

# Cancer Epidemiology, Biomarkers & Prevention



## The Analysis of Depression and Subsequent Cancer Risk in Taiwan

Ji-An Liang, Li-Min Sun, Chih-Hsin Muo, et al.

*Cancer Epidemiol Biomarkers Prev* 2011;20:473-475. Published OnlineFirst February 4, 2011.

**Updated Version** Access the most recent version of this article at:  
[doi:10.1158/1055-9965.EPI-10-1280](https://doi.org/10.1158/1055-9965.EPI-10-1280)

**Cited Articles** This article cites 8 articles, 4 of which you can access for free at:  
<http://cebp.aacrjournals.org/content/20/3/473.full.html#ref-list-1>

**E-mail alerts** [Sign up to receive free email-alerts](#) related to this article or journal.

**Reprints and Subscriptions** To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at [pubs@aacr.org](mailto:pubs@aacr.org).

**Permissions** To request permission to re-use all or part of this article, contact the AACR Publications Department at [permissions@aacr.org](mailto:permissions@aacr.org).

## Research Article

## The Analysis of Depression and Subsequent Cancer Risk in Taiwan

Ji-An Liang<sup>1,2</sup>, Li-Min Sun<sup>3</sup>, Chih-Hsin Muo<sup>4,5</sup>, Fung-Chang Sung<sup>4,5</sup>, Shih-Ni Chang<sup>4,6,7</sup>, and Chia-Hung Kao<sup>2,8</sup>

## Abstract

**Background:** Patients with depression are suggestive of having a tendency toward a marginally significant association with the subsequent cancer risk. The aim of this study was to evaluate the possible relationship between depression and cancer risk in Taiwan.

**Methods:** We used the data of the National Health Insurance system of Taiwan to assess this issue. The Cox proportional hazard regression analysis was conducted to estimate the effects of depression on the cancer risk.

**Results:** In patients with depression, there was no significant change in the risk of developing overall cancer or for the site-specific cancer and all showed the same direction (positive) except for colorectal cancer, which had a negative direction.

**Conclusions:** This population-based study did not find Taiwanese patients with depression to have a higher risk to develop overall cancer or site-specific cancer.

**Impact:** Depression does not increase cancer risk. *Cancer Epidemiol Biomarkers Prev*; 20(3); 473–5. ©2011 AACR.

## Introduction

Depression accounts for almost 12% of all total years lived with disability worldwide in 2000 (1) and is more common among Taiwanese than previously suggested (2). It has been proposed as a predisposing factor in the development of cancer, and 2 meta-analyses suggested a tendency toward a small and marginally significant association between depression and subsequent cancer risk (3, 4). To the best of our knowledge, there are no population-based studies which outline the possible relationship between depression and cancer in Taiwan. The aim of this

study was to investigate the risk of cancer among patients with depression in Taiwan.

## Methods

This study used data retrieved from The National Health Research Institute, containing all reimbursement claims records from 1996 to 2008 for 1 million randomly selected insureds (5).

In this study, we identified newly diagnosed depression patients in the period of 2000–2002 as the exposure group (ICD-9-CM 296.2–296.9). The index date for the depression patients was the date of their first medical visit. Subjects with the history of malignant cancer [International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) 140–208] diagnosed before index date or with missing information on age or sex were excluded. For the comparison group, we used a systematic random sampling method and selected 8 insured people without depression in the same period, with frequency matched with the depression group on age and sex.

Person-years of follow-up time were calculated for each person until cancer diagnosed or censored. We also considered hypertension (ICD-9-CM 401–405), diabetes mellitus (ICD-9-CM 250), hyperlipidemia (ICD-9-CM 272), and heart disease (ICD-9-CM 410–429) before the index date as baseline comorbidities.

We assessed the incidence density and rate ratio (RR) of cancer by each variable, using Poisson regression. The Cox proportion hazard regression analysis was used to estimate HR and 95% CI. All data measurements were

**Authors' Affiliations:** <sup>1</sup>Department of Radiation Oncology, China Medical University Hospital; <sup>2</sup>School of Medicine, College of Medicine, China Medical University, Taichung; <sup>3</sup>Department of Radiation Oncology, Zuoying Armed Forces General Hospital, Kaohsiung; <sup>4</sup>Management Office for Health Data, China Medical University Hospital; <sup>5</sup>Institute of Environmental Health, College of Public Health, and <sup>6</sup>The Ph.D. Program for Cancer Biology and Drug Discovery, China Medical University, Taichung; <sup>7</sup>Institute of Biomedical Sciences, Academia Sinica, Taipei; and <sup>8</sup>Department of Nuclear Medicine and PET Center, China Medical University Hospital, Taichung, Taiwan

**Note:** J-A. Liang and L-M. Sun contributed equally to this work.

**Corresponding Authors:** Chia-Hung Kao, Department of Nuclear Medicine and PET Center, China Medical University Hospital, No. 2, Yuh-Der Road, Taichung 404, Taiwan. Phone: 886-4-22052121-7412; Fax: 886-4-22336174. E-mail: d10040@mail.cmuh.org.tw; or Shih-Ni Chang, Management Office for Health Data, China Medical University Hospital, No. 2, Yuh-Der Road, Taichung 404, Taiwan. Phone: 886-4-22052121-7805; Fax: 886-4-22339216. E-mail: u9665856@cmu.edu.tw

doi: 10.1158/1055-9965.EPI-10-1280

©2011 American Association for Cancer Research.

**Table 1.** Comparisons of incidence density of cancer between depression group and nondepression group by characteristics

Variables	Depression								
	No				Yes				
	<i>n</i>	Case	Person-years	Rate <sup>a</sup>	<i>n</i>	Case	Person-years	Rate <sup>a</sup>	RR 95% CI
All	67,352	2,571	474,401	5.42	8,419	321	58,341	5.50	1.02 (0.90–1.14)
Sex									
Women	40,728	1,336	290,062	4.61	5,091	163	36,000	4.53	0.98 (0.84–1.16)
Men	26,624	1,235	184,339	6.70	3,328	158	22,342	7.07	1.06 (0.89–1.25)
Age, y									
<30	16,096	71	115,210	0.62	2,012	8	14,486	0.55	0.90 (0.43–1.86)
30–39	13,048	174	94,690	1.84	1,631	39	11,808	3.30	1.80 (1.27–2.54)
40–49	12,896	394	94,568	4.17	1,612	43	11,602	3.71	0.89 (0.65–1.22)
50–64	13,344	753	95,972	7.85	1,668	92	11,722	7.85	1.00 (0.81–1.24)
≥65	11,968	1,179	73,960	15.9	1,496	139	8,723	15.9	1.00 (0.84–1.19)
Occupation									
White collar	34,978	1,071	249,095	4.30	4,075	119	28,979	4.11	0.96 (0.79–1.15)
Blue collar	22,802	1,101	159,640	6.90	2,673	121	18,417	6.57	0.95 (0.79–1.15)
Others	9,572	399	65,666	6.08	1,671	81	10,945	7.40	1.22 (0.96–1.55)
Urbanization level									
1	20,272	690	143,772	4.80	2,583	88	18,151	4.85	1.01 (0.81–1.26)
2	19,252	731	136,461	5.36	2,631	95	18,262	5.20	0.97 (0.78–1.20)
3	12,103	429	84,959	5.05	1,352	54	9,309	5.80	1.15 (0.87–1.52)
4	15,720	721	109,170	6.60	1,853	84	12,619	6.66	1.01 (0.80–1.26)
Comorbidity									
Hypertension	13,743	1,028	90,298	11.4	2,422	170	15,681	10.8	0.95 (0.81–1.12)
Diabetes mellitus	4,710	361	30,214	12.0	898	68	5,520	12.3	1.03 (0.80–1.34)
Hyperlipidemia	7,006	478	48,429	9.87	1,386	79	9,376	8.43	0.85 (0.67–1.08)
Heart disease	10,276	754	66,916	11.3	2,445	147	15,964	9.2	0.82 (0.68–0.98)

<sup>a</sup>Per 1,000 person-year.

done by SAS statistical software (version 9.1 for Windows; SAS Institute Inc.), and the significance level was set to be 0.05.

## Results

The incidence of cancer was slightly higher in the depression group than in the nondepression group (5.50 vs. 5.42 per 1,000 person-years; Table 1). The incidence densities of cancer were higher in men and increased with age. The RR of cancer was higher in younger group than in the nondepression group (30–39 years of age, 3.30 vs. 1.84 per 1,000 person-years, RR = 1.80, 95% CI = 1.27–2.54).

The risk of cancer was not significant between the depression group and the nondepression group (adjusted HR = 1.03, 95% CI = 0.91–1.15; Table 2). Besides, the specific analyses on cancer type also did not observe any significant relationship between depression and cancer including hematologic malignancy, colorectal cancer,

lung cancer, breast cancer, uterus, cervical, ovary, and vaginal cancer, prostate cancer, and brain cancer.

## Discussion

The results did not show any significant relationship between the depression and cancer risk; however, the RR had the direction toward positive association for overall cancer and site-specific cancer except for the colorectal cancer.

One large study with long follow-up time conducted in Baltimore area showed that major depression was associated with a higher hazard for overall cancer, as well as for breast cancer and prostate cancer, and the authors suggested the association between depression and hormonally mediated cancers (6). Another nationwide cohort study from Denmark found that the standardized incidence ratio was 1.05 (95% CI = 1.03–1.07) and concluded that most of the excess risk could be attributed to an increased risk of tobacco-related cancers (7).

**Table 2.** HRs and 95% CIs of cancer associated with depression in Cox's regression analysis in different cancer

Variable	Case	Multivariate model, <sup>a</sup> HR (95% CI)
All cancers	2,892	1.03 (0.91–1.15)
Hematologic malignancy <sup>b</sup>	130	1.10 (0.64–1.87)
Colorectal cancer	408	0.77 (0.55–1.10)
Lung cancer	363	1.01 (0.65–1.58)
Breast cancer (women only)	325	1.09 (0.78–1.53)
Uterus, cervical, ovary, and vaginal cancer (women only)	208	1.16 (0.84–1.60)
Prostate cancer (men only)	123	1.33 (0.79–2.23)
Brain cancer	35	1.44 (0.55–3.76)

<sup>a</sup>Adjusted for age, sex, urbanization, and comorbidity.

<sup>b</sup>ICD-9-CM: hematologic malignancy, 200.xx–203.xx and 205.xx–208.xx; colorectal cancer, 153.xx and 154.xx; lung cancer, 162.xx; breast cancer, 174.xx and 175.xx; uterus, cervical, ovary, and vaginal cancer, 179.xx–184.xx; prostate cancer, 185.xx; brain cancer, 179.xx and 180.xx–184.xx.

Multivariate model (Table 2) analyses for our study showed no significant increment of the overall cancer risk for patients with depression. For the site-specific cancer analysis, we still could not find any significant relationship between depression and any cancer risk. All the directions were toward positive relationship except for the colorectal cancer. Our data showed that the HR for colorectal cancer was 0.77 (95% CI = 0.55–1.10). It may be comparable with The Danish cohort study, which detected a marginally significantly lower risk for reactive depression, and the possibility of decreased motivation for surveillance among patients with depressed mood should be considered (7). Positive relationship between depression and breast cancer may exist (6, 8), but most researches did not show this association (3). Although showing the tendency of positive relationship, our data did not support any significant finding for breast cancer either. We specified brain tumor to see whether there is an increased risk among patients with depression similar to the findings of the Danish cohort study. Unfortunately, 1.44 HR did not accompany with a significant higher risk.

In conclusion, this population-based retrospective cohort study failed to prove any significant association

between depression and subsequent overall or any site-specific cancer risk in Taiwan. Although meta-analyses suggested a tendency toward a marginally significant association, our data provide little, if any, support in the positive direction for most cancers.

#### Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

#### Grant Support

This study was supported by the National Sciences Council, Executive Yuan (grant numbers DOH 97-HP-1101, 2008–2010), China Medical University Hospital (grant number 1MS1, DMR-94-080), Taiwan Department of Health Clinical Trial and Research Center and for Excellence (grant number DOH 100-TD-B-111-004), and Taiwan Department of Health Cancer Research Center for Excellence (DOH100-TD-C-111-005).

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Received December 8, 2010; revised January 13, 2011; accepted January 14, 2011; published OnlineFirst February 4, 2011.

#### References

- Üstün TB, Ayuso-Mateos JL, Chatterji S, Mathers C, Murray CJ. Global burden of depressive disorders in the year 2000. *Br J Psychiatry* 2004;184:386–92.
- Chong MY, Tsang HY, Chen CS, Tang TC, Chen CC, Yeh TL, et al. Community study of depression in old age in Taiwan: prevalence, life events and socio-demographic correlates. *Br J Psychiatry* 2001;178:29–35.
- Oerlemans ME, Van Den Akker M, Schuurman AG, Kellen E, Buntinx F. A meta-analysis on depression and subsequent cancer risk. *Clin Pract Epidemiol Ment Health* 2007;3:29.
- McGee R, Williams S, Elwood M. Depression and the development of cancer: a meta-analysis. *Soc Sci Med* 1994;38:187–92.
- Lu JF, Hsiao WC. Does universal health insurance make health care unaffordable? Lessons from Taiwan. *Health Aff (Millwood)* 2003;22:77–88.
- Gross AL, Gallo JJ, Eaton WW. Depression and cancer risk: 24 years of follow-up of the Baltimore epidemiologic catchment area sample. *Cancer Causes Control* 2010;21:191–9.
- Dalton SO, Mellekjaer L, Olsen JH, Mortensen PB, Johansen C. Depression and cancer risk: a register-based study of patients hospitalized with affective disorders, Denmark, 1969–1993. *Am J Epidemiol* 2002;155:1088–95.
- Jacobs JR, Bovasso GB. Early and chronic stress and their relation to breast cancer. *Psychol Med* 2000;30:669–78.