Patients' perceptions of the negative effects following different prostate cancer treatments and the impact on psychological well-being: a nationwide survey

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Background: Although the prognosis of localised prostate cancer is good, the negative effects of prostate cancer treatment often impair patient quality of life. A growing number of men experience these negative effects over a longer time because of the increased incidence of and prolonged survival in prostate cancer, and the ageing of the population. Only a few studies have investigated the adverse effects of different prostate cancer treatments using large population-based samples.

Methods: We conducted a nationwide survey ($n = 1239$) to collect detailed information regarding the negative effects (i.e., the occurrence, perceived level and perceived bother since the beginning of the treatment) of prostate cancer treatments: radical prostatectomy, external beam radiotherapy, brachytherapy, hormone therapy and surveillance. Furthermore, we measured patient satisfaction with the outcome of the treatment and their psychological well-being (i.e., psychological symptoms and satisfaction with life) 5 years after diagnosis. The negative effects between the treatments were compared, and the determinants of satisfaction and psychological well-being were investigated.

Results: The negative effects of all types of active prostate cancer treatments were common and persistent (33–48% reported symptoms at 5 years) and showed the known differences between the treatments. Prostatectomy and the radiotherapies caused urinary leakage; radiotherapy also caused symptoms of urinary irritation; and external radiation also caused bowel dysfunction. Most symptoms were considered highly bothersome. Most respondents (81–93%) reported that their treatment negatively affected their sex lives; 70–92% reported sexual dysfunction; and 20–58% reported that their sex lives with their spouses had ended. Urinary symptoms were especially associated with poorer psychological outcomes. The perception of symptom level and bother had a greater effect on patient satisfaction and well-being than the symptoms per se.

Conclusion: Multiple and persistent negative effects follow active prostate cancer treatment, and these effects predict long-term patient satisfaction and psychological well-being. The harms and benefits associated with prostate cancer treatments should be considered when selecting whether and how to actively treat prostate cancer.

Prostate cancer is the most common cancer among men in developed countries, and 420 000 new cases were diagnosed in Europe in 2012 (http://globocan.iarc.fr). In Finland, the mean annual number from 2009–2013 was 4791 cases (www.cancerregistry.fi). The incidence of prostate cancer is increasing worldwide. This increase is partially because of the widespread testing for

prostate-specific antigen (PSA; Penson *et al*, 2008b; van Leeuwen *et al*, 2013; Wever *et al*, 2013; Schröder *et al*, 2014). Most prostate cancers are detected when they are localised and the prognosis is good, and the prevalence is increasing also because of the ageing of the population. Although survival is good, quality of life (QoL) outcomes are impaired by the negative effects due to various prostate cancer treatments (Potosky *et al*, 2004; Miller *et al*, 2005; Frank *et al*, 2007; Penson *et al*, 2008a, b; Roth *et al*, 2008; Smith *et al*, 2009; Lehto *et al*, 2010, 2013; Pardo *et al*, 2010).

Harmful, multiple and persistent adverse effects are common after all forms of active prostate cancer therapy: radical prostatectomy, external beam radiation, brachytherapy and hormone therapy. The most common negative effects include urinary, sexual and bowel dysfunction, all of which can reduce patient well-being and QoL (Miller *et al*, 2005; Northhouse *et al*, 2007; Penson *et al*, 2008a, b; Roth *et al*, 2008; Smith *et al*, 2009; Pardo *et al*, 2010; Lehto *et al*, 2013; Gavin *et al*, 2015). The negative effects vary by treatment method. All active prostate cancer treatments result in sexual difficulties; prostatectomy and radiotherapies also in urinary dysfunction; external radiotherapy also in bowel dysfunction; and hormone therapy causes, for example, hot flushes and mood disturbances. Consensus does not exist regarding whether the benefits of active treatment for early prostate cancer, compared with those of surveillance, outweigh the negative effects of the treatment (Denberg *et al*, 2006; Penson *et al*, 2008b; van den Bergh *et al*, 2009; Carter *et al*, 2015; Klotz *et al*, 2015).

Various treatment options for prostate cancer follow specific guidelines such as the European Association of Urology Prostate Cancer Guidelines (https://uroweb.org/guideline/prostate-cancer) and the American Urological Association Guidelines (https://www.auanet.org/education/clinical-practice-guidelines.cfm), which are based on the risk classification of the disease. However, the best treatment for long-term survival is still unknown (Wever *et al*, 2013). Specifically, no randomised controlled trial has compared prostatectomy with external beam radiotherapy. Patients usually participate in choosing their own treatments. This choice is important because different treatments can impair different areas of well-being and QoL. Differences in professional opinion concerning the best treatment option might complicate the situation for the patient at diagnosis (Denberg *et al*, 2006; Roth *et al*, 2008; Wever *et al*, 2013; Sooriakumaran *et al*, 2014). Both the prognosis and effect of the treatment on QoL should be considered when choosing a treatment for prostate cancer (Damber and Aus, 2008; Roth *et al*, 2008; Wever *et al*, 2013). Many men with localised prostate cancer do not benefit from definitive treatment (European Association of Urology Prostate Cancer Guidelines), and not all early local or locoregional prostate cancers require active treatment (Bul *et al*, 2013; Wever *et al*, 2013; Carter *et al*, 2015). In addition, the harms and benefits of population PSA screening are currently widely discussed (Auvinen *et al*, 2016). Screening with PSA detects some early prostate cancers that would never cause significant clinical problems during a man's lifetime. More information is needed to minimise the negative effects of prostate cancer and its treatments.

Using a population-based sample of men with prostate cancer diagnosis, we collected comprehensive information concerning the patient-reported negative effects (i.e., occurrence, perceived level and the perceived bother of the symptoms at any time, 'ever' and 'current') of different prostate cancer treatments 5 years after diagnosis. We also measured patient satisfaction with the outcome of the treatment and their psychological well-being (i.e., psychological symptoms and satisfaction with life) 5 years after diagnosis. The negative effects of the different treatments were compared, and the association among these negative effects, patient satisfaction and well-being was investigated.

PATIENTS AND METHODS

Sample and procedure. The Finnish Cancer Registry (www.cancerregistry.fi) collected a nationwide sample of every second incidence case diagnosed in Finland in 2004 on our behalf (Lehto *et al*, 2010; Lehto *et al*, 2015; Figure 1). We linked these data with the Finnish Population Register Centre and excluded patients who died before survey. After excluding patients without a recommendation from the treating hospital to participate in this study (11%), and those whose address was not available, we mailed a questionnaire to 1723 men between January and May 2009. A telephone line was provided to the patients for questions. A further questionnaire was sent to non-respondents 1 month later.

We accepted 1239 returned questionnaires (72%) for the study (Figure 1). These questionnaires represented 62.5% of the patients ($n = 1984$) who were alive at the time of the survey (70% of those who were < 65 years old, 67% of those who were 65–74 years old, 60% of those who were 75–84 years old, and 34.5% who were ⩾ 85 years old). The response rate and the age distribution of the
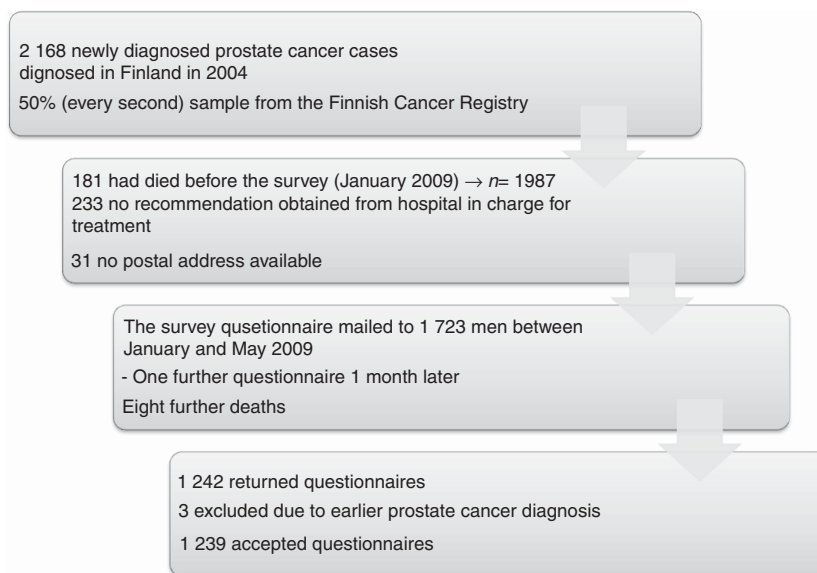

Figure 1. The study sample.

patients was similar across the five university hospital districts (geographic regions) in Finland (Lehto *et al*, 2010).

The questionnaire. The questionnaire was designed for the purposes of this study and constructed in collaboration with members of a prostate cancer patient organisation (Eturauhassyö-päpotilaiden tuki ry ERSY). These patients also participated in pilot studies to develop the questionnaire. The results of the first section of the questionnaire were previously reported (Lehto *et al*, 2015). The second section targeted the negative effects due to the treatment. We measured the occurrence, perceived level and the perceived bother of a given adverse effect at any time (ever) since the treatment with regard to each type of treatment the patient received, including radical prostatectomy, radiotherapies (i.e., external beam radiotherapy or brachytherapy), hormone therapy (other than neoadjuvant) and surveillance. (If any doubt or inconsistency appeared in the survey, then an expert medical researcher checked the treatment(s) implemented using the information the patient provided in the questionnaire or the information in the cancer registry data.). They were also asked whether the cancer had recurred.

The degree of the negative effects was evaluated with scales ranging from 0 (not at all) to 3 (a lot/strong/all the time) or with dichotomous no/yes answers. The patients were also asked whether they had had sex life with their spouse 6 months before the diagnosis (no/yes) and at any time after treatment (no/yes). Patient satisfaction was assessed using a scale ranging from 1 (completely adequate/satisfied) to 4 (completely inadequate/dissatisfied). Some open-ended questions including one regarding the negative effect(s) that the patient still suffered at the time of the survey were also asked.

Patient satisfaction with the overall outcome of the treatment and their psychological well-being were measured at the time of the survey. The patients indicated how satisfied they were with the outcome of their treatment using a scale ranging from 1 (completely satisfied) to 4 (completely dissatisfied). Psychological well-being was measured using two validated measures (Lehto *et al*, 2015): the psychological symptom items of the cancer-specific Rotterdam Symptom Checklist (deHaes *et al*, 1990), including irritability, depressed mood, nervousness, desperate feelings about the future, tension, anxiety, difficulty concentrating and worrying with scales ranging from 0 (not at all) to 3 (much), and the Satisfaction With Life Scale including statements: In most ways, my life is close to my ideal; The conditions of my life are excellent; I am satisfied with my life; So far I have the important things I want in life; If I could live my life over, I would change almost nothing (Diener *et al*, 1985).

We analysed the data using descriptive statistics and investigated the associations between the negative effects of the treatment and the outcome measures (i.e., satisfaction with outcome of the treatment, psychological symptoms and satisfaction with life) using a linear regression analysis (B = regression coefficient). All statistical analyses were performed using SPSS version 22 and Stata version 11.

Permissions and ethical aspects. The Ministry of Social Affairs and Health in Finland provided permission to obtain the Finnish Cancer Registry patient data. Experts in health psychology revised the questionnaire, and it was mailed to the patients from the National Public Health Institute (currently THL). The Ethics Committee of Helsinki University Hospital approved the research protocol.

RESULTS

The mean age of the respondents was 72 years old (range, 49–98 years), and thus the mean age at diagnosis has been 67 years old

(Table 1; Lehto *et al*, 2010, 2015). Approximately 80% were married or cohabiting, and 88% were retired. Nearly half (47%) reported receiving no or a very brief vocational education. Approximately 75% reported that they had another chronic condition (Table 1).

The most common treatments were radical prostatectomy (26%) and external beam radiation (24%) implemented as a single therapy (Table 1). Hormone (androgen deprivation) therapy was often used as an adjuvant treatment. However, 23% of the patients had undergone multiple treatments; thus, the total use of the different treatment modalities (alone or in combination) was higher. A total of 42% of the respondents received external beam radiotherapy, 33% received hormonal therapy, 32% received radical prostatectomy, 7% received surveillance and 6.5% received brachytherapy (Lehto *et al*, 2015). Hormonal therapy was often (65%) still going on at the time of the survey. Age was positively associated with hormonal therapy and surveillance but negatively associated with prosta-tectomy and brachytherapy. Having no other chronic condition was associated with prostatectomy. The Gleason score was positively associated with external radiotherapy and hormonal

Table 1. Demographic characteristics of the survey sample[a] and treatment for the prostate cancer (N = 1239)	
	% (n)
Age	
≤64	20 (248)
65–74	41 (503)
75–84	34 (423)
85 and over	5 (65)
Marital status	
Married or cohabiting	80 (988)
Divorced	7 (82)
Widow	8 (97)
Never married	4 (45)
Vocational education[b]	
No vocational education	25 (305)
Vocational courses or school	38 (465)
Some college or college graduate	21 (256)
University degree	14 (169)
Other chronic condition (own report)	
Any	74 (900)
Coronary heart disease	26 (311)
Musculoskeletal disease	18 (213)
Diabetes	15 (181)
Other cancer	7 (86)
Other	22 (267)
Gleason classification (x + x)[c]	
4 or less	10 (131)
5–6	40 (504)
7	26 (326)
8–10	13 (133)
Treatment for prostate cancer	
Radical prostatectomy alone	26 (319)
External beam radiotherapy alone	24 (292)
Hormonal therapy alone[d]	16 (202)
External beam radiotherapy + hormonal therapy	13 (163)
Surveillance alone[e]	6 (69)
Brachytherapy alone	5 (67)
Prostatectomy + external beam radiotherapy	4 (50)
Other combination	5 (73)

Note: some variables do not add up to 100% due to missing data.
[a]Finnish population is ethnically homogeneous in the age groups in question.
[b]The education level varied between the geographical areas in favour to the capital Helsinki area.
[c]From the Cancer Registry data, available for 88.3% of the respondents.
[d]Including orchiectomy.
[e]Either active surveillance or watchful waiting.

therapy but negatively associated with brachytherapy and surveillance. Six per cent of the patients reported that their prostate cancer had recurred; however, a higher proportion reported additional treatments, which were obviously due to a relapse.

Negative effects of the treatments. The negative effects by treatment are shown in Table 2. Patients treated with prostatectomy and radiotherapies commonly reported urinary and sexual difficulties, and those with external radiotherapy reported also bowel dysfunction. Depending on the treatment, 33–48% reported at least one current negative effect after 5 years, and this was more common after prostatectomy (B = 0.17, $P < 0.001$) and external radiotherapy (0.13, $P < 0.001$) but less common after brachytherapy (B = − 0.01, $P < 0.01$).

Urinary dysfunction. More than 70% of the patients reported urinary leakage after prostatectomy, and ~45% of those who were treated with external radiation or brachytherapy (Table 2). This symptom was more common after prostatectomy and external radiation ($P < 0.001$). This difference remained after adjusting for age. The perceived level of the leakage was also highest after prostatectomy (Figure 2A). Of those who received prostatectomy, 40% reported that the leakage had ceased within 3 months (Table 2), whereas 42% of patients receiving external radiation suffered from leakage for more than a year, and 50% of those patients reported that this symptom began as a late effect after the radiation therapy was over. Approximately 10% of the patients had urinary trouble (a qualitative report) at the time of the survey after prostatectomy, followed by 8% after external radiation, and 6% after brachytherapy. Approximately half of all patients reported that they had experienced unpleasant smell. This effect was more common after prostatectomy (age and Gleason score adjusted B = 0.29, $P < 0.001$) and less common after brachytherapy (B = − 0.09, $P = 0.086$).

Additional urinary symptoms, including burning during urination, increased frequency or blood in the urine, and retention or straining, were reported after radiation therapy, that is, external radiation and brachytherapy (Table 2). Brachytherapy was more closely associated with burning (B = 0.36, $P < 0.001$), increased frequency or blood in the urine (B = 0.23, $P < 0.1$) and urinary retention (B = 0.31, $P < 0.01$) than external radiation. Increased frequency/blood in the urine usually started during the radiotherapy, and it lasted longer than 1 year for 37% (external radiation) and 25% (brachytherapy) of the patients. Urinary retention lasted longer than a year for 30 and 44% of patients.

The urinary symptoms bothered 74 − 80% of the patients who reported them, and 7–10% reported these symptoms as a major bother (Table 2). The degree of the overall bother was predicted by most of the symptoms in prostatectomy and external radiation (Table 3). The most troublesome ($P < 0.001$) was the perceived level of the leakage; after prostatectomy also the level of the smell and after external beam radiotherapy also increased frequency/blood in the urine and retention were closely associated ($P < 0.001$) with the perceived overall bother. Age decreased the perceived bother of the urinary symptoms after prostatectomy ($P < 0.01$).

Bowel dysfunction. Approximately half of the patients suffered from bowel dysfunction during or after external beam radiotherapy, whereas only 15% did so after brachytherapy (Table 2). The most common symptoms were diarrhoea and bleeding from the anus/bowel. Diarrhoea lasted less than 3 months in approximately half of the patients after external radiation; however, it lasted longer than a year in 32%, and it started as a late effect in 25% of the patients. The bleeding was over in 3 months in 26% of the patients, whereas it lasted for more than a year in 59%. Approximately 15% of the patients reported bowel dysfunction at 5 years after external beam radiotherapy, whereas only 4% reported

this symptom after brachytherapy. Bowel dysfunction symptoms were considered harmful by 90% of the patients. Duration of diarrhoea was associated with the perceived bother of the bowel dysfunction (B = 0.24, $P = 0.021$).

Negative effects on sex life. All active treatments considerably affected patients' sex lives; specifically, 81 − 93% of respondents reported an effect (Table 2 and Figure 2B). Prostatectomy was reported as having a stronger effect on patients' sex lives ('ever' during the 5 years after diagnosis) than the other treatments, even after adjusting for age and the Gleason score (B = 0.23, $P < 0.001$). External beam radiotherapy (B = − 0.16, $P < 0.001$) and hormonal therapy (B = − 0.29, $P < 0.001$) had weaker effects. Of the patients who reported a permanent effect at five years, 67% indicated sexual difficulties after prostatectomy, and almost the same proportion after brachytherapy (Table 2). Permanent sexual difficulties were reported more often after prostatectomy (in 32% of all the patients) than after external radiation (11%) and brachytherapy (20%).

Between 70 and 92% of the patients reported sexual dysfunction (impotence, loss of libido/sexual desire, or the loss of both potency and desire) depending on the treatment received (Table 2). More dysfunction was reported after prostatectomy (B = 0.18, $P < 0.001$, adjusted for age), hormonal therapy (B = 0.11, $P < 0.001$), and external radiotherapy (B = 0.07, $P = 0.006$) than after the other treatments. Between 22 and 57% of the respondents reported impotence, most often after prostatectomy, whereas loss of sexual desire alone was rare (4–10%; Figure 2C). 18–25% reported the loss of both desire and potency after prostatectomy or radiotherapy, whereas 45% reported the loss of both after hormonal therapy.

Between 62 and 82% of the respondents reported having sex life with their spouse before treatment for prostate cancer (Table 2 and Figure 2D). Younger respondents (B = − 0.02, $P < 0.001$) and those without a comorbid chronic condition (B = 0.10, $P = 0.002$) reported having sex more often. A prior sex life had been most common when the chosen treatment was prostatectomy (B = 0.13, $P < 0.001$, when adjusted for age, the Gleason score and the presence of another chronic condition) but less common when it was surveillance (B = − 0.45, $P < 0.001$). The patients' sex lives decreased considerably after all treatments, and it ended in 38%, 30%, 20% and 58% of the patients receiving prostatectomy, external radiation, brachytherapy and hormone therapy, respectively. A post-treatment sex life was more common after radiation therapy (52 and 69% for external radiation and brachytherapy, respectively). 28% of the patients receiving hormone therapy reported having sex life with their spouse after treatment.

Across the different treatments, slightly different sexual effects predicted the overall effect of the treatment on sex life (Table 3). The most harmful effects across all treatments ($P < 0.001$) were the loss of both sexual desire and potency and the loss of sexual desire. The loss of potency showed a weaker association. A pre-treatment sex life with the spouse naturally predicted a stronger effect on sex life and the effect was weaker when post-treatment sex life was present. Age decreased the effect on sex life after prostatectomy ($P < 0.1$) and hormonal therapy ($P < 0.01$).

Side effects of hormonal therapy. The most common negative effect of hormonal therapy was hot flushes (73%) followed by sore breasts (52%), mood disturbances (46%) and oedema of the feet (34%; Figure 2E).

Patient satisfaction with the outcome of the treatment, psychological well-being, and the negative effects. Dissatisfaction with the treatment outcome at the time of the survey (i.e., proportion of patients reporting any amount of dissatisfaction) was highest after prostatectomy (42%). 34% of the patients were dissatisfied with the outcome of hormone therapy, 24% were

dissatisfied with the outcome of external beam radiation, 22% were dissatisfied with the outcome of brachytherapy and 15% were dissatisfied with the outcome of surveillance. The scale means were 1.55 (s.d. = 0.76), 1.48 (s.d. = 0.79), 1.35 (s.d. = 0.72), 1.34

(s.d. = 0.77), respectively, for the active therapies (satisfaction with surveillance was measured as no/yes).

Three-quarters of the respondents reported at least one psychological symptom (the Rotterdam Symptom Checklist) at

Table 2. Negative effects in different treatments				
	Prostatectomy (n = 402)	External beam radiation (n = 523)	Brachy therapy (n = 80)	Hormone therapy (n = 412)
Urinary tract symptoms				
Urinary leakage				
Reported: %	71	44	47	–
Perceived level: mean (s.d.)	1.07 (0.89)	0.64 (0.83)	0.73 (0.91)	–
Duration: %				
<3 Months	40	18	20	–
3–6 Months	13	8	9	–
6–12 Months	6	12	29	–
>1 Year	30	42	34	–
No information	12	21	9	–
Smell effect of urinary leakage: %	59	58	41	–
Perceived level of smell effect: mean (s.d.)	0.78 (0.74)	0.75 (0.76)	0.51 (0.70)	–
Burning during urination				
Reported: %	–	29	51	–
Perceived level: mean (s.d.)	–	0.36 (0.61)	0.72 (0.84)	–
Increased frequency or blood in urine				
Reported: %	–	46	61	–
Perceived level: mean (s.d.)	–	0.73 (0.90)	0.89 (0.85)	–
Urinary retention or straining				
Reported: %	–	30	44	–
Perceived level: mean (s.d.)	–	0.45 (0.77)	0.73 (0.96)	–
Bother of the urinary symptoms				
Reported, all above %	80	74	74	–
Perceived level of bother: %				
Not at all	20	21	25	–
A little	47	34	43	–
Somewhat	24	25	18	–
A lot	7	7	10	–
No information	3	12	3	–
Level of bother, mean (s.d.)	1.10 (0.82)	1.16 (0.93)	1.08 (0.94)	–
Bowel dysfunction				
Bowel symptoms total[a]	–	53	15[b]	–
Diarrhoea				
Reported: %	–	77	36	–
Duration: %				
<3 Months	–	47	25	–
3–12 Months	–	17	25	–
>1 Year	–	32	50	–
Bleeding from anus				
Reported: %	–	41	64	–
Duration: %				
<3 Months	–	26	33	–
3–12 Months	–	15	17	–
>1 Year	–	59	50	–
Bother of bowel symptoms				
Reported : %	–	88	91	–
Perceived level of bother. %				
Not at all	–	12	9	–
A little	–	41	55	–
Somewhat	–	36	18	–
A lot	–	11	18	–
Level of bother: mean (s.d.)	–	1.45 (0.86)	1.45 (0.93)	–
Impact on sex life				
Impact in sex life				
Reported: %	93	82	86	81
Perceived level: mean (s.d.)	2.35 (0.91)	1.89 (1.13)	1.78 (1.08)	2.16 (1.18)
Sexual dysfunction				
Reported total: %	92	79	70	84
Impotence	57	34	33	22
Loss of sexual desire	4	8	10	7
Loss of desire and potency	18	25	18	45
Sex life with spouse				
During 6 months before the treatment: %				
No	10	23	16	28
Yes	82	70	81	62
No spouse	8	7	3	10
After the treatment: %	55	52	69	28

Table 2. (Continued)				
	Prostatectomy (n = 402)	External beam radiation (n = 523)	Brachy therapy (n = 80)	Hormone therapy (n = 412)
A permanent negative effect (at 5 years)				
A permanent negative effect reported: %				
No	43	48	53	–
No information	9	15	15	–
Yes	48	37	33	–
The effects classified from qualitative reports %:				
Impotence or sexual difficulties	67	30	62	
Need for medication (tablet, injection) to get erection	9	2	8	
Urinary leakage or increased frequency	20	21	19	
Bowel symptoms	1	39	12	
Pain in lower abdomen/back/the scar	5	5	4	

Note: all symptoms were not asked from all treatments, because some symptoms are mostly treatment-specific.
[a]Data in brachytherapy insufficient (over 50% missing values).
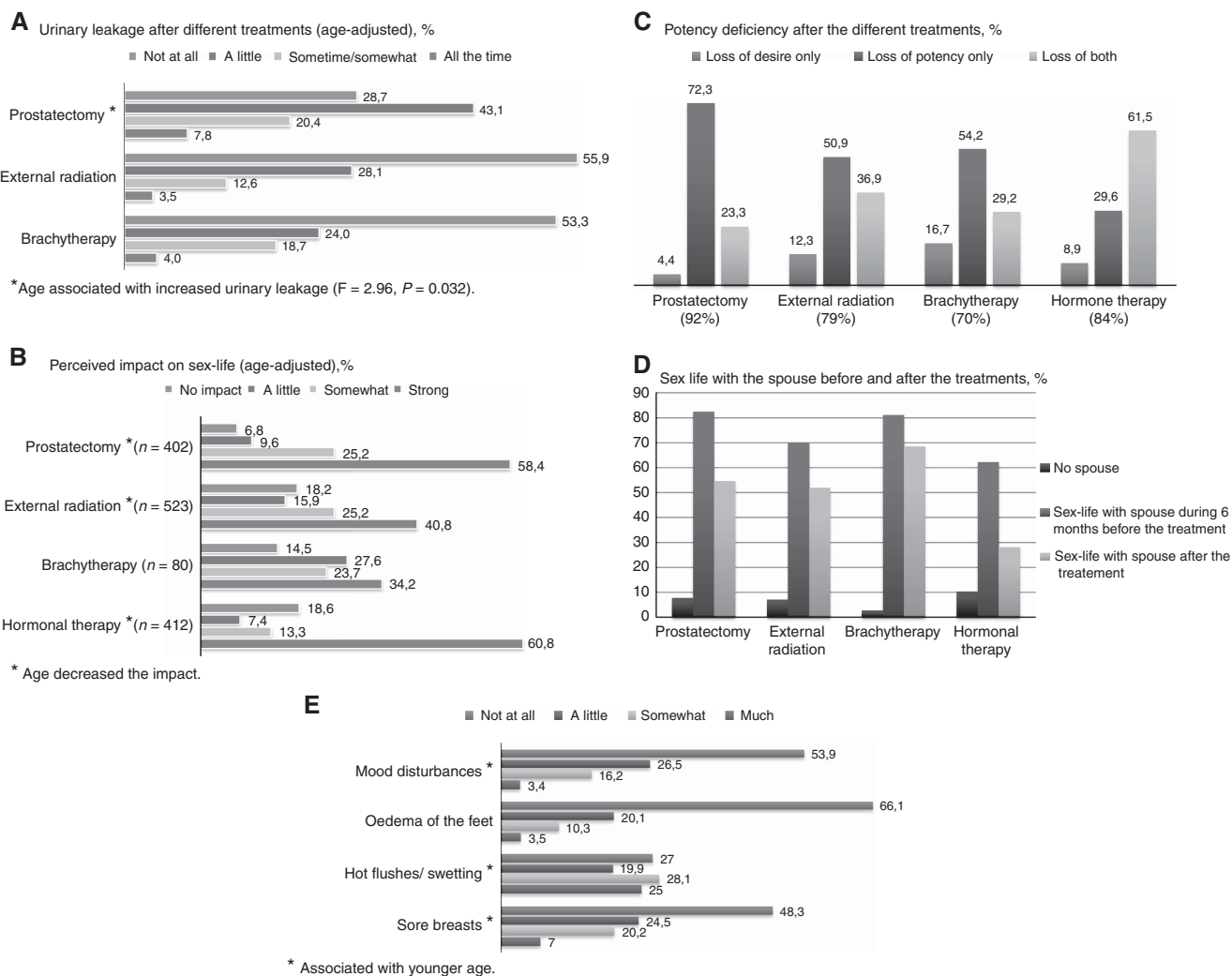[b]N = 11.

Figure 2. Negative effects in different treatments (Reproduced by kind permission Lehto *et al*, 2013). (**A**) Urinary leakage after different treatments (age-adjusted), %. (**B**) Perceived impact on sex life (age-adjusted), %. (**C**) Potency deficiency after different treatments, %. (**D**) Sex life with the spouse before and after the treatment, %. (**E**) Adverse effects of hormonal treatment, %.

the time of the survey (total scale mean n = 4.39, SD = 4.6; Lehto *et al*, 2015). The most common symptom was worrying (57%), followed by irritability (46%), nervousness (40%) and problems concentrating (39%). Regarding the satisfaction with life statements (the Satisfaction With Life Scale), the median response was 'mostly agree'. Brachytherapy was associated with a lower total level of psychological symptoms, whereas surveillance was associated with greater satisfaction with life (Lehto *et al*, 2015). Age was negatively associated with the total level of the psychological symptoms (B = − 0.05, P < 0.05 when adjusted

Table 3. Associations between the urinary and sexual adverse effects and overall perceived bother of them

	Prostatectomy	External radiation	Brachytherapy	Hormonal therapy
	B	B	B	B
Level of total bother of the urinary symptoms				
Predictors				
Age	− 0.02**	0.01	0.02	
Gleason	0.04	− 0.09†	0.12	
Level of urinary leakage	0.39***	0.40***	0.13	
Duration of urinary leakage	0.10**	0.18**	0.13	
Smell effect of urinary leakage	0.44***	0.17	− 0.10	
Burning during urinating		0.01	0.33	
Frequency or blood in urine		0.24***	− 0.04	
Retention or straining		0.24**	0.38†	
Coefficient of determination R² for the model	0.49	0.46	0.40	
Level of impact of treatment on sex life				
Predictors				
Age	− 0.01†	− 0.01	0.03	− 0.02**
Gleason	0.04	− 0.06	0.05	− 0.03
Impotence	0.64**	0.59***	0.38	0.83**
Loss of sexual desire	1.11***	1.19***	1.16***	1.44***
Loss of both desire and potency	1.19***	1.41***	1.50***	1.79***
Sex life with spouse during 6 months before treatment	0.18	0.65***	0.38	0.38**
Sex life with spouse after treatment	− 0.20*	− 0.22*	− 0.05	− 0.36*
Coefficient of determination R² for the model	0.31	0.36	0.40	0.38

Note: B = regression coefficient: association between the negative effects/symptoms and overall bother of them, by linear regression analysis, adjusted for age and Gleason, all variables in the model. ***P-value <0.001, **P-value <0.01, *P-value < 0.05, † P-value <0.1.

for treatment modality and recurrence). Reported recurrence was associated with more psychological symptoms ($B = 1.14$, $P < 0.05$).

Across the different treatments, different negative effects were associated with the outcomes (i.e., dissatisfaction with the treatment outcome and the well-being indicators (Table 4). The perceived level and the perceived bother of the symptoms (e.g., levels of bother of the urinary leakage and smell effect of the urinary leakage) were more strongly associated with the outcomes than the occurrence of the symptoms (measured as no/yes). Sexual dysfunction effects were more associated with the well-being outcomes among patients receiving prostatectomy than those receiving the other treatments. Sexual effects were of little consequence among the patients receiving radiation therapies, and their urinary symptoms explained most of the variation in the psychological well-being.

DISCUSSION

This nationwide survey collected detailed information regarding the negative effects of prostate cancer treatment by investigating patient perceptions of these effects and their bother at any time since the treatment during 5 years after diagnosis. We also measured patients' levels of satisfaction and psychological well-being five years after diagnosis. A 50%-patient sample from a national cancer registry enabled us to study all men in Finland who were diagnosed with prostate cancer over 1 year. The response rate was high (72%) for a postal survey addressing relatively elderly people. Of the patients in the cancer registry, 62.5% replied to our survey; only those over 84 years old were under-represented. The sample was representative of prostate cancer survivors 5 years after diagnosis. Along with the recent work from Ireland (Gavin et al, 2015), the current study is one of the first to describe the negative consequences of the various prostate cancer treatments in a population sample of patients of all ages.

As previously reported, the negative effects of all types of active prostate cancer treatments were common, often multiple, and

persisted over the long term (Miller et al, 2005; Smith et al, 2009; Pardo et al, 2010; Resnick et al, 2013; Gavin et al, 2015). The known differences by treatment method were as follows: prostatectomy and the radiotherapies cause urinary symptoms; external beam radiotherapy also causes bowel dysfunction; and all active treatments were followed by sexual difficulties. Some of the treatments typically induce immediate transitory side effects (prostatectomy) and some treatment-specific late effects (radiotherapies), and all treatments result in long-term effects. We found that most of the adverse effects were considered highly bothersome. Approximately 75% of the patients stated that their urinary symptoms bothered them, and 90% stated that their bowel dysfunction was bothersome. All treatments had the potential to seriously harm the patients' sex lives.

Because we recorded all negative effects since the beginning of the treatment, our study found high levels of negative effects when compared with previous research (Lehto et al, 2013). We do not have information regarding when most of these negative effects occurred during the 5 years or whether they had passed; however, we have qualitative data concerning the negative effects present at the time of the survey. Several studies have measured side effects at a specific time point (Potosky et al, 2004; Miller et al, 2005; Penson et al, 2008a; Smith et al, 2009; Pardo et al, 2010; Gavin et al, 2015) and reported that there were more negative effects after prostatectomy than after other treatments at 3 years (Smith et al, 2009; Pardo et al, 2010) or at 5 years (Potosky et al, 2004; Penson et al, 2008a) post-diagnosis/treatment. This finding is in agreement with our results. However, one study (Miller et al, 2005) reported few differences between prostatectomy and external beam radiotherapy after six years. More recently, no significant differences in urinary, bowel or sexual function were found between prostatectomy and radiotherapy when evaluated at 15 years (Resnick et al, 2013).

The high level of urinary leakage experienced by patients receiving prostatectomy was often decreased quickly, and permanent urinary troubles were only slightly more common after prostatectomy than after external beam radiotherapy or brachytherapy. Age was negatively associated with the perceived

Table 4. Negative effects of treatments associated with dissatisfaction with outcome of the treatment and psychological well-being

	Dissatisfaction with the outcome		Psychological symptoms		Satisfaction with life	
	B	P	B	P	B	P
A. Negative effects predicting psychological outcomes in prostatectomy						
Predictors						
Age	− 0.01	0.077	− 0.12	0.021		
Gleason					0.65	0.032
University education	0.27	0.026				
Have spouse					3.16	0.002
Musculoskeletal disease			2.07	0.032	− 3.72	0.001
Bother of urinary leakage	0.22	<0.001			− 1.28	0.017
Smell effect of urinary leakage			1.14	0.010	− 1.11	0.063
Impact on sex life	0.15	0.008			− 1.29	0.003
Sex life with spouse during 6 months before treatment	0.20	0.062				
Sex life with spouse after the treatment			− 1.39	0.029		
A permanent negative effect	0.25	0.011	1.38	0.025		
Coefficient of determination R² for the model	0.22		0.13		0.22	
B. Negative effects predicting psychological outcomes in external beam radiotherapy						
Predictors						
Age			− 0.12	0.074		
Gleason			0.65	0.070		
University education	0.41	0.067				
Have children					4.04	0.003
Musculoskeletal disease					− 1.97	0.092
Urinary leakage			0.91	0.092		
Smell effect of urinary leakage	0.36	0.004			− 1.33	0.026
Burning during urinating	0.22	0.092	1.43	0.024		
Urinary frequency or blood in urine					− 1.32	0.004
Late effect urinary frequency or blood in urine			2.36	0.014		
Impotence	0.33	0.080				
Bother of bowel dysfunction	0.23	0.022	1.11	0.044		
A permanent negative effect	0.52	0.003				
Satisfaction with sex life					1.03	0.005
Coefficient of determination R² for the model	0.34		0.27		0.26	
C. Negative effects predicting psychological outcomes in brachytherapy						
Predictors						
Age			− 0.20	0.052		
University education					4.94	0.021
Smell effect of urinary leakage			3.16	0.001		
Duration of urinary leakage					− 1.33	0.056
Duration of urinary frequency or blood in urine	0.29	0.030				
Bother of urinary symptoms					− 1.52	0.078
Coefficient of determination R² for the model	0.26		0.33		0.34	
D. Negative effects predicting psychological outcomes in hormonal therapy[a]						
Predictors						
Age			0.06	0.081		
University education	− 0.46	0.016	− 1.39	0.051		
Have spouse					1.08	0.068
Musculoskeletal disease					− 2.77	0.006
Diabetes			1.30	0.049		
Sex life with spouse during 6 months before treatment	0.21	0.032			− 1.49	0.074
Loss of sexual desire			2.08	0.034		
Mood disturbances	0.17	0.027	2.88	<0.001		
Sore breasts	0.19	0.007				
Oedema of feet	0.19	0.012				
Other symptom of hormonal treatment	0.24	0.074				
Satisfaction with sex life					1.08	<0.001
Coefficient of determination R² for the model	0.27		0.32		0.14	

Note: B = regression coefficient: association between negative effects and the well-being outcome (dissatisfaction with the outcome of treatment, psychological symptoms, satisfaction with life), by linear regression analysis. All variables adjusted for age and Gleason (in brachytherapy, Gleason ⩽7). Only the statistically significant are given.
[a]In 65% of the patients with hormonal therapy the treatment was going on.

bother of the urinary symptoms, which suggests that these symptoms are better tolerated as patients grow older age. However, prostatectomy most strongly affected patients' sex lives. Operation typically resulted in sexual dysfunction, especially impotence (75%), whereas impotence was less frequently associated with the other treatments (51–67%). The patients reported far more often permanent sexual difficulties after prostatectomy (32%) than after external radiation and brachytherapy (11% and 20%, respectively). This number was even higher when troubles solved with medication were included. This finding corroborates those of

previous studies (Potosky *et al*, 2004; Smith *et al*, 2009), indicating that prostatectomy often induces sexual dysfunction. The effect of prostatectomy on patients' sex lives was most likely stronger because these patients were younger, were more likely to have a sex life before treatment, and less likely to suffer from another chronic condition. Furthermore, prostatectomy typically led to impotence without the loss of sexual desire, which was strongly associated with perceived bother.

Among patients receiving external beam radiotherapy, urinary trouble and bowel dysfunction often started as a late effect after the treatment. Half of the patients reported bowel dysfunctions (diarrhoea or anal bleeding), and 25% reported these effects as late, and often lasting for more than a year. In addition, 15% reported bowel dysfunction after 5 years. The frequency of bowel dysfunction reported here matches previous reports, that is, 15–23% after 3 years (Smith *et al*, 2009; Pardo *et al*, 2010) and 13% after 6 years (Miller *et al*, 2005). The absence of a sex life with one's spouse occurred less frequently after radiotherapy than after the other treatments. Approximately half of the patients who underwent external beam radiotherapy reported having a sex life with their spouse after the treatment; this decrease was small because only 70% reported a pre-treatment sex life.

Brachytherapy seemed less harmful than the other treatments; it rarely resulted in bowel dysfunction, and its effect on patients' sex lives was smaller than those of other treatments. However, urinary irritation symptoms (burning, frequency and retention) remained common. These patients differed from others with regard to many preceding factors: they were younger, their cancers had better prognoses (i.e., smaller Gleason score; high-risk prostate cancer is not treated with brachytherapy), and they commonly reported pre-treatment sex lives. A comparison with the other treatments is complicated because brachytherapy was available only in certain hospital districts and it was widely used in one district. We previously found that psychological well-being after brachytherapy is better than that after other treatments (Lehto *et al*, 2015). Several studies have reported that brachytherapy causes fewer long-term side effects, especially sexual dysfunction and urinary incontinence (Frank *et al*, 2007; Aaltomaa *et al*, 2009; Pardo *et al*, 2010).

Surprisingly, patients receiving androgen deprivation therapy reported that their sex life was not more frequently affected than those receiving the other treatments; however, these patients were more likely to report a 'strong' effect. Age reduced the effect of hormonal therapy on sex life, and because only 62% of these patients reported having a sex life before treatment, they likely already had given up their sex life before their diagnosis, for example, due to ageing, illness or limitations in functional capacity. Thus, they had less sex lives to be affected. The decrease in having sex life with their spouse was nearly 60% of these patients; however, as many as 28% reported having a sex life with their spouse since the beginning of treatment.

We found that the negative effects of active prostate cancer treatment are associated with later satisfaction and psychological well-being. Urinary symptoms were more strongly associated with well-being outcomes than sexual difficulties. This result should not be generalised across all prostate cancer patients; individual differences in this matter are most likely strong. The association between sexual dysfunction and the treatment outcomes was somewhat stronger among patients receiving prostatectomy than those receiving other treatments. Some positive association was found between the Gleason score and better well-being. Could it be that patients with more severe diseases tolerate more negative effects of the treatment? On the whole, the perceived level and bother of the symptoms had a stronger effect on psychological outcomes than the occurrence of the symptoms *per se*.

We retrospectively measured the negative effects 5 years after the diagnosis of prostate cancer, and there may have been memory bias in the patients' recall of these effects. This might have biased

some of our findings. More severe and longer lasting effects might be better recalled than short-term consequences. However, the disturbing adverse effects due to cancer treatment are likely to be remembered, even years later. We assessed the effects associated with each treatment; however, nearly 25% of the patients received multiple treatments. Thus, these patients might have difficulty separating the effects of individual treatments from each other. Furthermore, we did not always ask when the symptoms occurred or how long they lasted (and when we did, the patients' answers tended to be incomplete). The current symptoms were recorded only as the presence of a negative effect at the time of the survey via quantitative reports that we classified later. The negative effects and well-being outcomes were measured simultaneously; thus, their associations do not allow for direct conclusions regarding causality. In addition, it would have been preferable to have information about the same symptoms in the population. These data would have helped assess the effects of prostate cancer treatment compared with the symptoms of same-aged men.

Our results describe the negative effects of the treatments implemented in 2004 and 2005. The treatments have developed since then; however, we believe that prostate cancer patients and survivors still face many of these negative effects. We believe that our results also indicate the present situation, especially by illustrating the perceived harmfulness and bother of the symptoms. However, a new survey should be conducted to obtain up-to-date information concerning the negative effects of prostate cancer in the population and to assess the effects of the developing treatments.

The abundance of the symptoms and their bothersome nature draws attention to the harms and benefits of the active treatment of prostate cancer. An on-going debate exists regarding how and whether to actively treat patients with early-stage prostate cancer (Denberg *et al*, 2006; Bul *et al*, 2013; Wever *et al*, 2013; Carter *et al*, 2015; Klotz *et al*, 2015). A related discussion concerns the appropriateness of population PSA screening for prostate cancer (van Leeuwen *et al*, 2013; Schröder *et al*, 2014; Auvinen *et al*, 2016).

Prostate cancer and its associated treatments affect the lives of an increasing proportion of the elderly male population and their partners (Lehto *et al*, 2017). A growing number of men experience the negative effects of these treatments and for a longer time. Thus, the well-being of prostate cancer patients and prostate cancer survivors is also important from a public health perspective. The negative effects of the treatments described herein and their effects on well-being should be carefully considered when selecting a treatment for prostate cancer. In addition, methods should be developed to alleviate the negative effects associated with treatments and promote the QoL of men with prostate cancer diagnosis.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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