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Determinants for choosing and adhering to active surveillance for localized prostate cancer: a nationwide population-based study

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Abstract

Objective: Knowledge about factors influencing choice of and adherence to active surveillance (AS) for prostate cancer (PC) is scarce. We aim to identify which factors most affected choosing and adhering to AS and to quantify their relative importance.

Design, Setting, and Participants: In 2015 we sent a questionnaire to all Swedish men aged ≤ 70 years registered in the National Prostate Cancer Register of Sweden who were diagnosed in 2008 with low-risk PC and had undergone prostatectomy, radiotherapy, or started on AS.

Outcome Measurements and Statistical Analysis: Logistic regression was used to calculate odds ratios (OR) with 95% confidence intervals (CI) for factors potentially affecting choice and adherence to AS.

Results: 1288 out of 1720 men (75%) responded, 451 (35%) chose AS and 837 (65%) underwent curative treatment. Of those starting on AS, 238 (53%) diverted to treatment within seven years. Most men (83%) choose AS because “My doctor recommended AS”. Factors associated with choosing AS over treatment were older age (OR 1.81, 95% CI 1.29-2.54), a Charlson Comorbidity Index >2 (OR 1.50, 95% CI 1.06–2.13), being unaccompanied when notified of the cancer diagnosis (OR 1.45, 95% CI 1.11-1.89). Men with a higher PSA at the time of diagnosis were less likely to adhere to AS (OR 0.26, 95% CI 0.10-0.63). The reason for having treatment after initial AS was “the PSA level was rising” in 55% and biopsy findings in 36%.

Conclusions: A doctor's recommendation strongly affects which treatment is chosen for men with low-risk PC. Rising PSA values were the main factor for initiating treatment for men on AS. These findings need be considered by health-care providers who wish to increase the uptake of and adherence to AS.

Strengths and limitations of this study:

- The strengths of our study include its population-based design, the high response rate for a study of its kind, the face-validated study-specific questionnaire, and the direct questions on reasons for choice and adherence.
- The retrospective design is a limitation, as the men's experiences during the seven-year follow-up might have affected their recollection of their experiences.
- We acknowledge that various selection mechanisms may have affected the men's choice of treatment and that several important factors therefor could have been missed.
- We did not have access to PSA (prostate specific antigen) levels during AS, only at diagnosis, which limits the possibility to investigate how PSA-monitoring affects adherence to AS.
- The study included Swedish men only and the findings might therefore not be generalizable to other cultural and health-care settings.

Introduction

A large proportion of men with prostate cancer (PC) are diagnosed with low-risk disease with a long-life expectancy even without curative treatment. Active surveillance (AS) has therefore emerged as the primary strategy for these men to reduce unnecessary treatment [1,2].

In Sweden, uptake of AS has increased steadily over the past decade and is now 80-90% [3]. However, the proportion of men with low-risk cancer who are on AS varies substantially between and within countries [2,4] Although notable rising trends are seen in e.g. North America, Australia and Europe [5], a 2014 survey in Japan noted that roughly half of urologists used AS in < 5% of men with low-risk PC and that only 27% stated that they would want to offer AS more frequently in the future [6]. Additionally, a considerable proportion of men on AS diverge to treatment over time without any clear evidence of disease progression [7,8].

In a systematic review on choice and adherence to AS, Kinsella et al [9] identifies several factors such as clinician's attitudes, family and social support, and patient education as potential determinants for choice and adherence to AS. However, no grading of these factors' relative importance was made.

We could not identify any previous studies on factors influencing choice of and adherence to AS in a nationwide population-based setting. In this nationwide population-based study, representing a period in time when Sweden experienced a rapid increase in AS [3], we used a questionnaire to identify which factors most affected choosing and adhering to AS, and to quantify the relative importance of different reasons for this, thereby identifying possibly influenceable determinants to increase the implementation of AS.

Material and methods

Study design and participants

We identified all men in the National Prostate Cancer Register of Sweden (NPCR) who were diagnosed in 2008 with low-risk PC at age 70 years or younger, had radical prostatectomy, radiotherapy or AS as primary treatment and were alive in 2015. The reason for choosing men diagnosed in 2008 was that we wished to assess reasons for diverting from AS to treatment after several years of AS. The reason for choosing men younger than 70 years with low-risk disease was to avoid getting men in watchful waiting mixed with the active surveillance group.

The NPCR has a capture rate of > 96% compared with the national cancer registry, to which registration is mandatory by law [10]. Low-risk disease was defined as Gleason score 6, prostate-specific antigen (PSA) < 10 ng/ml, and clinical stage T1 or T2.

Between February and October 2015, 1720 men were invited to participate via a letter, in which we presented the study and its purpose. The letter included a questionnaire and an addressed and stamped envelope for reply. The participants could also fill out the questionnaire online by using an individual code which was included in the letter. Men who failed to return the questionnaire were contacted by a research assistant via telephone and were sent a second questionnaire.

The Regional Ethical Review Board at Uppsala University approved of the study.

Questionnaire design

The questionnaire consisted of EPIC-26 and 49 study-specific questions (supplementary file). EPIC-26 is an instrument designed to assess pelvic organ function and bother after PC treatment [11]. The study-specific questions were developed after interviews with men living with PC, and were tested for face validity with one investigator accompanying the men while they completed the questionnaire. Questions not fully understood were changed to achieve clarity. The questionnaire was further validated in an unpublished pilot study among men not included in the present study. Our technique for developing a study-specific questionnaire is based on a one-concept–one-question method producing self-reported outcomes and has been previously described [12-14]. The questionnaire explored mental symptoms, quality of life, and overall satisfaction with care. The questionnaire also assessed experiences at the time of diagnosis and at follow-up, socio-demographics, smoking, alcohol consumption, physical activity, treatments, concurrent diseases (Charlson Comorbidity Index (CCI) [15]), and psychiatric problems (obtained by asking if they suffered from depression and/or any other mental illness).

Factors potentially associated with choice of and adherence to AS was further evaluated by two direct questions. Choice of AS was evaluated by the question "If you were on active surveillance for prostate cancer but later received treatment, or if you are still on active surveillance - which of the following alternative(s) influenced the decision?". Men had the possibility to grade the following alternatives from "I do not agree at all" to "I completely agree", "I am/was not particularly worried about the prostate cancer", "I did not want to risk leaking urine", "I did not want to risk impairing my sexual function", "I did not want to risk getting bowel problems", "I preferred not undergoing any treatment", "I wanted to

postpone any treatment until it was deemed necessary", "I felt uneasy about the available treatment strategies (surgery and radiotherapy)" and "My doctor recommended active surveillance". Adherence was evaluated by the question "Why was the active surveillance terminated and treatment initiated?" with the following alternatives where men had the possibility to choose more than one alternative, "The PSA level was rising", "The prostate biopsies showed a more aggressive tumour", "The initiative was mine and had nothing to do with the PSA level or prostate biopsies" and "The initiative was my doctor's and had nothing to do with the PSA level or prostate biopsies".

Patient and Public Involvement statement:

Men living with prostate cancer where involved in the study early on as we conducted individual interviews with a small number of respondents to explore their perspectives on living with prostate cancer. The study-specific questions were developed after these interviews. However, men with prostate cancer were not involved in the conduct, analysis of data or writing the manuscript in other ways.

Data collection, analysis, and statistical analysis

The questionnaires and cancer characteristics data from the NPCR were assembled in a database. Differences between responders and non-responders were analyzed. To assess factors associated with the initial choice of treatment, men were grouped by their initial treatment: curative or AS. To assess factors associated with adherence to AS, responders where grouped by whether they stayed on AS or diverged to treatment. Statements such as

"substantial information" were defined as the highest possible response to that specific question.

Missing data were handled using multiple imputations based on the method of chained equations [16]. Five imputation data sets were created. The maximum number of imputed answers where 4%.

The analysis of factors associated with choice and adherence to AS was carried out using logistic regression. A multivariate analysis was performed including age, retirement, education and CCI and it is these values that are presented. Odds ratios (ORs) with 95% confidence interval (CI) show the probability of choosing and adhering to AS.

Results

Patient characteristics

In all, 1288 (75%) of the 1720 invited men responded. Mean age at diagnosis was 63 years old (range 40–70) (Table 1a).

Non-responders were on average one year younger, had lower T-stage and lower PSA, were more likely to be diagnosed after PSA-testing, and were more likely to be initially managed with AS (data from the NPCR) (supplementary file).

A total of 451 (35%) chose AS and 837 (65%) underwent immediate treatment. Of the men who initially chose AS, 238 (53%) diverted to treatment within seven years, of whom 70% did so within the first three years (Table 1b and Figure 1).

The vast majority of men primarily consulted either a urologist or a medical oncologist, 18% consulted both a urologist and a medical oncologist.

Factors associated with choice (Figure 2)

Factors statistically associated with choosing AS over treatment included older age (OR 1.81, 95% CI 1.29-2.54 for men aged <60 yr vs men aged 66–70 yr), a CCI >2 (OR 1.50, 95% CI 1.06–2.13, compared with CCI 0), unaccompanied when being notified of the diagnosis (OR 1.45, 95% CI 1.11-1.89) and being presented with AS by the treating physician (OR 9.27, 95% CI 7.04-12.19). Factors statistically associated with not choosing AS over treatment included whether men were still working (OR 0.69, 95% CI 0.47-1.00) and/or had a T2 tumor (OR 0.40, 95% CI 0.29-0.56).

PSA at diagnosis (OR 0.67, 95% CI 0.40-1.13), time to reflect on treatment options (OR 0.93, 95% CI 0.63-1.39) and whether the men had seen both a urologist and a medical oncologist (OR 1.13, 95% CI 0.83-1.53) were not statistically significantly associated with choice.

Regarding the direct questions on why the men chose AS (Figure 3) (defined as completely or largely agreed),

- 83% “My doctor recommended AS”
- 74% “I did not want to risk leaking urine”
- 66% “I did not want to risk getting bowel problems”
- 64% “I am/was not particularly worried about the prostate cancer”
- 62% “I did not want to risk impairing my sexual function”,

- 55% “I wanted to postpone any treatment until it was deemed necessary”
- 49% “I felt uneasy about the available treatment strategies (surgery and radiotherapy)”
- 39% “I preferred not undergoing any treatment”

Factors associated with adherence (Figure 4)

Men with PC detected during investigation of LUTS (Lower Urinary Tract Symptoms) rather than screening was associated with adhering to AS (OR 1.78, 95% CI 1.16-2.72). Men with a higher PSA at the time of diagnosis (OR 0.26, 95% CI 0.10-0.63) were less likely to adhere to AS.

Regarding the direct question on reasons for diverting to treatment (Figure 5), (defined as completely or largely agreed)

- 55% “the PSA level was rising”
- 36% “the prostate biopsies showed a more aggressive tumor”
- 6% “the initiative was my doctor’s and had nothing to do with the PSA level or prostate biopsies”
- 3% “the initiative was mine and had nothing to do with the PSA level or prostate biopsies”

Discussion

In this nationwide population-based study, a doctor's recommendation was a strong predictor for choosing AS, as was patient characteristics such as older age and more concurrent diseases. Men without anyone accompanying them when they were notified of the cancer diagnosis were more likely to opt for AS. Regarding adherence to AS, a low PSA at the time of diagnosis was an important factor, both according to the multivariate analysis and the direct question. Further, men whose PC was detected during the investigation of LUTS was more likely to adhere to AS. A unique feature of our study is that we could quantify the relative importance of different potential reasons for choosing and adhering to AS, as the men could tick more than one reason and grade its importance.

A doctor´s recommendation emerged as strongest factor associated with choice. This is highlighted in our direct question on choice where a doctor's recommendation was the single strongest predictor for choosing AS with 83% stating that they chose AS because their doctor recommended it. In fact, more men specified a doctor's recommendation as a reason for choosing AS than the will to avoid side-effects from treatment. This is in line with the review article about factors influencing men's choice of and adherence to AS by Kinsella et al [9], in which a physician's recommendation was identified as an important element in choosing AS [17-20]. In light of the evidence from multiple studies for the importance of the physician's recommendation in favor for choosing AS, the most important cause of the rapid increase in uptake on AS in Sweden over the past decade[3], was probably the Swedish national guidelines' clear recommendation since 2007 of AS for men with low-risk PC. The recommendation was during this time period less clear in the European and US recommendations [21,22], in which AS was mentioned as an alternative to radical treatment rather than the first choice option.

That patient characteristics, such as a higher age, were associated with AS is in line with previous studies [18,23]. It is possible that some of these men might have diverted from AS to watchful waiting during the seven years of follow-up as the oldest had reached 77 years by 2015 and might not have been eligible for treatment.

On multivariate analysis, being unaccompanied when notified of the cancer diagnosis predicted choice of AS. This might reflect that these men are more prone to accept the physician's suggestion if no one else was influencing them to undergo treatment. This highlights the responsibility of the treating physician, not only directed towards the patients but also to their significant others, to facilitate an informed treatment decision. A recently published qualitative study by Mader et al stating that spousal and social support play important roles in helping men understand and accept their PC diagnosis and chosen care plan [24]. In our study, 18% of men saw both a urologist and a medical oncologist but this did not affect the choice of treatment.

The participants in our study were diagnosed in 2008. Since then, uptake on AS in Sweden has steadily increased and reached 74% by 2014 [3]. In our study, 35% initially chose AS and 47% were still on AS after seven years follow-up. This is in line with a study by Loeb et al from 2015 that reported 64 % adherence to AS after five years [25] as well as the PRIAS study where 50% diverted to treatment within five years, mostly due to protocol-based reclassification (biopsy-related, changes in T-stage and/or PSA-doubling time) [26].

The main patient reported driver behind diverting to treatment was a rise in PSA. Only 9% of the men stated that the decision to diverge from AS to treatment was not because of PSA and/or biopsy results. PSA is considered a poor marker for disease progression, which for

example was shown by Fall et al when looking at men with high-risk disease [27]. Several studies have shown that many men with low-risk PC overestimate the risk of living with an untreated cancer [28,29], something that might be further magnified by rising PSA. In the PIVOT study, no difference in mortality was detected between men who were randomized to radical prostatectomy or observation after nearly 20 years of follow-up [30]. Roughly half of the men in our study, who all had low-risk PC diverted to treatment within these seven years which represents a significant overtreatment. Adherence to AS protocols and additional methods for follow-up such as MRI [31] and evidence-based triggers for treatment might reduce the fear of living with untreated cancer and thereby reduce unnecessary treatment.

Interestingly, men whose PC was detected during the investigation of LUTS rather than through screening was more likely to adhere to AS. This finding persisted after adjusting for age, retirement and CCI. A possible explanation might be a higher degree of anxiety in the group whose PC was detected through screening rather through the investigation on LUTS, although we do not have any data to support this. A recently published review article on psychological distress during cancer-screening [32] indicated that psychological distress, although low and not a barrier to screening, might be present. There might also be a motivational difference where men diagnosed through screening actively sought the investigation of PC and might be more motivated to undergo treatment. Another possible explanation might be that men diagnosed through the investigation of LUTS might have received drugs that reduce PSA e.g. Finasteride.

The strengths of our study include its population-based design, the high response rate for a study of its kind, the face-validated study-specific questionnaire, and the direct questions on reasons for choice and adherence. We acknowledge that various selection mechanisms

affected the men's choice of treatment and that several important factors could have been missed. The retrospective design is a limitation, as the men's experiences during the seven-year follow-up might have affected their recollection of their experiences. We did not have access to PSA levels during AS, only at diagnosis, which limits the possibility to investigate how PSA monitoring affects adherence to AS. Regarding being unaccompanied when notified of the cancer diagnosis, it's important to acknowledge that while these where unaccompanied during the appointment, they still might have had support from people in their support network. The study included Swedish men only and the findings might therefore not be generalizable to other cultural and health-care settings.

Conclusions

A doctor´s recommendation strongly affects which treatment is chosen for men with low-risk PC. Rising PSA values were the main factor for initiating treatment for men on AS. These findings need to be considered by health-care providers who wish to increase the uptake of and adherence to AS.

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

Study concept and design: Bergengren, Garmo, Bratt, Johansson, Bill-Axelson.

Acquisition of data: Bergengren, Johansson, Bill-Axelson.

Analysis and interpretation of data: Bergengren, Garmo, Holmberg, Johansson, Bill-Axelson.

Drafting of the manuscript: Bergengren, Johansson, Bill-Axelson.

Critical revision of the manuscript for important intellectual content: Bergengren, Bratt, Holmberg, Johansson, Bill-Axelson.

Statistical analysis: Garmo.

Obtaining funding: Bill-Axelson.

Administrative, technical, or material support: Bill-Axelson

Supervision: Holmberg, Johansson, Bill-Axelson.

Other: None.

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Figure legends

Table 1a: Demographics, clinical characteristics and potential factors associated with the choice of treatment by treatment group. AS = Active surveillance; RP/RT = Radical prostatectomy or Radiotherapy. Numbers are frequencies with percentages in brackets unless otherwise stated.

Table 1b: Demographics, clinical characteristics and potential factors associated with adherence to active surveillance by treatment group. AS -> AS = Stayed on active surveillance; AS -> RP/RT = Diverted from active surveillance to Radical prostatectomy or Radiotherapy. Numbers are frequencies with percentages in brackets unless otherwise stated.

Figure 1: Flow chart showing patients participation and treatment.

Figure 2: Forrest plot illustrating choice. OR (Odds rations) shows the probability of choosing active surveillance as primary treatment. Adjusted for age, work status, education, and Charlson comorbidity index.

Figure 3: Bar chart illustrating the direct question on why men chose active surveillance as their primary treatment. Numbers are frequencies with percentages.

Figure 4: Forrest plot illustrating adherence. OR (Odds rations) shows the probability of adhering to active surveillance. Adjusted for age, work status, education, and Charlson comorbidity index.

Figure 5: Bar chart illustrating the direct question on time spent in active surveillance and why men terminated active surveillance. Numbers are frequencies with percentages.

Table 1a - Choice		AS		RP/RT		ALL	
n		451	'(100.0)	837	'(100.0)	1288	'(100.0)
Age, n (range)		64	(61 - 67)	62	(58 - 65)	63	(59 - 66)
Marital status n (%)							
	Married or domestic partner	367	'(81.4)	701	'(83.8)	1068	'(82.9)
	Other	73	'(16.2)	126	'(15.1)	199	'(15.5)
	Missing	11	(2.4)	10	'(1.2)	21	'(1.6)
Children n (%)							
	No children	36	'(8.0)	70	'(8.4)	106	'(8.2)
	Children	401	'(88.9)	747	'(89.2)	1148	'(89.1)
	Missing	14	'(3.1)	20	'(2.4)	34	'(2.6)
Work status, n (%)							
	Not retired	74	'(16.4)	211	'(25.2)	285	'(22.1)
	Retired	377	'(83.6)	626	'(74.8)	1003	'(77.9)
	Missing	0	'(0.0)	0	'(0.0)	0	'(0.0)
Education level, n (%)							
	Compulsory school	143	'(31.7)	208	'(24.9)	351	'(27.3)
	Secondary school	166	'(36.8)	347	'(41.5)	513	'(39.8)
	University	128	'(28.4)	265	'(31.7)	393	'(30.5)
	Missing	14	'(3.1)	17	'(2.0)	31	'(2.4)
Charlson comorbidity index, n (%)							
	0	129	'(28.6)	282	'(33.7)	411	'(31.9)
	1	142	'(31.5)	296	'(35.4)	438	'(34.0)
	2	85	'(18.8)	144	'(17.2)	229	'(17.8)
	>2	95	'(21.1)	115	'(13.7)	210	'(16.3)
Psychiatric illness, n (%)							
	No	411	'(91.1)	770	'(92.0)	1181	'(91.7)
	Yes (Depression/ Other)	40	'(8.9)	67	'(8.0)	107	'(8.3)
T-stage							
	T1ab	37	(8.2)	16	'(1.9)	53	'(4.1)
	T1c	354	(78.5)	599	'(71.6)	953	'(74.0)
	T2	60	(13.3)	222	'(26.5)	282	'(21.9)
PSA value at diagnosis, n (%)							
	0-3.0	31	(6.9)	41	'(4.9)	72	'(5.6)
	3.1-7.0	325	(72.1)	597	'(71.3)	922	'(71.6)
	7.1-10.0	95	(21.1)	199	'(23.8)	294	'(22.8)
Method of detection n (%)							
	Screening	228	(50.6)	481	'(57.5)	709	'(55.0)
	LUTS	161	(35.7)	216	'(25.8)	377	'(29.3)
	Other symptoms	51	(11.3)	109	'(13.0)	160	'(12.4)
	Missing	11	(2.4)	31	'(3.7)	42	'(3.3)
Alone when being notified of the cancer diagnosis n (%)							
	No	107	'(23.7)	256	'(30.6)	363	'(28.2)
	Yes	332	'(73.6)	568	'(67.9)	900	'(69.9)
	Missing	12	'(2.7)	13	'(1.6)	25	'(1.9)
Sufficient time from diagnosis until treatment decision, n (%)							
	No, i wanted a quicker decision	27	'(6.0)	48	'(5.7)	75	'(5.8)
	Yes	363	'(80.5)	739	'(88.3)	1102	'(85.6)
	No, i wanted more time to think	11	'(2.4)	35	'(4.2)	46	'(3.6)
	Missing	50	'(11.1)	15	'(1.8)	65	'(5.0)

Table 1b - Adherence	AS->AS		AS -> RP/RT		ALL	
	213	'(100.0)	238	'(100.0)	451	'(100.0)
Age, n (range)	65	(61 - 68)	64	(61 - 66)	64	(61 - 67)
Marital status n (%)						
Married or domestic partner	174	'(81.7)	193	'(81.1)	367	'(81.4)
Other	35	'(16.4)	38	'(16.0)	73	'(16.2)
Missing	4	'(1.9)	7	'(2.9)	11	'(2.4)
Children n (%)						
No children	20	'(9.4)	16	'(6.7)	36	'(8.0)
Children	186	'(87.3)	215	'(90.3)	401	'(88.9)
Missing	7	'(3.3)	7	'(2.9)	14	'(3.1)
Work status, n (%)						
Not retired	33	'(15.5)	41	'(17.2)	74	'(16.4)
Retired	180	'(84.5)	197	'(82.8)	377	'(83.6)
Missing	0	'(0.0)	0	'(0.0)	0	'(0.0)
Education level, n (%)						
Compulsory school	65	'(30.5)	78	'(32.8)	143	'(31.7)
Secondary school	78	'(36.6)	88	'(37.0)	166	'(36.8)
University	64	'(30.0)	64	'(26.9)	128	'(28.4)
Missing	6	'(2.8)	8	'(3.4)	14	'(3.1)
Charlson comorbidity index, n (%)						
0	56	'(26.3)	73	'(30.7)	129	'(28.6)
1	70	'(32.9)	72	'(30.3)	142	'(31.5)
2	36	'(16.9)	49	'(20.6)	85	'(18.8)
>2	51	'(23.9)	44	'(18.5)	95	'(21.1)
Psychiatric illness, n (%)						
No	189	'(88.7)	222	'(93.3)	411	'(91.1)
Yes (Depression/ Other)	24	'(11.3)	16	'(6.7)	40	'(8.9)
T-stage						
T1ab	26	'(12.2)	11	'(4.6)	37	(8.2)
T1c	156	'(73.2)	198	'(83.2)	354	(78.5)
T2	31	'(14.6)	29	'(12.2)	60	(13.3)
PSA value at diagnosis, n (%)						
0-3.0	23	'(10.8)	8	'(3.4)	31	(6.9)
3.1-7.0	151	'(70.9)	174	'(73.1)	325	(72.1)
7.1-10.0	39	'(18.3)	56	'(23.5)	95	(21.1)
Method of detection n (%)						
Screening	94	'(44.1)	134	'(56.3)	228	(50.6)
LUTS	89	'(41.8)	72	'(30.3)	161	(35.7)
Other symptoms	22	'(10.3)	29	'(12.2)	51	(11.3)
Missing	8	'(3.8)	3	'(1.3)	11	(2.4)
Alone when being notified of the cancer diagnosis n (%)						
No	44	'(20.7)	63	'(26.5)	107	'(23.7)
Yes	164	'(77.0)	168	'(70.6)	332	'(73.6)
Missing	5	'(2.3)	7	'(2.9)	12	'(2.7)
Sufficient time from diagnosis until treatment decision, n (%)						
No, i wanted a quicker decision	9	'(4.2)	18	'(7.6)	27	'(6.0)
Yes	152	'(71.4)	211	'(88.7)	363	'(80.5)
No, i wanted more time to think	5	'(2.3)	6	'(2.5)	11	'(2.4)
Missing	47	'(22.1)	3	'(1.3)	50	'(11.1)

Figure 1 - Flowchart

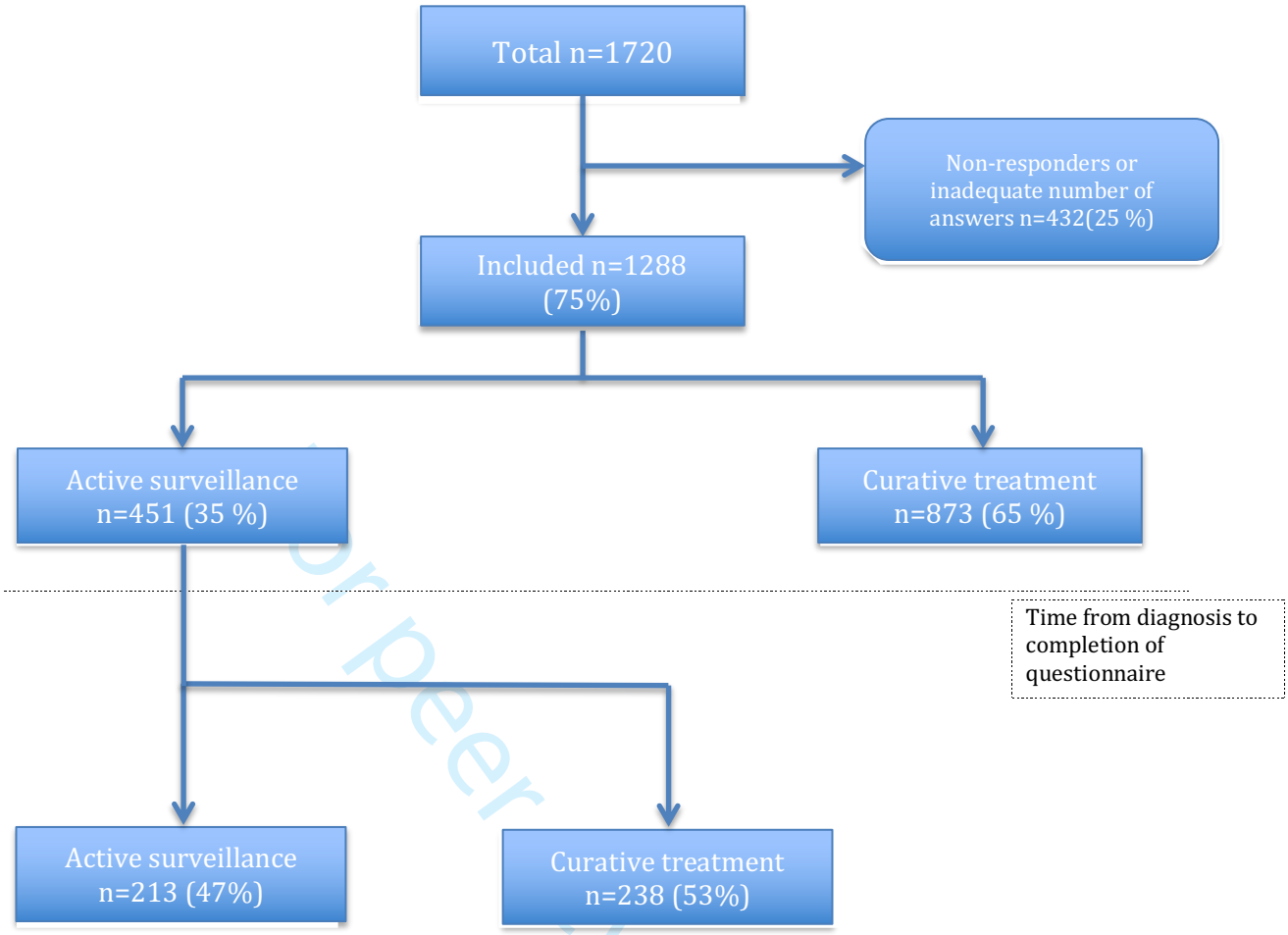


Figure 2 - Choice

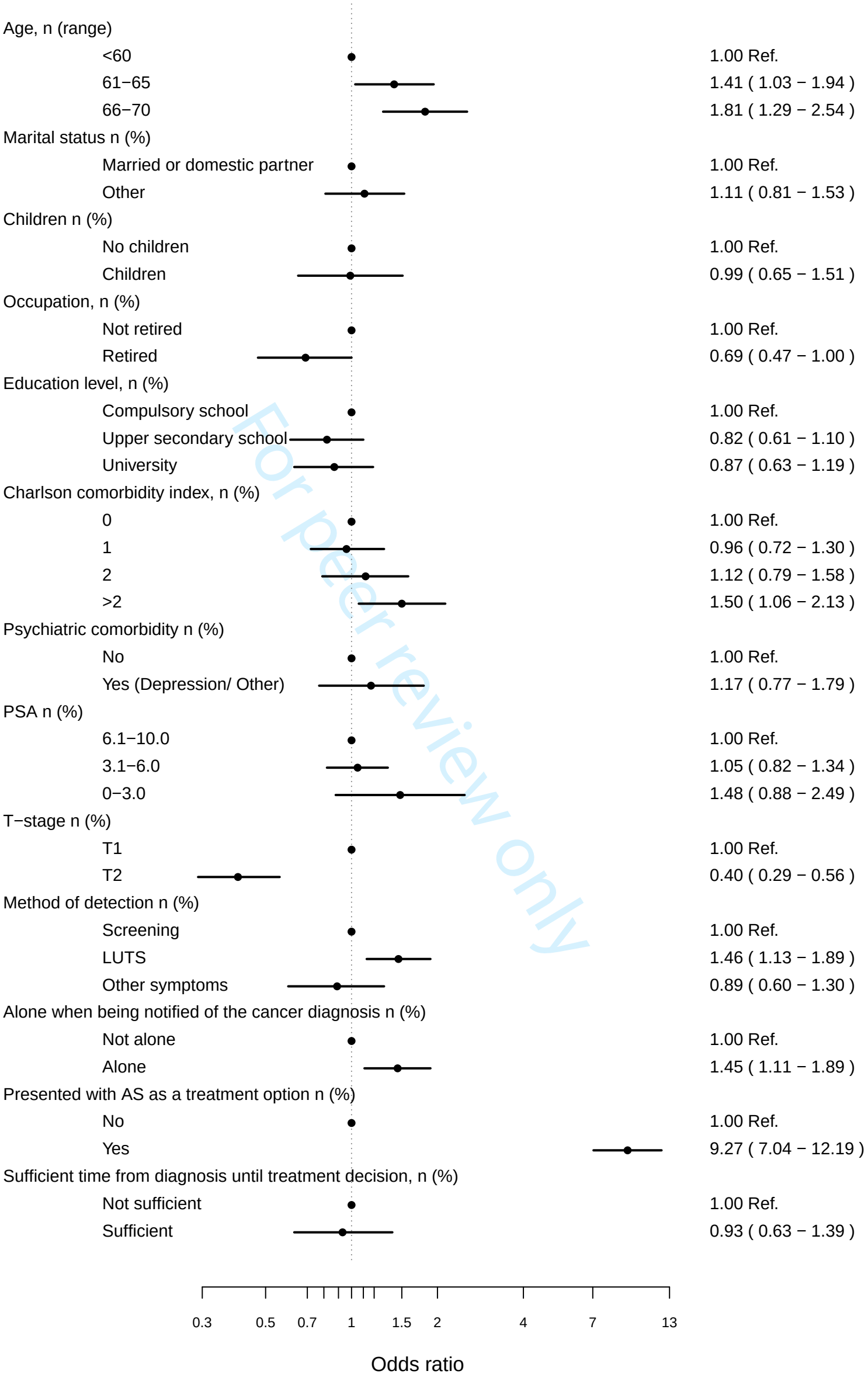
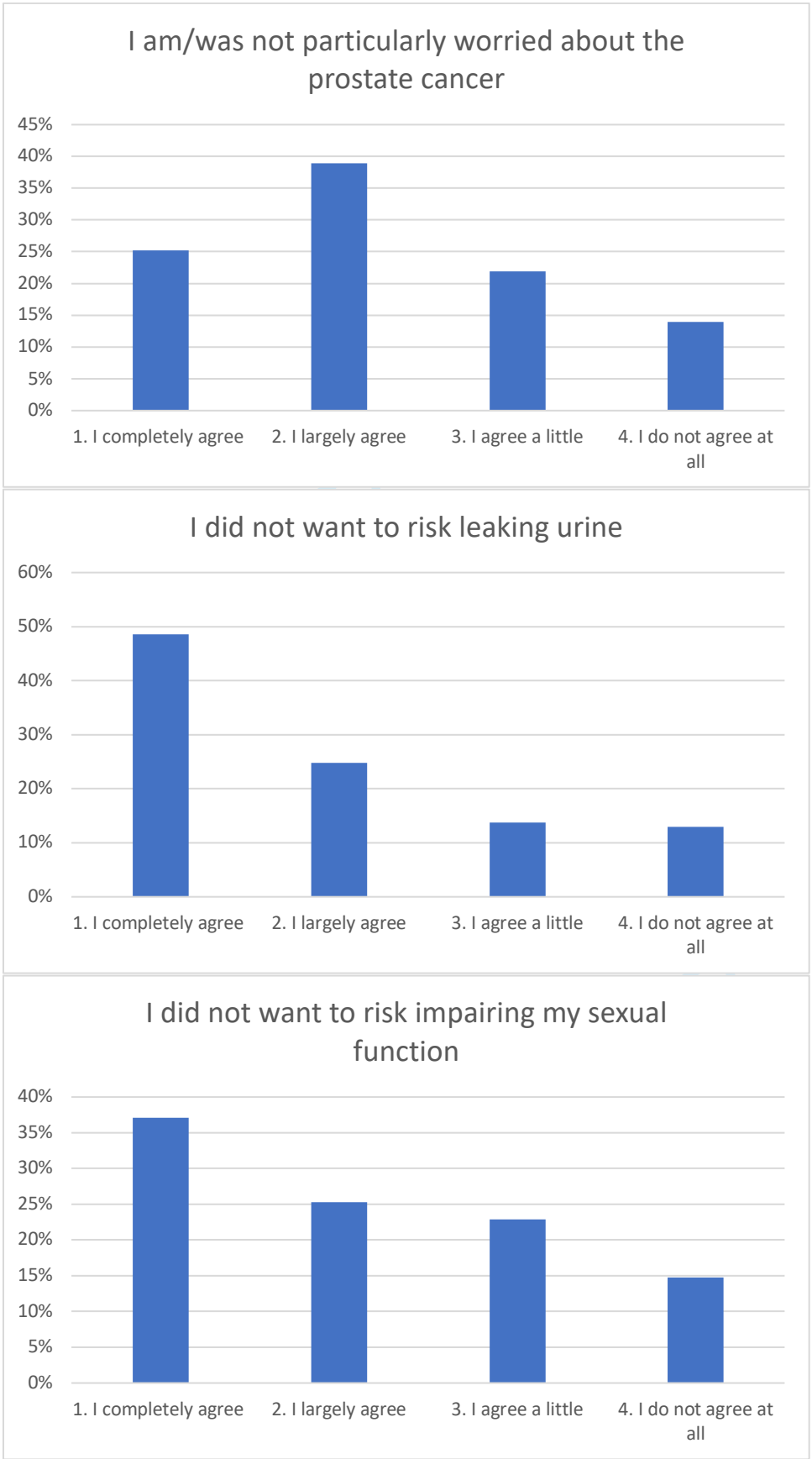
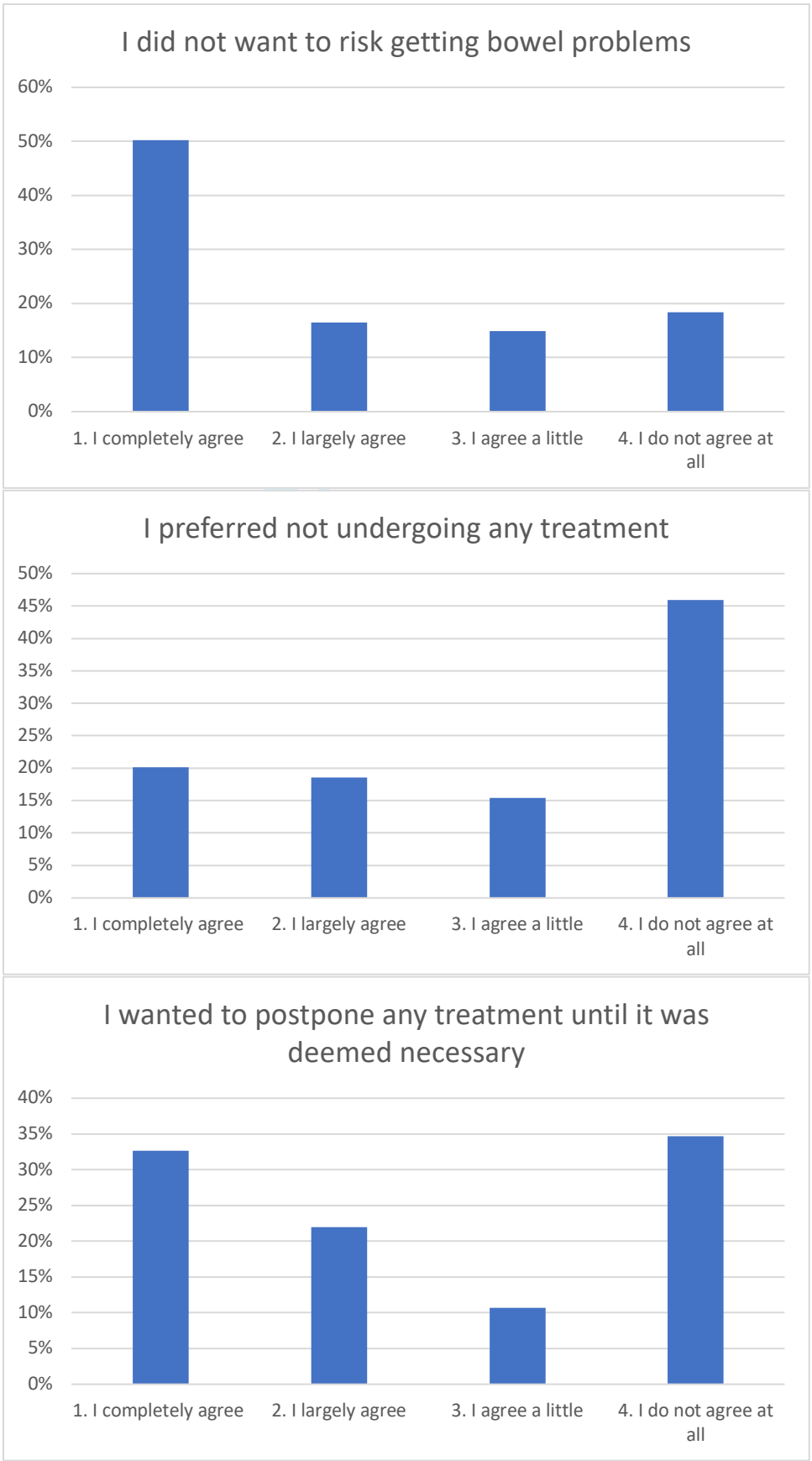
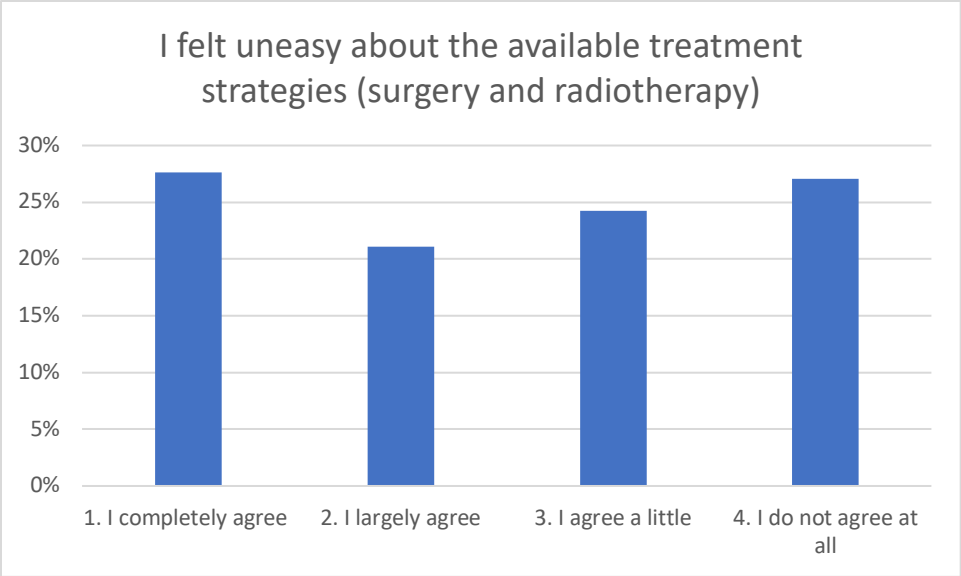


Figure 3 - direct question on why the men chose active surveillance




I did not want to risk getting bowel problems
60%
50%
40%
30%
20%
10%
0%
1. I completely agree
2. I largely agree
3. I agree a little
4. I do not agree at all
I preferred not undergoing any treatment
50%
45%
40%
35%
30%
25%
20%
15%
10%
5%
0%
1. I completely agree
2. I largely agree
3. I agree a little
4. I do not agree at all
I wanted to postpone any treatment until it was deemed necessary
40%
35%
30%
25%
20%
15%
10%
5%
0%
1. I completely agree
2. I largely agree
3. I agree a little
4. I do not agree at all


I felt uneasy about the available treatment strategies (surgery and radiotherapy)
30%
25%
20%
15%
10%
5%
0%
1. I completely agree
2. I largely agree
3. I agree a little
4. I do not agree at all

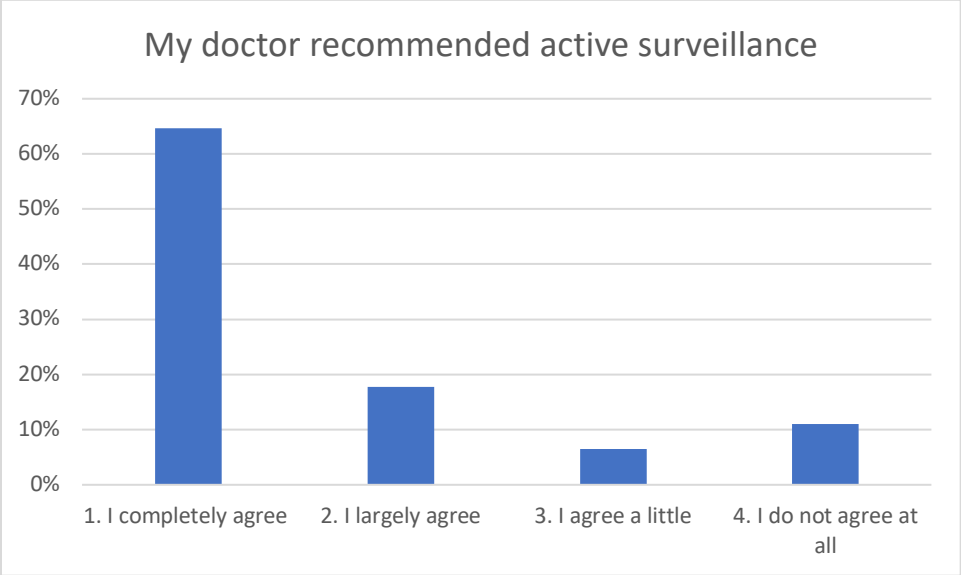

My doctor recommended active surveillance
70%
60%
50%
40%
30%
20%
10%
0%
1. I completely agree
2. I largely agree
3. I agree a little
4. I do not agree at all

Figure 4 - Adherence

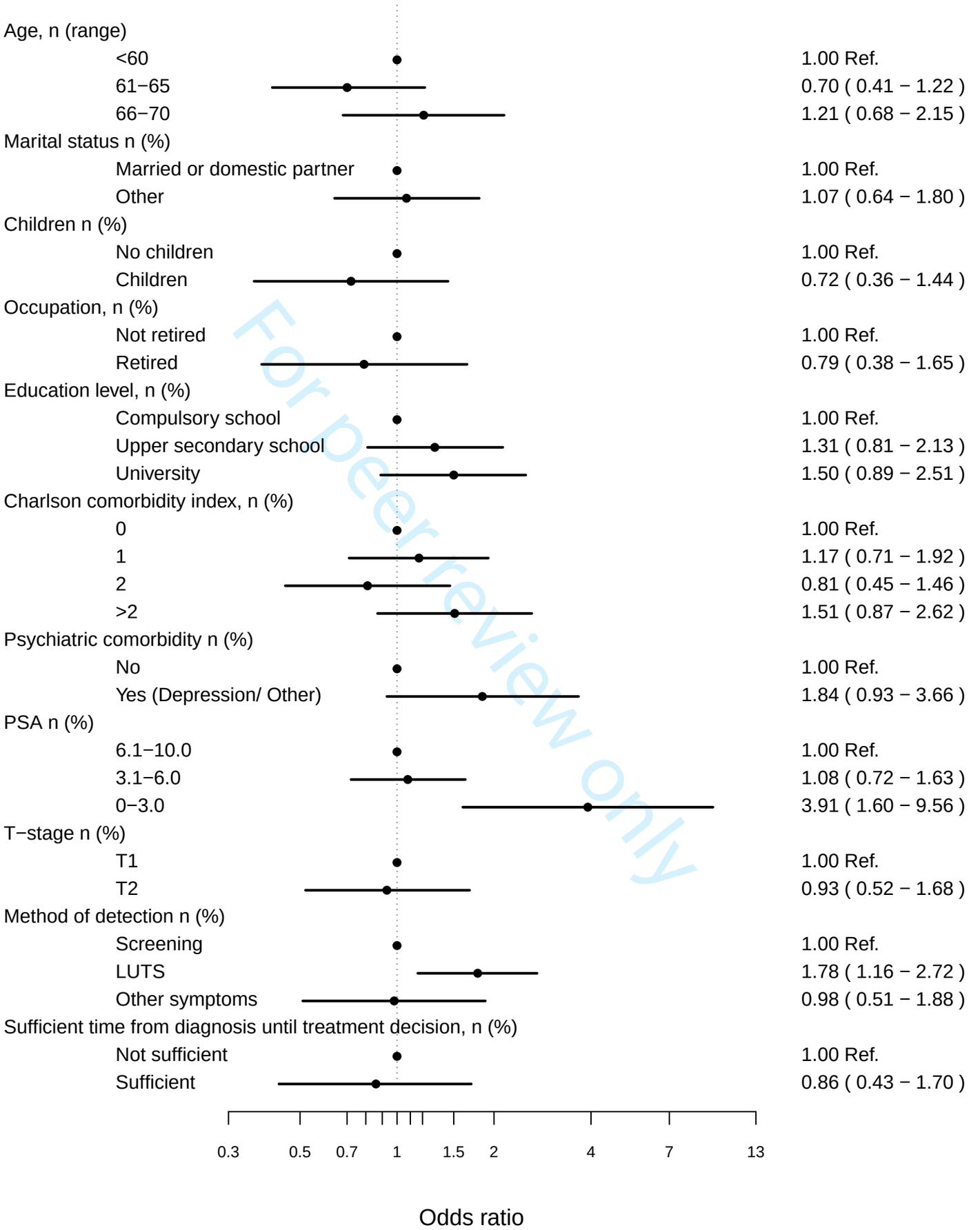
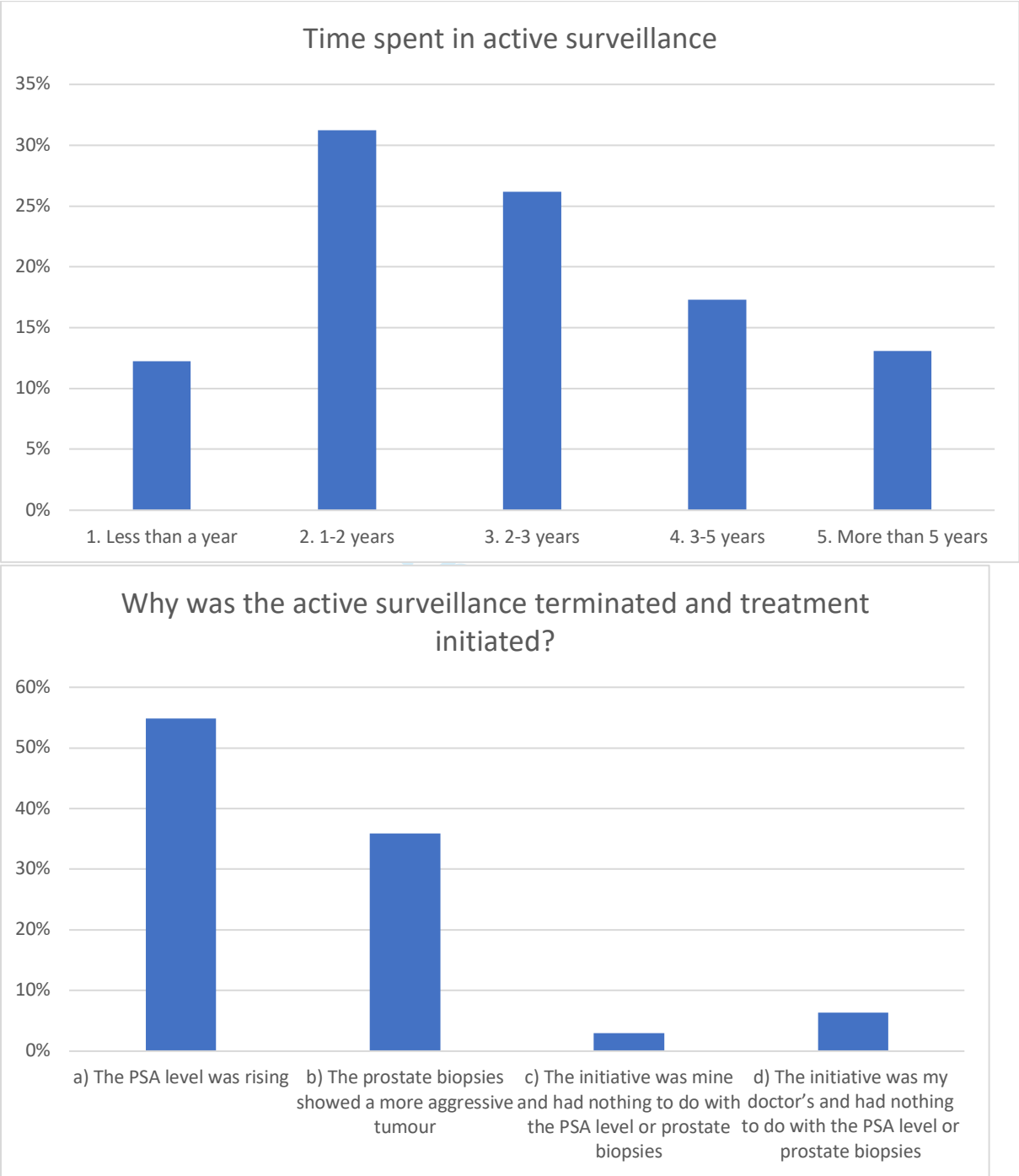


Figure 5 - direct question on why the men diverted from active surveillance



Health and Quality of Life in Men with Prostate Cancer

Thank you for taking part in this study.

A number of questions follow below (58 questions in part 1 and 17 questions in part 2). Provide the answers that best describe you and your situation. If more than one alternative is possible, the question will indicate as much. Please try to answer all the questions.

PLEASE OBSERVE that the term "active surveillance" is used in this questionnaire.
"Active surveillance" is a conservative treatment strategy for men with low-risk prostate cancer that involves close monitoring of the disease using PSA tests and repeat biopsies. When there are signs of disease progression, the patient receives curative treatment through surgery or radiotherapy. A patient is not in active surveillance if:

1) A decision to treat the prostate cancer by surgery or radiotherapy is taken within six months from the prostate cancer diagnosis.
2) Being monitored after having received treatment of any kind.

PART 1. Demographics and questions about quality of life

General Questions

1. In which year were you born?
(Give four figures, e.g. 1945)

2. Are you currently:

- ❑ Living with spouse or partner
- ❑ Not in a significant relationship
- ❑ In a significant relationship, but not living together

3. Do you have children?

❑ No ❑ Yes

4. Do you have grandchildren?

❑ No ❑ Yes

5. Are you currently:

- ❑ Employed
- ❑ Looking for work
- ❑ Retired
- ❑ On long-term sick leave
- ❑ On disability pension

6. What is the highest level of your education?

- ❑ Basic education or equivalent
- ❑ Upper secondary, vocational school or equivalent
- ❑ College or university

7. ***During the last 4 weeks***, how many hours per have you undertaken at least moderate physical exercise involving an elevated pulse rate (i.e. walking, cycling, swimming, etc.)?

- ❑ None
- ❑ Less than 1 hour per week
- ❑ 1-3 hours per week
- ❑ More than 3 and up to 7 hours per week
- ❑ More than 7 hours per week

8. What are your smoking habits? *(Only pick one answer)*

- ❑ Smoke everyday
- ❑ Smoke occasionally (less than 1 cigarette per day)
- ❑ Former smoker
- ❑ Never smoked

9. How many units of alcohol (see example below) do you typically drink on a day when you drink alcohol?

- ❑ 0 units of alcohol per week
- ❑ 1-5 units of alcohol per week
- ❑ 6-10 units of alcohol per week
- ❑ 11-20 units of alcohol per week
- ❑ More than 20 units of alcohol per week

In the UK, one unit of alcohol is for example:

10. How tall are you?

cm

11. How much do you weigh?

kg

12. Do you have or have you ever had any of the following illnesses? If so, which? *(Tick the appropriate box for each question)*

A.	Heart disease (e.g. angina, heart attack, or heart failure)	❑ No	❑ Yes
B.	High blood pressure	❑ No	❑ Yes
C.	Pains in the legs when walking owing to poor blood circulation	No	❑ Yes
D.	Lung disease (e.g. asthma, chronic bronchitis, or chronic obstructive pulmonary disease (COPD))	❑ No	❑ Yes
E.	Diabetes	❑ No	❑ Yes
F.	Kidney disease	❑ No	❑ Yes

G.	Liver disease	❑ No	❑ Yes
H.	Stroke	❑ No	❑ Yes
I.	Neurological disease (e.g. Parkinson's disease or MS)	❑ No	❑ Yes
J.	Other type of cancer than prostate cancer (in the last 5 years)	❑ No	❑ Yes
K.	Depression	❑ No	❑ Yes
L.	Other psychological illness	❑ No	❑ Yes
M.	Reumatism	❑ No	❑ Yes
N.	Paralysis	❑ No	❑ Yes
O.	HIV+ or AIDS	❑ No	❑ Yes

(modified from Charlson Comorbidity index Chaudhry et al 2005)

Questions About Quality of Life

Answer the following questions by circling the number that best fits your opinion.

13. ***During the last 4 weeks***, what has your quality of life been like?

1----------2----------3----------4----------5----------6----------7
No quality of life Best possible quality of life

14. ***During the last 4 weeks***, has your life felt meaningful?

1----------2----------3----------4----------5----------6----------7
Never All the time

15. ***During the last 4 weeks***, what has your physical stamina been like?

1----------2----------3----------4----------5----------6----------7
No stamina Best possible stamina

16. ***During the last 4 weeks***, what has your mental wellbeing been like?

1----------2----------3----------4----------5----------6----------7
No wellbeing Best possible wellbeing

17. ***During the last 4 weeks***, what has your physical health been like?

1----------2----------3----------4----------5----------6----------7
Worst imaginable health Best imaginable health

18. ***During the last 4 weeks***, what has your self-esteem been like?

1----------2----------3----------4----------5----------6----------7
No self-esteem Best imaginable self-esteem

Questions About Depression and Anxiety

19. ***During the last 4 weeks***, have you felt miserable or depressed?

1----------2----------3----------4----------5----------6----------7
Never All the time

20. ***During the last 4 weeks***, have you experienced worry or anxiety?

1----------2----------3----------4----------5----------6----------7
Never All the time

21. ***During the last 4 weeks***, have you had difficulties sleeping at night?

- ❑ No, never
- ❑ Yes, at least once this month
- ❑ Yes, at least once a week
- ❑ Yes, at least 3 times per week
- ❑ Yes, every night

22. ***During the last 4 weeks***, have you woken during the night with feelings of worry or anxiety?

- ❑ No, never
- ❑ Yes, at least once this month
- ❑ Yes, at least once a week
- ❑ Yes, at least 3 times per week
- ❑ Yes, every night

23. ***During the last 4 weeks***, have you taken any preparations to help you sleep?

- ❑ No, never
- ❑ Yes, at least once this month
- ❑ Yes, at least once a week
- ❑ Yes, at least 3 times per week

❑ Yes, every evening

24. ***During the last 4 weeks***, have you taken any tranquilizers (anti-anxiety medications)?

❑ No, never
❑ Yes, at least once this month
❑ Yes, at least once a week
❑ Yes, at least 3 times per week
❑ Yes, every day

25. ***During the last 4 weeks***, have you taken any anti-depressives, i.e medication against feeling low or depressed?

❑ No ❑ Yes

Questions About Information and Decision on Treatment

26. I was informed about my prostate cancer:

❑ At a meeting in person
❑ By telephone
❑ By mail
❑ In another way, which? _____

27. When you were informed about your prostate cancer, were you informed in a good way?
(Circle the number which best describes you or your situation)

1----------2----------3----------4----------5----------6----------7
Worst imaginable way Best imaginable way

28. Did you have a friend or relative with you when you were informed about your prostate cancer?

❑ No ❑ Yes

29. How much information have you received from your doctor? *(For each row, tick the box that best describes your perception)*

		No Information	Little Information	Quite a lot of Information	A great deal of Information
A.	About prostate cancer – the illness and its course	☐	☐	☐	☐
B.	About various treatment options for prostate cancer	☐	☐	☐	☐

C.	About side effects of the various treatment options	☐	☐	☐	☐
D.	About how the various treatments could affect your quality of life	☐	☐	☐	☐

30. Which treatment options were suitable to you, according to your perception of the information you received from your doctor? *(Multiple answers are possible)*

- ❑ Active surveillance (go to checks with PSA tests and MRI examinations, treatment will become relevant if the cancer becomes more serious)
- ❑ Surgical removal of the prostate (radical prostatectomy)
- ❑ Radiotherapy
- ❑ Other treatment, please specify: _____

31. How much did you influence the treatment decision-making?

- ❑ Not at all
- ❑ A little
- ❑ Moderately
- ❑ Very much

32. Are you satisfied with how much you were involved in the decision-making between radiotherapy, surgery or active surveillance?

- ❑ No, I wish I had been less involved in the decision-making
- ❑ No, I wish I had been more involved in the decision-making
- ❑ Yes, I am satisfied with how much I was involved in the decision-making

33. How much time passed between your prostate cancer diagnosis and the treatment decision-making?

- ❑ The treatment decision was made right after I received my diagnosis
- ❑ 1-4 weeks
- ❑ 2-3 months
- ❑ More than 3 months

34. In your opinion, were you given enough time to think before the treatment decision was made?

- ❑ No, I wish I had been given less time before the decision was made
- ❑ No, I wish I had been given more time before the decision was made
- ❑ Yes, I was given enough time before the decision was made

35. In your opinion, did the right amount of time pass between the treatment decision-making and the treatment start?

- ❑ *Not applicable,* I have not received treatment for my prostate cancer
- ❑ No, I wish there had been less time between the treatment decision-making and the treatment start

- ❑ No, I wish there had been more time between treatment decision and treatment start
- ❑ Yes, I am satisfied with the amount of time that passed between treatment decision-making and the treatment start

36. What type of doctor(s) did you discuss your prostate cancer with before the treatment decision was made?

- ❑ Urologist (doctor that performs prostate cancer surgery)
- ❑ Oncologist (doctor that gives radiotherapy treatment)
- ❑ Other type of doctor

37. Do you have access to a nurse navigator?

❑ No ❑ Yes ❑ I don't know

38. Where have you searched for information about prostate cancer? *(NB! Several alternatives possible.)*

- ❑ I have not searched for information about prostate cancer
- ❑ Internet
- ❑ Radio
- ❑ TV
- ❑ Newspapers
- ❑ Patient brochures
- ❑ Patients association
- ❑ Friends or family
- ❑ If elsewhere, please specify: _____

Questions About Your Treatment

39. Which alternatives below describes your situation? (*Cross of one alternative)*

- ❑ I am currently on active surveillance (i.e. my prostate cancer is closely monitored using PSA tests and repeat biopsies and curative treatment is initiated if the disease progresses)
- ❑ I started on active surveillance but have since received curative treatment
- ❑ I received treatment directly (within 6 months from my prostate cancer diagnosis)

40. If you have received treatment for prostate cancer, which treatment(s) have you received up to date?

(NB! Several alternatives are possible. You may, for example, have undergone an operation and radiotherapy, radiotherapy and hormone treatment, or just hormone treatment.)

- ❑ I have not had any treatment, I am on active surveillance
- ❑ Removal of the whole prostate gland (so-called radical prostatectomy)
- ❑ Radiotherapy of the prostate gland
- ❑ Hormone treatment in connection with radiotherapy of the prostate gland
- ❑ Only hormone treatment by injection (so-called GnRH-analogue)
- ❑ Only hormone treatment with pills (e.g. Bicalutamide, or Casodex)

❑ Testicles have been removed by means of operation

41. If you were on active surveillance for prostate cancer but later received treatment, or if you are still on active surveillance - which of the following alternative(s) influenced the decision?

❑ Not applicable, I was never on active surveillance, I received treatment directly

A. I am/was not particularly worried about the prostate cancer

❑ I completely agree
❑ I largely agree
❑ I agree a little
❑ I do not agree at all

B. I did not want to risk leaking urine

❑ I completely agree
❑ I largely agree
❑ I agree a little
❑ I do not agree at all

C. I did not want to risk impairing my sexual function

❑ I completely agree
❑ I largely agree
❑ I agree a little
❑ I do not agree at all

D. I did not want to risk getting bowel problems

❑ I completely agree
❑ I largely agree
❑ I agree a little
❑ I do not agree at all

E. I preferred not undergoing any treatment

❑ I completely agree
❑ I largely agree
❑ I agree a little
❑ I do not agree at all

F. I wanted to postpone any treatment until it was deemed necessary

❑ I completely agree
❑ I largely agree
❑ I agree a little
❑ I do not agree at all

G. I felt uneasy about the available treatment strategies (surgery and radiotherapy)

❑ I completely agree
❑ I largely agree
❑ I agree a little

❑ I do not agree at all

H. My doctor recommended active surveillance

❑ I completely agree
❑ I largely agree
❑ I agree a little
❑ I do not agree at all

42. What do you believe will happen in the future when it comes to your prostate cancer? *(Cross of one alternative.)*

❑ I believe that my disease will progress/recur and require treatment within 2 years
❑ I believe that my disease will progress/recur and require treatment within 5 years
❑ I believe that my disease will progress/recur and require treatment within 10 years
❑ I believe that my disease is harmless

43. If you were on active surveillance but then received treatment, please answer the following questions (A to C).

❑ Not applicable, I was never on active surveillance, I received treatment directly

A. For how long were you on active surveillance?

❑ Less than a year
❑ 1-2 years
❑ 2-3 years
❑ 3-5 years
❑ More than 5 years

B. Why was the active surveillance terminated and treatment initiated? *(NB! Several alternatives possible.)*

❑ The PSA level was rising
❑ The prostate biopsies showed a more aggressive tumour
❑ The initiative was mine and had nothing to do with the PSA level or prostate biopsies
❑ The initiative was my doctor's and had nothing to do with the PSA level or prostate biopsies
❑ If other reason, please specify: _____

C. If it was your initiative to terminate active surveillance and start treatment but the reason for this was not that the tumour was progressing, what was the reason: *(NB! Several alternatives possible.)*

❑ I was worried
❑ My partner was worried
❑ My friends were worried
❑ I wanted to avoid further biopsies
❑ I wanted to avoid the repeated PSA tests
❑ I just wanted to have treatment done
❑ Other reason

If other reason, please describe it:

_____

_____

44. Are you worried that your medical problems, if you have any, are related to prostate cancer?

- ❑ Not at all
- ❑ A little
- ❑ Moderately
- ❑ Very much

45. Do you believe that you will die from prostate cancer?

❑ No ❑ Yes

46. Have you told anyone about your prostate cancer? *(NB! Several alternatives possible.)*

- ❑ I have not told anyone about my prostate cancer
- ❑ Partner
- ❑ Children
- ❑ Grandchildren
- ❑ Close friend(s)
- ❑ Colleague(s)
- ❑ Other person(s)

47. If you are concerned about telling others about your prostate cancer, what are the reasons for this? *(NB! Several alternatives possible.)*

- ❑ Not applicable, I do not hesitate to tell others about the prostate cancer
- ❑ It felt too private
- ❑ I did not want to worry others
- ❑ I believe that people would act differently towards me if I told them about the prostate cancer
- ❑ I believe that telling others would affect my career
- ❑ Other reason

If other reason, please describe it:

_____

_____

Questions About Your Prostate Cancer Checks

48. Who monitors your prostate cancer? *(NB! Several alternatives possible.)*

- ❑ Doctor
- ❑ Nurse

49. When was your last prostate cancer check?

- ❑ Less than one week ago
- ❑ Less than one month ago
- ❑ Less than three months ago
- ❑ More than three months ago

50. When did you last take a PSA test?

- ❑ Less than one week ago
- ❑ 1-4 weeks ago
- ❑ 1-3 months ago
- ❑ More than three months ago

51. When is your next scheduled PSA test?

- ❑ In less than one week
- ❑ In 1-4 weeks
- ❑ In more than one month
- ❑ I don't know

52. In connection with your prostate cancer check, do you feel reminded of your cancer disease?

- ❑ Not at all
- ❑ A little
- ❑ Moderately
- ❑ Very much

53. In connections with your prostate cancer check, do you feel worried about what the PSA test will show?

- ❑ Not at all
- ❑ A little
- ❑ Moderately
- ❑ Very much

54. In connection with your prostate cancer checks, do you feel worried about needing to take new tissue samples (biopsies) from your prostate (if you are on active surveillance)?

- ❑ Not applicable, I have received treatment for prostate cancer
- ❑ Not at all
- ❑ A little
- ❑ Moderately
- ❑ Very much

55. In connection with your prostate cancer check, do you feel worried that your prostate cancer has spread (metastasized) to a different part of your body?

- ❑ Not at all

- ❑ A little
- ❑ Moderately
- ❑ Very much

56. If you feel worried in connection with your prostate cancer check, how long does the worry last?

- ❑ Not applicable, I am not worried before the prostate cancer check
- ❑ Only a day or so, at the time of the prostate cancer check
- ❑ From the day I receive the invitation to the time of the prostate cancer check
- ❑ From before I receive the invitation
- ❑ I am always, more or less, worried

57. Has your prostate cancer diagnosis had an affect on your life style in any way, and if so, in what areas?

A.	Type of food	☐ I eat less healthy	☐ Unchanged	☐ I eat healthier
B.	Exercise	☐ I exercise less	☐ Unchanged	☐ I exercise more
C.	Interest in social activities/relationships	☐ Less	☐ Unchanged	☐ More
D.	Interest in religion/philosophy	☐ Less	☐ Unchanged	☐ More

58. How has prostate cancer affected your economic situation?

- ❑ Impaired
- ❑ Unchanged
- ❑ Improved

PART II. Questionnaire for Symptoms (EPIC-26)

The next few questions concern problems you may be experiencing.
(Tick the appropriate box for each question)

1. ***Over the past 4 weeks***, how often has your urine leaked?

- ❑ More than once a day
- ❑ About once a day
- ❑ More than once a week
- ❑ About once a week
- ❑ Rarely or never

2. Which of the following alternatives best describes how well you have been able to control your urinating ***during the last 4 weeks***?

- ❑ No urinary control whatsoever
- ❑ Drip all the time
- ❑ Drip a little occasionally
- ❑ Full control

3. On average **over the last 4 weeks**, how many incontinence pads or adult diapers have you used per day owing to urine leakage?

- ❑ None
- ❑ 1 per day
- ❑ 2 per day
- ❑ 3 or more per day

4. How large a problem, if any, have the following symptoms been ***during the last 4 weeks***? (*Cross of one alternative for each sub-question.)*

		None	Very Little	Little	Moderate	Large
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	❑	❑	❑	❑	❑

5. Overall, how large a problem has urination been for you **during the last 4 weeks**? *(Tick the box that best describes your perception.)*

- ❑ No problem
- ❑ Very little problem
- ❑ Little problem
- ❑ Moderate problem
- ❑ Large problem

6. How large a problem, if any, have the following symptoms been for you? (*Cross of one alternative for each sub-question.)*

	None	Very Little	Little	Moderate	Large

A.	Urgent need to empty the bowel immediately	❑	❑	❑	❑	❑
B.	Need to empty the bowel often	❑	❑	❑	❑	❑
C.	Inability to control the bowel function	❑	❑	❑	❑	❑
D.	Bloody in faeces	❑	❑	❑	❑	❑
E.	Abdominal/pelvic/rectal pain	❑	❑	❑	❑	❑

7. Overall, how large a problem has your bowel emptying been for you ***during the last 4 weeks***? *(Tick the box that best describes your perception.)*

❑ No problem
❑ Very little problem
❑ Little problem
❑ Moderate problem
❑ Large problem

8. How would you rate each of the following ***during the last 4 weeks***? (*Cross of one alternative for each sub-question.)*

		Very Poor to Non-existent	**Poor**	**Modera**	**Good**	**Very Good**
A.	Your ability to get an erection	❑	❑	❑	❑	❑
B.	Your ability to achieve orgasm (climax)?	❑	❑	❑	❑	❑

9. How would you describe the usual quality of your erections ***during the last 4 weeks***? *(Tick the box that best describes your perception.)*

❑ None at all
❑ Not firm enough for any sexual activity
❑ Firm enough for masturbation and foreplay only
❑ Firm enough for intercourse

10. How would you describe the frequency of your erections ***during the last 4 weeks***? *(Tick the box that best describes your perception.)*

❑ I NEVER obtained an erection when desired
❑ Less than half of the times I wanted an erection
❑ Around half of the times I wanted an erection
❑ More than half of the times I wanted an erection
❑ Whenever I wanted an erection

11. Overall, how would you rate your sexual capability ***during the last 4 weeks***?

12. *(Tick the box that best describes your perception.)*

- ❑ Very poor
- ❑ Poor
- ❑ Moderate
- ❑ Good
- ❑ Very good

12. How large a problem have you had with your sexual capability ***during the last 4 weeks***?
(Tick the box that best describes your perception)

- ❑ No problem
- ❑ Very little problem
- ❑ Little problem
- ❑ Moderate problem
- ❑ Large problem

13. How large a problem, if any, have the following symptoms been for you during the last 4 weeks?
(*Cross of one alternative for each sub-question)*

		None	Very little problem	Little problem	Moderate problem	Large problem
A.	Hot flushes	❑	❑	❑	❑	❑
B.	Tenderness/ swelling in chest	❑	❑	❑	❑	❑
C.	Feeling low	❑	❑	❑	❑	❑
D.	Lacking energy	❑	❑	❑	❑	❑
E.	Change in body weight	❑	❑	❑	❑	❑

14. Which of the following medications/sexual aids have you tried and how did they work? (*Cross of one alternative for each sub-question)*

		Have not tried	Tried but it did not help	Helped but not using it now	Helps and I use it now and then	Helps and I always use it in connection with sexual activity
A.	Viagra, Sildenafil, Cialis, Levitra or other medications? If other pills, please give name: _____	❑	❑	❑	❑	❑
B.	Bondil (gel in urethra)?	❑	❑	❑	❑	❑
C.	Caverject (injection in the penis)?	❑	❑	❑	❑	❑
D.	Vacuum pump?	❑	❑	❑	❑	❑
E.	Other? If so, please state what: _____	❑	❑	❑	❑	❑

15. How long did your erection usually last with the aid of medication/sexual aid during the last 4 weeks?
(Tick the box that best describes your perception)

- ❑ Not relevant, I do not use medications or sexual aids

- ❑ Non-existent
- ❑ Insufficient for any kind of sexual activity
- ❑ Sufficient for masturbation and foreplay
- ❑ Sufficient for intercourse

16. Are you **satisfied** with your sexual life?
(Circle the number which best describes you or your situation)

1----------2----------3----------4----------5----------6----------7
Not at all satisfied Completely satisfied

Finally, we would like to ask you

17. Overall, how satisfied are you with the medical care you have received as a prostate cancer patient? (Personalised service, information, etc.)

(Circle the number which best describes you or your situation)

1----------2----------3----------4----------5----------6----------7
Not satisfied at all Completely satisfied

Is there anything else that you think is important concerning your illness that we have failed to ask about? Please write and tell us!

_____

_____

_____

THANK YOU FOR YOUR ANSWERS!

Appendix 2 – Drop-out analysis	No questioner data (n=432)		Questioner data (n=1288)		Received questioner (n=1720)		Fisher's exact test
Age, n (%)							
≤50	17	(3.9)	39	(3.0)	56	(3.3)	
51-60	170	(39.4)	401	(31.1)	571	(33.2)	0.003
61-65	128	(29.6)	488	(37.9)	616	(35.8)	
66-70	117	(27.1)	360	(28.0)	477	(27.7)	
T-stage, n (%)							
T1a	25	(5.8)	45	(3.5)	70	(4.1)	
T1b	6	(1.4)	8	(0.6)	14	(0.8)	0.04
T1c	320	(74.1)	953	(74.0)	1273	(74.0)	
T2	81	(18.8)	282	(21.9)	363	(21.1)	
PSA, n (%)							
≤3	48	(11.1)	72	(5.6)	120	(7.0)	
3.1-7	292	(67.6)	922	(71.6)	1214	(70.6)	<0.001
7.1-10	92	(21.3)	294	(22.8)	386	(22.4)	
Proportion positive cores, n (%)							
≤12.5%	137	(31.7)	378	(29.3)	515	(29.9)	
12.5-25%	107	(24.8)	380	(29.5)	487	(28.3)	
25.1-50%	126	(29.2)	359	(27.9)	485	(28.2)	0.15
>50%	27	(6.2)	111	(8.6)	138	(8.0)	
Missing data	35	(8.1)	60	(4.7)	95	(5.5)	
Mode of detection, n (%)							
Screening	203	(47.0)	709	(55.0)	912	(53.0)	
LUTS	145	(33.6)	377	(29.3)	522	(30.3)	0.024
Other symptoms	64	(14.8)	160	(12.4)	224	(13.0)	
Missing data	20	(4.6)	42	(3.3)	62	(3.6)	
Treatment according to NPCR, n (%)							
AS	202	(46.8)	476	(37.0)	678	(39.4)	
RP	187	(43.3)	660	(51.2)	847	(49.2)	0.002
RT	43	(10.0)	152	(11.8)	195	(11.3)	

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	Report numbers of outcome events or summary measures over time	8-10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-10
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-10
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15-16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Determinants for choosing and adhering to active surveillance for localized prostate cancer: a nationwide population-based study

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Determinants for choosing and adhering to active surveillance for localized prostate cancer: a nationwide population-based study

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Abstract

Objective: Knowledge about factors influencing choice of and adherence to active surveillance (AS) for prostate cancer (PC) is scarce. We aim to identify which factors most affected choosing and adhering to AS and to quantify their relative importance.

Design, Setting, and Participants: In 2015 we sent a questionnaire to all Swedish men aged ≤ 70 years registered in the National Prostate Cancer Register of Sweden who were diagnosed in 2008 with low-risk PC and had undergone prostatectomy, radiotherapy, or started on AS.

Outcome Measurements and Statistical Analysis: Logistic regression was used to calculate odds ratios (OR) with 95% confidence intervals (CI) for factors potentially affecting choice and adherence to AS.

Results: 1288 out of 1720 men (75%) responded, 451 (35%) chose AS and 837 (65%) underwent curative treatment. Of those starting on AS, 238 (53%) diverted to treatment within seven years. Most men (83%) choose AS because “My doctor recommended AS”. Factors associated with choosing AS over treatment were older age (OR 1.81, 95% CI 1.29-2.54), a Charlson Comorbidity Index >2 (OR 1.50, 95% CI 1.06–2.13), being unaccompanied when notified of the cancer diagnosis (OR 1.45, 95% CI 1.11-1.89). Men with a higher PSA at the time of diagnosis were less likely to adhere to AS (OR 0.26, 95% CI 0.10-0.63). The reason for having treatment after initial AS was “the PSA level was rising” in 55% and biopsy findings in 36%.

Conclusions: A doctor's recommendation strongly affects which treatment is chosen for men with low-risk PC. Rising PSA values were the main factor for initiating treatment for men on AS. These findings need be considered by health-care providers who wish to increase the uptake of and adherence to AS.

Strengths and limitations of this study:

- The strengths of our study include its population-based design, the high response rate for a study of its kind, the face-validated study-specific questionnaire, and the direct questions on reasons for choice and adherence.
- The retrospective design is a limitation, as the men's experiences during the seven-year follow-up might have affected their recollection of their experiences.
- We acknowledge that various selection mechanisms may have affected the men's choice of treatment and that several important factors therefor could have been missed.
- We did not have access to PSA (prostate specific antigen) levels during AS, only at diagnosis, which limits the possibility to investigate how PSA-monitoring affects adherence to AS.
- The study included Swedish men only and the findings might therefore not be generalizable to other cultural and health-care settings.

Introduction

A large proportion of men with prostate cancer (PC) are diagnosed with low-risk disease with a long-life expectancy even without curative treatment. Active surveillance (AS) has therefore emerged as the primary strategy for these men to reduce unnecessary treatment [1,2].

In Sweden, uptake of AS has increased steadily over the past decade and is now 80-90% [3]. However, the proportion of men with low-risk cancer who are on AS varies substantially between and within countries [2,4] Although notable rising trends are seen in e.g. North America, Australia and Europe [5], a 2014 survey in Japan noted that roughly half of urologists used AS in < 5% of men with low-risk PC and that only 27% stated that they would want to offer AS more frequently in the future [6]. Additionally, a considerable proportion of men on AS diverge to treatment over time without any clear evidence of disease progression [7,8].

In a systematic review on choice and adherence to AS, Kinsella et al [9] identifies several factors such as clinician's attitudes, family and social support, and patient education as potential determinants for choice and adherence to AS. However, no grading of these factors' relative importance was made.

We could not identify any previous studies on factors influencing choice of and adherence to AS in a nationwide population-based setting. In this nationwide population-based study, representing a period in time when Sweden experienced a rapid increase in AS [3], we used a questionnaire to identify which factors most affected choosing and adhering to AS, and to quantify the relative importance of different reasons for this, thereby identifying possibly influenceable determinants to increase the implementation of AS.

Material and methods

Study design and participants

We identified all men in the National Prostate Cancer Register of Sweden (NPCR) who were diagnosed in 2008 with low-risk PC at age 70 years or younger, had radical prostatectomy, radiotherapy or AS as primary treatment and were alive in 2015. The reason for choosing men diagnosed in 2008 was that we wished to assess reasons for diverting from AS to treatment after several years of AS. The reason for choosing men younger than 70 years with low-risk disease was to avoid getting men in watchful waiting mixed with the active surveillance group.

The NPCR has a capture rate of > 96% compared with the national cancer registry, to which registration is mandatory by law [10]. Low-risk disease was defined as Gleason score 6, prostate-specific antigen (PSA) < 10 ng/ml, and clinical stage T1 or T2.

Between February and October 2015, 1720 men were invited to participate via a letter, in which we presented the study and its purpose. The letter included a questionnaire and an addressed and stamped envelope for reply. The participants could also fill out the questionnaire online by using an individual code which was included in the letter. Men who failed to return the questionnaire were contacted by a research assistant via telephone and were sent a second questionnaire.

The Regional Ethical Review Board at Uppsala University approved of the study.

Questionnaire design

The questionnaire consisted of EPIC-26 and 49 study-specific questions (Appendix 1). EPIC-26 is an instrument designed to assess pelvic organ function and bother after PC treatment [11]. The study-specific questions were developed after interviews with men living with PC, and were tested for face validity with one investigator accompanying the men while they completed the questionnaire. Questions not fully understood were changed to achieve clarity. The questionnaire was further validated in an unpublished pilot study among men not included in the present study. Our technique for developing a study-specific questionnaire is based on a one-concept–one-question method producing self-reported outcomes and has been previously described [12-14]. The questionnaire explored mental symptoms, quality of life, and overall satisfaction with care. The questionnaire also assessed experiences at the time of diagnosis and at follow-up, socio-demographics, smoking, alcohol consumption, physical activity, treatments, concurrent diseases (Charlson Comorbidity Index (CCI) [15]), and psychiatric problems (obtained by asking if they suffered from depression and/or any other mental illness).

Factors potentially associated with choice of and adherence to AS was further evaluated by two direct questions. Choice of AS was evaluated by the question "If you were on active surveillance for prostate cancer but later received treatment, or if you are still on active surveillance - which of the following alternative(s) influenced the decision?". Men had the possibility to grade the following alternatives from "I do not agree at all" to "I completely agree", "I am/was not particularly worried about the prostate cancer", "I did not want to risk leaking urine", "I did not want to risk impairing my sexual function", "I did not want to risk getting bowel problems", "I preferred not undergoing any treatment", "I wanted to

postpone any treatment until it was deemed necessary", "I felt uneasy about the available treatment strategies (surgery and radiotherapy)" and "My doctor recommended active surveillance". Adherence was evaluated by the question "Why was the active surveillance terminated and treatment initiated?" with the following alternatives where men had the possibility to choose more than one alternative, "The PSA level was rising", "The prostate biopsies showed a more aggressive tumour", "The initiative was mine and had nothing to do with the PSA level or prostate biopsies" and "The initiative was my doctor's and had nothing to do with the PSA level or prostate biopsies".

Patient and Public Involvement statement:

Men living with prostate cancer where involved in the study early on as we conducted individual interviews with a small number of respondents to explore their perspectives on living with prostate cancer. The study-specific questions were developed after these interviews. However, men with prostate cancer were not involved in the conduct, analysis of data or writing the manuscript in other ways.

Data availability statement:

No additional data available.

Data collection, analysis, and statistical analysis

The questionnaires and cancer characteristics data from the NPCR were assembled in a database. Differences between responders and non-responders were analyzed. To assess factors associated with the initial choice of treatment, men were grouped by their initial treatment: curative or AS. To assess factors associated with adherence to AS, responders where grouped by whether they stayed on AS or diverged to treatment. Statements such as "substantial information" were defined as the highest possible response to that specific question.

Missing data were handled using multiple imputations based on the method of chained equations [16]. Five imputation data sets were created. The maximum number of imputed answers where 4%.

The analysis of factors associated with choice and adherence to AS was carried out using logistic regression. A multivariate analysis was performed including age, retirement, education and CCI and it is these values that are presented. Odds ratios (ORs) with 95% confidence interval (CI) show the probability of choosing and adhering to AS.

Results

Patient characteristics

In all, 1288 (75%) of the 1720 invited men responded. Mean age at diagnosis was 63 years old (range 40–70) (Table 1a).

Non-responders were on average one year younger, had lower T-stage and lower PSA, were more likely to be diagnosed after PSA-testing, and were more likely to be initially managed with AS (data from the NPCR) (Appendix 2).

A total of 451 (35%) chose AS and 837 (65%) underwent immediate treatment. Of the men who initially chose AS, 238 (53%) diverted to treatment within seven years, of whom 70% did so within the first three years (Table 1b and Figure 1). Prostate cancers comprised of 3% T1a, 1% T1b, 74% T1c and 22% T2 tumors.

The vast majority of men primarily consulted either a urologist or a clinical oncologist, 18% consulted both a urologist and a clinical oncologist.

Factors associated with choice

Factors statistically associated with choosing AS over treatment included older age (OR 1.81, 95% CI 1.29-2.54 for men aged <60 yr vs men aged 66–70 yr), a CCI >2 (OR 1.50, 95% CI 1.06–2.13, compared with CCI 0), unaccompanied when being notified of the diagnosis (OR 1.45, 95% CI 1.11-1.89) and being presented with AS by the treating physician (OR 9.27, 95% CI 7.04-12.19). Factors statistically associated with not choosing AS over treatment included whether men were still working (OR 0.69, 95% CI 0.47-1.00) and/or had a T2 tumor (OR 0.40, 95% CI 0.29-0.56). (Figure 2)

PSA at diagnosis (OR 0.67, 95% CI 0.40-1.13), time to reflect on treatment options (OR 0.93, 95% CI 0.63-1.39) and whether the men had seen both a urologist and a clinical oncologist (OR 1.13, 95% CI 0.83-1.53) were not statistically significantly associated with choice.

Regarding the direct questions on why the men chose AS (Figure 3) (defined as completely or largely agreed),

- 83% “My doctor recommended AS”
- 74% “I did not want to risk leaking urine”
- 66% “I did not want to risk getting bowel problems”
- 64% “I am/was not particularly worried about the prostate cancer”
- 62% “I did not want to risk impairing my sexual function”,
- 55% “I wanted to postpone any treatment until it was deemed necessary”
- 49% “I felt uneasy about the available treatment strategies (surgery and radiotherapy)”
- 39% “I preferred not undergoing any treatment”

Factors associated with adherence

Men with PC detected during investigation of LUTS (Lower Urinary Tract Symptoms) rather than screening was associated with adhering to AS (OR 1.78, 95% CI 1.16-2.72). Men with a higher PSA at the time of diagnosis (OR 0.26, 95% CI 0.10-0.63) were less likely to adhere to AS. (Figure 4)

Regarding the direct question on reasons for diverting to treatment (Figure 5), (defined as completely or largely agreed)

- 55% “the PSA level was rising”
- 36% “the prostate biopsies showed a more aggressive tumor”
- 6% “the initiative was my doctor’s and had nothing to do with the PSA level or prostate biopsies”

- 3% “the initiative was mine and had nothing to do with the PSA level or prostate biopsies”

Discussion

In this nationwide population-based study, a doctor’s recommendation was a strong predictor for choosing AS, as was patient characteristics such as older age and more concurrent diseases. Men without anyone accompanying them when they were notified of the cancer diagnosis were more likely to opt for AS. Regarding adherence to AS, a low PSA at the time of diagnosis was an important factor, both according to the multivariate analysis and the direct question. Further, men whose PC was detected during the investigation of LUTS was more likely to adhere to AS. A unique feature of our study is that we could quantify the relative importance of different potential reasons for choosing and adhering to AS, as the men could tick more than one reason and grade its importance.

A doctor´s recommendation emerged as strongest factor associated with choice. This is highlighted in our direct question on choice where a doctor’s recommendation was the single strongest predictor for choosing AS with 83% stating that they chose AS because their doctor recommended it. In fact, more men specified a doctor’s recommendation as a reason for choosing AS than the will to avoid side-effects from treatment. This is in line with the review article about factors influencing men's choice of and adherence to AS by Kinsella et al [9], in which a physician’s recommendation was identified as an important element in choosing AS [17-20]. In light of the evidence from multiple studies for the importance of the physician’s recommendation in favor for choosing AS, the most important

cause of the rapid increase in uptake on AS in Sweden over the past decade[3], was probably the Swedish national guidelines' clear recommendation since 2007 of AS for men with low-risk PC. The recommendation was during this time period less clear in the European and US recommendations [21,22], in which AS was mentioned as an alternative to radical treatment rather than the first choice option.

That patient characteristics, such as a higher age, were associated with AS is in line with previous studies [18,23]. It is possible that some of these men might have diverted from AS to watchful waiting during the seven years of follow-up as the oldest had reached 77 years by 2015 and might not have been eligible for treatment.

On multivariate analysis, being unaccompanied when notified of the cancer diagnosis predicted choice of AS. This might reflect that these men are more prone to accept the physician's suggestion if no one else was influencing them to undergo treatment. This highlights the responsibility of the treating physician, not only directed towards the patients but also to their significant others, to facilitate an informed treatment decision. A recently published qualitative study by Mader et al stating that spousal and social support play important roles in helping men understand and accept their PC diagnosis and chosen care plan [24]. In our study, 18% of men saw both a urologist and a clinical oncologist but this did not affect the choice of treatment.

The participants in our study were diagnosed in 2008. Since then, uptake on AS in Sweden has steadily increased and reached 74% by 2014 [3]. In our study, 35% initially chose AS and 47% were still on AS after seven years follow-up. This is in line with a study by Loeb et al from 2015 that reported 64 % adherence to AS after five years [25] as well as the PRIAS study

where 50% diverted to treatment within five years, mostly due to protocol-based reclassification (biopsy-related, changes in T-stage and/or PSA-doubling time) [26].

The main patient reported driver behind diverting to treatment was a rise in PSA. Only 9% of the men stated that the decision to diverge from AS to treatment was not because of PSA and/or biopsy results. PSA is considered a poor marker for disease progression, which for example was shown by Fall et al when looking at men with high-risk disease [27]. Several studies have shown that many men with low-risk PC overestimate the risk of living with an untreated cancer [28,29], something that might be further magnified by rising PSA. In the PIVOT study, no difference in mortality was detected between men who were randomized to radical prostatectomy or observation after nearly 20 years of follow-up [30]. Roughly half of the men in our study, who all had low-risk PC diverted to treatment within these seven years which represents a significant overtreatment. Adherence to AS protocols and additional methods for follow-up such as MRI [31] and evidence-based triggers for treatment might reduce the fear of living with untreated cancer and thereby reduce unnecessary treatment.

Interestingly, men whose PC was detected during the investigation of LUTS rather than through screening was more likely to adhere to AS. This finding persisted after adjusting for age, retirement and CCI. A possible explanation might be a higher degree of anxiety in the group whose PC was detected through screening rather through the investigation on LUTS, although we do not have any data to support this. A recently published review article on psychological distress during cancer-screening [32] indicated that psychological distress, although low and not a barrier to screening, might be present. There might also be a motivational difference where men diagnosed through screening actively sought the investigation of PC and might be more motivated to undergo treatment. Another possible

explanation might be that men diagnosed through the investigation of LUTS might have received drugs that reduce PSA e.g. Finasteride.

The strengths of our study include its population-based design, the high response rate for a study of its kind, the face-validated study-specific questionnaire, and the direct questions on reasons for choice and adherence. We acknowledge that various selection mechanisms affected the men's choice of treatment and that several important factors could have been missed. The retrospective design is a limitation, as the men's experiences during the seven-year follow-up might have affected their recollection of their experiences. We did not have access to PSA levels during AS, only at diagnosis, which limits the possibility to investigate how PSA monitoring affects adherence to AS. Regarding being unaccompanied when notified of the cancer diagnosis, it's important to acknowledge that while these where unaccompanied during the appointment, they still might have had support from people in their support network. The study included Swedish men only and the findings might therefore not be generalizable to other cultural and health-care settings.

Conclusions

A doctor´s recommendation strongly affects which treatment is chosen for men with low-risk PC. Rising PSA values were the main factor for initiating treatment for men on AS. These findings need to be considered by health-care providers who wish to increase the uptake of and adherence to AS.

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

Study concept and design: Bergengren, Garmo, Bratt, Johansson, Bill-Axelson.

Acquisition of data: Bergengren, Johansson, Bill-Axelson.

Analysis and interpretation of data: Bergengren, Garmo, Holmberg, Johansson, Bill-Axelson.

Drafting of the manuscript: Bergengren, Johansson, Bill-Axelson.

Critical revision of the manuscript for important intellectual content: Bergengren, Bratt, Holmberg, Johansson, Bill-Axelson.

Statistical analysis: Garmo.

Obtaining funding: Bill-Axelson.

Administrative, technical, or material support: Bill-Axelson

Supervision: Holmberg, Johansson, Bill-Axelson.

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Figure legends

Table 1a: Demographics, clinical characteristics and potential factors associated with the choice of treatment by treatment group. AS = Active surveillance; RP/RT = Radical prostatectomy or Radiotherapy. Numbers are frequencies with percentages in brackets unless otherwise stated.

Table 1b: Demographics, clinical characteristics and potential factors associated with adherence to active surveillance by treatment group. AS -> AS = Stayed on active surveillance; AS -> RP/RT = Diverted from active surveillance to Radical prostatectomy or Radiotherapy. Numbers are frequencies with percentages in brackets unless otherwise stated.

Figure 1: Flow chart showing patients participation and treatment.

Figure 2: Forrest plot illustrating choice. OR (Odds rations) shows the probability of choosing active surveillance as primary treatment. An OR above 1 favor AS. Adjusted for age, work status, education, and Charlson comorbidity index.

Figure 3: Bar chart illustrating the direct question on why men chose active surveillance as their primary treatment. Numbers are frequencies with percentages.

Figure 4: Forrest plot illustrating adherence. OR (Odds rations) shows the probability of adhering to active surveillance. An OR above 1 favor adhering to AS. Adjusted for age, work status, education, and Charlson comorbidity index.

Figure 5: Bar chart illustrating the direct question on time spent in active surveillance and why men terminated active surveillance. Numbers are frequencies with percentages.

Table 1a - Choice		AS		RP/RT		ALL	
n		451	'(100.0)	837	'(100.0)	1288	'(100.0)
Age, n (range)		64	(61 - 67)	62	(58 - 65)	63	(59 - 66)
Marital status n (%)							
	Married or domestic partner	367	'(81.4)	701	'(83.8)	1068	'(82.9)
	Other	73	'(16.2)	126	'(15.1)	199	'(15.5)
	Missing	11	(2.4)	10	'(1.2)	21	'(1.6)
Children n (%)							
	No children	36	'(8.0)	70	'(8.4)	106	'(8.2)
	Children	401	'(88.9)	747	'(89.2)	1148	'(89.1)
	Missing	14	'(3.1)	20	'(2.4)	34	'(2.6)
Work status, n (%)							
	Not retired	74	'(16.4)	211	'(25.2)	285	'(22.1)
	Retired	377	'(83.6)	626	'(74.8)	1003	'(77.9)
	Missing	0	'(0.0)	0	'(0.0)	0	'(0.0)
Education level, n (%)							
	Compulsory school	143	'(31.7)	208	'(24.9)	351	'(27.3)
	Secondary school	166	'(36.8)	347	'(41.5)	513	'(39.8)
	University	128	'(28.4)	265	'(31.7)	393	'(30.5)
	Missing	14	'(3.1)	17	'(2.0)	31	'(2.4)
Charlson comorbidity index, n (%)							
	0	129	'(28.6)	282	'(33.7)	411	'(31.9)
	1	142	'(31.5)	296	'(35.4)	438	'(34.0)
	2	85	'(18.8)	144	'(17.2)	229	'(17.8)
	>2	95	'(21.1)	115	'(13.7)	210	'(16.3)
Psychiatric illness, n (%)							
	No	411	'(91.1)	770	'(92.0)	1181	'(91.7)
	Yes (Depression/ Other)	40	'(8.9)	67	'(8.0)	107	'(8.3)
T-stage							
	T1ab	37	(8.2)	16	'(1.9)	53	'(4.1)
	T1c	354	(78.5)	599	'(71.6)	953	'(74.0)
	T2	60	(13.3)	222	'(26.5)	282	'(21.9)
PSA value at diagnosis, n (%)							
	0-3.0	31	(6.9)	41	'(4.9)	72	'(5.6)
	3.1-7.0	325	(72.1)	597	'(71.3)	922	'(71.6)
	7.1-10.0	95	(21.1)	199	'(23.8)	294	'(22.8)
Method of detection n (%)							
	Screening	228	(50.6)	481	'(57.5)	709	'(55.0)
	LUTS	161	(35.7)	216	'(25.8)	377	'(29.3)
	Other symptoms	51	(11.3)	109	'(13.0)	160	'(12.4)
	Missing	11	(2.4)	31	'(3.7)	42	'(3.3)
Alone when being notified of the cancer diagnosis n (%)							
	No	107	'(23.7)	256	'(30.6)	363	'(28.2)
	Yes	332	'(73.6)	568	'(67.9)	900	'(69.9)
	Missing	12	'(2.7)	13	'(1.6)	25	'(1.9)
Sufficient time from diagnosis until treatment decision, n (%)							
	No, i wanted a quicker decision	27	'(6.0)	48	'(5.7)	75	'(5.8)
	Yes	363	'(80.5)	739	'(88.3)	1102	'(85.6)
	No, i wanted more time to think	11	'(2.4)	35	'(4.2)	46	'(3.6)
	Missing	50	'(11.1)	15	'(1.8)	65	'(5.0)

Table 1b - Adherence	AS->AS		AS -> RP/RT		ALL	
	213	'(100.0)	238	'(100.0)	451	'(100.0)
Age, n (range)	65	(61 - 68)	64	(61 - 66)	64	(61 - 67)
Marital status n (%)						
Married or domestic partner	174	'(81.7)	193	'(81.1)	367	'(81.4)
Other	35	'(16.4)	38	'(16.0)	73	'(16.2)
Missing	4	'(1.9)	7	'(2.9)	11	'(2.4)
Children n (%)						
No children	20	'(9.4)	16	'(6.7)	36	'(8.0)
Children	186	'(87.3)	215	'(90.3)	401	'(88.9)
Missing	7	'(3.3)	7	'(2.9)	14	'(3.1)
Work status, n (%)						
Not retired	33	'(15.5)	41	'(17.2)	74	'(16.4)
Retired	180	'(84.5)	197	'(82.8)	377	'(83.6)
Missing	0	'(0.0)	0	'(0.0)	0	'(0.0)
Education level, n (%)						
Compulsory school	65	'(30.5)	78	'(32.8)	143	'(31.7)
Secondary school	78	'(36.6)	88	'(37.0)	166	'(36.8)
University	64	'(30.0)	64	'(26.9)	128	'(28.4)
Missing	6	'(2.8)	8	'(3.4)	14	'(3.1)
Charlson comorbidity index, n (%)						
0	56	'(26.3)	73	'(30.7)	129	'(28.6)
1	70	'(32.9)	72	'(30.3)	142	'(31.5)
2	36	'(16.9)	49	'(20.6)	85	'(18.8)
>2	51	'(23.9)	44	'(18.5)	95	'(21.1)
Psychiatric illness, n (%)						
No	189	'(88.7)	222	'(93.3)	411	'(91.1)
Yes (Depression/ Other)	24	'(11.3)	16	'(6.7)	40	'(8.9)
T-stage						
T1ab	26	'(12.2)	11	'(4.6)	37	(8.2)
T1c	156	'(73.2)	198	'(83.2)	354	(78.5)
T2	31	'(14.6)	29	'(12.2)	60	(13.3)
PSA value at diagnosis, n (%)						
0-3.0	23	'(10.8)	8	'(3.4)	31	(6.9)
3.1-7.0	151	'(70.9)	174	'(73.1)	325	(72.1)
7.1-10.0	39	'(18.3)	56	'(23.5)	95	(21.1)
Method of detection n (%)						
Screening	94	'(44.1)	134	'(56.3)	228	(50.6)
LUTS	89	'(41.8)	72	'(30.3)	161	(35.7)
Other symptoms	22	'(10.3)	29	'(12.2)	51	(11.3)
Missing	8	'(3.8)	3	'(1.3)	11	(2.4)
Alone when being notified of the cancer diagnosis n (%)						
No	44	'(20.7)	63	'(26.5)	107	'(23.7)
Yes	164	'(77.0)	168	'(70.6)	332	'(73.6)
Missing	5	'(2.3)	7	'(2.9)	12	'(2.7)
Sufficient time from diagnosis until treatment decision, n (%)						
No, i wanted a quicker decision	9	'(4.2)	18	'(7.6)	27	'(6.0)
Yes	152	'(71.4)	211	'(88.7)	363	'(80.5)
No, i wanted more time to think	5	'(2.3)	6	'(2.5)	11	'(2.4)
Missing	47	'(22.1)	3	'(1.3)	50	'(11.1)

Figure 1 - Flowchart

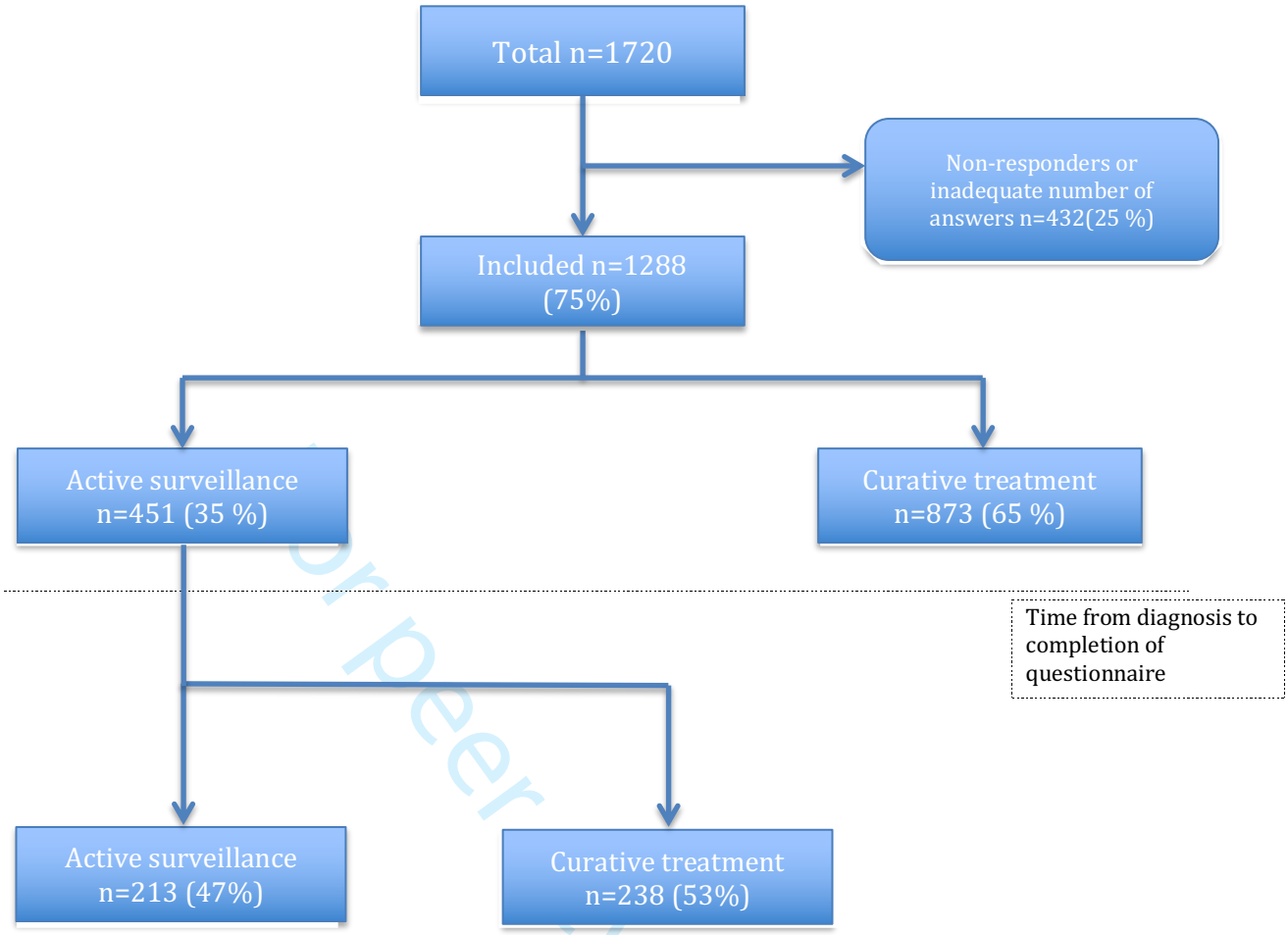


Figure 2 - Choice

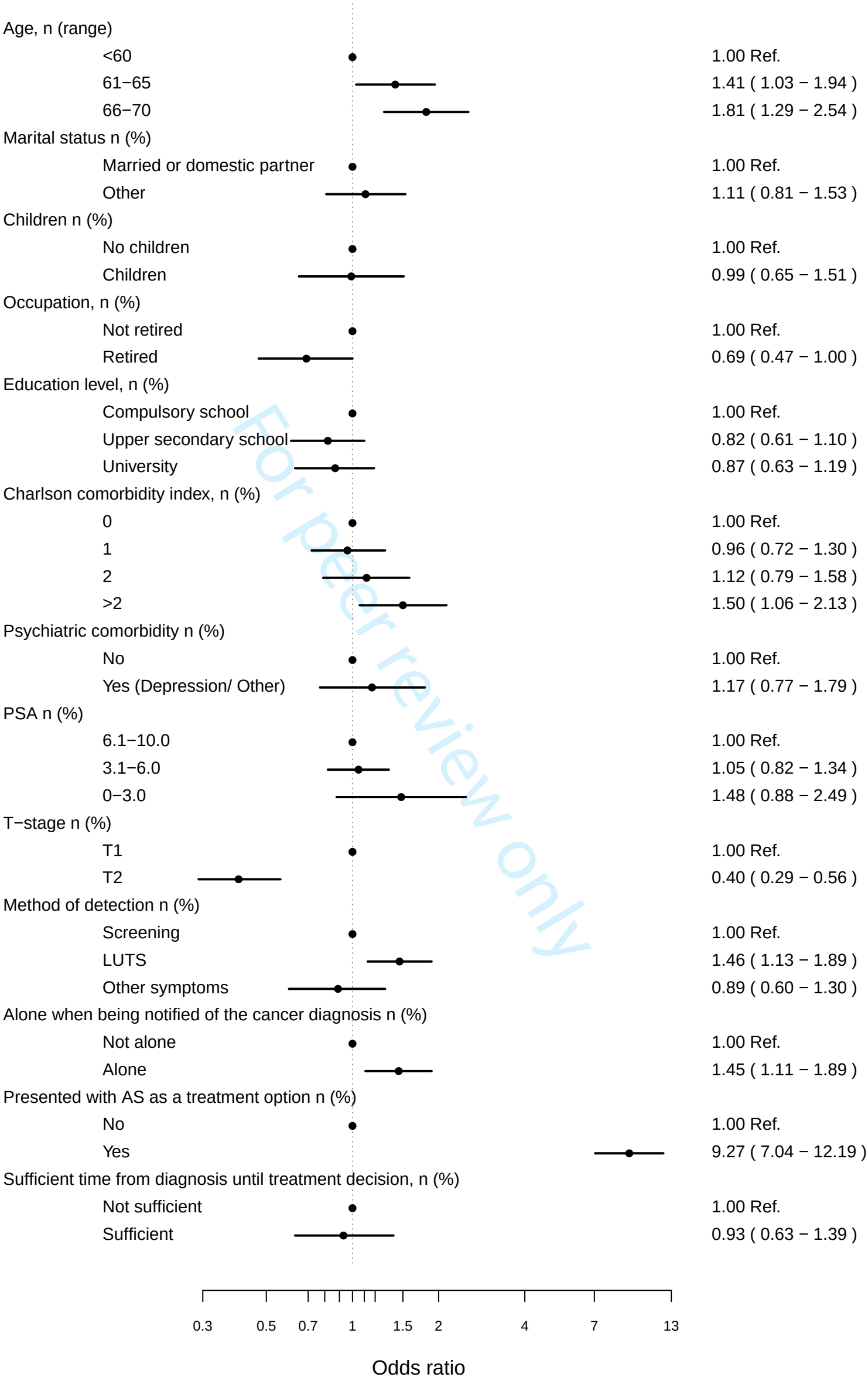


Figure 3 - direct question on why the men chose active surveillance

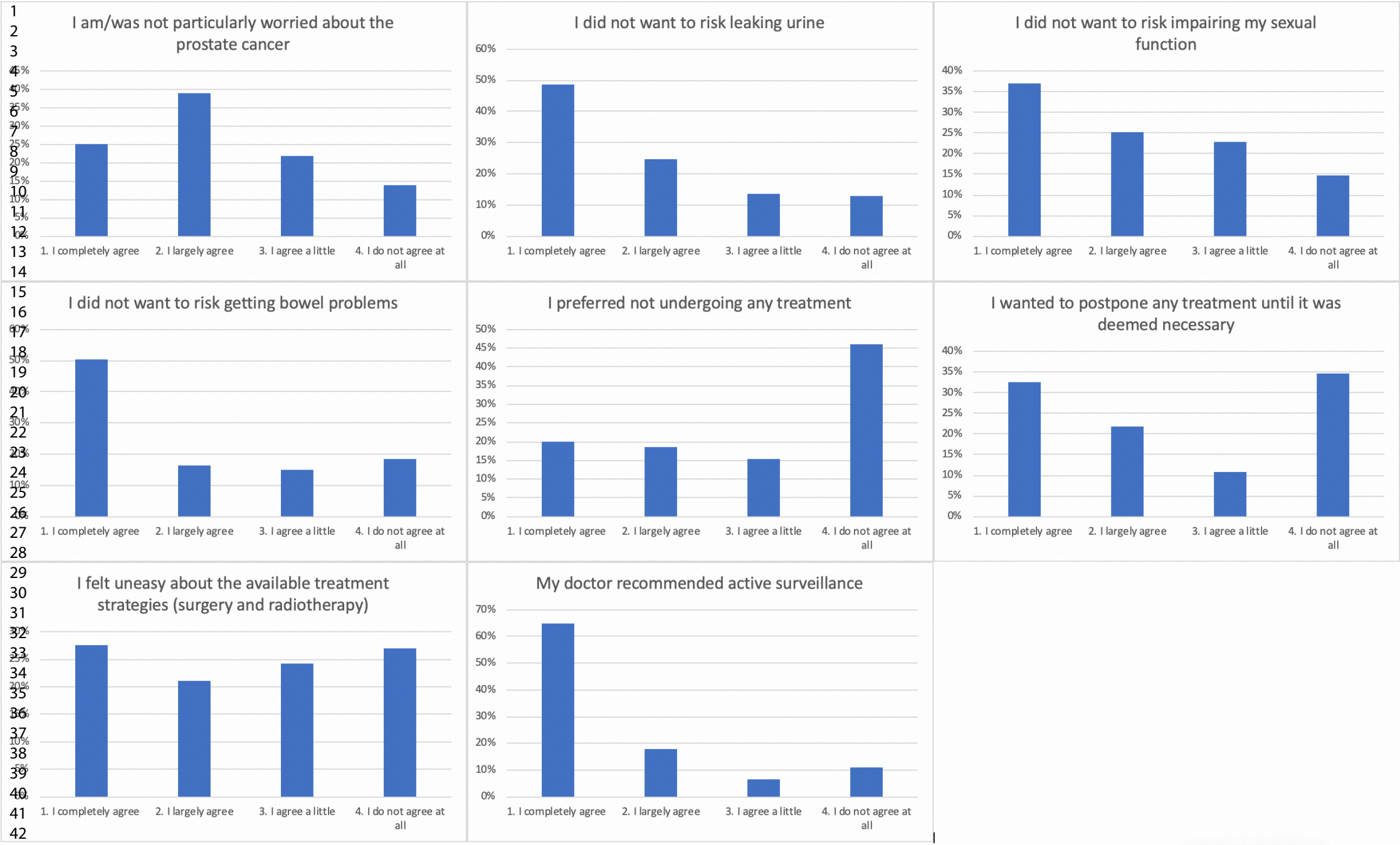


Figure 4 - Adherence

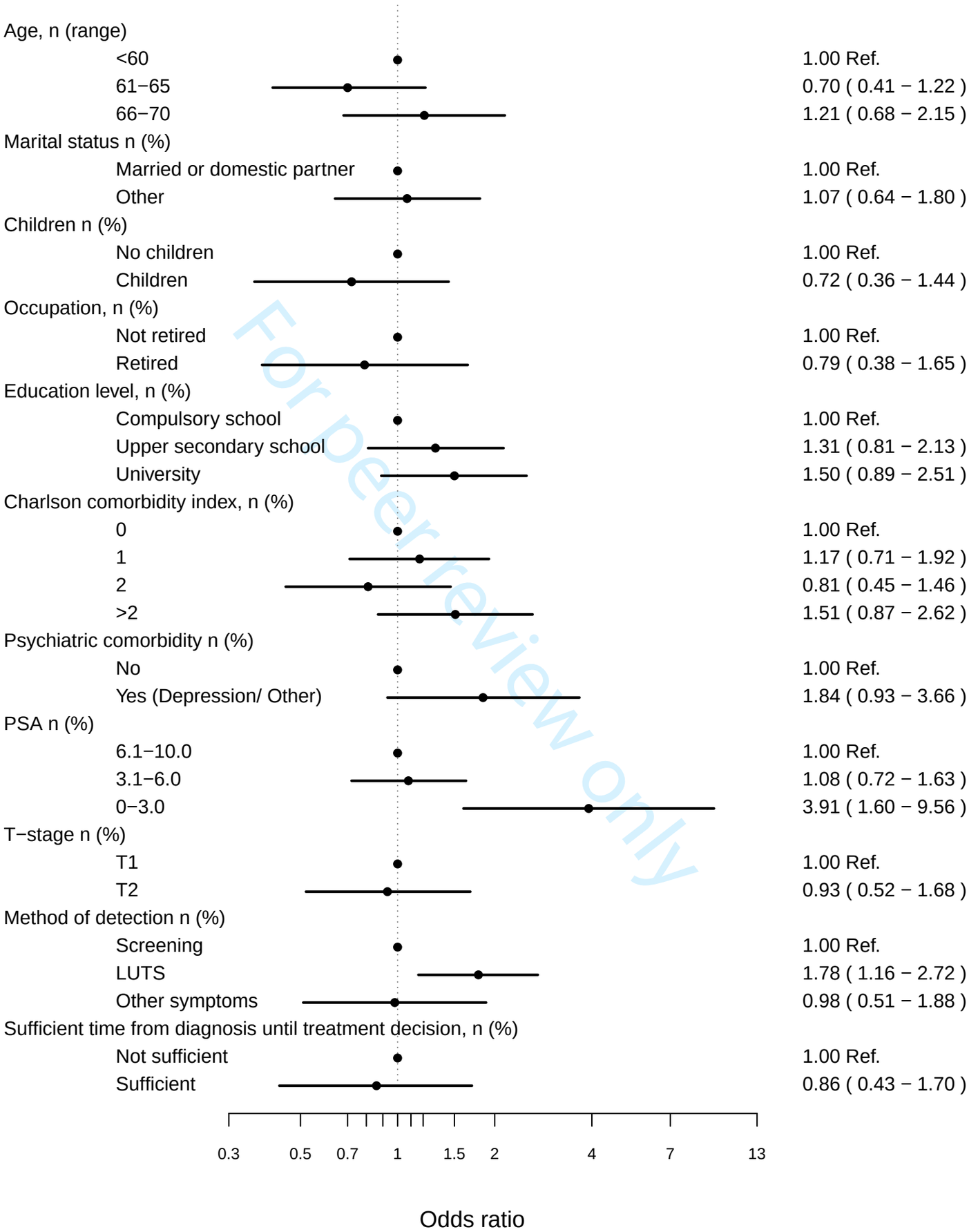
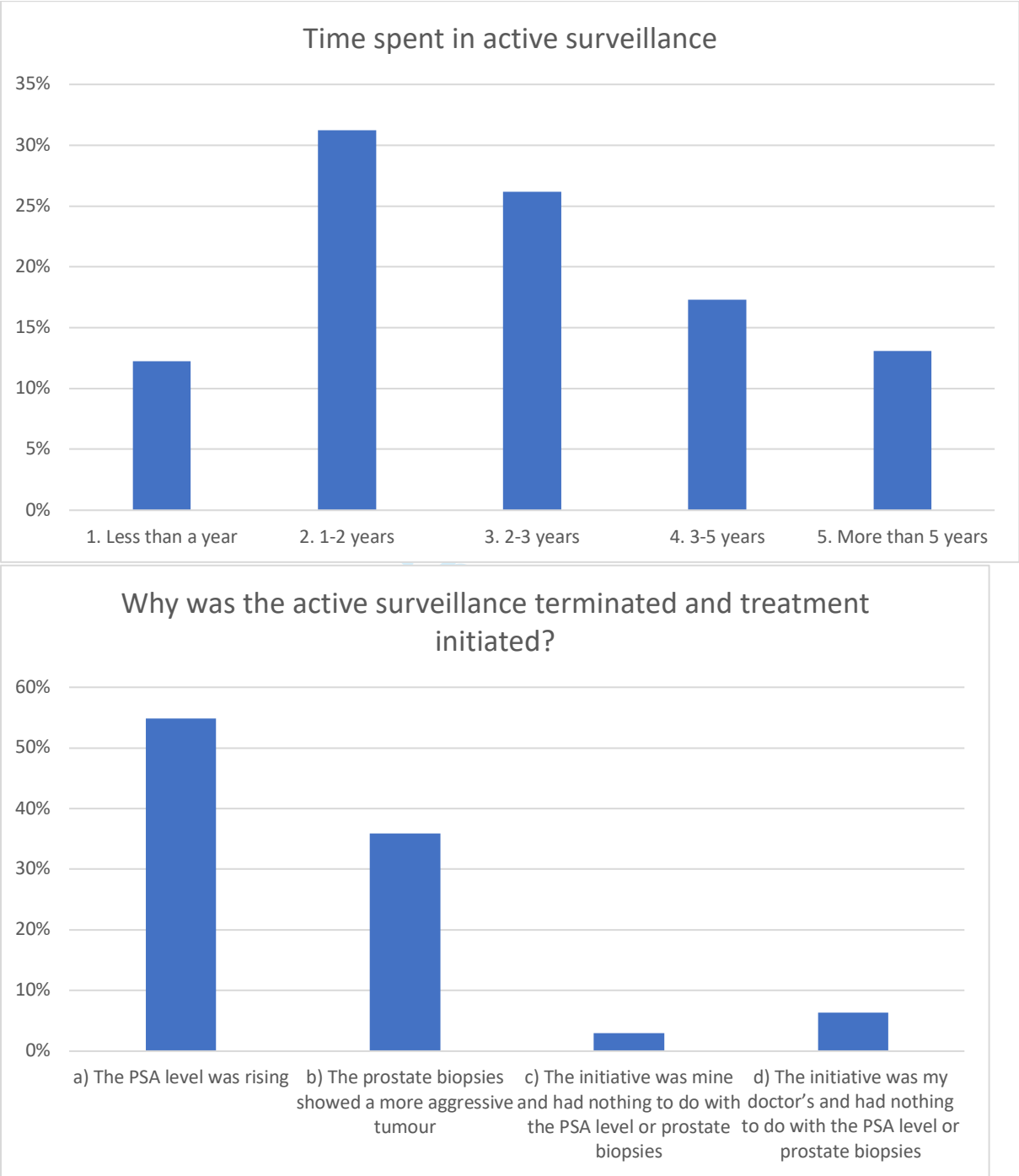


Figure 5 - direct question on why the men diverted from active surveillance



Health and Quality of Life in Men with Prostate Cancer

Thank you for taking part in this study.

A number of questions follow below (58 questions in part 1 and 17 questions in part 2). Provide the answers that best describe you and your situation. If more than one alternative is possible, the question will indicate as much. Please try to answer all the questions.

PLEASE OBSERVE that the term "active surveillance" is used in this questionnaire.
"Active surveillance" is a conservative treatment strategy for men with low-risk prostate cancer that involves close monitoring of the disease using PSA tests and repeat biopsies. When there are signs of disease progression, the patient receives curative treatment through surgery or radiotherapy. A patient is not in active surveillance if:

1) A decision to treat the prostate cancer by surgery or radiotherapy is taken within six months from the prostate cancer diagnosis.
2) Being monitored after having received treatment of any kind.

PART 1. Demographics and questions about quality of life

General Questions

1. In which year were you born?
(Give four figures, e.g. 1945)

2. Are you currently:

- ❑ Living with spouse or partner
- ❑ Not in a significant relationship
- ❑ In a significant relationship, but not living together

3. Do you have children?

❑ No ❑ Yes

4. Do you have grandchildren?

❑ No ❑ Yes

5. Are you currently:

- ❑ Employed
- ❑ Looking for work
- ❑ Retired
- ❑ On long-term sick leave
- ❑ On disability pension

6. What is the highest level of your education?

- ❑ Basic education or equivalent
- ❑ Upper secondary, vocational school or equivalent
- ❑ College or university

7. ***During the last 4 weeks***, how many hours per have you undertaken at least moderate physical exercise involving an elevated pulse rate (i.e. walking, cycling, swimming, etc.)?

- ❑ None
- ❑ Less than 1 hour per week
- ❑ 1-3 hours per week
- ❑ More than 3 and up to 7 hours per week
- ❑ More than 7 hours per week

8. What are your smoking habits? *(Only pick one answer)*

- ❑ Smoke everyday
- ❑ Smoke occasionally (less than 1 cigarette per day)
- ❑ Former smoker
- ❑ Never smoked

9. How many units of alcohol (see example below) do you typically drink on a day when you drink alcohol?

- ❑ 0 units of alcohol per week
- ❑ 1-5 units of alcohol per week
- ❑ 6-10 units of alcohol per week
- ❑ 11-20 units of alcohol per week
- ❑ More than 20 units of alcohol per week

In the UK, one unit of alcohol is for example:

10. How tall are you?

cm

11. How much do you weigh?

kg

12. Do you have or have you ever had any of the following illnesses? If so, which? *(Tick the appropriate box for each question)*

A.	Heart disease (e.g. angina, heart attack, or heart failure)	❑ No	❑ Yes
B.	High blood pressure	❑ No	❑ Yes
C.	Pains in the legs when walking owing to poor blood circulation	No	❑ Yes
D.	Lung disease (e.g. asthma, chronic bronchitis, or chronic obstructive pulmonary disease (COPD))	❑ No	❑ Yes
E.	Diabetes	❑ No	❑ Yes
F.	Kidney disease	❑ No	❑ Yes

G.	Liver disease	❑ No	❑ Yes
H.	Stroke	❑ No	❑ Yes
I.	Neurological disease (e.g. Parkinson's disease or MS)	❑ No	❑ Yes
J.	Other type of cancer than prostate cancer (in the last 5 years)	❑ No	❑ Yes
K.	Depression	❑ No	❑ Yes
L.	Other psychological illness	❑ No	❑ Yes
M.	Reumatism	❑ No	❑ Yes
N.	Paralysis	❑ No	❑ Yes
O.	HIV+ or AIDS	❑ No	❑ Yes

(modified from Charlson Comorbidity index Chaudhry et al 2005)

Questions About Quality of Life

Answer the following questions by circling the number that best fits your opinion.

13. ***During the last 4 weeks***, what has your quality of life been like?

1----------2----------3----------4----------5----------6----------7
No quality of life Best possible quality of life

14. ***During the last 4 weeks***, has your life felt meaningful?

1----------2----------3----------4----------5----------6----------7
Never All the time

15. ***During the last 4 weeks***, what has your physical stamina been like?

1----------2----------3----------4----------5----------6----------7
No stamina Best possible stamina

16. ***During the last 4 weeks***, what has your mental wellbeing been like?

1----------2----------3----------4----------5----------6----------7
No wellbeing Best possible wellbeing

17. ***During the last 4 weeks***, what has your physical health been like?

1----------2----------3----------4----------5----------6----------7
Worst imaginable health Best imaginable health

18. ***During the last 4 weeks***, what has your self-esteem been like?

1----------2----------3----------4----------5----------6----------7
No self-esteem Best imaginable self-esteem

Questions About Depression and Anxiety

19. ***During the last 4 weeks***, have you felt miserable or depressed?

1----------2----------3----------4----------5----------6----------7
Never All the time

20. ***During the last 4 weeks***, have you experienced worry or anxiety?

1----------2----------3----------4----------5----------6----------7
Never All the time

21. ***During the last 4 weeks***, have you had difficulties sleeping at night?

- ❑ No, never
- ❑ Yes, at least once this month
- ❑ Yes, at least once a week
- ❑ Yes, at least 3 times per week
- ❑ Yes, every night

22. ***During the last 4 weeks***, have you woken during the night with feelings of worry or anxiety?

- ❑ No, never
- ❑ Yes, at least once this month
- ❑ Yes, at least once a week
- ❑ Yes, at least 3 times per week
- ❑ Yes, every night

23. ***During the last 4 weeks***, have you taken any preparations to help you sleep?

- ❑ No, never
- ❑ Yes, at least once this month
- ❑ Yes, at least once a week
- ❑ Yes, at least 3 times per week

❑ Yes, every evening

24. ***During the last 4 weeks***, have you taken any tranquilizers (anti-anxiety medications)?

❑ No, never
❑ Yes, at least once this month
❑ Yes, at least once a week
❑ Yes, at least 3 times per week
❑ Yes, every day

25. ***During the last 4 weeks***, have you taken any anti-depressives, i.e medication against feeling low or depressed?

❑ No ❑ Yes

Questions About Information and Decision on Treatment

26. I was informed about my prostate cancer:

❑ At a meeting in person
❑ By telephone
❑ By mail
❑ In another way, which? _____

27. When you were informed about your prostate cancer, were you informed in a good way?
(Circle the number which best describes you or your situation)

1----------2----------3----------4----------5----------6----------7
Worst imaginable way Best imaginable way

28. Did you have a friend or relative with you when you were informed about your prostate cancer?

❑ No ❑ Yes

29. How much information have you received from your doctor? *(For each row, tick the box that best describes your perception)*

		No Information	Little Information	Quite a lot of Information	A great deal of Information
A.	About prostate cancer – the illness and its course	☐	☐	☐	☐
B.	About various treatment options for prostate cancer	☐	☐	☐	☐

C.	About side effects of the various treatment options	☐	☐	☐	☐
D.	About how the various treatments could affect your quality of life	☐	☐	☐	☐

30. Which treatment options were suitable to you, according to your perception of the information you received from your doctor? *(Multiple answers are possible)*

- ❑ Active surveillance (go to checks with PSA tests and MRI examinations, treatment will become relevant if the cancer becomes more serious)
- ❑ Surgical removal of the prostate (radical prostatectomy)
- ❑ Radiotherapy
- ❑ Other treatment, please specify: _____

31. How much did you influence the treatment decision-making?

- ❑ Not at all
- ❑ A little
- ❑ Moderately
- ❑ Very much

32. Are you satisfied with how much you were involved in the decision-making between radiotherapy, surgery or active surveillance?

- ❑ No, I wish I had been less involved in the decision-making
- ❑ No, I wish I had been more involved in the decision-making
- ❑ Yes, I am satisfied with how much I was involved in the decision-making

33. How much time passed between your prostate cancer diagnosis and the treatment decision-making?

- ❑ The treatment decision was made right after I received my diagnosis
- ❑ 1-4 weeks
- ❑ 2-3 months
- ❑ More than 3 months

34. In your opinion, were you given enough time to think before the treatment decision was made?

- ❑ No, I wish I had been given less time before the decision was made
- ❑ No, I wish I had been given more time before the decision was made
- ❑ Yes, I was given enough time before the decision was made

35. In your opinion, did the right amount of time pass between the treatment decision-making and the treatment start?

- ❑ *Not applicable,* I have not received treatment for my prostate cancer
- ❑ No, I wish there had been less time between the treatment decision-making and the treatment start

- ❑ No, I wish there had been more time between treatment decision and treatment start
- ❑ Yes, I am satisfied with the amount of time that passed between treatment decision-making and the treatment start

36. What type of doctor(s) did you discuss your prostate cancer with before the treatment decision was made?

- ❑ Urologist (doctor that performs prostate cancer surgery)
- ❑ Oncologist (doctor that gives radiotherapy treatment)
- ❑ Other type of doctor

37. Do you have access to a nurse navigator?

❑ No ❑ Yes ❑ I don't know

38. Where have you searched for information about prostate cancer? *(NB! Several alternatives possible.)*

- ❑ I have not searched for information about prostate cancer
- ❑ Internet
- ❑ Radio
- ❑ TV
- ❑ Newspapers
- ❑ Patient brochures
- ❑ Patients association
- ❑ Friends or family
- ❑ If elsewhere, please specify: _____

Questions About Your Treatment

39. Which alternatives below describes your situation? (*Cross of one alternative)*

- ❑ I am currently on active surveillance (i.e. my prostate cancer is closely monitored using PSA tests and repeat biopsies and curative treatment is initiated if the disease progresses)
- ❑ I started on active surveillance but have since received curative treatment
- ❑ I received treatment directly (within 6 months from my prostate cancer diagnosis)

40. If you have received treatment for prostate cancer, which treatment(s) have you received up to date?

(NB! Several alternatives are possible. You may, for example, have undergone an operation and radiotherapy, radiotherapy and hormone treatment, or just hormone treatment.)

- ❑ I have not had any treatment, I am on active surveillance
- ❑ Removal of the whole prostate gland (so-called radical prostatectomy)
- ❑ Radiotherapy of the prostate gland
- ❑ Hormone treatment in connection with radiotherapy of the prostate gland
- ❑ Only hormone treatment by injection (so-called GnRH-analogue)
- ❑ Only hormone treatment with pills (e.g. Bicalutamide, or Casodex)

❑ Testicles have been removed by means of operation

41. If you were on active surveillance for prostate cancer but later received treatment, or if you are still on active surveillance - which of the following alternative(s) influenced the decision?

❑ Not applicable, I was never on active surveillance, I received treatment directly

A. I am/was not particularly worried about the prostate cancer

❑ I completely agree
❑ I largely agree
❑ I agree a little
❑ I do not agree at all

B. I did not want to risk leaking urine

❑ I completely agree
❑ I largely agree
❑ I agree a little
❑ I do not agree at all

C. I did not want to risk impairing my sexual function

❑ I completely agree
❑ I largely agree
❑ I agree a little
❑ I do not agree at all

D. I did not want to risk getting bowel problems

❑ I completely agree
❑ I largely agree
❑ I agree a little
❑ I do not agree at all

E. I preferred not undergoing any treatment

❑ I completely agree
❑ I largely agree
❑ I agree a little
❑ I do not agree at all

F. I wanted to postpone any treatment until it was deemed necessary

❑ I completely agree
❑ I largely agree
❑ I agree a little
❑ I do not agree at all

G. I felt uneasy about the available treatment strategies (surgery and radiotherapy)

❑ I completely agree
❑ I largely agree
❑ I agree a little

- ❑ I do not agree at all

H. My doctor recommended active surveillance

- ❑ I completely agree
- ❑ I largely agree
- ❑ I agree a little
- ❑ I do not agree at all

42. What do you believe will happen in the future when it comes to your prostate cancer? *(Cross of one alternative.)*

- ❑ I believe that my disease will progress/recur and require treatment within 2 years
- ❑ I believe that my disease will progress/recur and require treatment within 5 years
- ❑ I believe that my disease will progress/recur and require treatment within 10 years
- ❑ I believe that my disease is harmless

43. If you were on active surveillance but then received treatment, please answer the following questions (A to C).

- ❑ Not applicable, I was never on active surveillance, I received treatment directly

A. For how long were you on active surveillance?

- ❑ Less than a year
- ❑ 1-2 years
- ❑ 2-3 years
- ❑ 3-5 years
- ❑ More than 5 years

B. Why was the active surveillance terminated and treatment initiated? *(NB! Several alternatives possible.)*

- ❑ The PSA level was rising
- ❑ The prostate biopsies showed a more aggressive tumour
- ❑ The initiative was mine and had nothing to do with the PSA level or prostate biopsies
- ❑ The initiative was my doctor's and had nothing to do with the PSA level or prostate biopsies
- ❑ If other reason, please specify: _____

C. If it was your initiative to terminate active surveillance and start treatment but the reason for this was not that the tumour was progressing, what was the reason: *(NB! Several alternatives possible.)*

- ❑ I was worried
- ❑ My partner was worried
- ❑ My friends were worried
- ❑ I wanted to avoid further biopsies
- ❑ I wanted to avoid the repeated PSA tests
- ❑ I just wanted to have treatment done
- ❑ Other reason

If other reason, please describe it:

_____

_____

44. Are you worried that your medical problems, if you have any, are related to prostate cancer?

- ❑ Not at all
- ❑ A little
- ❑ Moderately
- ❑ Very much

45. Do you believe that you will die from prostate cancer?

❑ No ❑ Yes

46. Have you told anyone about your prostate cancer? *(NB! Several alternatives possible.)*

- ❑ I have not told anyone about my prostate cancer
- ❑ Partner
- ❑ Children
- ❑ Grandchildren
- ❑ Close friend(s)
- ❑ Colleague(s)
- ❑ Other person(s)

47. If you are concerned about telling others about your prostate cancer, what are the reasons for this? *(NB! Several alternatives possible.)*

- ❑ Not applicable, I do not hesitate to tell others about the prostate cancer
- ❑ It felt too private
- ❑ I did not want to worry others
- ❑ I believe that people would act differently towards me if I told them about the prostate cancer
- ❑ I believe that telling others would affect my career
- ❑ Other reason

If other reason, please describe it:

_____

_____

Questions About Your Prostate Cancer Checks

48. Who monitors your prostate cancer? *(NB! Several alternatives possible.)*

- ❑ Doctor
- ❑ Nurse

49. When was your last prostate cancer check?

- ❑ Less than one week ago
- ❑ Less than one month ago
- ❑ Less than three months ago
- ❑ More than three months ago

50. When did you last take a PSA test?

- ❑ Less than one week ago
- ❑ 1-4 weeks ago
- ❑ 1-3 months ago
- ❑ More than three months ago

51. When is your next scheduled PSA test?

- ❑ In less than one week
- ❑ In 1-4 weeks
- ❑ In more than one month
- ❑ I don't know

52. In connection with your prostate cancer check, do you feel reminded of your cancer disease?

- ❑ Not at all
- ❑ A little
- ❑ Moderately
- ❑ Very much

53. In connections with your prostate cancer check, do you feel worried about what the PSA test will show?

- ❑ Not at all
- ❑ A little
- ❑ Moderately
- ❑ Very much

54. In connection with your prostate cancer checks, do you feel worried about needing to take new tissue samples (biopsies) from your prostate (if you are on active surveillance)?

- ❑ Not applicable, I have received treatment for prostate cancer
- ❑ Not at all
- ❑ A little
- ❑ Moderately
- ❑ Very much

55. In connection with your prostate cancer check, do you feel worried that your prostate cancer has spread (metastasized) to a different part of your body?

- ❑ Not at all

- ❑ A little
- ❑ Moderately
- ❑ Very much

56. If you feel worried in connection with your prostate cancer check, how long does the worry last?

- ❑ Not applicable, I am not worried before the prostate cancer check
- ❑ Only a day or so, at the time of the prostate cancer check
- ❑ From the day I receive the invitation to the time of the prostate cancer check
- ❑ From before I receive the invitation
- ❑ I am always, more or less, worried

57. Has your prostate cancer diagnosis had an affect on your life style in any way, and if so, in what areas?

A.	Type of food	☐ I eat less healthy	☐ Unchanged	☐ I eat healthier
B.	Exercise	☐ I exercise less	☐ Unchanged	☐ I exercise more
C.	Interest in social activities/relationships	☐ Less	☐ Unchanged	☐ More
D.	Interest in religion/philosophy	☐ Less	☐ Unchanged	☐ More

58. How has prostate cancer affected your economic situation?

- ❑ Impaired
- ❑ Unchanged
- ❑ Improved

PART II. Questionnaire for Symptoms (EPIC-26)

The next few questions concern problems you may be experiencing.
(Tick the appropriate box for each question)

1. ***Over the past 4 weeks***, how often has your urine leaked?

- ❑ More than once a day
- ❑ About once a day
- ❑ More than once a week
- ❑ About once a week
- ❑ Rarely or never

2. Which of the following alternatives best describes how well you have been able to control your urinating ***during the last 4 weeks***?

- ❑ No urinary control whatsoever
- ❑ Drip all the time
- ❑ Drip a little occasionally
- ❑ Full control

3. On average **over the last 4 weeks**, how many incontinence pads or adult diapers have you used per day owing to urine leakage?

- ❑ None
- ❑ 1 per day
- ❑ 2 per day
- ❑ 3 or more per day

4. How large a problem, if any, have the following symptoms been ***during the last 4 weeks***? (*Cross of one alternative for each sub-question.)*

		None	Very Little	Little	Moderate	Large
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	❑	❑	❑	❑	❑

5. Overall, how large a problem has urination been for you **during the last 4 weeks**? *(Tick the box that best describes your perception.)*

- ❑ No problem
- ❑ Very little problem
- ❑ Little problem
- ❑ Moderate problem
- ❑ Large problem

6. How large a problem, if any, have the following symptoms been for you? (*Cross of one alternative for each sub-question.)*

	None	Very Little	Little	Moderate	Large

A.	Urgent need to empty the bowel immediately	❑	❑	❑	❑	❑
B.	Need to empty the bowel often	❑	❑	❑	❑	❑
C.	Inability to control the bowel function	❑	❑	❑	❑	❑
D.	Bloody in faeces	❑	❑	❑	❑	❑
E.	Abdominal/pelvic/rectal pain	❑	❑	❑	❑	❑

7. Overall, how large a problem has your bowel emptying been for you ***during the last 4 weeks***? *(Tick the box that best describes your perception.)*

❑ No problem
❑ Very little problem
❑ Little problem
❑ Moderate problem
❑ Large problem

8. How would you rate each of the following ***during the last 4 weeks***? (*Cross of one alternative for each sub-question.)*

		Very Poor to Non-existent	**Poor**	**Modera**	**Good**	**Very Good**
A.	Your ability to get an erection	❑	❑	❑	❑	❑
B.	Your ability to achieve orgasm (climax)?	❑	❑	❑	❑	❑

9. How would you describe the usual quality of your erections ***during the last 4 weeks***? *(Tick the box that best describes your perception.)*

❑ None at all
❑ Not firm enough for any sexual activity
❑ Firm enough for masturbation and foreplay only
❑ Firm enough for intercourse

10. How would you describe the frequency of your erections ***during the last 4 weeks***? *(Tick the box that best describes your perception.)*

❑ I NEVER obtained an erection when desired
❑ Less than half of the times I wanted an erection
❑ Around half of the times I wanted an erection
❑ More than half of the times I wanted an erection
❑ Whenever I wanted an erection

11. Overall, how would you rate your sexual capability ***during the last 4 weeks***?

12. *(Tick the box that best describes your perception.)*

- ❑ Very poor
- ❑ Poor
- ❑ Moderate
- ❑ Good
- ❑ Very good

12. How large a problem have you had with your sexual capability ***during the last 4 weeks***?
(Tick the box that best describes your perception)

- ❑ No problem
- ❑ Very little problem
- ❑ Little problem
- ❑ Moderate problem
- ❑ Large problem

13. How large a problem, if any, have the following symptoms been for you during the last 4 weeks?
(*Cross of one alternative for each sub-question)*

		None	Very little problem	Little problem	Moderate problem	Large problem
A.	Hot flushes	❑	❑	❑	❑	❑
B.	Tenderness/ swelling in chest	❑	❑	❑	❑	❑
C.	Feeling low	❑	❑	❑	❑	❑
D.	Lacking energy	❑	❑	❑	❑	❑
E.	Change in body weight	❑	❑	❑	❑	❑

14. Which of the following medications/sexual aids have you tried and how did they work? (*Cross of one alternative for each sub-question)*

		Have not tried	Tried but it did not help	Helped but not using it now	Helps and I use it now and then	Helps and I always use it in connection with sexual activity
A.	Viagra, Sildenafil, Cialis, Levitra or other medications? If other pills, please give name: _____	❑	❑	❑	❑	❑
B.	Bondil (gel in urethra)?	❑	❑	❑	❑	❑
C.	Caverject (injection in the penis)?	❑	❑	❑	❑	❑
D.	Vacuum pump?	❑	❑	❑	❑	❑
E.	Other? If so, please state what: _____	❑	❑	❑	❑	❑

15. How long did your erection usually last with the aid of medication/sexual aid during the last 4 weeks?
(Tick the box that best describes your perception)

- ❑ Not relevant, I do not use medications or sexual aids

- ❑ Non-existent
- ❑ Insufficient for any kind of sexual activity
- ❑ Sufficient for masturbation and foreplay
- ❑ Sufficient for intercourse

16. Are you **satisfied** with your sexual life?
(Circle the number which best describes you or your situation)

1----------2----------3----------4----------5----------6----------7
Not at all satisfied Completely satisfied

Finally, we would like to ask you

17. Overall, how satisfied are you with the medical care you have received as a prostate cancer patient? (Personalised service, information, etc.)

(Circle the number which best describes you or your situation)

1----------2----------3----------4----------5----------6----------7
Not satisfied at all Completely satisfied

Is there anything else that you think is important concerning your illness that we have failed to ask about? Please write and tell us!

_____

_____

_____

THANK YOU FOR YOUR ANSWERS!

Appendix 2 – Drop-out analysis	No questioner data (n=432)		Questioner data (n=1288)		Received questioner (n=1720)		Fisher's exact test
Age, n (%)							
≤50	17	(3.9)	39	(3.0)	56	(3.3)	
51-60	170	(39.4)	401	(31.1)	571	(33.2)	0.003
61-65	128	(29.6)	488	(37.9)	616	(35.8)	
66-70	117	(27.1)	360	(28.0)	477	(27.7)	
T-stage, n (%)							
T1a	25	(5.8)	45	(3.5)	70	(4.1)	
T1b	6	(1.4)	8	(0.6)	14	(0.8)	0.04
T1c	320	(74.1)	953	(74.0)	1273	(74.0)	
T2	81	(18.8)	282	(21.9)	363	(21.1)	
PSA, n (%)							
≤3	48	(11.1)	72	(5.6)	120	(7.0)	
3.1-7	292	(67.6)	922	(71.6)	1214	(70.6)	<0.001
7.1-10	92	(21.3)	294	(22.8)	386	(22.4)	
Proportion positive cores, n (%)							
≤12.5%	137	(31.7)	378	(29.3)	515	(29.9)	
12.5-25%	107	(24.8)	380	(29.5)	487	(28.3)	
25.1-50%	126	(29.2)	359	(27.9)	485	(28.2)	0.15
>50%	27	(6.2)	111	(8.6)	138	(8.0)	
Missing data	35	(8.1)	60	(4.7)	95	(5.5)	
Mode of detection, n (%)							
Screening	203	(47.0)	709	(55.0)	912	(53.0)	
LUTS	145	(33.6)	377	(29.3)	522	(30.3)	0.024
Other symptoms	64	(14.8)	160	(12.4)	224	(13.0)	
Missing data	20	(4.6)	42	(3.3)	62	(3.6)	
Treatment according to NPCR, n (%)							
AS	202	(46.8)	476	(37.0)	678	(39.4)	
RP	187	(43.3)	660	(51.2)	847	(49.2)	0.002
RT	43	(10.0)	152	(11.8)	195	(11.3)	

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	Report numbers of outcome events or summary measures over time	8-10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-10
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-10
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15-16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.