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Short report

A contribution of *Patient Reported Outcomes* data to measuring clinical value in prostate cancer: pilot study.

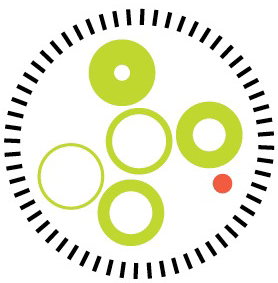
Henrik Møller (1)
Heidi Jeanet Larsson (1)
Karina Edvardsen (2)
Christina Richardt Pedersen (2)
Ulla Geertsen (3)

(1) Regionernes Kliniske Kvalitetsudviklingsprogram. The Danish Clinical Registries (RKKP).

(2) Region Syddanmark

(3) Odense University Hospital

Correspondance: Lead epidemiologist, dr.med. Henrik Møller (henrik.moller@rkkp.dk)



RKKP Working Paper

List of tables and figures (in sequence of appearance)

Introduction

The five government regions in Denmark have been pursuing a joint project on value-based health care, with each region having the lead role for component projects. Region South Denmark has led a project on prostate cancer, using clinical database data patient-reported outcomes (PRO) data.

The present report provides a concise summary of this prostate cancer project.

Data and methods

The analysis is based on surgically treated prostate cancer patients at Odense University Hospital, operated during 2016-2018. Data were extracted from the clinical quality database for prostate cancer that is hosted at The Danish Clinical Registries (RKKP), end these data were linked with PRO survey data collected at the hospital during 2017-2018.

Composite value scores were computed in two ways. Firstly, we computed the mean quality score from eight component items, including two items from the clinical database and six items from the PRO survey. Secondly, we derived the binary "All eight" composite score with the value of 1 for a survey return with all eight components favourable and 0 for other returns.

The statistical analysis used contingency tables with Chi-Square tests for linear trend over categories, and univariate and multivariate logistic regression analyses.

All analyses in the present report are cross-sectional, and ignore the repeated measures that arise when a man answers the PRO survey at multiple points in time. Conditional analyses that respect the repeated measures data structure will be reported separately for the specific outcomes of urinary continence and erectile function.

Results

Figure 1 illustrates the construction of the analysis dataset. There were 445 candidate patient records in the clinical database, and 961 patient reported outcomes (PRO) records from Odense University Hospital. The two files were merged by the unique Danish central population registration number for each man. Data cleaning reduced this to 427 unique patients with 916 PRO returns.

Table 1 gives an overview of the 427 patient records. Height and weight were not available in the majority of patients, and body mass index were therefore not available as a covariate for analysis. Almost all the patients were operated with endoscopic (robotic) surgery, and a nerve-sparing technique was used in 48% of patients.

Readmission to hospital within 30 days from prostatectomy occurred in 11% of patients. The 89% with no readmission were assigned a value score of 1 for the purpose of calculating indices of clinical value. The readmitted patients were assigned a score of 0. Similarly, the 98% of patients with three or fewer bed-days were assigned a value score of 1.

Table 2 shows tabulations of the 916 PRO returns. There were similar numbers of returns from the three first surveys (0, 90, 180 days), but fewer returns from the survey 360 days after diagnosis. We used six questions in the survey instrument to assign clinical value scores at each point in time. For example, the men who responded that they used none or only one diaper per day were assigned the value score 1, and men using more diapers were assigned the score 0. For five of the six questions, more than half of responses were positive. For erectile function, only 29% of PRO responses were positive, with the man reporting little or no difficulty getting and maintaining an erection.

Table 3 shows the pattern of contribution of PRO returns for the men. Only 6% of the men contributed all four surveys, and the first three returns were available from 124 men.

The eight component value scores were combined in two different ways. Firstly, we computed the mean composite score for each man at each point in time. This index can vary from 0 to 8. The average score was 6.7 at the time of diagnosis, and 4.7, 5.4 and 5.9 at the three later time points **(Figure 2)**.

Secondly, we derived the binary "All eight" index, assigning the value of 1 to returns that were all positive. **Figure 3** shows how this index varied from 36% at time of diagnosis to 4%, 7% and 11% at the three subsequent time points. For the remainder of the analyses, we used the binary composite index. Note that these analyses are cross-sectional. They use all the PRO returns and they ignore the inter-dependence of returns from the same man.

Table 4 shows the "All eight" binary index at the four time points for the entire study population, and in strata of the available covariates. For example, a positive "All eight" response at time of diagnosis was reported by 50% of patients in their 40s and by 24% of patients in their 70s. The linear trend over the four age-groups was statistically significant (p=0.02).

Strong and consistent patterns were seen for age, where younger men had higher value scores than older men, and for nerve-sparing resection which was associated with higher reported value scores. Less consistent patterns were seen for PSA and T stage. Low PSA and low T stage were associated with higher value scores. There was no association with comorbidity or with Gleason grade.

For multivariate analysis, we explored the data at the 180 days time point. Nerve-sparing surgery was strongly associated with the favourable "All eight" outcome (OR=9.55; 95% CI: 2.15-42.51; p=0.003) (**Table 5**). High age, high PSA and high T stage were associated with low value scores. In mutually adjusted analysis, the effect of nerve-sparing surgery was robust (OR=9.40) and remained statistically significant, whereas the effects of the other three covariates were reduced, and borderline statistical significance remained only for age.

Discussion

The present short report serves primarily to illustrate the possible conceptual and computational practice of analysis of composite value indicators.

The current interest in patient reported outcome data is evidence of an emerging or increasing interest in the patient perspective on clinical value and outcomes. The patient interest is likely to persist alongside established

specialist clinical guidelines, the latter for example regarding the clinical indications for particular interventions and therapies. Conflicting interests may occur, for example between the control of disease and the patient-experienced quality of life, or between avoiding short-term mortality and the long-term patient experience.

In our experience, the principal learning from the present project was the realisation of a degree of subjectivity and perhaps even arbitrariness in the process of assigning relative value to events and responses, and in the weighting of component scores.

In Tables 1 and 2 we assigned quality scores to eight components. There is no easy way to do this objectively. Instead of 0 and 1 value scores for each component, more detailed ranking scores could have been used. Moreover, we effectively weighted the eight component areas equally, but could also have decided that some components were more important than others. In a separate project on stroke care and outcomes, we used a formal Delphi process, where a panel of patients and health professionals decided on the weighting of the different value components.

The selected components of value were decided by a larger project group, with representation of multiple interests. The decision process was guided overall by a concern for the value for the patient, but practical considerations on data availability played a role as well. For example, there was a strong desire to include a verified standard measure of surgical complications, but we were forced to use readmission and bed-days as alternative measures.

In the present project, we also perceived some conceptual difficulty in operating with composite scores with a mixture of unspecific qualities like quality of life and more specific patient reports of incontinence or impotence. In order for the measures at the four time points to be comparable, the items on bed-days and readmission were carried through, and used at all four time points.

The present dataset has the particular complexity of multiple measurements over time, and the overall dimensionality of the data is very high. We recommend that the design of similar studies and projects should define the

data analysis plan explicitly. This would help guide the analysis, but should not preclude secondary explorative analyses of the data.

With respect to case-mix adjustment and confounder control, we consider that the analysis plan should not prescribe *a priori* an approach with multiple adjustments for a range of covariates, as this may exhaust the statistical power and lead to spurious biases due to over-adjustment. We recommend that the analysis plan entertains sensitivity analyses, so that the effects of specific adjustments can be seen and used in the interpretation of results.

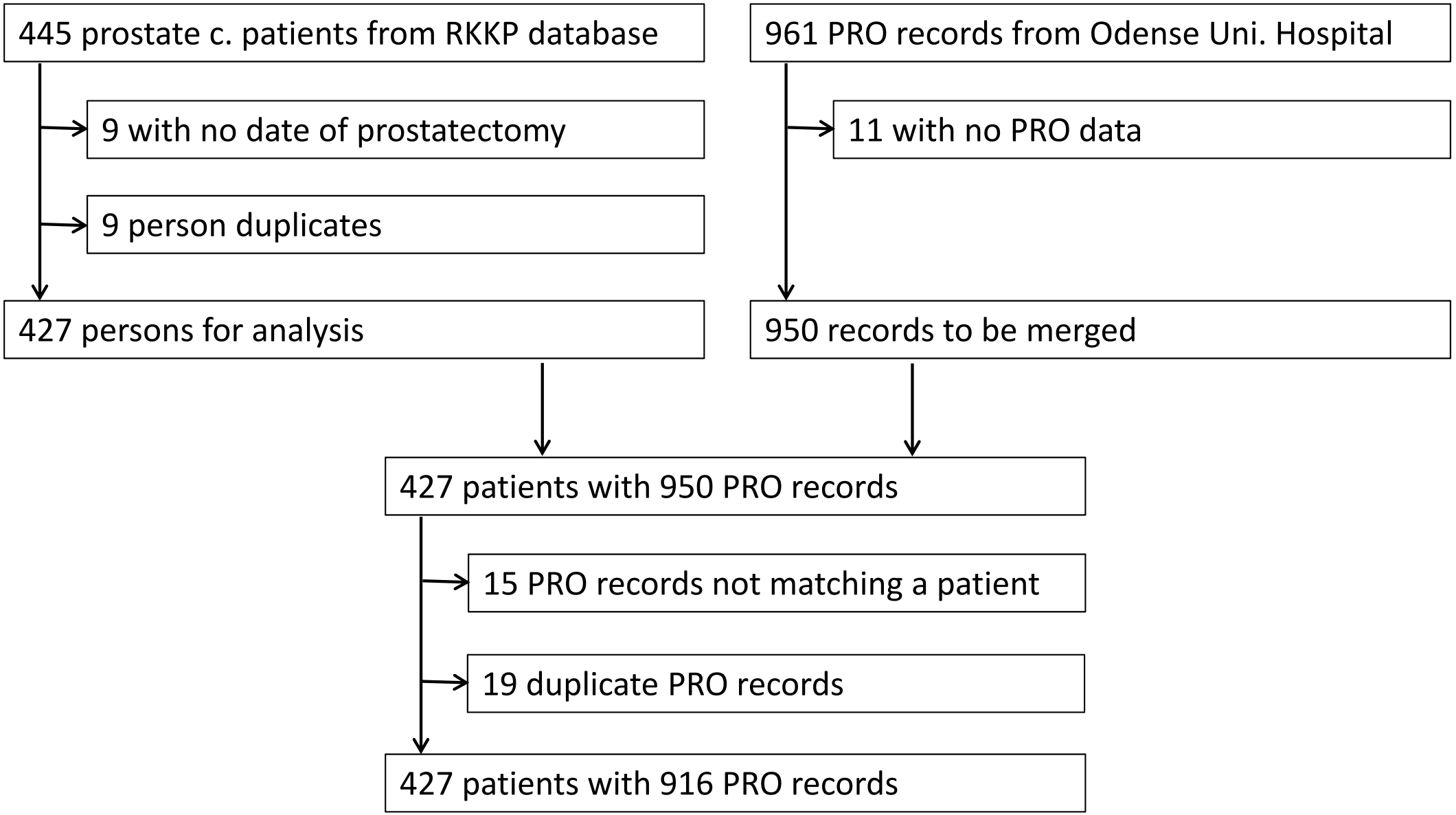

445 prostate c. patients from RKKP database
961 PRO records from Odense Uni. Hospital
9 with no date of prostatectomy
11 with no PRO data
9 person duplicates
427 persons for analysis
950 records to be merged
427 patients with 950 PRO records
15 PRO records not matching a patient
19 duplicate PRO records
427 patients with 916 PRO records

Table 1. Overview of data material of 427 prostate cancer patients.

		N	%	Assigned quality score
Age at diagnosis	40s	5	1	
	50s	83	19	
	60s	253	59	
	70s	86	20	
Hight	*Available*	*76*	*18*	
	NA	*351*	*82*	
Weight	*Available*	*88*	*21*	
	NA	*339*	*79*	
Charlson index	0	328	77	
	1	64	15	
	2+	35	8	
RP year	2016	39	9	
	2017	257	60	
	2018	131	31	
PSA at diagnosis	0-9.9	249	58	
	10-19.9	104	24	
	20+	44	10	
	NA	30	7	
Gleason grade	<7	57	13	
	7	300	70	
	>7	19	4	
	NA	51	12	
T stage	0-2	309	72	
	3-4	111	26	
	NA	7	2	
Operation type	Open	4	1	
	Endoscopic	423	99	
Nerve-sparing technique	0	224	52	
	1	203	48	
Genindlæggelse inden for 30 dage efter prostatektomi				
	0	378	89	1
	1	49	11	0
Indlagt mere end 3 dage efter prostatektomi				
	0	419	98	1
	1	8	2	0

Table 2. Overview of data material for 916 PRO returns.

			N	%	Assigned quality score	%
Year of PRO	2017		450	49		
	2018		466	51		
PRO batch	0		276	30		
	90		274	30		
	180		244	27		
	360		122	13		
"Hvor mange bleer eller indlæg har du brugt pr. dag for at kunne kontrollere din utæthed for urin?"						
25 - Bleer	1	Ingen	386	42	1	
	2	1	180	20	1	62
	3	2	107	12	0	
	4	3+	243	27	0	
"Problemer med at dryppe eller holde på vandet"						
27 - Dryppe	1	Ingen problemer	203	22	1	
	2	Meget små problemer	252	28	1	50
	3	Små problemer	181	20	0	
	4	Moderate problemer	164	18	0	
	5	Store problemer	116	13	0	
"Har du haft problemer med at få eller bevare en erektion?"						
20 - Erektion	1	Slet ikke	120	13	1	
	2	Lidt	147	16	1	29
	3	En del	153	17	0	
	4	Meget	496	54	0	
"Hvor meget påvirker prostatakræft dit helbred?"						
41 - QoL	1	Slet ikke	411	45	1	
	2	Lidt	329	36	1	81
	3	Noget	118	13	0	
	4	En hel del	49	5	0	
	5	Meget	9	1	0	
"Hvordan vil du vurdere din samlede livskvalitet i den forløbne uge?"						
43 - QoL	1	1: Meget dårligt	15	2	0	
	2	2	23	3	0	
	3	3	59	6	0	
	4	4	132	14	0	
	5	5	228	25	1	
	6	6	320	35	1	
	7	7: Særdeles godt	139	15	1	75
"Hvordan vil du vurdere dit samlede helbred i den forløbne uge?"						
44 - QoL	1	1: Meget dårligt	6	1	0	
	2	2	11	1	0	
	3	3	48	5	0	
	4	4	95	10	0	
	5	5	217	24	1	
	6	6	353	39	1	
	7	7: Særdeles godt	186	20	1	83

Table 3. 427 men with 916 PRO returns. Patterns of PRO returns, by time since operation

Time (days) since operation					
0	90	180	360	N	%
1				69	16
1	1			75	17
1	1	1		100	23
1	1	1	1	24	6
1	1		1	1	0
1		1		6	1
1		1	1	1	0
	1			16	4
	1	1		28	7
	1	1	1	29	7
	1		1	1	0
		1		11	3
		1	1	45	10
			1	21	5
				427 men	
276	274	244	122	--> 916 PRO returns	

Figure 2. Mean composite value score

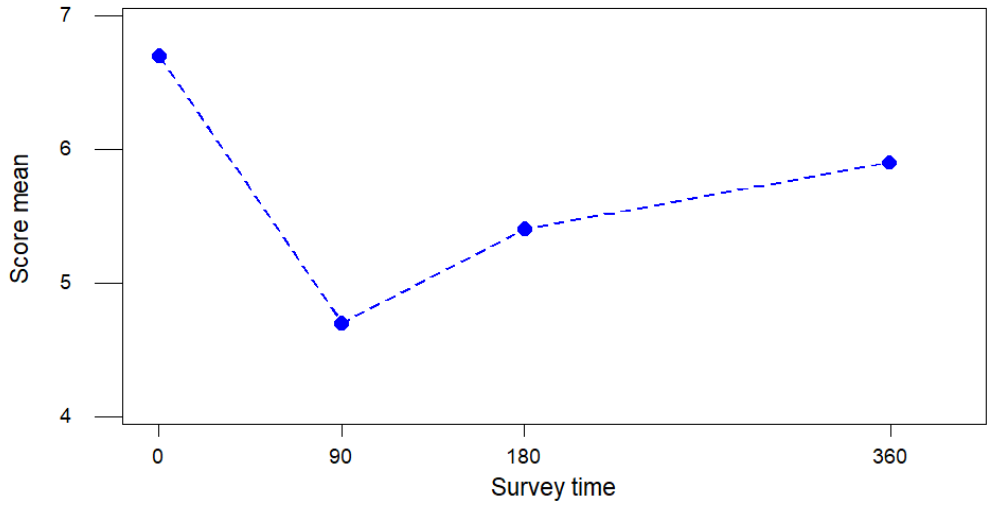


Figure 3. Prevalence of “All eight” component value scores.

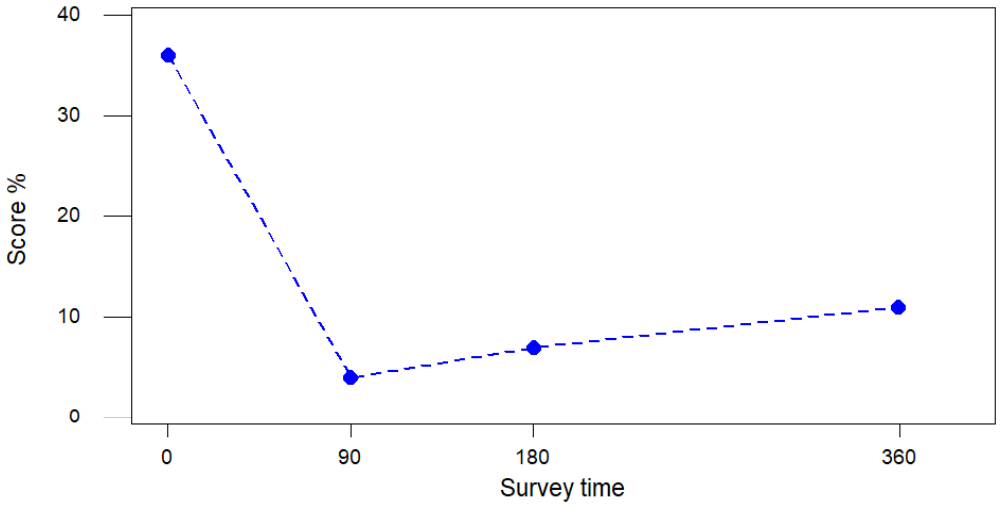


Table 4. Univariate analysis of the "All eight" binary outcome. Percentages of men and p-values for trend over categories.

		All eight value scores (%)			
PRO survey time (days after operation)		0	90	180	360
All men		36	4	7	11
Age at diagnosis	40s	**50**	**0**	**33**	**50**
	50s	**45**	**15**	**16**	**27**
	60s	**37**	**2**	**5**	**7**
	70s	**24**	**2**	**2**	**0**
		0.02	*0.005*	*0.001*	*0.001*
Charlson index	0	38	5	8	13
	1	27	5	6	7
	2+	35	0	0	0
		0.35	*0.58*	*0.18*	*0.13*
RP year	2016			9	**19**
	2017	35	5	7	**7**
	2018	37	3		
		0.77	*0.58*	*0.75*	*0.04*
PSA at diagnosis	0-9.9	**40**	**8**	**9**	13
	10-19.9	**31**	**0**	**2**	4
	20+	**20**	**0**	**0**	9
		0.02	*0.009*	*0.03*	*0.31*
Gleason grade	<7	35	11	11	16
	7	39	4	7	9
	>7	36	9	0	0
		0.83	*0.2*	*0.25*	*0.23*
T stage	0-2	35	5	9	12
	3-4	37	3	2	8
		0.72	*0.42*	*0.09*	*0.56*
Nerve-sparing technique	0	**29**	**1**	**2**	**2**
	1	**44**	**9**	**13**	**20**
		0.01	*0.001*	*0.001*	*0.001*

Bold type denotes statistically significant trend over the categories.

Table 5. Cross-sectional analysis of "All eight" binary value score according to PRO returns at 180 days

		Univariate				Mutually adjusted			
Predictor		OR	95% CI		p	OR	95% CI		p
Age	Per year	0.88	0.81	0.96	0.003	0.92	0.84	1.01	0.08
PSA	10-19 vs. 0-9	0.21	0.03	1.61	0.13	0.39	0.05	3.16	0.37
T	3,4 vs. 0,2	0.20	0.03	1.54	0.12	0.37	0.05	3.02	0.35
Nerve-sparing	Y vs. N	9.55	2.15	42.51	0.003	9.40	1.49	59.46	0.017