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Problems sleeping with prostate cancer: Exploring possible risk factors for sleep disturbance in a population-based sample of survivors

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Abstract

Purpose: To investigate the prevalence of sleeping problems in prostate cancer survivors and to explore the role of predisposing, precipitating and perpetuating factors in this process. Methods: Using a cross-sectional design, 3,348 prostate cancer survivors between 2-18 years post-diagnosis reported experiences of insomnia using the QLQC30, along with their sociodemographic characteristics, health status, and treatment(s) received. The EQ5D-5L and QLQPR25 assessed survivors' overall and prostate cancer-specific health-related quality of life. A hierarchical multiple regression analysis was constructed with three blocks: (1) predisposing (e.g. demographics at diagnosis), (2) precipitating (e.g. disease extent, treatment), and (3) perpetuating factors (e.g. side effects). Results: Nineteen percent of survivors reported significant problems sleeping. The final model accounted for 31% of the variance in insomnia scores ($p < .001$). In order of magnitude, associates of sleep disturbance were: urinary symptoms ($\beta = .22$; $p < .001$), experiencing symptoms of depression/anxiety ($\beta = .18$; $p < .001$), hormone treatment-related symptoms ($\beta = .12$; $p = .001$), pain ($\beta = .10$; $p < .001$), and bowel symptoms ($\beta = .06$; $p = .005$). Having a lower education and more comorbidities at diagnosis also predicted sleep problems. Conclusion: Results suggest that it is the ongoing adverse effects of prostate cancer and its treatment (e.g. urinary symptoms) that put survivors most at risk of sleep problems. Strong associations with symptoms of depression/anxiety were also observed. Findings highlight the need for health care practitioners to treat and manage adverse effects of prostate cancer treatment in order to mitigate sleep disturbance in survivors.

Keywords: Prostate cancer; insomnia; adverse side effects; depression; anxiety; pain

Running head: Sleep disturbance in prostate cancer survivors

Introduction

The diagnosis and treatment of prostate cancer is associated with a wide range of adverse effects, many of which can have a detrimental impact on the quality of life of survivors [1-3]. Most research to date has concentrated on the specific physical adverse effects of the disease and its treatment (e.g. erectile dysfunction, urinary incontinence and bowel problems), with less work focusing on more general symptoms such as insomnia or sleep disturbance [4]. Nevertheless, insomnia has been shown to be a common problem among survivors of many types of cancer [5-7], including those with prostate cancer [8,9,6]. The negative effects of sleep disturbance have been well documented, with those suffering from insomnia at a much higher risk of a range of problems. However, while some work has begun to shed light on the potential factors that put survivors at risk of sleep difficulties, there is still a dearth of knowledge in terms of how various factors combine to exacerbate these problems.

Along with fatigue, sleep disturbance is the most commonly reported symptom in prostate cancer survivors [8,1], although estimates of the prevalence of sleep difficulties vary significantly across studies, ranging from as low as 8% to as high as 53% of survivors [4]. Beyond prostate cancer, as many as 74% of patients with advanced cancer can be classified as "poor sleepers" [10]. The lack of agreement here is potentially due to the many different ways in which sleep problems can be defined and measured. While the general consensus is that insomnia involves a persistent difficulty in initiating and/or maintaining sleep [11], this term is typically used in the context of a clinical diagnosis so may not present a complete picture of the range of sleep disturbances that may be experienced by cancer survivors.

In prostate cancer, a likely influence on sleep quality is the particular treatment undertaken by patients. A number of studies have suggested that undergoing any form of active treatment puts survivors at greater risk of sleep problems [12], although some treatments have a more detrimental effect than others. In particular, androgen deprivation therapy (ADT) has

been associated with greater levels of sleep disturbances [13]. This is most likely due to the side effects of ADT, with some work showing that sleep problems in this group are mediated by associated symptoms, such as night sweats and nocturia [14,15,13,12]. Such side effects have also been shown to lead to insomnia in breast cancer survivors [12]. However, other common side effects associated with prostate cancer treatment, such as urinary problems, can also lead to night time waking and potentially exacerbate sleep problems further [13].

It could of course be the case that prostate cancer survivors already had a risk of developing symptoms of insomnia prior to treatment, or indeed may have had problems with sleeping that pre-dated their diagnosis. For example, one study [9] reported that half of prostate cancer survivors who met the criteria for chronic insomnia syndrome (specifically defined as a difficulty initiating or maintaining sleep for at least three nights a week, leading to significant daytime impairment) reported sleep difficulties prior to their cancer diagnosis. Indeed, in the general population, certain risk factors for insomnia have been identified, including, for example, younger age [16]. These factors may influence the likelihood of survivors experiencing sleep difficulties, irrespective of disease extent and treatment undertaken.

Reflecting the diverse elements associated with sleep disturbance, an influential theory of insomnia has proposed that sleep difficulties are caused by a combination of (1) predisposing, (2) precipitating, and (3) perpetuating, factors [17]. This theory, often referred to as the "three Ps" model, has also been adapted to explain insomnia in cancer survivors [18-21]. Specifically, predisposing factors have been considered to be those that put individuals at risk of sleep problems prior to diagnosis (e.g. sociodemographic characteristics at diagnosis), precipitating factors are those that trigger sleep difficulties upon diagnosis and treatment, while perpetuating factors have been viewed as those factors that maintain sleep disturbances post diagnosis.

We argue that a similar approach can be applied to understanding sleep disturbance in prostate cancer, however our conceptualisation of the "three Ps" model deviates slightly from previous work. In other studies, the adverse effects resulting from cancer treatment have been classified as precipitating factors [18], while perpetuating factors have been viewed as the actions that people take in order to compensate for, or cope with, sleepiness (for example caffeine consumption, or time spent in bed). We propose, however, that the adverse effects of cancer and treatment are better viewed as perpetuating factors, as these relate to the ongoing, often chronic, experiences of survivors that extend beyond the initial diagnosis and treatment of cancer. These could include the aforementioned urinary problems and night sweats, as well as a range of other physical effects of cancer and its treatment.

Sleep problems may also be perpetuated by psychological factors, such as symptoms of depression or anxiety. It is known that such symptoms co-occur with sleep disturbance in cancer [18], however the exact nature of the relationship between insomnia and depression/anxiety is unclear. Large scale longitudinal studies suggest a bidirectional relationship between the two [22] meaning that the experience of each disorder predicts the later onset of the other. Some work also suggests that an increase in anxiety levels in cancer survivors can lead to an increased risk of insomnia incidence [23,20]. It is possible that experiencing high levels of anxiety may perpetuate ongoing sleep difficulties, particularly given that prostate cancer survivors are known to experience fears of recurrence [24]. We hence conceptualise psychological variables here as *potentially* perpetuating sleep disturbance.

In sum, a greater understanding of the factors that put prostate cancer survivors at risk of sleep problems is merited. In this study we aimed to systematically explore how the previously defined predisposing, precipitating and perpetuating factors are associated with sleep disturbance across different phases of prostate cancer survivorship.

Methods

Sample and Design

This study formed part of the PiCT*ure* (Prostate Cancer Treatment, your experience) project which was designed to investigate the experiences of a representative sample of prostate cancer survivors in the Republic of Ireland (RoI) and Northern Ireland (NI) [25]. Survivors were identified from two population-based cancer registries and a countrywide stratified sample of 12,322 men was identified (see supplementary figure for an overview of sample recruitment). Inclusion criteria included being at least 2 years post diagnosis, being over the age of 18, and not suffering from any form of cognitive impairment that would interfere with study participation [25]. This was determined by health care professionals and was included to ensure that the respondents would be in a position to give fully informed consent. Following screening for eligibility by health care professionals (General Practitioners in the RoI and Urology Clinical Nurses in NI), a total of 6,559 survivors were invited to complete a postal questionnaire between April and September 2012. In addition to a cover letter, a consent form was included which recipients were asked to sign and return alongside the questionnaire in a prepaid envelope. Non-respondents received two written reminders approximately two weeks apart. The study was ethically approved by the Irish College of General Practitioners and from each of the five NI Trusts. Written informed consent was obtained from all participants included in the study.

Instruments

Sleep disturbance

Survivors completed the EORTC QLQC30 (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire) which is a widely used, valid and reliable

measure of health related quality of life in cancer survivors [26]. In addition to giving rise to five functional scales and a global health score, this measure includes nine symptom scales, one of which pertains to insomnia which constituted the outcome measure for the current study. To measure the extent of sleep problems, survivors were asked to rate whether they had experienced trouble sleeping during the past week on a four point scale ("Not at all", "A little", "Quite a bit", or "Very Much"). Responses were standardised as recommended [26] to give a score of 0-100, with higher scores associated with greater levels of sleep disturbance.

Predisposing factors

Socio-demographic variables and health status at diagnosis were classified as predisposing factors. Survivors were asked to indicate their date of birth (which was used to calculate their age at diagnosis) along with their marital status at diagnosis, education level at diagnosis, employment status at diagnosis, and whether they had any children under the age of 16 at diagnosis. Survivors were also asked whether they had any additional health problems at diagnosis including, for example, heart disease, diabetes, high blood pressure, diverticular disease, and/or other health problems. A total comorbidity score was computed reflecting to the total number of health conditions reported by respondents.

Precipitating factors

Precipitating factors were considered to be those relating to cancer diagnosis and treatment. Survivors were classified by disease extent at the time of diagnosis based on clinical stage and Gleason Grade (GG). This information was obtained from the National Cancer Registry Ireland (NCRI) and the Northern Ireland Cancer Registry records. Following previous guidelines [27], survivors with stage I/II disease and a GG of 2-7 at diagnosis were classified as having localised disease, whereas those with stage III/IV disease and any GG were classified as having locally advancing/advanced disease. Survivors with any other combinations of stage and GG as well

as those missing either a stage or grade classification and therefore could not be clearly identified as having either localised or advanced disease were included in a third category ("other"). Time since diagnosis was also recorded.

In addition, survivors indicated through self-report whether they had received any of the following treatments for their cancer: Radical Prostatectomy (RP), External Beam Radiation Therapy (EBBT), Brachytherapy (BT), Watchful Waiting (WW), and/or Androgen Deprivation Therapy (ADT). In relation to ADT, survivors also indicated whether this was a treatment they had undergone previously or were undergoing currently.

Perpetuating factors

Perpetuating factors were considered to be any ongoing effects of prostate cancer diagnosis and treatment and other indicators of quality of life. These were assessed using two scales. Firstly, survivors completed the QLQ PR25 (Quality of Life Questionnaire-Prostate 25) which measures prostate cancer specific symptoms [28]. Here, survivors indicated the extent to which they encountered problems in urinary (7 items) and bowel functions (4 items), and other possible treatment-related symptoms (6 items) such as hot flushes, swelling and/or fluctuations in weight. There were also specific questions relating to those who wore an incontinence aid and those who had engaged in sexual activity in the last 4 weeks, however, for the purposes of this study, these subscales were not included in the analysis as such symptoms were only applicable to a smaller subset of men [29]. For all items, survivors indicated the extent that they had experienced problems in the last week (or in the last four weeks for some treatment-related symptoms, such as weight loss or gain) on a scale of 1 (not at all) to 4 (very much). As recommended [28], subscales were computed for each domain and scores standardised from 0-100, with higher scores indicating greater problems. The

QLQP25 has been previously demonstrated to have acceptable psychometrics properties and clinical validity [30].

Survivors also completed the EQ5D-5L which is a widely used instrument for assessing generic health-related quality of life developed by the EuroQoL group [31] and has been demonstrated to have good reliability and validity in cancer patients [32]. This required survivors to indicate if they had any problems in the following domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Items were rated on a five point scale ranging from 1 (no problems) to 5 (severe problems). Following an established procedure, responses were categorised into a binomial variable representing whether survivors exhibited any problems in each domain (0=no problems; 1=any problems, as indicated by a response of 2 or above).

Statistical analysis

Descriptive statistics were calculated including means, ranges, and standard deviations. No violations regarding assumptions of linearity and homoscedasticity were observed. Examination of correlations amongst independent variables revealed no problems with multicollinearity. The outcome variable (insomnia subscale) was positively skewed, which is in line with previous research using the QLQ-C30 [33,34]. A number of the predictor variables were also positively skewed including all symptom subscales of the QLQPR25 and the total number of comorbid conditions experienced. Linear regression modelling can still be employed in predicting non-normally distributed data such as this, especially in cases where the sample size is large, and where the other assumptions are met [35]. A hierarchical multiple regression model was hence constructed to examine the associations between the three blocks of factors and problems sleeping: (1) Predisposing factors at diagnosis (age, education, employment status, marital status, having children living at home), (2)

Precipitating factors (disease extent at diagnosis, time since diagnosis and treatment, specifically having undergone RP, ERBT, and ADT, either current or previous treatment), and (3) Perpetuating factors (three symptom scales of QLQ PR25 and five subscales of EQ5D-5L). Missing data were handled using the pairwise deletion method. Associations with sleep problems were assessed using two-sided t-tests and p values of <0.05 considered significant.

Results

Descriptive statistics

Following questionnaire dispatch, 5% of respondents were deemed ineligible (see Figure 1). After removing these, a total of 3,348 survivors were included in the study (adjusted response rate = 54%). Analysis of the available information from registry records revealed that survivors who were less than 60 years old at diagnosis were more likely to respond than those above the age of 60. No difference was observed in time since diagnosis between responders and non-responders meaning that each survival phase was well represented [25].

Table 1 displays descriptive statistics for the measures used. At diagnosis the majority of survivors were married s (83%), had completed at least primary education (67%), were not in employment (51%), and had no children living at home (78%). Most (56%) reported at least one other health problems at diagnosis, with the most commonly reported problem being high blood pressure (30%), followed by heart disease (13%) and diabetes (7%). Forty three percent were classified as having localised disease at diagnosis with 15% having advanced disease. The most common treatment was ERBT (51%), followed by ADT (47% had either currently or previously received ADT) with 28% having undergone RP. Due to small numbers undergoing BT (6%) and watchful waiting (8%), these were not included in the final model.

Examination of prostate cancer specific symptoms revealed most survivors did not report significant problems in the three domains, although the most common of these were urinary symptoms (M = 19.76; SD = 18.34), followed by treatment related symptoms (M = 10.62; SD = 12.80), and bowel symptoms (M = 7.29; SD = 12.57). Results from all EQ5D-5L subscales showed the most commonly reported problem was pain (37%), followed by problems with usual activities (35%), mobility (33%), and anxiety/depression (28%). Only a small proportion of survivors (13%) reported problems with self-care.

When examining the QLQC30 insomnia subscale (see Figure 1), it can be seen that while the majority of the sample (54%) reported having no trouble sleeping in the past week, almost half reported some problems with 19% experiencing at least "quite a bit" of trouble sleeping (M = 23.57; SD = 30.18).

Hierarchical Regression Analysis

Table 2 displays the results of the regression analysis. All three blocks of factors were significant contributors to the model. Firstly, when entering predisposing factors into Block 1, 5.2% of the variance in sleep problems were accounted for, with significant associates at diagnosis being: a greater number of comorbid conditions ($\beta = .17$, $p < .001$), a lower level of education ($\beta = -.09$, $p < .001$), having no children at home ($\beta = -.05$, $p = .01$), not being in employment ($\beta = -0.6$, $p = .01$), and being younger ($\beta = -.05$, $p = .03$). After entering the precipitating factors into Block 2 of the model, a further 1.5% of variance in sleep problems was accounted for ($p < .001$). At this step, significant associates were: undergoing ADT currently ($\beta = .10$, $p = .001$), and having more advanced disease ($\beta = .05$, $p = .02$). Education, employment status, age, and comorbid conditions at diagnosis remained significant associates of sleep problems at this stage, however, many of these associations disappeared when entering the perpetuating factors into Block 3 of the model. This step contributed the largest

proportion of variance (24%) to levels of sleep disturbance ($p < .001$). Overall the final model was significant and explained a total of 31% of the variance in problems sleeping ($F(19,2391) = 56.41$; $p < .001$). In order of magnitude, the strongest predictors were: urinary symptoms ($\beta = .22$ $p < .001$), problems with anxiety/depression ($\beta = .18$, $p < .001$), treatment related symptoms ($\beta = .12$, $p < .001$), pain ($\beta = .10$, $p < .001$), bowel symptoms ($\beta = .06$, $p = .005$), a lower level of education at diagnosis ($\beta = -.05$, $p = .007$), and a greater number of comorbid conditions at diagnosis ($\beta = .04$, $p = .033$).

Discussion

Our results fit with a growing body of literature which suggests that sleep disturbance is a common problem for prostate cancer survivors [8,4] In spite of having a reasonably high quality of life, many survivors in our sample reported at least some difficulties sleeping, which is consistent with previous QLQC30 reference data for this group [36]. When compared to population norms [33] the mean insomnia score we observed ($M = 24$; $SD = 30$) was higher than that of males in the general population ($M = 19$; $SD = 27$). This implies that, in spite of a large variability in experience, sleep disturbance is a relatively common concern for prostate cancer survivors. We have shown that, although a number of predisposing and precipitating factors may put survivors at risk of sleep difficulties, the factors that we have classified as perpetuating factors, specifically the ongoing side effects of prostate cancer and its treatment, appear to have the strongest associations with sleep disturbance.

Physical side effects of cancer

Prostate cancer diagnosis and treatment can give rise to a range of physical adverse effects [1-3] and it is clear from the results of our study that many of these effects are

independently related to the experience of sleep problems. The strongest predictor here was urinary symptoms, which fits with a number of studies and reviews in the area [4]. It is likely that experiencing a more frequent need to urinate directly contributes to sleep problems owing to more night time waking [9].

Interestingly, although we initially found in step 2 of our model that survivors undergoing current ADT experienced higher levels of sleep disturbance, a result consistent with other work in the area [12], any differences in sleep difficulties between treatment groups disappeared when accounting for such side effects. These results go beyond the findings of previous studies to suggest that it is the adverse physical and psychological effects of prostate cancer and its treatment, rather than the treatment per se, that gives rise to problems sleeping. This highlights the importance of managing side effects for all prostate cancer survivors, regardless of treatment undergone. However, currently interventions and medications to manage side effects are not widely employed [37].

Related to this, it is also notable that another strong predictor of sleep difficulties was survivors' reported levels of pain. In the general population, longitudinal studies have similarly documented that those with a higher level of bodily pain are more likely to develop insomnia syndrome [23]. Other studies suggest that those in chronic pain have an average "sleep debt" of 42 minutes per week (defined as the difference between self-reported sleep duration and the quantity of sleep respondents felt they needed), in comparison to 14 minutes of sleep debt for those who did not suffer from pain [38]. The fact that pain predicted sleep problems in our sample, independently of other prostate specific symptoms, illustrates the importance of acknowledging this factor in the follow up treatment of survivors, including those who are up to 17 years post diagnosis.

Depression, anxiety and sleep disturbance

The second strongest associate with sleep difficulties in our sample was the experience of depression and anxiety, a finding consistent with a number of studies in the area. For example, within prostate cancer one study found that half of survivors with clinically significant depression also exhibited clinically significant insomnia [8]. More generally, other work has demonstrated that mental health, as opposed to physical health, better predicts chronic insomnia in a 7.5 year follow up [16]. Yet, while the relationship between insomnia and mental health has been well established, there is some disagreement as to whether higher levels of depression/anxiety lead to insomnia, or vice versa. For example, in one population-based longitudinal study of almost 25,000 participants [22] it was found that both depression and insomnia significantly predicted the later onset of the other disorder. Sleep difficulties can be viewed as both a symptom and a correlate of various psychological disorders and, given the cross-sectional nature of our study design, we cannot be sure of the direction of this relationship in our sample. It is possible that the co-occurrence of sleep disturbance and depression in cancer survivors may stem from specific biologic processes following treatment. In prostate cancer it has also been argued that sleep disturbances result from specific neurobiological mechanisms which may in turn lead to a greater likelihood of experiencing symptoms of depression [39].

Given that prostate cancer survivors are known to be at risk of depression and anxiety [40,41], it is also reasonable to presume that such factors in themselves could contribute to higher likelihood of night time waking. As with other cancers, prostate cancer survivors can experience fears of recurrence, a type of anxiety which can significantly impact on survivors' quality of life [42]. Some studies also suggest that cancer survivors are at risk of developing post-traumatic stress disorder (PTSD) following diagnosis and treatment [43]. Given the well established relationships between PTSD and insomnia [44] it seems likely that worsening mental health might lead to difficulties sleeping in this group. However, it is also important to acknowledge that insomnia often occurs independently of anxiety or depression in prostate

cancer [9]. Closer analysis of our results revealed that of those survivors who did not experience any problems with depression and/or anxiety, 10% still experienced significant sleep difficulties (defined as at least "quite a bit of trouble sleeping"). Conversely, 28% of those reporting problems with depression/anxiety experienced no sleep disturbance. This clearly illustrates that poor mental health is not the only factor associated with sleep difficulties.

Limitations

In considering our results, a number of limitations must be acknowledged. Firstly, for the purposes of this study, we conceptualised sleep disturbance simply as an individual's perceptions of whether they have any trouble sleeping. There are other more objective ways of assessing sleep difficulties and of establishing clinically significantly levels of insomnia [4], but this were beyond the scope of the current study. We did not take into account whether survivors took any sleep-inducting medications or indeed whether survivors had any previously diagnosed sleep disorder, both of which may have influenced the results. Also, older survivors may have been underrepresented in our study based on analysis of non-responders, and this group may be more likely to experience problems sleeping. Finally, the cross-sectional nature of the design means we must be cautious in interpreting the results, especially with respect to the temporal interpretation of our findings. Nevertheless, this study has a number of key strengths. Most notably, it involved a large population-based sample of survivors, including long term survivors, who had undergone a range of treatments for prostate cancer, and therefore can give insight into the associates of sleep difficulties in a range of individuals at different stages of survivorship.

Conclusions and implications

It is clear from the results of our study that many prostate cancer survivors exhibit problems sleeping. An important consideration for health care practitioners is therefore how

best to treat and manage symptoms of insomnia within this group. While many US cancer centres screen survivors for sleep disorders, very few conduct a thorough sleep evaluation [7]. Despite evidence that cognitive-behavioural therapy is the most effective treatment for insomnia [45], those that do attempt to treat insomnia in cancer tend to employ sleep hygiene and/or pharmacotherapy. Our findings suggest that, in treating sleep difficulties, health care practitioners should work to effectively manage both general and specific adverse effects of prostate cancer treatment, in addition to behavioural modification techniques.

In conclusion, we have shown how sleep disturbance is clearly associated with both the physical and psychological symptoms associated with prostate cancer. This further strengthens the need for practitioners to acknowledge and treat the adverse effects of treatment in order to better enhance survivor well-being.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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The authors declare they have no other conflicts of interest. The two PIs have full control of all the primary data collected and agree to allow the journal to review this if required. The dataset is not publicly available due to the fact that survivors never issued consent for their data to be made publicly available.

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Table 1: Descriptive statistics for sample

Categorical variables	No.	%
Marital status		
Married/cohabiting	2753	83%
Other	558	17%
Missing	*37*	*1%*
Total	**3348**	**100%**
Education		
Primary	1187	36%
Secondary (High School)	1122	34%
Third level (College/University or above)	899	27%
Missing	*140*	*4%*
Total	**3348**	**100%**
Employment status at diagnosis		
Employed/self-employed	1455	44%
Other	1689	51%
Missing	*204*	*6%*
Total	**3348**	**100%**
Children living at home		
Some children living at home	729	78%
No children living at home	*2619*	22%
Total	**3348**	**100%**
Disease extent at diagnosis		
Localised	1449	43%
Locally advancing/advanced	502	15%
Other	1244	37%
Missing	*153*	*5%*
Total	**3348**	**100%**
Treatment*		
RP	934	28%
ERBT	1718	51%
BT	183	6%
ADT past	912	27%
ADT current	657	20%
Watchful waiting	258	8%
* Note that treatment types are not mutually exclusive. Survivors could have undergone more than one of the above.		
Mobility (EQ5D)		
Problems	1086	33%
No problems	2118	63%
Missing	144	4%
Total	**3348**	**100%**
Self-care(EQ5D)		
Problems	419	13%
No problems	2798	84%
Missing	131	4%
Total	**3348**	**100%**
Usual activities (EQ5D)		
Problems	1184	35%

No problems	2019	60%
Missing	145	4%
Total	**3348**	**100%**
Pain (EQ5D)		
Problems	1236	37%
No problems	1962	59%
Missing	150	5%
Total	**3348**	**100%**
Anxiety/depression (EQ5D)		
Problems	939	28%
No problems	2239	67%
Missing	170	5%
Total	**3348**	**100%**

Continuous variables	**Mean**	**SD**	**Range**	**N**
Survivor age	71.57	7.94	37-95	3319
Time since diagnosis (years)	6.42	3.57	2-17	3348
Number of comorbidities	0.86	0.97	0-7	3348
Urinary symptoms (QLQ-PR25)	19.76	18.34	0-100	2653
Bowel symptoms (QLQ-PR25)	7.29	12.57	0-100	2783
Treatment related symptoms (QLQ-PR25)	10.62	12.80	0-100	2891
Sleep disturbance (Insomnia subscale of QLQ-C30)	23.57	30.18	0-100	3174

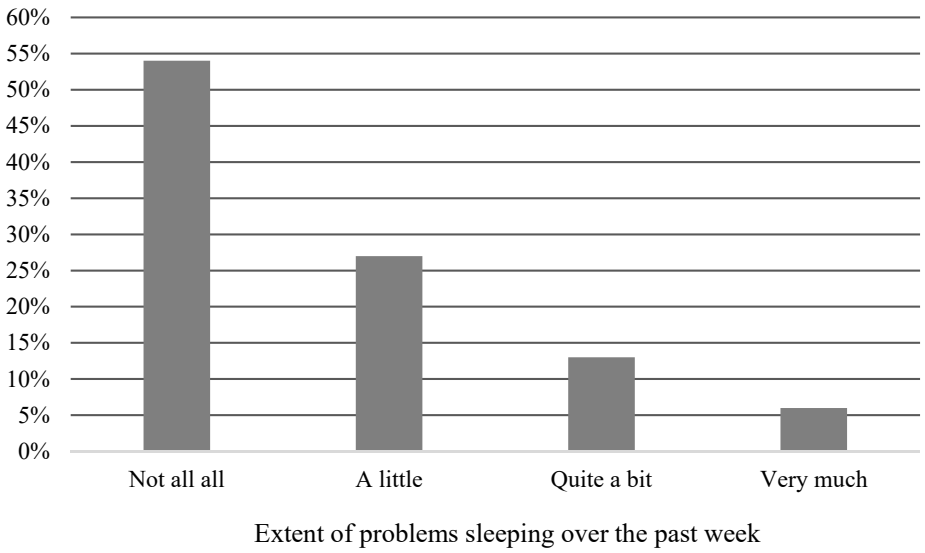

Figure 1: Proportion of survivors reporting the extent of problems sleeping (based on scores from the QLQ-C30 insomnia subscale)

Table 2: Hierarchical Multiple Regression Analysis

Variables	β	p	t	B	SE	CI95%	
Step 1: Predisposing factors							
Age	-.048*	.033	-2.139	-.181	.085	-.347	-.015
Marital status [other=0; married/cohabiting=1]	-.038	.056	-1.914	-3.084	1.611	-6.244	.076
Education level [higher = higher level of education]	-.093***	.000	-4.578	-3.497	.764	-4.994	-1.999
Children at home [no = 0; yes = 1]	-.054**	.007	-2.689	-3.979	1.480	-6.881	-1.077
Employment status [other=0; employed=1]	-.056*	.012	-2.512	-3.401	1.354	-6.056	-.746
Comorbidity [higher = more pre-existing conditions]	.173***	.000	8.564	5.377	.628	4.146	6.609
R^2 Change=0.052							
Step 2: Precipitating factors							
Age	-.095***	.000	-3.655	-.361	.099	-.555	-.168
Marital status [other=0; married/cohabiting=1]	-.039	.050	-1.958	-3.142	1.605	-6.288	.005
Education level [higher = higher level of education]	-.090***	.000	-4.445	-3.381	.761	-4.873	-1.889
Children at home [no = 0; yes = 1]	-.048*	.018	-2.359	-3.506	1.486	-6.420	-.591
Employment status [other=0; employed=1]	-.064**	.006	-2.766	-3.859	1.395	-6.595	-1.124
Comorbidity [higher = more pre-existing conditions]	.171***	.000	8.435	5.293	.628	4.062	6.523
Time since diagnosis in years [higher = greater time]	.042	.064	1.855	.354	.191	-.020	.728
Disease extent [higher = more advanced]	.051*	.015	2.436	2.129	.874	.415	3.842
Treatment RP [no = 0; yes = 1]	-.005	.856	-.181	-.352	1.947	-4.169	3.465
Treatment ERBT [no = 0; yes = 1]	-.012	.662	-.437	-.732	1.675	-4.018	2.553
Treatment ADT Previous	.037	.137	1.489	2.457	1.650	-.780	5.693
Treatment ADT Current	.108***	.000	4.486	7.866	1.754	4.427	11.304
R^2 Change=0.015							
Step 3: Perpetuating factors							
Age	-.033	.144	-1.461	-.126	.086	-.296	.043
Marital status [other=0; married/cohabiting=1]	-.020	.235	-1.188	-1.647	1.386	-4.365	1.072
Education level [higher = higher level of education]	-.046**	.009	-2.630	-1.735	.660	-3.029	-.441
Children at home [no = 0; yes = 1]	-.020	.249	-1.154	-1.484	1.286	-4.006	1.038
Employment status [other=0; employed=1]	-.031	.120	-1.554	-1.878	1.208	-4.246	.491
Comorbidity [higher = more pre-existing conditions]	.038*	.038	2.081	1.168	.561	.067	2.269

Time since diagnosis in years [higher = greater time]	.016	.415	.815	.134	.165	-.189	.458
Disease extent [higher = more advanced]	-.004	.837	-.205	-.156	.760	-1.647	1.335
Treatment RP [no = 0; yes = 1]	-.014	.571	-.566	-.955	1.686	-4.261	2.351
Treatment ERBT [no = 0; yes = 1]	-.022	.368	-.900	-1.311	1.457	-4.168	1.546
Treatment ADT Previous	.013	.571	.612	.880	1.438	-1.940	3.700
Treatment ADT Current	-.009	.676	-.418	-.667	1.596	-3.797	2.463
Urinary symptoms [higher = worse]	.218***	.000	10.188	.359	.035	.290	.428
Bowel symptoms [higher = worse]	.056**	.005	2.783	.135	.048	.040	.229
Treatment-related symptoms [higher = worse]	.115***	.000	5.242	.272	.052	.170	.374
Mobility problem [no problems = 0; problems = 1]	.029	.235	1.187	1.829	1.541	-1.192	4.851
Self-care problems [no problems = 0; problems = 1]	.018	.385	.870	1.658	1.906	-2.081	5.396
Problems with usual activities [no problems = 0; problems = 1]	.044	.073	1.792	2.758	1.539	-.260	5.776
Pain [no problems = 0; problems = 1]	.096***	.000	4.395	5.940	1.352	3.290	8.590
Anxiety/depression [no problems = 0; problems = 1]	.181***	.000	9.155	11.980	1.309	9.414	14.546
	R^2 Change=0.24						
	Adjusted R^2=0.31						