Ejaculatory Dysfunction in Patients Presenting to a Men’s Health Clinic: A Retrospective Cohort Study

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ABSTRACT

Introduction: Prevalence and bother of ejaculatory dysfunction (EjD) has yet to be evaluated in a men’s health referral population.

Aim: To evaluate the prevalence and associated risk factors of EjD in men presenting to a men’s health clinic.

Methods: A retrospective review examined patients presenting to an outpatient men’s health clinic who completed the Sexual Health Inventory for Men and the Male Sexual Health Questionnaire Ejaculatory Dysfunction (MSHQ-EjD) Short Form. Patient factors including demographics, comorbidities, and medication were examined. Descriptive statistics and multivariable logistic regression were used.

Main Outcome Measures: The main outcomes of this study are Sexual Health Inventory for Men and MSHQ-EjD scores.

Results: A total of 63 (24%) of patients presenting to the urology clinic were characterized as having EjD based on questionnaire responses. The mean age for men with EjD was 53.8 years, while those without was 42.6 years (P < .001). Of men with EjD, 74.6% were at least moderately bothered (MSHQ-EjD ≥3). Men with EjD were more likely to have erectile dysfunction (77.8%) compared with those without (21%, P < .001) as well as a history of a pelvic cancer (20.6% vs 6%, P = .001). On multivariable regression, erectile dysfunction (odds ratio: 15.04, 95% confidence interval: 6.76–35.92, P < .0001) and alpha inhibitor prescription (odds ratio: 6.82, 95% confidence interval: 1.57–30.16, P = .01) were associated with a higher odds of EjD. ED was found to be a mediator of the relationship between EjD and age, as the age association was lost in the ED population on multivariable regression compared with the non-ED population where it remained significant.

Conclusions: EjD is common among patients presenting to a men’s health clinic and may present at varying ages, though it is more common in those aged 50 years or older; it is independent of age and race. EjD is associated with erectile dysfunction, pelvic cancer history, and use of alpha inhibitors, presenting a population that could be considered for screening.

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Key Words: Ejaculatory Dysfunction; Delayed Ejaculation; Erectile Dysfunction; Men’s Health

INTRODUCTION

Ejaculatory dysfunction (EjD), other than premature ejaculatory, are a combination of potentially distressing conditions that include anejaculation, delayed ejaculation (DE), decreased force of ejaculate volume, and decreased perceived ejaculate volume.1–2 Premature ejaculation has been well characterized in the literature with regard to prevalence, risk factors, and associated clinical characteristics.3 However, the equivalent data with regard to other EjD are not nearly as robust. As EjD has the potential to cause patients and their partners significant distress and various treatments do exist, these range of conditions warrant significant attention.2,4–7

Prior prevalence estimates and risk factor associations for EjD have been examined in population-based cohorts or in patients
presenting with specific conditions such as lower urinary tract symptoms (LUTS), benign prostatic hypertrophy, or erectile dysfunction (ED).8–12 In particular, a multinational survey of more than 12,000 men between 50 and 80 years of age found 46% with reduced amount of ejaculate and 5% with anejaculation.12 EjD was particularly prevalent among men aged 70–80 years and was correlated with LUTS severity. Beyond this study, most have focused on men presenting with a single condition rather than a subpopulation of men. Among men with ED, 57.8% were found to have some form of EjD, and cardiac disease and certain medications (antipsychotics and antidepressants) were found to increase the risk of development of EjD.8

Although EjD has been characterized within the general population and within certain specific conditions, men presenting for consultation within a men’s health clinic have yet to be studied. As male sexual dysfunction increases with age and the impact that EjD may have on a man and/or his partner should not be underestimated as it can be associated with significant distress, sexual dissatisfaction, and relationship strain, it warrants continued investigation.1 We therefore sought to characterize the prevalence and risk factors for EjD in a population of men referred to a men’s health clinic.

### METHODS

#### Study Population

This retrospective review was approved by the institutional review board and covered patients presenting to an outpatient urology men’s health clinic at an academic teaching hospital from March 1, 2019 to October 31, 2019. Specifically, this clinic receives referrals for patients with ED, EjD, infertility, Peyronie’s disease, hypogonadism, vasectomy and reversal of vasectomy, and patients with non-oncologic testicular pathology (eg, varicocele, chronic pain, and so on). A chart review was performed on all patients, regardless of known EjD or not, who completed 2 questionnaires (Sexual Health Inventory for Men [SHIM] and Male Sexual Health Questionnaire Ejaculatory Dysfunction [MSHQ-EjD] Short Form) that were routinely collected for all new patients.13,14 All surveys were administered by medical assistants without a physician present before their visit to limit bias. This study was limited to male patients, and those patients who had incomplete surveys were excluded from the study. The electronic medical records of qualifying patients were further reviewed to obtain information regarding patient demographics, comorbidities, and medication usage.

#### Table 1. Baseline demographics and comorbidities of the patient population

|                  | EjD       | No EjD    | P-value |
|------------------|-----------|-----------|---------|
| **Total**        | 63        | 200       |         |
| Age (mean (SD))  | 53.76 (15.63) | 42.60 (14.35) | <.001   |
| <30              | 5 (11.9)  | 37 (88.1) | <.001   |
| 30–39            | 11 (14.9) | 63 (85.1) |         |
| 40–49            | 7 (13.7)  | 44 (86.3) |         |
| 50–59            | 13 (31.7) | 28 (68.3) |         |
| 60–69            | 14 (48.3) | 15 (51.7) |         |
| 70+              | 13 (50.0) | 13 (50.0) | .157    |
| Race (%)         |           |           |         |
| White            | 43 (28.1) | 110 (71.9)|         |
| Asian            | 8 (16.0)  | 42 (84.0) |         |
| Other            | 12 (20.0) | 48 (80.0) |         |
| **Sexual function, mean (SD)** | | | |
| SHIM score       | 11.90 (5.95) | 20.19 (5.63) | <.001   |
| MSHQ-EjD score   | 5.98 (3.59) | 12.36 (2.51) | <.001   |
| Bother score     | 3.10 (1.56) | 1.02 (1.49)  | <.001   |
| **Comorbidities (%)** | | | |
| Erectile dysfunction | 49 (77.8) | 42 (21.0)  | <.001   |
| Hyperlipidemia   | 11 (17.5) | 39 (19.5) | .861    |
| Diabetes         | 4 (6.3)   | 9 (4.5)   | .797    |
| Hypogonadism     | 12 (19.0) | 59 (29.5) | .142    |
| LUTS             | 12 (19.0) | 19 (9.5)  | .068    |
| History of pelvic cancer | 13 (20.6) | 12 (6.0)  | .001    |
| **Current prescription (%)** | | | |
| Antiepileptic or antipsychotic | 17 (27.0) | 28 (14.0) | .028    |
| Alpha inhibitor  | 7 (11.1)  | 6 (3.0)   | .024    |
| Opioid           | 30 (47.6) | 54 (27.0) | .004    |

EjD = ejaculatory dysfunction; LUTS = lower urinary tract symptoms; MSHQ-EjD = Male Sexual Health Questionnaire Ejaculatory Dysfunction; SD = standard deviation; SHIM = Sexual Health Inventory for Men.
### Table 2. Multivariable regression for odds of development of EjD, bother by EjD, strength of ejaculation, and volume of ejaculate with sociodemographic factors, comorbidities, and medications

| Age       | EjD OR (95% CI)       | *P*-value | Bother OR (95% CI) | *P*-value | Strength OR (95% CI) | *P*-value | Volume OR (95% CI) | *P*-value |
|-----------|----------------------|-----------|--------------------|-----------|----------------------|-----------|--------------------|-----------|
| <30       | 1.01 (0.98–1.04)     | .24       | 1.02 (0.99–1.04)   | .18       | 1.07 (1.04–1.10)     | <.0001    | 1.07 (1.04–1.10)   | <.0001    |
| 30–39     | 1.16 (0.33–4.56)     | .82       | 0.68 (0.28–1.68)   | .40       | 1.74 (0.64–5.09)     | .29       | 0.83 (0.31–2.26)   | .71       |
| 40–49     | 0.95 (0.23–4.16)     | .95       | 0.74 (0.28–1.93)   | .53       | 1.92 (0.64–6.00)     | .25       | 1.28 (0.46–3.67)   | .63       |
| 50–59     | 2.34 (0.61–9.79)     | .23       | 0.80 (0.28–2.24)   | .67       | 11.30 (3.62–38.77)   | <.0001    | 4.37 (1.56–12.99)  | .006      |
| 60–69     | 2.63 (0.59–12.55)    | .21       | 1.70 (0.50–5.94)   | .39       | 10.05 (2.5–45.87)    | .002      | 4.99 (1.43–18.80)  | .01       |
| 70+       | 1.69 (0.34–8.84)     | .52       | 2.35 (0.56–11.31)  | .26       | 21.49 (3.91–178.92)  | .001      | 42.36 (6.20–875.2) | .001      |
| Race      |                      |           |                    |           |                      |           |                    |           |
| White     | 0.58 (0.18–1.69)     | .34       | 0.31 (0.13–0.70)   | .007      | 1.18 (0.49–2.80)     | .71       | 0.90 (0.38–2.08)   | .80       |
| Asian     | 0.94 (0.36–2.36)     | .89       | 0.61 (0.29–1.26)   | .19       | 1.11 (0.50 – 2.47)   | .79       | 1.32 (0.61 – 2.83) | .48       |
| Other     |                      |           |                    |           |                      |           |                    |           |
| Comorbidities |                   |           |                    |           |                      |           |                    |           |
| Erectile dysfunction | 15.04 (6.76–35.92)  | <.0001    | 6.92 (3.50–14.26)  | <.0001    | 9.72 (4.58–21.95)    | <.0001    | 4.27 (2.13–8.76)   | <.0001    |
| Hyperlipidemia | 0.43 (0.15–1.14)   | .10       | 1.08 (0.47–2.47)   | .85       | 0.45 (0.17–1.16)     | .11       | 0.67 (0.26–1.61)   | .37       |
| Diabetes  | 0.34 (0.06–1.54)     | .18       | 0.85 (0.18–4.23)   | .83       | 0.80 (0.14–6.72)     | .81       | 0.44 (0.08–2.30)   | .32       |
| Hypogonadism | 1.03 (0.42–2.46)    | .94       | 1.47 (0.76–2.85)   | .25       | 2.02 (0.96–4.31)     | .07       | 1.81 (0.89–3.72)   | .11       |
| LUTS      | 0.80 (0.27–2.23)     | .67       | 0.71 (0.26–1.90)   | .49       | 2.28 (0.71–8.05)     | .18       | 1.48 (0.50–4.41)   | .48       |
| History of pelvic cancer | 1.57 (0.50–4.93)   | .44       | 0.49 (0.16–1.51)   | .22       | 2.33 (0.58–10.28)    | .24       | 2.87 (0.82–11.04)  | .11       |
| Medications |                   |           |                    |           |                      |           |                    |           |
| Antiepileptic or antipsychotic | 0.79 (0.27–2.23)  | .67       | 1.80 (0.69–4.76)   | .23       | 0.89 (0.29–2.64)     | .84       | 0.77 (0.26–2.22)   | .64       |
| Alpha inhibitor | 6.82 (1.57–30.16) | .01       | 8.69 (1.84–64.24)  | .01       | 2.46 (0.46–13.49)    | .29       | 3.55 (0.68–18.59)  | .12       |
| Opioid   | 1.75 (0.73–4.15)     | .20       | 1.16 (0.56–2.36)   | .68       | 1.08 (0.47–2.41)     | .85       | 1.66 (0.77–3.57)   | .19       |

CI = confidence interval; EjD = ejaculatory dysfunction; LUTS = lower urinary tract symptoms; OR = odds ratio.
Table 3. Average SHIM, MSHQ, and bother scores stratified by sociodemographic factors and comorbidities

| Age     | SHIM    | MSHQ-EjD | Bother score |
|---------|---------|----------|-------------|
| <30     | 20.5 ± 5.5 | 12.7 ± 2.2 | 1.0 ± 1.5 |
| 30–39   | 20.8 ± 4.8 | 12.3 ± 3.3 | 1.2 ± 1.7 |
| 40–49   | 20.4 ± 5.0 | 12.3 ± 2.4 | 1.2 ± 1.6 |
| 50–59   | 16.8 ± 7.2 | 9.8 ± 3.9  | 1.3 ± 1.6 |
| 60–69   | 13.6 ± 7.2 | 7.2 ± 4.4  | 2.6 ± 2.0 |
| 70+     | 10.3 ± 5.7 | 6.6 ± 2.9  | 3.0 ± 1.5 |

| Race    | SHIM    | MSHQ-EjD | Bother score |
|---------|---------|----------|-------------|
| White   | 17.9 ± 7.0 | 10.5 ± 4.1 | 1.8 ± 1.8 |
| Asian   | 18.6 ± 6.0 | 11.6 ± 3.4 | 1.1 ± 1.7 |
| Other   | 18.8 ± 6.6 | 11.0 ± 3.8 | 1.3 ± 1.6 |

| SHIM score | SHIM    | MSHQ-EjD | Bother score |
|------------|---------|----------|-------------|
| 22–25      | 24.0 ± 1.1 | 13.3 ± 2.2 | 0.5 ± 1.1 |
| 17–21      | 19.0 ± 1.3 | 10.7 ± 3.3 | 1.7 ± 1.5 |
| 12–16      | 14.3 ± 1.5 | 9.0 ± 3.0  | 2.7 ± 1.7 |
| 8–11       | 9.6 ± 1.1  | 8.2 ± 3.0  | 2.3 ± 1.9 |
| 1–7        | 5.7 ± 0.9  | 5.6 ± 3.6  | 3.2 ± 1.7 |

| Comorbidities | SHIM    | MSHQ-EjD | Bother score |
|---------------|---------|----------|-------------|
| Erectile dysfunction | 10.1 ± 4.2 | 7.6 ± 3.5 | 2.7 ± 1.8 |
| Hyperlipidemia   | 16.2 ± 7.3 | 10.4 ± 3.7 | 1.7 ± 1.8 |
| Diabetes         | 10.3 ± 5.3 | 8.3 ± 3.3  | 2.9 ± 2.0 |
| Hypogonadism     | 19.4 ± 5.2 | 11.5 ± 3.0 | 1.3 ± 1.5 |
| LUTS             | 13.6 ± 6.3 | 8.3 ± 4.0  | 2.1 ± 1.9 |
| History of pelvic cancer | 12.8 ± 7.5 | 6.7 ± 4.9 | 2.0 ± 1.7 |

| Medications | SHIM    | MSHQ-EjD | Bother score |
|-------------|---------|----------|-------------|
| Antiepileptic or antipsychotic | 15.3 ± 7.2 | 8.8 ± 4.4 | 2.1 ± 1.7 |
| Alpha inhibitor | 15.5 ± 7.6 | 7.8 ± 4.9 | 2.9 ± 1.7 |
| Opioid       | 16.1 ± 7.4 | 9.4 ± 4.5 | 2.0 ± 1.8 |

EjD = ejaculatory dysfunction; LUTS = lower urinary tract symptoms; MSHQ EjD = Male Sexual Health Questionnaire Ejaculatory Dysfunction Short Form; SHIM = Sexual Health Inventory for Men.

Survey Instruments

2 validated surveys—the SHIM and MSHQ-EjD—were administered to patients.15,16 The SHIM instrument is a widely used measure of erectile function consisting of 5 questions and a total score ranging from 1 to 25. The MSHQ-EjD is a measure of ejaculatory function consisting of 4 questions with Likert scale response options, each ranging from 0 to 5.

Statistical Methods

Patient characteristics and survey responses were analyzed using descriptive statistics, including proportions, median, and mean ± standard deviation (SD). Categorical variables were analyzed by the χ2 test or Fisher’s exact test as appropriate. Normally distributed continuous variables were analyzed by Student’s t-test, whereas skewed continuous variables were analyzed by the Wilcoxon rank sum test.

For the purpose of multivariable logistic regression analysis, we dichotomized outcome variables. SHIM scores less than 18 were considered to be ED. A response of “About half the time” or less for “How often have you been able to ejaculate when having sexual activity?” was considered EjD. A response of at least “A little bothered” for the question “If you have had any ejaculation difficulties, have you been bothered by this?” was considered as bothered by EjD. A response “Somewhat less strong than it used to be” or less for “How would you rate the strength of your ejaculation?” was considered poor strength. A response of “Somewhat less than it used to be” or less for “How would you rate the amount or volume of semen or fluid when you ejaculate?” was considered poor volume.

Independent factors associated with EjD, EjD bother, and ejaculatory strength and volume were investigated by multivariate logistic regression. All data were analyzed using R v3.5.3 (R Foundation for Statistical Computing). The significance level for all statistical tests was set at 0.05, and all tests were 2 sided.

RESULTS

In total, for all 263 men completing the questionnaires with unknown EjD status, 63 men (24%) were identified by their questionnaire response as having EjD compared with 200 men
Table 4. Multivariable regression with age and race in patients with ED vs those without ED (variables controlled for: age, race, hypogonadism, diabetes, LUTS, history of pelvic cancer, antiepileptic medications, antipsychotic medications, and opioid prescription).

| Age (years) | ED OR (95% CI)  | P-value | Reference | EjD OR (95% CI)  | P-value | Reference |
|-------------|-----------------|---------|-----------|-----------------|---------|-----------|
| <30         | 0.98 (0.94–1.02) | .63     | Ref       | 0.99 (0.94–1.04) | .19     | Ref       |
| 30–49       | 0.99 (0.94–1.04) | .39     |           | 1.18 (1.03–1.35) | .48     |           |
| 50–59       | 1.20 (1.06–1.36) | .04     |           | 1.00 (0.93–1.08) | .33     |           |
| 60–69       | 1.54 (1.07–2.20) | .04     |           | 0.22 (0.15–0.32) | .0007   |           |
| 70+         | 1.54 (1.00–2.36) | .04     |           | 0.41 (0.30–0.57) | .90     |           |

CI = confidence interval; ED = erectile dysfunction; EjD = ejaculatory dysfunction; OR = odds ratio.

Patients with ED had significantly higher odds of developing EjD (OR: 15.04, 95% CI: 6.76–35.92, P = 0.0001), being bothered by EjD (OR: 6.92, 95% CI: 3.50–14.26, P < 0.0001), and having low strength of ejaculation (OR: 9.72, 95% CI: 4.58–21.95, P < 0.0001) or volume of ejaculate (OR: 4.27, 95% CI: 2.13–8.76, P < 0.0001; Table 3). Comorbidities such as hyperlipidemia, diabetes, hypogonadism, and LUTS were not associated with measures of ejaculation. Importantly, when patients were stratified into those with and without ED and compared on multivariable regression, those without ED retained an overall significant association with age (OR: 1.06, 95% CI: 1.02–1.11, P = .01; Table 4). In contrast, patients with ED did not display an association between EjD and age (Table 4) suggesting ED is a mediator of the association between EjD and age.

Both the SHIM and MSHQ-EjD were inversely related to age—that is total scores decreased as age increased (Table 3). In contrast, the MSHQ-EjD bother score increased as age increased. In total, 84.1% of men with EjD were at least a little bothered (MSHQ-EjD ≥ 2) and 74.6% were at least moderately bothered (MSHQ-EjD ≥ 3).
DISCUSSION

While prior analyses of EjD have focused on the general population and those with LUTS or ED, our analysis sought to examine the prevalence of EjD in patients presenting to a men’s health clinic. This study population therefore captures men presenting with a variety of conditions that a urologist may encounter such as ED, infertility, Peyronie’s disease, hypogonadism, and various testicular pathologies. Within our population, the rate of EjD was 24%. As the majority of these patients were not referred for EjD, this represents a high percentage of a condition that may negatively impact quality of life and therefore warrants attention among providers caring for a similar patient population. As the mean MSQH-EjD bother score was 3.1 of 5 (moderately bothered), there is opportunity here to screen and treat these patients. Overall, EjD appeared to be associated with age, particularly in those older than 70 years of age, when examined within the population without ED. However, this association was lost when the ED population was examined alone suggesting that ED is a mediator of EjD. Those men with EjD were more affected by ED and were more bothered by their EjD. ED and alpha inhibitors were associated with development of EjD, whereas other underlying comorbidities were not. There were not significant associations with race/ethnicity suggesting that all are similarly affected and bothered.

The prevalence of EjD within the general population was established by Rosen et al. in 2003 when they performed a multinational survey (the United States and 6 European countries) in 50- to 80-year-old men using 2 different questionnaires: the Danish Prostatic Symptom Score for sexual function and the International Index of Erectile Function (of which SHIM is a derivative). The authors found high rates of ED with 48.7% of their sample reporting difficulty with achieving an erection which increased with age. With regard to EjD, 46.2% had reduced volume or anejaculation. Similar to our study, age was a predictor of sexual dysfunction and men with more comorbidities (eg, hypertension, diabetes, cardiac disease, and so on) tended to have more EjD. In addition, there was a trend of increasing ejaculation difficulty with age with 74.3% of men aged 70–80 years reporting difficulty. Severity of LUTS was associated with increasing EjD; however, this was based on International Prostate Symptom Score unlike in our study which utilized diagnosis codes which could explain the discordant findings. While their study utilized a similar ED questionnaire and a different sexual function questionnaire, it reports a similar age and co-morbidity outcomes for EjD albeit with lower prevalence given the population surveyed.

The remaining studies in the literature have focused on men with specific conditions such as ED or LUTS. Paduch, et al examined survey data utilizing the MSHQ-EjD from participants screened for a clinical trial examining testosterone replacement in men with EjD. While the trial was specifically examining men with EjD, 88% reported some baseline issue with a high level of bother at 68% similar to reported in our study. Furthermore, a study of aggregate data from trials of tadalafil versus placebo, which covered over 12,000 men, found 57.8% reported abnormal ejaculatory function based on IIEF questions 9 and 10. The higher prevalence than we report here may be due attributed to the presence of ED in all patients. The frequency of EjD was also found to increase with severity of ED and the authors found a similar trend of EjD with increasing comorbidity (e.g. cardiac disease). Interestingly, EjD was found to be associated with younger age which is contrary to what we report here. The relationship between EjD and ED may be due to a perceived lack of control which could be distracting causing loss of erections. Furthermore, the loss of erectile strength may lead to more EjD leading to a detrimental cycle. EjD is probably best studied in the subset of patients experiencing LUTS. A number of studies have examined this association utilizing, mainly, the International Prostate Symptom Score to assess LUTS and a variety of sexual dysfunction questionnaires to examine EjD (for example the Danish Prostatic Symptom Score for sexual function, MSHQ, Brief Sexual Function Inventory, and International Continence Society Questionnaire sexual function). As summarized by Hellstrom et al., all studies have found increased odds of EjD with LUTS, and generally, these odds increase with severity. Corona et al reported in a series of 2,437 men, of whom 29.9% had EjD, either DE or premature ejaculation, that 26% of patients with DE had hypogonadism with a hazard ratio of 1.83 (95% CI: 1.14–3.94) suggesting that testosterone may be a mediator of EjD. While we were unable to find a correlation between hypogonadism and EjD, we did not measure serum testosterone levels and relied on diagnostic codes which may explain this finding.

As demonstrated in the present study, EjD may be undiagnosed in many patients while causing significant bother. The underlying reason for lack of diagnosis is unknown and may include, but not be limited to, a lack of recognition, hesitancy by the patient or provider to explore symptoms, or time constraints within a modern healthcare setting. Various treatments are available for a variety of EjD conditions including DE, anejaculation, and anorgasmia. While sex therapy can depend on availability of qualified therapists, various pharmacologic treatments have been described including alpha-1 adrenergic receptor antagonists selective serotonin reuptake inhibitors and tramadol. However, many treatments remain off-label and efficacy is varied which may add to distress for patients, therefore more research is required to better treat these conditions.

The present study has several limitations that warrant mention. First, there is inherent selection bias as the surveys were conducted in a urology clinic for those patients referred for urologic conditions. However, we sought to examine the prevalence of EjD within a specific subset of the urologic population. In addition, not every patient filled out a survey, and therefore, theoretically we could be examining those patients more willing to complete a survey on EjD (eg, those with either high level or very low level of dysfunction). However, this is unlikely as there are high completion rates of questionnaires before clinic visits as it is a requirement
before evaluation. Second, while we did use 2 validated questionnaires for clinical sexual dysfunction and ED, responses could be subjective, and we did not objectively measure ejaculatory latency time with a stopwatch as has been performed in clinical trials for treatment. In addition, diagnoses of comorbidities, such as LUTS or hypertension, were based on chart review rather than further questionnaires or quantitative data which may confound the results. Finally, the data were obtained from a tertiary referral academic center and therefore may not be generalizable.

In conclusion, this study suggests that EjD is prevalent among patients presenting to a man’s health clinic and that patients are bothered by it. EjD, in this population, appears to be associated with development of ED, and could be screened for by providers if they care for a similar population of patients given the potential for significant bother it presents to patients.

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