UNIVERSITY OF TWENTE.

N. IRELAND Cancer Registry

Burden of PSA testing

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Master thesis Health Sciences
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27-06-2017

Preface

I present my thesis for the master study Health Sciences entitled 'Burden of PSA testing'. The project was established by collaboration between the University of Twente and the N. Ireland Cancer Registry, Queen's University Belfast. For the work, I have been hosted by the N. Ireland Cancer Registry for the past four months.

I have been greatly supported by many people during the work of this thesis. I would like to start by thanking all staff in the Northern Ireland Cancer Registry for making the time in Belfast really enjoyable. In particular I would like to thank Dr Anna Gavin (Registry Director) and Dr Therese Kearney. I would like to extend my thanks and appreciation to Dr David Donnelly and Prof Linda Sharp, both of whom offered expert guidance with the statistical element of my thesis. A very special thanks to my supervisors Prof Sabine Siesling and Dr Jeannette van Manen in the Netherlands for their valid support and comments. They have been a great support and were always very enthusiastic during Skype meetings about my project and activities around it. I also would like to thank Movember and Prostate Cancer UK which funded the project to gather the data made available to me for this project and the wider Life After Prostate Cancer Diagnosis (LAPCD) team. Finally, I would like to thank the men who took the time to respond to the LAPCD survey, without them this piece of work would not have been possible.

I also would like to thank my parents for supporting me during my whole study, financially and emotionally. I would like to thank them and Joris for being a great support when I decided to take the chance to complete my master thesis abroad. In the beginning it was a bit scary, but with their help I made a great start and settled quickly into Belfast; so much that I have decided to come back in September for a few months to work within the Northern Ireland Cancer Registry. Thanks as well to the friends from my parent's home town and from Enschede who supported me doing my internship abroad. Special thanks to the friends who visited me in Belfast. We had fantastic weekends and I loved showing you all around Belfast and telling you the history of the city.

Thank you all for supporting me during my stay in Belfast! I had a really great time and I am looking forward to coming back to Belfast.

Linda Vis

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Abstract

Aim: Increasingly it is recognised that PSA testing for prostate cancer does not meet the criteria for screening. However, the use of PSA testing has led to a large increase in cases diagnosed which could represent overdiagnosis. Prostate cancer treatments have recognised long term side effects. The aim of this work is to investigate the difference between symptomatically and PSA diagnosed men in general characteristics and prostate cancer related physical outcomes, and to estimate the health burden on men with PSA detected prostate cancer.

Participants: Men aged 40-74 diagnosed with prostate cancer 18-42 months previously in England, N. Ireland, Scotland and Wales.

Method: A cross-sectional postal survey sent to prostate cancer survivors 18-42 months post-diagnosis, to gather information about the prostate cancer related physical outcomes (EPIC-26 and EORTC QLQ C30 fatigue subscale). Questions included whether responders were symptomatic at diagnosis or detected by a PSA test without symptoms. Reported outcomes between these two groups were compared using univariate and multivariate logistic regression analysis.

Results: 35,823 men responded (response rate of 60.8%), from which 13,086 men (aged under 75) reported being diagnosed symptomatically and 3,994 men by PSA testing. PSA diagnosed men were younger, had a lower stage of disease, lower Gleason score, less comorbidities and had a more affluent status, compared to symptomatically diagnosed men. PSA diagnosed men also reported less bother with urinary incontinence (16.3% vs 21.7%), urinary irritation (10.3% vs 20.1%), sexual function (15.1% vs 21.7%), bowel function (15.4% vs 23.3%), hormonal function (11.2% vs 22.2%) and fatigue (17.2% vs 31.1%), than symptomatic men after treatment. All differences between symptomatically and PSA diagnosed men in prostate cancer related physical outcomes were significant. These differences remained significant after univariate and multivariate logistic regression analysis which took differences in general characteristics into account.

Conclusion: While PSA diagnosed men reported significant symptoms after treatment, these were less for urinary incontinence, urinary irritation, sexual function, bowel function, hormonal function and fatigue, than for symptomatic men. We estimate that over 7,000 men per year are diagnosed with prostate cancer by PSA testing in the UK. Many of them have serious negative impacts as a result of PSA testing. Besides the prostate cancer related outcomes there is also an economic aspect of PSA testing. Research is required to look at the value of PSA testing with the aspect of costs in mind.

Introduction

Prostate cancer is the most commonly diagnosed cancer in Western countries and the second most common diagnosed cancer worldwide (1,2). It can be diagnosed in men who present symptomatically or in asymptomatic men by a prostate specific antigen (PSA) test as part of a general/private health check. The introduction of PSA testing at the end of the 1980s resulted in a rapid increase in prostate cancer incidence, with a peak in 1992 in the United States (US) (3). Due to more men receiving an earlier diagnosis, the incidence of local tumours has increased 40-50% in Europe and the US (from 4 per 1000 men in 1987 to 6 per 1000 men in 1996) (3,4). However, controversies exist in the effectiveness of PSA testing as a screening test for prostate cancer. The numbers of metastatic cancers diagnosed has remained constant (5) resulting in what appears to be a decrease in late diagnosed cancers due to the overall increase in numbers diagnosed. The proportions for metastatic cancer have decreased by 65% (from 0.68 per 1000 patients in 1995 to 0.24 per 1000 patients in 2000) (3). The introduction of PSA testing also coincided with a lowering in prostate cancer related mortality from a rate of 21-28% (4,6), however this decrease may also be explained by improved anti-cancer therapies, earlier use of hormonal therapy and earlier detection of recurrent disease (3,7). The research of Bannon and Gavin (5) showed that although the number of deaths in Northern Ireland remained constant, the mortality rate from prostate cancer decreased. The increased number of men diagnosed and the decreased mortality rate has resulted in an increase in the prevalence of men living after a diagnosis of prostate cancer. The PLCO study showed no mortality benefit from PSA testing (8).

The message to diagnose cancer early through screening tests are applied for cervical, bowel and breast cancer and so men see PSA testing as a way of diagnosing prostate cancer early. However, PSA testing does not meet the criteria for organized large scale population screening (9,10), although it can be used as part of an individual's diagnosis. Therefore shared-decision making between the clinician and patient is recommended in Europe and the US for men at risk of prostate cancer (6,11). One of the main problems is that PSA testing can lead to diagnosis of clinically insignificant tumours (overdiagnosis) (3,4). There is also lead time bias where men are aware for longer of their diagnosis due to early detection before clinical symptoms, but with no impact on mortality. Men that are diagnosed with prostate cancer, but would have died of other causes before the time of clinical diagnosis, are also considered overdiagnosed (3). Because of this the U.S. Preventive Services Task Force (11) states that men 75 years and older should not be screened by PSA testing, because men with a life expectancy less than 10 years are unlikely to benefit from PSA testing. Research showed that between 23-43% of the PSA detected cancers are overdiagnosed (3,4). Research by Schröder et al. (6) indicated that 781 men need to be invited (NNI) for a PSA test and 27 men need to be detected (NND) with prostate cancer to prevent one men dying from prostate cancer. Clinicians and patients, when faced with a diagnosis of prostate cancer, whether presented symptomatically or via PSA test, opt for treatment which can result in moderate to severe side effects and unnecessary costs (3,7).

Research indicates that men diagnosed by PSA testing are younger, have a lower stage of disease, have a lower Gleason score, are more likely to have an aggressive treatment, have less comorbidities and are more affluent, in comparison with symptomatically diagnosed men (12–14). Research also indicated that PSA tested men were more likely to report less side effects in terms of urinary incontinence, bowel problems and fatigue (12). However, to our knowledge the difference in general characteristics and quality of life outcomes of PSA tested and symptomatic men has never been studied in a UK wide population, within 4 years post-diagnosis. This information can help in the

debate about the use and effects of PSA testing in asymptomatic men and perhaps influence future uptake of PSA testing.

This research aims to answer the questions ‘What is the difference in general characteristics between men diagnosed by PSA testing and men diagnosed symptomatically?’ and ‘What is the estimated health burden on men linked with PSA testing?’.

Method

This study is undertaken as part of the 'Life After Prostate Cancer Diagnosis' (LAPCD) study. The methods of this study have been described in a previous publication (15), however below is a short summary of the methods used.

Ethical approval

The LAPCD study has received the following approvals: Newcastle and North Tyneside 1 Research Ethics Committee (15/NE/0036), Health Research Authority Confidentiality Advisory Group (15/CAG/0110), NHS Scotland Public Benefit and Privacy Panel (0516-0364), Office of Research Ethics, Northern Ireland (16/NI/0073) and NHS R&D approval from Wales, Scotland and Northern Ireland.

Participants

In total, 58,930 men aged 40 or over diagnosed with prostate cancer 18-42 months previously were surveyed by postal questionnaire in England, Wales, Scotland and Northern Ireland. In England, Wales and Northern Ireland the cancer registries were used to identify eligible men, and in Scotland hospital activity data (with cross checking against the Scottish Cancer Registry to confirm a diagnosis of prostate cancer) was used. For this study only results from men younger than 75 years at time of diagnosis were included as PSA testing is not recommended for men 75 years and older (11).

Survey

Men were asked to report all treatments received by answering yes/no to a list of treatments (radical prostatectomy, external beam radiotherapy, brachytherapy, hormone therapy, active surveillance and watchful waiting). Men were also asked about their overall health, method of diagnosis, symptoms, difficulties in life, emotional well-being, and sociodemographic characteristics. The EPIC-26 and EORTC QLQ-C30 Fatigue symptom scale questionnaires were used to measure the physical health-related quality-of-life of the symptomatic and PSA diagnosed respondents. The EPIC-26 questionnaire is made up of 5 sections; urinary incontinence, urinary irritation (including obstruction), bowel, sexual, and hormonal function (16). Fatigue was included as a subscale with three items (17). All domains are scored out of a total of 100. For the EPIC-26 questionnaire, a lower score for each outcome represents more problems/poorer functioning. For the fatigue subscale, a higher score represents a worse experience of fatigue. For the other parts of the survey other validated questions were used. A structure of the survey and the survey itself are included in Appendix A.

Stage and Gleason grade (GG) at diagnosis, nation and deprivation for all men were extracted from the cancer registries (England, Wales and Northern Ireland) or from hospital records (Scotland).

Statistical analysis

Health-related quality of life outcomes of men diagnosed symptomatically and men diagnosed by PSA testing (most likely confirmed with a biopsy) were compared. These subgroups were created based on the self-reported method of diagnosis (Question 7 of the survey: How were you diagnosed? Please tick all that apply). The men who ticked the boxes 'I attended my GP with urinary symptoms' or 'I attended my GP with other symptoms' were categorised as symptomatic, the men who ticked the boxes 'I had no symptoms and my GP offered to test my PSA as part of a general health check', 'I had no symptoms and I asked my GP to measure my PSA', or 'I had a PSA test as part of a private health

check' were categorised as PSA tested, and the men who ticked the box 'Other' were categorised as other. Men with contradictory answers were also categorised as other.

The analysis consisted of three parts. In the first part descriptive statistics were used to report the differences in symptomatically and PSA diagnosed men. Initially three subgroups were created (i.e. symptomatic, PSA tested, and other), however, analysis of the different subgroups showed that the men who ticked the option 'I had no symptoms and my GP offered to test my PSA (blood test) as part of a general health check' may have had symptoms which caused the GP concern but not the patient. These men were categorised as a separate subgroup ('GP offered to test PSA') and were, together with the subgroup 'Other', excluded in the analysis. A description of differences between symptomatically and PSA diagnosed men is presented in Table 1. A descriptive table of all subgroups is included in supplementary table 1 (Appendix B). Significant differences between the PSA tested and symptomatic men were analysed by chi-square tests.

In the second part outcomes were reported for PSA tested versus symptomatic prostate cancer patients again for all men younger than 75 years. The proportions of men that experienced a poor physical outcome were reported relative to the men that did not experience that physical outcome as poor. The variables age, stage, Gleason score, treatment type, comorbidities and deprivation status were included in this descriptive table as the literature indicated that these variables best explain the differences between symptomatic and PSA tested men (12–14). A table with all responders is included in supplementary table 2 (Appendix B). Z-tests for proportions were used to report the significant differences between symptomatic and PSA tested men.

In the third part of the analysis the impact of PSA testing was analysed using multivariate regression models. First the assumptions of linear regression were tested with the use of a scatterplot, histogram, p-p plot, Durbin-Watson test, and collinearity test, however analysis revealed that the normality assumptions (i.e. histogram and p-p plot) were violated. Second, the linear outcomes were transformed into log-linear outcomes for a log-linear regression analysis. However, this analysis showed a poorer fit of the model. Third, the linear outcomes were transformed into binary outcomes for a binary logistic regression analysis. To our knowledge no cut-off points were available for urinary incontinence, urinary irritation, sexual function, bowel function and hormonal function. Therefore, a cut-off point of 20% of the worst self-reported scores was used for these symptoms. These men were labelled as having a poor experience on these symptoms. A sensitivity analysis was performed at the cut-off points of 25% and 30% to examine the sensitivity of the chosen cut-off point of 20%. The fatigue subscale was analysed with a recently published cut-off value of 39 (18). A score of 39 or higher represents a poorer experience of fatigue, and so is of higher clinical importance. Patients with missing values from the outcome under investigation were excluded from analysis. All variables were transformed into binary variables. A separate category was made for missing values, which were then excluded throughout, with the exception of stage and Gleason, because these categories can sometimes reflect some aspect of patient care.

Univariate analysis and multivariate analysis were performed. For each outcome a multivariate regression model was made that included all variables. Then, for each model the non-significant variables were excluded. Lastly, the fit of the models was tested by R square and the collinearity by the variance Inflation Factor (VIF). For each model, there was an increased R square, i.e. a better fit of the model, compared to when one of the significant variables was taken out of the model. Also, the

VIF was between 1 and 5 for all variables, which indicated that the variables showed no important correlation. The results of this study were extrapolated in estimating the health burden of PSA testing on national level. Significance was set at a 5% level. In order to prevent disclosure of potentially identifiable respondent data, cells with counts less than five were simply reported as <5.

Analyses were performed using SPSS v22 (19).

Results

A total of 35,823 men responded, a response rate of 60.8%. However, this study excluded the men 75 years and older. 26,919 men (75.1% of all respondents) were under the age of 75 years. 48.6% of these men reported that they were diagnosed symptomatically and 14.8% of these men were diagnosed through PSA testing as defined for this study. The column 'All respondents' includes all the men younger than 75 years who responded on the questionnaire. The overall numbers showed that almost two-third of the men (63.1%) were between 65 and 74 years old, 31.7% had stage I disease, 40.7% had a Gleason score of 7, 24.2% reported having the treatment surgery only, 60.8% were not employed (2.5%) or retired (58.3%), 80.4% were married or had a civil partnership, 93.9% were heterosexual, 94.1% were white, 35.5% reported one comorbidity, 84.6% were from England and 26.4% were from the least deprived quintile, at questionnaire completion. (see table 1)

The further analysis included only the men diagnosed symptomatically or by PSA testing. 17,080 men (63.4% of all respondents <75) reported being diagnosed symptomatically (76.6%) or by PSA testing (screening) (23.4%). The general characteristics of the respondents indicate that PSA tested men were younger at diagnosis, had a lower stage and Gleason score at diagnosis compared to symptomatic men. The results also indicate that PSA tested men had less comorbidities and were from a more affluent background than symptomatically diagnosed men. A higher percentage of PSA tested men received surgery only and brachytherapy only, while a higher percentage of symptomatic men were treated with hormone therapy only, external beam radiotherapy only, and with the combination of hormone therapy and external beam radiotherapy. (see table 1)

Table 1: General characteristics of respondents

	Symptomatic (%) (n= 13,086) (48.6%)	**PSA tested (%)** (n= 3,994) (14.8%)	**All respondents (%)*** (n= 26,919) (100.0%)	**P-value****
Age at diagnosis, mean (SD)	65.63 (5.8)	64.78 (6.1)	65.55 (5.9)	<0.001
Age at diagnosis				<0.001
- <55	639 (4.9%)	266 (6.7%)	1,392 (5.2%)	
- 55-64	4,169 (31.9%)	1,380 (34.6%)	8,529 (31.7%)	
- 65-74	8,274 (63.2%)	2,348 (58.8%)	16,992 (63.1%)	
- Unknown/missing	<5	0 (0.0%)	6 (0.0%)	
Stage				<0.001
- 1	3,899 (29.8%)	1,349 (33.8%)	8,542 (31.7%)	
- 2	3,115 (23.8%)	1,146 (28.7%)	6,862 (25.5%)	
- 3	2,797 (21.4%)	728 (18.2%)	5,395 (20.0%)	
- 4	1,702 (13.0%)	174 (4.4%)	2,669 (9.9%)	
- Unknown/missing	1,573 (12.0%)	597 (14.9%)	3,451 (12.8%)	
Gleason score				<0.001
- 2-6	3,526 (26.9%)	1,180 (29.5%)	7,615 (28.3%)	
- 7	4,955 (37.9%)	1,790 (44.8%)	10,951 (40.7%)	
- 8-10	3,382 (25.8%)	645 (16.1%)	5,805 (21.6%)	
- Unknown/missing	1,223 (9.3%)	379 (9.5%)	2,548 (9.5%)	
Treatment				<0.001
- Surgery	2,817 (21.5%)	1,239 (31.0%)	6,516 (24.2%)	
- External beam radiotherapy	1,044 (8.0%)	254 (6.4%)	2,135 (7.9%)	
- Brachytherapy	383 (2.9%)	248 (6.2%)	1,075 (4.0%)	
- Hormone therapy	771 (5.9%)	84 (2.1%)	1,269 (4.7%)	
- Active surveillance	1,179 (9.0%)	383 (9.6%)	2,488 (9.2%)	
- Watchful waiting	616 (4.7%)	178 (4.5%)	1,309 (4.9%)	
- Surgery and external beam radiotherapy	421 (3.2%)	151 (3.8%)	904 (3.4%)	
- Surgery, hormone therapy and external beam radiotherapy	422 (3.2%)	147 (3.7%)	844 (3.1%)	
- Hormone therapy and external beam radiotherapy	3,337 (25.5%)	829 (20.8%)	6,351 (23.6%)	*
- Unknown/missing	2,096 (16.0%)	481 (12.0%)	4,028 (15.0%)	

Employment status				<0.001
- Employed	4,703 (35.9%)	1,667 (41.7%)	9,935 (36.9%)	
- Not employed/retired	8,112 (62.0%)	2,250 (56.3%)	16,374 (60.8%)	
- Other/missing	271 (2.1%)	77 (1.9%)	610 (2.3%)	
Marital status				<0.001
- Married/partnership	10,528 (80.5%)	3,352 (83.9%)	21,635 (80.4%)	
- Single (separated, divorced, widowed, single)	2,260 (17.3%)	560 (14.0%)	4,623 (17.2%)	
- Other/unknown/missing	298 (2.3%)	82 (2.1%)	661 (2.5%)	
Sexuality				0.502
- Heterosexual/straight	12,354 (94.4%)	3,784 (94.7%)	25,281 (93.9%)	
- Homosexual/bisexual	164 (1.3%)	53 (1.3%)	359 (1.3%)	
- Don't know/prefer not to answer/missing	568 (4.3%)	157 (3.9%)	1,279 (4.8%)	
Ethnicity				0.001
- White	12,433 (95.0%)	3,736 (93.5%)	25,333 (94.1%)	
- (British) Asian/Black (British) /African/Caribbean/Mixed	324 (2.5%)	140 (3.5%)	834 (3.1%)	
- Other/missing	329 (2.5%)	118 (3.0%)	752 (2.8%)	
Comorbidities				<0.001
- No comorbidities	3,943 (30.1%)	1,488 (37.3%)	8,439 (31.3%)	
- 1	4,546 (34.7%)	1,468 (36.8%)	9,556 (35.5%)	
- 2	2,543 (19.4%)	634 (15.9%)	5,070 (18.8%)	
- 3	1,172 (9.0%)	223 (5.6%)	2,181 (8.1%)	
- 4 or more	882 (6.7%)	181 (4.5%)	1,673 (6.2%)	
Nation				<0.001
- England	10,920 (83.4%)	3,413 (85.5%)	22,768 (84.6%)	
- Wales	920 (7.0%)	316 (7.9%)	1,929 (7.2%)	
- Scotland	869 (6.6%)	147 (3.7%)	1,432 (5.3%)	
- Northern Ireland	377 (2.9%)	118 (3.0%)	790 (2.9%)	
Socioeconomic status (deprivation quintiles)				<0.001
- 1 – Affluent	3,346 (25.6%)	1,271 (31.8%)	7,104 (26.4%)	
- 2	3,345 (25.6%)	1,072 (26.8%)	6,929 (25.7%)	
- 3	2,687 (20.5%)	788 (19.7%)	5,511 (20.5%)	
- 4	1,988 (15.2%)	499 (12.5%)	3,980 (14.8%)	
- 5 – Deprived	1,416 (10.8%)	285 (7.1%)	2,764 (10.3%)	
- Unknown/missing	304 (2.3%)	79 (2.0%)	631 (2.3%)	

* The column 'All respondents' includes the men younger than 75 from the categories 'GP offered PSA test' and 'Other', and the men who did not answer the question about the method of diagnosis.

** P-value compares the symptomatic and PSA tested men.

Outcomes – general

PSA tested men were less likely to report poor urinary incontinence, urinary irritation, sexual problems, bowel problems, hormonal problems and fatigue, compared to symptomatically diagnosed men. In general, poorer physical outcomes were reported by men with a higher stage of disease, higher Gleason score, those with more comorbidities and from a more deprived area. The experience by age was not the same for all symptoms. Younger men reported poorer urinary incontinence and urinary irritation more than older men while poorer sexual function was more associated with older age groups. Symptomatic men reported poorer bowel function, hormonal function and fatigue with a younger age, while PSA tested men reported poorer experiences at an older age.

Both symptomatic and PSA tested men experienced the poorest urinary incontinence after treatments that included surgery, the poorest sexual function, hormonal function and fatigue after treatments that included hormone therapy (HT), and the poorest bowel function after treatments that included external beam radiotherapy (EBRT). Symptomatic men reported the poorest urinary irritation after active surveillance (AS), while PSA tested reported this poorest after the treatment combination of surgery, hormone therapy and external beam radiotherapy. (see table 2)

Table 2: Proportions of symptoms by age, stage, Gleason, treatment, comorbidities and deprivation for all men <75

	Poor urinary incontinence score[a,c]		Poor urinary irritation score[a,c]		Poor sexual score[a,c]		Poor bowel score[a,c]		Poor hormonal score[a,c]		Poor fatigue score[b,c]	
Method of diagnosis	Symp-toms %	PSA %	Symp-toms %	PSA %	Symp-toms %	PSA %	Symp-toms %	PSA %	Symp-toms %	PSA %	Symp-toms %	PSA %
Overall number (n)	2,584	609	2,226	364	2,673	575	2,734	562	2,677	419	3,772	644
Overall scores	21.7	16.3**	20.1	10.3**	21.7	15.1**	23.3	15.4**	22.2	11.2**	31.1	17.2**
Age at diagnosis												
- <55 (n= 905)	25.6	18.1*	24.7	11.4**	13.6	8.5%*	25.4	14.6**	23.7	10.7**	33.3	14.6**
- 55-64 (n= 5,549)	23.8	16.6**	21.8	10.2**	19.4	11.6%**	23.6	13.9**	24.3	10.5**	32.2	15.3**
- 65-74 (n= 10,622)	20.2	15.9**	18.7	10.3**	23.6	18.0%**	22.9	16.4**	20.9	11.6**	30.4	18.6**
- Missing/ unknown (n= 4)	33.3	0.0	50.0	0.0	66.7	0.0%	100.0	0.0	66.7	0.0	50.0	0.0
Stage												
- 1 (n= 5,248)	20.4	14.8**	22.4	11.7**	15.1	10.7**	21.5	13.5**	13.6	6.9**	26.9	13.7**
- 2 (n= 4,261)	23.6	18.1**	17.8	8.2**	19.6	15.7*	22.6	13.8**	16.8	9.9**	28.7	16.9**
- 3 (n= 3,525)	23.2	18.6*	18.0	9.3**	28.6	22.7*	26.4	21.2*	30.1	17.6**	31.8	21.3**
- 4 (n= 1,876)	17.7	13.7	21.2	14.9	32.3	31.1	23.9	25.3	40.3	35.2	44.3	31.6*
- Missing/ unknown (n= 2,170)	22.6	14.3*	21.0	11.1**	18.8	10.0**	22.9	13.0**	20.3	8.5**	30.7	16.3**
Gleason score												
- 2-6 (n= 4,706)	20.3	12.6**	22.3	11.5**	13.2	10.0*	18.2	11.2**	11.4	5.3**	26.6	11.7**
- 7 (n= 6,745)	23.2	18.6**	17.0	8.0**	21.3	14.9**	24.1	15.4**	19.9	9.6**	28.6	17.5**
- 8-10 (n= 4,027)	21.3	18.0	21.5	12.9**	30.3	25.7*	27.3	23.0*	35.8	25.4**	38.6	26.8**
- Missing/ unknown (n= 1,602)	20.6	14.3*	21.8	13.4**	24.9	14.0**	23.6	15.8*	24.9	13.1**	33.7	16.3**
Treatment												
- Surgery (n= 1,562)	36.4	30.4**	12.6	4.9**	19.0	13.4**	13.9	5.9**	8.0	3.8**	20.7	12.0**
- EBRT (n= 4,056)	15.8	7.3**	19.8	11.1*	24.0	14.9*	30.7	24.1	19.8	11.8*	30.7	15.8**
- BT (n= 1,298)	9.6	5.5	21.4	17.8	7.3	4.6	21.4	19.8	6.1	2.9	18.5	11.2*
- HT (n= 631)	13.3	5.4	22.7	8.8*	29.7	28.8	14.2	18.1	39.3	31.9	38.7	29.2
- AS (n= 572)	14.1	6.1**	29.8	13.3**	6.7	3.6*	12.9	7.2*	5.9	2.2*	21.3	9.4**
- WW (n= 4,166)	16.3	6.2*	24.6	11.0**	8.9	7.9	14.5	6.3*	5.9	2.4	23.5	10.5**
- Surgery + EBRT (n= 569)	35.2	25.9*	14.4	6.7*	22.9	22.4	28.9	22.7	11.1	4.3*	26.0	16.7*
- Surgery + HT + EBRT (n= 855)	36.2	31.0*	23.3	20.0	31.7	30.0	32.6	37.1	35.3	25.9*	39.5	22.7**
- HT + EBRT (n= 794)	15.1	6.6**	20.1	11.5**	26.0	20.6*	33.6	26.1**	35.6	24.5**	37.3	26.9**
- Unknown/ missing (n= 2,577)	20.1	12.4**	22.6	14.2**	27.5	18.2**	25.4	16.4**	31.2	16.4**	42.6	22.8**
Comorbidities												
- None (n= 5,431)	17.9	14.4*	14.0	8.4**	16.4	10.5**	15.5	10.3**	16.0	7.8**	19.2	10.0**
- 1 (n= 6,014)	20.1	16.3*	18.4	9.3**	19.9	15.4**	20.4	14.5**	19.5	8.7**	26.1	14.9**
- 2 (n= 3,177)	24.7	18.6*	23.6	12.5**	25.0	19.0*	28.3	21.7*	25.3	18.5**	39.3	26.0**
- 3 (n= 1,395)	26.7	18.9*	29.7	13.8**	32.6	20.5**	37.9	27.5*	35.0	20.6**	54.2	34.8**
- 4 or more (n= 1,063)	31.8	22.2*	33.4	23.2*	31.2	30.6	40.6	28.6*	39.3	22.9**	56.9	41.5**
Socioeconomic status (deprivation quintiles)												
- 1 – affluent (n= 4,617)	19.0	14.9*	17.7	9.5**	16.3	11.4**	20.1	15.2**	16.3	9.2**	24.2	15.5**
- 2 (n= 4,417)	18.8	15.5*	18.0	10.7**	20.4	14.3**	22.4	15.2**	20.2	10.0**	28.4	16.1**
- 3 (n= 3,475)	21.7	17.9*	20.2	10.3**	24.9	19.8*	24.4	16.5**	23.6	13.0**	33.0	18.5**
- 4 (n= 2,487)	24.6	17.4*	22.7	9.8**	23.7	16.5**	24.8	12.2**	26.5	13.2**	37.1	17.5**
- 5 – deprived (n= 1,701)	31.2	20.4**	27.0	13.9**	30.4	20.8*	29.2	20.4*	33.6	17.0**	43.1	25.2**
- Unknown/ missing (n= 383)	22.1	15.3	21.4	10.0*	17.6	8.2*	24.1	13.2*	23.8	10.4*	31.3	14.7*

Significant difference between symptomatic and PSA tested men; *p<0.05, **p<0.001

[a] Urinary incontinence, urinary irritation, sexual function, bowel function and hormonal function are based on the EPIC-26 (17)

[b] Fatigue is based on the EORT QLQ C30 Fatigue subscale (18)

[c] Poor scores were based on the 20% lowest values (urinary incontinence: 0-65, urinary irritation: 0-69, sexual function: 0-1, bowel function: 0-79, hormonal function: 0-63, fatigue: 39-100)

Outcomes – symptomatic vs PSA tested

The univariate binary logistic regression analysis showed a significant difference between symptomatically and PSA diagnosed men in all self-reported prostate cancer related physical outcomes. After adjusting for significant confounders (see footnotes below table 3), the risk of poor urinary incontinence, urinary irritation, sexual function, bowel function, hormonal function and fatigue after treatment was significant lower for PSA tested than for symptomatically diagnosed men (see table 3; all p<0.001). These differences persisted for all outcomes after adjustments for confounders. The adjusted analysis revealed that PSA tested men had 1.5 times (1/0.69) less risk of urinary incontinence, 2.0 times (1/0.50) less risk of urinary irritation, 1.3 times (1/0.79) less risk of sexual problems, 1.5 times (1/0.67) less risk of bowel problems, 1.7 times (1/0.59) less risk of hormonal problems, and 1.8 times (1/0.56) less risk of fatigue, after treatment, compared to symptomatically diagnosed men. The sensitivity analysis with cut-off levels of 25% and 30% did not show important differences in the results.

Table 3: Patient-reported health-related quality of life outcomes prostate cancer

	Proportion		**Univariate**		**Multivariate model**	
	Sympto-matic	PSA tested	OR* (95% CI)	p-value	OR* (95% CI)	p-value
EPIC-26: Urinary incontinence	21.7%	16.3%	0.71 (0.64 – 0.78)	<0.001	0.69[a] (0.62 – 0.77)	<0.001
EPIC-26: Urinary irritation	20.1%	10.3%	0.46 (0.41 – 0.52)	<0.001	0.50[b] (0.45 – 0.57)	<0.001
EPIC-26: Sexual function	21.7%	15.1%	0.64 (0.58 – 0.71)	<0.001	0.79[c] (0.71 – 0.87)	<0.001
EPIC-26: Bowel function	23.3%	15.4%	0.60 (0.54 – 0.66)	<0.001	0.67[d] (0.60 – 0.74)	<0.001
EPIC-26: Hormonal function	22.2%	11.2%	0.44 (0.39 – 0.49)	<0.001	0.59[e] (0.52 – 0.66)	<0.001
EORTC QLQ C30: Fatigue	31.1%	17.2%	0.46 (0.42 – 0.50)	<0.001	0.56[f] (0.51 – 0.62)	<0.001

* Symptomatic men were used as the reference group in the ORs (odds ratios)

[a] Adjusted for stage, Gleason score, treatment, marital status, ethnicity, comorbdities, nation and deprivation

[b] Adjusted for age, stage, Gleason score, treatment, marital status, comorbdities, nation and deprivation

[c] Adjusted for age, stage, Gleason score, treatment, comorbidities, nation and deprivation

[d] Adjusted for age, Gleason score, treatment, marital status, comorbidities, nation and deprivation

[e] Adjusted for age, stage, Gleason score, treatment, marital status, sexuality, comorbidities, nation and deprivation

[f] Adjusted for age, stage, Gleason score, treatment, employment, marital status, sexuality, comorbidities, nation and deprivation

Discussion

To our knowledge this is the largest study to date in the world of self-reported outcomes in men with prostate cancer which reflects recent PSA testing patterns. This study showed that similar to the literature (12–14) PSA diagnosed men were younger, had a lower stage of disease, lower Gleason score, less comorbidities and had a more affluent status, compared to symptomatically diagnosed men. While PSA diagnosed men reported significant symptoms after treatment, these were less for urinary incontinence, urinary irritation, sexual function, bowel function, hormonal function and fatigue, than for symptomatic men.

The survey questions allowed us to split the men by method of diagnosis i.e. symptomatic vs PSA tested, thus enabling the investigation into the effects of PSA testing on men's health. To improve discrimination between PSA tested (screened) men and those presenting symptomatically, we excluded men where the PSA test was organised by their GP. We found that PSA diagnosed men were more likely to have surgery than men who presented symptomatically. This is similar to other studies (12,14,20,21). Similar to Schröder et al. (22) men diagnosed symptomatically tended to be treated with the combination of hormone therapy and external beam radiotherapy, reflecting their stage of disease and treatment options. Hormone therapy was low in PSA tested men and was more likely to be given to symptomatically diagnosed men. This can also be seen in studies by Van Leeuwen et al. (20), Drummond et al. (12), Postma et al. (14), and Schröder et al. (21).

Differences in symptomatic and PSA tested men between the nations were observed. A higher proportion of men diagnosed by symptoms were observed in Scotland, compared to the other nations. This could be due to the variation in methods used to identify patients that were eligible to be surveyed (Scotland from hospital data; England, Wales and Northern Ireland from cancer registries) and also that Scottish GPs were less favourably disposed to do a PSA test with asymptomatic men (22).

To our knowledge no clinically validated cut-off values were available for the EPIC-26 subscales used in this study. Therefore we used cut-off values based on the worst 20% scores. As a result, it is not possible to see whether the differences between the symptomatic and PSA tested men are clinically relevant. For fatigue a validated cut-off was used to study the fatigue the men reported. However, if this cut-off value is transformed to a ratio, about 25% of the worst self-reported scores are included.

After treatment PSA tested men were less likely to report poor urinary incontinence, urinary irritation, sexual function, bowel function, hormonal function and fatigue, compared with symptomatically diagnosed men. This corroborates with the study of Drummond et al. (12) where PSA tested men reported less urinary incontinence, bowel problems and hormonal effects (hot flashes/sweats). The study of Heijnsdijk et al. (4) suggested that this could be due to the younger age of PSA diagnosed men. However, our study has adjusted for age, and indicated only a small influence. The study of Drummond et al. (12) also showed that symptomatically diagnosed men experienced more severe fatigue than PSA diagnosed men, as a result of higher odds of anxiety, depression and stress in symptomatically diagnosed men. Although the results for physical symptoms are the same in these two studies, in the study of Drummond et al. (12) half of the men were >5 years post-diagnosis, and they had categorised men with an inconsistent answer as symptomatic, while the mode of diagnosis was unknown.

For both symptomatic and PSA tested men, the poorest urinary incontinence was reported after treatments that included surgery. Younger men, men with stages 2 and 3, and men with a Gleason score of 7 experienced poorer urinary incontinence than older men, men with stages 1 and 4 and men with a Gleason score of 2-6 and 8-10 did, this could be due to that surgery is preferably given to younger men with a less advanced disease. The poorest sexual function, bowel function, hormonal function and fatigue were experienced by symptomatic and PSA tested men with a higher stage and high Gleason score. This could also be related to the given treatment. The treatments that include hormone therapy and/or external beam radiotherapy may cause these symptoms and are preferably given to older men with a more advanced stage of disease.

Overall, the symptomatic men experienced poorer physical symptoms compared with PSA tested men, even after adjustments for confounders. Men with higher stages (except for urinary incontinence and urinary irritation), higher Gleason scores, and more comorbidities had a poorer experience of physical symptoms. This could be due to these men receiving more intense treatment to treat their prostate cancer. Also men from a more deprived area had a poorer experience of physical symptoms. A possible reason could be that these men did not have the financial resources to alleviate the burden of their symptoms.

The analysis of the differences between symptomatically and PSA diagnosed men showed that most differences were statistically significant. This could be due to the large study population. It would be hard to say whether the results are clinically relevant. However, the odds ratios in table 3 indicate a sizable difference between the two groups, even after adjusting for all significant variables. PSA tested men have 1.3 to 2.0 times less risk on poor physical outcomes after treatment, compared to symptomatically diagnosed men. This would indicate a clinically relevant difference between symptomatic and PSA tested men. Although PSA tested men reported less poor physical outcomes compared to symptomatic men, using PSA testing as a screening tool for prostate cancer would not necessarily be a solution, because still 23-43% of the PSA detected cancers are overdiagnosed (3,4). As a result, part of the men in this study, diagnosed by PSA testing, may be overdiagnosed cases and experience poor quality of life outcomes as a result of treatment they would otherwise never had experienced.

Limitations

This research had several limitations. The question on the survey asking men the method of diagnosis allowed the responders to tick multiple boxes. Some men ticked multiple contradictory boxes. As a result it was not possible to divide these men into the symptomatic or PSA tested group, these men were therefore put in the group ‘Other’. The men who ticked the box ‘Other’ in the research question had the possibility to respond in a free-text box. The study of Nayoan et al. (23) (within the LAPCD study) showed that a huge amount of men had recorded information about their symptoms in the free-writing box, but yet these men did not perceive their problems as symptoms. The comments may have helped with assigning these men, and men with contradictory answers, to the correct diagnosis group. These comments may have added greatly to this paper and may have shown stronger differences between PSA and symptomatically diagnosed men, because it could have made the allocation of the subgroups more accurate.

No comparison was made with the physical scores of men without prostate cancer to see what part of the reported patient outcomes could be explained by the result of treatment and what part by elderly

complaints. A general population study has been organised as part of the total LAPCD study, however results from this study are not yet analysed. The comparison between men in the general population and men with prostate cancer may also reduce the differences noted in patient reported outcome studies when comparing symptomatic and PSA tested men, as symptomatic men are older and therefore would have more physical burdens even without prostate cancer.

The Gleason score was coded as 2-6, 7, and 8-10. The category with a Gleason score of 7 represented the men with the score 3+4 and the score 4+3. However, there is a significant difference between these two groups. The study of Stark et al. (24) showed that men with the standardised Gleason score of 4 + 3 were 3.1 times more likely to develop bony metastasis and prostate cancer related death, compared to men with a Gleason score of 3 + 4.

Lastly, as the analysis of this study was based on self-reported characteristics and patient outcomes, this could possibly have led to recall bias (25). As a result, there could be differences in accuracy of the answers the men gave. Men with more severe side effects could have remembered their problems better than men without or with only slight side effects. The free-text comments that men made could have helped to improve the accuracy of the answers the men gave. However, this study was performed 4 years post-diagnosis, which made it less likely that the men would have forgotten their symptoms. Participating in this study was also voluntary, which could have led to non-response bias. The study of Cheung et al. (26) indicated that the health outcomes in a voluntarily study are underestimated, because men with better health outcomes are more likely to respond to a questionnaire. A comparison of responders and non-responders in age, ethnicity, stage and deprivation for all men (all ages) that was sent the questionnaire of the LAPCD study showed a significant difference in all these variables. The table with responders and non-responders can be seen in supplementary table 3 (Appendix B). If all men would have responded this could have led to worse quality of life outcomes than showed in the results.

Strengths

This large study had a high response rate and consisted of clinical data and patient related outcomes that looked at the self-reported physical side effects of men treated for prostate cancer, separated for men diagnosed by PSA testing and men diagnosed symptomatically. To our knowledge, the difference between PSA tested men and symptomatically diagnosed men in urinary incontinence, urinary irritation, bowel function, sexual function, hormonal function and fatigue has not been studied in total before.

Conclusion

Based on the evidence from randomised trials the PSA test does not meet the criteria as a screening test (6,8,9). However, in this study, with the application of strict criteria to identify men detected by PSA testing, at least 14.8% of men responded that they had been asymptomatic and had their prostate cancer diagnosed by a PSA test. Men diagnosed with prostate cancer by PSA testing were younger, had a lower stage of disease, had less comorbidities and reported better outcomes in terms of urinary incontinence, urinary irritation, sexual function, bowel function, hormonal function and fatigue after treatment compared to symptomatically diagnosed men. However, the PSA tested men had negative outcomes.

Extrapolating the results of this work to the population of the UK where about 46,700 men are diagnosed annually with prostate cancer (27), the burden of PSA testing on men's health can be calculated. With a conservative estimate, 14.8% of men (n= 6,912) are detected by PSA testing resulting in 1,127 men with urinary incontinence (16.3% of 6,912 men), 712 men with urinary irritation (10.3%), 1,044 men with difficulties in sexual function (15.1%), 1,064 men with bowel problems (15.4%), 774 men with hormonal related difficulties (11.2%), and 1,189 men with fatigue (17.2%). However, some men will have had multiple physical difficulties. This represents a significant annual burden in the absence of hard evidence of mortality benefit from PSA testing.

This study documents only the prostate cancer treatment related outcomes. There are also negative outcomes from prostate biopsies (27) and also an economic burden of PSA testing. Research is required to look at the value of PSA testing with the aspect of costs in mind.

Acknowledgments

The Life After Prostate Cancer Diagnosis study was funded by the Movember Foundation, in partnership with Prostate Cancer UK, as part of the Prostate Cancer Outcomes programme, grant number BO26/MO. We would like to record our thanks to all the men who participated in any of the surveys forming part of the LAPCD study. The contribution of staff at the National Cancer Registration and Analysis Service of Public Health England, the N. Ireland Cancer Registry (funded by the Public Health Agency NI), the Information Services Division (including the Scottish Cancer Registry), and the Welsh Cancer Intelligence and Surveillance Unit is also gratefully acknowledged.

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Appendix

Appendix A: Questionnaire

The EPIC-26 and EORTC QLQ C30 Fatigue subscale were used in this study. The EPIC-26 questionnaire is made up of 5 sections; urinary incontinence, urinary irritation, bowel, sexual, and vitality/hormonal function (16). Fatigue was included as a subscale with three items (17), these items were included as question 28, 29 and 30. The questions about the different domains of the EPIC-26 were included as follows:

Question	**Part of the EPIC-26**
10-13a	Urinary incontinence
13b-e	Urinary irritation
15-16	Bowel function
17-21	Sexual function
22	Hormonal function

The structure of the whole questionnaire was as follows:

Question	**Questionnaire**
1-6	EQ-5D-5L
7	Method of diagnosis
8	Treatment type
9a	Decision making
9b	Decision regret scale
10-22	EPIC-26
23-24	EORTC PR25
25-27	Sexual activity aids
28-30	EORTC QLQ C30 Fatigue scale
31-48	Social difficulties inventory (SDI)
49	Physical activity
50-56	Short Warwick-Edinburgh mental well-being scale
57-62a	K6 (Australian scoring values used)
62b-76	Patient empowerment scale
77	Impact of disease
78-88	General characteristics

Reference Number

Life After Prostate Cancer Diagnosis: Patient Reported Outcomes Survey

More men are now living longer after a diagnosis of prostate cancer. We want to find out what life is really like for this group of men. Your answers will benefit other men with prostate cancer in the future by providing information to help clinical teams, service providers and policy makers make decisions about how to improve the quality of services for prostate cancer patients. We would be grateful if you would complete this survey, which asks for information about your health and quality of life.

If you have **not** had a diagnosis of prostate cancer this questionnaire is not relevant to you.
Please tick the "no" box below and please accept our apologies for contacting you. Please return the blank questionnaire in the envelope provided and we will correct our records. If you have any questions about this survey please contact the FREEPHONE helpline number: **0808 801 0678**.

Have you ever been told by a doctor that you have prostate cancer?

Yes ☐ **No** ☐

If you have ticked yes to the first question please complete the rest of the survey.

If you have ticked no, please accept our apologies and send the questionnaire back to us in the envelope provided.

The survey
This survey is made up of eight sections and will take approximately 30 minutes to complete.

Who should complete the questionnaire?
The questions should be answered by the person named in the letter that came with this questionnaire. If that person needs help to answer the questions then the answers should be given from their point of view – not from the point of view of the person who is helping.

Completing the questionnaire
For each question please tick clearly inside the box of the response that best represents your views, using a black or blue pen. Do not worry if you make a mistake. Just cross out the mistake and put a tick in the correct box. Do not write your name or address anywhere on the questionnaire. The more questions in this survey that you complete, the more we can understand what life is like for those living with and beyond prostate cancer. However, if you feel unable or uncomfortable about answering any of the questions, leave it blank and move on to the next one.

The information you give us will be kept **securely** and treated in **confidence**. We will not publish any personal information that could allow anyone to identify you. We are very grateful for your time and effort in completing this survey.

If you have any queries about the questionnaire, please call the FREEPHONE helpline number: **0808 801 0678**

You can find more information about the study at:
http://www.lifeafterprostatecancerdiagnosis.com/

Section One: Your overall health

Under each heading, please tick ONE box that best describes your health TODAY

1. MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

2. SELF-CARE

I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

3. USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

4. PAIN / DISCOMFORT

I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

5. ANXIETY / DEPRESSION

I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

Are there any additional HEALTH issues that are of concern to you?

6. We would like to know how good or bad your health is TODAY.

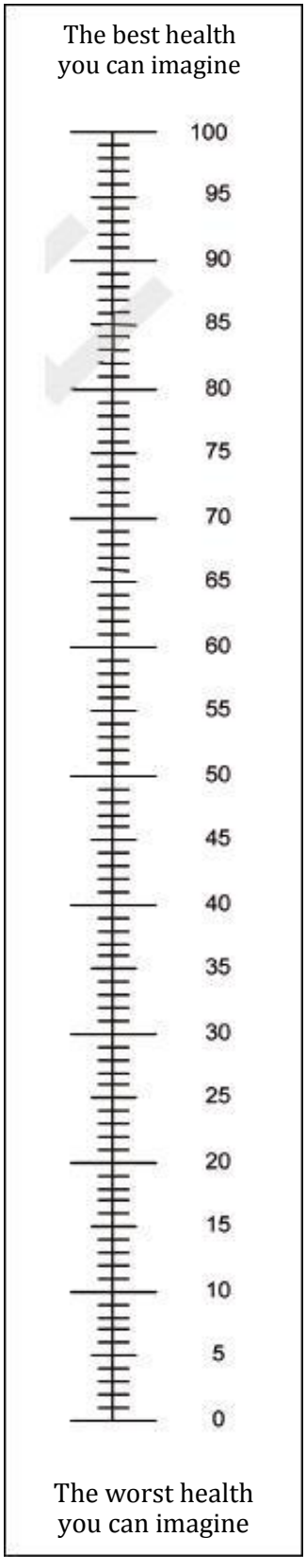
This scale is numbered from 0 to 100.

100 means the best health you can imagine.
0 means the worst health you can imagine.

Mark an X on the scale to indicate how your health is TODAY.

Now, please write the number you mark on the scale in the box below.

YOUR HEALTH TODAY = ☐



Section Two: Your diagnosis and treatment

7. How were you diagnosed? *Please tick **all that apply***

- ☐ I attended my GP with urinary symptoms (e.g. urinating frequently, blood in urine)
- ☐ I attended my GP with other symptoms (e.g. back pain, joint pain)
- ☐ I had no symptoms and my GP offered to test my PSA (blood test) as part of a general health check
- ☐ I had no symptoms and I asked my GP to measure my PSA (blood test)
- ☐ I had symptoms and I asked my GP to measure my PSA (blood test)
- ☐ I had a PSA test as part of a private health check
- ☐ Other — Please tell us about this:

8. Please tell us which treatments you have had following your diagnosis of prostate cancer *Please tick **all** the options that apply.*

A. Have you had surgery (prostatectomy)? No ☐ Yes ☐

If **no**, go to **B**

If **yes**, what type of surgery? Please tick one box

Open prostatectomy ☐
Operation performed through a cut in the abdomen above the pubic bone area (retropubic prostatectomy) or a cut in the area between the testicles and back passage (perineal prostatectomy).

Laparoscopic (keyhole) prostatectomy ☐
Operation performed through small incisions in the abdominal wall.

Robotic prostatectomy ☐
Operation performed with the assistance of a surgical robot (Da Vinci prostatectomy).

I don't know what kind of operation I had ☐

B. Have you had radiotherapy? No ☐ Yes ☐

If **no**, go to **C**

If **yes**, what type of radiotherapy? Please tick all that apply

External beam radiotherapy (with or without hormone treatment) ☐
Radiotherapy uses high-energy X-ray beams to treat the whole prostate. This form of treatments includes both 3-dimensional conformal radiotherapy (3D-CRT) and intensity modulated radiotherapy (IMRT).

Permanent seed (low-dose) brachytherapy ☐
This involves implanting radioactive seeds into the prostate gland.

Temporary (high-dose) brachytherapy (with or without external beam radiotherapy or hormone treatment) ☐
This involves inserting a source of high-dose radiation into the prostate gland for a few minutes.

I don't know what type of radiotherapy or brachytherapy I had ☐

C. Have you had any of the following treatments?

Please tick all that apply.

High intensity focused ultrasound (HIFU) ☐
This treatment uses ultrasound waves to heat and destroy cancer cells in the prostate.

Cryotherapy ☐
This treatment uses freezing and thawing to kill the cancer cells in the prostate.

Chemotherapy (not including hormones) ☐

Hormone treatment (either continuous or on/off treatment) ☐

Abiraterone and/or Enzalutamide ☐

D. Are doctors and nurses currently monitoring <u>your</u> prostate cancer?

No ☐ Yes ☐

If **no**, go to question **9**

If **yes**, what type of monitoring? Please tick one box.

Active Surveillance ☐
*Surveillance is monitoring of low risk, slow growing **localised prostate cancer** with the aim of avoiding or delaying **curative treatment** (e.g. surgery, radiotherapy).This involves having regular tests.*

Watchful waiting ☐
Watchful waiting is a way of monitoring prostate cancer that isn't causing any symptoms or problems. The aim is to keep an eye on the cancer over the long term and only having treatment if the cancer deteriorates or the patient gets symptoms. This involves fewer tests than in active surveillance.

Clinical follow-up during or after one of the treatments mentioned above in 8A, B or C ☐

I am unsure about the type of monitoring I am currently having ☐

9a. Do you think your views were taken into account when the team of doctors and nurses caring for you were discussing which treatment you should have? Please tick one of the following boxes:

- ☐ Yes, definitely
- ☐ Yes, to some extent
- ☐ No, my views were not taken into account
- ☐ I didn't know my treatment was being discussed by a team of doctors / nurses
- ☐ Not sure / can't remember

9b. Please answer the following questions whether or not you were <u>actively</u> involved in the decisions made about your treatment.

Please think about the decisions you made about your treatment for prostate cancer after talking to your doctor, surgeon, nurse, health care professional etc.

*Please show how you feel about these statements by ticking **one** box on each row.*

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
a. It was the right decision	☐	☐	☐	☐	☐
b. I regret the choice that was made	☐	☐	☐	☐	☐
c. I would go for the same choice if I had to do it over again	☐	☐	☐	☐	☐
d. The choice did me a lot of harm	☐	☐	☐	☐	☐
e. The decision was a wise one	☐	☐	☐	☐	☐

Please add anything else you would like to tell us about your diagnosis, treatment, and the decision making process.

Section Three: How things are for you now

We understand that some of the following questions are very sensitive, but we would really appreciate you answering them if possible. As with the rest of the questionnaire, your answers will be kept confidential and no one will be able to identify you.

*Please tick **one** box for each question.*

10.	Over the **past 4 weeks,** how often have you leaked urine**?**
More than once a day	☐
About once a day	☐
More than once a week	☐
About once a week	☐
Rarely or never	☐

11.	Which of the following best describes your urinary control **during the last 4 weeks?**
No urinary control whatsoever	☐
Frequent dribbling	☐
Occasional dribbling	☐
Total control	☐

12.	How many pads <u>per day</u> did you usually use to control leakage **during the last 4 weeks?**
None	☐
1 pad per day	☐
2 pads per day	☐
3 or more pads per day	☐

13.	How big a problem, if any, has each of the following been for you **during the last 4 weeks?** *Please tick **one** box on each line.*				
	No problem	Very small problem	Small problem	Moderate problem	Big problem
a. Dripping or leaking urine	☐	☐	☐	☐	☐
b. Pain or burning on urination	☐	☐	☐	☐	☐
c. Bleeding with urination	☐	☐	☐	☐	☐
d. Weak urine stream or incomplete emptying	☐	☐	☐	☐	☐
e. Need to urinate frequently during the day	☐	☐	☐	☐	☐

14.	Overall, how big a problem has your urinary function been for you **during the last 4 weeks?** *Please tick **one** box.*
No problem	☐
Very small problem	☐
Small problem	☐
Moderate problem	☐
Big problem	☐

15.	How big a problem, if any, has each of the following been for you **during the last 4 weeks**? *Please tick **one** box on each line.*				
	No problem	Very small problem	Small problem	Moderate problem	Big problem
a. Urgency to have a bowel movement	☐	☐	☐	☐	☐
b. Increased frequency of bowel movements	☐	☐	☐	☐	☐
c. Losing control of your stools	☐	☐	☐	☐	☐
d. Bloody stools	☐	☐	☐	☐	☐
e. Abdominal/ Pelvic/Rectal pain	☐	☐	☐	☐	☐

16.	Overall, how big a problem have your bowel habits been for you **during the last 4 weeks**? *Please tick **one** box.*
No problem	☐
Very small problem	☐
Small problem	☐
Moderate problem	☐
Big problem	☐

17.	How would you rate each of the following **during the last 4 weeks**? *Please tick **one** box on each line.*				
	Very poor to none	Poor	Fair	Good	Very good
a. Your ability to have an erection	☐	☐	☐	☐	☐
b. Your ability to reach orgasm (climax)	☐	☐	☐	☐	☐

18.	How would you describe the usual QUALITY of your erections **during the last 4 weeks?** *Please tick **one** box.*
None at all	☐
Not firm enough for any sexual activity	☐
Firm enough for masturbation and foreplay only	☐
Firm enough for intercourse	☐

*Please tick **one** box for each question.*

19.	How would you describe the FREQUENCY of your erections **during the last 4 weeks?**
I NEVER had an erection when I wanted one	☐
I had an erection LESS THAN HALF the time I wanted one	☐
I had an erection ABOUT HALF the time I wanted one	☐
I had an erection MORE THAN HALF the time I wanted one	☐
I had an erection WHENEVER I wanted one	☐

20.	Overall, how would you rate your ability to function sexually **during the last 4 weeks?**
Very poor	☐
Poor	☐
Fair	☐
Good	☐
Very good	☐

21.	Overall, how big a problem has your sexual function or lack of sexual function been for you **during the last 4 weeks?**
No problem	☐
Very small problem	☐
Small problem	☐
Moderate problem	☐
Big problem	☐

22.	How big a problem **during the last 4 weeks**, if any, has each of the following been for you? *Please tick **one** box on each line.*				
	No problem	Very small problem	Small problem	Moderate problem	Big problem
Hot flushes	☐	☐	☐	☐	☐
Breast tenderness/enlargement	☐	☐	☐	☐	☐
Feeling depressed	☐	☐	☐	☐	☐
Lack of energy	☐	☐	☐	☐	☐
Change in body weight	☐	☐	☐	☐	☐

During the last 4 weeks *Please tick **one** box on each line.*				
	Not at all	A little	Quite a bit	Very much
23. To what extent were you interested in sex?	☐	☐	☐	☐
24. To what extent were you sexually active (with or without intercourse)?	☐	☐	☐	☐

25. Have you used any medications to aid or improve erections since your prostate cancer diagnosis? (e.g. tablets, penis injections, gels) *Please tick **one** box.*

☐	☐	☐	☐	☐	☐	☐
I was not offered this	I was offered this but did not want it	I was offered this but have not tried it	I was offered this and tried it, but it was not helpful	I was offered this and it helped, but I am not using it now	I was offered this, it helps and I use it sometimes	I was offered this, it helps and I use it often

26. Have you used any devices to aid or improve erections since your prostate cancer diagnosis? (e.g. vacuum pump, penile prosthesis) *Please tick **one** box.*

☐	☐	☐	☐	☐	☐	☐
I was not offered this	I was offered this but did not want it	I was offered this but have not tried it	I was offered this and tried it, but it was not helpful	I was offered this and it helped, but I am not using it now	I was offered this, it helps and I use it sometimes	I was offered this, it helps and I use it often

27. Have you used any specialist services to help with your sex life following your diagnosis of prostate cancer? (e.g. counselling, psychosexual clinics, psychology)
*Please tick **one** box.*

☐	☐	☐	☐	☐	☐
I was not offered this	I was offered this but did not want it	I was offered this but have not tried it	I was offered this and tried it, but it was not helpful	I was offered this and it helped, but I am not using it now	I was offered this, it helps and I am still using the service

During the past week: *Please tick **one** box on each line.*

	Not at all	A little	Quite a bit	Very much
28. Did you need to rest?	☐	☐	☐	☐
29. Have you felt weak?	☐	☐	☐	☐
30. Were you tired?	☐	☐	☐	☐

Please add anything else you would like to tell us about your symptoms or the side effects of your treatment.

Section Four: Your everyday life

On each line please tick the box that best describes your answer. Please

tick the **'no difficulty box'** if a question **does not apply to you**.

During the past month:	No difficulty	A little difficulty	Quite a bit of difficulty	Very much difficulty
31. Have you had any difficulty maintaining your independence?	☐	☐	☐	☐
32. Have you had any difficulty in carrying out your domestic chores? (e.g. cleaning, gardening, cooking, shopping)	☐	☐	☐	☐
33. Have you had any difficulty with managing your own personal care? (e.g. bathing, dressing, washing)	☐	☐	☐	☐
34. Have you had any difficulty with looking after those who depend on you? (e.g. children, dependent adults, pets)	☐	☐	☐	☐
35. Have any of those close to you (e.g. partner, children, parents) had any difficulty with the support available to them?	☐	☐	☐	☐
36. Have you had any difficulties with benefits? (e.g. Statutory Sick Pay, Personal Independence Payments, Attendance Allowance, Universal Credit)	☐	☐	☐	☐
37. Have you had any financial difficulties?	☐	☐	☐	☐
38. Have you had any difficulties with financial services? (e.g. loans, mortgages, pensions, insurance)	☐	☐	☐	☐
39. Have you had any difficulty concerning your work? (or education if you are a student)	☐	☐	☐	☐
40. Have you had any difficulty with planning for your own or your family's future? (e.g. care of dependents, legal issues, business affairs)	☐	☐	☐	☐
41. Have you had any difficulty with communicating with those closest to you? (e.g. partner, children ,parents)	☐	☐	☐	☐

During the past month:	No difficulty	A little difficulty	Quite a bit of difficulty	Very much difficulty
42. Have you had any difficulty with communicating with others? (e.g. friends, neighbours, colleagues, dates)	☐	☐	☐	☐
43. Have you had any difficulty concerning plans to have a family?	☐	☐	☐	☐
44. Have you had any difficulty concerning your appearance or body image?	☐	☐	☐	☐
45. Have you felt isolated?	☐	☐	☐	☐
46. Have you had any difficulty with getting around? (e.g. transport, car parking, your mobility)	☐	☐	☐	☐
47. Have you had any difficulty in carrying out your recreational activities (e.g. hobbies, pastimes, social pursuits)	☐	☐	☐	☐
48. Have you had any difficulty with your plans to travel or take a holiday?	☐	☐	☐	☐

49. In the **past week**, on how many days have you done a total of 30 minutes or more of physical activity, which was enough to raise your heart rate?

(This may include sport, exercise and brisk walking or cycling for recreation or to get to and from places, ***but should not include housework or physical activity that is part of your job.)***

Please tick ***one*** *box.*

☐	☐	☐	☐	☐	☐	☐	☐
None	**1 day**	**2 days**	**3 days**	**4 days**	**5 days**	**6 days**	**7 days**

Please add anything else you would like to tell us about how your prostate cancer has had an impact on your everyday life.

Section Five: Your emotional wellbeing

Below are some statements about feelings and thoughts. Please tick the box on each line that best describes your experience of each over **the last 2 weeks.**

STATEMENTS	None of the time	Rarely	Some of the time	Often	All of the time
50. I've been feeling optimistic about the future	☐	☐	☐	☐	☐
51. I've been feeling useful	☐	☐	☐	☐	☐
52. I've been feeling relaxed	☐	☐	☐	☐	☐
53. I've been dealing with problems well	☐	☐	☐	☐	☐
54. I've been thinking clearly	☐	☐	☐	☐	☐
55. I've been feeling close to other people	☐	☐	☐	☐	☐
56. I've been able to make up my own mind about things	☐	☐	☐	☐	☐

The following questions ask about how you have been feeling during the **past 30 days**.
For each question, please tick the box on each line that best describes how often you had this feeling.

During the past 30 days, about how often did you feel...

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
57. ...nervous?	☐	☐	☐	☐	☐
58. ...hopeless?	☐	☐	☐	☐	☐
59. ...restless or fidgety?	☐	☐	☐	☐	☐
60. ...so depressed that nothing could cheer you up?	☐	☐	☐	☐	☐
61. ...that everything was an effort?	☐	☐	☐	☐	☐
62. ...worthless?	☐	☐	☐	☐	☐

Please add anything else you would like to tell us about how your prostate cancer has had an impact on your emotional well-being.

Section Six: Looking to the future

Even if you are now free from prostate cancer please complete this section.

Please read the statements carefully and tick your responses to them. *Please tick **one** box on each line.* **If a question does not apply to you please leave it blank**.

	Strongly agree	Agree	Disagree	Strongly disagree
62. I am capable of coping with my prostate cancer	☐	☐	☐	☐
63. I have all the information I need to manage my prostate cancer	☐	☐	☐	☐
64. I am capable of helping health professionals reach decisions related to my prostate cancer	☐	☐	☐	☐
65. My family are very supportive	☐	☐	☐	☐
66. I need the support of my family and friends	☐	☐	☐	☐
67. My family and friends still rely on me	☐	☐	☐	☐
68. I can adapt to the changes in my lifestyle	☐	☐	☐	☐
69. Health professionals are happy to include me in decisions related to my prostate cancer	☐	☐	☐	☐
70. I want my family and friends to continue to rely on me	☐	☐	☐	☐
71. My friends are always supportive	☐	☐	☐	☐
72. I still feel useful in my daily life	☐	☐	☐	☐
73. My spiritual beliefs help me cope with my prostate cancer	☐	☐	☐	☐
74. I accept that I have to change my lifestyle	☐	☐	☐	☐
75. Complementary therapies help me cope with my prostate cancer	☐	☐	☐	☐
76. I have a lot of confidence in my local GP	☐	☐	☐	☐
	No impact	A little impact	Quite a bit of impact	Very much impact
77. How much of an impact has prostate cancer had on your life?	☐	☐	☐	☐

What have been the most important issues that you have faced since your prostate cancer diagnosis?

Section Seven: Questions about you

78. How old are you (in years)?

☐

79. What is your **legal** marital status? *Please tick **one** box.*

- ☐ Married
- ☐ In civil partnership
- ☐ Separated
- ☐ Divorced/dissolved civil partnership
- ☐ Widowed/surviving partner from civil partnership
- ☐ Single (never married/never in civil partnership)
- ☐ Other

80. What was your employment status before your diagnosis of prostate cancer? *Please tick **one** box.*

- ☐ Full time employment
- ☐ Part time employment
- ☐ Self employed
- ☐ Looking after family/home
- ☐ Retired
- ☐ Unemployed, seeking work
- ☐ Unemployed, unable to work for health reasons
- ☐ Other

81. What is your employment status currently? *If on sick leave answer in relation to your usual employment status. Please tick **one** box.*

- ☐ Full time employment
- ☐ Part time employment
- ☐ Self employed
- ☐ Looking after family/home
- ☐ Retired
- ☐ Unemployed, seeking work
- ☐ Unemployed, unable to work for health reasons
- ☐ Other

82. To which of these ethnic groups would you say you belong? *Please tick **one** box.*

White

- ☐ English/Welsh/Scottish/Northern Irish/British
- ☐ Irish
- ☐ Gypsy or Irish Traveller
- ☐ Any other White background

Mixed/Multiple ethnic groups

- ☐ White and Black Caribbean
- ☐ White and Black African
- ☐ White and Asian
- ☐ Any other Mixed/multiple ethnic background

Asian / British Asian

- ☐ Indian
- ☐ Pakistani
- ☐ Bangladeshi
- ☐ Chinese
- ☐ Any other Asian background

Black/African/Caribbean/Black British

- ☐ Black African
- ☐ Black Caribbean
- ☐ Any other Black / African / Caribbean background

Other ethnic group

- ☐ Arab
- ☐ Any other ethnic group

83. Do you consider yourself… *Please tick **one** box.*

- ☐ Heterosexual / straight
- ☐ Homosexual / gay
- ☐ Bisexual
- ☐ Don't know
- ☐ Prefer not to answer

84. Which, if any, of the following conditions do you have? *Please tick **all** the boxes that apply.*

- ☐ A heart condition
- ☐ Angina
- ☐ High blood pressure
- ☐ Asthma or other chronic chest problem
- ☐ Liver disease
- ☐ Problems with your stomach, bowels or gallbladder
- ☐ Problems with your pancreas
- ☐ Kidney disease
- ☐ Diabetes
- ☐ Stroke
- ☐ Alzheimer's disease or dementia
- ☐ Epilepsy
- ☐ Other long standing neurological problem
- ☐ A diagnosis of arthritis

85. How tall are you? ……feet…….inches OR ……centimetres ☐ Don't know

86. How much do you weigh? ……..stone……pounds OR ….kilograms… grams ☐ Don't know

87. Have you <u>ever in your lifetime</u> seen a health care professional (such as a GP, psychiatrist, psychologist, social worker, counsellor, psychotherapist, mental health nurse, or any other such professional) for problems with your emotions or nerves or your use of alcohol or drugs?

☐ Yes ☐ No

88. Do you look after, or give any help or support (not part of your paid employment) to family members, friends, neighbours or others because of either:

- Long term physical or mental health disability, or
- Problems relating to old age

☐ Yes ☐ No

Is there anything else you would like to tell us about what life has been like for you following your prostate cancer diagnosis?

Please would you tell us who filled in this survey? *Please tick **one** box.*

☐ The person to whom this survey was sent

☐ A representative of the person to whom this survey was sent (e.g. partner, family member, friend)

Section Eight: Future contact

Follow-up survey

Thank you for completing this survey. We will be **contacting you again in a year time** for the follow-up survey. If you decide at that time you would rather not complete the survey again there is no obligation to do so.

Follow-up interview

As part of this work we are going to be interviewing a small number of men and some partners /spouses to gain a better understanding of their experience. This will only involve men and their partners / spouses who indicate they are interested in being interviewed. We would normally only be able to interview either the participant or their partner/spouse. We will not be interviewing couples together.

If you or your partner/spouse is interested in being involved in the interview, please tick the relevant boxes below.

☐ I am interested in being interviewed for this work

☐ My partner / spouse is interested in being interviewed for this work

We are sorry we will not be able to contact all those who would like to participate in the interview, but we will make sure that we get the views of a varied group. If you are one of the group we would like to interview we will write to you explaining how to get in touch with us to find out more about the interview. If you are still interested, we would arrange a time for the interview. If you think your partner/spouse would like to be interviewed, we would follow a similar process by making the initial contact with you by letter.

You have completed the survey.
Thank you for your time.

If you would like to know more about this study then please visit our website: http://www.lifeafterprostatecancerdiagnosis.com/

We *very much appreciate the time and thought you have put into completing this survey. If reflecting on your situation has caused anxiety or uncertainty in any way, please do not hesitate to contact your specialist cancer nurse or call one of the specialist nurses on Prostate Cancer UK's Confidential Help Line.*

Prostate Cancer UK's Confidential Help Line telephone: ***0800 074 8383***

(Free from UK landlines)

(Monday – Friday 9-6pm, Wednesday 10-8pm).

They are there to listen to your concerns, and offer support and helpful information

Appendix B: Supplementary tables

Supplementary table 1

General characteristics of all respondents <75

	Symptomatic (%) (n= 13086) (48.6%)	**PSA tested (%)** (n= 3994) (14.8%)	**GP offered PSA test (%)** (n= 4584) (17.0%)	**Other (%)** (n= 4095) (15.2%)	**All respondents (%)*** (n= 26919) (100.0%)	**P-value** **
Age at diagnosis, mean (SD)	65.63 (5.8)	64.78 (6.1)	66.08 (5.6)	65.31 (6.1)	65.55 (5.9)	<0.001
Age at diagnosis						<0.001
- <55	639 (4.9%)	266 (6.7%)	185 (4.0%)	240 (5.9%)	1,392 (5.2%)	
- 55-64	4,169 (31.9%)	1,380 (34.6%)	1,320 (28.8%)	1,343 (32.8%)	8,529 (31.7%)	
- 65-74	8,274 (63.2%)	2,348 (58.8%)	3,079 (67.2%)	2,511 (61.3%)	16,992 (63.1%)	
- Unknown/missing	<5	0 (0.0%)	0 (0.0%)	<5	6 (0.0%)	
Stage						<0.001
- 1	3,899 (29.8%)	1,349 (33.8%)	1,618 (35.3%)	1,306 (31.9%)	8,542 (31.7%)	
- 2	3,115 (23.8%)	1,146 (28.7%)	1,280 (27.9%)	1,032 (25.2%)	6,862 (25.5%)	
- 3	2,797 (21.4%)	728 (18.2%)	894 (19.5%)	757 (18.5%)	5,395 (20.0%)	
- 4	1,702 (13.0%)	174 (4.4%)	231 (5.0%)	438 (10.7%)	2,669 (9.9%)	
- Unknown/missing	1,573 (12.0%)	597 (14.9%)	561 (12.2%)	562 (13.7%)	3,451 (12.8%)	
Gleason score						<0.001
- 2-6	3,526 (26.9%)	1,180 (29.5%)	1,413 (30.8%)	1,152 (28.1%)	7,615 (28.3%)	
- 7	4,955 (37.9%)	1,790 (44.8%)	2,091 (45.6%)	1,667 (40.7%)	10,951 (40.7%)	
- 8-10	3,382 (25.8%)	645 (16.1%)	663 (14.5%)	870 (21.2%)	5,805 (21.6%)	
- Unknown/missing	1,223 (9.3%)	379 (9.5%)	417 (9.1%)	406 (9.9%)	2,548 (9.5%)	
Treatment						<0.001
- Surgery	2,817 (21.5%)	1,239 (31.0%)	1,176 (25.7%)	1,026 (25.1%)	6,516 (24.2%)	
- External beam radiotherapy	1,044 (8.0%)	254 (6.4%)	435 (9.5%)	292 (7.1%)	2,135 (7.9%)	
- Brachytherapy	383 (2.9%)	248 (6.2%)	252 (5.5%)	157 (3.8%)	1,075 (4.0%)	
- Hormone therapy	771 (5.9%)	84 (2.1%)	152 (3.3%)	203 (5.0%)	1,269 (4.7%)	
- Active surveillance	1,179 (9.0%)	383 (9.6%)	463 (10.1%)	359 (8.8%)	2,488 (9.2%)	
- Watchful waiting	616 (4.7%)	178 (4.5%)	248 (5.4%)	199 (4.9%)	1,309 (4.9%)	
- Surgery and external beam radiotherapy	421 (3.2%)	151 (3.8%)	158 (3.4%)	135 (3.3%)	904 (3.4%)	
- Surgery, hormone therapy and external beam radiotherapy	422 (3.2%)	147 (3.7%)	109 (2.4%)	135 (3.3%)	844 (3.1%)	
- Hormone therapy and external beam radiotherapy	3,337 (25.5%)	829 (20.8%)	1,035 (22.6%)	935 (22.8%)	6,351 (23.6%)	
- Unknown/missing	2,096 (16.0%)	481 (12.0%)	556 (12.1%)	654 (16.0%)	4,028 (15.0%)	
Employment status						<0.001
- Employed	4,703 (35.9%)	1,667 (41.7%)	1,617 (35.3%)	1,553 (37.9%)	9,935 (36.9%)	
- Not employed/retired	8,112 (62.0%)	2,250 (56.3%)	2,855 (62.3%)	2,439 (59.6%)	16,374 (60.8%)	
- Other/unknown/missing	271 (2.1%)	77 (1.9%)	112 (2.4%)	103 (2.5%)	610 (2.3%)	
Marital status						<0.001
- Married/partnership	10,528 (80.5%)	3,352 (83.9%)	3,646 (79.5%)	3,227 (78.8%)	21,635 (80.4%)	
- Single (separated, divorced, widowed, single)	2,260 (17.3%)	560 (14.0%)	823 (18.0%)	749 (18.3%)	4,623 (17.2%)	
- Other/unknown/missing	298 (2.3%)	82 (2.1%)	115 (2.5%)	119 (2.9%)	661 (2.5%)	
Sexuality						<0.001
- Heterosexual/straight	12,354 (94.4%)	3,784 (94.7%)	4,284 (93.5%)	3,826 (93.4%)	25,281 (93.9%)	
- Homosexual/bisexual	164 (1.3%)	53 (1.3%)	67 (1.5%)	61 (1.5%)	359 (1.3%)	
- Don't know/prefer not to answer/missing	568 (4.3%)	157 (3.9%)	233 (5.1%)	208 (5.1%)	1,279 (4.8%)	
Ethnicity						<0.001
- White	12,433 (95.0%)	3,736 (93.5%)	4,294 (93.7%)	3,802 (92.8%)	25,333 (94.1%)	
- (British) Asian/Black (British)/African/ Caribbean/Mixed	324 (2.5%)	140 (3.5%)	168 (3.7%)	160 (3.9%)	834 (3.1%)	
- Other/missing	329 (2.5%)	118 (3.0%)	122 (2.7%)	133 (3.2%)	752 (2.8%)	
Comorbidities						<0.001
- No comorbidities	3,943 (30.1%)	1,488 (37.3%)	1,402 (30.6%)	1,270 (31.0%)	8,439 (31.3%)	
- 1	4,546 (34.7%)	1,468 (36.8%)	1,719 (37.5%)	1,387 (33.9%)	9,556 (35.5%)	

- 2	2,543 (19.4%)	634 (15.9%)	891 (19.4%)	779 (19.0%)	5,070 (18.8%)	
- 3	1,172 (9.0%)	223 (5.6%)	337 (7.4%)	364 (8.9%)	2,181 (8.1%)	
- 4 or more	882 (6.7%)	181 (4.5%)	235 (5.1%)	295 (7.2%)	1,673 (6.2%)	
Nation* **						<0.001
- England	10,920 (83.4%)	3,413 (85.5%)	3,940 (86.0%)	3,489 (85.2%)	22,768 (84.6%)	
- Wales	920 (7./%)	316 (7.9%)	330 (7.2%)	294 (7.2%)	1,929 (7.2%)	
- Scotland	869 (6.6%)	147 (3.7%)	154 (3.4%)	204 (5.0%)	1,432 (5.3%)	
- Northern Ireland	377 (2.9%)	118 (3.0%)	160 (3.5%)	108 (2.6%)	790 (2.9%)	
Socioeconomic status (deprivation quintiles)						<0.001
- 1 – Affluent	3,346 (25.6%)	1,271 (31.8%)	1,170 (25.5%)	1,071 (26.2%)	7,104 (26.4%)	
- 2	3,345 (25.6%)	1,072 (26.8%)	1,228 (26.8%)	1,017 (24.8%)	6,929 (25.7%)	
- 3	2,687 (20.5%)	788 (19.7%)	944 (20.6%)	850 (20.8%)	5,511 (20.5%)	
- 4	1,988 (15.2%)	499 (12.5%)	677 (14.8%)	608 (14.8%)	3,980 (14.8%)	
- 5 – Deprivation	1,416 (10.8%)	285 (7.1%)	456 (9.9%)	447 (10.9%)	2,764 (10.3%)	
- Missing	304 (2.3%)	79 (2.0%)	109 (2.4%)	102 (2.5%)	631 (2.3%)	

* The column 'All respondents' includes the men younger than 75 who did not respond to the question about the method of diagnosis.

** P-value compares the groups symptomatic, PSA tested, GP offered PSA test, and other.

Supplementary table 2

In supplementary table 2 shows that the proportions of men with poor physical outcomes (i.e. urinary incontinence, urinary irritation, sexual function, bowel function, hormonal function and fatigue) increase with higher stage, higher Gleason score (except for urinary incontinence and urinary irritation), more comorbidities and a more deprived area. For age, only the sexual function gets poorer with increasing age. The urinary incontinence and urinary irritation are poorer with a younger age.

Men experienced the poorest urinary incontinence after treatments that included surgery, the poorest sexual function, hormonal function and fatigue after treatments that included hormone therapy, and the poorest bowel function after treatments that included external beam radiotherapy. The urinary irritation score was poorest after active surveillance.

Supplementary table 2: Physical outcomes by description for all men <75 years.

Age at diagnosis, mean (SD)	**Poor urinary incontinence score**[a,c]	**Poor urinary irritation score**[a,c]	**Poor sexual score**[a,c]	**Poor bowel score**[a,c]	**Poor hormonal score**[a,c]	**Poor fatigue score**[b,c]
Overall number (n)	4,900	3,735	5,018	4,967	4,648	6,668
Overall scores	19.9%	16.3%	19.8%	20.6%	18.8%	26.8%
Age at diagnosis						
- <55 (n= 905)	23.1%	17.9%	12.3%	20.8%	19.7%	26.7%
- 55-64 (n= 5,549)	21.7%	17.1%	16.9%	20.0%	19.8%	26.4%
- 65-74 (n= 10,622)	18.7%	15.7%	22.0%	20.9%	18.2%	27.0%
- Missing/ unknown (n= 4)	25.0%*	50.0%*	66.7%*	100.0%*	66.7%*	50.0%
Stage						
- 1 (n= 5,248)	18.3%	17.8%	14.0%	18.8%	11.7%	23.1%
- 2 (n= 4,261)	21.4%	14.4%	18.3%	19.7%	14.5%	24.9%
- 3 (n= 3,525)	22.1%	14.8%	26.2%	23.7%	26.5%	28.5%
- 4 (n= 1,876)	17.4%	19.3%	33.0%	24.0%	39.6%	42.4%
- Missing/ unknown (n= 2,170)	19.4%*	16.4%*	17.3%*	19.7%*	16.8%*	25.3%*
Gleason score						
- 2-6 (n= 4,706)	17.8%	17.8%	12.5%	15.8%	9.7%	21.7%
- 7 (n= 6,745)	21.3%	13.7%	19.1%	21.0%	16.5%	24.8%
- 8-10 (n= 4,027)	20.8%	18.9%	29.2%	26.1%	33.6%	36.0%
- Missing/ unknown (n= 1,602)	18.4%*	17.0%*	23.4%*	21.2%*	22.2%*	30.0%*
Treatment						
- Surgery (n= 1,562)	33.8%	9.5%	17.3%	10.4%	6.5%	17.1%
- EBRT (n= 4,056)	13.7%	16.2%	21.3%	27.9%	18.0%	27.4%
- BT (n= 1,298)	7.9%	18.5%	6.0%	20.8%	5.2%	15.6%
- HT (n= 631)	12.4%	19.5%	30.5%	15.2%	38.1%	37.9%
- AS (n= 572)	10.6%	22.7%	5.7%	11.0%	4.9%	16.7%
- WW (n= 4,166)	12.7%	18.8%	9.7%	11.6%	5.1%	20.4%
- Surgery + EBRT (n= 569)	33.5%	12.1%	23.5%	27.4%	9.9%	24.0%
- Surgery + HT + EBRT (n= 855)	35.7%	20.9%	30.6%	32.3%	33.6%	36.5%
- HT + EBRT (n= 794)	12.6%	7.2%	24.5%	31.4%	32.4%	34.3%
- Unknown/ missing (n= 2,577)	18.8%*	19.6%*	25.2%*	23.7%*	27.5%*	37.3%*
Comorbidities						
- None (n= 5,431)	16.8%	11.4%	14.9%	13.3%	12.9%	16.1%
- 1 (n= 6,014)	18.8%	14.7%	17.9%	18.3%	16.2%	22.3%
- 2 (n= 3,177)	22.1%	19.7%	23.1%	26.2%	23.3%	35.3%
- 3 (n= 1,395)	25.0%	25.0%	30.3%	34.7%	32.1%	50.1%
- 4 or more (n= 1,063)	28.9%*	28.8%*	31.5%*	36.9%*	33.8%*	51.2%*
Socioeconomic status (deprivation quintiles)						
- 1 – affluent (n= 4,617)	17.4%	14.0%	15.2%	18.1%	13.9%	21.2%
- 2 (n= 4,417)	17.7%	14.6%	18.2%	19.9%	16.9%	24.5%
- 3 (n= 3,475)	20.1%	16.2%	22.4%	21.3%	19.7%	28.0%

- 4 (n= 2,487)	22.3%	18.8%	22.1%	21.7%	23.2%	31.6%
- 5 – deprived (n= 1,701)	28.3%	23.6%	28.0%	26.7%	29.7%	39.0%
- Unknown/ missing (n= 383)	21.2%*	17.3%*	17.2%*	20.9%*	20.1%*	28.2%*

* Significant; $p<0.05$

[a] Urinary incontinence, urinary irritation, sexual function, bowel function and hormonal function are based on the EPIC-26 (16)

[b] Fatigue is based on the EORT QLQ C30 Fatigue subscale (18)

[c] Poor scores were based on the 20% lowest values (urinary incontinence: 0-65, urinary irritation: 0-69, sexual function: 0-1, bowel function: 0-79, hormonal function: 0-63, fatigue: 39-100)

Supplementary table 3

General characteristics compared between non-responders and responders for all men within the LAPCD study.

	Non-responders	Responders	Total	p-value
Age				
- <55	5.6%	3.9%	4.6%	<0.001
- 55-64	21.7%	23.8%	23.0%	
- 65-74	38.5%	47.4%	43.9%	
- 75-84	27.7%	22.6%	24.6%	
- 85+	6.0%	2.3%	3.7%	
- Missing/ unknown	0.5%	0.0%	0.2%	
Ethnicity				
- White	88.0%	94.2%	91.8%	<0.001
- Mixed	0.6%	0.3%	0.4%	
- Asian	2.7%	1.1%	1.7%	
- Black	5.2%	1.9%	3.2%	
- Other	1.1%	0.6%	0.8%	
- Missing/ unknown	2.4%	1.9%	2.1%	
Stage				
- 1	33.7%	31.1%	32.1%	<0.001
- 2	20.5%	24.4%	22.9%	
- 3	16.3%	20.1%	18.6%	
- 4	11.7%	10.6%	11.0%	
- Missing/ unknown	17.9%	13.8%	15.4%	
Socioeconomic status (deprivation quintiles)				
- 1 - least deprived	19.2%	26.3%	23.5%	<0.001
- 2	21.5%	26.0%	24.2%	
- 3	20.7%	20.7%	20.7%	
- 4	19.1%	14.8%	16.5%	
- 5 - most deprived	16.8%	10.2%	12.8%	
- Missing/ unknown	2.7%	2.1%	2.3%	