

## 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

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**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 1M51, 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).

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

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# BLOOD CANCER DISCOVERY

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

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