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### Authors

Punnen, Sanoj  
Cooperberg, Matthew R  
Sadetsky, Natalia  
[et al.](#)

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## Among potent men post radical prostatectomy, does the need for phosphodiesterase inhibitors have an impact on sexual bother scores?

**Sanoj Punnen, Matthew R. Cooperberg, Natalia Sadetsky, and Peter R. Carroll**

Department of Urology, UCSF Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, CA, USA

### Abstract

- To determine whether the current definition of potency, inclusive of phosphodiesterase inhibitor (PDEi) use, is valid with respect to sexual bother (SB). This will be assessed by characterizing the effect of PDEi use on SB scores in men who are potent post radical prostatectomy.
- The study population consisted of patients who were potent both before and after radical prostatectomy, with at least 2 years of follow-up.
- Disease-specific quality of life data were evaluated by the University of California, Los Angeles, Prostate Cancer Index (PCI) survey.
- The relationships between changes in sexual function (SF) and SB and use of PDEi over time were evaluated by mixed model analysis controlling for age, clinical risk group, marital status, and time of PCI assessment.
- Of the 246 patients who met the study criteria, 39% reported PDEi use at some point after treatment.
- PDEi use was not associated with improved SF ( $P = 0.81$ ).
- Furthermore, PDEi use was not associated with a change in SB ( $P = 0.36$ ).
- Both SF and SB were significantly associated with time of assessment and age, and SF and SB each improved over time.
- In addition, SB was significantly associated with marital status.
- In this analysis, there was no difference in SF scores between men who were potent with or without the use of PDEi.
- Furthermore, there was no difference in SB scores between men who were potent with or without the use of PDEi.
- This suggests that the current, inclusive, definition of potency is valid with respect to SB.

### Keywords

radical prostatectomy; phosphodiesterase inhibitors; sexual bother; CaPSURE

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Correspondence: Sanoj Punnen, University of California, San Francisco, Department of Urology, 1600 Divisadero St, Box 1695, San Francisco, CA 94143-1695, USA. PunnenSP@urology.ucsf.edu.

### CONFLICT OF INTEREST

None declared.

## INTRODUCTION

For men with localized prostate cancer, radical prostatectomy achieves excellent cancer control [1,2]. However, surgery is known to impact sexual function (SF) and sexual bother (SB) [3–6]. The use of phosphodiesterase inhibitors (PDEi) improves SF – specifically erectile function – in patients after surgery for prostate cancer [7,8]. Potency following surgery is most commonly defined as having erections sufficient for intercourse with or without the use of PDEi [9]. However, this definition – inclusive of medication use – does not consider the extent to which men who are potent after surgery with the use of PDEi may be bothered by having to take a medication.

Previous studies have suggested a complex relationship between SF and SB, with findings of inconsistent correlation between the two domains [10–12]. For example, a recent study showed that even men with good erectile function post surgery were troubled by their broader sexual outcomes, resulting in worsening SB and quality of life [11]. Therefore, it may not be sufficient to assume patients with good erections post radical prostatectomy have no SB.

More than half of patients typically use PDEi to improve their SF post surgery [13–15]. However, no study has assessed whether the use of PDEi in potent men affects SB. Without knowing the impact of PDEi use on SB in potent men, we cannot assume that the current definition of potency, inclusive of PDEi use, is valid with respect to SB. Therefore, this study aimed to characterize the effect of PDEi use on SF and SB scores in men who were potent before and following prostatectomy in a large national prostate cancer registry.

## PATIENTS AND METHODS

The Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE™) is a national cancer registry accruing men with biopsy-proven prostate cancer from 40 primarily community-based urology practices across the USA. Men are recruited, by participating urologists, at the time of prostate cancer diagnosis and initial and follow-up clinical data are reported. All patients provide written, informed consent under local and central institutional review board approval. Patients are treated as per their clinician's usual standard of practice and followed until death or withdrawal from the study. Health-related quality of life data are ascertained using self-administered questionnaires including the University of California, Los Angeles (UCLA), Prostate Cancer Index (PCI), which are mailed to patients semi-annually. Details regarding CaPSURE's methodology have been reported previously [16].

Within the CaPSURE database, men who were diagnosed with prostate cancer between 1995 and 2005 and were potent both before (without the use of PDEi) and 2 years after (with or without the use of PDEi) radical prostatectomy comprised the study population. Potency was defined as having erections sufficient for intercourse on a self-administered questionnaire (PCI). Inclusion criteria included having 2 years of follow-up post surgery, consisting of baseline and at least two assessments in the 2 years post treatment. Exclusion criteria included receiving any neoadjuvant/adjuvant or salvage therapy for prostate cancer or the use of PDEi prior to surgery. PDEi use post surgery was determined by a self-administered medication questionnaire.

The UCLA PCI is a self-administered questionnaire that measures urinary, bowel and sexual function and bother in men with prostate cancer. It is a well validated and reliable tool in the assessment of health-related quality of life and outcomes research [17–19]. SF is assessed using eight items, which address erectile function and other aspects of sexuality, and a summary score from 0 to 100 is provided. SB is assessed by one question on bother in the

previous 4 weeks and is similarly scored. Higher scores on both SF and SB relate to higher health-related quality of life in those areas.

## STATISTICAL ANALYSIS

Baseline demographic and clinical characteristics of the study population were evaluated using chi-squared analysis for categorical variables and ANOVA for continuous variables. The association of PDEi use with SB over time was analysed using a repeated measures model. This analysis was used because it takes into account the correlation of the repeated measurement of the outcome within patients and accounts for any missing variables. The repeated measures model included PDEi use, time period and an interaction between PDEi and time. The interaction term was used to determine whether SB differed after radical prostatectomy according to PDEi use. The model also included age at diagnosis, marital status, D'Amico clinical risk classification [20] and time of assessment. Although the number of comorbidities was associated with PDEi use, it was not associated with either SF or SB outcomes and was therefore not included in the model.

## RESULTS

Of the 13 000 men in the CaPSURE registry, 4589 patients had localized prostate cancer treated via surgery alone. Of these patients, 2935 men were excluded for lack of complete baseline and postoperative quality of life or medication data and 1408 men were excluded due to lack of baseline and post treatment potency. This left 246 patients who met the study criteria (Fig. 1). Within this group, 96 (39%) reported PDEi use at some point after treatment and 150 (61%) did not. Patients who used PDEi appeared to be younger and had a significantly lower number of comorbidities than those who did not use PDEi (Table 1).

In the mixed model analysis, PDEi use was not associated with improved SF. Adjusted mean (standard error) SF scores over the 24 months of follow-up for PDEi users and non-users were 58.9 (3.0) and 58.6 (3.0), respectively ( $P = 0.81$ ). SF was significantly associated with time of assessment and age at diagnosis ( $P < 0.001$ ).

PDEi use was not associated with a change in SB score. Adjusted mean (standard error) SB scores over the 24 months of follow-up for PDEi users and non-users were 76.7 (5.1) and 78.5 (5.1), respectively ( $P = 0.36$ ). SB was significantly associated with time of assessment ( $P < 0.001$ ), age at diagnosis ( $P = 0.016$ ) and marital status ( $P = 0.002$ ). Both SF and SB improved over time; however, neither outcome returned to baseline levels (Fig. 2).

## DISCUSSION

The present study evaluated 246 men in a large, community based prostate cancer registry who were potent at baseline and 2 years post radical prostatectomy, and found that PDEi use did not impact mean SF scores. More important to the objective of this study, we found that PDEi use did not appear to impact SB scores. In both PDEi users and non-users, SF and SB improved over time from surgery, but failed to return to baseline levels.

Within the study cohort, it appeared that older patients (>70 years) and patients with more comorbidities (>3) were less likely to use PDEi. It could be that older or more comorbid patients had less concern about their sexual health and therefore less interest in taking a medication for it.

Health-related quality of life after treatment for prostate cancer has been extensively studied. Surgery for prostate cancer can have a significant impact on both SF and SB outcomes. SF, on the PCI, reflects a score based on eight items assessing SF, of which four relate to erectile function. Therefore, SF scores are well correlated with potency [3,10,12]. This explains the

similarities in SF score between users and non-users in this study, since only potent men were selected. However, previous studies have illustrated a very complex relationship between SF and SB [10,12].

In a prior CaPSURE study of 5135 men treated for prostate cancer, the authors found a divergence between potent and impotent men in their SF and SB scores [12]. However, the authors stated that the large range of scores in both groups denotes a complex picture of SF and SB. It was also noted that a simple documentation of patient-reported potency, post treatment, is not a sufficient measure of health-related quality of life. The use of well validated instruments is essential. Similarly, a study of 183 men treated with radical prostatectomy found that SB worsens after surgery, even in men with good erectile function, and includes shame, embarrassment and a reduction in general life happiness [11]. This further implies that SF or potency itself may not be a surrogate for sexual-health-related quality of life in all men.

Current definitions of potency include the ability to achieve successful erections, with or without the use of PDEi [9]. The use of PDEi post radical prostatectomy has been studied extensively and is known to increase SF [7,8,21]. However, given the lack of correlation between SF and SB after surgery for prostate cancer, it should not be assumed that achieving good SF with PDEi excludes the possibility of SB. In addition, no prior study has specifically looked at the impact of PDEi use on SB in potent men post surgery for prostate cancer. The present study assessed this, and found no difference in the SB scores between PDEi users and non-users. This suggests that the use of medication to improve SF and potency did not have an impact on SB and lends support to the suggestion that the current definition of potency – with or without PDEi – is valid with respect to SB.

However, other studies have disagreed with our findings. A recent study of 620 men, post radical prostatectomy, found that men not using PDEi were twice as likely to report improved SB compared with men that were using it [10]. However, it was not clear from the study whether SB was a cause or result of men using PDEi. Similarly, another study of men who underwent radical prostatectomy showed that the use of sexual aids was associated with a two-fold worse SB and a greater risk for worsening SB [22]. However, neither of these studies set out to evaluate the difference between SB in PDEi users and non-users and the observed results were a product of sub-analysis. Furthermore, both studies involved potent and impotent men, whereas the present study included only potent men. This may explain the difference in observations as an impotent man using PDEi may be expected to have worse SB than a potent man using PDEi.

The current study found that SB was associated with age at diagnosis of prostate cancer, marital status and time of assessment since surgery. Other studies have noted similar findings [22,23] and additional associations. Within the CaPSURE database, a study of post prostatectomy men found that those with a high school education or less were more likely to have worse SB than men who were college graduates [10]. This has been verified by Knight *et al.* [24], who showed that men with less education experienced worse health-related quality of life across a wide range of domains including sexual health. This underscores the importance of patient education prior to surgery for prostate cancer and suggests that improved understanding of expectations post surgery may lead to better health-related quality of life outcomes.

The strengths of the current study were the use of a large prostate cancer registry with complete follow-up to 2 years on 246 men followed with a well validated questionnaire. However, the study has some limitations. Of the 13 000 patients in the CaPSURE data set, 4589 were treated with radical prostatectomy, of whom 3181 met the inclusion criteria of

being potent at baseline and 2 years post surgery. However, of these 3181 patients, only 246 had complete baseline and postoperative quality of life data. Therefore, there is a concern for selection bias since results apply only to those patients who responded to the quality of life questionnaire. Second, SB was assessed using the UCLA PCI. Although, the overall questionnaire has been validated in the use of health-related quality of life studies, the single question pertaining to SB has not. In addition, PDEi use was measured by responses to a self-administered medication questionnaire without verification via prescription records or patient charts. However, patients are mailed these questionnaires every 6 months and any significant misclassification of the exposure to PDEi should be apparent in the lack of consistency in repeated responses to PDEi use on the questionnaire. Finally, since CaPSURE does not contain data on the exact timing and duration of PDEi use, this study was unable to comment on this in the PDEi user group.

Potency is most commonly defined as having successful erections with or without the use of PDEi. In this analysis, there was no difference in the SB scores between men who were potent with or without the use of PDEi. This suggests that the current, inclusive, definition of potency is probably valid with respect to SB outcomes.

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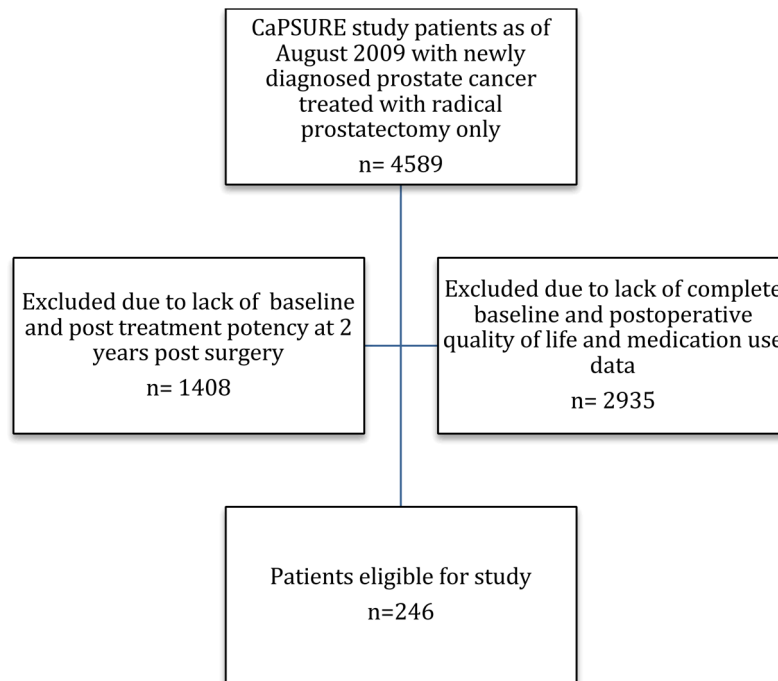
## Abbreviations

<b>SF</b>	sexual function
<b>SB</b>	sexual bother
<b>PDEi</b>	phosphodiesterase inhibitors
<b>CaPSURE</b>	Cancer of the Prostate Strategic Urologic Research Endeavor
<b>UCLA PCI</b>	University of California, Los Angeles, Prostate Cancer Index

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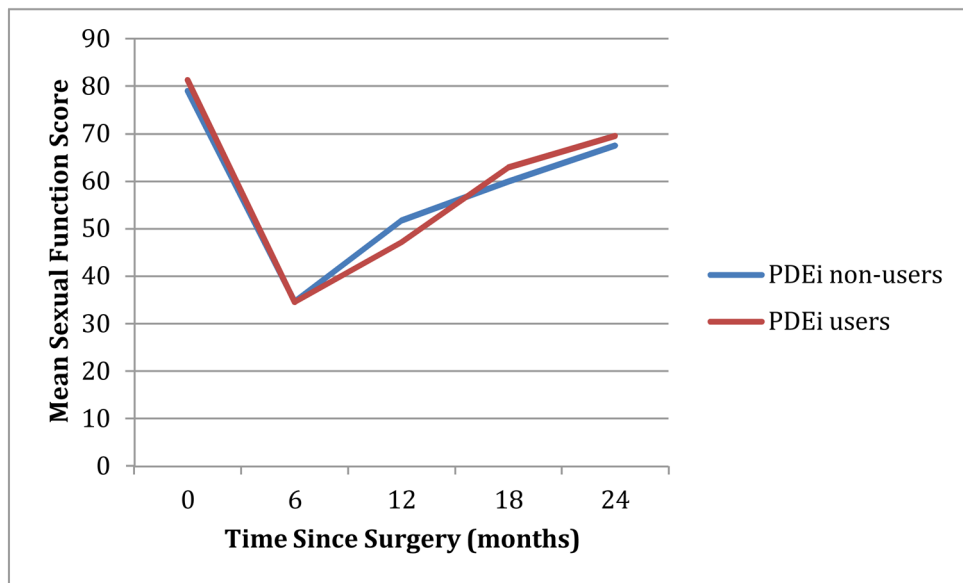
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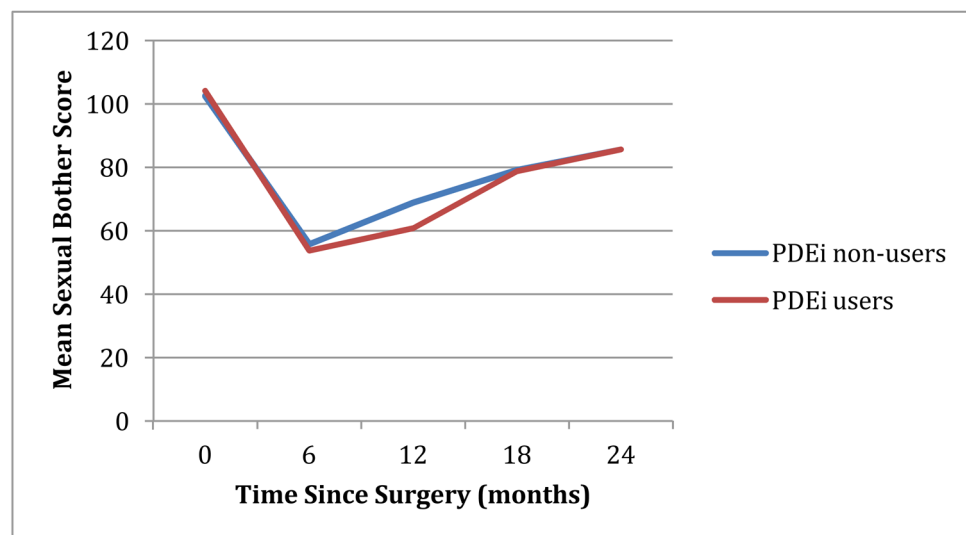


**FIG. 1.**  
Patient selection and flow chart.





(a)



(b)

**FIG. 2.** Mean SF (a) and SB (b) over 2 years in PDEi users and non-users.

**TABLE 1**

Demographic and clinical characteristics of study patients

Study characteristic	Value	No PDEi, N (%)	PDEi, N (%)	P
Age at diagnosis	<65	32 (21)	31 (32)	0.09
	65–70	84 (56)	51 (53)	
	>70	34 (23)	14 (15)	
Clinical risk	Low	86 (59)	52 (60)	0.92
	Intermediate	44 (30)	26 (30)	
	High	16 (11)	8 (9)	
Number of comorbidities	None	26 (17)	25 (26)	<0.01
	1–2	96 (64)	66 (69)	
	3	28 (19)	5 (5)	
BMI	Normal (<25.0)	36 (24)	24 (26)	0.69
	Overweight (25.0–29.9)	85 (57)	55 (59)	
	Obese (30.0–34.9)	29 (19)	14 (15)	
Race/ethnicity	AA	6 (4)	3 (3)	0.92
	White	137 (91)	88 (92)	
	Other	7 (5)	5 (5)	
Education level	<HS	8 (5)	6 (6)	0.41
	HS grad	28 (19)	13 (14)	
	Some college	30 (20)	14 (15)	
	College or grad school	84 (56)	63 (66)	
Household income	<\$50 000	45 (31)	20 (22)	0.20
	\$50 000–\$75 000	30 (21)	26 (28)	
	>\$75 000	71 (49)	47 (51)	
Relationship status	In relationship	149 (99)	95 (99)	0.75
	Single	1 (1)	1 (1)	

BMI, body mass index; AA, African American; HS, high school.