

# Interpretation of Domain Scores on the EPIC—How Does the Domain Score Translate into Functional Outcomes?



Aaron A. Laviana,\* Agustin Hernandez, Li-Ching Huang, Zhiguo Zhao, Tatsuki Koyama, Ralph Conwill, Karen Hoffman, Irene D. Feuerer, Michael Goodman, Ann S. Hamilton, Xiao-Cheng Wu, Lisa E. Paddock, Antoinette Stroup, Matthew R. Cooperberg, Mia Hashibe, Brock B. O'Neil, Sherrie H. Kaplan, Sheldon Greenfield, David F. Penson and Daniel A. Barocas

From the Departments of Urology (AAL, AH, DFP, DAB), Biostatistics (L-CH, ZZ, TK, IDF) and Surgery (IDF) and Office of Patient and Community Education (RC), Patient Advocacy Program, Vanderbilt Ingram Cancer Center, Vanderbilt University Medical Center, Nashville, Tennessee, Department of Radiation Oncology, University of Texas MD Anderson Center (KH), Houston, Texas, Department of Epidemiology, Emory University Rollins School of Public Health (MG), Atlanta, Georgia, Department of Preventive Medicine, Keck School of Medicine at University of Southern California (ASH), Los Angeles, Department of Urology (MRC), University of California-San Francisco, San Francisco and Department of Medicine, University of California-Irvine (SHK, SG), Irvine, California, Department of Epidemiology, Louisiana State University New Orleans School of Public Health (X-CW), New Orleans, Louisiana, Department of Epidemiology, Cancer Institute of New Jersey, Rutgers Health (LEP, AS), New Brunswick, New Jersey, and Department of Family and Preventive Medicine, University of Utah School of Medicine (MH) and Department of Urology (BBO), University of Utah Health, Salt Lake City, Utah

### Abbreviations and Acronyms

AS = active surveillance

CEASAR = Comparative Effectiveness Analysis of Surgery and Radiation

EBRT = external beam radiotherapy

EPIC-26 = Expanded Prostate Cancer Index Composite-Short Form

MCID = minimum clinically important difference

PRO = patient reported outcome

PSA = prostate specific antigen

RALP = robot-assisted laparoscopic prostatectomy

**Purpose:** The EPIC-26 (Expanded Prostate Cancer Index Composite-Short Form) is a validated questionnaire for measuring health related quality of life. However, the relationship between domain scores and functional outcomes remains unclear, leading to potential confusion about expectations after treatment. For instance, does a sexual function domain score of 80 mean that a patient can achieve erection sufficient for intercourse? Consequently we sought to determine the relationship between the domain score and the response to obtaining the best possible outcome for each question.

**Materials and Methods:** Using data from the CEASAR (Comparative Effectiveness Analysis of Surgery and Radiation) study, a multicenter, prospective study of men diagnosed with localized prostate cancer, we analyzed 11,464 EPIC-26 questionnaires from a total of 2,563 men at baseline through 60 months of followup who were treated with robotic prostatectomy, radiotherapy or active surveillance. We dichotomized every item into its best possible outcome and assessed the percent of men at each domain score who achieved the best result.

**Results:** For every EPIC-26 item the frequency of the best possible outcome was reported by domain score category. For example, a score of 80 to 100 on sexual function corresponded to 97% of men reporting erections sufficient for

Accepted for publication June 5, 2019.

The corresponding author certifies that, when applicable, a statement(s) has been included in the manuscript documenting institutional review board, ethics committee or ethical review board study approval; principles of Helsinki Declaration were followed in lieu of formal ethics committee approval; institutional animal care and use committee approval; all human subjects provided written informed consent with guarantees of confidentiality; IRB approved protocol number; animal approved project number.

Supported by the PCACO (Paul Calabresi Career Development Award for Clinical Oncology) K12 (NIH [National Institutes of Health] Institutional Research Career Development K12 grant mechanism) (AAL), AHRQ (Agency for Healthcare Research and Quality) Grants 1R01HS019356 and 1R01HS022640, NCATS (National Center for Advancing Translational Sciences) Grant UL1TR000011 (Vanderbilt Institute of Clinical and Translational Research), NIH and NCI (National Cancer Institute) Grant 5T32CA106183, and PCORI (Patient-Centered Outcomes Research Institute) Award CE12-11-4667.

No direct or indirect commercial, personal, academic, political, religious or ethical incentive is associated with publishing this article.

\* Correspondence: Department of Urology, Vanderbilt University Medical Center, A1302 Medical Center North, Nashville, Tennessee 37232 (telephone: 615-589-0542; FAX: 615-322-8990; e-mail: [aaron.a.laviana@vumc.org](mailto:aaron.a.laviana@vumc.org)).

**Editor's Note:** This article is the second of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 1277 and 1278.

intercourse while at a score of 40 to 60 only 28% reported adequate erections. Also, at a score of 80 to 100 on the urinary incontinence domain 93% of men reported rarely or never leaking vs 6% at a score of 61 to 80.

**Conclusions:** Our findings indicate a novel way to interpret EPIC-26 domain scores, demonstrating large variations in the percent of respondents reporting the best possible outcomes over narrow domain score differences. This information may be valuable when counseling men on treatment options.

**Key Words:** prostatic neoplasms, patient reported outcome measures, quality of life, urinary incontinence, penile erection

DESPITE continuous advances in the detection and treatment of localized prostate cancer, long-term survival remains similar among varying treatment options.<sup>1-6</sup> As a result, patients and providers have placed increasing importance on the risks of treatment and longitudinal health related quality of life outcomes.<sup>7,8</sup> Although many analyses exist, in most retrospective, cross-sectional data were used and/or they lacked baseline data, of which the latter is helpful to predict posttreatment outcomes.<sup>9-11</sup> Furthermore, score misinterpretation is frequent and clinical interpretability is often poor with physicians and patients unsure of what the scores actually mean.<sup>12</sup>

To bridge the gap between the research and clinical applicability of measuring functional outcomes the EPIC-26, a 26-item PRO questionnaire, has been frequently used to assess health related quality of life before and after prostate cancer treatment.<sup>13,14</sup> This questionnaire, which measures urinary incontinence, urinary irritation, and sexual, bowel and hormonal function, is convenient to use in practice and has good internal consistency, reliability and discriminative validity.<sup>13-15</sup> Nevertheless, although it is widely disseminated, clinical interpretation remains elusive. For example, if the sexual function domain score of a patient is 80, what is the probability of that patient achieving erection sufficient for intercourse?

In this study we analyzed the relationship between individual best item responses and the domain score for several thousand EPIC-26 questionnaires in a longitudinal cohort study of men with localized prostate cancer.<sup>16</sup> In essence, by translating these domain scores into a probabilistic outcome, eg helping patients understand the likelihood of retaining or regaining erections firm enough for intercourse, we sought to enrich patient and provider expectations with varying treatments for all clinically relevant outcomes of the EPIC-26.

## MATERIALS AND METHODS

### Analytical Cohort

The CEASAR study is a multicenter, longitudinal, prospective, population based, observational study of men diagnosed with localized prostate cancer in 2011 to 2012,

which was designed to measure the impact of contemporary treatment strategies on functional outcomes (ClinicalTrials.gov NCT0136286). The CEASAR methodology was previously described.<sup>17</sup> Briefly, study eligibility criteria included men 80 years old or younger with clinical cT1 or cT2 disease, PSA less than 50 ng/dl and no nodal involvement or metastasis on clinical evaluation who were enrolled in the study within 6 months of diagnosis and underwent RALP, EBRT or AS. Patient reported outcomes, including the EPIC-26 survey, were collected via mail survey at enrollment, and 6, 12, 36 and 60 months after enrollment. This study includes followup through September 2018. Local institutional review board approval was obtained at all sites (IRB No. 110299).

### Expanded Prostate Cancer Index Composite-Short Form

The primary outcome measure in the CEASAR study was patient reported, disease specific function as measured by the EPIC-26 questionnaire. The EPIC-26 measures sexual function, bowel function, hormone therapy side effects, urinary incontinence, and urinary irritative and obstructive symptoms. The 26 individual items have 4 to 5 response options reflecting a range of function from poor to excellent (supplementary fig. 1, <https://www.jurology.com>).

Responses to individual items are scored from 0 to 100 and the domain score is calculated as an average of scores on the questions in that domain. Thus, the domain score is a continuous scale ranging from 0 to 100 with a higher score indicating better function. In previous studies the MCID between scores was estimated, that is the change in score which would be noticeable to the patient. To aid in interpretation this noticeable change was 4 to 6 for the hormone domain, 5 to 7 for the urinary irritative domain, 6 to 9 for the urinary incontinence domain and 10 to 12 for the sexual domain.<sup>18,19</sup> Although urinary bother is part of the urinary incontinence and irritative domains, we believe that it was important to include this and so it is listed as part of the urinary irritative domain for classification purposes.

To determine the percent of men who had the best possible outcome on each question across the range of domain scores each question was dichotomized into the best outcome vs any other response. For example, we dichotomized "How would you describe the usual QUALITY of your erections over the last 4 weeks?" into the best possible response of "Firm enough for intercourse" vs any lesser response.

In addition to analyzing all 26 questions for score interpretation, we singled out key items based on clinical relevance to the patient advisory panel and the prostate

cancer health care providers on our research team. Overall pad use, leakage frequency, erection quality and whether erections were sufficient for intercourse, which were deemed the most clinically relevant questions, were subsequently assessed in more detail.

### Statistical Analysis

Patient demographic and baseline characteristics are summarized as the median and quartile for continuous variables and the frequency and percent for categorical variables. For each EPIC-26 functional item the frequency (percent) of the best possible outcome is reported by domain score category, including 0 to 20, 21 to 40, 41 to 60, 61 to 80 and 81 to 100. To translate a functional domain score into a more intuitive specific functional item we used logistic regression models from all data time points to estimate the likelihood of having the best possible outcome for each item using the functional domain score (range 0 to 100) as a continuous predictor.

To account for inclusion of the correlated data collected at multiple surveys from each participant we applied the generalized estimation equation method. To visualize the relationship of the domain score with each EPIC-26 item we plotted the logistic regression predicted probability of the best possible outcome against the corresponding domain score. The same approach was used in a sensitivity analysis estimating the likelihood of having the best 2 possible outcomes on each EPIC-26 item. We assumed that the relationship between the domain score and specific items did not change with time or by treatment and we combined the data from various surveys when fitting the logistic regression models. Statistical significance was considered at 2-sided  $p \leq 5\%$ . All analyses were done with R, version 3.5 (<https://www.R-project.org/>).

## RESULTS

### Patient Characteristics and Demographics

The parent CEASAR study accumulated 3,709 men, of whom 432 were excluded from study for failing to meet inclusion criteria. Additionally, 521 men were excluded because they underwent a treatment other than AS, EBRT or RALP, leaving 2,756 available for consideration. Of these men 2,563 (93%) completed a baseline survey and at least 1 survey thereafter and were included in the current study.

The survey response rate was 89% (2,446 participants) at 6 months, 86% (2,377) at 12 months, 78% (2,143) at 36 months and 70% (1,935) at 60 months. Thus, 11,464 EPIC-26 questionnaires were included in analysis (fig. 1). Table 1 lists descriptive characteristics of the overall cohort. Median age in quartiles at enrollment was 64 years (58, 69) and 1,884 men (74%) were white. Disease was D'Amico low, intermediate and high risk in 1,151 (45%), 988 (39%) and 418 men (16%), respectively, and PSA was 4 to 10 ng/ml in 1,693 (66%).

Table 2 summarizes patient responses to the best possible outcome on each question at baseline, and

at 6, 12, 36 and 60 months. Table 3 details the percent of men in each domain score stratum who reported the best possible outcome. As domain scores improved so did the percent of men who reported the best possible outcome. Figure 2 shows these relationships. Each curve illustrates the relationship between the individual item and the domain score, and demonstrates the distinct kinetics with different degrees of elasticity shown by every question. The most elastic areas were those in which a small change in the domain score was associated with the greatest difference in the proportion of men who reported the best response to an individual item. None of these curves demonstrated linear kinetics and further details on these most clinically relevant domain trends are provided.

On sensitivity analysis to estimate the likelihood of having the best 2 possible outcomes on each question the results mirrored those of the primary analysis (supplementary fig. 2, <https://www.jurology.com>).

### Urinary Incontinence

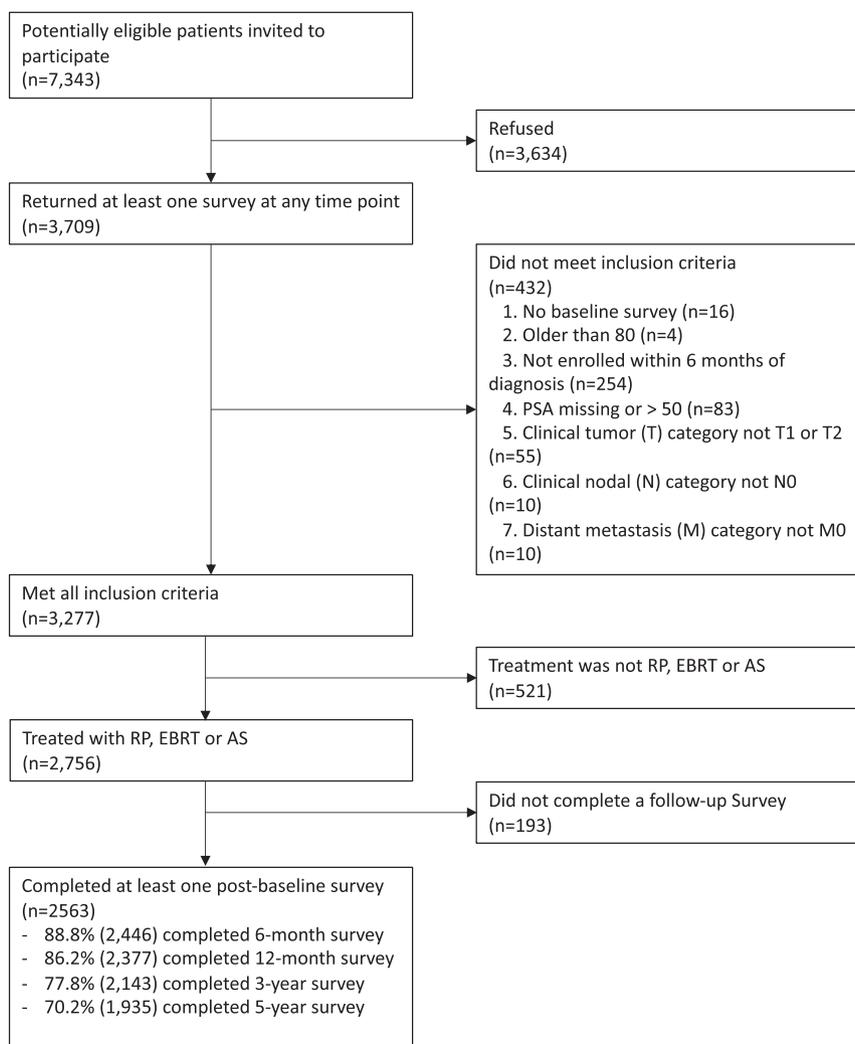
In the urinary incontinence domain the 2 items which we considered most clinically relevant had distinct relationships with the domain score. At a domain score between 41 and 60, 1% of patients reported rarely or never leaking, and between 61 and 80 only 6% reported being dry. However, 93% of men reported being dry between scores 81 and 100 (table 3). This relationship was represented by a steep, narrow and right shifted curve (fig. 2, A). In contrast, the need for pads was most elastic between domain scores of 40 to 80 with 27% of respondents reporting no pad use at a score between 41 and 60 vs 89% at 61 and 80. Above a domain score of 80 pad use was rarely reported. This curve was notably more shifted to the left and more broadly based than the question pertaining to leakage (fig. 2, A).

### Urinary Bother

Question 5 on the EPIC-26 pertains to urinary bother. This curve was notably right shifted and even at domain scores of 81 to 100 only 58% of men reported having no problem with urination overall. This decreased to 8% for domain scores of 61 to 80.

### Sexual Function

We dichotomized the quality of erections category into firm enough for intercourse vs any lesser response. With a score between 41 and 60 on the sexual domain score only 28% of patients reported erections sufficient for intercourse. Further, when the sexual domain score was 61 to 80 erections sufficient for intercourse were reported by 72% of patients vs 97% at scores of 81 to 100. The greatest elasticity was noted between a sexual domain



**Figure 1.** CEASAR study analytical cohort with 5-year data. *RP*, radical prostatectomy.

score of 40 and 80 (fig. 2, *D*). In contrast, when analyzing the overall sexual function item (EPIC-26 question 11), the curve was more shifted to the right with a steep change in elasticity between scores 81 to 100. Scores less than 80 were highly indicative of poor sexual function with only 55% and 2% of men reporting very good overall sexual function at scores of 61 to 80 and 41 to 60, respectively.

## DISCUSSION

As we continue to emphasize the need for shared decision making, it is essential that providers and patients alike have accurate information on outcomes.<sup>20,21</sup> While the main CEASAR study provided high quality data on the comparative harms of different treatments of localized prostate cancer based on the EPIC-26 domain scores, the current study provides a means to interpret these domain scores for application in clinical practice.

Overall our study has many areas of clinical significance and it is important for several reasons. 1) These findings allow us to better counsel men with newly diagnosed, localized prostate cancer by detailing the realistic probabilities of being impotent or needing pads when undergoing treatment. The current study makes this information more clinically useful by enabling the translation of domain scores into relevant functional outcomes which are easy to interpret. For example, using our previous 3-year CEASAR data we found an adjusted mean score difference of  $-16.2$  in the sexual function score for RALP vs AS.<sup>16</sup> If the preoperative sexual function domain score of a patient was 100, we can say that if the score remains between 81 and 100, 97% of men in that range could achieve erection sufficient for intercourse vs only 72% with a score of 61 to 80. The development of further predictive models is currently under way.

2) This study demonstrates that the probability distributions of functional outcomes are nonlinear

**Table 1.** Patient demographics and baseline characteristics in CEASAR study from 2011 to 2012

No. pts	2,563	
Median age at diagnosis (IQR)	64 (58–69)	
No. race (%):		
White	1,884	(74)
Black	359	(14)
Hispanic	187	(7)
Asian	80	(3)
Other	37	(1)
No. education (%):		
Less than high school	250	(10)
High school graduate	500	(21)
Some college	533	(22)
College graduate	562	(23)
Graduate or professional school	588	(24)
No. marital status (%):		
Not married	474	(20)
Married	1,953	(80)
No. TIBI (Total Illness Burden Comorbidity) score (%):		
0–2	690	(28)
3–4	1,024	(42)
5 or Greater	731	(30)
No. D'Amico prostate Ca risk (%):		
Low	1,151	(45)
Intermediate	988	(39)
High	418	(16)
No. ng/ml PSA (%):		
0—Less than 4	529	(21)
4—Less than 10	1,693	(66)
10—Less than 20	257	(10)
20–50	84	(3)
No. clinical stage (%):		
T1	1,943	(76)
T2	609	(24)
No. biopsy Gleason score (%):		
6 or less	1,331	(52)
3 + 4	707	(28)
4 + 3	264	(10)
8,9,10	253	(10)
No. any yr 1 hormone therapy (%):		
No	2,157	(86)
Yes	346	(14)
No. accrual site (%):		
Louisiana	725	(28)
Utah	206	(8)
Atlanta	309	(12)
Los Angeles County, CA	731	(29)
New Jersey	411	(16)
CaPSURE™ (Cancer of the Prostate Strategic Urologic Research Endeavor)	181	(7)

(table 3 and fig. 2). When viewed according to dichotomous functional outcomes (eg pads—yes/no or erections firm enough for intercourse—yes/no), one can see that the MCID has a varying effect on function depending on the domain score. For example, a decrease from 81 to 100 to a score of 61 to 80 on the urinary irritative domain corresponds to a 52% and 2% chance, respectively, of reporting no urination frequency while a similar decrease in sexual function corresponds to a 97% and 72% chance, respectively, of achieving erection sufficient for intercourse. As a result these data suggest that the MCID depends on and varies along the continuum of starting domain scores rather than being fixed.<sup>18</sup>

3) The EPIC-26 domain scores are psychometrically validated. This tool is invaluable for comparing the functional outcomes of different treatment options and studying the trajectory of functional outcomes with time. Nevertheless, a numerical domain score may be difficult for patients and providers alike to interpret.<sup>18,22,23</sup> Fortunately this instrument comprises easily interpretable items which may better resonate with the patient actual experiences of side effects. For example, previous groups have attempted to define potency as a sexual function domain score greater than 60 and very potent as a score greater than 80.<sup>24</sup> Nevertheless, at a sexual function domain score between 61 to 80 our data show that only 2% of patients reported very good erections and 29% reported achieving erection when they wanted. We believe that the ability to make these data more granular helps better define expectations after treatment.

Our study demonstrates that each individual item has a unique relationship or kinetic with the domain score. Thus, the domain score can be translated into a likelihood of retaining or regaining specific functional capabilities in a way that the patient and the provider can understand. We understand that the individual items and the domain score are highly associated but our primary objective enabled the individual items to have improved clinical interpretability, which may be more meaningful to the patient than the generalized domain scores themselves. Furthermore, robust data suggest that PROs correlate with improved clinical care,<sup>25,26</sup> increased referrals<sup>27</sup> and improved care processes.<sup>28</sup> Continuing to improve our understanding of PROs will hopefully only improve these stated benefits.<sup>29</sup>

Our study is not without limitations. 1) Our data analysis does not consider PROs from time points other than those studied and it does not distinguish among treatment types. Nevertheless, given the large sample size, prolonged followup and range of treatments provided, we strongly believe that this encapsulates most patients with localized disease. Furthermore, while treatment type affects the domain score,<sup>16</sup> scoring is the same regardless of treatment. A score of 60 on sexual function has the same meaning regardless of whether a patient underwent AS, EBRT or RALP. We also assume that the EPIC domain scores are the same regardless of time point.

2) Item dichotomization at the highest level may not represent the entire spectrum of patient expectation and some patients may consider other cutoff points clinically meaningful. For example, erection sufficient for foreplay instead of intercourse may be highly relevant for some patients.

**Table 2. Patient choice on each EPIC-26 item collected at every survey from baseline through 5 years**

EPIC-26 Item No./Question (pt choice)	Survey Time % (No. pts)					
	Baseline 100 (2,563)	6 Mos 100 (2,446)	1 Yr 100 (2,377)	3 Yrs 100 (2,143)	5 Yrs 100 (1,935)	Overall 100 (11,464)
<i>Urinary incontinence</i>						
1/Rarely or never leaks:						
Yes	73 (1,809)	47 (1,155)	50 (1,150)	48 (1,026)	48 (918)	54 (6,058)
No	27 (681)	53 (1,282)	50 (1,156)	52 (1,093)	52 (993)	46 (5,205)
2/Total urinary control:						
Yes	66 (1,644)	43 (1,042)	44 (1,038)	41 (867)	40 (762)	47 (5,353)
No	34 (851)	57 (1,393)	56 (1,314)	59 (1,254)	60 (1,154)	53 (5,966)
3/No pads:						
Yes	92 (2,297)	71 (1,733)	77 (1,808)	78 (1,668)	76 (1,464)	79 (8,970)
No	8 (196)	29 (702)	23 (550)	22 (463)	24 (451)	21 (2,362)
4a/No problem with dripping:						
Yes	70 (1,752)	46 (1,126)	48 (1,139)	49 (1,041)	47 (904)	53 (5,962)
No	30 (750)	54 (1,311)	52 (1,213)	51 (1,078)	53 (1,009)	47 (5,361)
<i>Urinary irritative</i>						
4b/No pain or burning with urination:						
Yes	83 (2,062)	89 (2,152)	89 (2,091)	92 (1,952)	93 (1,772)	89 (10,029)
No	17 (434)	11 (278)	11 (263)	8 (175)	7 (141)	11 (1,291)
4c/No bleeding with urination:						
Yes	93 (2,303)	98 (2,354)	98 (2,287)	97 (2,047)	98 (1,853)	97 (10,844)
No	7 (175)	2 (57)	2 (57)	3 (59)	2 (42)	3 (390)
4d/No weak stream or incomplete emptying:						
Yes	46 (1,163)	60 (1,468)	61 (1,433)	62 (1,313)	61 (1,166)	58 (6,535)
No	54 (1,340)	40 (978)	39 (918)	38 (816)	39 (747)	42 (4,799)
4e/No frequency of urination:						
Yes	37 (930)	39 (945)	41 (966)	45 (959)	44 (849)	41 (4,649)
No	63 (1,572)	61 (1,487)	59 (1,398)	55 (1,181)	56 (1,072)	59 (6,691)
5/Overall, no problem with urinary function:						
Yes	50 (1,223)	42 (1,009)	46 (1,071)	49 (1,046)	48 (917)	47 (5,266)
No	50 (1,242)	58 (1,414)	54 (1,247)	51 (1,083)	52 (998)	53 (5,984)
<i>Bowel function</i>						
6a/No rectal urgency:						
Yes	77 (1,927)	75 (1,837)	72 (1,699)	74 (1,583)	72 (1,379)	74 (8,425)
No	23 (580)	25 (599)	28 (664)	26 (549)	28 (536)	26 (2,928)
6b/No bowel frequency:						
Yes	82 (2,047)	80 (1,943)	80 (1,894)	83 (1,755)	81 (1,555)	81 (9,194)
No	18 (457)	20 (487)	20 (465)	17 (368)	19 (353)	19 (2,130)
6c/No fecal incontinence:						
Yes	93 (2,332)	91 (2,207)	90 (2,124)	90 (1,901)	89 (1,706)	91 (10,270)
No	7 (174)	9 (220)	10 (225)	10 (218)	11 (203)	9 (1,040)
6d/No bloody stools:						
Yes	95 (2,389)	96 (2,330)	95 (2,245)	94 (2,005)	96 (1,834)	95 (10,803)
No	5 (113)	4 (101)	5 (117)	6 (125)	4 (80)	5 (536)
6e/No pain with bowel movements:						
Yes	84 (2,097)	88 (2,135)	87 (2,050)	89 (1,903)	89 (1,711)	87 (9,896)
No	16 (409)	12 (296)	13 (305)	11 (228)	11 (202)	13 (1,440)
7/No problems with bowel function:						
Yes	79 (1,964)	75 (1,832)	75 (1,754)	75 (1,597)	76 (1,470)	76 (8,597)
No	21 (527)	25 (600)	25 (594)	25 (535)	24 (465)	24 (2,721)
<i>Sexual function</i>						
8a/Very good erections:						
Yes	24 (582)	7 (175)	8 (188)	9 (192)	9 (168)	12 (1,305)
No	76 (1,854)	93 (2,192)	92 (2,076)	91 (1,887)	91 (1,714)	88 (9,723)
8b/Very good orgasm:						
Yes	29 (709)	13 (306)	14 (330)	16 (329)	15 (289)	18 (1,963)
No	71 (1,733)	87 (2,052)	86 (1,966)	84 (1,741)	85 (1,579)	82 (9,071)
9/Erections firm enough for intercourse:						
Yes	56 (1,380)	28 (669)	32 (739)	33 (689)	32 (598)	37 (4,075)
No	44 (1,066)	72 (1,698)	68 (1,569)	67 (1,389)	68 (1,272)	63 (6,994)
10/Erections whenever desired:						
Yes	40 (973)	18 (419)	20 (467)	22 (457)	23 (417)	25 (2,733)
No	60 (1,450)	82 (1,914)	80 (1,832)	78 (1,596)	77 (1,428)	75 (8,220)
11/Very good sexual function:						
Yes	22 (541)	8 (178)	9 (206)	10 (206)	10 (185)	12 (1,316)
No	78 (1,885)	92 (2,153)	91 (2,082)	90 (1,857)	90 (1,678)	88 (9,655)
<i>Hormonal</i>						
13a/No hot flashes:						
Yes	89 (2,195)	85 (2,034)	86 (2,004)	90 (1,885)	91 (1,724)	88 (9,842)
No	11 (273)	15 (361)	14 (332)	10 (214)	9 (169)	12 (1,349)

(continued)

**Table 2.** (continued)

EPIC-26 Item No./Question (pt choice)	Survey Time % (No. pts)					Overall 100 (11,464)
	Baseline 100 (2,563)	6 Mos 100 (2,446)	1 Yr 100 (2,377)	3 Yrs 100 (2,143)	5 Yrs 100 (1,935)	
13b/No breast tenderness:						
Yes	96 (2,335)	97 (2,275)	94 (2,160)	95 (1,969)	96 (1,797)	96 (10,536)
No	4 (88)	3 (81)	6 (140)	5 (105)	4 (73)	4 (487)
13c/No problem with depression:						
Yes	64 (1,581)	67 (1,609)	65 (1,518)	68 (1,417)	68 (1,282)	66 (7,407)
No	36 (881)	33 (786)	35 (800)	32 (677)	32 (609)	34 (3,753)
13d/No problem with low energy:						
Yes	50 (1,247)	52 (1,236)	46 (1,085)	52 (1,089)	51 (971)	50 (5,628)
No	50 (1,231)	48 (1,164)	54 (1,251)	48 (1,022)	49 (924)	50 (5,592)
1e/No change in body wt:						
Yes	77 (1,913)	74 (1,767)	71 (1,656)	75 (1,569)	74 (1,394)	74 (8,299)
No	23 (563)	26 (630)	29 (685)	25 (533)	26 (502)	26 (2,913)

Further analysis with additional cutoff points would be needed to determine this. With that said, our sensitivity analysis incorporates the best 2 answers on each question and shows results comparable to those of our primary analysis, supporting our methodology.

3) These results have not been externally validated. Nevertheless, the longitudinal, population based design, the diverse cohort and the focus on contemporary treatments in the CEASAR study

provide a representative data set for this type of analysis.<sup>16</sup>

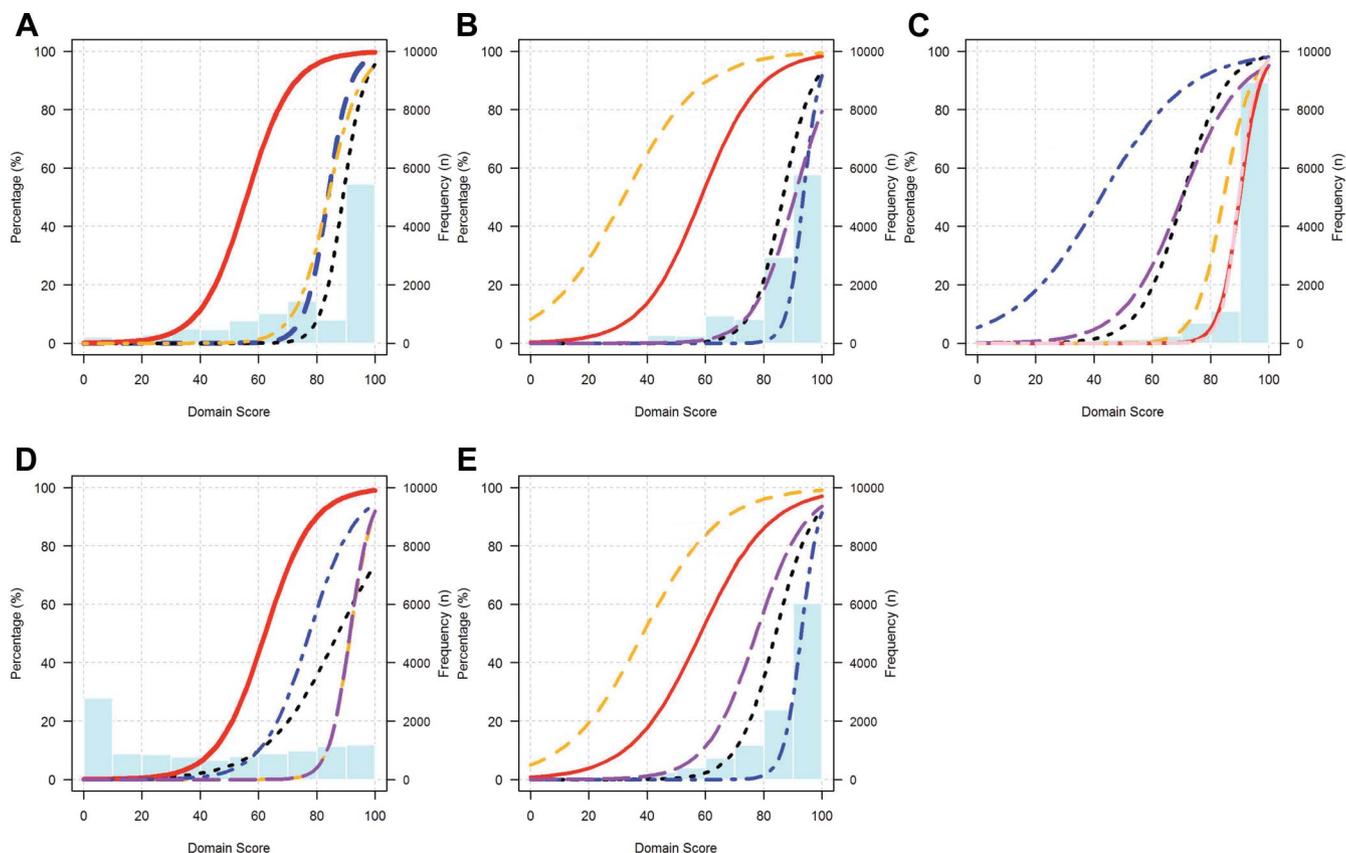
## CONCLUSIONS

The EPIC-26 provides a validated means to compare functional outcomes across treatments and with time. Nevertheless, interpreting domain scores can be challenging for patients and providers. In this study we sought to translate domain scores into

**Table 3.** Patient choice on each EPIC-26 item at 5-year survey by corresponding domain score category

EPIC-26 Item (No./question)	Domain Score % (No. pts)					Combined
	0–20	21–40	41–60	61–80	81–100	
Urinary incontinence:	100 (384)	100 (781)	100 (1,251)	100 (2,466)	100 (6,263)	100 (11,145)
1/Rarely or never leaks	0	0 (1)	1 (10)	6 (160)	93 (5,833)	54 (6,004)
2/Total urinary control	0	0 (1)	1 (12)	5 (114)	82 (5,162)	47 (5,289)
3/No pads	0	9 (70)	27 (333)	89 (2,207)	99 (6,213)	79 (8,823)
4a/No problem with dripping	0	1 (8)	4 (45)	14 (343)	88 (5,482)	53 (5,878)
Urinary irritative:	100 (38)	100 (112)	100 (524)	100 (1,760)	100 (8,728)	100 (11,162)
4b/No pain or burning with urination	0	2 (2)	39 (206)	74 (1,310)	96 (8,382)	89 (9,900)
4c/No bleeding with urination	0	59 (66)	84 (439)	93 (1,643)	99 (8,636)	97 (10,784)
4d/No weak stream or incomplete emptying	0	2 (2)	2 (9)	9 (160)	72 (6,296)	58 (6,467)
4e/No frequency of urination	0	0	1 (3)	2 (39)	52 (4,557)	41 (4,599)
5/Overall no problem with urinary function	5 (2)	1 (1)	2 (10)	8 (138)	58 (5,043)	47 (5,266)
Bowel function:	100 (22)	100 (88)	100 (256)	100 (940)	100 (10,031)	100 (11,337)
6a/No rectal urgency	0	0	2 (6)	9 (88)	83 (8,313)	74 (8,407)
6b/No bowel frequency	0	1 (1)	7 (18)	20 (187)	90 (8,986)	81 (9,192)
6c/No fecal incontinence	0	7 (6)	23 (57)	56 (519)	97 (9,684)	91 (10,266)
6d/No bloody stools	10 (2)	51 (44)	74 (188)	84 (787)	97 (9,772)	95 (10,793)
6e/No pain with bowel movements	0	17 (15)	39 (98)	53 (497)	93 (9,277)	87 (9,887)
7/No problems with bowel function	10 (2)	2 (2)	2 (4)	6 (54)	85 (8,515)	76 (8,577)
Sexual function:	100 (3,678)	100 (1,643)	100 (1,462)	100 (1,871)	100 (2,321)	100 (10,975)
8a/Very good erections	0	0 (6)	1 (9)	2 (43)	54 (1,236)	12 (1,294)
8b/Very good orgasm	1 (42)	4 (67)	6 (92)	14 (268)	64 (1,484)	18 (1,953)
9/Erections firm enough for intercourse	0 (2)	3 (51)	28 (405)	72 (1,339)	97 (2,257)	37 (4,054)
10/Erections whenever desired	0 (3)	2 (26)	6 (82)	29 (533)	90 (2,079)	25 (2,723)
11/Very good sexual function	0 (3)	0 (1)	1 (11)	2 (37)	55 (1,259)	12 (1,311)
Hormonal:	100 (31)	100 (145)	100 (635)	100 (1,914)	100 (8,430)	100 (11,155)
13a/No hot flashes	3 (1)	20 (29)	50 (318)	73 (1,406)	96 (8,057)	88 (9,811)
13b/No breast tenderness	6 (2)	57 (75)	79 (489)	91 (1,703)	99 (8,258)	96 (10,527)
13c/No problem with depression	0	1 (1)	8 (53)	25 (483)	81 (6,825)	66 (7,362)
13d/No problem with low energy	0	0	1 (9)	5 (105)	65 (5,480)	50 (5,594)
13e/No change in body wt	0	5 (7)	18 (11)	41 (786)	87 (7,348)	74 (8,252)

Each patient choice was yes.



**Figure 2.** EPIC-26 domain scores and dichotomized best possible outcomes of each question in that domain. *n*, number. Curves indicate relationship of domain score to percent of men who reported best possible outcome at that score. Light blue curve indicates number of men reporting in each domain interval. **A**, urinary incontinence. Dark blue curve indicates question 1 (rarely or never leaks). Black curve indicates question 2 (total urinary control). Red curve indicates question 3 (no pads). Yellow curve indicates question 4a (no dripping problem). **B**, urinary irritative. Red curve indicates question 4b (no pain or burning with urination). Yellow curve indicates question 4c (no bleeding with urination). Black curve indicates question 4d (no weak stream or incomplete emptying). Dark blue curve indicates question 4e (no frequent urination). Purple curve indicates question 5 (overall no problem with urinary function), which was included in this domain for classification but not used to calculate overall urinary irritative domain score. **C**, bowel function. Red curve indicates question 6a (no rectal urgency). Yellow curve indicates question 6b (no bowel frequency). Black curve indicates question 6c (no fecal incontinence). Dark blue curve indicates question 6d (no bloody stools). Purple curve indicates question 6e (no pain with bowel movement). Pink curve indicates question 7 (no bowel function problems). **D**, sexual function. Yellow curve indicates question 8a (very good erections). Black curve indicates question 8b (very good orgasm). Red curve indicates question 9 (erections firm enough for intercourse). Dark blue curve indicates question 10 (erections whenever desired). Purple curve indicates question 11 (very good sexual function). **E**, hormonal function. Red curve indicates question 13a (no hot flashes). Yellow curve indicates question 13b (no breast tenderness). Black curve indicates question 13c (no depression problem). Dark blue curve indicates question 13d (no low energy problem). Purple curve indicates question 13e (no body weight change).

the probability of obtaining pertinent outcomes, such as the need for incontinence pads or achieving erections sufficient for intercourse, highlighting that the percent of patients who report the best

possible outcomes varies widely over narrow domain score differences. This information may be valuable when counseling men on treatment options.

## REFERENCES

1. Albertsen PC, Hanley JA, Fine J et al: 20-year outcomes following conservative management of clinically localized prostate cancer. *JAMA* 2005; **293**: 2095.
2. Fenton JJ, Weyrich MS, Durbin S et al: Prostate-specific antigen-based screening for prostate cancer. Evidence report and systematic review for the US Preventive Services Task Force. *JAMA* 2018; **319**: 1914.
3. Eiffler JB, Alvarez J, Koyama T et al: More judicious use of expectant management for localized prostate cancer during the last 2 decades. *J Urol* 2017; **197**: 614.
4. Weiner AB and Kundu SD: Prostate cancer: a contemporary approach to treatment and outcomes. *Med Clin North Am* 2018; **102**: 215.
5. Wilt TJ, Jones KM, Barry MJ et al: Follow-up of prostatectomy versus observation for early prostate cancer. *N Engl J Med* 2017; **377**: 132.

6. Hamdy FC, Donovan JL, Lane JA et al: 10-year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. *N Engl J Med* 2016; **375**: 1415.
7. Litwin MS, Gore JL, Kwan L et al: Quality of life after surgery, external beam irradiation, or brachytherapy for early-stage prostate cancer. *Cancer* 2007; **11**: 2239.
8. Reeve BB, Wang M, Weinfurt K et al: Psychometric evaluation of PROMIS sexual function and satisfaction measures in a longitudinal population-based cohort of men with localized prostate cancer. *J Sex Med* 2018; **15**: 1792.
9. Stanford JL, Feng Z, Hamilton AS et al: Urinary and sexual function after radical prostatectomy for clinically localized prostate cancer: the Prostate Cancer Outcomes Study. *JAMA* 2000; **283**: 354.
10. Sanda MG, Dunn RL, Michalski J et al: Quality of life and satisfaction with outcome among prostate-cancer survivors. *N Engl J Med* 2008; **358**: 1250.
11. Tyson MD, Koyama T, Lee D et al: Effect of prostate cancer severity on functional outcomes after localized treatment: comparative effectiveness analysis of surgery and radiation study results. *Eur Urol* 2018; **74**: 26.
12. Chipman JJ, Sanda MG, Dunn RL et al: Measuring and predicting prostate cancer related quality of life changes using the Expanded Prostate Cancer Index Composite for Clinical Practice (EPIC-CP). *J Urol* 2014; **191**: 638.
13. Wei JT, Dunn RL, Litwin MS et al: Development and validation of the Expanded Prostate Cancer Index Composite (EPIC) for comprehensive assessment of health-related quality of life in men with prostate cancer. *Urology* 2000; **56**: 899.
14. Szymanski KM, Wei JT, Dunn RL et al: Development and validation of an abbreviated version of the Expanded Prostate Cancer Index Composite instrument for measuring health-related quality of life among prostate cancer survivors. *Urology* 2010; **76**: 1245.
15. Chang P, Szymanski KM, Dunn RL et al: Expanded Prostate Cancer Index Composite for Clinical Practice: development and validation of a practical health related quality of life instrument for use in routine clinical care of patients with prostate cancer. *J Urol* 2011; **186**: 865.
16. Barocas DA, Alvarez J and Resnick MJ: Association between radiation therapy, surgery, or observation for localized prostate cancer and patient-reported outcomes after 3 years. *JAMA* 2017; **317**: 1126.
17. Barocas DA, Chen V, Cooperberg M et al: Using a population-based observational cohort study to address difficult comparative effectiveness research questions: the CEASAR study. *J Comp Eff Res* 2013; **2**: 445.
18. Skolarus TA, Dunn RL, Sanda MG et al: Minimally important differences for the Expanded Prostate Cancer Index Composite Short Form. *Urology* 2015; **85**: 101.
19. Ellison JS, He C and Wood DP: Stratification of post-prostatectomy urinary function using Expanded Prostate Cancer Index Composite. *Urology* 2013; **81**: 56.
20. Protopapa E, Meulen JVD, Moore C et al: Patient-reported outcome (PRO) questionnaires for men who have radical surgery for prostate cancer: a conceptual review of existing instruments. *BJU Int* 2017; **129**: 468.
21. Unger JM, Vaidya R, Gore JL et al: Key design and analysis principles for quality of life and patient-reported outcomes in clinical trials. *Urol Oncol* 2019; **37**: 324.
22. Resnick MK, Barocas DA, Morgans AK et al: The evolution of self-reported urinary and sexual dysfunction over the last two decades: implications for comparative effectiveness research. *Eur Urol* 2015; **67**: 1019.
23. Resnick MJ, Barocas DA, Morgans AK et al: Contemporary prevalence of pretreatment urinary, sexual, hormonal and bowel dysfunction. Defining the population at risk for harms of prostate cancer treatment. *Cancer* 2014; **120**: 1263.
24. Schroeck FR, Donatucci CF, Smathers EC et al: Defining potency: a comparison of the International Index of Erectile Function short version and the Expanded Prostate Cancer Index Composite. *Cancer* 2008; **113**: 2687.
25. Gerhardt WE, Mara CA, Kudel I et al: System-wide implementation of patient-reported outcomes in routine clinical care at a children's hospital. *Joint Comm J Qual Patient Saf* 2018; **44**: 441.
26. Detmar SB, Martin MJ, Schornagel JH et al: Health-related quality-of-life assessment and patient-physician communication: a randomized controlled trial. *JAMA* 2002; **288**: 3027.
27. Espallargues M, Valderas JM and Alonso J: Provision of feedback on perceived health status to health care professionals: a systematic review of its impact. *Med Care* 2000; **38**: 175.
28. Geenhalgh J and Meadows K: The effectiveness of the use of patient-based measures of health in routine practice in improving the process and outcome of patient-care: a literature review. *J Eval Clin Pract* 1999; **5**: 401.
29. Knaup C, Koesters M, Schoefer D et al: Effect of feedback of treatment outcome in specialist mental healthcare; meta-analysis. *Br J Psychiatry* 2009; **195**: 15.