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Original Article

Non-apnea sleep disorders will increase subsequent liver cancer risk – A nationwide population-based cohort study

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ABSTRACT

Introduction: It is well known that patients with sleep disorders (SD) have an increased risk of cardiovascular disease, diabetes mellitus, obesity, and total mortality. However, little information exists regarding the relationship between non-apnea SD and the risk of cancer. The goal of this study was to determine if any association between SD and malignancy exists in Taiwan.
Methods: We used data from the National Health Insurance system of Taiwan to assess this issue. The SD cohort contained 42,351 patients, and each patient was randomly frequency-matched by age and sex with two people from the general population without SD. The Cox's proportional hazard regression analysis was conducted to estimate the effects of SD on cancer risk.
Results: In patients with SD, the overall risk of developing cancer was significantly higher than in normal healthy subjects (adjusted Hazard ratio [HR] = 1.12, 95% confidence interval = 1.06–1.18). This held true even when we analyzed males and females separately. In regards to individual types of cancer, the risk for developing liver cancer among patients with SD was significantly higher than in subjects without SD. For breast cancer the risk showed a marginally significant increase.
Conclusion: The nationwide population-based cohort study found Taiwanese patients with SD have a higher risk of developing cancer, particularly liver cancer and, possibly, breast cancer.

1. Introduction

Sleep problems are not uncommon in the general population [33]. A previous study conducted in the Los Angeles metropolitan area found the prevalence of sleep disorders to be 32.2% [2]. The similar result was also reported for Asians [5]. A lack of quality sleep can cause accidents, affect relationships and mental prowess, and have detrimental effects on health outcomes such as increasing the risk of cardiovascular disease, diabetes mellitus, obesity, and total mortality [17]. When looking at the relationship between sleep problems and cancer, most researchers have focused on the issue of cancer induced sleep disturbance [1,7,10,21,27,28]. There is little information discussing the possible reverse causality – non-apnea sleep disorders (SD) may increase cancer risk. Thompson et al. [31] found that a short duration of sleep can increase the risk of colorectal adenoma, and a couple of studies have suggested that long sleepers or the combination of physical activity and a good-night's sleep might reduce the risk of breast cancer [19,32]. Poor sleep enhances proinflammatory cytokine production and may induce immunosuppression [11,12]. Immunosuppression plays an important role in the initiation process of cancer for patients after organ transplant, as well as for patients who are HIV

Abbreviations: SD, sleep disorders; HR, Hazard ratio; NHI, National Health Insurance; NHRI, National Health Research Institute; CI, confidence interval; RR, rate ratio.

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positive [23,25]. Based on the links between the conditions and diseases mentioned above, we were interested in exploring the possible relationship between SD and cancer risk. In this study we tried to test the hypothesis that SD can increase the risk of developing cancer.

To the best of our knowledge, no published population-based study has investigated the relationship between SD and cancer risks. The aim of this study is to determine if there is any association between cancer risk and SD in Taiwan. The results presented in this paper were from a retrospective cohort study to assess the possibility of a higher risk of developing malignancy in patients with SD. The original database was derived from the National Health Insurance (NHI) system in Taiwan.

2. Methods

2.1. Study design and data collection

This study used data retrieved from the medical claims database of Taiwan's Universal NHI program. The NHI program covers more than 96% of the country's population and has contracted with 97% of all hospitals and clinics in Taiwan [16]. The National Health Research Institute (NHRI), which established and maintains the claims database, created a research dataset containing all reimbursement claims records from 1996 to 2008 for one million randomly selected insured patients. Details of this population-based program have been described in a previous study [14].

In the period from 2000 January to 2001 December newly diagnosed subjects with SD were identified using the ICD-9-CM code 780.5 and 307.4 (except for sleep apnea syndrome [ICD-9-CM code 780.51, 780.53, 780.57]) as the exposure cohort. We defined the first diagnosis of SD in the database as index date, and we also excluded subjects with SD before 2000 to ensure our study subjects had never had SD before the beginning of the insurance program.

Subjects with a history of malignant cancer (ICD-9-CM code 140–208) diagnosed before the index date were excluded. We also used the database to randomly select two insured people without SD or a history of cancer as a control group in the same period, frequency matched with the SD cohort using age and sex. This study analyzed a total of 127,053 subjects.

2.2. Study end-point

We used the unique personal-identification number of the subject as a link to the registry of Catastrophic Illness Patient Database in order to search for new diagnoses of cancer as the outcome of this study. The diagnosis of cancer in the program needs histological confirmation. Both the SD patient cohort and the comparison cohort were started using the same index date; observation was completed when cancer was diagnosed or censored prior to or on December 31, 2008. Length of follow-up time was calculated for each patient diagnosed with cancer. The completion date was defined as the date of death in the follow-up period or the date of last withdrawal from the NHI program.

2.3. Statistical analysis

We compared the distribution differences of socio-demographic variables and baseline co-morbidities between the SD cohort and non-SD cohort using the Chi-square test. We also estimated sex, age, urbanization level, and co-morbidities specific cancer incidence density and rate ratios by the population person-year for two cohorts. The townships within which subjects registered for insurance were grouped into four levels of urbanization, level 1 being the highest and level 4 the lowest level of urbanization, based on a score calculated by incorporating variables indicating population density (people/km^2) and the population ratio of the elderly, agriculture workers, different educational levels, and the number of physicians per 100,000 people [15].

The Cox proportional-hazards regression models were conducted to assess the influence of the SDs on cancer risk. When the association was significant, a Hazard ratio (HR) and 95% confidence interval (95% CI) were reported. Models were adjusted for age, sex, levels of urbanization, and co-morbidities. The co-morbidities included hypertension (ICD-9-CM code: 401–405), diabetes mellitus (ICD-9-CM code: 250), hyperlipidemia (ICD-9-CM code: 272), and heart disease (ICD-9-CM code: 410–429). The same model was used for the sex- and cancer type-specific analysis. We also analyze the Hazard ratio of liver cancer after controlling for liver cancer-related co-morbidities: hypertension, diabetes mellitus, hyperlipidemia, heart disease, alcoholic liver damage (ICD-9-CM code: 571.0, 571.1 and 571.3), non-alcoholic liver damage (ICD-9-CM code: 571.8), hepatitis B (ICD-9-CM code: V02.61, 070.20, 070.22, 070.30, 070.32), hepatitis C (ICD-9-CM code: V02.62, 070.41, 070.44, 070.51, 070.54), cirrhosis (ICD-9-CM code: 571.2, 571.5, 571.6), and alcoholism (ICD-9-CM code: 303 and 305.0).

A two-tail P value of less than 0.05 was considered to indicate statistical significance. SAS 9.1 statistical software (SAS Institute, Inc., Cary, NC, USA) was used to perform the analysis.

3. Results

3.1. Subject characteristics

For the period 2000–2001 we identified 42,351 patients with SD; this group was comprised of 26,079 (61.6%) women and 16,272 (38.4%) men, with a mean age of 49.0 at baseline (Table 1). Age and sex distributions were similar in both groups, with the most prevalent age group being 50–64 years of age (23.8%). Compared with the non-SD group, subjects with SD were more likely to have hypertension (33.6% vs. 20.9%, $p < 0.0001$), diabetes mellitus (10.9% vs. 7.3%, $p < 0.0001$), hyperlipidemia (17.2% vs. 9.4%, $p < 0.0001$), and heart disease (27.8% vs. 13.5%, $p < 0.0001$).

3.2. Rate ratio and risk of cancer

During the follow-up period of 310,866 person-years in the SD cohort and 618,434 person-years in the non-SD cohort, we identified a total of 5898 cancer cases (Table 2). Overall, the incidence of cancer was higher in the SD cohort than in the non-SD group (6.77 vs. 6.13 per 1000 person-years). In both cohorts, men (8.02 and 8.99 per 1000 person-years, RR = 1.12, 95% CI = 1.04–1.21) had greater incidence of cancer than women (5.00 and 5.46 per 1000 person-years, RR = 1.09, 95% CI = 1.01–1.18). Compared with the non-SD cohort, the RR was highest in those less than 30 years old (RR = 1.92, 95% CI = 1.25–2.95).

In the Cox proportional-hazards regression model adjusting for covariates in Table 1, subjects with SD were more associated with increased risk of cancer (HR = 1.12, 95% CI = 1.06–1.18). The risk of cancer associated with SD was statistically significantly in both women (HR = 1.08, 95% CI = 1.00–1.17) and men (HR = 1.14, 95% CI = 1.06–1.24) (Table 3).

In addition, the cancer specific analysis is displayed in Table 4. We only observed that patients with SD had significantly increased risk of developing liver cancer (HR = 1.64, 95% CI = 1.42–1.89) and marginally significantly increased risk of developing breast cancer (HR = 1.17, 95% CI = 0.98–1.39). The SD patients are more likely to have liver cancer-related co-morbidities, including alcoholic liver damage, non-alcoholic liver damage, hepatitis B, hepatitis C, cirrhosis, and alcoholism, than non-SD patients (all p-values were

Table 1
Baseline characteristics between the sleep disorder group and the non-sleep disorder group in 2000–2001.

Variables			Sleep disorder				*p*-value
	Total *N* = 127,053		No *N* = 84,702		Yes *N* = 42,351		
	N	(%)	*n*	(%)	*n*	(%)	
Sex							1.00
Women	78,237	(61.6)	52,158	(61.6)	26,079	(61.6)	
Men	48,816	(38.4)	32,544	(38.4)	16,272	(38.4)	
Age (years)							1.00
<30	19,500	(15.4)	13,000	(15.4)	6500	(15.4)	
30–39	22,194	(17.5)	14,796	(17.5)	7398	(17.5)	
40–49	26,904	(21.2)	17,936	(21.2)	8968	(21.2)	
50–64	30,198	(23.8)	20,132	(23.8)	10,066	(23.8)	
⩾65	28,257	(22.2)	18,838	(22.2)	9419	(22.2)	
Mean (SD)[a]	49.0	(18.0)	48.9	(18.2)	49.2	(17.7)	0.005
Urbanization level							<0.0001
1	37,169	(29.3)	25,514	(30.1)	11,655	(27.5)	
2	36,010	(28.3)	24,158	(28.5)	11,852	(28.0)	
3	22,370	(17.6)	14,771	(17.4)	7599	(17.9)	
4	31,500	(24.8)	20,255	(23.9)	11,245	(26.5)	
Co-morbidity							
Hypertension	31,919	(25.1)	17,701	(20.9)	14,218	(33.6)	<0.0001
Diabetes mellitus	10,793	(8.5)	6186	(7.3)	4607	(10.9)	<0.0001
Hyperlipidemia	15,234	(12.0)	7968	(9.4)	7266	(17.2)	<0.0001
Heart disease	23,203	(18.3)	11,448	(13.5)	11,755	(27.8)	<0.0001

Chi-square test.
[a] Student *t*-test.

Table 2
Comparisons of incidence density of cancer between the sleep disorder group and the non-sleep disorder group by characteristics.

Variables	Sleep disorder						RR	(95% CI)
	No			Yes				
	Cases	Person-years	Rate[a]	Cases	Person-years	Rate[a]		
All	3793	618,434	6.13	2105	310,866	6.77	1.10	(1.05–1.16)**
Sex								
Women	1927	385,710	5.00	1067	195,481	5.46	1.09	(1.01–1.18)*
Men	1866	232,724	8.02	1038	115,405	8.99	1.12	(1.04–1.21)*
Age (years)								
<30	42	98,044	0.43	41	49,886	0.82	1.92	(1.25–2.95)*
30–39	207	111,856	1.85	135	56,847	2.37	1.28	(1.03–1.59)*
40–49	506	138,306	3.66	333	69,176	4.81	1.32	(1.15–1.51)**
50–64	1135	152,105	7.46	648	75,427	8.59	1.15	(1.05–1.27)*
⩾65	1903	118,083	16.1	948	59,550	15.9	0.99	(0.91–1.07)
Urbanization level								
1	1038	188,671	5.50	518	86,725	5.97	1.09	(0.98–1.21)
2	1012	177,557	5.70	547	87,998	6.22	1.09	(0.98–1.21)
3	639	107,305	5.95	353	55,467	6.36	1.07	(0.94–1.22)
4	1104	144,870	7.62	687	80,696	8.51	1.12	(1.02–1.23)*

RR = rate ratio, compared to non-sleep disorder group.
[a] Per 1000 person-year.
* *p*-Value <0.05.
** *p*-Value <0.001.

less than 0.0001, Table 5). Table 6 also shows that the SD patients had an appreciatively increased risk of 40% for developing liver cancer (HR = 1.40, 95% CI = 1.21–1.62) after controlling liver cancer-related variables. We also analyzed the relations between different risk factors and liver cancer, and the results reveal all but alcoholism had higher risks for liver cancer (Table 7).

4. Discussion

Our studies found that patients with SD had a significantly higher risk of developing all cancer, especially liver cancer. For female patients, it also showed a marginally significant higher risk of developing breast cancer.

The epidemiology data from Surveillance Epidemiology and End Results showed that the overall cancer rates for all racial and ethnic groups combined decreased by 0.7% per year between 1999 and 2006 [9]. However, it is an inverse trend for the age-adjusted cancer rate in Taiwan, which revealed a steady increase, and reached 270 new cases per 100,000 people in 2007. Since 1982 cancer has become the leading cause of death in the Taiwanese general population [30]. As this issue continues to be a challenge for the public health system in Taiwan, it has come to the attention of the government, thus resulting in population-based investigations

Table 3
Hazard ratios and 95% confidence interval of cancer associated with sleep disorder in Cox's regression analysis.

Variables	Model 1		Model 2		Model 3	
	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)
leep disorder						
No	1.00	(reference)	1.00	(reference)	1.00	(reference)
Yes	1.11	(1.05–1.17)**	1.12	(1.05–1.17)**	1.12	(1.06–1.18)***
Women						
Sleep disorder						
No	1.00	(reference)	1.00	(reference)	1.00	(reference)
Yes	1.10	(1.02–1.19)*	1.10	(1.02–1.18)*	1.08	(1.00–1.17)*
Men						
Sleep disorder						
No	1.00	(reference)	1.00	(reference)	1.00	(reference)
Yes	1.13	(1.05–1.22)*	1.12	(1.04–1.21)*	1.14	(1.06–1.24)*

Model 1: unadjusted.
Model 2: adjusted for age and urbanization.
Model 3: adjusted for age, urbanization, and co-morbidity (included hypertension, diabetes mellitus, hyperlipidemia and heart disease).
* p-Value <0.05.
** p-Value <0.001.
*** p-Value <0.0001.

regarding cancer preventive epidemiology. The Taiwanese NHI system health insurance program covers more than 96% of the population and maintains contracts with 97% of hospitals and clinics, which has been the case since the end of 1996, so the generalizability is undoubted. It provides us with a good resource to approach population-based studies. We recently used it as the material to evaluate the risk of malignancy for patients with end-stage renal disease and published some positive findings [14]. This current study used a similar design and tried to determine if SD increases the risk of cancer.

In order to create a control group we randomly frequency matched each SD patient with two people from the general population without SD but with similar age and same sex. Table 1 reveals that more SD people live in areas with lower urbanization levels. The possible explanation is that the areas of lower urbanization in Taiwan normally represent lower socioeconomic status as well as lower incomes and educational levels. Prior papers indicated that sleep disorders are independently associated with lower income and lower educational levels [5,26]. Major medical illnesses had significantly higher prevalence in the SD group (Table 1). This is unsurprising due to the fact that a significant association exists between sleep disorders and chronic physical diseases (such as diabetes, hypertension, hypercholesterolemia, or other chronic diseases) [24].

Unadjusted analysis found patients with SD had a higher risk of developing cancer overall, and this was also true when we analyzed females and males separately. All age groups except for the oldest age group showed significantly higher cancer risks for the SD cohort. All the urbanization levels showed the same trend of

Table 4
Hazard ratios and 95% confidence interval of cancer associated with sleep disorder in Cox's regression analysis in different cancer.

Variables	Sleep disorder				HR	(95% CI)
	No		Yes			
	Case	%	Case	%		
Colorectal cancer	568	0.67	275	0.65	0.97	(0.84–1.13)
Liver cancer	432	0.51	354	0.84	1.64	(1.42–1.89)***
Lung cancer	509	0.60	264	0.62	1.07	(0.91–1.24)
Melanoma	16	0.02	4	0.01	0.37	(0.12–1.14)
Skin cancer	76	0.09	31	0.07	0.83	(0.54–1.27)
Breast cancer (women only)	369	0.71	212	0.81	1.17	(0.98–1.39)
Cervical cancer (women only)	151	0.29	68	0.26	0.96	(0.72–1.29)
Prostate cancer (men only)	167	0.51	104	0.64	1.15	(0.89–1.49)
Brain tumor	46	0.05	17	0.04	0.75	(0.42–1.33)
Other cancers	1459	1.72	776	1.83	1.05	(0.96–1.15)

ICD-9-CM: colorectal cancer, 153.xx and 154.xx; liver cancer, 155.xx; lung cancer, 162.xx; melanoma: 172.xx; skin cancer: 173.xx breast cancer, 174.xx and 175.xx; cervical cancer, 180.xx; prostate cancer, 185.xx; brain cancer, 191.xx.
Adjusted for age, urbanization, and co-morbidity (included hypertension, diabetes mellitus, hyperlipidemia and heart disease).
*** p-Value <0.0001.

Table 5
Liver cancer-related co-morbidity between the sleep disorder group and the non-sleep disorder group.

Variables	Sleep disorder				p-Value[a]
	No N = 84,702		Yes N = 42,351		
	n	%	n	%	
Alcoholic liver damage	273	0.32	456	1.08	<0.0001
Non-alcoholic fatty liver disease	559	0.66	606	1.43	<0.0001
Hepatitis B	626	0.74	773	1.83	<0.0001
Hepatitis C	332	0.39	468	1.11	<0.0001
Cirrhosis	676	0.80	755	1.78	<0.0001
Alcoholism	163	0.19	346	0.82	<0.0001

Alcoholic liver damage ICD-9-CM: 571.0, 571.1 and 571.3.
Non-alcoholic fatty liver disease ICD-9-CM: 571.8.
Hepatitis B ICD-9-CM: V02.61, 070.20, 070.22, 070.30, 070.32.
Hepatitis C ICD-9-CM: V02.62, 070.41, 070.44, 070.51, 070.54.
Cirrhosis ICD-9-CM: 571.2, 571.5, 571.6.
Alcoholism ICD-9-CM: 303 and 305.0.
[a] Chi-square test.

Table 6
Hazard ratios and 95% confidence interval of liver cancer associated with the sleep disorder group and the non-sleep disorder group.

Variables	Non-sleep disorder	Sleep disorder	Crude		Adjusted	
	Cases	Cases	HR	(95% CI)	HR	(95% CI)
All	432	354	1.63	(1.42–1.88)***	1.40	(1.21–1.62)***
Female	174	132	1.51	(1.20–1.89)***	1.23	(0.97–1.56)
Male	258	222	1.73	(1.45–2.08)***	1.54	(1.28–1.87)***

Adjusted for age, urbanization, and co-morbidity (included hypertension, diabetes mellitus, hyperlipidemia, heart disease, alcoholic liver damage, non-alcoholic liver damage, Hepatitis B, Hepatitis C and cirrhosis) and alcoholism.
*** $p < 0.0001$.

Table 7
Hazard and 95% confidence interval of liver cancer-related comorbidity.

Variables	N	Case	HR	(95% CI)
Alcoholic liver damage	729	23	4.66	(3.08–7.07)***
Non-alcoholic fatty liver disease	1165	25	3.03	(2.03–4.51)***
Hepatitis B	1399	58	8.68	(6.63–11.4)***
Hepatitis C	800	75	16.4	(12.9–20.8)***
Cirrhosis	1431	145	18.9	(157–22.6)***
Alcoholism	509	5	1.93	(0.80–4.67)

Alcoholic liver damage ICD-9-CM: 571.0, 571.1 and 571.3.
Non-alcoholic fatty liver disease ICD-9-CM: 571.8.
Hepatitis B ICD-9-CM: V02.61, 070.20, 070.22, 070.30, 070.32.
Hepatitis C ICD-9-CM: V02.62, 070.41, 070.44, 070.51, 070.54.
Cirrhosis ICD-9-CM: 571.2, 571.5, 571.6.
HR, Hazard ratio, adjusted for age and sex.
*** p-Value < 0.0001.

higher cancer risk within the SD group with a marginally significant difference. The relatively small sample size caused by separating them into four groups could weaken the statistical power of this finding.

In our Cox-regression model with adjustments for sex, age, urbanization, and co-morbidity (model 3) we found the HR for the overall cancer is 1.12 with a 95% CI of 1.06–1.18. This value is more reliable because we were able to control for many of the possible confounders from the database. The same model (except without the adjustment for sex) was used for women and men and also showed similar findings. Women with SD had a marginally significantly higher cancer risk, and men had a significantly higher cancer risk. We validated our hypothesis that SD did increase the risk of cancer, and this novel finding can be partially attributed to the large sample size in this population-based study. One of the possible reasons for a higher cancer risk in the SD cohort could be the pathway of sleep disorders-immunosuppression-cancer. Sleep deprivation leads to the suppression of immune surveillance, which may permit the establishment and growth of malignant clones (e.g., immunosuppression from increased cortisol, etc.) [7].

Our data showed different directions for various cancers. Higher risks of liver, lung, breast, prostate, and other cancers, and lower risks of brain tumor, melanoma, skin, cervical, and colorectal cancers were observed. However, only liver cancer showed a significantly higher risk. One of the possible reasons for higher liver cancer risk is that liver cancer is thought to be a virus-related malignancy [3,13]; therefore, it may be linked to our hypothesis of a sleep disorders-immunosuppression-viral infection-cancer pathway. Patients with SD in Taiwan tend to try Chinese herbal medicines and that could have been liver toxic [4]. Primary liver cancer is the second most common malignancy in Taiwan [30], and the large number of cases in the study could enforce the statistics power. Breast cancer showed a marginally significant increase in risk in the SD group. Epidemiologic studies are now beginning to emerge suggesting that women who work at night, and who experience sleep deprivation, circadian disruption, and exposure to light-at-night are at an increased risk for breast cancer [6,8]. Wu et al. found a significant decline in postmenopausal breast cancer risk with increasing self-reported hours of sleep among Chinese women in Singapore, and possibly via its effect on melatonin levels [35]. In addition, the suggestion of lower breast cancer risk in long sleepers in the Finnish Twin Cohort also adds to the body of evidence for a possible anticarcinogenic effect of melatonin [32]. In our target group, we collected all patients who fit the ICD9 code for SD and sleep disturbances (except for obstructive sleep apnea in our analysis because it has different causes and biological effects compared to other sleep problems), which included the phase-shift disruption of the 24-h sleep–wake cycle (code number 30745) and disruptions of the 24-h sleep–wake cycle (code number 78055). Although the majority of our patients suffered from sleep disorders, we still had eight patients in these two codes (data not shown). Patients with similar symptoms might have been coded into others, which may have diluted our power to detect any statistical significance in breast cancer.

One of the strengths of this study is its population-based design due to its generalizability. However, one major limitation that needs to be addressed is that there is no information regarding life style or behavior of the patient on the NHI database, so it is impossible to adjust for behavior related factors such as smoking and alcohol consumption. Smokers might have a higher risk of sleep disorders [18], and smoking might be a confounder between SD and smoking-related cancers. According to the Surgeon General's Report, lung, oral, pharynx, larynx, esophagus, kidney, bladder, pancreas, stomach, and cervical cancers are all smoking-related [22]. Our data did not show any significant difference in these cancers. However, a study from Taiwan suggested habitual alcohol drinking, betel quid chewing, and cigarette smoking are associated with an increased risk of liver cancer [34]. For alcohol consumption, clinical investigations supported a relationship between sleep disturbance and alcohol use, but variability in the definition and measurement of these domains and a preponderance of cross-sectional studies made uncertain the strength and direction of the association [29]. Chronic alcohol use of greater than 80 g/day for more than 10 years increases the risk of liver cancer approximately 5-fold, but alcohol use of less than 80 g/day is not associated with a significant increase in risk [20]. Table 5 validated the theory that alcoholic liver damage and alcoholism are more frequently seen in the SD group, and it may partially explain the significantly higher risk of liver cancer for patients with SD. However, after controlling the possible confounders, Table 6 reveals the adjusted HR of liver cancer for patients with SD is still significantly higher, and Table 7 does not show a higher risk of liver cancer for patients with alcoholism.

In conclusion, this population-based retrospective cohort study suggested that SD may associate with an increased risk for the subsequent liver cancer, and possibly breast cancer. The apparent increased alcohol use in the SD group remains a possible confounder. Further studies with controls for alcohol use and other possible confounders are mandatory to truly uncover the possible link between SD and cancer risk. Nevertheless, the findings from

this study may arouse the attention of the NHI of Taiwan to reconsider the policy regarding follow-up and cancer screening in patients with SD.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: doi:10.1016/j.sleep.2012.02.005.

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