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ORIGINAL ARTICLE

Short- and long-term use of medication for psychological distress after the diagnosis of cancer

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Abstract
Purpose This study investigated the short- and long-term use of medication for psychological distress after the diagnosis of cancer.
Methods Longitudinal data from the Taiwan National Health Insurance database were used to follow 35,137 cancer patients for 2.5 years after being diagnosed in 2006 and 2007.
Results Among those patients who survived for at least 180 days, 20.9 % had used psychotropic medications; sedatives were the most frequently prescribed (14.3 %), followed by antidepressants (5.5 %), anxiolytics (3.6 %), and antipsychotics (2.7 %). Lung cancer, prostate cancer, and oral cancer showed a significant association with the regular use of medication in the first 180 days. Among patients who survived for at least 2.5 years, 4.8 % still used psychotropic medication on a regular basis. Lung cancer and prostate cancer were associated with such prolonged use.
Conclusions This longitudinal study found that the type of cancer was significantly associated with the use of psychotropic drugs after the diagnosis was made. It provided information about the trajectory of that use and found that a small number of patients were still using those medications after 2.5 years.

Keywords Psychological distress · Psychotropic medication · Cancer · Long-term demand · Medication possession ratio

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Abbreviations

MPR	Medication possession ratio
NHI	National Health Insurance
NHIA	National Health Insurance Administration
OR	Odds ratio

Introduction

Cancer is a leading cause of death in developed countries [1]. Its impact on mental health is also significant. Research has shown that 25–30 % of all newly diagnosed patients and those with recurrent cancer experienced significantly elevated levels of emotional distress, and around 50 % of those received psychiatric diagnoses [2–5]. Studies of distress in long-term survivors have reported mixed results. Several [6–8] have demonstrated persistent symptoms of depression, anxiety, pain,

or fatigue, while others have indicated no difference in the frequency of those symptoms from that in the general population [9, 10].

Pharmacological therapy either alone or in combination with psychosocial intervention has been demonstrated to be beneficial for cancer patients with depression [11–13]. Previous studies have reported the prevalence rates for and the types of psychotropic drugs prescribed for cancer patients; these studies were based on cross-sectional data for prescriptions for sedatives, antidepressants, anxiolytics, and antipsychotics. The reasons for the use of these drugs included depression, anxiety, insomnia, pain, and treatment-related emesis [14, 15]. Little research has investigated the association between type of cancer and the use of psychotropic medication or long-term patterns of use. Braun et al. [9] recently reported that cancer patients who survived for 5 years or longer appeared to use psychotropic medication at a rate similar to that of cancer-naïve controls. It is unclear how the level of use might vary from time to time among long-term cancer survivors and what factors might be associated with persistently high use of psychotropic medications by these patients. We hypothesized that there might be differences in the use of medication among patients with different types of cancer and that the use of such medication would be reduced and stable after a period of time.

The aims of this study, therefore, were to investigate the short- and long-term use of medications for psychological distress after the diagnosis of cancer and to determine what factors were associated with such use.

Methods

This is a retrospective population study based on data from Taiwan's National Health Insurance (NHI) databank. NHI covers almost all Taiwanese for medical services in almost all outpatient settings and hospitals [16]. Once a patient is diagnosed with a malignancy, the National Health Insurance Administration (NHIA) issues a catastrophic illness registry card to the patient and then provides that patient with all NHI healthcare services related to treatment of that cancer without copayments.

Data source

The NHI database includes comprehensive claims and registration data and has detailed information about health services, procedures, and prescriptions provided through NHI. It also includes data on diagnoses and background information on patients, physicians, and healthcare institutions. The NHI system codes diagnoses using the International Classification of Diseases, Ninth Revision (ICD-9). The quality of NHI data is considered to be reliable, because the NHIA routinely audits data submitted by healthcare institutions in order to prevent fraud.

The database we acquired contained person-level longitudinal NHI claims and registration data for the entire national population of patients who were newly diagnosed with cancer between January 1, 2006 and June 30, 2007. We also acquired longitudinal NHI registration data for healthcare institutions.

Study participants

We used SAS software version 9.1.3 (SAS Institute Inc., Cary, NC) to extract, organize, and link each patient's data. We selected the date of the first cancer registry as the index date for the beginning of observation (n = 79,868) but included only patients with the ten most common types of cancer (n = 57,224). Because we focused on the regular use of psychotropic medication after the diagnosis of cancer, we excluded patients with a previous diagnosis of cancer and those who had at least one prescription for medication for psychological distress within the 2 years immediately prior to their index date (n = 40,080). Finally, we excluded patients with missing data for the essential variables in our study. For each patient in the study (n = 35,137), we had a complete 2.5-year follow-up. (Fig. 1).

Research variables

We classified the medications for psychological distress as antidepressants, anxiolytics, sedatives, and antipsychotics in accordance with the study of cancer patients by Derogatis et al. [14]. Although several of these medications are used to control chemotherapy-induced nausea and vomiting, The National Comprehensive Cancer Network recommends that they be used only temporarily for this [17]. Control of emesis would not be a long-term indication. Our outcome variables were binary variables reflecting regular use of psychotropic medication in the five 180-day periods after the diagnosis of cancer. NHI regulations require that prescriptions be renewed every 180 days. A value of 1 indicated regular use and a value of 0 denoted non-regular use. We defined regular medication use in a period as a medication possession ratio (MPR) ≧50 % for the period. MPR is the ratio of "the number of days for which medication is prescribed in a period" to "the number of days alive in that period." MPR is a common index for measuring medication adherence, and it is also a suitable outcome measure for investigating the long-term or regular use of medication [18]. Many studies of medication adherence in chronic disease adopted a MPR≧80 % as the indicator of regular use [19]; however, we believed that a MPR≧50 % for psychotropic medication was already a sign of severe psychiatric distress and consistent with other studies [20, 21].

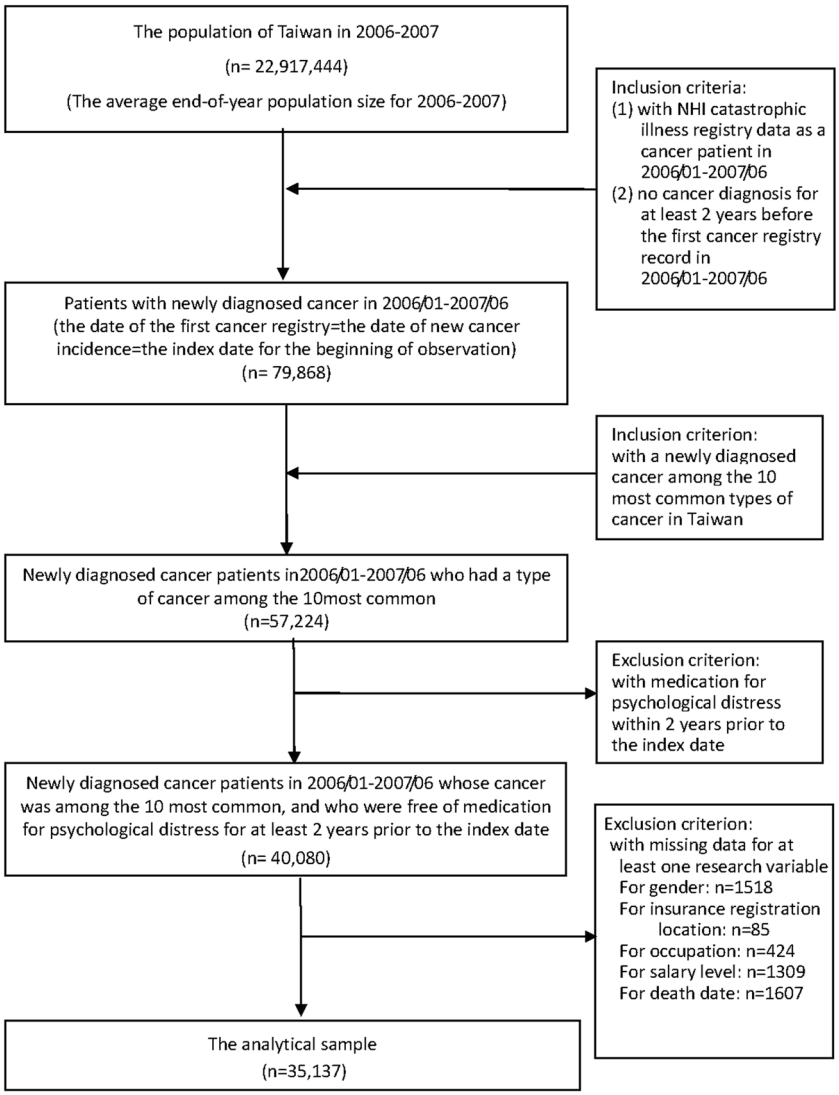

Fig. 1 The process of selection of study subjects

We used NHI data to establish a set of factors which might potentially influence the use of mediation for psychological distress. Patient characteristics at the time of the diagnosis of cancer included gender, age, and type of cancer; rather than using the more general Charleston Comorbidity Index, we selected comorbid conditions generally associated with use of medications for psychological distress. These included diabetes mellitus (DM), hypertension, chronic obstructive pulmonary disease (COPD), chronic liver disease, coronary arterial disease (CAD), and cerebral vascular accident (CVA) [22]. We created a binary variable to denote the existence of comorbidity for each of these conditions and also a binary variable to indicate the existence of at least one of these conditions.

We generated a set of binary variables to indicate the level of urbanization of a patient's NHI registration location according to the local population density and the local pattern of industry [23]. With regard to socioeconomic status, we included a set of categorical variables showing the position of NHI registration and the salary tertile. The project was approved by the Institutional Review Board (IRB) of National Taiwan University Hospital (NTUH-REC No. 201307046W). All individual identification numbers were scrambled to protect privacy.

Statistical analysis

Stata Software version 9 was used (StataCorp, College Station, TX) for descriptive statistics and multivariable regression analysis. Binary variables indicating use of medication were reported as counts and percentages. The chi-square test was used to assess differences between subgroups of cancer patients.

On the basis of the MPR levels in the five 180-day periods after the diagnosis of cancer, we defined patterns of long-term medication use. We regarded the persistent regular use of psychotropic medication as regular use for all the five 180-day periods after the diagnosis.

We used logit regression analysis to identify factors associated with regular medication use in the first 180 days after diagnosis, as well as factors associated with persistent regular medication use over the five 180-day periods after the diagnosis. Statistical significance was set as $p \leq 0.05$.

Results

Study participants and their survival rates

Among patients with the ten most common types of cancer, 17.5 % died within 180 days after the diagnosis. Table 1 shows the study subjects' demographic, socioeconomic, and clinical characteristics separately for patients who survived at least 180 days and for those who died within 180 days after the diagnosis. The data show that the two groups of patients had significant differences for each characteristic we investigated.

Table 2 shows the survival rates over the 2.5 years following the diagnosis of cancer for different types of cancer, separately by gender. Among male patients, those with lung cancer and those with liver cancer had the poorest prognosis. Only 18.3 % of male lung cancer patients and 35.1 % of male liver cancer patients survived for 2.5 years after that diagnosis, while 80.6 % of prostate cancer patients survived at least 2.5 years. Among female patients, those with lung cancer and those with liver cancer also had a poor prognosis. Only 30.6 % of female lung cancer patients and 40.3 % of female liver cancer patients survived for 2.5 years after that diagnosis, while 92.3 % of breast cancer patients survived at least 2.5 years.

Proportions of cancer patients who regularly used psychotropic medications

Supplemental Table S1 shows the proportions of patients who regularly used medication for psychological distress among those who survived at least 180 days after the diagnosis of cancer. The table reports the proportions for different types of cancer and for all ten common types of cancer combined, as well as the proportions for all types of psychotropic medications combined and separately for antidepressants, anxiolytics, sedatives, and antipsychotics.

The overall rate of use during the first 180-day period was 20.88 % in the population that survived at least 180 days. Among the four drug classes, sedatives were most commonly prescribed for each type of cancer except prostate cancer; antidepressants were the second most common for each type of cancer except prostate cancer. Because many patients with prostate cancer used imipramine for enuresis, and imipramine is classified as an antidepressant, antidepressants were the drug class most commonly prescribed for prostate cancer.

Lung cancer patients had the highest overall use of psychotropic mediation in the first 180 days, as 30.1 % of them took medication regularly. Head and neck cancer patients ranked second at 28.1 %. The lowest proportion of regular use, 13.3 %, was for patients with skin cancer.

The overall use of medication for psychological distress decreased slightly over time during the first 2.5-year period after diagnosis (Fig. 2). Patients with liver cancer showed an increasing trend for the use of medication, while patients with oral cancer showed a decreasing trend. Both lung cancer and prostate cancer patients had a high use of medication, and both of these groups showed a fluctuating trend in use. Both genders showed similar trends (data not shown).

Factors associated with regular use of psychotropic medication in the first 180-day period after diagnosis

Table 3 shows the factors associated with regular use of psychotropic medication in the first 180 days after diagnosis in male cancer patients. Compared to skin cancer, oral cancer (odds ratio (OR) = 2.8, $p < 0.001$) and lung cancer (OR = 2.7, $p < 0.001$) were associated with a significantly greater use of psychotropic medication. Prostate cancer (OR = 2.5, $p < 0.001$) and stomach cancer (OR = 1.4, $p < 0.001$) were also associated with greater use of medication. Comorbidity at the time of cancer diagnosis was also associated with a higher level of medication use (OR = 1.1, $p < 0.01$). Male cancer patients in big cities appeared to use medication less (OR = 0.8, $p < 0.01$). The region of location of NHI registration was also an influential factor.

Regarding factors associated with the regular use of psychotropic medication in the first 180 days after diagnosis by female cancer patients, compared to skin cancer, lung cancer (OR = 2.6, $p < 0.001$), oral cancer (OR = 2.0, $p < 0.01$), cervical cancer (OR = 1.6, $p < 0.01$), and liver cancer (OR = 1.5, $p < 0.05$) were all associated with a greater use of psychotropic medication (details not shown). Women under 35 used less medication ($p < 0.05$). Women with better occupations (e.g., government employees, teachers, or employees with regular employers) or women with NHI registration through local governments also tended to use less medication ($p < 0.05$).

Long-term patterns of use of medication by cancer patients who survived at least 2.5 years after diagnosis

With regard to the pattern of long-term use of psychotropic medication shown in Table 4, on average, 4.8 %

Table 1 Comparison of the characteristics of patients who survived at least 180 days and those who passed away within 180 days after the diagnosis of cancer

Characteristics	Patients surviving at least 180 days		Patients passing away within 180 days		p value for χ^2 test
	n	%	*n*	%	
Gender					$p < 0.001$
Male	15,641	46.03	4534	73.68	
Female	13,342	53.97	1620	26.32	
Age at cancer diagnosis (in years)					$p < 0.001$
<35	1048	3.62	106	1.72	
35–44	4047	13.96	408	6.63	
45–54	7141	24.64	914	14.85	
55–64	6243	21.54	1089	17.70	
65–74	6149	21.22	1558	25.32	
75–84	3816	13.17	1636	26.58	
≥85	539	1.86	443	7.20	
Region of the NHI registration location at cancer diagnosis					$p < 0.001$
Taipei region	9902	34.16	1843	29.95	
Northern region	3616	12.48	744	12.09	
Central	4917	16.97	1057	17.18	
Southern	4921	16.98	1201	19.52	
The farthest South (two counties)	4851	16.74	1102	17.91	
Eastern	776	2.68	207	3.36	
Urbanization level of the NHI registration location at cancer diagnosis					$p < 0.001$
Big city	14,391	49.65	2718	44.17	
Small city or town	9997	34.49	2212	35.94	
Remote or rural area	4595	15.85	1224	19.89	
Occupation type in the NHI registry at cancer diagnosis					$p < 0.001$
Government employee or teacher	1581	5.45	271	4.4	
NHI registration through employers of other types	9153	31.58	1525	24.78	
NHI registration through labor unions	5445	18.79	892	14.49	
Veterans or their dependents	252	0.87	62	1.01	
Family dependents with no jobs	294	1.01	92	1.49	
NHI registration through local governments	5349	18.46	1342	21.81	
Members of families in poverty/residents in religious or charitable institutions	175	0.60	64	1.04	
NHI registration through farmers/fishermen/crewmen unions	6734	23.23	1906	30.97	
Salary class in the NHI registry at cancer diagnosis					$p < 0.001$
The bottom tertile of the population	12,460	42.99	3096	50.31	
The middle tertile	10,694	36.90	2414	39.23	
The top tertile	5829	20.11	644	10.46	
Comorbidity at cancer diagnosis					
Diabetes					$p < 0.001$
No	25,839	89.15	5282	85.83	
Yes	3144	10.85	872	14.17	
Hypertension					$p < 0.001$
No	22,362	77.15	4522	73.48	
Yes	6623	22.85	1632	26.52	
Ischemic heart disease					$p < 0.001$
No	27,442	94.68	5649	91.79	
Yes	1541	5.32	505	8.21	

Table 1 (continued)

Characteristics	Patients surviving at least 180 days		Patients passing away within 180 days		p value for χ^2 test
	n	%	*n*	%	
Comorbidity at cancer diagnosis					
Cerebrovascular accident					$p < 0.001$
No	27,904	96.28	5686	92.40	
Yes	1079	3.72	468	7.60	
Chronic obstructive pulmonary disease					$p < 0.001$
No	27,892	96.24	5602	91.03	
Yes	1091	3.76	552	8.97	
Chronic liver disease/cirrhosis					$p < 0.001$
No	25,440	87.78	4423	71.87	
Yes	3543	12.22	1731	28.13	
Cancer type					$p < 0.001$
Malignant neoplasm of rectum and rectosigmoid colon	6459	22.29	646	10.50	
Malignant neoplasm of breast	5503	18.99	93	1.51	
Malignant neoplasm of liver and intrahepatic bile ducts	3107	10.72	2296	37.31	
Malignant neoplasm of trachea, bronchus, and lung	3072	10.60	1896	30.81	
Malignant neoplasm of lip, oral cavity, and pharynx	4103	14.16	373	6.06	
Malignant neoplasm of stomach	1698	5.86	641	10.42	
Malignant neoplasm of prostate	1945	6.71	83	1.35	
Malignant neoplasm of cervix uteri	1611	5.56	59	0.96	
Malignant melanoma of skin	838	2.89	35	0.57	
Malignant neoplasm of body of uterus	647	2.23	32	0.52	

Table 2 Post-diagnosis survival rates among cancer patients, for the ten most common types of cancer

Cancer type	(*n*) at diagnosis	180-day survival rate % (*n*)	1-year survival rate % (*n*)	1.5-year survival rate % (*n*)	2-year survival rate % (*n*)	2.5-year survival rate % (*n*)
Male						
Colon	(*n* = 4296)	91.2 (3919)	85.7 (3682)	81.0 (3481)	76.8 (3299)	72.7 (3125)
Liver	(*n* = 4229)	56.1 (2372)	47.5 (2007)	42.0 (1778)	38.6 (1633)	35.1 (1485)
Oral	(*n* = 4188)	91.7 (3839)	80.2 (3357)	70.9 (2968)	66.2 (2771)	63.4 (2657)
Lung	(*n* = 3366)	57.8 (1946)	40.3 (1358)	29.5 (992)	22.9 (771)	18.3 (617)
Prostate	(*n* = 2028)	95.9 (1945)	92.7 (1880)	88.5 (1794)	84.8 (1720)	80.6 (1635)
Stomach	(*n* = 1548)	73.1 (1131)	62.0 (960)	54.3 (841)	49.0 (759)	45.9 (710)
Skin	(*n* = 513)	94.0 (482)	89.3 (458)	85.0 (436)	81.9 (420)	80.1 (411)
Female						
Breast	(*n* = 5589)	98.3 (5496)	97.1 (5427)	95.6 (5344)	93.9 (5246)	92.3 (5156)
Colon	(*n* = 2809)	90.4 (2540)	85.7 (2407)	81.1 (2279)	76.6 (2151)	72.9 (2049)
Cervical	(*n* = 1670)	96.5 (1611)	92.0 (1537)	88.1 (1471)	84.9 (1417)	82.6 (1379)
Lung	(*n* = 1602)	70.3 (1126)	56.2 (901)	44.9 (720)	37.2 (596)	30.6 (491)
Liver	(*n* = 1174)	62.6 (735)	53.8 (632)	48.9 (574)	44.5 (522)	40.3 (473)
Stomach	(*n* = 791)	71.7 (567)	59.4 (470)	51.1 (404)	46.4 (367)	43.9 (347)
Uterus	(*n* = 679)	95.3 (647)	92.6 (629)	90.0 (611)	88.1 (598)	86.5 (587)
Skin	(*n* = 360)	98.9 (356)	96.4 (347)	93.1 (335)	91.4 (329)	89.4 (322)
Oral	(*n* = 288)	91.7 (264)	80.9 (233)	73.3 (211)	69.8 (201)	68.1 (196)

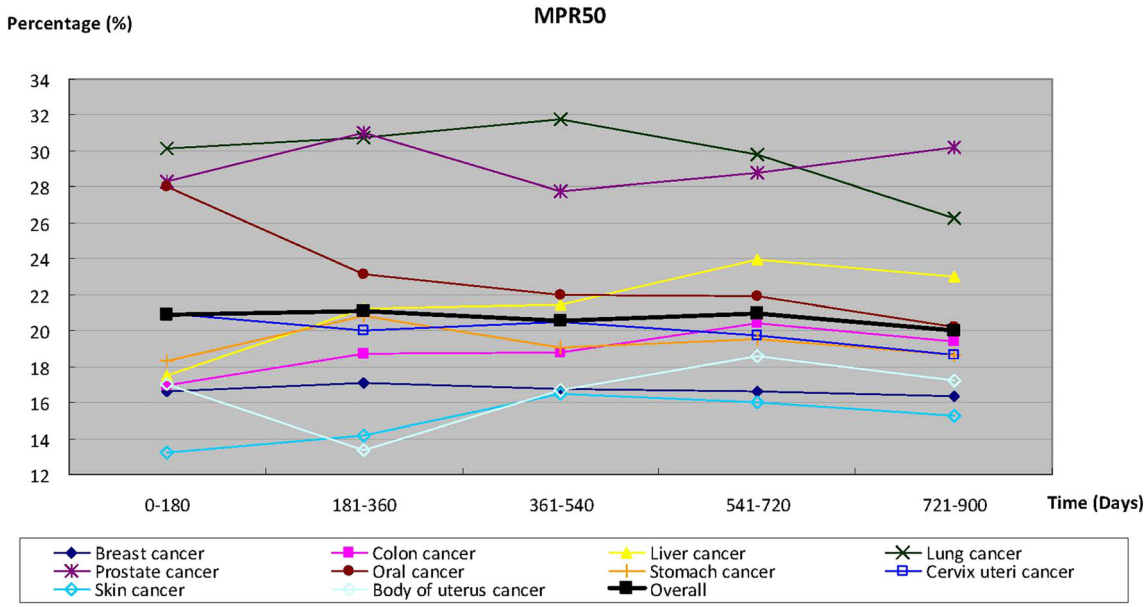

Fig. 2 Proportions of patients regularly using medication for psychological distress in the five 180-day periods after cancer onset

of all patients used psychotropic drugs regularly in all five 180-day periods, while 62.8 % had no period with regular use in all five 180-day periods.

Comparison among types of cancer indicates that lung and prostate cancer patients were the two groups at higher risk for persistent regular use of psychotropic medication. Males with oral cancer patients also showed high use in the early periods after the diagnosis.

Supplemental Table S2.1 presents factors associated with persistent regular use of psychotropic medications in the five 180-day periods after the diagnosis in male cancer patients. Compared to skin cancer, lung cancer (OR = 3.8, $p < 0.001$), oral cancer (OR = 3.1, $p < 0.01$), and prostate cancer (OR = 2.7, $p < 0.01$) were associated with significantly greater use of psychotropic medication. Comorbidity at the time of the diagnosis of cancer was also related to a higher level of medication use (OR = 1.3, $p < 0.01$). No demographic or socioeconomic factors were statistically significant for male cancer patients with regard to level of drug use.

Data about the use of psychotropic medications in the five 180-day periods after the diagnosis by female cancer patients are shown in Supplemental Table S2.2. Lung cancer (OR = 3.7, $p < 0.001$) was associated with a higher demand for psychiatric medication. Comorbidity at the time of the diagnosis was also associated with a higher level of medication use (OR = 1.4, $p < 0.05$). Compared to women in the bottom salary tertile in the NHI registry, women in a higher salary grade tended to use less medication ($p < 0.05$).

Discussion

Among cancer patients who survived at least 180 days after the diagnosis, 20.9 % used psychotropic medication regularly during that period, and sedatives were used most frequently. The proportion of patients who used psychotropic mediation regularly remained stable over the 2.5 years after the diagnosis. Among patients who survived at least 2.5 years, 4.8 % still used psychotropic medications on a regular basis. Lung cancer and prostate cancer were associated with such persistent use.

Instead of examining the use of psychotropic medication during a specific period of cancer treatment, this study investigated the regular use of these drugs after the diagnosis and focused on patients with newly diagnosed cancer and newly diagnosed psychological distress. In Taiwan, the Distress Thermometer has become a routine screening tool used with cancer patients nationwide, and hospitals provide psychosocial support accordingly [24]. In a survey administered to 1579 patients admitted for cancer treatment, 51 % reported that they had been prescribed at least one psychotropic medication [14]. A longitudinal 8-month follow-up study of Chinese women after surgery for breast cancer [25] showed a declining trend in psychological distress after surgery, but 49 % of their study participants had psychological distress over those 8 months. Some Western studies reported similar findings [26]. A large survey of newly diagnosed cancer patients ($n = 4496$) showed that the overall prevalence rate of psychological distress was 35.1 %, and the rates for different types of cancer varied; the rates were 43.4 % for lung cancer,

Table 3 Factors associated with regular use of psychotropic medications in the first 180-day period after the diagnosis of cancer, for male patients who survived 180 days

Explanatory variables	OR		95 % CI
The type of cancer at diagnosis[a] (reference: skin cancer)			
Colon cancer	1.322		0.999–1.748
Liver cancer	1.243		0.931–1.659
Oral cancer	2.789	***	2.100–3.705
Lung cancer	2.666	***	2.001–3.551
Prostate cancer	2.521	***	1.908–3.329
Stomach cancer	1.429	*	1.050–1.944
Age in years (reference <35)			
35–44	1.063		0.815–1.387
45–54	1.083		0.840–1.398
55–64	1.112		0.859–1.439
65–74	1.096		0.843–1.426
75–84	0.850		0.645–1.120
≧85	0.837		0.571–1.227
Region of the NHI registration location at the onset of cancer (reference: East)			
Taipei region	0.811		0.647–1.017
North except Taipei	0.686	**	0.542–0.867
Central	0.822		0.657–1.028
South	0.667	***	0.532–0.836
The farthest south (Kaohsiung and Ping-Tung)	0.590	***	0.468–0.742
Urbanization level of the NHI registration location at the onset of cancer (reference: remote or rural area)			
Big city	0.825	**	0.724–0.940
Small city or town	0.919		0.818–1.033
Occupation type in the NHI registry at the onset of cancer (reference: NHI registration through farmers/fishermen/crewmen unions)			
Government employee or teacher	0.938		0.747–1.178
NHI registration through employers of other types	0.984		0.839–1.154
NHI registration through labor unions	1.112		0.959–1.290
Veterans or their dependents	0.953		0.641–1.416
Family dependents with no jobs	1.256		0.833–1.894
NHI registration through local governments	1.007		0.840–1.207
Members of families in poverty/residents in religious or charitable institutions	1.152		0.714–1.858
Salary class in the NHI registry at the onset of cancer (reference: the bottom tertile of the population)			
The middle tertile	0.959		0.835–1.102
The top tertile	0.910		0.799–1.037
Comorbidity (reference: none)			
Some comorbidity	1.116	**	1.027–1.212
No. of observations	15,634		
Breast cancer	1.260		0.917–1.733
Colon cancer	1.283		0.929–1.773
Cervical cancer	1.644	**	1.181–2.288
Lung cancer	2.592	***	1.859–3.614
Liver cancer	1.530	*	1.070–2.188
Stomach cancer	1.448		0.999–2.099
Uterus cancer	1.263		0.870–1.834
Oral cancer	2.049	**	1.353–3.103
Age in years (reference <35)			
35–44	1.486	**	1.130–1.954

Table 3 (continued)

Explanatory variables	OR		95 % CI
45–54	1.826	***	1.401–2.381
55–64	1.768	***	1.347–2.322
65–74	1.623	**	1.223–2.152
75–84	1.402	*	1.034–1.899
≧85	1.722	*	1.115–2.660
Region of the NHI registration location at the onset of cancer (reference: East)			
Taipei region	1.078		0.804–1.445
North except Taipei	0.781		0.575–1.061
Central	0.927		0.690–1.246
South	0.938		0.698–1.262
The farthest south (Kaohsiung and Ping-Tung)	0.912		0.676–1.230
Urbanization level of the NHI registration location at the onset of cancer (reference: remote or rural area)			
Big city	0.897		0.761–1.057
Small city or town	0.965		0.830–1.121
Occupation type in the NHI registry at the onset of cancer (reference: NHI registration through farmers/fishermen/crewmen unions)			
Government employee or teacher	0.746	*	0.580–0.960
NHI registration through employers of other types	0.835	*	0.701–0.994
NHI registration through labor unions	0.864		0.729–1.024
Veterans or their dependents	0.798		0.418–1.525
Family dependents with no jobs	1.231		0.826–1.835
NHI registration through local governments	0.814	*	0.663–0.998
Members of families in poverty/residents in religious or charitable institutions	0.948		0.534–1.682
Salary class in the NHI registry at the onset of cancer (reference: bottom tertile of the population)			
The middle tertile	0.880		0.765–1.012
The top tertile	0.874		0.758–1.008
Comorbidity (reference: none)			
Some comorbidity	1.002		0.903–1.111
No. of observations	13,342		
Log-likelihood ratio test statistic for model significance	Wald χ^2 (31) = 191.35-***		

CI confidence interval, *OR* odds ratio

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

35.4 % for liver cancer, 35.1 % for head and neck cancer, 31.6 % for colon cancer, 30.5 % for prostate cancer, and 29.6 % for gynecological cancer [3].

Our study found that 20.9 % of patients who survived at least 180 days used psychiatric medication in those first 180 days. Because our study focused on the regular use of psychotropic medication, and controlled for the influences of pre-existent malignancy and mental problems, it is not surprising that we found lower prevalence rates for the use of psychotropic medications than the surveys mentioned above.

Clusters of psychological symptoms and classes of psychiatric drugs in cancer patients

Major symptoms of psychological distress among cancer patients include sleep disturbance, anxiety, depression, and somatization [14]. As shown in one prospective study, 36.6 % of cancer patients reported symptoms of insomnia, and 43 % met the diagnostic criteria for insomnia syndrome during their first cycle of chemotherapy [27]. Our results with regard to the distribution of classes of psychotropic medications clearly demonstrated this. In the first 180-day period after the

Table 4 Long-term use of psychotropic medications by patients with different types of cancer, for those who survived at least 2.5 years after the diagnosis

Male patients' major cancer types	Colon (n = 3125)	Oral (n = 2657)	Prostate (n = 1635)	Liver (n = 1485)	Stomach (n = 710)	Lung (n = 617)	Skin (n = 411)	P value for χ^2 test
Regular use for all the five 180-day periods	3.17 (n = 99)	5.12 (n = 136)	**7.58** (n = 124)	4.11 (n = 61)	3.94 (n = 28)	**6.48** (n = 40)	1.95 (n = 8)	297.357*
No period with regular use	59.94 (n = 1873)	53.07 (n = 1410)	41.47 (n = 678)	55.42 (n = 823)	60.56 (n = 430)	46.19 (n = 285)	64.48 (n = 265)	
Regular use in earlier periods	6.88 (n = 215)	**12.16** (n = 323)	**11.80** (n = 193)	5.12 (n = 76)	7.32 (n = 52)	**10.70** (n = 66)	6.81 (n = 28)	
Regular use in later periods	7.30 (n = 228)	5.83 (n = 155)	**8.69** (n = 142)	7.88 (n = 117)	6.90 (n = 49)	7.78 (n = 48)	7.79 (n = 32)	
Sporadic regular use or non-regular use	22.72 (n = 710)	23.82 (n = 633)	30.46 (n = 498)	27.47 (n = 408)	21.27 (n = 151)	28.85 (n = 178)	18.98 (n = 78)	
Female patients' major cancer types	**Breast (n = 5156)**	**Colon (n = 2049)**	**Cervical (n = 1379)**	**Uterus (n = 587)**	**Lung (n = 491)**	**Liver (n = 473)**	**Stomach (n = 347)**	**Skin (n = 322)**	**P value for χ^2 test**
Regular use for all the five 180-day periods	3.49 (n = 180)	4.05 (n = 83)	3.48 (n = 48)	3.24 (n = 19)	**7.13** (n = 35)	5.29 (n = 25)	4.03 (n = 14)	1.86 (n = 6)	139.80*
No period with regular use	61.17 (n = 3154)	55.54 (n = 1138)	55.98 (n = 772)	61.67 (n = 362)	41.55 (n = 204)	50.74 (n = 240)	55.04 (n = 191)	60.87 (n = 196)	
Regular use in earlier periods	8.13 (n = 419)	6.64 (n = 136)	**9.57** (n = 132)	7.16 (n = 42)	**9.78** (n = 48)	6.77 (n = 32)	8.36 (n = 29)	5.59 (n = 18)	
Regular use in later periods	5.59 (n = 288)	7.71 (n = 158)	5.95 (n = 82)	6.30 (n = 37)	7.33 (n = 36)	**8.46** (n = 40)	7.49 (n = 26)	7.76 (n = 25)	
Sporadic regular use or non-regular use	21.63 (n = 1115)	26.06 (n = 534)	25.02 (n = 345)	21.64 (n = 127)	34.22 (n = 168)	28.75 (n = 136)	25.07 (n = 87)	23.91 (n = 77)	

*$p < 0.001$

diagnosis, sedatives for insomnia were the most commonly prescribed drugs.

Trends in the regular use of medication for psychological distress over time after the diagnosis of cancer

Patients with different types of cancer showed different trends in the regular use of medication for psychological distress over time after the diagnosis. Two types of cancer were particularly noteworthy: liver cancer and oral cancer. Among patients with liver cancer, the proportion of regular use was 17.0 % in the first 180-day period, and it increased to 23.0 % in the fifth 180-day period. For patients with oral cancer, the proportion was 28.1 % in the first 180-day period, and it decreased to 20.2 % in the fifth 180-day period. Determination of the reasons for this difference requires further study.

Information about an individual patient's long-term pattern of the regular use of medication sheds light on the types of cancer associated with persistent psychological distress. Our data indicated that 4.75 % of cancer patients who survived for at least 2.5 years had persistent psychological distress, and patients with lung or prostate cancer were more likely to continue to use psychotropic medications. Without specific data for individual patients, the reasons for persistent distress are unknown. A previous study showed that the prevalence of psychological distress did not change during the year after curative resection in patients with lung cancer [28]; however, a recent study by Braun et al. [9] found that the level of psychological distress among 5-year cancer survivors was no different from that of cancer-naïve controls. Epstein et al. [29] did note that heavy drinking and heavy smoking were associated with both depression and specific types of cancer; however, information about a history of drinking or smoking was not available to us. Our study provides some indication of the prevalence of distress in the intervening years; however, the determination of which patients may be at risk for psychological distress requires further study.

Clinically, Hammerlid et al. reported a high incidence of anxiety soon after the diagnosis of head and neck cancer, and depression reached a peak about 3 months after the initial treatment of these patients; the rates of both returned to near pre-treatment levels within 12 months. [30]. Similarly, our results showed a high demand for medication for psychological distress (28 %) in the first 6 months after diagnosis and a lower level of demand (23 %) thereafter. Cancer therapy including surgery, radiation, and chemotherapy or combinations of these can be an important factor since treatment is often finished within 6 months. These first 6 months for newly diagnosis head and neck cancer patients are the most crucial

period for psychological support and a systematic assessment of patients' distress and need for supportive care is important.

On the other hand, we found that patients with lung cancer and prostate cancer used psychotropic medication regularly (approximately 30 %) during both the short time interval and the long time interval. Dinh et al. reported the association between androgen deprivation therapy and depression in patients with localized prostate cancer, and the risk of depression increased with the duration of that therapy from 12 % with fewer than 6 months of treatment, to 26 % with 7 to 11 months, and 37 % with longer than 12 months of treatment [31]. A survey done in England by Ream et al. found high levels of psychological distress in men living with prostate cancer for 2 to 24 months prior to the survey and receiving various kinds of treatment; however, they did not mention the trend of this unmet need [32]. Our findings showed a consistent high level of medication use as a result of psychological distress for a long period of time. Although we were unable to identify the treatment modality for each patient with prostate cancer, the Cancer Registry did show that a majority of our patients had undergone androgen deprivation therapy by surgery, radiation, hormonal therapy, or a combination of these. A strategy to improve long-term health-related quality of life including the need for medication for psychological distress is clearly warranted for men with prostate cancer.

In our study, patients with lung cancer showed a trend in medication use similar to that of patients with prostate cancer. Rauma et al. reported a permanent reduction in health-related quality of life including depression and psychological distress among survivors of non-small cell lung cancer. [33] A high percentage of lung cancer in Taiwan is adenocarcinoma, however [34]. This suggests that an assessment for psychological distress is important but also depends on the type of cancer and the therapeutic modality [35].

This study did have several limitations. Neither clinical diagnoses of the psychological disorders nor the stage of cancer at the time of diagnosis was cited. Treatment modalities and treatment outcomes were not noted in the record. There was no comparison data for the use of psychotropic medications by the general population. Because patients with a catastrophic illness registry card receive all medications without copayment from their surgeon, oncologist, and/or psychiatrist, there is no information as to whether the prescription was initiated by a physician or requested by the patient. The specialties of the prescribing physicians were not indicated; however, a previous study showed that missed rates of psychiatric morbidity did not differ significantly by physician specialty or primary cancer site [36]. Finally, the assumption that medication prescription equals medication consumption is not always the case. The trend of the demand in this report, however, indicated that physicians prescribed medications when patients required them and stopped prescribing them when they did not.

Conclusions

This longitudinal study found that the type of cancer was significantly associated with the use of psychotropic drugs after the diagnosis. It provided information on the trajectory of that use and found that a small number of patients were still using these medications after 2.5 years. The findings highlighted the need for ongoing assessments of the level of psychological distress among cancer patients.

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Compliance with ethical standard

Conflict of interest The authors declare that they have no competing interests.

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