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Abbreviations:
DAQS, dietary antioxidant quality score; eGFR, estimated glomerular filtration rate; MET, metabolic equivalent; NHANES, National Health and Nutrition Examination Surveys; PAQ, Physical Activity Questionnaire; PIR, poverty:income ratio; vit A, vitamin A; vit C, vitamin C; vit E, vitamin E

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Combined association between dietary antioxidant quality score and leisure-time physical activity on sleep pattern in cancer survivors: a cross-sectional study of National Health and Nutrition Examination Surveys database

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Abstract

This study aimed to explore the combined association between the dietary antioxidant quality score (DAQS) and leisure-time physical activity on sleep patterns in cancer survivors. Data of cancer survivors were extracted from the National Health and Nutrition Examination Surveys database in 2007–2014 in this cross-sectional study. Weighted multivariable logistic regression models were used to estimate OR and 95 % CI for the association of DAQS and leisure-time physical activity on sleep patterns. The combined association was also assessed in subgroups of participants based on age and use of painkillers and antidepressants. Among the eligible participants, 1133 had unhealthy sleep patterns. After adjusting for covariates, compared with low DAQS level combined with leisure-time physical activity level < 600 MET·min/week, high DAQS level combined with leisure-time physical activity ≥ 600 MET·min/week was associated with lower odds of unhealthy sleep patterns (OR = 0·41, 95 % CI: 0·23, 0·72). Additionally, the association of high DAQS level combined with high leisure-time physical activity with low odds of unhealthy sleep patterns was also significant in < 65 years old (OR = 0·30, 95 % CI: 0·13, 0·70), non-painkiller (OR = 0·39, 95 % CI: 0·22, 0·71), non-antidepressant (OR = 0·49, 95 % CI: 0·26, 0·91) and antidepressant (OR = 0·11, 95 % CI: 0·02, 0·50) subgroups. DAQS and leisure-time physical activity had a combined association on sleep patterns in cancer survivors. However, the causal associations of dietary nutrient intake and physical activity with sleep patterns in cancer survivors need further clarification.

Cancer is a leading cause of human deaths at present and becomes a major public health issue over the world[1]. According to the American Cancer Society, 1 958 310 new cancer cases and 609 820 cancer deaths are projected to occur in the USA in 2023[2]. Significant strides in cancer screening, diagnostics and therapeutics have contributed to a growing population of cancer survivors in recent decades[3,4]. However, cancer survivors are at risk of physical and psychological morbidity in the years after treatment completion, including increased sleep disturbance[5].

Sleep pattern is a compositive sleep behaviour, including sleep duration, sleeping difficulties and sleep disorders, reflecting the sleep conditions of individuals. A prior study showed that between 30 % and 80 % of cervical cancer survivors demonstrated unhealthy sleeping patterns, such as insomnia, excessive sleep, sleep disorders and sleep difficulties[6]. Sleep plays an important role in the regulation of immunity, metabolism and body repair in humans[7]. A poor sleep condition is closely associated with increased pain, decreased life quality, anxiety and depression in patients with cancer and thus has a greater negative impact on their prognoses[8]. Therefore, adequately understanding and addressing sleep problems in cancer survivors is important for improving the disease prognoses and living quality.

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It is known that the occurrence of cancer is closely linked to oxidative stress and chronic inflammation, which can activate growth factors and inflammatory factors, leading to abnormal transformation of normal cells and the proliferation and invasion of tumour cells[9]. On the other hand, inflammatory process disorder can activate sleep-related inflammatory molecules, affecting the sleep and circadian rhythms, and further result in sleep disorders, sleep deprivation and other sleep problems[10,11]. Hence, oxidative stress and chronic inflammation may be involved in both sleep process and cancer development.

In addition to clinical therapies, diet and physical activity are major regulatable and controllable lifestyle factors associated with the health maintenance in patients with cancer[12]. Adequate intake of dietary components with antioxidant and anti-inflammatory properties, such as vitamin A (vit A), vitamin E (vit E), vitamin C (vit C), Zn, Se and Mg, can help reduce the oxidative stress and chronic inflammatory response, thereby improving sleep conditions and prognoses in cancer patients[13–15]. Similarly, keeping a high level of physical activity can enhance the body's antioxidant response, and these individuals are more likely to achieve better sleep quality and disease prognoses[16–18]. In fact, more than one-third of cancer patients are sedentary or not engage in leisure-time physical activity for long periods of time, leading to an increased risk of adverse outcomes[19]. Higher levels of leisure-time physical activity can counteract the negative effects of sedentary behavior[19]. However, the combined association between antioxidant/anti-inflammatory dietary nutrient intake and leisure-time physical activity on sleep patterns in cancer survivors is still unclear.

Herein, this study aims to explore the combined association between the composite index of multiple antioxidant and anti-inflammatory dietary components (including vit A, vit E, vit C, Zn, Se and Mg), namely the dietary antioxidant quality score (DAQS), and the leisure-time physical activity on sleep patterns in cancer survivors, in order to provide insight for improving cancer survivors' living quality.

Methods

Study design and population

Data of cancer survivors in this cross-sectional study were extracted from the National Health and Nutrition Examination Surveys (NHANES) database in 2007–2014. The NHANES survey is conducted by the Centers for Disease Control and Prevention and the National Center for Health Statistics jointly, with the aim to assess the nutritional and health status of the noninstitutionalised population in the USA. It includes a complex, multistage stratified probability sample based on selected counties, blocks, households and persons within households. The National Center for Health Statistics' well-trained professionals conducts interviews in participants' homes, and extensive physical examinations were conducted at mobile exam centers. For more details, please visit the NHANES website: https://wwwn.cdc.gov/nchs/nhanes/index.htm.

We initially included 2173 cancer survivors who have information on sleep patterns (including sleep duration, sleeping difficulties and sleep disorders) assessment, dietary intake and physical activity. The exclusion criteria were (1) having an extreme energy intake (< 500 kcal or > 8000 kcal for male; < 500 kcal or > 5000 kcal for female) and (2) missing information on the study variables, including sedentary time, BMI, leucocytes, lymphocyte, neutrophil, estimated glomerular filtration rate, marital status and education level. The final sample size was 1936. The NHANES survey was approved by the institutional review board of the National Center for Health Statistics. Since the study data were de-identified, and all the participants have provided informed consent, no ethical approval from our agency's institutional review board was required.

Definition of sleep patterns

Assessment of sleep pattern was on the basis of three sleep related factors, including sleep duration, sleeping difficulties and sleep disorders. Sleep duration was self-reported through the question 'How much sleep do you usually get at night on weekdays or workdays?' The quantity of time recorded was grouped as short (< 7 h per night), normal (7–9 h per night) and long (> 9 h per night)[20]. The responses to 'Have you ever told a doctor or other health professional that you have trouble sleeping?' and 'Have you ever been told by a doctor or other health professional that you have a sleep disorder?' were respectively used to assess the sleeping difficulties and sleep disorders. A short/long sleep duration, having sleeping difficulties and having sleep disorders were respectively classified as 0, whereas normal sleep duration, non-sleeping difficulties and non-sleep disorders were respectively classified as 1. Then scores of the above three sleep related factors were used to generate overall sleep scores, ranging from 0 to 3. An overall sleep score of 3 indicated a healthy sleep pattern, while the score of 0, 1 or 2 indicated an unhealthy sleep pattern[21–23].

Assessment of dietary intake and calculation of dietary antioxidant quality score

Dietary total energy intake was calculated through information on 'total nutrient intakes' and 'total dietary supplements' collected from two 24-hour dietary recalls in the NHANES. The first recall was conducted in person, and later recall was conducted 3–10 d after the first one via a phone call. Also, information on dietary supplements intake was collected at the NHANES household interview through a dietary supplement questionnaire. The dietary antioxidant quality score was assessed by dietary intake as well as supplements. DAQS calculation was according to the aggregate score of the six nutrients, including vit A, vit E, vit C, Zn, Se and Mg[24,25]. Specifically, the intake of each nutrient was compared with its recommended intake level, and that less than 2/3 of the recommended intake level was classified as 0, otherwise classified as 1. The aggregate score ranged from 0 to 6, and a higher score indicated a higher dietary antioxidant level. We divided the DAQS into three levels according to the tertiles, where DAQS of 0–3 represented a low dietary antioxidant level, DAQS of 4–5 represented a median dietary antioxidant level and DAQS of 6 represented a high dietary antioxidant level. More details on dietary recommendation of vitamins and minerals are shown elsewhere: https://www.ncbi.nlm.nih.gov/books/NBK56068/table/summarytables.t2/?report=objectonly;https://www.ncbi.nlm.nih.gov/books/NBK545442/table/appJ_tab3/?report=objectonly.

Assessment of leisure-time physical activity

Information on leisure-time physical activity was collected using the NHANES Physical Activity Questionnaire (PAQ). The questions used to assess leisure-time physical activity included PAQ655 (days vigorous recreational activities), PAD660 (minutes vigorous recreational activities), PAQ640 (number of days walk or bicycle), PAD645 (minutes walk or bicycle for transportation), PAQ670

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(days moderate recreational activities) and PAD675 (minutes moderate recreational activities). The physical activity level was transformed into energy consumption using the formula: energy consumption = recommended metabolic equivalent (MET) × daily duration of the activities (min) × weekly frequency of activities. The unit of energy consumption was MET·min/week. Therefore, leisure-time physical activity = PAQ655 × PAD660 × 8 + PAQ640 × PAD645 × 4 + PAQ670 × PAD675 × 4. In accordance with the previous study, leisure-time physical activity was divided into two categories, including low level (< 600 MET·min/week) and high level (≥ 600 MET·min/week)[26,27].

Variables selection

We also selected potential covariates from the database, including (1) demographic variables (age, gender, race, educational level, poverty:income ratio (PIR) and marital status), (2) physical examination variables (height, weight, BMI, WBC, lymphocyte, neutrophil and estimated glomerular filtration rate), (3) lifestyle information (smoking, drinking, physical work and sedentary time) and (4) diseases and medication that associated with cancer or sleep quality (hypertension, diabetes mellitus, dyslipidaemia, cardiovascular disease (CVD), chronic obstructive pulmonary disease, antineoplastic agents use, painkiller use, anxiolytics/sedatives/hypnotics use, antidepressant use, cancer site and cancer duration).

Demographic variables and physical examination variables were collected by well-trained NHANES interviewers at mobile exam centers and transferred to laboratory for further testing. In our analyses, PIR was divided into low level (PIR ≤ 1·01) and high level (PIR > 1·01). BMI were divided into three levels, including < 25 kg/m^2 (underweight/normal), 25–30 kg/m^2 (overweight) and ≥ 30 kg/m^2 (obese)[28]. The estimated glomerular filtration rate was calculated by the following formula: estimated glomerular filtration rate = 175 × standardised Scr − 1·154 × age−0·203 × 1·212 (if black) × 0·742 (if female), where GFR is expressed as ml/min/1·73 m^2 of body surface area41 and Scr is expressed in mg/dl[29].

Lifestyle information was collected during the NHANES household interview. Participants who claimed to have smoked fewer than 100 cigarettes in their lives were labeled as 'non-smoking'. The answer to another question 'Does you now smoke cigarettes?' was used to further divided participants into 'current smoking' and 'former smoking'. Alcohol consumption was also captured by questionnaires, and the drinking patterns were divided into non-drinking, light drinking, moderate drinking and heavy drinking[30]. Physical work was assessed according to the formula: physical work = days vigorous work × minutes vigorous-intensity work × 8 + number of days moderate work × minutes moderate-intensity work × 4[31]. Sedentary time was similarly self-reported via questionnaires, which were divided into < 480 min/d (low level sedentary activity) and ≥ 480 min/d (high level sedentary activity)[32].

Hypertension was defined by the laboratory inspection (a measured systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 80 mm Hg), self-reported hypertension or currently use of hypotensive drugs. Diabetes mellitus was defined according to a self-reported diagnosis, the use of oral hypoglycemic agents or insulin, glycosylated Hb ≥ 6·5 %, a plasma glucose level ≥ 200 mg/dl at 2 h after the oral glucose tolerance test or a fasting glucose level ≥ 126 mg/dl. Patients with total cholesterol ≥ 200 mg/dl (5·2 mmol/l) or TAG ≥ 150 mg/dl (1·7 mmol/l) or low-density lipoprotein cholesterol ≥ 130 mg/dl (3·4 mmol/l) or high-density lipoprotein cholesterol ≤ 40 mg/dl (1·0 mmol/l) or self-report hypercholesteremia or receiving lipid-lowering therapy were identified as dyslipidemia. CVD was diagnosed according to the positive answer to the multiple-choice question: 'Have you ever been told you had (congestive) heart failure, coronary heart disease, angina/angina pectoris, heart attack and stroke' or using of cardiovascular drugs in any one or more diseases or medications. Cchronic obstructive pulmonary disease was defined as a positive response to any of the following questions: (1) 'Has a doctor or other health professional ever told you that you have chronic bronchitis?' (2) 'Has a doctor or other health professional ever told you that you have emphysema?' (3) 'Has a doctor or other health professional ever told you that you have chronic obstructive pulmonary disease?' (4) 'Are you over 40 years old and have a history of smoking or chronic bronchitis and take one of the following medications: mast cell stabilisers, inhaled corticosteroids, leukotriene modifiers or selective phosphodiesterase-4 inhibitors?' In addition, cancer site, cancer duration and medication use situations were assessed by questionnaires.

Statistical analysis

Normally distributed data were described using mean (standard error) (mean (SE)), and *t* test was utilised for comparison between the healthy sleep pattern group and the unhealthy sleep pattern group. Enumeration data were expressed as frequency and constituent ratio (*n* (%)), and χ^2 was used for comparison. According to the NHANES guideline, day 1 dietary sample weights were used to adjust for oversampling, nonresponse rates, non-coverage and day of week. Weighted univariable logistic regression analysis was utilised to screen covariates that significantly associated with unhealthy sleep patterns in cancer survivors (with two-sided $P < 0{\cdot}05$ was considered as statistically significant). Weighted multivariable logistic regression models were used to estimate OR and 95 % CI for the association of DAQS, leisure-time physical activity and the combined effects between them on sleep patterns. Low-DAQS level combined with leisure-time physical activity < 600 MET·min/week was recognised as reference (the worst condition in our study), other combined associations between DAQS levels and leisure-time physical activity levels (five types of combined associations) on unhealthy sleep pattern were analysed compared to the reference. Model 1 was unadjusted model. Model 2 adjusted for covariates including age, race, PIR, cancer site, painkiller, anxiolytics/sedatives/hypnotics, antidepressant and total energy intake. In addition, subgroup analyses of age, painkiller use and antidepressant use were performed to assess the combined associations between DAQS levels and leisure-time physical activity levels on unhealthy sleep pattern. Statistical analyses were performed using R (version 4.2.0, Institute for Statistics and Mathematics) and SAS 9.4 (SAS Institute).

Results

Characteristics of cancer survivors

Figure 1 shows the flowchart of the participants screening. There were 2444 cancer survivors in the NHANES database in 2007–2014. We initially included individuals aged ≥ 20 years old, with information on sleep pattern, dietary intake and physical activity (*n* 2173). Then, those who have extreme energy intake (*n* 24) or missing information on sedentary time (*n* 7), BMI (*n* 37), WBC (*n* 120), lymphocyte (*n* 6), neutrophil (*n* 0), estimated glomerular filtration rate (*n* 41), marital status (*n* 1) or education level (*n* 1) were excluded. Finally, 1936 were eligible.

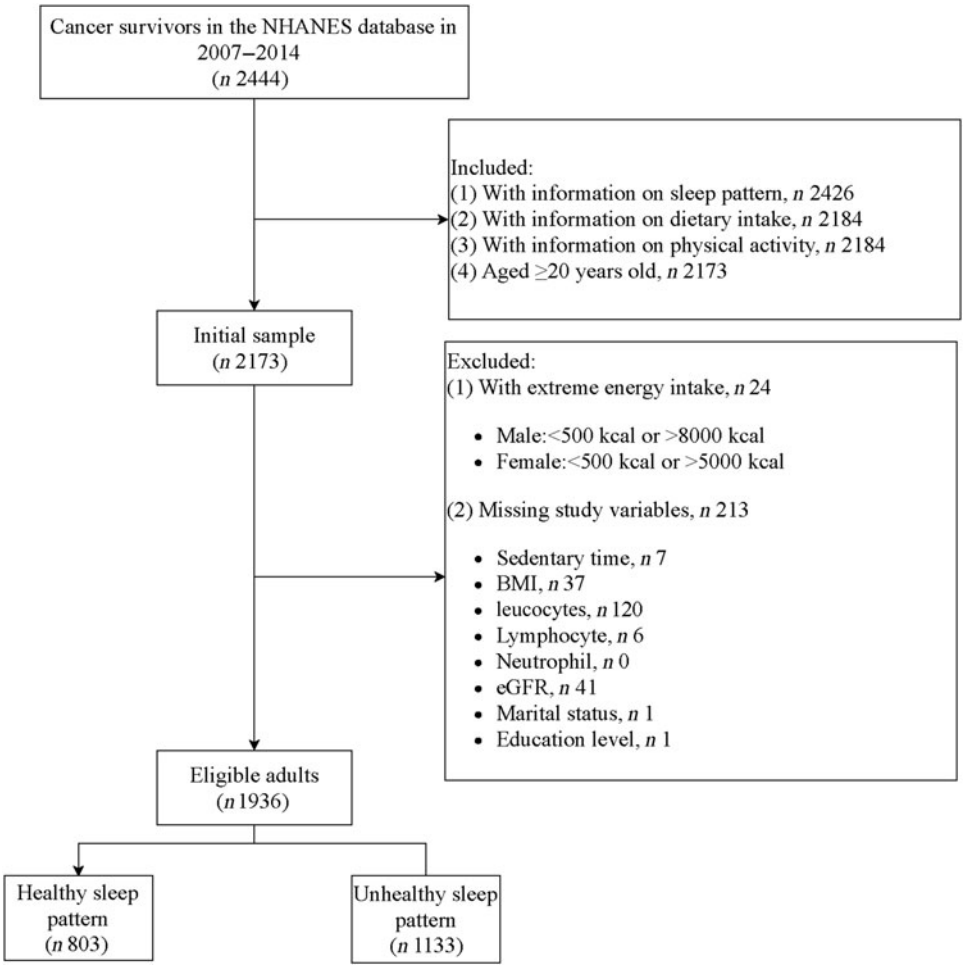

Figure 1. Flow chart of cancer survivors screening.

Table 1 shows the characteristics of cancer survivors between the healthy sleep pattern group and the unhealthy sleep pattern group. Among the eligible patients, 1133 had unhealthy sleep patterns. The average age of cancer survivors was 61·55 years old and 1070 (58·74 %) were female. Skin cancer accounted for the majority (34·4 %), followed by respiratory cancer (12·0 %) and reproductive system cancer (11·8 %). More than half of the participants (55·0 %) had a cancer duration > 5 years. The mean DAQS was significantly different between the healthy sleep pattern group and the unhealthy sleep pattern group (4·25 *v.* 4·03), in which the average vit A intake was significant higher in the healthy sleep pattern group than that in the unhealthy sleep pattern group (775·29 mg *v.* 69·16 mg). In addition, compared to the healthy sleep pattern group, the proportion of individuals with leisure-time physical activity levels < 600 MET·min/week was higher in the unhealthy sleep pattern group ($P < 0·001$).

Associations of dietary antioxidant quality score and leisure-time physical activity with unhealthy sleep patterns in cancer survivors

We first screened the covariates associated with unhealthy sleep patterns in cancer survivors (online Supplementary Table S1). The results showed that age (OR = 0·66, 95 % CI: 0·49, 0·88), race (Non-Hispanic White: OR = 0·57, 95 % CI: 0·39, 0·84), PIR (PIR > 1·01: OR = 0·43, 95 % CI: 0·29, 0·65), cancer site (skin: OR = 1·86, 95 % CI: 1·20, 2·88; digestive system: OR = 2·02, 95 % CI: 1·06, 3·83), painkiller (OR = 1·89, 95 % CI: 1·21, 2·96), anxiolytics/sedatives/hypnotics (OR = 7·04, 95 % CI: 3·55, 13·96) and antidepressant (OR = 2·00, 95 % CI: 1·23, 3·25) were all significantly associated with unhealthy sleep patterns.

Then, we explored the associations of DAQS and leisure-time physical activity with unhealthy sleep patterns in cancer survivors (Table 2). After adjusting for covariates, the highest tertile of DAQS level (OR = 0·60, 95 % CI: 0·36, 0·99) and leisure-time physical activity ≥ 600 MET·min/week (OR = 0·76, 95 % CI: 0·58, 1·00) were both associated with lower odds of unhealthy sleep patterns in cancer survivors. We further assessed the combined associations between different DAQS levels and leisure-time physical activity levels on unhealthy sleep patterns (Table 3). Compared with low DAQS level combined with leisure-time physical activity level < 600 MET·min/week, median level of DAQS combined with leisure-time physical activity ≥ 600 MET·min/week (OR = 0·62, 95 % CI: 0·43, 0·88) or high level of DAQS combined with leisure-time physical activity ≥ 600 MET·min/week (OR = 0·41, 95 % CI: 0·23, 0·72) was linked to lower odds of unhealthy sleep patterns.

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Table 1. Characteristics of cancer survivors with different sleep patterns (Mean values with their standard errors; numbers and percentages)

	Total (*n* 1936)		Healthy sleep pattern (*n* 803)		Unhealthy sleep pattern (*n* 1133)		
Variables	Mean	SE	Mean	SE	Mean	SE	*P*
Age, years, Mean (SE)	61·55	0·47	63·91	0·60	59·89	0·56	<0·001
	n	%	*n*	%	*n*	%	
Age, years, *n* (%)							<0·001
< 65	836	53·5	268	45·6	568	59·0	
≥ 65	1100	46·5	535	54·4	565	41·0	
Gender, *n* (%)							0·150
Male	866	41·3	387	44·1	479	39·3	
Female	1070	58·7	416	55·9	654	60·8	
Race, *n* (%)							0·022
Non-Hispanic Black	257	5·3	88	4·1	169	6·1	
Non-Hispanic White	1365	86·9	597	89·3	768	85·2	
Mexican American	126	2·4	45	2·3	81	2·5	
Other	188	5·4	73	4·2	115	6·3	
PIR, *n* (%)							<0·001
≤ 1·01	265	8·5	69	4·6	196	11·3	
> 1·01	1539	84·8	672	89·1	867	81·8	
Unknown	132	6·7	62	6·3	70	6·9	
Marital status, *n* (%)							0·106
Married/living with partner	1199	67·1	528	70·7	671	64·6	
Spinsterhood/divorced/widowed/separated	737	32·9	275	29·3	462	35·4	
	Mean	SE	Mean	SE	Mean	SE	
Height, cm, Mean (SE)	167·52	0·34	167·60	0·52	167·47	0·47	0·855
Weight, kg, Mean (SE)	80·90	0·62	78·85	0·71	82·34	0·91	0·003
BMI, kg/m^2, *n* (%)							0·027
< 25	560	30·8	240	31·0	320	30·8	
(25, 30)	664	34·5	302	38·6	362	31·6	
≥ 30	712	34·7	261	30·5	451	37·7	
Physical work, MET·min/week, *n* (%)							0·717
< 600	1383	70·0	573	69·5	810	70·4	
≥ 600	553	30·0	230	30·6	323	29·6	
Sedentary time, min/d, *n* (%)							0·529
< 480	1233	58·3	512	59·5	721	57·5	
≥ 480	703	41·7	291	40·6	412	42·5	
Smoking, *n* (%)							0·089
No	891	46·8	399	49·5	492	44·9	
Former	747	37·9	319	38·3	428	37·7	
Now	298	15·3	85	12·2	213	17·4	
Drinking, *n* (%)							0·288
No	545	22·7	225	23·2	320	22·4	
Light	400	21·5	150	19·8	250	22·8	
Moderate	430	28·0	200	30·0	230	26·5	

(*Continued*)

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Table 1. (*Continued*)

Variables	Total (*n* 1936)		Healthy sleep pattern (*n* 803)		Unhealthy sleep pattern (*n* 1133)		*P*
	Mean	SE	Mean	SE	Mean	SE	
Heavy	185	11·3	89	12·6	96	10·4	
Unknown	376	16·5	139	14·5	237	17·9	
Hypertension, *n* (%)							0·892
No	488	30·3	208	30·1	280	30·5	
Yes	1448	69·7	595	69·9	853	69·6	
DM, *n* (%)							0·968
No	1471	80·4	619	80·4	852	80·5	
Yes	465	19·6	184	19·6	281	19·5	
Dyslipidaemia, *n* (%)							0·636
No	334	17·5	136	16·8	198	18·0	
Yes	1602	82·5	667	83·2	935	82·0	
CVD, *n* (%)							0·896
No	1233	70·3	520	70·1	713	70·5	
Yes	703	29·7	283	29·9	420	29·5	
COPD, *n* (%)							0·038
No	1650	85·3	713	87·8	937	83·6	
Yes	286	14·7	90	12·2	196	16·4	
Cancer site, *n* (%)							0·118
Urinary	291	9·2	141	12·1	150	7·2	
Digestive	111	4·4	40	3·8	71	4·9	
Reproductive	240	11·8	79	10·3	161	12·9	
Respiratory	261	12·0	114	13·5	147	11·0	
Skin	507	34·4	217	32·8	290	35·6	
Hematopoietic	49	2·7	27	3·8	22	1·9	
Thyroid	37	2·1	13	1·3	24	2·6	
Neural/cerebric	8	0·4	0	0·0	8	0·6	
Others	95	5·5	39	5·8	56	5·3	
2 sites	158	8·0	69	7·8	89	8·3	
3 sites	13	0·8	6	0·8	7	0·8	
≥ 3 sites	2	0·1	1	0·1	1	0·1	
Unknown	164	8·6	57	8·2	107	9·0	
Cancer duration, years, *n* (%)							0·424
≤ 1	249	14·1	106	14·9	143	13·5	
(1, 3)	239	11·7	89	10·8	150	12·3	
(3, 5)	200	10·7	96	12·8	104	9·2	
> 5	1089	55·0	456	53·4	633	56·2	
Unknown	159	8·6	56	8·1	103	8·9	
Antineoplastic agents, *n* (%)							0·825
No	1683	87·1	709	87·6	974	86·6	
Antimetabolite	71	3·7	22	3·3	49	3·9	
Other antineoplastic agents	182	9·3	72	9·1	110	9·5	

(*Continued*)

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Table 1. (*Continued*)

	Total (*n* 1936)		Healthy sleep pattern (*n* 803)		Unhealthy sleep pattern (*n* 1133)		
Variables	Mean	SE	Mean	SE	Mean	SE	*P*
Painkiller, *n* (%)							0·001
No	1705	89·3	732	93·0	973	86·7	
Yes	231	10·7	71	7·0	160	13·3	
ASH, *n* (%)							<0·001
No	1794	92·7	784	98·4	1010	88·7	
Yes	142	7·3	19	1·6	123	11·3	
Antidepressant, *n* (%)							0·001
No	1615	81·0	718	88·2	897	75·9	
Yes	321	19·0	85	11·8	236	24·1	
Total energy intake, kcal, Mean (SE)	1935·69	28·01	1917·29	33·11	1948·68	39·64	0·525
WBC, 1000/μl, Mean (SE)	7·16	0·08	6·95	0·10	7·31	0·11	0·020
Lymphocyte, 1000/μl, Mean (SE)	2·02	0·03	1·94	0·04	2·08	0·05	0·080
Neutrophil, 1000/μl, Mean (SE)	4·33	0·06	4·21	0·08	4·41	0·08	0·063
eGFR, ml/min/1·73 m^2, *n* (%)							0·735
< 60	276	10·9	116	11·3	160	10·7	
≥ 60	1660	89·1	687	88·7	973	89·3	
	Mean	SE	Mean	SE	Mean	SE	
DAQS, Mean (SE)	4·12	0·05	4·25	0·07	4·03	0·08	0·041
DAQS levels, *n* (%)	*n*	%	*n*	%	*n*	%	0·070
Low	679	30·1	252	25·9	427	33·0	
Median	948	51·2	408	53·2	540	49·7	
High	309	18·8	143	20·9	166	17·3	
	Mean	SE	Mean	SE	Mean	SE	
Vit A, mcg, Mean (SE)	683·76	29·50	775·29	59·64	619·16	23·81	0·016
Vit E, mg, Mean (SE)	9·25	0·27	9·68	0·48	8·94	0·35	0·237
Vit C, mg, Mean (SE)	213·61	13·99	211·26	16·64	215·27	20·42	0·878
Zn, mg, Mean (SE)	17·77	0·44	19·01	0·90	16·90	0·60	0·086
Se, mcg, Mean (SE)	125·26	2·34	125·06	3·02	125·40	3·66	0·946
Mg, mg, Mean (SE)	337·75	8·84	353·44	14·98	326·68	9·46	0·112
Leisure-time physical activity, MET·min/week, *n* (%)							0·001
< 600	1263	61·3	495	55·7	768	65·3	
≥ 600	673	38·7	308	44·3	365	34·8	
	Mean	SE	Mean	SE	Mean	SE	
Sleep duration, h/d, Mean (SE)	7·00	0·04	7·69	0·03	6·51	0·06	<0·001
Sleep duration levels, h/d, *n* (%)							<0·001
7–9	1167	65·0	803	100·0	364	40·3	
< 7	704	32·6	0	0·0	704	55·6	
> 9	65	2·4	0	0·0	65	4·1	
Sleeping difficulties, *n* (%)							<0·001
No	1249	61·3	803	100·0	446	34·0	
Yes	687	38·7	0	0·0	687	66·0	

(*Continued*)

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Table 1. (*Continued*)

Variables	Total (*n* 1936)		Healthy sleep pattern (*n* 803)		Unhealthy sleep pattern (*n* 1133)		*P*
	Mean	SE	Mean	SE	Mean	SE	
Sleep disorders, *n* (%)							<0·001
No	1697	86·6	803	100·0	894	77·2	
Yes	239	13·4	0	0·0	239	22·8	

PIR, poverty:income ratio; MET, metabolic equivalent; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; ASH, anxiolytics, sedatives and hypnotics; eGFR, estimated glomerular filtration rate; DAQS, dietary antioxidant quality score; vit A, vitamin A; vit E, vitamin E; vit C, vitamin C.
Comparisons used *t* test and χ^2 test.

Table 2. Associations of DAQS and leisure-time physical activity with unhealthy sleep patterns in cancer survivors (Odds ratios and 95 % confidence intervals)

Variables	Model 1			Model 2			Model 3		
	OR	95 % CI	*P*	OR	95 % CI	*P*	OR	95 % CI	*P*
DAQS	0·85	0·73, 0·99	0·039	0·84	0·70, 1·00	0·050	0·85	0·71, 1·03	0·090
DAQS levels									
Low		Ref			Ref			Ref	
Median	0·73	0·54, 1·00	0·050	0·75	0·53, 1·05	0·092	0·76	0·54, 1·08	0·124
High	0·65	0·43, 0·98	0·039	0·57	0·34, 0·93	0·026	0·60	0·36, 0·99	0·046
Leisure-time physical activity									
< 600		Ref			Ref			Ref	
≥ 600	0·67	0·53, 0·84	0·001	0·73	0·56, 0·95	0·019	0·76	0·58, 1·00	0·048

DAQS, dietary antioxidant quality score; Ref, reference.
Model 1: unadjusted model.
Model 2: adjusted for age, race, PIR, cancer site, painkiller, ASH, antidepressant and total energy intake.
Model 3: adjusted for covariables in the adjustment of model 2 and DAQS or leisure-time physical activity adjusted for each other.

Table 3. Combined association between DAQS and leisure-time physical activity on unhealthy sleep patterns in cancer survivors (Odds ratios and 95 % confidence intervals)

Variables	Model 1			Model 2		
	OR	95 % CI	*P*	OR	95 % CI	*P*
Low DAQS and leisure-time physical activity < 600		Ref			Ref	
Median DAQS and leisure-time physical activity < 600	0·73	0·50, 1·07	0·105	0·77	0·50, 1·17	0·211
High DAQS and leisure-time physical activity < 600	0·77	0·44, 1·34	0·346	0·70	0·35, 1·41	0·308
Low DAQS and leisure-time physical activity ≥ 600	0·69	0·41, 1·16	0·158	0·83	0·48, 1·44	0·495
Median DAQS and leisure-time physical activity ≥ 600	0·55	0·39, 0·78	0·001	0·62	0·43, 0·88	0·010
High DAQS and leisure-time physical activity ≥ 600	0·43	0·23, 0·78	0·007	0·41	0·23, 0·72	0·003

DAQS, dietary antioxidant quality score; Ref, reference.
Model 1: unadjusted model.
Model 2: adjusted for age, race, PIR, cancer site, painkiller, ASH, antidepressant, and total energy intake.

Combined associations between different dietary antioxidant quality score levels and leisure-time physical activity levels on sleep patterns in age, painkiller use and antidepressant use subgroups

We also investigated the combined associations between different DAQS levels and leisure-time physical activity levels on sleep patterns in cancer survivors with different age and medication situations (Fig. 2). The combined association between high DAQS level and high leisure-time physical activity level had a negative association with unhealthy sleep patterns in age < 65 years old (OR = 0·30, 95 % CI: 0·13, 0·70), non-painkiller (OR = 0·39, 95 % CI: 0·22, 0·71), non-antidepressant (OR = 0·49, 95 % CI: 0·26, 0·91) and antidepressant (OR = 0·11, 95 % CI: 0·02, 0·50) use subgroups. No interaction effect was observed between age or medication situations and DAQS combined with leisure-time physical activity on sleep patterns in cancer survivors (all $P > 0·05$), indicating these two factors may not impact the associations.

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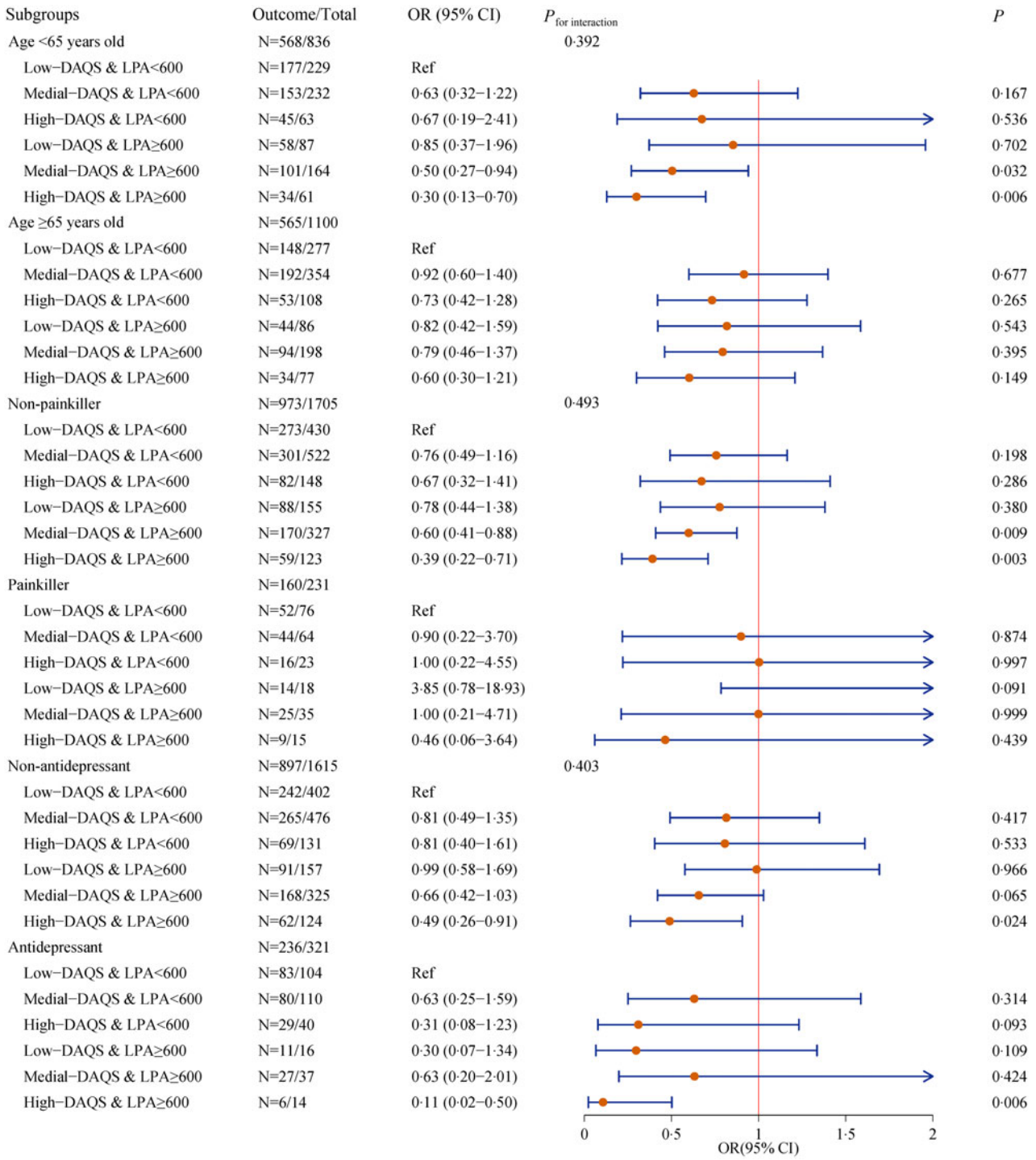

Figure 2. Subgroup analyses of combined association between different DAQS levels and leisure-time physical activity levels on unhealthy sleep patterns in cancer survivors. DAQS, dietary antioxidant quality score.

Discussion

This cross-sectional study explored the combined association between different DAQS levels and leisure-time physical activity levels on sleep patterns in cancer survivors. The study results indicated that higher DAQS combined with higher leisure-time physical activity levels was associated with lower odds of unhealthy sleep patterns in cancer survivors. Moreover, this joint association was also found in aged < 65 years old, non-painkiller, non-antidepressant and antidepressant use subgroups.

Dietary habits and physical activity are common factors influencing human health. Growing scientific evidence has suggested that a healthy sleep pattern is strongly associated with improved adverse outcomes for cancer survivors, and therefore, it is necessary to investigate the beneficial factors that can improve sleep in this population[33,34]. However, to the best of our knowledge, no study has discussed the combined association between DAQS and leisure-time physical activity on sleep patterns in cancer survivors. In the current study, we included the

representative population in the USA from the NHANES database and explored the combined association between DAQS and leisure-time physical activity on sleep patterns. We found that compared to cancer survivors with low levels of both DAQS and leisure-time physical activity, those who had both higher DAQS and higher leisure-time physical activity levels seemed to have lower odds of unhealthy sleep patterns.

The DAQS and leisure-time physical activity were, respectively, negatively associated with the odds of unhealthy sleep pattern, which was in accordance with previous studies. A cross-sectional study among women with diabetes mellitus conducted by Daneshzad et al.[35] showed that subjects in the highest tertile of the ferric reducing ability of plasma and the oxygen radical absorbance capacity score compared to those in the lowest tertile of these scores had, respectively, 94 % and 87 % lower risk of poor sleep. Differently, we used the DAQS to reflect the dietary antioxidant capacity, which not only included dietary vitamins indexes but also dietary minerals. In addition, interventions to promote leisure-time physical activity and/or exercise-based rehabilitation may improve quality of life among cancer survivors[36]. It has been reported that adequate adherence to the 2018 diet and exercise recommendations of the World Cancer Research Fund/American Institute for Cancer Research can possibly result in less oxidative stress, lower risk to chemo- and radiotoxicity, lower risk of relapse and increased quality of life in breast cancer survivors[37]. Based on these evidences, we speculated that DAQS and leisure-time physical activity may be at the same time involved in sleep conditions improvement in cancer survivors. Although DAQS and leisure-time physical activity were both beneficial factors for quality of life in cancer survivors, causal associations of these two indexes with sleep patterns are still needed to be clarified.

The DAQS included many ingredients that have been proven to have antioxidant effects in previous studies, which may be involved in pathways associated with physical activity and/or sleep quality. Vit C supplementation helped to reduce oxygen-free radicals produced by radiation and chemotherapy and relieved patients of symptoms related to cancer treatment, such as fatigue, insomnia and sleep disturbances[38,39]. Vit E acts through antioxidant mechanisms to initiate T-cell activation signals, enhance inflammatory cytokine secretion and natural killer cell responses and reduce the risk of infection[40]. Zn and Se, essential trace elements, play crucial roles in the development and maintenance of immune cells and mammalian redox biology. Insufficient Zn and Se levels may lead to impaired humoral function and cell-mediated immunity[41]. A cross-sectional analysis basing on the NHANES database showed that serum Zn, Zn:Cu ratio and Zn:Se ratio were all associated with a reduced likelihood of self-reported sleep disturbance in adults[42]. Another study found that Mg ions might influence sleep duration by regulating circadian rhythms, with people who slept longer having significantly higher levels of Mg[38]. Mg has a crucial role in numerous biological processes, including oxidative phosphorylation, energy production, glycolysis and protein and nucleic acid synthesis[43]. Mg deficiency may produce overexcitation of the central nervous system, while severe Mg deficiency is thought to cause weakness, muscle pain and nighttime cramps[44]. Besides, among the DAQS components, we only found the average vit A concentration was significantly different between healthy sleep pattern group and unhealthy sleep pattern group (775·29 mcg *v.* 619·16 mcg). Previous human studies reported that lower vit A intake levels were associated with disturbed wake–sleep cycles[45]. Vit A may influence biological rhythms and various diseases, including but not limited to metabolic syndromes, CVD, cancers and inflammations through retinoid-related orphan receptors, constituting an important part of the molecular mechanism of biorhythm regulation[46,47]. Nevertheless, the potential mechanisms that combined association between DAQS and leisure-time physical activity on sleep pattern in cancer survivors are still unclear.

Hypothesised biologic mechanisms that physical activity influencing sleep quality in cancer survivors could through the main pathways including metabolic and sex hormones, inflammation and immunity[48]. The growing evidence from experimental studies indicated that prolonged and uninterrupted sitting are associated with impaired glucose metabolism and increased systemic inflammation[49]. Low leisure-time physical activity and prolonged sitting may also contribute to increased risk of cachexia, thromboembolic events and fatigue, which all influence survival after cancer[50]. Traditional exercise training focuses on moderate-to-vigorous intensity physical activity and exercise, which can be challenging for patients who are older and have substantial physical and psychosocial barriers, high frailty, comorbidity burden, more advanced disease and cancer survivors[51–53]. Therefore, increasing light-intensity physical activity and exercise and reducing sedentary behavior are also recognised as important[31]. Although with the limited evidence available, the WHO in its 2020 guidelines on physical activity and sedentary behaviour strongly recommends limiting the amount of sedentary time and substituting it with any physical activity to improve health, particularly for individuals with long-term diseases[54].

Additionally, the combined association between DAQS and leisure-time physical activity on sleep pattern was also found in < 65 years old, non-painkiller, non-antidepressant and antidepressant use subgroups. Previous studies have reported that higher dietary antioxidant levels were associated with better nutritional status and better sleep quality in the elderly population[18,55]. DNA damage, telomere dysfunction, epigenetic disruption, mitogenic signalling and oxidative stress increase with ageing[56–59]. However, we did not observe the combined association between higher levels of DAQS and leisure-time physical activity on lower odds of unhealthy sleep pattern in cancer survivors aged ≥ 65 years, which we speculated that may because the influencing from more healthier body condition and higher adherence to medical advice in younger persons. Furthermore, this combined association was found in non-painkiller, non-antidepressant and antidepressant subgroups. Although painkiller and antidepressant act on the nervous system, their usage was generally in accordance with medical advice, and clinicians may also recommend periodic inspection on relative indexes of drug metabolism. Therefore, whether the use of such drugs can affect the combined association between DAQS and leisure-time physical activity on sleep patterns is still unclear.

This study was the first to explore the combined association between DAQS and leisure-time physical activity on sleep patterns in cancer survivors, which may provide some references for the improvement of living quality in these populations with unhealthy sleep patterns. Basing on the NHANES database, the study subjects were the representative population in the USA so that our findings were relatively credible. However, there are still some limitations in our research. We could not conclude causal associations of DAQS and leisure-time physical activity with sleep patterns in cancer survivors due to the study design was cross-sectional. The information on dietary intake, sleeping and leisure-time physical activity were self-reported, which may cause recalling biases.

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Information on dietary intake was collected through 24-hour dietary recalls in the NHANES, which could only reflect the short-term dietary intake status instead of the long-term influencing. The database only collected data of sleeping in 2005–2014, and data of dietary supplement were collected starting from 2007, and therefore, the data we used for analyses were 2007–2014 considering both sleep and dietary information. The exclusion of persons missing information on study variables may result in selection bias. Additionally, detailed information on painkiller type, which may affect sleep patterns, was not available in the database.

Conclusion

Higher level of DAQS combined with higher level of leisure-time physical activity was associated with lower odds of unhealthy sleep patterns in cancer survivors. These findings indicated that, in addition to dietary, focusing on combined effect among multi-angle lifestyle factors has significance in management of cancer survivors and improving their living quality.

Supplementary material. For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114524001831

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R. Y., X. L., L. Z. and X. H. designed the study. R. Y. and X. L. wrote the manuscript. F. P., C. L., Y. N., S. W. and S. S. collected, analysed and interpreted the data. L. Z. and X. H. critically reviewed, edited and approved the manuscript. All authors read and approved the final manuscript.

There are no conflicts of interest.

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