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REVIEW ARTICLE

Are we sleeping on the job? Insomnia among men with prostate cancer

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***Abstract*:** Prostate cancer is one of the most commonly diagnosed cancers in men and almost half of male cancer survivors in the US have had a prostate cancer diagnosis. Insomnia is common among cancer patients and survivors. There is evidence that cognitive behavioural therapy can be used to effectively manage insomnia among women with breast cancer. The aim of this review was to investigate the prevalence, risk factors and management of insomnia among men with prostate cancer. The effect of insomnia on the psychological health and health-related quality of life of these patients and/or survivors is also discussed. Increased awareness and knowledge of this symptom among men with prostate cancer may facilitate improved diagnosis, and management of insomnia in this large population. This in turn may improve the health-related quality of life of these men. Therefore, research into the effective management of insomnia among men with prostate cancer is essential.

***Keywords*:** prostate cancer; insomnia; androgen deprivation therapy; radiotherapy; health-related quality of life; depression; anxiety

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Introduction

Prostate cancer is the most commonly diagnosed cancer among men in Western countries. There will be an estimated 1.7 million incidences of prostate cancer globally by 2030[1]. The number of survivors is also rising, with 43% of male cancer survivors in the US having had a prostate cancer diagnosis[2]. Currently the 10- and 15-year relative survival of men with prostate cancer in the US is more than 90%[2]. These trends are attributed to the widespread use of prostate specific antigen (PSA) testing, which has resulted in men being diagnosed with prostate cancer at a younger age, and with less advanced disease[3-4], ageing populations and improved survival[5-7].

There is no consensus on the optimum treatment of men with localised disease[8,9]. Radical prostatectomy and radiotherapy are the most commonly used treatments for localised prostate cancer; active surveillance or watchful waiting are appropriate management strategies in some cases, and brachytherapy is becoming more common. Androgen deprivation therapy (ADT) is frequently used as a neo-adjuvant or adjuvant treatment, and as a primary treatment for older men and those with recurrent or more advanced cancer. Each treatment carries the potential for general and disease-specific adverse effects or symptoms, which can be acute or chronic, lasting throughout survivorship[3,10,11]. These symptoms can negatively affect the global health-related quality of life (HRQoL) of men with prostate cancer[3,8,10,12] and are associated with increased risks of depression, anxiety and distress among survivors[20]. Much of the focus has been on the physical disease-specific symptoms including urinary incontinence, sexual dysfunction and bowel problems experienced by men with prostate cancer, while more general symptoms including insomnia have received less attention in this patient group[3,8,10,11,14].

Insomnia or sleep disturbance is a common symptom,

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which affects cancer patients[21,29]. Insomnia is defined as difficulty initiating and/or maintaining sleep, or non-restorative sleep, lasting for at least one month and resulting in clinically significant daytime impairment or distress[30]. Insomnia often goes unrecognised, it can be poorly managed and has negative effects on the HRQoL of cancer patients[29,31,32]. The aim of this review was to investigate the prevalence, risk factors and management of insomnia among men with prostate cancer.

Methods

A search on PubMed was conducted using the terms ("sleep initiation and maintenance disorders" OR "sleep"[All Fields] AND "initiation"[All Fields] AND "maintenance"[All Fields] AND "disorders"[All Fields]) OR "sleep initiation and maintenance disorders"[All Fields] OR "insomnia"[All Fields] AND ("prostatic neoplasms" OR ("prostatic"[All Fields] AND "neoplasms"[All Fields]) OR "prostatic neoplasms"[All Fields] OR ("prostate"[All Fields] AND "cancer"[All Fields]) OR "prostate cancer"[All Fields]).

Findings from multi-cancer site studies, which included men with prostate cancer, were used if they presented prostate cancer-specific information[21,22,24-26]. However, studies that gave only the overall findings were excluded[23,27,28].

Results

Methodologies to assess insomnia among men with prostate cancer

There is no optimum method to measure or assess insomnia or sleep disturbances. Both subjective measurements (*e.g.*, questionnaires and sleep diaries) and objective measurements (*e.g.*, wrist actigraphy) have been employed to assess insomnia among men with prostate cancer.

The questionnaires most commonly used to measure insomnia include the Insomnia Severity Index (ISI), the Pittsburgh Sleep Quality Index (PSQI), the General Sleep Disturbance Scale (GSDS), the Athens Insomnia Scale (AIS) and the Medical Outcomes Study (MOS) Sleep Scale, all of which assess various aspects of sleep over a period of between one week and one month prior to the completion of the questionnaire[33-37]. A number of HRQoL instruments also assess sleep disturbances or insomnia as one of a number of possible symptoms experienced by people with cancer. One of the most commonly used is the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 which asks, during the past week '*Have you had trouble sleeping?*'[38]. The Insomnia Diagnostic Interview[39] and sleep diaries, as a repeated measure of sleeping patterns and habits, have also been used as subjective measures of insomnia[40]. The most common objective measurement of insomnia among men with prostate cancer is the wrist actigraphy, which measures sleep-wake circadian activity rhythms by recording movements to estimate a number of sleep parameters, including the total sleep time and number of nocturnal awakenings in a research environment or in the patient's own sleeping environment[41].

Prevalence of insomnia among men with prostate cancer

Insomnia or sleep disturbances among men with prostate cancer has been investigated in both cross-sectional and longitudinal studies (**Table 1**)[8,14,15,17,18,21,24,25,42-48].

Within cross-sectional studies, between 8% and 53% of men with prostate cancer were reported to experience insomnia[15,17,18,21,42-44]. Difficulties with both initiating and maintaining sleep have been described[42,44].

One of the largest cross-sectional studies described that the prevalence of clinical levels of insomnia was 32% among 861 men with localised prostate cancer, who were between 24 and 37 months post-treatment with radiotherapy, brachytherapy or radical prostatectomy[43]. Another study reported that almost one-third of 327 prostate cancer survivors (32%) also experienced insomnia between 4 and 10 years post-radical prostatectomy[42]. Both of these studies used the ISI to measure sleeping difficulties. One of the first studies to investigate the effects of prostate cancer on the HRQoL of men found that a similar proportion of the 172 men with prostate cancer investigated (*i.e.*, 29%) experienced insomnia as measured using the EORTC-QLQ-C30[17].

Davidson *et al.* observed lower rates, with 18% of 155 men attending genitourinary clinics (141 of whom had prostate cancer) having insomnia (including men who reported difficulty sleeping in at least 7 of the previous 28 nights) and consequent negative effects on daytime functioning, as measured by a Sleep Survey[21]. These men were approximately 4 years post-diagnosis and one-third were currently receiving treatment. The lowest prevalence of insomnia was reported by Lilleby *et al.*, in 1999; among 303 men in Norway, who were 1–10 years post-treatment, the prevalence of sleeping difficulties were 15%, 13% and 8% among men treated with radical prostatectomy, radiotherapy and watchful waiting, respectively[18].

The highest prevalence of clinically significant insomnia among men with prostate cancer was 53%, ob-

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Table 1. Prevalence of insomnia among men with prostate cancer

Year	Author	Country	Insomnia assessment instrument	Study design	Patients	Findings/Comment
2013	Bill-Axelson A *et al.*[8]	Sweden	Survey questions: During the past 6 months, (i) Have you had difficulty in sleeping at night? (ii) Have you taken sleeping pills?	Longitudinal: diagnosis to 8 years post-treatment	272 men with non-metastatic prostate cancer randomised to receive radical prostatectomy (N = 136) or watchful waiting (N = 136); Mean age 64 years	• Insomnia was consistently reported at 30%–40% in both treatment groups over 8-year follow-up
2002	Davidson JR *et al.*[21]	Canada	Sleep survey questionnaire	Cross-sectional	982 patients with cancer at mixed sites, of whom 141 had prostate cancer	• 18.1% of men with prostate cancer reported insomnia, and 14.8% were taking sleep medication. • Overall, initiation of insomnia coincided with cancer diagnosis in 48% of the cases and was chronic (>6 months) for 75% of cancer patients. • Those who were fatigued were 2.5 times more likely to have insomnia than others.
2009	Dirksen SR *et al.*[44]	USA	Insomnia Severity Index[34]	Cross-sectional	51 prostate cancer patients currently undergoing treatment; Mean age of 74 years, 51% had stage IV prostate cancer	• 53% had clinically significant insomnia; 45% had difficulty initiating sleep and 55% maintaining sleep; 37% had problems with both initiating and maintaining sleep. • Correlation was identified between radiation therapy and insomnia severity (r = 0.31, p = 0.03) and depression (r = 0.37, p = 0.01).
2005	Hervouet S *et al.*[43]	Canada	Insomnia Severity Index[34]	Cross-sectional	861 men with prostate cancer, 24–37 months post-treatment, treated with radical prostatectomy (N = 281), brachytherapy (N = 188) or radiotherapy (N = 392); Mean age = 68 years	• 31.9% had clinical levels of insomnia. • Prevalence of insomnia was highest post-radiotherapy (35%), intermediate at post-radical prostatectomy (30%) and lowest post-brachytherapy (29%). • Differences by treatment were not statistically significant.
2005	Jønler M *et al.*[15]	Scandinavian Prostate Cancer Group 5 (SPCG-5) study	EORTC QLQ-C30[39]	Cross-sectional	917 untreated patients with metastatic prostate cancer; Mean age = 72.5 years	• 20% experienced insomnia. • Insomnia was the third highest (worst) symptom score after fatigue and pain.
1994	Kornblith AB *et al.*[17]	USA	EORTC QLQ-C30[39]	Cross-sectional	172 prostate cancer patients and 83 spouses or partners; 55% treated with ADT, 28% with radical prostatectomy and/or radiotherapy only, 18% had not been placed on any treatment	• 29% and 37% of patients and spouses, respectively, reported sleep disturbances. • Insomnia was not associated with HRQoL of patients or survivors. Pain, fatigue and urinary problems did affect patients' HRQoL.
1999	Lilleby W *et al.*[18]	Norway	EORTC QLQ-C30[39]	Cross-sectional	Men with localised prostate cancer who had undergone radiotherapy (N = 154) and radical prostatectomy (N = 108) or men undergoing watchful waiting (N = 41) at least one year post-treatment	• 15%, 13% and 8% of patients treated with radical prostatectomy, radiotherapy and watchful waiting, respectively, reported sleep difficulties.

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Year	Author	Country	Insomnia assessment instrument	Study design	Patients	Findings/Comment
2011 (b)	Miaskowski C *et al.*[49]	USA	Pittsburgh Sleep Quality Index (PSQI) at baseline[35]. General Sleep Disturbance Scale (GSDS)[36] administered at each time point.	Longitudinal: at simulation visit, every other week for 6 weeks during treatment and 4 months post-treatment	82 patients with non-metastatic prostate cancer who underwent primary or adjuvant radiotherapy; Mean age = 67 years; 51% received ADT prior to the initiation of radiotherapy, 10% had radical prostatectomy prior to radiotherapy, 9.8% also had brachytherapy	• 24.4% displayed sleep disturbances on the GSDS at the simulation visit. • Self-reported sleep disturbance increased during radiotherapy specifically from weeks 1–9, and decreased following completion of radiotherapy. Inter-individual differences existed in the sleep trajectories. However, inter-individual differences existed in the sleep trajectories. None of the incremental increases in sleep disturbances reached clinical significance (*i.e.*, score $\geqslant$43) during the study. Predictors of higher levels of sleep disturbance included younger age, higher levels of trait anxiety and depressive symptoms and higher levels of sleep disturbance at the initiation of radiotherapy.
2005	Savard J *et al.*[42]	Canada	Insomnia Severity Index[34]	Cross-sectional	327 men with prostate cancer treated with radical prostatectomy between 4 and 10 years previously; 37% had surgery only or a combination of treatments (ADT 29%, ADT + radiotherapy 29%, radiotherapy 5%); Mean age = 66 years	• 31.5% of the patients reported non-specific sleep difficulties 20.5% (CI 95%, 16.3%–25.3%) reported taking sleep-promoting substance in the past month. • 18% met specific criteria for insomnia. Of those, 14% had trouble initiating sleep only, 34% had difficulty maintaining sleep and 52% had a mixed difficulty of initiating and maintaining sleep at least 3 nights per week; median duration of sleep difficulties was 59 months for 95%. 5% had sub-acute insomnia (1–6 months). • In most of these latter cases (95%), insomnia was chronic (duration of 6 months or more). Nearly half of the patients with insomnia reported the onset of their sleep difficulties following their cancer diagnosis. A similar proportion had no comorbid clinical levels of anxiety or depression. Risk factors for the presence of insomnia included a younger age, poor prognosis, presence of intestinal pain, depression and androgen blockade-related symptoms.
2009	Savard J *et al.*[24]	Canada	Insomnia diagnostic interview[33]	Longitudinal: perioperative phase (T1) and two months later (T2)	991 patients with non-metastatic cancer at mixed sites, scheduled to receive curative surgery; 269 patients (27%) had prostate cancer	• Prevalence of insomnia (syndrome and symptoms) among men with prostate cancer at T1 and T2 were 37.8% and 27.8%, respectively. • Prevalence of insomnia syndrome alone at T1 and T2 was 15.8% and 15.9% respectively among men with prostate cancer. • The highest rates of insomnia were found in breast cancer patients and the lowest rates were observed in prostate cancer patients.

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Year	Author	Country	Insomnia assessment instrument	Study design	Patients	Findings/Comment
2011	Savard J *et al.*[25]	Canada	Insomnia diagnostic interview[33]	Longitudinal: perioperative phase (T1), 2 (T2), 6 (T3), 10 (T4), 14 (T5) and 18 (T6) months post-surgery	962 patients with non-metastatic cancer at mixed sites, scheduled to receive curative surgery; 235 patients (24%) had prostate cancer	• Prevalence of insomnia among men with prostate cancer was between 36% (T1) and 25% (T6). • 15% (*N* = 36) of men had their first episode of insomnia during the study. 29% (*N* = 68) of men had insomnia, which was persistent for at least two consecutive time points; 36% (*N* = 84) had a remission from insomnia (for 29.8% the remission only lasted for one time interval); 13% (*N* = 30) had a relapse during the course of the study. • Prevalence of insomnia syndrome was quite constant throughout the study with between 12% and 15% of men with PCa experiencing insomnia syndrome.
2013	Savard J *et al.*[47]	Canada	Insomnia Severity Index[34]	Longitudinal: prior to treatment (T1, baseline); at 1, 2, 4, 6, 8, 12 and 16 months post-surgery	60 men with non-metastatic prostate cancer scheduled to receive radiotherapy with ADT (*N* = 28) or without ADT (*N* = 32)	• Insomnia scores were highest for those treated with ADT at baseline, 14% in the radiotherapy and 22% in the ADT-radiotherapy groups had a clinical score for insomnia. • Insomnia scores in men treated with ADT-radiotherapy increased throughout treatment. Differential effects of short- and long-term ADT use were observed. Insomnia scores increased from baseline to 6 months in long-term ADT users but began to decrease at 6 months in short-term ADT users. Effects of ADT on insomnia were mediated by frequent hot flashes and night sweats. The authors suggested a transient effect of ADT on insomnia; that men can adapt to the negative effect of ADT on sleep. Scores for insomnia were relatively low in radiotherapy patients (14% to 22%). Relationship between radiotherapy and insomnia was mediated most strongly by excessive urinary frequency.
2015	Savard J *et al.*[48]	Canada	Insomnia Severity Index[34]	Longitudinal, population-based epidemiological study	263 men with prostate cancer followed from baseline to 18 months post-recruitment	• ADT was related to increased insomnia, mediated through somatic symptoms, in particular night sweats. The highest ISI scores corresponded to the peak exposure to ADT.
2012	Zucca AC *et al.*[26]	Australia	EORTC QLQ-C30[39]	Cross-sectional	863 long-term survivors, 5 to 6 years post-diagnosis with cancer at mixed sites; 133 (15%) had prostate cancer	• 13.4% of men with prostate cancer had insomnia symptoms; lower than those with breast, lympho-hematopoietic, thyroid and other endocrine, head and neck, and lung cancer patients; higher than those with melanoma, colorectal, gynaecological and urogenital cancer. • 20.2% of men with prostate cancer experienced two or more symptoms.

*ADT: Androgen deprivation therapy; European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30

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served in a small study of older men (*N* = 51) with a mean age of 74 years[44]. More than half of these men (51%) had stage IV metastatic disease and they had received a range of treatments. In contrast, of 917 older men (mean age 72.5 years) with untreated metastatic prostate cancer, who took part in the Scandinavian Prostate Cancer Group study, 20% experienced insomnia[15].

Several studies used objective measures to assess insomnia among men with prostate cancer[27,45]. Hanisch *et al.* found that the total sleep time of 60 prostate cancer patients undergoing ADT was 5.9 h and the sleep efficiency, *i.e.* the ratio of time asleep to the time in bed, was 75% as measured by wrist actigraphy[45]. Miaskowski *et al.* reported that approximately 30% of cancer patients (*N* = 185) at mixed sites (44% with prostate cancer) did not sleep well as defined by a sleep efficacy of <80%. However, specific results of men with prostate cancer were not reported[27]. Both studies found poor concordance between actigraphy measures and subjective measures of sleep[27,45].

Prevalence of insomnia syndrome among men with prostate cancer

One cross-sectional study reported that 18% of prostate cancer survivors (up to 10 years post-radical prostatectomy) suffered from the more serious condition, that is insomnia syndrome[42]. Insomnia syndrome was defined by the authors as: (a) difficulty initiating (*i.e.*, 30 min or more to fall asleep) or maintaining sleep (*i.e.*, 30 min or more of nocturnal awakenings); (b) these difficulties occur at least three nights per week; and (c) sleep disturbance causing significant daytime impairment (*e.g.*, fatigue, mood disturbances) or marked distress in the month prior to questionnaire completion.

Changes in the prevalence of insomnia among prostate cancer patients throughout the disease trajectory

Longitudinal studies reported changes in the prevalence of insomnia throughout the disease trajectory, from cancer diagnosis to the period during which men with prostate cancer underwent treatment(s) and post-treatment[8,24,25,47-50].

Among 269 men with non-metastatic prostate cancer scheduled to receive radical prostatectomy, the highest prevalence of insomnia was in the time between receiving a prostate cancer diagnosis and having surgery, when 38% of men had insomnia, as assessed by an Insomnia Diagnostic Interview[24]. Prevalence of insomnia decreased throughout the study to 25% at 18 months post-diagnosis[25]. Of these, approximately 15% experienced insomnia syndrome, and rates of insomnia syndrome were relatively stable throughout the 18 months follow-up study[24,25].

The authors identified a number of different sleep trajectories throughout the cancer care pathway. Among prostate cancer patients who were good sleepers at diagnosis, between 87% (14 months post-recruitment) and 93% (18 months post-recruitment) remained good sleepers; for those who had insomnia symptoms at diagnosis, between 18% (2 months post-recruitment) and 44% (18 months post-recruitment) continued to have insomnia symptoms; and of those who had insomnia syndrome at diagnosis, between 64% (6 months post-recruitment) and 87% (14 months post-recruitment) continued to experience insomnia syndrome[24,25]. However, sleep trajectories were individual and men frequently alternated between sleeping states during the study, experiencing both insomnia remission and relapses between time points. Overall, the rates of insomnia persistence, remission and relapse among men with non-metastatic prostate cancer was 29%, 36% and 13% respectively during the first 18 months of the cancer trajectory post-surgery.

Similarly, insomnia was found to increase during radiotherapy and to decline upon treatment completion and up to 4 months post-treatment[49,50]. Miaskowski *et al.* observed that among 82 men who received either primary or adjuvant radiotherapy for non-metastatic prostate cancer, 24% experienced insomnia prior to treatment initiation[49]. Again, considerable inter-individual differences in sleep trajectories were observed throughout the study period.

However, it is not uncommon for men to receive more than one treatment modality, for example, neo-adjuvant or adjuvant ADT and radiotherapy. One group attempted to dissect the discrete effects of individual treatments and treatment combinations on insomnia[47,48]. Among 60 men with non-metastatic diseases treated with radiotherapy or ADT with radiotherapy, the prevalence of insomnia at baseline (22% and 14%, respectively) and throughout treatment was higher among those who received ADT and radiotherapy compared to those treated with radiotherapy only (mean 35% and 17%, respectively)[47]. In a recent study, ADT was found to be related to increased insomnia among 263 men with non-metastatic prostate cancer; with the highest prevalence at 39%, coinciding with the greatest exposure to ADT[48].

In contrast, in a randomised controlled trial of 347 men who were recruited to the Scandinavian Prostate Cancer Group-4 trial and who received either radical prostatectomy or watchful waiting, 30%–40% of men in both treatment groups consistently had insomnia up to 8 years post-treatment[8].

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These studies demonstrate that while the prevalence of insomnia decreases post-treatment, insomnia is a chronic condition for many men with prostate cancer, which lasts long into survivorship[8,14,18,21,25,42-49].

Prevalence of insomnia among partners and spouses of men with prostate cancer

One cross-sectional study investigated the prevalence of insomnia among spouses and/or partners of men with prostate cancer. In the US, Kornblith *et al.* reported in 1994 that 37% of the 83 participating spouses experienced insomnia or sleep disturbances, which was higher than that experienced by their partners with prostate cancer (29%)[17].

Insomnia and different cancer sites

Insomnia is associated with different cancer sites to variable degrees[51]. In studies directly comparing different cancer sites, the prevalence of insomnia was lower in men with prostate cancer than in women with breast cancer, as well as among men and women with colorectal, lung, head and neck cancers[22,24,26]. In contrast, the prevalence of insomnia syndrome was similar among men with localised prostate cancer (18%) and women with breast cancer (19%)[42].

Furthermore, among patients with advanced cancer, a diagnosis of prostate, breast, lung, and gastrointestinal cancer was associated with increased likelihood of insomnia[28]. Insomnia among prostate cancer patients was also reportedly higher than in the general population[19].

Risk factors for the development of insomnia among men with prostate cancer

Within cancer populations, risk factors associated with insomnia have been categorised as: (i) predisposing factors (including increasing age, family and/or personal history, and high trait anxiety particularly the hyperarousability trait), (ii) precipitating factors (*e.g.*, a stressful event including cancer diagnosis, as well as disease factors, treatment symptoms and stress), and (iii) perpetuating factors (behavioural and cogitative factors), which contribute to the maintenance of insomnia[51].

Predisposing factors

Age

Unlike populations without cancer, insomnia is inversely related with age in patients with cancer at mixed sites[21,23,28,44] and also among men with prostate cancer[42,49]. Younger men are also more likely to develop insomnia syndrome[42], suggesting that younger men may have more trouble adjusting to their 'new normality' and consequently, are more susceptible to chronic sleeping difficulties.

Marital status

Unmarried men are at a higher risk of experiencing insomnia[42,49].

Psychological health and insomnia

The relationship between psychological health and insomnia is not completely understood. Men with prostate cancer who experience poor psychological health including anxiety, depression and distress more often experience insomnia[8,21,42,44,49]. For example, men with prostate cancer with high trait anxiety have been found to have a higher prevalence of insomnia[42,49]. There is also evidence of an increased risk of insomnia among men with depression[42,44,49]; 52% of prostate cancer patients with insomnia in one study had clinically significant depression[44]. However, similar proportions of men with and without these negative emotional states experienced insomnia in another study[42]. Furthermore, insomnia is one of the symptoms observed to increase the risk of anxiety and depression among prostate cancer survivors[20]. The relationship between depression, anxiety and distress on the development and maintenance of insomnia among men with prostate cancer may be bi-directional and requires further research.

Different coping styles have been shown to predict sleeping patterns in patients with breast and prostate cancer. Avoidance coping is predictive of worse sleep, whereas approach coping is predictive of better sleep among men with prostate cancer (N = 23) who were treated with radiotherapy[50].

Personal history of insomnia

Men with sleeping problems at diagnosis were more likely to consistently have sleeping problems throughout the cancer care trajectory[8,24,25].

Precipitating factors

Cancer diagnosis

Being diagnosed with cancer is a stressful event. In retrospective studies, a high proportion of men reported that their insomnia coincided with their prostate cancer diagnosis[21,24,25,42]. One such study described that the onset of symptoms was secondary to prostate cancer diagnosis in

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54% of men experiencing insomnia syndrome[42]. The majority of longitudinal studies described the highest prevalence of insomnia, or highest insomnia scores indicating worse symptomology, at the time point closest to diagnosis[23-25,49]. In one longitudinal study, 15% of the men reported that their first episode of insomnia coincided with their diagnosis[24,25]. In addition, in studies reporting on the differential effects of cancer stages on insomnia, a worse prognosis is a risk factor for insomnia[42].

Cancer treatment

As described above, prostate cancer treatments have differential effects on insomnia among patients and survivors. In a large population-based study of 3,348 prostate cancer survivors, insomnia was experienced by men treated with ADT, radiotherapy, active surveillance/watchful waiting, radical prostatectomy and brachytherapy up to 18 years into survivorship[14]. However, insomnia was consistently reported to be higher in men treated with ADT or radiotherapy or a combination of these modalities[14,25,44,45,47-50].

The effects of various treatments on the initiation and maintenance of insomnia have been shown to be mediated through the treatment side effects experienced by men with prostate cancer, particularly night sweats/hot flashes and nocturia[27,28,42,45,47,48]. An interaction between these symptoms has also been proposed whereby when men wake up due to night sweats, they also empty their bladder, thus prolonging the length of time they are awake at night[47]. Other common symptoms that have been shown to increase risk of insomnia are pain and intestinal problems[42]. While there is some evidence that men can adapt to the adverse effects of ADT on insomnia[47], the management of insomnia may be improved by a greater use of interventions to treat the adverse effects experienced by men following their diagnosis of, and treatment for prostate cancer.

Perpetuating factors

New behaviours that begin following a cancer diagnosis and during treatment, including day time napping, sleep monitoring and unhelpful beliefs about sleep, all contribute to the maintenance of insomnia into survivorship[42].

Impact of insomnia on men with prostate cancer

HRQoL

In studies investigating the HRQoL of men with prostate cancer, insomnia is consistently the symptom that receives the highest score[19] or one of the highest scores, indicating worse symptomology[8,12,14,15,23,26]. Higher symptomology is associated with lower HRQoL among men with prostate cancer into survivorship[14]. However, not all studies found that sleeping difficulties negatively affected general HRQoL[17,47]. Kornblith *et al.* found that pain, fatigue and urinary problems, but not insomnia, were associated with HRQoL among 172 prostate cancer patients[17]. Daytime fatigue and low energy have been commonly associated with insomnia among cancer patients, including men with prostate cancer[21,27,32,44,47,49] and are negatively associated with many HRQoL subscales[49].

Insomnia and risk of prostate cancer mortality

There is some evidence that baseline HRQoL domains including insomnia are predictive of survival among men with prostate cancer[12,13,22]. Insomnia, as part of a symptom cluster including pain and fatigue, is associated with more adverse outcomes in older cancer patients[22]. However, HRQoL domains did not add to the ability of predictive models which included biochemical and clinical data[13].

A large prospective study of 305,057 men in the US found that neither insomnia nor work schedule (*i.e.*, rotating and fixed shifts) were associated with prostate cancer mortality over a 28-year follow-up[52]. However, the adjusted relative risk (RR) of fatal prostate cancer was significantly higher among men who slept for 3–5 h (RR 1.64, 95% confidence intervals (CI) 1.06, 2.54) and 6 h (RR 1.28, 95% CI 0.98, 1.67) per night, compared to those who slept for 7 h per night during the first 8 years of follow-up. The authors suggested that a short sleep duration could affect the later stages of prostate carcinogenesis.

Management of insomnia among men with prostate cancer

Pharmaceutical management of insomnia among men with prostate cancer was not uncommon, with between 20% and 25% of cancer patients regularly take sleeping pills[21,42,53,54]. However, in many cases this management

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is unsuccessful with levels of insomnia remaining high[44,53].

Behavioural therapy in the form of individualised sleep plans, stimulus control, relaxation training and sleep restriction have been used to manage insomnia in cancer populations[55]. However, cognitive behavioural therapy (CBT) aimed at changing beliefs and attitudes about insomnia in conjunction with behavioural therapy, is considered the gold standard, non-pharmaceutical management of insomnia. CBT has been found to successfully improve many dimensions of insomnia including increased sleep effectiveness, and reduced sleep latency, nocturnal awakenings and insomnia severity in cancer patients who received CBT compared to those who did not[56-58]. A recent systematic review concluded that the quality of the evidence supported a strong recommendation for the use of CBT among cancer survivors experiencing insomnia[58]. CBT interventions also had a positive effect on daytime fatigue, at least in the short term[57]. However, the majority of these studies have been undertaken among women with localised breast cancer[55,56,58].

Three randomised controlled trials (RCT) investigating the effect of CBT on insomnia included men with prostate cancer. Of these, Garland *et al.* included 8 men with prostate cancer (7% of total)[59] and Ritterband *et al.* included 4 men[60], but the cancer site was not identified and neither trial presented results specifically for men with prostate cancer. One RCT encompassed 150 patients with cancer at mixed sites including men with prostate cancer (N = 34; 23%) suffering from insomnia for at least 6 months[53]. This intervention involved 5 small group CBT sessions, which were delivered by an oncology nurse with specialist training. This intervention was successful up to the final measurement time point 6 months post-intervention, at reducing sleep latency and nocturnal awakenings, and at increasing sleep efficacy measured both subjectively and objectively. A mean reduction in insomnia symptoms of almost 1 h was observed in the CBT group compared to the usual treatment group. More than half (51%) of the CBT arm achieved the criterion for normal sleep compared to 34% in the control group following treatment, but this difference was not observed at the 6-month follow-up. Those in the CBT group also had increased HRQoL outcomes, including decreased fatigue, anxiety and depression post-treatment and at follow-up compared to the control group. However, results by cancer site were not reported; therefore, it is unknown whether this CBT intervention was effective in men with prostate cancer.

Discussion

This review illustrates that insomnia is common among men with prostate cancer, affecting 8%–53% of men during the cancer care trajectory, from diagnosis up to 18 years post-diagnosis. However, studies investigating the prevalence of insomnia and/or factors associated with insomnia or sleep disturbances within this cancer population were very heterogeneous with regard to the study design, instruments used to investigate insomnia prevalence and the age, cancer stage, treatment received, and time point during the cancer trajectory of the study participants. In addition, many of the studies involved a relatively small number of participants. It is likely that these differences explain the wide variation in the prevalence of insomnia reported in this cancer group. It also makes it difficult to draw conclusions regarding risk factors for the development and maintenance of insomnia.

Despite this, some trends are suggested. For many men, insomnia begins with their prostate cancer diagnosis. Younger men with prostate cancer are more likely to experience insomnia, which is contrary to those without cancer. This suggested that younger men may find it more difficult to adjust to their new normality[61], which may involve multiple adverse effects from their prostate cancer diagnosis and/or its treatment including impotence, urinary incontinence, bowel symptoms and fatigue. Furthermore, younger men are more likely to have dependents, mortgages and to be in employment. Their working life may be disrupted with long periods of sick leave and/or early retirement with consequent changes in their financial circumstances, all of which are associated with financial stress and strain among men with prostate cancer[62]. All of these factors can result in an altered self-image and changes in intimate relationships[61].

Men who received treatment were more likely to experience insomnia than those who were untreated, including those with metastatic prostate cancer. Insomnia has been found to be high prior to surgery, and during treatment, especially during radiotherapy as well as ADT, with slight decreases in the prevalence of insomnia post-treatment. There is less information on the effect of other treatments, including brachytherapy, on insomnia. However, insomnia is also common during survivorship[14]. The effects of various treatments on the initiation and maintenance of insomnia is likely to be mediated, at least in part, through the adverse effects of treatment. Two such common adverse effects, night sweats/hot flashes and nocturia, cause night time waking[27,28,42,45,47,48]. These symptoms have also been proposed to have an additive effect whereby when men wake up due to night

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sweats, they may also empty their bladder, thus prolonging the length of time they are awake at night and possibly making it more difficult to resume sleep[47]. Some men can adapt to the adverse effects of ADT[47]; however, the management of insomnia may be improved by treating adverse treatment side effects with greater use of interventions such as the cool pad pillow topper, which reduces the frequency/severity of hot flushes and sleep disturbance among women, and a greater use of incontinence medication (*e.g.*, tolterodine)[47,63].

Men with a personal and/or family history of insomnia, those who experience distress, anxiety and/or depression, and men with later stages of cancer are at an increased risk of insomnia. The spouses/partners of these men may also be at a higher risk of insomnia; however, its prevalence will have to be investigated further. More research into the risk factors of insomnia is required, along with the effects of insomnia on cancer outcomes, where trends towards worse outcomes were observed among men with prostate cancer who experience insomnia.

Currently, up to one-quarter of men with prostate cancer who experience insomnia are being managed pharmacologically, but this is not necessarily effective as evidenced by the persistent high levels of insomnia. CBT has been shown to effectively manage insomnia in some cancer populations. However, despite the high incidence and prevalence of prostate cancer, there is a dearth of research into the management of insomnia in this cancer population. Development of interventions to manage this distressing symptom is required.

Conclusion

Insomnia is common among men with prostate cancer undergoing treatment and also into survivorship. More than 20% of men with prostate cancer who experience insomnia are prescribed hypnotic medication. Prostate cancer treatment modalities have differential effects on insomnia; men treated with ADT experience the highest prevalence of insomnia but the incidence is also high among those who receive radiotherapy. Those most at risk include men with a history of insomnia, younger men, unmarried men, and those experiencing adverse effects (particularly night sweats and urinary problems such as nocturia) following their diagnosis and treatment. Insomnia is associated with lower HRQoL and has negative effects on the psychological health of survivors. CBT has been shown to successfully manage cancer-related insomnia in women with breast cancer. However, despite the burden of prostate cancer to men, research into the management of insomnia among men with prostate cancer is lacking. Increased use of interventions to manage treatment side effects and the development of CBT interventions to manage insomnia are necessary to address insomnia in this large cancer population. This in turn may lead to an improvement in the HRQoL and psychological health of men with prostate cancer into survivorship.

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Conflict of interest

The author declares no potential conflict of interest with respect to the research, authorship, and/or publication of this article.

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