Meta-Analysis of Observational Studies in Epidemiology

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The association between sleep duration and prostate cancer

A systematic review and meta-analysis

Ranlu Liu[a,b,*], Shangrong Wu[a,b], Baoling Zhang[a,b], Mingyu Guo[a,b], Yang Zhang[a,b]

Abstract

The association between sleep duration and prostate cancer (PCa) risk is still unclear. We performed a systematic review and meta-analysis to explore if sleep duration is associated with PCa in men.

A comprehensive literature search was conducted in November 2019 based on the Pubmed, Embase, and Cochrane databases. After extracting the data, the random effects model was used to calculate the pooled Risk Ratio (RR) and it's 95% confidence interval (CI) to represent the correlation between sleep duration and PCa risk.

Overall, we included 6 studies in our meta-analysis. Our pooled results showed that neither short sleep (RR = 0.99; 95%CI:0.91-1.07, $P = .74$) nor long sleep (RR = 0.88; 95%CI:0.75-1.04, $P = .15$) was associated with the risk of PCa.

Sleep duration has no significant effect on PCa risk. Long sleep may have a potential protective effect on PCa incidence.

Abbreviations: CI = confidence intervals, NOS = Newcastle-Ottawa score, PCa = prostate cancer, RR = risk ratio.

Keywords: prostate cancer, sleep duration, meta-analysis

1. Introduction

Prostate Cancer (PCa) is the most common cancer among men and the second most common fatal cancer among men in the United States.[1] PCa is a hormone - regulated tumor. Androgens play an important role in the development of tumors. Many factors might be associated with the risk of PCa. A number of factors can be used to build mathematical models for the prediction and diagnosis of PCa, such as age, pentraxin 3, prostate-specific antigen, absence of bladder outlet obstruction, etc.[2,3] While sleep is very important for physical and mental health.[4] Sleep duration, quality of sleep, and so on might be related to the development of some diseases.[5,6]

Many studies have shown an association between sleep duration and cancer, although their conclusions are inconsistent.[7–9] To date, we still don't know the relationship between sleep duration and PCa risk. Therefore, we conduct a systematic review and a comprehensive meta-analysis in order to further investigate this issue.

2. Materials and methods

This meta-analysis was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement guidelines strictly.[10] All data used in this article were from the original article and had previously been ethically approved. So ethical approval was not necessary for our article.

2.1. Literature search

We performed a comprehensive literature search based on Pubmed, Embase, and Cochrane databases. The retrieval time limit is from the beginning of database construction to November 29, 2019. There is no restriction on the retrieval language. The flow diagram is shown in Figure 1. The retrieval algorithm is as follows: ("sleep") ("prostate cancer" or "prostate neoplasm" or "prostate carcinoma"). At the same time, the references included in the literature were searched to supplement the relevant literature.

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This article does not contain any studies with human participants or animals performed by any of the authors.

For this type of study, formal consent is not required. Consent for publication All authors consent this article for publication.

All data generated or analyzed during this study are included in this published article.

Ranlu Liu, Degree of Doctor of Medicine

Shangrong Wu, Baoling Zhang, Mingyu Guo, Yang Zhang, Degree of Bachelar of Medicine

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The datasets generated during and/or analyzed during the current study are publicly available.

[a] *Department of Urology, The Second Hospital of Tianjin Medical University,* [b] *Tianjin Institute of Urology, Tianjin, China.*

[*] *Correspondence: Ranlu Liu, Department of Urology, The Second Hospital of Tianjin Medical University, Tianjin, China (e-mail address: m18822321838@163.com).*

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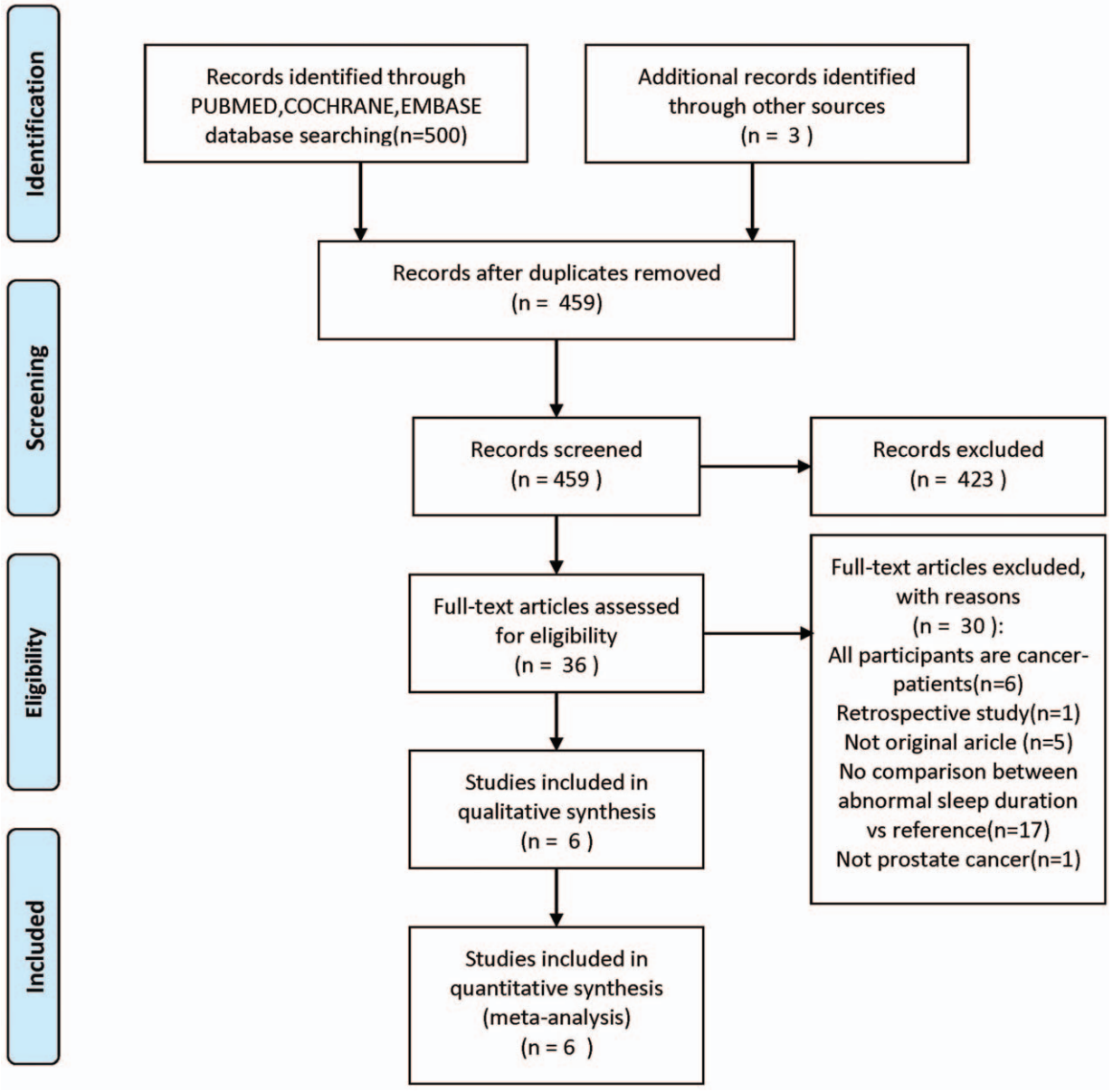

Figure 1. Literature search for the meta-analysis.

2.2. Selection criteria

The following modified PICOS guided eligibility screening of studies:

(1) participants: adult population;
(2) intervention: not applicable;
(3) comparisons: exposure group vs reference group (short or long sleep duration as the exposure of interest);
(4) outcomes: morbidity of PCa as the outcome of interest; reported the relative risk (RR), hazard ratio or odds ratio, and 95% confidence intervals (CIs) for the association between the sleep duration and PCa risk.
(5) study design: prospective study.

Studies were excluded if they

(1) had duplicated data;
(2) were reviews, reports, animal experiments, or genetic and cell studies; or
(3) had insufficient data.

2.3. Quality assessment

Four independent reviewers (S Wu, B Zhang, M Guo, and Y Zhang) used the Newcastle-Ottawa Scale (NOS) to assess the quality of studies.[11] NOS is a 9-star system, which includes 3 dimensions: selection (4 items), comparability (1 item), and exposure/outcome (3 items). Studies of 1 to 3 stars were categorized as low quality, 4 to 6 stars as moderate quality and 7 to 9 stars as high quality.

2.4. Data extraction

Data is extracted independently by 4 reviewers (S Wu, B Zhang, M Guo, and Y Zhang) and conflicts are resolved through discussion during the data extraction process. Data were

extracted using a predeveloped worksheet: author, year of publication, country of study, study design, number of patients, sleep reference category; category for "short" and "long" sleep duration, the RR, OR or hazard ratio for PCa risk for both short and long sleep duration; corresponding 95% CI, follow-up time, and NOS scores.

2.5. Statistical methods

STATA 12.0 software was used for analysis. For studies that reported separate effect size estimates for the risk of PCa, we combined these risk estimates within each study, weighted by the inverse of the variance. RR values were used to assess the risk of morbidity between the exposure group and the reference group. The analysis results were presented in the form of 95%CI. Heterogeneity was examined by Cochrane Q statistical method (the level of significance was set at 0.1)[12] and evaluated by I^2. The smaller the I^2 value, the smaller the heterogeneity. A P value $<.1$ for Cochran Q and $I^2>50\%$ were used as a cut-off for significant heterogeneity.[13] In order to increase the CI of the results, the DerSimonian and Laird random effects model were used for analysis in this study.

In the sensitivity analysis, the meta-analysis was re-conducted after omitting each study in turn. Publication bias shall be detected by Egger test and Begg test.[14]

3. Results

3.1. Study searches and characteristics

The detailed process of literature search is shown in Figure 1. A total of 6 eligible studies[15–20] were eventually included in this meta-analysis. All of the studies were designed as cohort studies. Quality scores evaluated by the NOS ranged from 6 to 8. The reference categories of sleep duration in each study were classified as 7 hours,[19] 7 to 8 hours,[16–18,20] 8 hours.[15] The main characteristics of all included studies have been summarized in Table 1.

3.2. Sleep duration and PCa risk

We analyzed the relationship between sleep duration and PCa risk from 6 studies. The relationship between short sleep and PCa risk is shown in Figure 2A. The relationship between long sleep duration and PCa risk is shown in Figure 2B.

Obviously, the pooled results showed that the short sleep was not associated with PCa risk (RR = 0.99; 95%CI:0.91-1.07, $P=.74$) and the long sleep was not associated with PCa as well (RR = 0.88; 95%CI:0.75-1.04, $P=.15$). In the aspect of heterogeneity, the pooled results of the 6 studies we included were of low heterogeneity for short sleep ($I^2=0\%$, $P_{Heterogeneity}=.53$, Figure 2A) and significant heterogeneity for long sleep ($I^2=56.2\%$, $P_{Heterogeneity}=.04$, Figure 2B). To explore the sources of heterogeneity, we stratified the studies by region subtypes. The results showed that neither short nor long sleep was associated with PCa for different people from different regions (Table 2).

3.3. Sensitivity analysis and publication bias

Sensitivity analysis demonstrated that no individual study influenced the overall results for short sleep (Fig. 3A) and long

Table 1

We included 6 similar observational studies and recorded the number of characteristic.

Study(year)	Country	Design	sleep duration	No. of total paticipants	No. of Pca patients	Reference category	Short duration of sleep	Long duration of sleep	follow-up time(years)	NOS score
Kakizaki2008	Japan	Prospective cohort	≤6	2671	21	7-8 h	≤6 h	≥9 h	6(1995-2001)	7
			7-8	15127	87					
			≥9	4522	19					
Gapstur2014	America	Prospective cohort	3-5	9891	155	7 h	3-5 h	10-12 h	28(1982-2010)	7
			6	51997	801					
			7	119827	1859					
			8	108766	1842					
			9	11899	226					
			10-12	2809	46					
Markt2015	Sweden	Prospective cohort	<5	533	43	8 h	≤5 h	≥9 h	13(1997-2010)	7
			6	4106	201					
			7	5571	332					
			8	2559	193					
			≥ 9	207	16					
Dickerman2016	Finland	Prospective cohort	<7	1744	99	7-8 h	<7 h	>8 h	30(1981-2012)	6
			7-8	7771	405					
			>8	1653	92					
Markt2016	America	Prospective cohort	<5	701	99	8 h	<5 h	≥10 h	23(1987-2010)	8
			6	6257	752					
			7	15220	1894					
			8	8328	1235					
			9	1432	246					
			≥10	203	35					
Gu2016	America	Prospective cohort	<5	4302	299	7-8 h	<5 h	≥9 h	11(1995-2006)	8
			5-6	53099	4076					
			7-8	109976	9199					
			≥ 9	5950	470					

NOS = Newcastle-Ottawa Scale, Pca = prostate cancer.

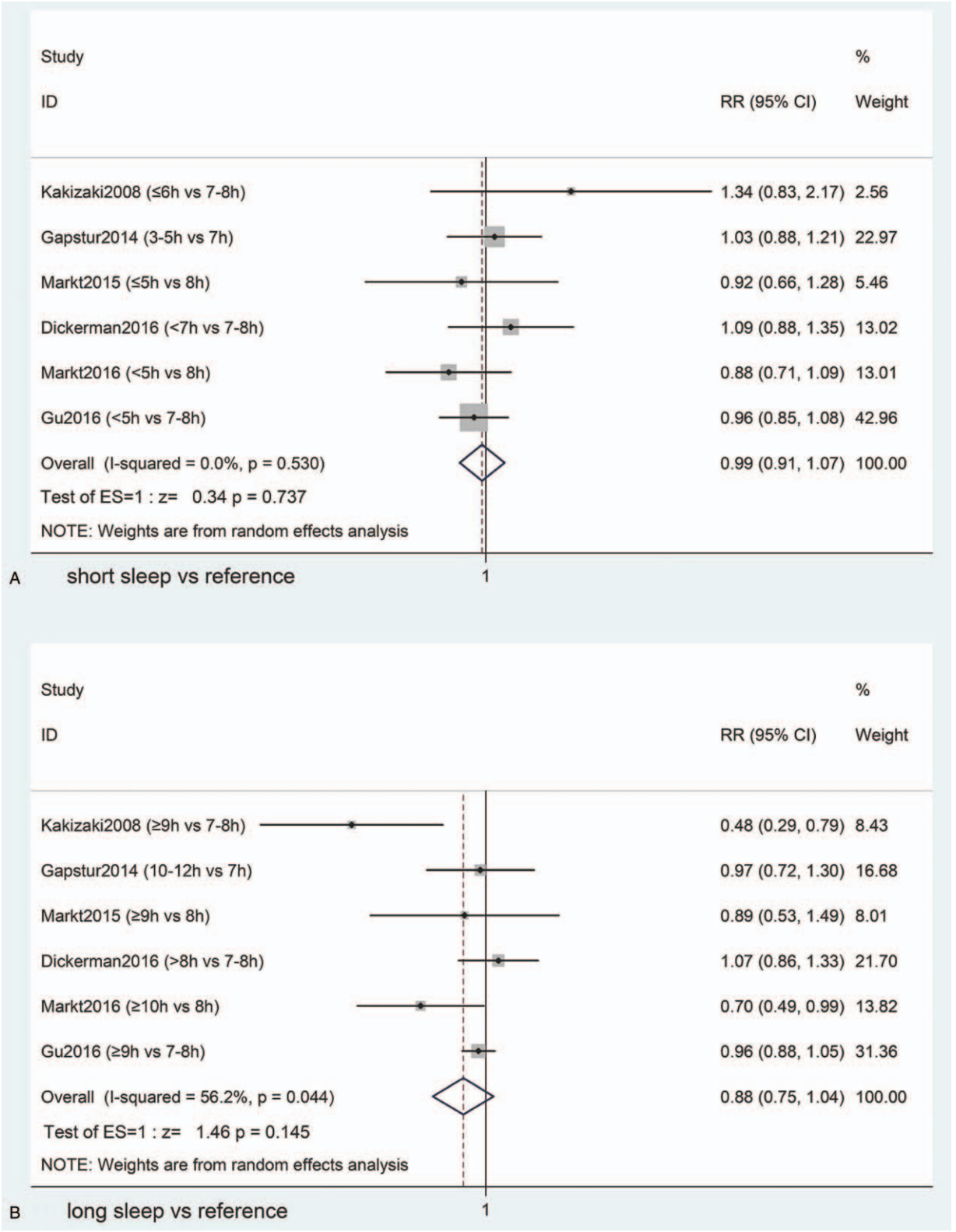

Figure 2. Forest plot for the association of sleep duration and prostate cancer mortality.

sleep (Fig. 3b). There was no evidence of publication bias in this meta-analysis for short sleep (Begg tests: $P = .45$; Egger tests: $P = .46$, Fig. 4A) and for long sleep (Begg tests: $P = .24$; Egger tests: $P = .13$, Fig. 4B).

4. Discussion

This study incorporated 6 available published cohort studies and provided a qualitative estimate of the association between sleep duration and PCa risk. After integrating all the available

Table 2

Subgroup analyses for the effect of sleep duration on risk of prostate cancer.

Subgroup	Author and Publication year of study	RR(95%CI)	*P* value	Heterogeneity	
				I^2	$P_{Heterogeneity}$
Asia					
Short sleep	Kakizaki2008	1.34(0.83,2.17)	.233	–	–
Long sleep		0.48(0.29,0.79)	.004	–	–
America					
Short sleep	Gapstur2014, Markt2016, Gu2016	0.97 (0.89,1.05)	.399	0.0%	.509
Long sleep		0.92 (0.79,1.07)	.258	33.9%	.220
Europe					
Short sleep	Markt2015, Dickerman2016	1.04 (0.87,1.24)	.693	0.0%	.398
Long sleep		1.04 (0.85,1.27)	.697	0.0%	.519

evidence, we found that neither short (RR = 99; 95%CI:0.91-1.07; $P = .74$) nor long(RR = 0.88; 95%CI:0.75-1.04, $P = .15$) sleep duration was associated with PCa.

Reviewing previous studies, Kakizaki et al[17] showed an increased but not statistically significant risk of PCa in men who slept less than 6 hours per night. Another study[19] showed that short sleep (3-5 hours) was associated with an increased risk of PCa during the first 8 years of follow-up, compared to 7 hours of sleep per night. But after 28 years of follow-up time, the final results of this study[19] showed that sleep duration was not associated with PCa risk. Given that the follow-up time of Kakizaki et al was only 6 years, we suspect that their conclusions would have changed if they had been followed longer. In fact, most studies[15,16,19,20] showed that short sleep was not associated with PCa risk, which supported our conclusion. In our subgroup analysis of the region factor, the results showed that short sleep was not associated with PCa risk in any region of the world. For long sleep duration, although with no statistical significant, we suggest that there might be a potential protective effect of long sleep on PCa incidence. Kakizaki et al[17] found that men who slept more than 9 hours per night had a 52% lower risk of PCa. Markt et al[16] also considered that sleep ≥9 hours can reduce the risk of PCa. While other studies[15,18,19] showed that a non-statistically significant decreased risk of PCa for men with long sleep duration. In fact, people of different regions and ethnicities have different lifestyles, so they are at different risk for different types of cancer. We may be able to diagnose cancer in part by reference to the patient's ethnicity. Although our subgroup analysis of region factor did not show any association between long sleep and PCa risk. But that may change as more studies emerge.

Previous biological explanations for the association between sleep duration and cancer risk have focused on melatonin. Because previous studies thought that insufficient sleep was associated with lower melatonin levels, presumably due to the increased exposure to light from nighttime activities.[21,22] Although the exact molecular mechanism is still unclear, melatonin may play an anti-cancer role by inhibiting cell proliferation and stimulating differentiation and apoptosis.[23] And the lack of melatonin can promote tumor growth.[24] There is also a lot of evidence show that melatonin has an anti-tumor effect.[25–27] Some reports claimed that night work could reduce the level of melatonin and be associated with increased risk of cancers.[28–30] In fact, night work might be associated with the decrease of melatonin levels, but that didn't mean sleep duration was directly related to the level of melatonin.[31,32] Short sleep duration might indicate that sleep quality was good and short sleep didn't affect melatonin secretion. In addition, some factors that affect sleep duration, such as aging and nocturia, were also related to the risk of PCa. As is known to all, Sleep duration decreased with aging,[33] and the probability of PCa was associated with aging.[1] Therefore, aging might play an important role in exploring the relationship between sleep duration and PCa risk. Besides, the probability of nocturia increased with age, and nocturia was significantly associated with PCa in older men.[34] These are all potential biases in the association between sleep time and PCa risk. In order to eliminate the interference of these influencing factors as much as possible, the data we adopted were adjusted for multivariate before meta-analysis, which reduced the bias caused by various factors to some extent.

Overall, our results suggested that sleep duration was not associated with PCa risk. Long sleep may have a potential protective effect on PCa incidence. The association between sleep duration and PCa risk and more reasonable classification of sleep duration warrant further investigation.

5. Limitation

Several limitations should be acknowledged in the meta-analysis. First, the information on sleep duration comes mainly from questionnaires, rather than objective measures, which might make our classification of exposure factors less accurate. Second, sleep duration is influenced by many factors. For example, short sleep duration may be caused by pathological changes in the body. Long sleep may indicate poor sleep quality, which may also be due to pathological changes in the body, such as sleep apnea syndrome. These pathologic changes may be directly related to PCa. Finally, the follow-up time of our included literature varied greatly, which may have influenced the results.

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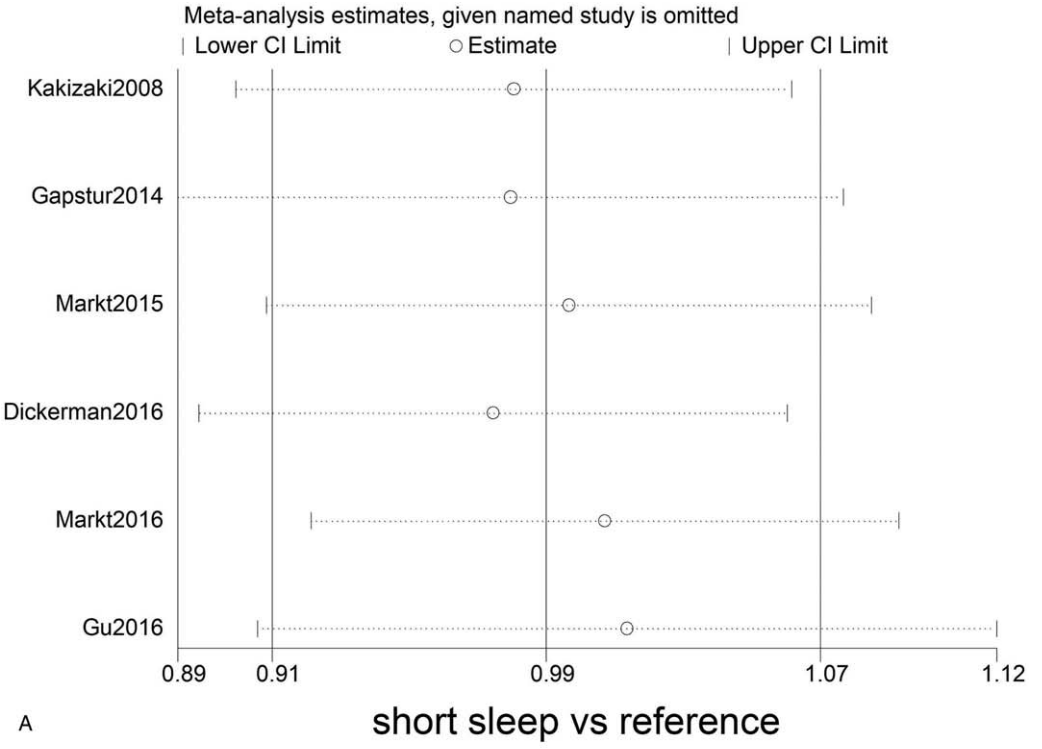
Author contributions

S Wu, B Zhang, M Guo, and Y Zhang used the NOS to assess the quality of studies. Data is extracted independently by S Wu, B Zhang, M Guo, and Y Zhang, and conflicts are resolved through discussion during the data extraction process. S Wu and R Liu conducted meta-analysis,prepared all of the figures and tables, and wrote the main manuscript. All authors reviewed the manuscript.



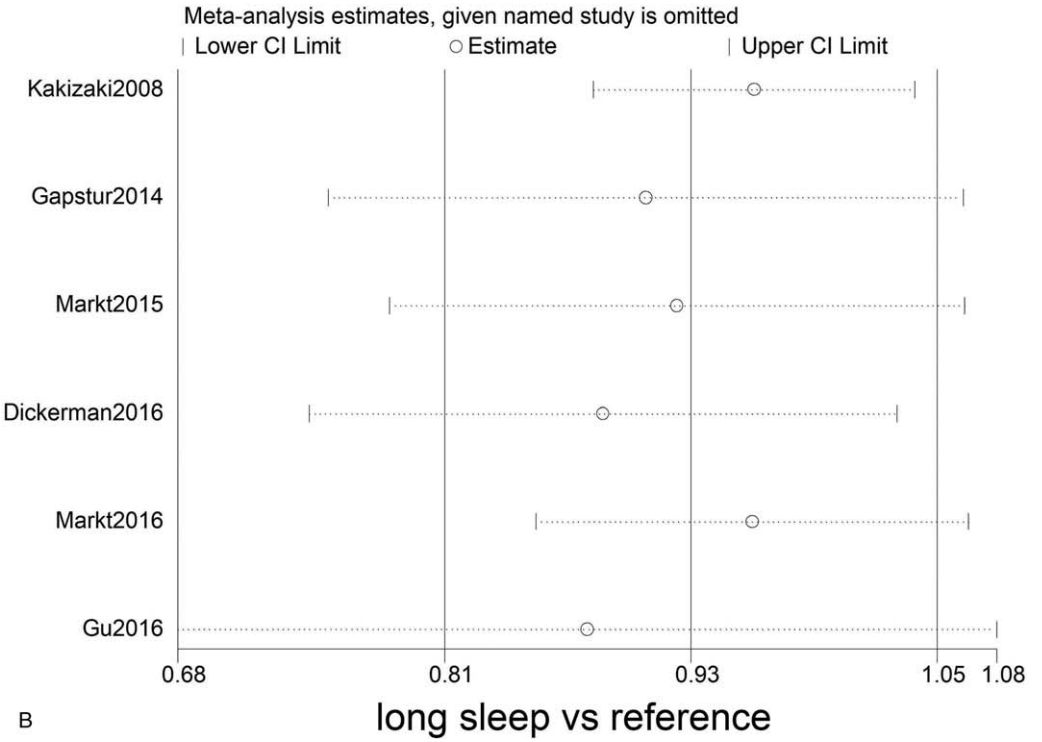


Figure 3. Sensitivity analysis for the association between sleep duration and prostate cancer in this meta-analysis. Through sensitivity analysis, we found that the results of the literature included are stable and accurate.

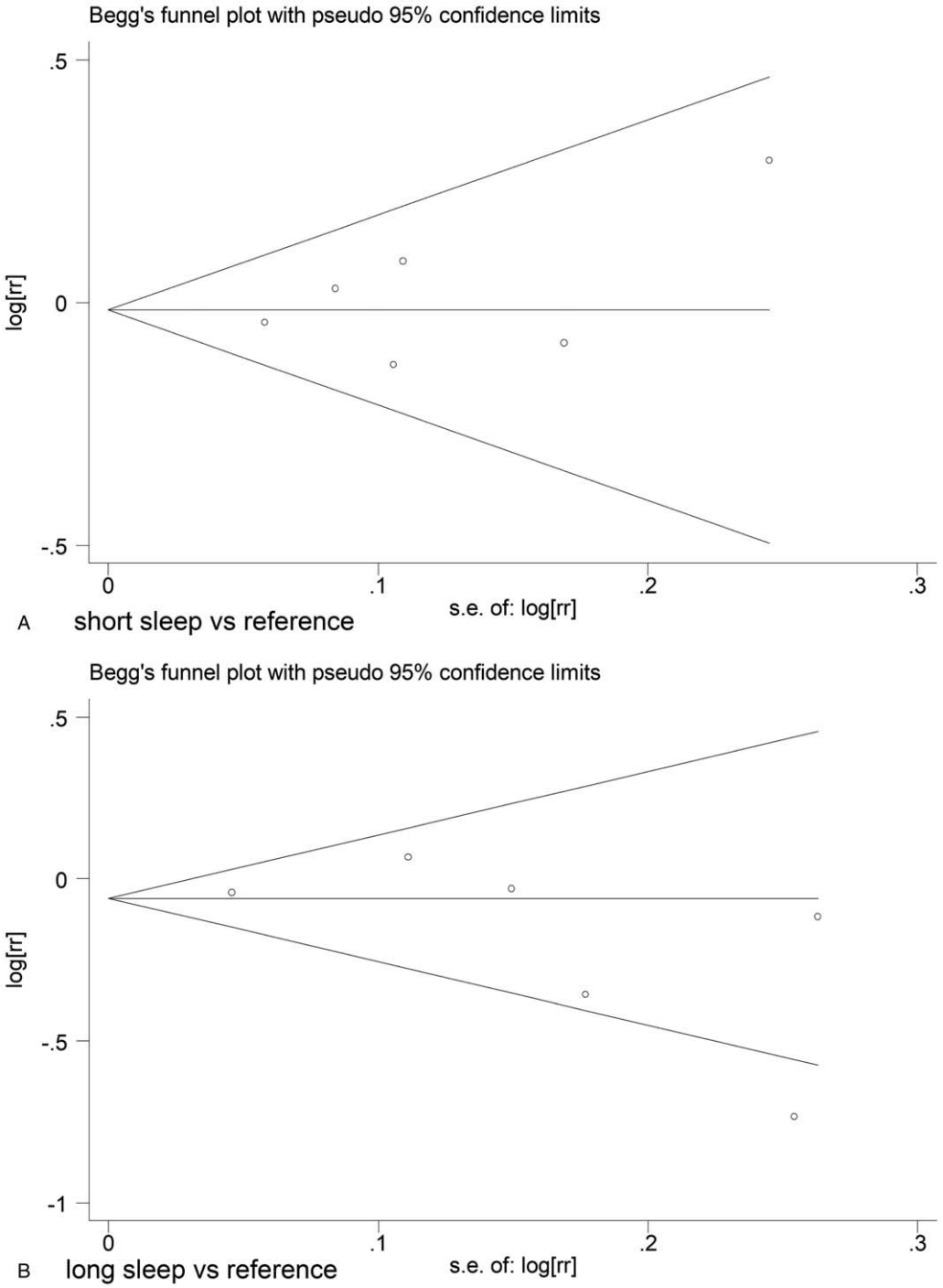


Figure 4. Funnel plots based on risk ratio (Begg test). No statistical publication bias was found in all literature.

References

[1] Siegel RL, Miller KD, Jemal A. Cancer statistics [J]. CA: A Cancer Journal for Clinicians 2019;69:7–34.

[2] Cormio L, Cindolo L, Troiano F, et al. Development and internal validation of novel nomograms based on benign prostatic obstruction-related parameters to predict the risk of prostate cancer at first prostate biopsy [J]. Front Oncol 2018;8:

[3] Cormio L, Lucarelli G, Selvaggio O, et al. Absence of bladder outlet obstruction is an independent risk factor for prostate cancer in men undergoing prostate biopsy [J]. Medicine (Baltimore) 2016;95:e2551.

[4] Chaput J-P, Gray CE, Poitras VJ, et al. Systematic review of the relationships between sleep duration and health indicators in school-aged children and youth [J]. Applied physiology, nutrition, metabolism 2016;41:S266–82.

[5] St-Onge M-P, Grandner MA, Brown D, et al. Sleep duration and quality: impact on lifestyle behaviors and cardiometabolic health: a scientific statement from the American Heart Association [J]. Circulation 2016;134:e367–86.

[6] Shan Z, Ma H, Xie M, et al. Sleep duration and risk of type 2 diabetes: a meta-analysis of prospective studies [J]. Diabetes Care 2015;38: 529–37.

[7] Heckman CJ, Kloss JD, Feskanich D, et al. Associations among rotating night shift work, sleep and skin cancer in Nurses' Health Study II participants [J]. Occupational and environmental medicine 2017; 74:169–75.
[8] Luojus MK, Lehto SM, Tolmunen T, et al. Sleep duration and incidence of lung cancer in ageing men [J]. BMC public health 2014;14:295.
[9] Jiao L, Duan Z, Sangi-Haghpeykar H, et al. Sleep duration and incidence of colorectal cancer in postmenopausal women [J]. British journal of cancer 2013;108:213.
[10] Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement [J]. Annals of internal medicine 2009;151:264–9.
[11] Wells G. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses[C] Symposium on Systematic Reviews: Beyond the Basics. 2000
[12] Handoll HH. Systematic reviews on rehabilitation interventions [J]. Archives of physical medicine rehabilitation 2006;87:875.
[13] Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses [J]. BMJ 2003;327:557–60.
[14] Seagroatt V, Stratton I. Bias in meta-analysis detected by a simple, graphical test, Test had 10% false positive rate [J]. BMJ 1998;316:470.
[15] Markt SC, Grotta A, Nyren O, et al. Insufficient sleep and risk of prostate cancer in a large swedish cohort [J]. Sleep 2015;38:1405–10.
[16] Markt SC, Flynn-Evans EE, Valdimarsdottir UA, et al. Sleep duration and disruption and prostate cancer risk: A 23-year prospective study [J]. Cancer Epidemiology Biomarkers and Prevention 2016;25:302–8.
[17] Kakizaki M, Inoue K, Kuriyama S, et al. Sleep duration and the risk of prostate cancer: The Ohsaki Cohort Study [J]. British journal of cancer 2008;99:176–8.
[18] Gu F, Xiao Q, Chu LW, et al. Sleep duration and cancer in the NIH-AARP diet and health study cohort [J]. PLoS One 2016;11:e0161561.
[19] Gapstur SM, Diver WR, Stevens VL, et al. Work schedule, sleep duration, insomnia, and risk of fatal prostate cancer [J]. American journal of preventive medicine 2014;46(3 SUPPL. 1):S26–33.
[20] Dickerman BA, Markt SC, Koskenvuo M, et al. Sleep disruption, chronotype, shift work, and prostate cancer risk and mortality: a 30-year prospective cohort study of Finnish twins [J]. Cancer Causes and Control 2016;27:1361–70.
[21] Wu AH, Wang R, Koh W-P, et al. Sleep duration, melatonin and breast cancer among Chinese women in Singapore [J]. Carcinogenesis 2008; 29:1244–8.
[22] Sigurdardottir LG, Markt SC, Rider JR, et al. Urinary melatonin levels, sleep disruption, and risk of prostate cancer in elderly men [J]. Euro Urol 2015;67:191–4.
[23] Blask DE, Dauchy RT, Sauer LA. Putting cancer to sleep at night [J]. Endocrine 2005;27:179–88.
[24] Blask DE, Brainard GC, Dauchy RT, et al. Melatonin-depleted blood from premenopausal women exposed to light at night stimulates growth of human breast cancer xenografts in nude rats [J]. Cancer Res 2005;65:11174–84.
[25] Fathizadeh H, Mirzaei H, Asemi Z. Melatonin: an anti-tumor agent for osteosarcoma [J]. Cancer Cell Int 2019;19:319.
[26] Shafabakhsh R, Mirzaei H, Asemi Z. Melatonin: a promising agent targeting leukemia [J]. Journal of cellular biochemistry 2019.
[27] Reiter RJ, Rosales-Corral SA, Tan D-X, et al. Melatonin, a full service anti-cancer agent: inhibition of initiation, progression and metastasis. International journal of molecular sciences 2017;18:843.
[28] Schernhammer ES, Berrino F, Krogh V, et al. Urinary 6-Sulphatoxymelatonin levels and risk of breast cancer in premenopausal women: the ORDET cohort. Cancer Epidemiology Prevention Biomarkers 2010; 19:729–37.
[29] Viswanathan AN, Hankinson SE, Schernhammer ES. Night shift work and the risk of endometrial cancer [J]. Cancer Res 2007;67:10618–22.
[30] Hansen J. Increased breast cancer risk among women who work predominantly at night [J]. Epidemiology 2001;12:74–7.
[31] Sturgeon SR, Luisi N, Balasubramanian R, et al. Sleep duration and endometrial cancer risk. Cancer causes & control: CCC 2012;23: 547–53.
[32] Erren TC. Sleep duration and cancer risk: time to use a "sleep-years" index? [M]. 2012;Springer,
[33] Akerstedt T, Ghilotti F, Grotta A, et al. Sleep duration, mortality and the influence of age [J]. European journal of epidemiology 2017;32:881–91.
[34] Markland AD, Vaughan CP, Johnson TM2nd, et al. Prevalence of nocturia in United States men: results from the National Health and Nutrition Examination Survey [J]. The Journal of urology 2011;185: 998–1002.