Development of a Novel Patient-Reported Outcome Measure to Assess Hormonal-Based Treatment Symptoms and Their Impacts in Patients with Prostate Cancer

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Introduction

- Treatment of advanced prostate cancer typically includes surgical or chemical castration, such as androgen deprivation therapy (ADT), to suppress testosterone and prevent the prostate cancer cells from further growth.[1]
- Commonly used ADT treatments are gonadotropin-releasing hormone (GnRH) agonists (e.g., leuprolide) and antagonists (e.g., degarelix, relugolix).[1]
- ADT treatment-related adverse events may include hot flashes, fatigue, loss of libido, and erectile dysfunction.[1]
- While several prostate cancer-specific patient-reported outcome (PRO) measures exist, these do not adequately cover the spectrum of patient-relevant symptoms and impacts of hormonal-based treatments.

Objectives

The aims of this study were to:

- Determine the most important ADT-related symptoms and their impacts on patients with prostate cancer through concept elicitation (CE) interviews.
- To inform the content of a novel PRO measure to assess symptoms and impacts associated with hormonal-based treatments, specifically ADT, on men with prostate cancer.

Methods

- Participants living in the United States were recruited based on the following inclusion criteria:
  - Male
  - ≥ 18 years
  - Fluent in English
  - Diagnosed with prostate cancer
  - Either:
    - Treated with a GnRH agonist or antagonist as monotherapy, OR
    - At least 6 months of GnRH agonist or antagonist monotherapy before adding another treatment for prostate cancer (and on this combination therapy for no more than 3 months in total)
- CE interviews were semi-structured, ~75 minutes, and conducted over the telephone.
- Interviews explored participants' experiences with ADT, focusing on ADT-related symptoms and their impacts.
- Participants were asked if they would attribute the symptoms specifically to their ADT rather than to any other factors (e.g., their prostate cancer, other conditions, other treatments, etc.).
- If not spontaneously mentioned, concepts of interest were probed by interviewers.
- CE interviews were conducted to the point of saturation (when there were no new concepts emerging from subsequent interviews).
- Interviews were audio-recorded, transcribed verbatim, and analyzed thematically using NVivo, software allowing for systematic evaluation of themes captured in qualitative data.
- Findings from the CE interviews were reviewed with clinical experts who provided additional insights regarding the relationship of symptoms and their impacts to hormonal-based treatments.
- Due to the proximity of treatment-related symptoms to the patient experience on ADT, the focus here is on the patient-reported ADT-specific symptoms.

Results

- Findings are reported for 12 participants, after which saturation was reached.
- The mean (standard deviation; SD) age of participants was 56.8 (7.48) years, 33.3% were African American, and the mean (SD) time on their most recent ADT was 15.5 (11.5) months. **(Table 1)**

Table 1. Participant Demographics, Clinical Characteristics, and Treatment History (N = 12)

Age	
Age (in years), mean (SD)	56.8 (7.48)
Race & Ethnicity, n (%)	
White/Caucasian	8 (66.7%)
Black/African American	4 (33.3%)
Hispanic/Latino	1 (8.3%)
Not Hispanic/Latino	11 (91.7%)
Clinician-reported Clinical Characteristics	
Months since prostate cancer diagnosis, mean (SD)	17.2 (10.32)
Current state of prostate cancer*, n (%) (not mutually exclusive)	
Localized	10 (83.3%)
Locally advanced	2 (16.7%)
Non-metastatic castration resistant	1 (8.3%)
Clinician-reported Treatment Experiences	
GnRH Agonist or Antagonist – Current, n (%)	12 (100.0%)
Months on most recent GnRH Agonist or Antagonist, mean (SD)	15.5 (11.5)

Abbreviations: SD = standard deviation, GnRH = gonadotropin-releasing hormone.
* Clinicians could indicate multiple states of prostate cancer.

Symptoms Related to ADT

- A total of 21 symptoms were discussed across the interviews. **(Table 2)**
- Key symptoms reported by ≥ 10 participants (spontaneously or probed) included: fatigue or lack of energy (n = 11), reduced sexual interest or desire (n = 10), and pain or tenderness at the injection site (n = 10). **(Table 2)**
- These key symptoms were attributed to their ADT by at least half of the participants. **(Table 2)**

Impacts Related to ADT

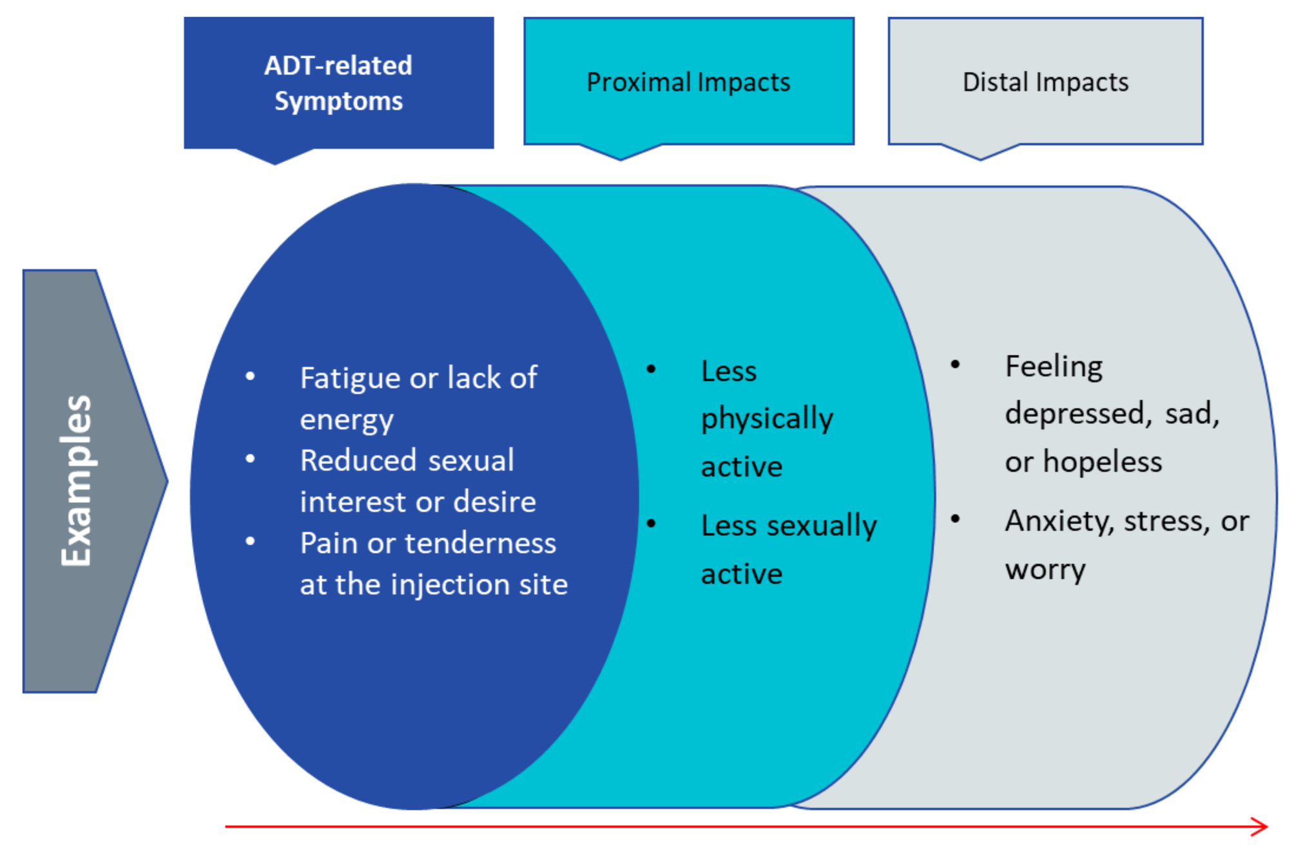
- Proximal impacts of symptoms (either spontaneously or probed) included being less sexually active (n = 10) and being less physically active (n = 9). **(Table 2, Figure 1)**
- Other spontaneously reported proximal impacts reported by > 4 participants included sleep impacts (n = 8) and physically draining or moving slower (n = 6).
- Distal impacts of symptoms (either spontaneously or probed) included feeling depressed, sad, or hopeless (n = 9) as well as anxiety, stress, or worry (n = 9). **(Table 2, Figure 1)**
- Other spontaneously reported distal impacts reported by > 4 participants included reduced intimacy with partner (n = 9), less socially engaged (n = 9), impact on self-esteem or self-image impact (e.g., feeling less masculine; n = 6), adjustment to exercise (n = 6), and mentally draining (n = 5).

Table 2. Symptoms and Impacts Related to ADT (N = 12)

Symptom	S (n)	P (n)	Total (n)	Attr. to ADT (n)
Fatigue or lack of energy*	9	2	11	8
Pain or tenderness at injection site*	8	2	10	10
Reduced sexual interest or desire*	8	2	10	5
Hot flashes (night sweats)*	6	2	8	6
Headaches	5	3	8	2
Insomnia or sleep problems*	6	2	8	1
Difficulty maintaining erection*	3	5	8	2
Urinary symptoms	6	0	6	2
Weight gain or feeling fat*	3	3	6	4
Dry mouth*	2	4	6	3
Joint pain or muscle stiffness*	2	4	6	3
Loss of muscle mass*	1	5	6	1
Cognitive difficulties*	1	4	5	2
Nausea or vomiting	1	3	4	2
Reduced seminal flow	1	2	3	1
Kidney or back pain	1	2	3	0
Reduced appetite	2	0	2	0
Diarrhea	1	1	2	1
Fever	1	0	1	0
Dizziness	1	0	1	0
Enlarged or tender breasts/nipples	0	1	1	1
Impact				
Being less sexually active*	5	5	10	-
Being less physically active*	7	2	9	-
Feeling depressed, sad, or hopeless*	5	4	9	-
Anxiety, stress, or worry*	8	1	9	-

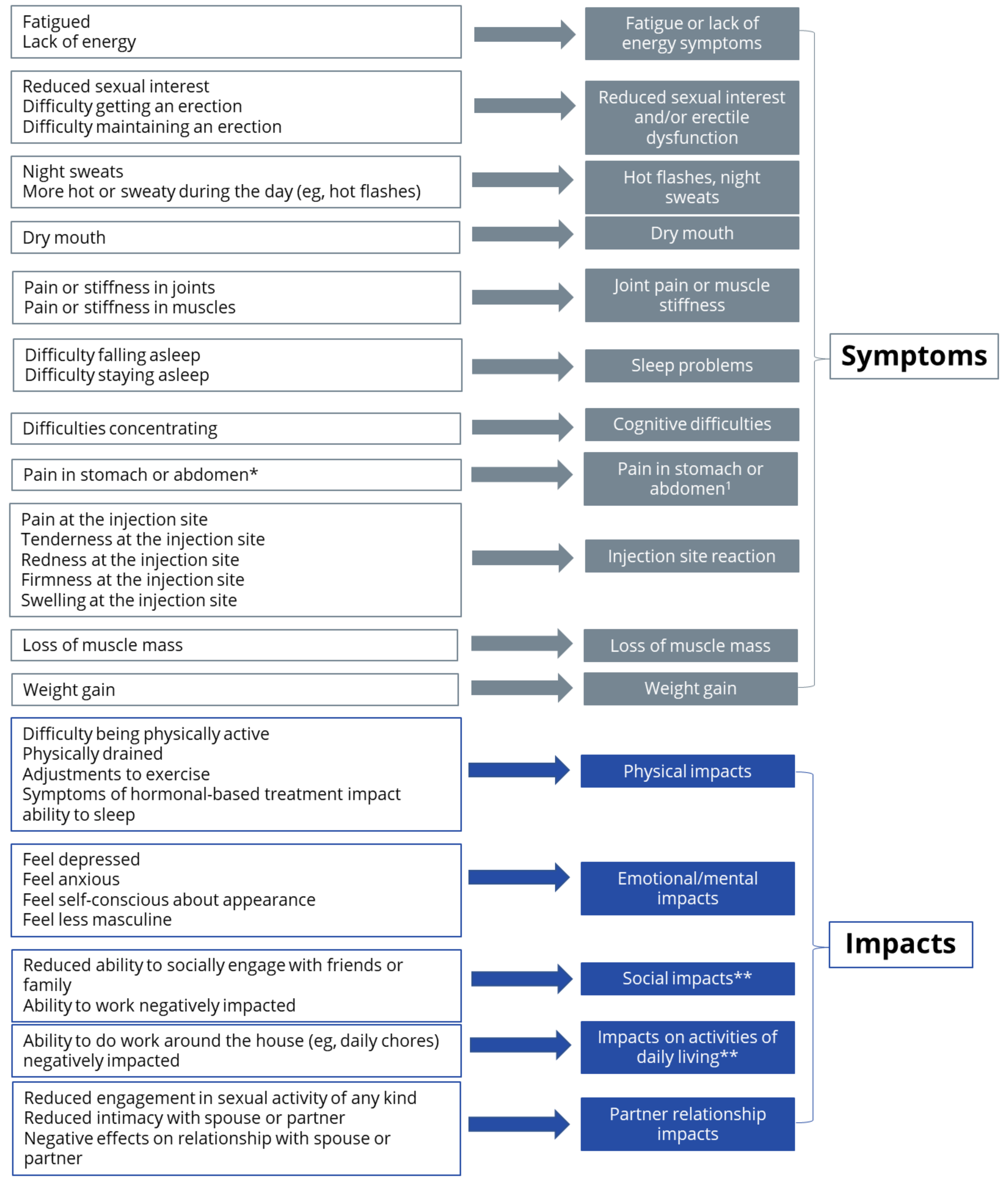
Abbreviations: Attr. = attributed, P = probe, S = spontaneous.
* Included in the draft conceptual framework based on importance to patients, and attribution to ADT according to both patient report and clinical expert input.

Figure 1. Symptoms and Proximal and Distal Impacts


ADT-related Symptoms
Proximal Impacts
Distal Impacts
Examples
Fatigue or lack of energy
Reduced sexual interest or desire
Pain or tenderness at the injection site
Less physically active
Less sexually active
Feeling depressed, sad, or hopeless
Anxiety, stress, or worry
Proximal concept to treatment benefit
Distal concept to treatment benefit

- The resulting conceptual model from these interviews led to a draft measure for ADT-related symptoms and impacts. **(Figure 2)**

Figure 2. Draft Measure Conceptual Framework


Items
Concept Measured
Fatigued
Lack of energy
Fatigue or lack of energy symptoms
Reduced sexual interest
Difficulty getting an erection
Difficulty maintaining an erection
Reduced sexual interest and/or erectile dysfunction
Night sweats
More hot or sweaty during the day (eg, hot flashes)
Hot flashes, night sweats
Dry mouth
Dry mouth
Pain or stiffness in joints
Pain or stiffness in muscles
Joint pain or muscle stiffness
Difficulty falling asleep
Difficulty staying asleep
Sleep problems
Difficulties concentrating
Cognitive difficulties
Pain in stomach or abdomen*
Pain in stomach or abdomen[1]
Pain at the injection site
Tenderness at the injection site
Redness at the injection site
Firmness at the injection site
Swelling at the injection site
Injection site reaction
Loss of muscle mass
Loss of muscle mass
Weight gain
Weight gain
Symptoms
Difficulty being physically active
Physically drained
Adjustments to exercise
Symptoms of hormonal-based treatment impact ability to sleep
Physical impacts
Feel depressed
Feel anxious
Feel self-conscious about appearance
Feel less masculine
Emotional/mental impacts
Reduced ability to socially engage with friends or family
Ability to work negatively impacted
Social impacts**
Ability to do work around the house (eg, daily chores) negatively impacted
Impacts on activities of daily living**
Reduced engagement in sexual activity of any kind
Reduced intimacy with spouse or partner
Negative effects on relationship with spouse or partner
Partner relationship impacts
Impacts

*Symptom added based on clinician input.
**Social impacts and impacts on daily living were added based on patient feedback (not probed).

Conclusions

- The CE interviews provided rich qualitative data from men with prostate cancer on their ADT-related symptom and impact experiences.
- The findings were used to draft a de novo PRO tool focusing on the patient-relevant symptoms and impacts of hormonal-based treatments for prostate cancer, which will be debriefed in further interviews.

References

1. Perlmutter MA, Lepor H. Androgen deprivation therapy in the treatment of advanced prostate cancer. Rev Urol. 2007;9 Suppl 1(Suppl 1):S3-S8.

Disclosures

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