

Influencing factors of depressive symptoms in patients with malignant tumour

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Abstract

Objective: To assess the influencing factors of depressive symptoms in malignant tumour patients.

Methods: Participants were 2079 inpatients with malignant tumour (1291: depressive symptoms; 788 no depressive symptoms). Univariable and multivariable logistic regression were used to evaluate sociodemographic and clinical factors influencing depressive symptoms.

Results: Risk factors were family income \leq 5000 yuan (odds ratio [OR]: 4.966, 95% confidence interval [Cl]: 2.938–8.395) and 5001–10,000 yuan (OR: 3.111, 95% Cl: 1.840–5.260); Karnofsky Performance Status of 70 (OR: 2.783, 95% Cl: 1.281–6.042) and 80 (OR: 1.834, 95% Cl: 1.139–2.953); disease course \leq 1 year; palliative treatment (OR: 2.288, 95% Cl: 1.292–4.055); progressive disease (OR: 1.876, 95% Cl: 1.284–2.739); pain (OR: 1.973, 95% Cl: 1.555–2.505); cancer type: lung (OR: 3.199, 95% Cl: 1.938–5.279), oesophagus (OR: 3.288, 95% Cl: 1.673–6.464), cervix (OR: 1.542, 95% Cl: 1.056–2.253) and partial knowledge of disease condition (OR: 2.366, 95% Cl: 1.653–3.385). Return to work (OR: 0.503, 95% Cl: 0.348–0.727) and physical exercise (OR: 0.437, 95% Cl: 0.347–0.551) were protective against depressive symptoms. **Conclusions:** Several factors affected depressive symptoms in malignant tumour patients, including income, disease type and course, palliative treatment, return to work and physical exercise.

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Keywords

Influencing factor, depressive symptom, malignant tumour, sociodemographic, clinical, China, regression

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Introduction

Malignant tumour has become a major cause of global mortality and its management is a huge health burden for healthsystems.^{1,2} According to care the International Agency for Research on Cancer, the cancer burden in China is substantial and the incidence of cancer is still rising.^{3,4} Although substantial improvements have been made in the clinical treatment of malignant tumour, its overall prognosis remains unfavourable.⁵ The diagnosis of malignant tumour and the resulting deterioration in health status are a psychological challenge for patients, as the disease has a substantial effect on patients' physical appearance, physical ability, family, occupation, economic status and emotions during diagnosis and treatment.⁶ More attention should be paid to psychosocial states in cancer patients.

Depression is a common psychological disease that is comorbid with malignant tumour. There is evidence from previous studies that the prevalence of depressive symptoms is substantial in patients with malignant tumours.⁷ One study reported that the prevalence of depression among head and neck cancer patients varies from 13% to 40% at diagnosis, 25% to 52% during treatment and 11% to 45% in the first 6 months following treatment.8 The prevalence of major depressive disorder in breast cancer patients is estimated as 10% to 33%.⁹ It has also been reported that the incidence of major depression in malignant tumour patients is approximately 15% in

oncological and haematological settings.¹⁰ Cancer treatment causes metabolic and endocrine changes, and chronic pain may also increase the susceptibility to depression tumour patients.^{11,12} malignant of Depression damages the immune system and promotes the progression of malignant tumours, which leads to worse disease outcomes.¹³ Depression also increases patient treatment noncompliance, such as failure to attend consultation appointments, and leads to poorer treatment response.¹⁴ A better understanding of the influencing factors of depression may not only prolong the lives of patients, but also improve their quality of life.¹⁵ Many studies have explored the risk factors for depression in different cancers. Lee et al. showed that higher educational level, stressor severity and anxiety severity were associated with depression in patients with head and neck cancer and lung cancer.¹⁶ Other studies have found that levels of blood cytokines. such interleukin-10. interleukin-6. as interleukin-8 and tumour necrosis factor- α . are associated with depression status in patients with cancer.¹⁷ However, these studies used only clinical or laboratory examination indexes and did not analyse important social factors such as work status. The aim of this study was to identify the influencing factors of depressive symptoms in patients with malignant tumours, focusing on demographic, clinical and social characteristics. The findings may help clinicians to prevent depressive symptoms in patients with malignant tumours.

Methods

Study design and participants

Potential participants in this cross-sectional study were inpatients with malignant tumours from the following departments of the Affiliated Cancer Hospital of Xinjiang Medical University: pulmonary medicine, gastroenterology, breast radiotherapy, chest and abdomen radiotherapy, gynaecology radiotherapy, head and neck radiotherapy, and integrated traditional Chinese and Western medicine. Participants were selected according to the following inclusion criteria: malignant tumour confirmed by pathology or cytology, aged 18 to 85 years, ability to fully understand the questionnaire content and provision of written consent. Excluded patients were those with cognitive impairment and severe weakness owing to disease or treatment; those who did not agree to participate in the study; patients diagnosed with schizophrenia, schizoaffective disorder or bipolar I disorder; patients with depressive symptoms caused by another medical condition or induced by substances (defined using the International Classification of Diseases, Tenth Revision) and patients with severe anxiety and acute confusional states associated with drug toxicity. The reporting of this study conforms to the STROBE guidelines.¹⁸ All participants provided informed consent and the study was approved by the ethics committee of the Affiliated Cancer Hospital of Xinjiang Medical University (approval number: G-201554).

Assessment and diagnosis of depressive symptoms

The Zung Self-Rating Depression Scale (SDS) is a self-report questionnaire that has been previously used to evaluate the presence of depressive symptoms in

malignant tumour patients.¹⁹ The SDS comprises 20 items scored on a scale of 1 to 4. The raw SDS score ranges from 20 to 80, and a standard score is calculated by multiplying raw scores by 1.25, resulting in a total standard score from 25 to 100. The severity of depressive symptoms is defined as <53, no depressive symptoms; 63 to 72, moderate depressive symptoms; and 72 to 100, severe depressive symptoms.²⁰

Variables and data collection

Important risk factors were selected based on the sociodemographic and clinical data collected from all patients. Sociodemographic information comprised sex, age, race (Han population or minority population), residence (city or country), education (illiterate, junior, senior or college), marital status (married or single), monthly family income (\leq 5000, 5001-10,000 or >10,000 yuan), work status (working or not working), physical exercise (engagement in exercise or no exercise). comprised Clinical data Karnofsky Performance Status (KPS) score (60, 70, 80, 90 or 100), cancer type (head and neck, lung, breast, oesophagus, stomach, colorectum, cervix, thyroid or others), disease course (≤ 1 month, 2–6 months, 7–12 months or >1 year), cancer stage (I, II, III or IV), therapy (re-examination, chemotherapy or/and radiotherapy or palliative treatment), disease state (stable, progression or newly diagnosed), metastasis or not, awareness of condition (no idea, partial knowledge or full knowledge), pain or not and history of hypertension or diabetes.

Definitions of variables

Pain intensity was evaluated using a numerical rating scale and classified into none (0 points), mild (1–3), moderate (4–6) and severe (7-10).²¹ Physical activity was defined as any type of planned, structured and repeated physical activity, including any body movement produced by skeletal muscle contraction for improving or maintaining physical fitness.²² The KPS is a performance status scale that evaluates patient status and is administered by a health-care provider. Patients were assigned to 1 of 10 categories (ranging from 0 (dead) to 100 (normal activity, no evidence of disease).²³ A detailed definition of KPS score is shown in Supplementary Table 1.

Statistical analysis

EpiData 3.1 (EpiData Association, Odense, Denmark) was used to establish a database, and double entry was used to ensure the correctness of the input data. Statistical analysis was conducted using R 4.0.2 software (www.r-project.org). Quantitative variables with normal or approximately normal distribution were expressed as mean \pm standard deviation (SD). One-way analysis of variance was used for betweengroup comparisons. Quantitative variables with skewed distributions were represented interquartile bv median and range. Enumeration data were presented as case and frequency (N [%]). The influencing factors of depressive symptoms in patients with malignant tumour were preliminarily analysed using the chi-square test (χ^2) and odds ratios (ORs) and 95% confidence intervals (CIs). Statistically significant factors in the univariable analysis were included in a logistic regression analysis using a backward stepwise regression method. The results of the above analysis were used to conduct multivariable logistic regressions for breast cancer, lung cancer, colorectal cancer and cervical cancer to explore the influencing factors of depressive symptoms in specific tumour populations. Of the factors examined in the multivariable logistic regression, the main factors were selected for an efficacy analysis to test the sample size efficacy. All statistical analyses were two-sided, and P < 0.05 was considered statistically significant.

Results

Background characteristics of participants

In total, 2178 patients with malignant tumour were enrolled in this study. After excluding patients with impaired cognition owing to disease or treatment; severely weak patients; those who did not agree to participate in the study; those diagnosed with schizophrenia, schizoaffective disorder or bipolar I disorder; those with depressive symptoms caused by another medical condition or induced by substances; and those with severe anxiety and acute confusional states associated with drug toxicity, 2079 remained (response participants rate: 95.45%). All participants were divided а depressive symptoms into group (n = 1291) and a non-depressive symptoms group (n = 788) according to the presence of depressive symptoms. The screening process is shown in Figure 1. The men:women sex ratio was 1:1.82. The average age of all patients was 54.62 ± 11.43 years and 86.24% of patients were married. Of participants, 1473 (70.85%) were Han, 54.65% were educated to junior high school level or below, 1285 lived in the city and 57.53% had a monthly family income below 5000 yuan. Of participants, 1036 engaged in physical exercise. Only 233 patients returned to work and 1846 did not return to work or retired. Most of the 2079 participants had KPS scores of 80 (33.09%) or 90 (52.86%). There were 321 patients with lung tumour, 512 patients with breast cancer, 305 patients with colorectal cancer and 305 patients with cervical cancer. Of patients, 53.39% had a disease course longer than 6 months and 26.84% patients had disease progression. Regarding treatment, 51.23% patients had



Figure 1. Participant screening process.

received radiotherapy, chemotherapy or concurrent chemoradiotherapy. Of patients, 639 were at stage IV, 725 had tumour metastasis and 60 had no knowledge of their disease state. A total of 235 patients had hypertension and 130 had diabetes. Detailed patient data are shown in Table 1.

Univariable analysis for malignant tumour patients with depressive symptoms

A univariable analysis was conducted to compare the characteristics of malignant tumour patients with or without depressive symptoms. The results showed significant differences between the depressive symptoms group and the non-depressive symptoms group on sex ($\chi^2 = 13.918$, P < 0.001), age ($\chi^2 = 61.662$, P < 0.001), place of residence $(\chi^2 = 31.634, P < 0.001)$, education $(\chi^2 = 125.227, P < 0.001)$, marital status $\chi^2 = 19.798$, P < 0.001, monthly family income ($\chi^2 = 199.74$, P < 0.001), work status ($\chi^2 = 92.701$, P < 0.001), physical exercise $(\gamma^2 = 214.075, P < 0.001)$, KPS (P < 0.001),score cancer stage $(\gamma^2 = 119.365, P < 0.001)$, disease course

 $(\chi^2 = 57.251, P < 0.001)$, therapy $(\chi^2 = 102.383, P < 0.001)$, disease state $(\chi^2 = 191.774, P < 0.001)$, tumour metastasis $(\chi^2 = 134.579, P < 0.001)$, pain $(\chi^2 = 84.292, P < 0.001)$, condition awareness $(\chi^2 = 128.204, P < 0.001)$, history of hypertension $(\chi^2 = 5.598, P < 0.001)$ and type of cancer $(\chi^2 = 10.317, P < 0.001)$ (Table 2).

Logistic regression analysis for depressive symptoms in malignant tumour patients

The data showed that the following factors increased the risk of depressive symptoms in malignant tumour patients: monthly family income \leq 5000 yuan (OR = 4.966, 95% CI: 2.938–8.395, P < 0.001) and 5001 to 10,000 yuan (OR = 3.111, 95% CI: 1.840-5.260, P < 0.001), KPS score of 70 95% (OR = 2.783,CI: 1.281-6.042, P = 0.010) and 80 (OR = 1.834, 95% CI: 1.139-2.953, P = 0.013), disease course \leq 12 months (*P* < 0.05), palliative treatment (OR = 2.288,95% CI: 1.292-4.055, P = 0.005),progressive disease (OR = 1.876,95% CI: 1.284-2.739, P = 0.001), pain (OR = 1.973, 95% CI: 1.555-2.505, P < 0.001), cancer type lung

	All patients
Characteristic	(n = 2079)
Sex, n (%)	
Men	736 (35.40)
Women	1343 (64.60)
Age, years, n (%)	
<40	210 (10.10)
	585 (28.14)
51-60	632 (30.40)
61–85	652 (31.36)
Race, n (%)	()
Han	1473 (70.85)
Minority	606 (29.15)
Residence, n (%)	Residence. n (%)
City	1285 (61.81)
Country	794 (38.19)
Education, n (%)	
Illiterate	39 (6.69)
lunior	997 (47.96)
Senior	563 (27.08)
College	380 (18.28)
Marital status, n (%)	
Married	1793 (86 24)
Single	286 (13.76)
Monthly family income yuan	n (%)
< 5000	1196 (57 53)
5001-10.000	771 (37.09)
>10.001	112 (5.39)
Work, n (%)	
No	1846 (88,79)
Yes	233 (11 21)
Physical exercise, n (%)	200 (11.21)
No	1043 (50.17)
Yes	1036 (49.83)
KPS. n (%))
60	13 (0.63)
70	135 (6.49)
80	688 (33.09)
90	1099 (52.86)
100	44 (6.93)
Type of cancer, n (%)	()
Head and neck	45 (2.16)
Lung	321 (15.44)
Breast	5 3 (24.68)
Oesophagus	120 (5 77)
Stomach	216 (10 39)
Colorectum	305 (14.67)
	,
	(continued)

 Table I. Baseline data for 2079 cancer patients.

Table I. Continued.

Characteristic	All patients (n = 2079)
Corvix	305 (14 67)
Thyroid	78 (3 75)
Others	176 (8 47)
Disease course n (%)	170 (0.17)
	238 (11 45)
2–6 months	731 (35.16)
7-12 months	357 (17 17)
> vear	753 (36.22)
Cancer stage, n (%))
	332 (15.97)
1	553 (26.60)
111	555 (26.70)
IV	639 (30.74)
Therapy, n (%)	()
Re-examination	832 (40.02)
Chemotherapy or/	1065 (51.23)
and radiotherapy	· · · · · ·
Palliative treatment	182 (8.75)
Disease state, n (%)	
Stable	1348 (64.84)
Progression	558 (26.84)
Newly diagnosed	173 (8.32)
Metastasis, n (%)	
No	1354 (65.13)
Yes	725 (34.87)
Condition awareness, n (%)	
No idea	60 (2.89)
Partial knowledge	375 (18.04)
Full knowledge	1644 (79.08)
Pain, n (%)	
No	1290 (62.05)
Yes	789 (37.95)
Hypertension, n (%)	
No	1844 (88.70)
Yes	235 (11.30)
Diabetes, n (%)	
No	1949 (93.75)
Yes	130 (6.25)

KPS, Karnofsky Performance Status.

(OR = 3.199, 95% CI: 1.938-5.279, P < 0.001), oesophagus (OR = 3.288, 95% CI: 1.673-6.464, P < 0.001) and cervix (OR = 1.542, 95% CI: 1.056-2.253, P = 0.025) and partial knowledge of disease

	No depressive	Depressive			
Characteristic	symptoms n = 788	symptoms n = 1291	χ^2	Р	OR (95% CI)
Sex. n (%)			13.918	< 0.001	
Men	239 (30.33)	497 (38.50)			1.438 (1.190–1.737)
Women	549 (69.67)	794 (61.50)			1.000
Age, years, n (%)		()	61.662	<0.001	
<40	100 (12.69)	110 (8.52)			1.000
41–50	272 (34.52)	313 (24.24)			1.046 (0.763-1.435)
51-60	242 (30.71)	390 (30.21)			1.465 (1.069–2.007)
61-85	174 (22.08)	478 (37.03)			2.497 (1.810-3.445)
Race, n (%)			0.420	0.157	
Han	651 (82.61)	1052 (81.49)			1.000
Minority	137 (17.39)	239 (18.51)			1.080 (0.657-1.362)
Residence, n (%)			31.634	<0.001	(,
City	548 (69.54)	737 (57.09)			1.000
Country	240 (30.46)	554 (42.91)			1.716 (1.423-2.070)
Education, n (%)			125.227	<0.001	
Illiterate	34 (4.31)	105 (8.13)			4.433 (2.863–6.868)
lunior	286 (36.29)	711 (55.07)			3.568 (2.791-4.566)
Senior	244 (30.96)	319 (24.71)			1.878 (1.442–2.444)
College	224 (28.43)	156 (12.08)			1.000
Marital status, n (%)	()	()	19.798	<0.001	
Married	714 (90.61)	1079 (83.58)			1.000
Single	74 (9.39)	212 (16.42)			1.896 (1.431-2.511)
Monthly family income,		()	199.74	<0.001	· · · · · ·
yuan, n (%)					
<5000	309 (39.21)	887 (68.71)			9.034 (5.751-14.200)
5001-10,000	394 (50.00)	377 (29.20)			3.013 (1.910-4.750)
≥10,001	85 (10.79)	27 (2.09)			1.000
Work, n (%)			92.701	< 0.001	
No	632 (80.20)	1214 (94.04)			1.000
Yes	156 (19.80)	77 (5.96)			0.257 (0.192-0.343)
Physical exercise, n (%)			214.075	< 0.001	
No	233 (29.57)	810 (62.74)			1.000
Yes	555 (70.43)	481 (37.26)			0.249 (0.206-0.301)
Type of cancer, n (%)			10.317	<0.001	
Head and neck	13 (1.65)	32 (2.48)			3.278 (1.681-6.393)
Lung	46 (5.84)	275 (21.30)			7.873 (5.504–11.263)
Breast	293 (37.18)	220 (17.04)			1.000
Oesophagus	15 (1.90)	105 (8.13)			9.051 (5.122-15.995)
Stomach	83 (10.53)	133 (10.30)			2.134 (1.542–2.954)
Colorectum	159 (20.18)	146 (11.31)			1.215 (0.913–1.615)
Cervix	78 (9.90)	227 (17.58)			3.876 (2.840–5.290)
Thyroid	60 (7.61)	18 (1.39)			0.377 (0.214–0.665)
Others	41 (5.20)	135 (10.46)			4.385 (2.967–6.482)

Table 2. Univariable analysis of factors associated with depressive symptoms in cancer patients.

Characteristic	No depressive symptoms	Depressive symptoms	~ ²	D	
	11=700	11-1271	λ	1	
KPS score, n (%)			162.732	<0.001	
60	1 (0.13)	12 (0.93)			19.414 (2.460–153.279)
70	13 (1.65)	122 (9.45)			15.18 (7.823–29.478)
80	183 (23.22)	505 (39.12)			4.464 (3.065–6.506)
90	502 (63.71)	597 (46.24)			1.925 (1.347-2.749)
	89 (11.29)	55 (4.26)	110 275	.0.001	1.000
Cancer stage, n (%)			119.365	<0.001	
1	186 (23.60)	146 (11.31)			1.000
II	253 (32.11)	300 (23.24)			1.511 (1.149–1.986)
III	200 (25.38)	355 (27.50)			2.261 (1.713–2.984)
IV	149 (18.91)	490 (37.96)			4.191 (3.154–5.565)
Disease course, n (%)			57.251	<0.001	
\leq I month	52 (6.60)	186 (14.41)			3.174 (2.261–4.455)
2–6 months	249 (31.60)	482 (37.34)			1.718 (1.393–2.118)
7–12 months	133 (16.88)	224 (17.35)			1.495 (1.155–1.934)
>I year	354 (44.92)	399 (30.91)			1.000
Therapy, n (%)			102.383	<0.001	
Re-examination	407 (51.65)	425 (32.92)			1.000
Chemotherapy or/ and radiotherapy	359 (45.56)	706 (54.69)			1.883 (1.564–2.268)
Palliative treatment	22 (2.79)	160 (12.39)			6.966 (4.371–11.098)
Disease state, n (%)			191.774	<0.001	
Stable	657 (83.38)	691 (53.52)			1.000
Progression	96 (12.18)	462 (35.79)			4.577 (3.584–5.843)
Newly diagnosed	35 (4.44)	138 (10.69)			3.747 (2.548-5.515)
Metastasis, n (%)			134.579	<0.001	
No	636 (80.71)	718 (55.62)			1.000
Yes	152 (19.29)	573 (44.38)			3.34 (2.711–4.112)
Pain, n (%)	. ,	. ,	84.292	<0.001	, , , , , , , , , , , , , , , , , , ,
No	588 (74.62)	702 (54.38)			1.000
Yes	200 (25.38)	589 (45.62)			2.467 (2.031–2.996)
Condition awareness, n (%)		, , , , , , , , , , , , , , , , , , ,	128.204	<0.001	
No idea	9 (1.14)	51 (3.95)			4.468 (2.186–9.141)
Partial knowledge	54 (6.85)	321 (24.86)			4.688 (3.459–6.357)
Full knowledge	725 (92.01)	919 (71.19)			1.000
Hypertension, n (%)			5.598	0.018	
No	716 (90.86)	1128 (87.37)			1.000
Yes	72 (9.14)	163 (12.63)			1.438 (1.072-1.926)
Diabetes, n (%)	. = (()	1.600	0,206	
No	746 (94.67)	203 (93.18)			1.000
Yes	42 (5.33)	88 (6.82)			1.300 (0.89–1.898)

Table 2. Continued.

KPS, Karnofsky Performance Status; OR, odds ratio; CI, confidence interval.

condition (OR = 2.366, 95% CI: 1.653-P < 0.001). 3.385, Return to work (OR = 0.503,95% CI: 0.348 - 0.727, P < 0.001) and physical exercise (OR = 0.437,95% CI: 0.347 - 0.551, P < 0.001) reduced the risk of depressive symptoms in patients with malignant tumours (Table 3).

Subgroup analysis of different tumour types

As shown in Table 4, monthly family income $\leq 10,000$ yuan (P < 0.05), KPS score of 80 (OR = 3.552, 95% CI: 1.685-7.488, P < 0.001),progressive disease (OR = 2.994,95% CI: 1.144-7.836, P = 0.025), pain (OR = 2.143, 95% CI: 1.377-3.335, P < 0.001) and partial knowledge of disease condition (OR = 3.017, 95%CI: 1.275–7.141, P = 0.0102) increased the risk of depressive symptoms in breast patients. Return work cancer to 95% 0.240 - 0.848, (OR = 0.452,CI: P = 0.013) and physical exercise 95% CI: 0.307-0.745. (OR = 0.478,P = 0.001) were protective factors for depressive symptoms in breast cancer patients. In lung cancer patients, progressive disease (OR = 3.801, 95% CI: 1.422-10.165, P = 0.008) was a risk factor for depressive symptoms whereas return to work (OR = 0.216, 95% CI: 0.046–1.007, P = 0.051) physical and exercise (OR = 0.270,95% CI: 0.121-0.602, P = 0.001) were protective factors for depressive symptoms (Table 5). For patients with colorectal cancer, pain was a risk factor for depressive symptoms (OR = 2.053,95% CI: 1.097-3.842 P = 0.024) and physical exercise reduced of depressive the risk symptoms 95% CI: (OR = 0.357,0.193 - 0.663, P = 0.001) (Table 6). In addition, monthly family income < 10,000 yuan (P < 0.05), dis-7 to 12 months ease duration of 1.427-57.318. 95% CI: (OR = 9.045,

P = 0.019) and partial knowledge of their disease condition (OR = 3.133, 95% CI: 1.445–6.793, P = 0.004) increased the risk of depressive symptoms in cervical cancer patients (Table 7).

Power analysis and sample size determination

The G* Power software (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) and the existing sample size were used for power analysis to test the efficiency of the backward stepwise regression model. The results showed that of the main study variables (monthly family income, work status, physical exercise, tumour metastasis and pain), the lowest statistical power value was 0.959 for tumour metastasis, indicating that the sample size was sufficient for good performance of the backward stepwise regression model.

Discussion

This study collected clinical data from 2079 malignant tumour patients and evaluated the risk factors for depressive symptoms in those patients. The results showed that monthly family income $\leq 10,000$ yuan, KPS score of 70 and 80, disease course ≤ 1 year, palliative treatment, progressive disease, pain and partial knowledge of disease condition were risk factors for depressive symptoms in malignant tumour patients. Return to work and physical exercise were protective factors for depressive symptoms in patients with malignant tumour.

In this study, higher family income levels were associated with a lower risk of depressive symptoms. Patients with higher incomes experience less worry about the economic burden of cancer treatment and fewer depressive symptoms, and their family burden may be lower than that of patients with lower incomes.²⁴ Sharp and her colleagues found that 49% of 654

Variable	β	SE	OR (95% CI)	Р
Sex				
Men	-0.275	0.161	0.759 (0.554–1.041)	0.087
Women	0.000	_	1.000	_
Age, years				
<40	0.000	_	1.000	_
	-0.095	0.199	0.909 (0.616-1.343)	0.633
51–60	0.188	0.203	1.207 (0.81–1.797)	0.355
>60	0.292	0.215	1.339 (0.878-2.041)	0.175
Monthly family income, yuan		0.2.0		
< 5000	1 603	0 268	4 966 (2 938-8 395)	< 0.001
5001-10 000	1.135	0.268	3 1 1 (1 840–5 260)	< 0.001
	0.000	-		_
Work	0.000		1.000	
No	0.000	_	1 000	_
Yos	0.000	0188	0.503 (0.348, 0.727)	~0.001
Physical exercise	-0.007	0.100	0.505 (0.548-0.727)	<0.001
No	0.000		1.000	
NO Yee	0.000	_		~ 0.001
les	-0.827	0.110	0.437 (0.347-0.331)	<0.001
	1 5 1 2	1 1 5 2	4 5 4 1 (0 474 42 472)	0.100
80	1.513	1.155	4.341 (0.474 - 43.473)	0.107
70	1.023	0.396	2.783 (1.281-6.042)	0.010
80	0.606	0.243	1.834 (1.139–2.953)	0.013
90	0.255	0.223	1.291 (0.834–1.999)	0.252
100	0.000	_	1.000	-
Disease course	0.500	0.044		
≤I month	0.589	0.264	1.801 (1.073–3.024)	0.026
2–6 months	0.403	0.163	1.496 (1.088–2.058)	0.013
7–12 months	0.382	0.17	1.465 (1.049–2.044)	0.025
>l year	0.000	-	1.000	-
Therapy				
Re-examination	0.000	-	1.000	-
Chemotherapy or/and radiotherapy	0.112	0.154	1.118 (0.827–1.511)	0.469
Palliative treatment	0.828	0.292	2.288 (1.292–4.055)	0.005
Disease state				
Stable	0.000	_	1.000	-
Progression	0.629	0.193	1.876 (1.284–2.739)	0.001
Newly diagnosed	-0.148	0.281	0.863 (0.497–1.497)	0.599
Metastasis				
No	0.000	-	1.000	-
Yes	0.265	0.209	1.304 (0.865–1.965)	0.206
Pain				
No	0.000	-	1.000	-
Yes	0.68	0.122	1.973 (1.555–2.505)	<0.001
Condition awareness				
No idea	0.36	0.423	1.433 (0.625–3.287)	0.395

 Table 3. Stepwise logistic regression analysis of factors associated with depressive symptoms in cancer patients.

Table	3. (Contir	nued.
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Variable	β	SE	OR (95% CI)	Р
Partial knowledge	0.861	0.183	2.366 (1.653–3.385)	<0.001
Full knowledge	0.000	_	1.000	-
Cancer stage				
1			1.000	
II	-0.052	0.171	0.95 (0.679–1.328)	0.763
III	-0.118	0.182	0.889 (0.622-1.269)	0.517
IV	-0.016	0.233	0.984 (0.623–1.552)	0.944
Type of cancer				
Head and neck	0.557	0.405	1.745 (0.789–3.861)	0.169
Lung	1.163	0.256	3.199 (1.938–5.279)	<0.001
Breast			1.000	
Oesophagus	1.190	0.345	3.288 (1.673-6.464)	<0.001
Stomach	0.045	0.234	1.046 (0.662–1.654)	0.846
Colorectum	-0.208	0.2	0.812 (0.549–1.202)	0.299
Cervix	0.433	0.193	1.542 (1.056–2.253)	0.025
Thyroid	-0.557	0.344	0.573 (0.292-1.125)	0.106
Others	0.637	0.237	1.892 (1.189–3.01)	0.007
AIC	2753.550		. , ,	

KPS, Karnofsky Performance Status; SE, standard error; OR, odds ratio; CI, confidence interval; AIC, Akaike information criterion.

cancer patients had a heavy treatmentrelated economic burden and family income was an independent risk factor for depressive symptoms in malignant tumour patients.²⁵ The KPS score reflects patient function; lower scores indicate worse health status.²⁶ Several studies have indicated that lower KPS score is an independent prognostic factor for survival in cancer patients;^{27,28} thus, low function may increase patients' fear and anxiety. In this study, KPS scores of 70 and 80 increased the risk of patient depressive symptoms by 1.783 and 0.834 times, respectively. Additionally, depressive symptoms were related to disease course. Patients with a disease course ≤ 1 year had a higher risk of depressive symptoms. This may be because patients with a longer disease course have passed the initial period of disease denial, have begun to accept the reality of the disease and are willing to actively cooperate with treatment.⁸ Palliative treatment provides symptomatic support for the clinical symptoms of cancer patients; although it relieves clinical symptoms, it cannot control the further development and metastasis of malignant tumours.²⁹ In this study, patients receiving palliative treatment had a higher risk of depressive symptoms. This study also showed that progressive disease and tumour metastasis affected the risk of depressive symptoms in patients with malignant tumour, which supports previous study findings.³⁰ This may be because patients with progressive disease and tumour metastasis experience greater psychological anxiety and despair. According to data from a meta-analysis, 55% of patients receiving anticancer treatment and 64% with advanced metastatic or terminal disease experience pain.³¹ Studies have shown that pain substantially affects the psychology of patients, and moderate to severe pain leads to severe depressive symptoms in patients.³² The present findings showed that pain increased the risk of patient depressive symptoms by 0.973

Variable	β	SE	OR (95% CI)	Р
Sex				
Men	-1.1 94	1.160	0.303 (0.031-2.944)	0.303
Women			1.000	
Age, years				
<u>≤</u> 40			1.000	
41–50	0.024	0.323	1.024 (0.544–1.929)	0.941
51–60	-0.174	0.349	0.840 (0.424–1.665)	0.617
>60	0.315	0.426	1.371 (0.595–3.157)	0.459
Monthly family income, yuan				
\leq 5000	1.859	0.486	6.417 (2.474–16.645)	<0.001
5001-10,000	1.241	0.477	3.458 (1.359-8.799)	0.009
>10,000			1.000	
Work				
No			1.000	
Yes	-0.795	0.322	0.452 (0.24-0.848)	0.013
Physical exercise				
No			1.000	
Yes	-0.737	0.226	0.478 (0.307-0.745)	0.001
KPS				
60	0.512	1.507	1.669 (0.087–31.975)	0.734
70	1.144	0.9	3.138 (0.537–18.325)	0.204
80	1.267	0.381	3.552 (1.685–7.488)	<0.001
90	0.136	0.306	1.146 (0.629–2.087)	0.656
100			1.000	
Disease course				
\leq I month	1.059	0.831	2.882 (0.565–14.703)	0.203
2–6 months	0.260	0.368	1.297 (0.631–2.669)	0.479
7–12 months	0.292	0.308	1.339 (0.732–2.451)	0.344
>l year			1.000	
Therapy				
Re-examination			1.000	
Chemotherapy or/and radiotherapy	0.114	0.329	1.121 (0.589–2.135)	0.728
Palliative treatment	-1.300	0.848	0.273 (0.052-1.436)	0.125
Disease state				
Stable			1.000	
Progression	1.097	0.491	2.994 (1.144–7.836)	0.025
Newly diagnosed	-0.313	1.213	0.731 (0.068–7.882)	0.796
Metastasis				
No			1.000	
Yes	-0.450	0.606	0.638 (0.194–2.092)	0.458
Pain				
No			1.000	
Yes	0.762	0.226	2.143 (1.377–3.335)	<0.001
Condition awareness				
No idea	-1.333	1.615	0.264 (0.011–6.246)	0.409
Partial knowledge	1.104	0.440	3.017 (1.275–7.141)	0.012
Full knowledge			1.000	

 Table 4. Logistic regression analysis of related factors for breast cancer population.

Variable	β	SE	OR (95% CI)	Р
Cancer stage				
I				
II	0.278	0.264	1.321 (0.787-2.215)	0.292
III	-0.087	0.318	0.917 (0.491-1.711)	0.784
IV	0.291	0.636	1.338 (0.384-4.654)	0.648
AIC	702.746			

Table 4. Continued.

KPS, Karnofsky Performance Status; SE, standard error; OR, odds ratio; CI, confidence interval; AIC, Akaike information criterion.

 Table 5. Logistic regression analysis of related factors for lung cancer population.

Variable	β	SE	OR (95% CI)	Р
Sex				
Men	-0.664	0.469	0.515 (0.205-1.291)	0.157
Women			1.000	
Age, years				
≤40			1.000	
41–50	-2.149	1.583	0.117 (0.005-2.595)	0.175
51–60	-0.778	1.542	0.459 (0.022-9.431)	0.614
>60	-0.956	1.529	0.385 (0.019-7.696)	0.532
Monthly family income, yuan				
≤5000	1.292	0.955	3.640 (0.560-23.646)	0.176
5001-10,000	0.427	0.980	1.532 (0.224–10.465)	0.663
>10,000			1.000	
Work				
No			1.000	
Yes	-1.532	0.785	0.216 (0.046-1.007)	0.051
Physical exercise				
No			1.000	
Yes	-1.310	0.410	0.27 (0.121-0.602)	0.001
KPS				
60	_	_	_	0.990
70	13.216	1088.359	_	0.990
80	1.47	1.59	4.349 (0.193–98.138)	0.355
90	1.02	1.48	2.774 (0.152-50.488)	0.491
100			1.000	
Disease course				
\leq I month	1.029	0.895	2.799 (0.485–16.162)	0.250
2–6 months	0.107	0.478	1.113 (0.436–2.843)	0.823
7–12 months	0.190	0.552	1.210 (0.410-3.571)	0.730
>I year			1.000	
Therapy				
Re-examination			1.000	
Chemotherapy or/and radiotherapy	0.150	0.479	1.162 (0.455–2.969)	0.754
Palliative treatment	0.757	0.798	2.131 (0.446–10.187)	0.343

13

Variable	β	SE	OR (95% CI)	Р
Disease state				
Stable			1.000	
Progression	1.335	0.502	3.801 (1.422-10.165)	0.008
Newly diagnosed	-1.416	1.065	0.243 (0.030-1.956)	0.184
Metastasis				
No			1.000	
Yes	0.852	0.598	2.343 (0.726-7.559)	0.154
Pain				
No			1.000	
Yes	0.680	0.524	1.973 (0.707–5.509)	0.194
Condition awareness				
No idea	-0.478	1.394	0.62 (0.040-9.535)	0.732
Partial knowledge	-0.110	0.640	0.896 (0.255-3.144)	0.864
Full knowledge			1.000	
Cancer stage				
I			1.000	
II	-0.374	0.752	0.688 (0.157-3.004)	0.619
III	-1.092	0.763	0.335 (0.075-1.495)	0.152
IV	-0.986	0.823	0.373 (0.074-1.874)	0.231
AIC	264.873			

Table 5. Continued.

KPS, Karnofsky Performance Status; SE, standard error; OR, odds ratio; CI, confidence interval; AIC, Akaike information criterion.

times, indicating that pain is an independent risk factor for depressive symptoms in patients with malignant tumours. Patients experiencing pain may have inflammation, which is associated with a high risk of depression because inflammation can induce neurogenesis and synaptic plasticity impairment.³³ Clinicians should pay attention to inflammation in cancer patients to prevent inflammation-induced stress and depressive symptoms.³⁴ A study by Ghoshal et al. indicated that patients with cancer prefer to have full knowledge of their diagnoses and prognoses.³⁵ Deeper understanding of their disease increases patient compliance. Patients who are unaware or partly informed about their disease may be fearful and therefore have a higher risk of cancer-related negative emotions than those who are informed. In the present study, different cancer types had different effects on the risk of depressive

symptoms. Compared with breast cancer patients, lung, oesophageal and cervical cancer patients had a higher risk of depressive symptoms. Previous studies have estimated that the prevalence of depressive symptoms in lung, oesophageal and cervical cancer patients is very high.^{16,36} This may be because the incidence of these kinds of tumours is also very high, which may lead to a high prevalence of depressive symptoms in people with these cancers.

One previous study demonstrated that depressive symptoms in cancer patients improved over 18 months after return to work.³⁷ The present findings support this and indicate that return to work can reduce the risk of depressive symptoms in patients with malignant tumours. This may be because work increases family income and relieves the financial pressure caused by cancer treatment. Cancer patients who return to work experience a richer

Variable	ß	SE		P
Variable	ρ	JE	OK (33% CI)	r
Sex	0.205	0.004		0.100
Men	-0.385	0.294	0.680 (0.382–1.211)	0.190
vvomen			1.000	
Age, years			1.000	
	0.490	0 5 7 4		0 270
41-50 51 40	-0.460	0.536	0.019(0.210-1.709)	0.370
51-60 > 40	-0.261	0.521	0.770(0.277-2.137)	0.017
>00 Monthly family income yuan	-0.139	0.554	0.855 (0.500-2.427)	0.766
	0.827	0.678	2 288 (0 605-8 644)	0 222
5001-10.000	0.139	0.670	1,150,(0,303-4,365)	0.222
>10,000	0.157	0.001	1.150 (0.505-1.505)	0.050
Work			1.000	
No			1.000	
Yes	-0.773	0 558	0.462 (0.155–1.378)	0 166
Physical exercise	0.775	0.550	0.102 (0.103 1.370)	0.100
No			1 000	
Yes	-1 029	0315	0 357 (0 193–0 663)	0 00 1
KPS	1.027	0.010		0.001
60	13.336	855.5	_	0.988
70	1.491	1.213	4,441 (0,412-47,839)	0.219
80	1.116	0.935	3.052 (0.489–19.059)	0.233
90	0.961	0.916	2.615 (0.434–15.736)	0.294
100			1.000	
Disease course				
<i month<="" td=""><td>-0.526</td><td>0.72</td><td>0.591 (0.144-2.425)</td><td>0.465</td></i>	-0.526	0.72	0.591 (0.144-2.425)	0.465
2–6 months	0.262	0.399	1.299 (0.594-2.841)	0.512
7–12 months	-0.165	0.452	0.848 (0.35–2.056)	0.715
>I year			1.000	
Therapy				
Re-examination			1.000	
Chemotherapy or/and radiotherapy	0.512	0.415	1.668 (0.739–3.767)	0.218
Palliative treatment	1.376	0.691	3.957 (1.021–15.332)	0.047
Disease state			,	
Stable			1.000	
Progression	0.073	0.451	1.076 (0.444–2.607)	0.871
Newly diagnosed	0.727	0.648	2.069 (0.581–7.37)	0.262
Metastasis				
No			1.000	
Yes	0.873	0.559	2.394 (0.800-7.162)	0.118
Pain				
No			1.000	
Yes	0.720	0.320	2.053 (1.097-3.842)	0.024
Condition awareness				
No idea	0.523	0.833	1.687 (0.33-8.625)	0.53
Partial knowledge	0.658	0.499	1.931 (0.725–5.138)	0.188
Full knowledge			1.000	

Table 6. Logistic regression analysis of related factors for col-	orectal cancer population.
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Variable	β	SE	OR (95% CI)	Р
Cancer stage				
I				
II	-0.374	0.752	0.688 (0.157-3.004)	0.619
III	-1.092	0.763	0.335 (0.075-1.495)	0.152
IV	-0.986	0.823	0.373 (0.074–1.874)	0.231
AIC	422.789			

Table 6. Continued.

KPS, Karnofsky Performance Status; SE, standard error; OR, odds ratio; CI, confidence interval; AIC, Akaike information criterion.

Variable	β	SE	OR (95% CI)	Р
Age, years				
			1.000	
41–50	0.521	0.511	1.684 (0.619–4.581)	0.308
51–60	0.585	0.527	1.794 (0.639–5.037)	0.267
>60	0.851	0.572	2.342 (0.763–7.191)	0.137
Monthly family income, yuan				
≤5,000	3.295	1.256	26.976 (2.299–316.54)	0.009
5,001-10,000	2.740	1.277	15.486 (1.267–189.268)	0.032
>10,000			1.000	
Work				
Νο			1.000	
Yes	-0.838	0.637	0.432 (0.124-1.506)	0.188
Physical exercise			· · · · · · · · · · · · · · · · · · ·	
, No			1.000	
Yes	-0.383	0.330	0.682 (0.357-1.301)	0.245
KPS			· · · · · · · · · · · · · · · · · · ·	
70	13.081	415.57	-	0.975
80	0.504	0.835	1.656 (0.322-8.506)	0.546
90	-0.060	0.769	0.942 (0.209–4.25I)	0.938
100			1.000	
Disease course				
\leq I month	0.771	0.803	2.163 (0.448–10.436)	0.337
2–6 months	0.802	0.729	2.231 (0.534–9.318)	0.271
7–12 months	2.202	0.942	9.045 (1.427-57.318)	0.019
>I year			1.000	
Therapy				
Re-examination			1.000	
Chemotherapy or/and radiotherapy	-0.149	0.730	0.861 (0.206-3.604)	0.838
Palliative treatment	0.197	0.975	1.217 (0.18-8.235)	0.84
Disease state				
Stable			1.000	

Table 7. Logistic regression analysis of related factors for cervical cancer population.

Table II Contantaca.	Table	7.	Continued.
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Variable	β	SE	OR (95% CI)	Р
Progression	-0.72	0.763	0.487 (0.109–2.173)	0.346
Newly diagnosed	-0.200	0.610	0.819 (0.247–2.708)	0.743
Metastasis				
No			1.000	
Yes	0.130	0.820	1.139 (0.228–5.675)	0.874
Pain				
No			1.000	
Yes	0.458	0.340	1.581 (0.812–3.079)	0.178
Condition awareness				
No idea	0.393	0.880	1.481 (0.264-8.309)	0.655
Partial knowledge	1.142	0.395	3.133 (1.445–6.793)	0.004
Full knowledge			1.000	
Cancer stage				
1			1.000	
II	-0.075	0.455	0.928 (0.381-2.262)	0.869
111	-0.038	0.520	0.962 (0.347-2.667)	0.941
IV	2.035	1.067	7.656 (0.946–61.942)	0.056
AIC	348.816			

KPS, Karnofsky Performance Status; SE, standard error; OR, odds ratio; CI, confidence interval; AIC, Akaike information criterion.

environment and more social interactions. This can improve neurogenesis in the dentate gyrus of the hippocampus, which is required for learning, memory and emotional behaviours, and reduce the risk of patients.³⁸ depression in cancer Additionally, work distracts patients and gives them less time to think about their disease. Physical exercise was another protective factor of depressive symptoms in patients with malignant tumours in this study. Physical exercise reduces the risk of depressive symptoms and improves the quality of life of cancer patients.³⁹ Physical exercise reduces the risk of depressive symptoms in cancer patients because it improves immune function and relieves patients' anxiety and tension; this further improves sleep and appetite, promotes digestion and increases the body's tolerance to pain.^{40,41} Using a mouse model, Crupi et al. showed that brain inflammation, impairment and hippocampal plasticity are associated with anxiety and depression.⁴²

Cognitive function and neurogenesis may be impaired in cancer patients because of chemotherapy, which may cause mood disorders and depressive symptoms in these patients.⁴³ Exercise improves brain function and brain plasticity, especially adult hippocampal neurogenesis, and so could be a useful novel treatment method for depression.⁴⁴ Patients with maligant tumours should engage in appropriate exercise to improve brain function, sleep quality and appetite to prevent the occurrence of depressive symptoms. If possible, patients with malignant tumours should go back to work and take part in more social activities to prevent the occurrence of depressive symptoms.

The present study identified several factors that affected depressive symptom status in patients with cancer. These findings may help in quickly identifying cancer patients with a high risk of depressive symptoms. Patients diagnosed with cancer may experience psychosocial and physical pressure.45 Depressive symptoms lead to poor treatment response, increase hospital admission rate and are associated with poorer prognosis and higher cancer mortality; most worryingly, they can also lead to mortality and suicide.⁴⁶ Therefore, clinicians must take timely preventive measures against depressive symptoms in cancer patients with a high risk of such symptoms, and reduce the occurrence rate of depressive symptoms using psychological counselling. Malignant tumour patients with depressive symptoms should receive appropriate psychosocial interventions, psychological treatment or antidepressants, which may help to improve adherence to cancer treatments and reduce the poor prognosis rate in cancer patients. Social support should be provided for patients with lower incomes and heavy family burdens.

There were some study limitations. First, the study included a relatively small number of patients (especially for some subgroups) from a single institution, which may have reduced the statistical power. The findings should be generalized with caution. Second, depressive symptoms were assessed using a self-report patient rating scale, which may have resulted in uncontrolled bias. Third, some important variables associated with depression were not assessed. For example, specific temperament traits predict perceived stress,⁴⁷ indicating that people with different temperament traits may have different risks of depression. Additionally, one previous study showed that temperament traits correlate with depression status in cancer patients receiving palliative care.48 Fourth, there are currently no structured interviews or validated assessment tools for neuropsychiatric disorders, which may reduce the validity of the exclusion criteria for these patients and may have reduced the statistical power of our study. To confirm the present findings, more well-designed studies are required using longer scales and a wider range of reliable variables.

Conclusion

In this study, we evaluated the factors affecting the risk of depressive symptoms in malignant tumour patients. The results showed that monthly family income <10,000 yuan, KPS scores of 70 and 80, disease course of ≤ 1 year, palliative treatment, progressive disease, pain, partial knowledge of disease condition, return to work and physical exercise were influencing factors for depressive symptoms in patients with malignant tumours. These findings may help clinicians to conduct timely preventive interventions for cancer patients with a high risk of depressive symptoms. Additionally, these results could inform the use of appropriate treatments, including psychosocial interventions and antidepressants, for malignant tumour patients with depressive symptoms.

Declaration of Conflicting Interest

The authors declare that there is no conflict of interest.

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References

1. Fitzmaurice C, Allen C, Barber RM, et al. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015: a systematic analysis for the Global Burden of Disease Study. *JAMA Oncol* 2017; 3: 524–548.

- Liu Y, Zhou H, Zheng J, et al. Identification of immune-related prognostic biomarkers based on the tumor microenvironment in 20 malignant tumor types with poor prognosis. *Front Oncol* 2020; 10: 1008.
- Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018; 68: 394–424.
- 4. Feng RM, Zong YN, Cao SM, et al. Current cancer situation in China: good or bad news from the 2018 Global Cancer Statistics? *Cancer Commun (Lond)* 2019; 39: 22.
- Miller KD, Nogueira L, Mariotto AB, et al. Cancer treatment and survivorship statistics, 2019. CA Cancer J Clin 2019; 69: 363–385.
- Le L, Yu L, Guan C, et al. Epidemiology, etiology, screening, psychotherapy of malignant tumor patients with secondary depressive disorder. *Curr Pharm Des* 2018; 24: 2591–2596.
- Akimana B, Abbo C, Balagadde-Kambugu J, et al. Prevalence and factors associated with major depressive disorder in children and adolescents at the Uganda Cancer Institute. *BMC Cancer* 2019; 19: 466.
- Korsten LHA, Jansen F, De Haan BJF, et al. Factors associated with depression over time in head and neck cancer patients: a systematic review. *Psychooncology* 2019; 28: 1159–1183.
- Blanco C, Markowitz JC, Hellerstein DJ, et al. A randomized trial of interpersonal psychotherapy, problem solving therapy, and supportive therapy for major depressive disorder in women with breast cancer. *Breast Cancer Res Treat* 2019; 173: 353–364.
- 10. Ostuzzi G, Matcham F, Dauchy S, et al. Antidepressants for the treatment of depression in people with cancer. *Cochrane Database Syst Rev* 2018; 4: Cd011006.
- 11. Adam S, Thong MSY, Martin-Diener E, et al. Identifying classes of the pain, fatigue, and depression symptom cluster in longterm prostate cancer survivors-results from the multi-regional Prostate Cancer Survivorship Study in Switzerland (PROCAS). Support Care Cancer 2021; 29: 6259–6269.

- Van Santen HM, Chemaitilly W, Meacham LR, et al. Endocrine health in childhood cancer survivors. *Pediatr Clin North Am* 2020; 67: 1171–1186.
- Robson MJ, Quinlan MA and Blakely RD. Immune system activation and depression: roles of serotonin in the central nervous system and periphery. ACS Chem Neurosci 2017; 8: 932–942.
- Erim DO, Bensen JT, Mohler JL, et al. Prevalence and predictors of probable depression in prostate cancer survivors. *Cancer* 2019; 125: 3418–3427.
- Perez-Tejada J, Aizpurua-Perez I, Labaka A, et al. Distress, proinflammatory cytokines and self-esteem as predictors of quality of life in breast cancer survivors. *Physiol Behav* 2020: 113297.
- 16. Lee Y, Hung CF, Chien CY, et al. Comparison of prevalence and associated factors of depressive disorder between patients with head and neck cancer and those with lung cancer at a tertiary hospital in Taiwan: a cross-sectional study. *BMJ Open* 2020; 10: e037918.
- 17. Liu WJ, Wang XD, Wu W, et al. Relationship between depression and blood cytokine levels in lung cancer patients. *Med Sci* (*Paris*) 2018; 34: 113–115.
- Von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med* 2007; 147: 573–577. (Note, you will probably need to renumber your references after this addition).
- Dunstan DA and Scott N. Clarification of the cut-off score for Zung's self-rating depression scale. *BMC Psychiatry* 2019; 19: 177.
- 20. Guo C and Huang X. Hospital anxiety and depression scale exhibits good consistency but shorter assessment time than Zung selfrating anxiety/depression scale for evaluating anxiety/depression in non-small cell lung cancer. *Medicine (Baltimore)* 2021; 100: e24428.
- 21. Su WC, Chuang CH, Chen FM, et al. Effects of Good Pain Management (GPM) ward program on patterns of care and pain

control in patients with cancer pain in Taiwan. *Support Care Cancer* 2021; 29: 1903–1911.

- Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA, et al. American College of Sports Medicine position stand. Exercise and physical activity for older adults. *Med Sci Sports Exerc* 2009; 41: 1510–1530.
- 23. Tandon P, Reddy KR, O'Leary JG, et al. A Karnofsky performance status-based score predicts death after hospital discharge in patients with cirrhosis. *Hepatology* 2017; 65: 217–224.
- 24. Hajjay A, Hassan SAM, Rayes R, et al. Risk factors linked to depression after treatment in cancer survivors in Jeddah, Saudi Arabia. *Cureus* 2021; 13: e12710.
- 25. Sharp L, Carsin AE and Timmons A. Associations between cancer-related financial stress and strain and psychological well-being among individuals living with cancer. *Psychooncology* 2013; 22: 745–755.
- 26. Della Pepa GM, Caccavella VM, Menna G, et al. Machine learning-based prediction of 6-month postoperative Karnofsky Performance Status in patients with glioblastoma: capturing the real-life interaction of multiple clinical and oncologic factors. *World Neurosurg* 2021; 149: e866–e876.
- Lie HC, Hjermstad MJ, Fayers P, et al. Depression in advanced cancer–assessment challenges and associations with disease load. J Affect Disord 2015; 173: 176–184.
- Pérez-Cruz PE, Langer P, Carrasco C, et al. Spiritual pain is associated with decreased quality of life in advanced cancer patients in palliative care: an exploratory study. *J Palliat Med* 2019; 22: 663–669.
- 29. Vinches M, Neven A, Fenwarth L, et al. Clinical research in cancer palliative care: a metaresearch analysis. *BMJ Support Palliat Care* 2020; 10: 249–258.
- Zhao L, Li X, Zhang Z, et al. Prevalence, correlates and recognition of depression in Chinese inpatients with cancer. *Gen Hosp Psychiatry* 2014; 36: 477–482.
- Reis-Pina P, Acharya A and Lawlor PG. Cancer pain with a neuropathic component: a cross-sectional study of its clinical characteristics, associated psychological distress, treatments, and predictors at referral to a

cancer pain clinic. J Pain Symptom Manage 2018; 55: 297–306.

- 32. Huang G, Liu G, Zhou Z, et al. Successful treatment of refractory cancer pain and depression with continuous intrathecal administration of dexmedetomidine and morphine: a case report. *Pain Ther* 2020; 9: 797–804.
- Crupi R, Cambiaghi M, Deckelbaum R, et al. n-3 fatty acids prevent impairment of neurogenesis and synaptic plasticity in B-cell activating factor (BAFF) transgenic mice. *Prev Med* 2012; 54: S103–S108.
- Manigault AW, Kuhlman KR, Irwin MR, et al. Vulnerability to inflammation-related depressive symptoms: moderation by stress in women with breast cancer. *Brain Behav Immun* 2021; 94: 71–78.
- 35. Ghoshal A, Salins N, Damani A, et al. To tell or not to tell: exploring the preferences and attitudes of patients and family caregivers on disclosure of a cancer-related diagnosis and prognosis. J Glob Oncol 2019; 5: 1–12.
- Tsatsou I, Parpa E, Tsilika E, et al. A systematic review of sexuality and depression of cervical cancer patients. *J Sex Marital Ther* 2019; 45: 739–754.
- Dorland HF, Abma FI, Van Zon SKR, et al. Fatigue and depressive symptoms improve but remain negatively related to work functioning over 18 months after return to work in cancer patients. *J Cancer Surviv* 2018; 12: 371–378.
- Smail MA, Smith BL, Nawreen N, et al. Differential impact of stress and environmental enrichment on corticolimbic circuits. *Pharmacol Biochem Behav* 2020; 197: 172993.
- Kozik TM, Hickman MC, Schmidt S, et al. An exerciSe program to improve depression And sleep Disorders in oncology patients: the SAD study. *Eur J Oncol Nurs* 2018; 37: 19–22.
- 40. Yamada PM, Teranishi-Hashimoto C and Bantum EO. Paired exercise has superior effects on psychosocial health compared to individual exercise in female cancer patients. *Support Care Cancer* 2021; 29: 6305–6314.
- 41. Witlox L, Schagen SB, De Ruiter MB, et al. Effect of physical exercise on cognitive

function and brain measures after chemotherapy in patients with breast cancer (PAM study): protocol of a randomised controlled trial. *BMJ Open* 2019; 9: e028117.

- Crupi R, Cambiaghi M, Spatz L, et al. Reduced adult neurogenesis and altered emotional behaviors in autoimmune-prone B-cell activating factor transgenic mice. *Biol Psychiatry* 2010; 67: 558–566.
- Das A, Ranadive N, Kinra M, et al. An overview on chemotherapy-induced cognitive impairment and potential role of antidepressants. *Curr Neuropharmacol* 2020; 18: 838–851.
- 44. Sun L, Sun Q, Qi J, et al. Adult hippocampal neurogenesis: an important target associated with antidepressant effects of exercise. *Rev Neurosci* 2017; 28: 693–703.
- 45. Götze H, Friedrich M, Taubenheim S, et al. Depression and anxiety in long-term

survivors 5 and 10 years after cancer diagnosis. *Support Care Cancer* 2020; 28: 211–220.

- 46. Chen J, Hua Y, Su L, et al. The effect of psychological condition before radiotherapy on prognosis in 390 patients initially treated for nasopharyngeal carcinoma. *Support Care Cancer* 2021; 28: 211–220.
- 47. Infortuna C, Gratteri F, Benotakeia A, et al. Exploring the gender difference and predictors of perceived stress among students enrolled in different medical programs: a cross-sectional study. *Int J Environ Res Public Health* 2020; 17: 6647.
- Unseld M, Vyssoki B, Bauda I, et al. Correlation of affective temperament and psychiatric symptoms in palliative care cancer patients. *Wien Klin Wochenschr* 2018; 130: 653–658.