PC (RI=35.6% vs 30.9%, p=0.021; Figure S2); among respondents of any other race/ethnicity compared with White respondents (RI=38.3% vs 29.6%, p<0.001; Figure S3); and among respondents with ≥1 cardiovascular comorbidity compared with those with no cardiovascular comorbidities (RI=38.4% vs 31.6%, p=0.011; Figure S4). Further, impact on sexual interest was ranked higher in importance to White respondents compared with respondents of any other race/ethnicity (RI=26.8% vs 21.9%, p=0.009; Figure S3). Lastly, risk of cardiovascular events (RI=13.0% vs 9.7%, p=0.004) and the need to take an additional medication to prevent a testosterone surge (RI=8.0% vs 6.2%, p=0.003) were more important to respondents aged ≥65 years vs those aged <65 years (Figure S5). No statistically significant differences in average RI estimates were observed between ADT-naïve and ADT-experienced respondents (Figure S6).

Discussion

The current study assessed the treatment preferences of US patients with PC and provided contemporary insights from the patient perspective into the importance of various attributes associated with currently available ADT options. The findings suggest that respondents, on average, preferred an oral, once-daily ADT pill taken at home over any of the less frequently administered injectable alternatives that must be received at a physician's office. Among the total sample and across all subgroups, mode of administration was the most important attribute, explaining approximately 30–40% of the variation in treatment choice. Impact on sexual interest and time to testosterone recovery after treatment discontinuation were also viewed by respondents as highly important, in relation to the other attributes. The need to take a pill to prevent a testosterone surge at ADT initiation and the risk of cardiovascular events had the least influence on treatment choice. A latent class analysis of the same data sample identified a minority of patients (19.4%) who preferred infrequent intramuscular injections to a once-daily pill; these patients were more likely to be ADT-experienced and aged ≥65 years.[22] The current analysis suggests that ADT experience and age may not be independently associated with preferring injectable administration of ADT.

A prior systematic review of 79 DCE studies which examined treatment choice across multiple oncology indications, including PC, reported that treatment administration-related attributes were ranked in the top three most important attributes in nearly one-third of the studies.[23] The findings from the current study further highlight the importance of providing an oral administration option to patients with PC. Moreover, these results indicate that mode of administration is more important to respondents with advanced PC, racial/ethnic minorities, and those who have cardiovascular

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comorbidities, relative to those with localized PC, White patients, and those with no cardiovascular comorbidities, respectively. Hence, the lower burden of a once-daily ADT pill may be even more important for certain subpopulations of patients when choosing a PC treatment. Of note, preferences for a once-daily pill over injectable ADTs were similar for patients aged ≥65 years and <65 years, as well as ADT-naïve and ADT-experienced respondents with PC, which suggests that patients' willingness to take a once-daily ADT pill is not affected by their age or prior experience with injectable ADTs.

A prior DCE study, which assessed preferences for hypothetical PC treatments among antiandrogen-naïve patients with nonmetastatic PC, found that impact on libido and the ability to maintain an erection were influential attributes in treatment choice.[24] In a previous systematic review, sexual dysfunction was also identified as an important consideration in treatment decisions among patients with PC.[25] The results from the current study generally align with this prior literature, as impact on sexual interest and time to testosterone recovery after treatment discontinuation were the second and third most important attributes overall, respectively, when choosing PC treatment.

As noted above, there are differences between GnRH receptor agonists and antagonists in time to testosterone recovery after treatment discontinuation. Patients treated with long-term GnRH receptor agonists can take multiple years to recover to normal testosterone levels after treatment discontinuation, which can negatively impact patients' quality of life and sexual function.[4,5,26] In contrast, GnRH receptor antagonists have been associated with faster testosterone recovery after treatment discontinuation.[6] This may be especially relevant for patients with nonmetastatic PC who are eligible for intermittent ADT, as these patients are less likely to experience the adverse effects of ADT, including sexual dysfunction, due to limited treatment exposure.[6,27]

To facilitate patients' ability to make informed decisions about their healthcare, the American Urological Association provides guidance and resources on implementing shared-decision making in clinical practice as a part of routine urological care.[28] Shared decision-making would help patients with PC to fully understand their treatment options, as well as the anticipated benefits, risks, and outcomes associated with each option. The current study identified significant differences in patient preferences for attributes of ADT based on patient characteristics including cancer stage, race/ethnicity, presence of cardiovascular comorbidities, and age. Being aware of these variations in preferences among patients eligible for ADT may aid physicians in making ADT treatment decisions. Additional characteristics that may not be available in a patient's medical record, such as insurance type or plans for being sexually active, may also influence patient preferences regarding their PC treatment. For the patient to make an informed decision, the physician should be able to clearly explain in lay language the differences of each ADT option, including their mode of administration, OOP costs, impact on sexual function, likelihood of recovery post-treatment discontinuation, and cardiovascular risk. While some physicians may not have the time or specialized expertise (eg, cardiovascular expertise or knowledge of OOP costs) for these conversations, ultimately, they are needed to truly incorporate the patient's voice in decision-making. Future research on best practices for implementing shared decision-making in treatment choices for patients with PC is warranted.

Limitations

The findings of this study should be interpreted in the context of relevant limitations. First, clinical characteristics, comorbidities, and PC procedures and treatments were all self-reported by respondents, and these data could not be verified against medical records. Any inaccuracies in recall may have resulted in misclassification of respondents into subgroups, particularly based on ADT experience, cardiovascular comorbidities, or cancer stage. Additionally, the cross-sectional study design does not permit inferences to be made regarding causality, and longitudinal data would be needed to evaluate whether the treatment preferences of patients with PC change over time and throughout the course of the disease. The web-based survey administration may limit the ability to generalize results to patient subpopulations who reside in more remote, rural communities with inadequate internet access. Moreover, since patients who could not complete the survey independently were ineligible to participate, findings may not be generalizable to extremely ill or frail patients with PC. According to the Prostate Cancer Foundation,[29] approximately 60% of those diagnosed with PC are ≥65 years of age, whereas 53% of patients with PC in the current study were in that age group; as such, the younger average age in the study sample may also limit the generalizability of results. The study also did not factor in continuous vs intermittent ADT regimens. Studies including a 2023 meta-analysis of 12 randomized trials suggest that intermittent ADT has advantages over continuous

therapy, including reduced toxicity and a positive impact on quality of life.[16,30] As OOP costs and some adverse events would likely be lower for patients treated with intermittent vs continuous ADT, patient preferences for ADT attributes may differ depending on the regimen.

The DCE design was informed by a literature review and qualitative research, although patient characteristics not captured in the survey may result in biased preference estimates. Furthermore, stated preferences do not have complete fidelity with actual treatment choices. Nevertheless, prior research has supported the external validity of DCE methodology,[31] which increases confidence that the findings reasonably reflect the real-world treatment choices that patients with PC might make. While the current study included qualitative interviews with patients to evaluate the content of the survey, further qualitative research would be needed to understand the reasons underlying patient preferences for ADT.

Conclusions

Our findings indicate respondents would prefer to be treated for their PC by taking a daily pill at home instead of less frequent injections at a doctor's office. Preferences for an oral mode of administration for ADT were stronger among respondents with advanced PC, racial/ethnic minorities, and those with cardiovascular comorbidities. Notably, the preferences of ADT-experienced and ADT-naïve respondents were similar; both groups preferred a once-daily oral ADT option irrespective of prior experience with injectable alternatives. Further, variations in preferences for ADT attributes across subgroups were observed, which provides insight for healthcare providers into the types of ADT that patients with different characteristics may prefer. However, given that treatment decisions are highly personal, the optimal treatment option for any individual patient can only be determined through open dialogue between the physician and the patient and discussion of the different attributes of all available treatment options.

Abbreviations

ADT, androgen deprivation therapy; DCE, discrete choice experiment; GnRH, gonadotropin-releasing hormone; IRB, institutional review board; OOP, out-of-pocket; PC, prostate cancer; RI, relative importance; SD, standard deviation; US, United States; Δ, difference in mean preference weights.

Data Sharing Statement

The study data are not publicly available due to the data collection only being granted exemption determination from an IRB for this specific protocol. The data presented in this study can be made available upon reasonable request from the corresponding author for non-commercial use.

Ethics Approval and Informed Consent

The final protocol and informed consent documentation were reviewed by Sterling International Review Board (Atlanta, GA); an exemption determination was granted on October 28, 2021 (IRB Protocol #: 9398-MMaculaitis). All participants provided their informed consent electronically.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Consent for Publication

The manuscript neither contains nor reports on details of any images, videos, recordings, or any other information that could potentially identify any individual respondent. The study team only had access to and analyzed deidentified participant data. The study informed consent statement advised participants that their survey answers would be combined with those of other survey participants and the results would be reported in the aggregate.

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Disclosure

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