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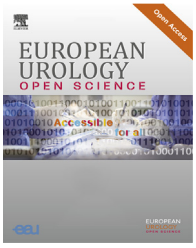

European Association of Urology

Prostate Cancer

An Overview of Patient-reported Outcomes for Men with Prostate Cancer: Results from the PIONEER Consortium

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Abstract

Background and objective: Patient-reported outcome measures (PROMs) are increasingly being used to capture the patients' perspective of their functional status and quality of life (QoL). Big data can help us better understand patient-reported outcomes (PROs). Using prospectively collected data from the Prostate Cancer Diagnosis and Treatment Enhancement Through the Power of Big Data in Europe (PIONEER) consortium, we aimed to describe the functional status and QoL in men with prostate cancer (PCa) treated with active surveillance (AS), radical prostatectomy (RP), and radiotherapy (RT), and to demonstrate the applicability of PROM data on a large scale and at a European level.
Methods: We identified data sources that collected QoL data using the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30, EORTC QLQ-PR25, or Expanded Prostate Cancer Index Composite (EPIC)-26/50 questionnaires. Aggregated summary scores for urinary, bowel, and sexual dysfunction, global health status, and QoL were shared for each data source.
Key findings and limitations: We identified eight data sources originating from various settings: routine hospital data, embedded research PRO collection, survey data collected by a patient organization, multi-institutional prospective cohort study, and registry data. PRO data were available for 709 men on AS, 20 508 on RP, and

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3417 on RT, with a median time between diagnosis and PROM assessment ranging from 1 to 8.7 yr. Most men were diagnosed with Gleason ≤7 disease, and T1 or T2 PCa. We observed that sexual dysfunction was the most affected PRO and found large differences between data sources.

Conclusions and clinical implications: Our results support the feasibility of PRO assessment using big data in Europe. Implementation of PROMs in clinical practice and the use of standardized methods could improve value-based health care provision.

Patient summary: In this study, we combined several data sources that reported urinary, bowel, and sexual dysfunction, global health status, and quality of life. We identified eight data sources and show that sexual function is the most affected domain after treatment.

1. Introduction

The use of patient-reported outcomes (PROs) in routine clinical care is increasing [1]. Long-term PRO data confirms that radical prostatectomy (RP) can result in sexual and urinary dysfunction, whereas radiotherapy (RT) can lead to sexual and bowel dysfunction [2]. While men following active surveillance (AS) do not report such treatment-related side effects, AS can have an impact on mental health [3]. As such, assessing long-term outcomes using PROs is becoming increasingly important in informing clinical care and facilitates shared decision-making [4]. Centers across Europe have started to collect patient-reported outcome measures (PROMs) to quantify PROs. This offers the opportunity to also utilize PRO data in a big data context including the inclusion and assessment of different stakeholders, which reflects the diversity of populations across Europe (eg, countries, comorbidities, and inclusion of noncenters of excellence).

Different complementary sources of health care data allow us to delve deeper into understanding PROs. This includes establishing norms, assessing data distribution, and determining the proportions of patients meeting change or threshold standards [5]. Such norms can be delineated across various subpopulations, a capability previously constrained by limited single-center PRO data and patient-generated health data.

In this study, as part of the Prostate Cancer Diagnosis and Treatment Enhancement Through the Power of Big Data in Europe (PIONEER) consortium [6], an international multistakeholder collaboration led by the European Association of Urology, it is attempted for the first time to analyze European PRO using a big data approach, combining PROMs from different data sources. We aim to present an overview of the PROs in men with prostate cancer (PCa) across data sources collected prospectively across Europe, and to demonstrate the applicability of PROM data on a large scale and at a European level.

2. Patients and methods

2.1. Study population

Although the use of PROs in routine clinical care is increasing, currently, PRO collection is not standardized in clinical practice (ie, the outcome to be measured and the use of measurement). To enable the use of PRO data in a big data context, Calvert et al [1] suggest the use of "core outcome sets incorporating PROs" specifically designed for routine clinical practice. As part of the PIONEER consortium, a core outcome set (ie, the collection of outcomes that should be measured and reported in randomized clinical trials, and standard clinical care) for PCa patients has been developed and the following PROs were prioritized: bowel, urinary, and sexual dysfunction, and overall quality of life (QoL) [7]. PIONEER recommends the use of the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and EORTC QLQ-PR25 questionnaires in both research and daily clinical practice for the localized setting [8]. We therefore focused on the selected "core" PROs, as assessed by the EORTC QLQ-C30 and EORTC QLQ-PR25 questionnaires. In addition, we also included the Expanded Prostate Cancer Index Composite (EPIC; EPIC-26 or EPIC-50) PROM, as this was identified to be the most frequently used PROM in PCa [8] and recommended by the International Consortium for Health Outcomes Measurement standard data set for localized and locally advanced PCa [9].

To identify PRO data across the EU, we shared an online survey via the PIONEER social media channels and contacted consortium partners as well as other European PRO data initiatives to identify PRO datasets. Subsequently, we contacted data teams who indicated collecting PROs using EORTC QLQ-C30, EORTC QLQ-PR25, or EPIC. EORTC QLQ-C30 incorporates five functional scales (physical, role, cognitive, emotional, and social), three symptom scales (fatigue, pain, and nausea and vomiting), and a global health/QoL scale; all scales range from 0 to 100 [10]. For functional scales and the global health/QoL scale, higher scores represent a better level of functioning; for the symptom scales, lower scores represent a better level of function. EORTC QLQ-PR25 is a module for PCa-specific PROs (urinary symptoms, incontinence aid, bowel symptoms, hormonal treatment-related symptoms, sexual activity, and sexual function) and follows the same scoring and interpretation as EORTC QLQ-C30, in which lower scores represent better function. This module is an addition to EORTC QLQ-C30 specifically for PCa patients [11]. The minimally important differences (MIDs) of EORTC QLQ-C30 for physical function and global QoL ranged from –7 to –11 and from –6 to –7,

respectively, for deterioration [12]. EPIC incorporates five domains for PCa-specific health (urinary incontinence, urinary irritable/obstructive, bowel, sexual, and hormonal concerns), and domain-specific function and bother subscales; all scales range from 0 to 100, in which higher scores represent better function [13]. The MIDs for EPIC-26 are 6–9 for urinary incontinence, 5–7 for urinary irritative/obstructive, 4–6 for bowel, 10–12 for sexual, and 4–6 for hormonal concerns [14]. In our analyses, we only selected patients who underwent AS, RP, or RT as initial treatment given that we specifically focused on the localized and locally advanced disease setting.

Eight data sources shared or previously published PRO data. Data sources originated from the European PCa patient organization survey (Europa Uomo Patient Reported Outcome Study [EUPROMS]), embedded research PRO collection (cross-sectional studies within European Randomized study of Screening for Prostate Cancer [ERSPC] Rotterdam and Prostate cancer Research International Active Surveillance [PRIAS] study), routine hospital data from a high-volume academic center (Vita-Salute San Raffaele University Milan), multi-institutional prospective cohort study data (the Mental Wellbeing and Quality of Life in Prostate Cancer [MIND-P] study; German Cancer Society/Deutsche Krebsgesellschaft [DKG]; Utrecht Prostate Cohort for Cancer Treatment Intervention Studies and Long-term Evaluation [UPC], which includes patients from the UMC Utrecht and the Sint-Antonius hospital [NCT04228211]), and a national registry (the Patient Reported Outcomes Following Initial Treatment and Long-term Evaluation of Survivorship [PROFILES] registry in combination with the Netherlands Cancer Registry).

EUPROMS is a cross-sectional survey initiated by Europa Uomo and collected PROs of 2943 men from 24 European countries to present a patient-to-patient perspective of PROs [15]. Venderbos et al [16] presented cross-sectional PRO data among men treated actively with RP and RT from the ERSPC Rotterdam, and among men managed with AS from the PRIAS study. Data from Vita-Salute San Raffaele University originate from a prospective database that aims at evaluating postoperative outcomes of PCa patients treated with RP at a high-volume academic tertiary referral center in Italy. The PROFILES registry contains PRO data from studies set up by researchers from The Netherlands Comprehensive Cancer Organisation (IKNL) and Tilburg University (Tilburg, The Netherlands) in collaboration with medical specialists from Dutch hospitals. The data are linked to clinical data from The Netherlands Cancer Registry. Their study collected PROM data in 2014 and 2015 from PCa patients diagnosed in 2007–2013. The MIND-P study was an eight-center prospective cohort study in the UK recruiting newly diagnosed PCa patients between 2021 and 2023 [17]. Physical, mental, and social well-being PROs were collected periodically at up to 12 mo across patients undergoing numerous management options. UPC data were collected from March 2020 until September 2023 for the analyses in this study. Only patients who underwent RT were included. PRO data from the DKG originates from 136 centers including 18 452 men who were treated with RP, 2608 treated with RT, and 359 treated with AS [18,19].

2.2. Statistical analyses

Unless aggregated data were published, we developed a script tailored to each dataset since PRO data are not mapped to the standard common data model (ie, Observational Medical Outcomes Partnership Common Data Model) [20]. The custom R script was intended to describe the patient cohorts within each dataset, and to calculate the median and interquartile range (IQR) of each PRO at the patient's latest PROM assessment after treatment stratified by initial treatment (AS, RP, or RT). As a result of our approach, only aggregated results were shared. We summarized the aggregated PRO data in a graphical overview using R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria). For institutions outside the Erasmus Medical Center Rotterdam, data sharing agreements and collaboration letters were put in place to share the aggregated data or data published previously. Since the patients in the cohort of the UPC study used EPIC-50 and the other data sources used EPIC-26, we combined the summary score of bowel, urinary, and sexual dysfunction of EPIC-26 and EPIC-50. Data from PROFILES, DKG, MIND-P, and EUPROMS were reported for the time from diagnosis to PROs, while for the other data sources, these were reported for the time from treatment to PROs.

3. Results

Data were available for 709 men on AS, 20 508 on RP, and 3417 on RT (Fig. 1 and Supplementary Table 1). The pooled median age (weighed by sample size) of men at diagnosis was 68 yr (95% confidence interval [CI] 66–69) for men on AS, 66 yr (95% CI 66–66) for men on RP, and 74 yr (95% CI 67–74) for men on RT (Table 1). Most men were diagnosed with Gleason 6 or 7, and T1 or T2 PCa, which suggests that most men received RT without adjuvant androgen deprivation therapy. The median time between diagnosis and PRO completion ranged from 1 to 8.7 yr. Only the DKG and the MIND-P study reported PROs 1 yr after treatment. Most data sources used the EPIC questionnaire to evaluate the functional outcomes after treatment; only the PROFILES registry used the EORTC QLQ-C30 and EORTC QLQ-PR25 questionnaires.

For urinary dysfunction, we observed that men opting for RP showed the lowest scores, compared with men opting for AS or RT across all data sources (see Fig. 2). Among those opting for RP (range of median scores: 71–92), the lowest median score is reported by men from the EUPROMS study (median score of 71). Among those who opted for RT (range of median scores: 92–100), the lowest median score was reported by the MIND-P study (ie, 92). Men opting for AS reported an approximate ceiling effect in which the lowest median score was 97, as reported by the MIND-P study (range of median scores: 97–100).

For bowel dysfunction, we observed that the difference in median scores between treatment modalities did not

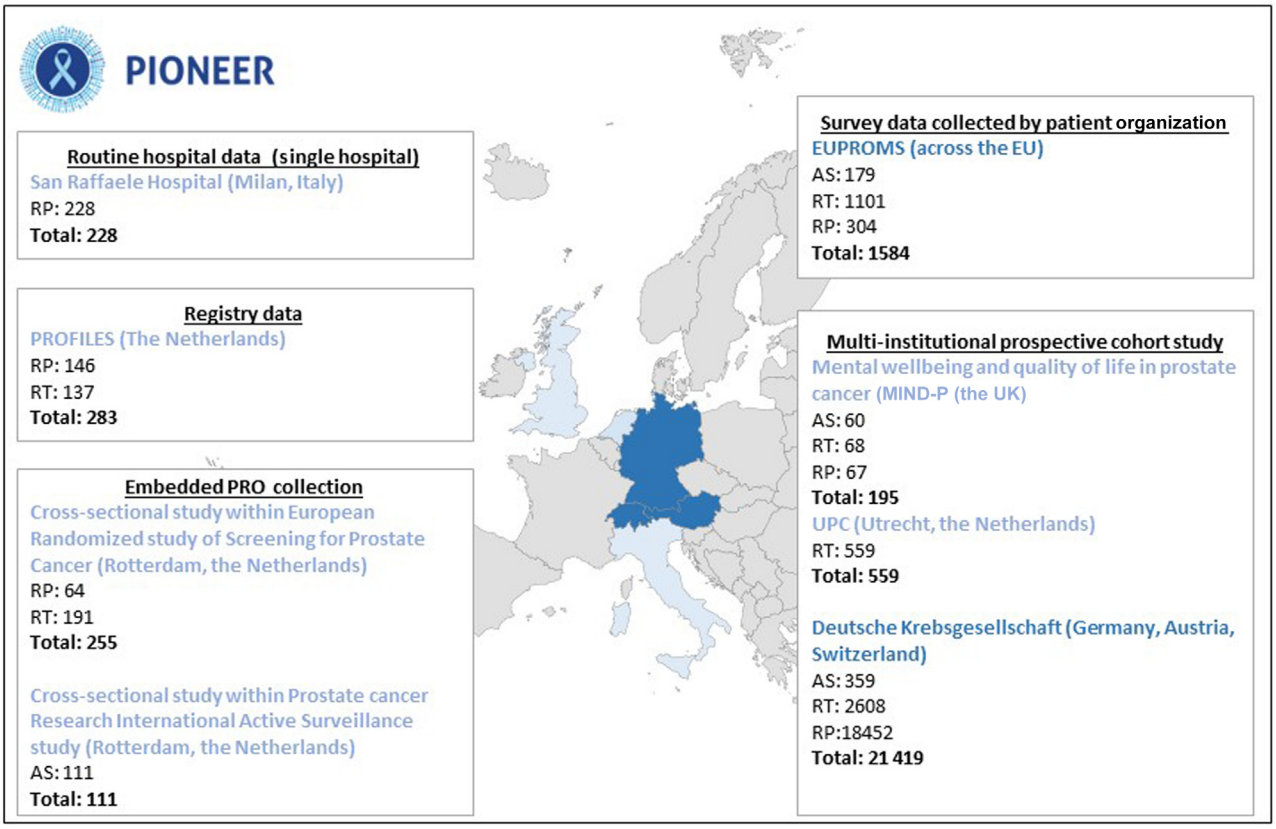

Fig. 1 – Origin of the data. AS = active surveillance; EU = European Union; EUPROMS = Europa Uomo Patient Reported Outcome Study; MIND-P = Mental Wellbeing and Quality of Life in Prostate Cancer; PRO = patient-reported outcome; PROFILES = Patient Reported Outcomes Following Initial Treatment and Long-term Evaluation of Survivorship; RP = radical prostatectomy; RT = radiotherapy; UPC = Utrecht Prostate Cohort for Cancer Treatment Intervention Studies and Long-term Evaluation.

show large differences (range of median scores across all treatment modalities: 92–100); however, the 25th percentile of these scores was the lowest for men opting for RT, compared with men who opted for AS or RP. While the range of scores for men opting for RP and AS was relatively small, the widest range of scores was observed in men opting for RT.

For sexual dysfunction, we observed that men who opted for RT (range of median scores: 17–46) or RP (range of median scores: 6–40) showed lower scores than those opting for AS (range of median scores: 44–57). Among those opting for RP, there was large heterogeneity between data sources. To elaborate, the highest score was observed in the Milan database (ie, 40), and the lowest score was observed in the ERSPC Rotterdam cohort (ie, 6). It must be noted that respondents within the ERSPC Rotterdam cohort were older (median age 69.7 yr, IQR 68.6–72.0) than respondents from the Milan study (median age 62.3 yr, IQR 56.3–67.6), while the median times between diagnosis and PROMs were 5.9 yr (IQR 4.6–7.6) and 8.0 yr (IQR 4.0–11.0), respectively. For men opting for RT and AS, there was limited heterogeneity in scores between data providers.

Overall QoL was reported by PROFILES, the MIND-P study, the Milan database, and the UPC study. These cohorts show that overall QoL was less affected than the function outcomes since these median scores range from 90 (RT: PROFILES) to 96 (RP: Milan).

4. Discussion

In this study, we evaluated urinary, bowel, and sexual dysfunction, global health status, and QoL among men with localized and locally advanced PCa across Europe, based on datasets available to the PIONEER consortium or for which the necessary results have been made publicly accessible. In this big data approach, we identified PRO data of 709 men on AS, 20 508 on RP, and 3417 on RT from at least four different data sources for each treatment. We observed that—compared with men opting for AS—sexual dysfunction was the highest among men who underwent active treatment. We also showed that urinary dysfunction was affected mostly among men who underwent RP across all data sources. However, it is important to mention that, even within a large country, there are large differences in reported PROs between centers [21]. To elaborate, Sibert et al [21] (ie, the DKG data) have shown that the median EPIC-26 score for urinary dysfunction 1 yr after RP ranged from 51 to 87 among different operating sites within Germany. We also observed that the scores for bowel dysfunction showed large variance between men opting for RT, while this was less pronounced among men opting for AS and RP. This variance is probably attributable to neither the differences in sample size since the data sources included more men on RT than on AS nor the differences in doses of RT after treatment [22]. These variations could,

Table 1 – Baseline characteristics for each study stratified by treatment

Variable	Treatment															
	AS				RP						RT					
	Study															
	EUPROMS	DKG	MIND-P	PRIAS	EUPROMS	ERSPC	DKG	MIND-P	Milan	PROFILES	EUPROMS	ERSPC	DKG	MIND-P	PROFILES	UPC
Age at diagnosis (yr), median (IQR)	NR	69.0 (63.0–74.0)	68.0 (62.8–74.0)	66.0 (61.0–70.0)	NR	69.7 (68.6–72.0)	66.0 (61.0–71.0)	65.0 (57.8–68.0)	62.3 (56.3–67.6)	64.0 (59.0–67.0)	NR	65.8 (61.5–70.0)	74.0 (69.0–78.0)	71.0 (65.0–76.0)	69.0 (65.0–73.0)	71.0 (66.0–75.0)
Age categories if no continuous variable has been reported, *n* (%)																
<55	16 (8.9)				128 (12)						9 (3.0)					
55–59	16 (8.9)				212 (19)						37 (12)					
60–64	40 (22)				304 (28)						44 (14)					
65–69	41 (23)				286 (26)						73 (24)					
70–74	32 (18)				139 (13)						83 (27)					
75–79	23 (13)				29 (2.6)						53 (17)					
80+	11 (6.1)				3 (0.27)						5 (1.6)					
Gleason, *n* (%) [a]																
6	67 (60)	320 (89)	47 (78)	111 (100)	126 (20)	46 (72)	4310 (23)	1 (1.5)	95 (42)		31 (20)	151 (91)	589 (23)	1 (1.5)		72 (13)
7	36 (32)	38 (11)	13 (22)	0 (0)	381 (61)	18 (28)	10 638 (58)	59 (87)	91 (41)		63 (41)	15 (9.0)	1375 (53)	40 (60)		370 (67)
8	5 (4.5)	0 (0)	0 (0)	0 (0)	69 (11)	0 (0)	2337 (13)	2 (2.9)	27 (12)		33 (21)	0 (0)	404 (15)	13 (19)		82 (15)
9–10	3 (2.7)	1 (0.3)	0 (0)	0 (0)	50 (8.0)	0 (0)	1167 (6.3)	6 (8.8)	11 (4.9)		27 (18)	0 (0)	240 (9.2)	13 (19)		32 (5.8)
Missing/unknown	68	0	0	0	475	0	0	0	4	146	150	25	0	0	137	3
T stage, *n* (%)																
T1	76 (46)	318 (89)	1 (1.7)	89 (80)	223 (23)	40 (66)	13 063 (71)	2 (2.9)	128 (58)	71 (49)	58 (22)	125 (65)	1495 (57)	1 (1.5)	40 (29)	262 (50)
T2	77 (46)	39 (11)	57 (97)	22 (20)	559 (57)	21 (34)	4765 (26)	42 (62)	77 (3)	55 (38)	123 (46)	66 (35)	886 (34)	39 (58)	54 (39)	204 (39)
T3	6 (3.6)	2 (0.6)	1 (1.7)	0 (0)	158 (16)	0 (0)	611 (3.3)	24 (35)	15 (6.8)	19 (13)	65 (25)	0 (0)	209 (8.0)	26 (39)	40 (29)	56 (11)
T4	7 (4.2)	0 (0)	0 (0)	0 (0)	33 (3.4)	0 (0)	12 (0.1)	0 (0)	0 (0)	0 (0)	19 (7.2)	0 (0)	18 (6.9)	1 (1.5)	3 (2.2)	2 (0.4)
Missing/unknown	14	0	1	0	128	3	1	0	8	1	39	0	0	0	0	35
PSA (ng/ml), median (IQR)	NR	6.0 (4.0–8.0)	5.9 (4.2–7.2)	5.8 (4.3–7.4)	NR	4.9 (3.9–8.3)	7.0 (5.0–11.0)	6.6 (4.9–8.6)	6.1 (4.7–8.5)	NR	NR	7.1 (5.2–9.4)	8.0 (6.0–13.0)	9.1 (6.9–16.7)	NR	
Missing/unknown	–	0		0	–	0	3		3	–	–	0	1		–	
Time between diagnosis and PROM or fixed PROM measurement (yr), median (IQR) [b]	3 or 4	1	1	6.3 (5.4–7.1)	3 or 4	5.9 (4.6–7.6)	1	1	8.0 (4.0–11.0)	3.9 (2.9–4.8)	5	8.7 (5.6–11.3)	1	1	3.8 (2.5–5.0)	1 (0.8–2)
Number of responders																
Urinary dysfunction	179	341	60	111	1101	64	17 994	68	204	146	304	191	2424	67	136	551
Bowel dysfunction	179	338	60	111	1101	63	17 492	68	168	145	304	189	2293	67	135	545
Sexual dysfunction	179	348	60	111	1101	62	18 135	68	191	83	304	182	2496	67	60	429
Global health status									228	146					137	555
Quality of life			60					68	219	143				67	131	552

AS = active surveillance; DKG = German Cancer Society/Deutsche Krebsgesellschaft; ERSPC = European Randomized study of Screening for Prostate Cancer; EUPROMS = Europa Uomo Patient Reported Outcome Study; IQR = interquartile range; ISUP = International Society of Urological Pathology; MIND-P = Mental Wellbeing and Quality of Life in Prostate Cancer; NR = not reported in the original study; PRIAS = Prostate cancer Research International Active Surveillance study; PROFILES = Patient Reported Outcomes Following Initial Treatment and Long-term Evaluation of Survivorship; PROM = patient-reported outcome measure; PSA = prostate-specific antigen; RP = radical prostatectomy; RT = radiotherapy; UPC = Utrecht Prostate Cohort for Cancer Treatment Intervention Studies and Long-term Evaluation.

[a] To harmonize the characteristics between studies, we combined Gleason 3 + 4 (ISUP 2) and Gleason 4 + 3 (ISUP 3).

[b] In the EUPROMS study, the age at diagnosis was reported as a categorical variable. Therefore, we derived the time between diagnosis and questionnaire completion based on median differences between age at questionnaire completion and the categorical age at diagnosis.

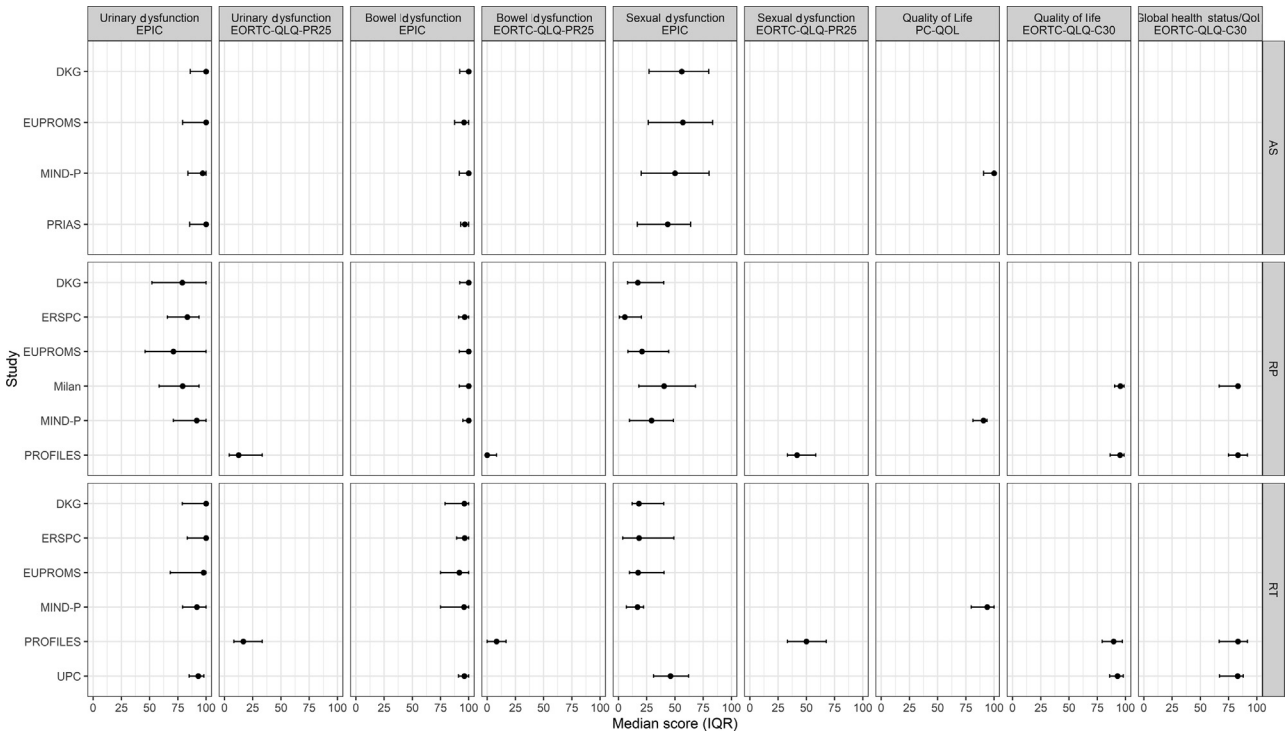

Fig. 2 – PRO score for each study and each QoL domain. We used the nomenclature of the EPIC domain scores as recommended by the core outcome set of PIONEER, but we did not change the scoring scale (ie, dysfunction instead of function) [10]. For urinary, bowel, and sexual function, high EPIC scores indicate better function, while low EORTC QLQ-PR25 scores represent better function. AS = active surveillance; DKG = German Cancer Society/Deutsche Krebsgesellschaft; EORTC = European Organization for Research and Treatment of Cancer; EPIC = Expanded Prostate Cancer Index Composite; ERSPC = European Randomized study of Screening for Prostate Cancer; EUPROMS = Europa Uomo Patient Reported Outcome Study; IQR = interquartile range; MIND-P = Mental Wellbeing and Quality of Life in Prostate Cancer; PIONEER = Prostate Cancer Diagnosis and Treatment Enhancement Through the Power of Big Data in Europe; PRIAS = Prostate cancer Research International Active Surveillance study; PRO = patient-reported outcome; PROFILES = Patient Reported Outcomes Following Initial Treatment and Long-term Evaluation of Survivorship; QoL = quality of life; RP = radical prostatectomy; RT = radiotherapy; UPC = Utrecht Prostate Cohort for Cancer Treatment Intervention Studies and Long-term Evaluation.

however, suggest that bowel function impairment is a heterogeneous outcome [23].

Data from EUPROMS previously showed that urinary dysfunction, as reported by clinical investigator–initiated studies, might not accurately represent a patient's perceived functional outcome [15,24]. In our study, we also found significant differences in reported urinary dysfunction between data sources. This highlights the need for real-world data outside controlled clinical settings and the importance of recognizing how PROs are captured. To elaborate, Månsson et al [25] observed worse bowel function after radical cystectomy among patients who received PROMs from a neutral third party compared than reported by the surgeon or institution. We found limited differences between EUPROMS and the other data sources for bowel dysfunction. However, for sexual dysfunction, we observed large differences between data sources among those who underwent active treatment. For example, the median difference in reported sexual dysfunction among men opting for RP between EUPROMS and Milan was above the MID (21 vs 40), and men who underwent RT in the UPC study showed higher scores for sexual function than all other data sources. On the contrary, data from DKG did not show large differences as compared with other studies, which can suggest that inclusion and assessment of diverse data sources lead to a better representation of PROs. A comparison of the EUPROMS results against studies reported in the literature [24] showed that the largest discrepancy was observed for the study of Barocas et al [26], which collected PROs as part of a prospective longitudinal population-based cohort study. One reason for these differences in perceived sexual dysfunction is that patients—although they consider it a problem—appear to accept the consequence of the treatment [27].

To improve the uptake of PROs in daily clinical practice, the assessment of PRO data after treatment should be standardized [1,28,29]. A way to effectively collect PROMs is to collect these as electronic PROMs (ePROMs) [30]. It has been shown that the response rate of PROMs increased from 33% to 72% after the introduction of ePROMs [31]. However, responses using ePROMs decrease over time as well [32], so it is important to incorporate both short- and long-term PROMs as an integral part of clinical practice to ensure that feedback from patients is incorporated in decision-making [33].

There are some limitations to this study. The data sources followed different protocols including different timeframes being compared, and we could not adjust for case-mix, disease status, and pretreatment PROs, limiting statistical inferences. Another limitation is that to date no crosswalk has been established between EPIC and EORTC QLQ-PR25 [34], so we were unable to compare functional

outcomes one to one. However, data from PROFILES (ie, EORTC QLQ-C30 and EORTC QLQ-PR25) show a similar pattern of scores to those from other datasets that used EPIC, although scoring is reversed. Future studies should consider differences in case-mix to analyze PROs including pretreatment scores. This would allow a better comparison between treatment modalities. This enriched understanding serves to enhance the utility of PROMs in two ways. First, at the population level, PRO data can be used as an outcome in prognostic models to identify patient groups who require extra care [1] and enable a comparison of outcomes across health care providers [35]. Second, at an individual level, PRO data can help with the early identification and monitoring of a patient's side effects [36,37], and can improve patient-physician communication [1,5].

5. Conclusions

Our results show that treatment of PCa is complicated by sexual dysfunction, bowel dysfunction, and urinary incontinence. Importantly, our results support the feasibility of PRO assessment using big data in Europe and serve as a call to action for better implementation of PROMs in clinical practice.

Author contributions: Sebastiaan Remmers had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Remmers, Beyer, Van Hemelrijck, Roobol, Venderbos.
Acquisition of data: Remmers, Beyer, Lalmahomed, Prinsen, Horevoorts, Sibert, Kowalski, Barletta, Brunckhorst, Gandaglia, van der Voort van Zyp, Smith, Deschamps, Van Hemelrijck.
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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2024.11.009.

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