Population-Based Cohort Analyses of the Bidirectional Relationship Between Type 2 Diabetes and Depression

Pei-Chun Chen, phd[1]
Yen-Ting Chan, msc[2]
Hua-Fen Chen, md, msc[3,4]
Ming-Chung Ko, md, msc[5]
Chung-Yi Li, phd[6,7]

OBJECTIVE—This study addresses the strength of association for the bidirectional relationship between type 2 diabetes and depression.

RESEARCH DESIGN AND METHODS—We used two cohort studies with the same source of database to determine the link between depression and type 2 diabetes. The data analyzed included a random sample of 1 million beneficiaries selected from the National Health Insurance claims in 2000. The analysis of diabetes predicting the depression onset consisted of 16,957 diabetic patients and the same number of sex- and age-matched nondiabetic control subjects. The analysis of depression predicting diabetes onset included 5,847 depressive patients and 5,847 sex- and age-matched nondepressive control subjects. The follow-up period was between 2000 and 2006, and onset of end points was identified from ambulatory care claims. The Cox proportional hazards regression model adjusted for potential confounders was used to estimate relative hazards.

RESULTS—The first cohort analysis noted an incidence density (ID) of 7.03 per 1,000 person-years (PY) and 5.04 per 1,000 PY for depression in diabetic and nondiabetic subjects, respectively, representing a covariate-adjusted hazard ratio (HR) of 1.43 (95% CI 1.16–1.77). The second cohort analysis noted an ID of 27.59 per 1,000 PY and 9.22 per 1,000 PY for diabetes in depressive and nondepressive subjects, respectively. The covariate-adjusted HR was stronger at 2.02 (1.80–2.27) for incident diabetes associated with baseline depression.

CONCLUSIONS—The two cohort studies provided evidence for the bidirectional relationship between diabetes and depression, with a stronger association noted for the depression predicting onset of diabetes.

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Although the underlining mechanisms for the relationship between depression and diabetes have not been fully understood (1), comprehensive evidence has shown a clear clustering of depression among diabetic patients (2–4).The putative causal link between depression and diabetes has been reported by a number of cohort studies (5–8). In a meta-analysis of 13 eligible studies, Mezuk et al. (9) reported a pooled significantly increased relative risk (RR) of 1.60 for incident type 2 diabetes associated with baseline depression. Unlike the studies of depression predicting the onset of diabetes, evidence concerning whether there is also an increased risk of depression in diabetic patients has been neither comprehensive nor evident. The putative association of diabetes predicting the onset of depression has been shown in some studies (10,11) but not in others (12,13).

Although diabetes has a strong association with the presence of depression, it is still unclear whether diabetes itself increases the risk of developing depression. Diabetes may increase the risk of depression mainly because of the sense of threat and loss associated with suffering from this disease and its complications, which may last for the entire life. Pompili et al. (14) evaluated the perceived quality of life and its association with suicide risk in Italian patients with diabetes and found that patients with diabetes showed greater hopelessness and suicide ideation than other internal medicine outpatients.

The prevalence rates of diabetes and depression have been increasing during the past decade in Taiwan (15,16), which entails substantial health care burden and adverse health consequences. Knowledge of the strengths of bidirectional relationships between diabetes and depression would be of help in setting preventive strategies aiming to reduce the presence of concomitant depression symptoms among diabetes. Although the bidirectional relationship between diabetes and depression have been frequently investigated in different settings with various methodologies, to our knowledge, there have been only two studies to date that conducted such analyses based on the same population and the same source of data (17,18). One study was performed in subjects ≥45 years of age (17); the other analysis was restricted to women ≥50 years of age (18). Information on a young population is not available. We thus examined this issue using claims data from the Taiwan National Health Insurance (NHI) program, which provides health care coverage to all ages of residents in Taiwan.

RESEARCH DESIGN AND METHODS

Source of data

The data analyzed in this study were claims of 1 million beneficiaries randomly selected from all beneficiaries insured in

From the [1]Institute of Epidemiology and Preventive Medicine, National Taiwan University College of Public Health, Taipei, Taiwan; the [2]Department of Health, Centers for Disease Control, ROC Executive Yuan, Taipei, Taiwan; the [3]Department of Endocrinology, Far Eastern Memorial Hospital, Panchiao, New Taipei City, Taiwan; the [4]School of Medicine, Fujen Catholic University, New Taipei City, Taiwan; the [5]Department of Surgery, Taipei City Hospital City, Taipei, Taiwan; the [6]Department and Institute of Public Health, College of Medicine, National Cheng Kung University, Tainan, Taiwan; and the [7]Department of Public Health, College of Public Health, China Medical University, Taichung, Taiwan.
Corresponding author: Ming-Chung Ko, mingchung77@gmail.com.
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2000, with age and sex distributions nearly identical to the entire insured population of Taiwan (19). The claims were retrieved from the National Health Insurance Research Database (NHIRD) provided by the Bureau of National Health Insurance (BNHI). The NHIRD provides all inpatient and ambulatory medical claims for ~96% of Taiwanese people (20,21). To ensure the accuracy of claim files, the BNHI performs quarterly expert reviews on a random sample for every 50–100 ambulatory and inpatient claims. False reports of diagnosis would yield severe penalties from the BNHI (22). By the end of 1996, BNHI had contracted with 97% of the island-wide hospitals and clinics, with 99% of the total Taiwanese population enrolled in the program (21). Therefore, information obtained from the NHIRD is believed to be complete and accurate. We used several NHIRD datasets in this study, including ambulatory care visit claims (ACVC), Inpatient Expenditures by Admissions (IEA), and Registry for Beneficiaries (RB). Access to research data has been approved by the Review Committee of the National Health Research Institutes.

The cohort analysis of the association between diabetes and risk of new-onset depression

An individual was classified as a diabetic patient if she or he had a diagnosis of type 2 diabetes (ICD-9-CM: 250 × 0 or 250 × 2) at any time in ACVC of 2000 and then experienced another one or more diagnoses within the subsequent 12-month follow-up periods. The first and last outpatient visits within 1 year had to be >30 days apart to avoid accidental inclusion of miscoded patients (23). The eligible diabetic patients must have no prior history of depression (ICD-9-CM: 296, 309, or 311) (3) diagnosis since 1 January 1997. In total, 16,957 prevalent diabetic patients were included in the diabetic group. The control subjects were 16,957 insurers randomly selected, sex and age matched to the diabetic group, from all beneficiaries free from both diabetes and depression in 1997–2000.

We linked the diabetic and control subjects to ACVC in 2000–2006 for possible episodes of diagnosis for depression. The index date for each diabetic patient was the date of his or her first diabetes diagnosis. The index date for subjects in the control group was the first date of enrollment in NHI. If their first date of enrollment was before 1 January 2000, the index date was set as 1 January 2000. The 7-year follow-up period began as early as 1 January 2000 and ended 31 December 2006. The age of each study subject was calculated by the difference in time between the index date and the date of birth. We grouped the area of each member's insurance unit, either the beneficiaries' residential area or location of their employment, into four geographic areas (north, central, south, and east) or urbanization status (urban and rural) according to the National Statistics of Regional Standard Classification (24), and such information was obtained from the RB.

The age- and sex-specific hazard rates were determined with person-years (PY) as the denominator under the Poisson assumption. To assess the independent associations of diabetes with the risks of depression, we conducted Cox proportional hazards regression models with age, sex, geographic area, urbanization statuses, and various comorbidities adjusted simultaneously in the model. We adjusted geographic variables for the presence of an urban-rural difference in the accessibility to medical care in Taiwan (25). The comorbidities considered in our analysis included a number of medical diagnoses considered to pose a long-term risk for depressive symptoms (12) and several macrovascular complications that could substantially affect diabetic patients' quality of life and psychological well-being (14). Information of comorbidities was retrieved from the IEA from the first day of 1997 to the date of encountering a depression diagnosis, or to the date of censoring, which was either the date of withdraw from the insurance or date of the end of follow-up, i.e., 31 December 2006. All statistical analyses were performed with SAS (version 9.2; SAS Institute, Cary, NC). A P value <0.05 was considered statistically significant.

The cohort analysis of the association between depression and risk of incident diabetes

The second cohort analysis managed to assess whether depression predicts the onset of diabetes. The depression subjects were also identified from the above-mentioned 1 million beneficiaries. An individual was classified as a depression patient if she or he had a depression diagnosis (ICD-9-CM: 296, 309, or 311) at any time in 2000, and she or he must have no prior history of diabetes (ICD-9-CM: 250 × 0 or 250 × 2). In total, 5,847 subjects with depression were identified to form the depression group. The control subjects (n = 5,847) were randomly selected and sex and age matched to the depressive patients from all nondepression insurers. The control subjects must have been free from both depression and diabetes in 1997–2000.

We linked the subjects from both groups to ACVC in 2000–2006 for possible episodes of diagnosis of diabetes. The index date for each depression subject was the date of his or her first depression diagnosis in 2000. The index date for subjects in the control group was the first date of enrollment to NHI. If their first date of enrollment was before 1 January 2000, the index date was set as 1 January 2000. The 7-year follow-up period began as early as 1 January 2000 and ended 31 December 2006. The methods of calculation of age and grouping one's beneficiaries' residential area or location of employment were the same as those described in the first cohort analysis. The statistical analysis used in the second cohort analysis was also similar to that used in the first cohort analysis. The only difference was that we did not take into account the risk factors for diabetes, since many of the risk factors for diabetes were related to one's diet, lifestyle, and compliance to medical advice, but such information was not included in the NHI claims.

RESULTS

The cohort analysis for the risk of depression in relation to diabetes

Male subjects dominated the sample in both diabetic and control groups (53.5%), and diabetic patients were of the same age as their matched controls (mean age ± SD, 60.1 ± 13.2 vs. 60.3 ± 13.1 years). Distributions of urbanization level and geographic location of residential areas were essentially the same between the two groups. On the other hand, the respective prevalence of prior admission due to cancer, hypertension, rheumatoid arthritis, lung disease, and peripheral artery disease was higher in diabetic patients than in control subjects. Moreover, diabetic patients were also more likely than control subjects to suffer from commonly seen diabetes complications and disease consequences, including stroke (7.3 vs. 5.2%), cardiovascular disease (6.1 vs. 4.8%), nontraumatic hip fracture (1.0 vs. 0.3%), and lower-extremity amputations (1.0 vs. 0.2%) (Table 1).

Table 2 shows the overall and age- and sex-specific incidence densities (IDs) of

Table 1—*Demographic data of the diabetic and control cohorts*

	Control group		Diabetic group	
	n	%	*n*	%
Sex				
Male	9,072	53.5	9,072	53.5
Female	7,868	46.4	7,868	46.4
Age (years)				
<35	492	2.9	492	2.9
35–44	1,407	8.3	1,407	8.3
45–54	3,663	21.6	3,663	21.6
55–64	4,443	26.2	4,443	26.2
>64	6,952	41	6,952	41
Mean age (SD)	60.1	(13.2)	60.3	(13.1)
Urbanization of residential area				
Urban	7,563	44.6	6,918	40.8
Satellite	5,036	29.7	4,714	27.8
Rural	4,290	25.3	5,206	30.7
Geographic location of residential area				
North	8,699	51.3	7,987	47.1
Center	3,120	18.4	2,713	16
South	4,765	28.1	5,664	33.4
East	356	2.1	492	2.9
Risk factors for depression*				
Cancer (140–239)	543	3.2	848	5.0
Hypertension (401–405)	1,272	7.5	2,883	17.0
Rheumatoid arthritis (714)	203	1.2	237	1.4
Lung disease (466, 491, 492)	458	2.7	492	2.9
Peripheral artery disease (443)	2	<0.1	17	0.1
Diabetes complications*				
Stroke (430–438)	882	5.2	1,238	7.3
Cardiovascular disease (410, 414)	814	4.8	1,034	6.1
Nontraumatic hip fracture (820)	51	0.3	170	1.0
Lower-extremity amputation (84.1, 84.10–84.18)	34	0.2	170	1.0
Overall†	16,957	100.0	16,957	100.0

*Numbers in parenthesis are ICD-9-CM codes. †Inconsistency between total population and population summed for individual variable was because of missing information.

depression for the two study groups. Over the 7-year study period, diabetic patients had an ID of 7.03 (95% CI 6.52–7.55) per 1,000 PY. The control subjects had a lower ID at 5.04 (4.62–5.46) per 1,000 PY. Diabetic patients were observed to suffer from a higher ID than control subjects irrespective of age and sex. Concerning the age-specific ID, it tended to increase with age regardless of sex among control subjects. However, for the diabetic patients, the lowest age-specific ID of depression was noted in male subjects 45–54 years of age (4.93 [3.76–6.10] per 1,000 PY) and in female subjects 55–64 years of age (7.66 [6.20–9.12] per 1,000 PY). Table 2 also shows covariate-adjusted hazard ratios (HRs) of depression in association with diabetes. Compared with control subjects, diabetic patients had a significantly increased hazard of depression (HR 1.43 [95% CI 1.16–1.77]). The corresponding figures for male and female subjects were 1.39 [1.08–1.79] and 1.48 [1.14–1.92]. However, these two sex-specific HRs were not significantly different (*P* value for diabetes-sex interaction is 0.0749). On the other hand, the diabetes and age interaction was significant for both male and female subjects. The highest age-specific HR was noted in subjects <35 years of age in both male and female subjects with an HR of 1.81 (1.13–2.91) and 2.16 (1.39–3.37), respectively. For both sexes, the age-specific HR gradually decreased as age increased.

The cohort analysis for the risk of diabetes in relation to depression

Female subjects (59.6%) were dominant in the depression group. The mean ± SD age for the depression group was 44.5 ± 17.6 years, with a majority of study subjects <45 years of age (54.9%). The distributions of urbanization and geographic locations of residential areas were similar between the two groups (Table 3). Table 4 shows overall and age- and sex-specific ID and HR of diabetes onset for the depression and nondepression groups. The overall ID of diabetes for the depression and nondepression groups was estimated at 27.59 per 1,000 PY and 16.45 per 1,000 PY, respectively. The ID of diabetes increased with age for both men and women, and depressive subjects consistently had a higher ID of diabetes than the nondepressive subjects for all sex and age stratifications. The depressive subjects were associated with a significantly increased HR (2.02 [95% CI 1.80–2.27]), with a greater RR estimate for women (2.23 [1.89–2.62]) than for men (1.83 [1.56–2.16), but this sex difference was not statistically significant (*P* = 0.0721). The age-stratified analyses revealed that age significantly interacted with depression on the risk of diabetes for both men and women (both $P < 0.0001$), in which younger depressive patients were associated with higher HRs than older patients. The depressive women <35 years of age were significantly associated with the most increased HR (3.50 [2.47–4.97]), followed by depressive men <35 years of age (3.46 [2.37–5.04]). The depressive men and women 34–44 years of age had an HR of 2.13 (1.51–3.00) and 2.21 (1.54–3.18), respectively. The elevated HRs for depressive men >54 years of age and depressive women >64 years of age were no longer statistically significant.

CONCLUSIONS—The current study revealed a bidirectional association between diabetes and depression. Similar to a meta-analysis that included 13 publications of depression (9), our observations showed that the relationship between depression and incidence of diabetes was stronger than between diabetes and incidence of depression. The bidirectional relationships between diabetes and depression appreciably weakened with increased age in both sexes.

The link between diabetes and depression

Several prospective studies have assessed the association between diabetes and risk of developing depression and showed contradictory findings (1,6,11–13,17,26). Mezuk et al. (9) have reported in their meta-analysis of these studies that the pooled RR was 1.15 (95% CI 1.02–1.30).

Table 2—*Overall and age- and sex-specific relative hazards of depression in association with diabetes*

Variables	Control group			Diabetic group			
	No. patients	No. events	ID (per 1,000 PY) (95% CI)†	No. patients	No. events	ID (per 1,000 PY) (95% CI)†	Adjusted HR (95% CI) in association with depression group
Men (years)							
<35	263	5	2.97 (0.42–5.52)	263	10	5.64 (2.07–9.21)	1.81 (1.13–2.91)§
35–44	896	19	3.19 (1.76–4.62)	901	31	5.38 (3.48–7.28)	1.62 (1.04–2.51)§
45–54	2,175	49	3.39 (2.44–4.34)	2,175	68	4.93 (3.76–6.10)	1.37 (0.91–2.06)§
55–64	2,259	58	3.91 (2.90–4.92)	2,254	80	5.80 (4.53–7.07)	1.38 (0.83–2.28)§
>64	3,479	116	5.68 (4.64–6.72)	3,479	142	7.51 (6.28–8.74)	1.23 (0.79–1.91)§
Total	9,072	247	4.30 (3.76–4.84)	9,072	331	6.13 (5.47–6.79)	1.39 (1.08–1.79)‖
Women (years)							
<35	229	6	4.08 (0.88–7.28)	228	13	8.89 (4.07–13.71)	2.16 (1.39–3.37)§
35–44	507	18	5.19 (2.78–7.60)	501	26	7.91 (4.84–10.98)	1.50 (0.95–2.37)§
45–54	1,482	58	5.82 (4.32–7.32)	1,484	73	7.70 (5.94–9.46)	1.27 (0.85–1.91)§
55–64	2,180	80	5.47 (4.27–6.67)	2,188	105	7.66 (6.20–9.12)	1.32 (0.82–2.12)§
>64	3,470	134	6.42 (5.33–7.51)	3,467	165	8.49 (7.20–9.78)	1.25 (0.76–2.06)§
Total	7,868	296	5.87 (5.20–6.54)	7,868	382	8.06 (7.26–8.87)	1.48 (1.14–1.92)‖
Overall*	16,957	543	5.04 (4.62–5.46)	16,957	713	7.03 (6.52–7.55)	1.43 (1.16–1.77)¶

The *P* value for diabetes-age interaction is <0.0001 in both sexes. The *P* value for diabetes-sex interaction is 0.0749. *Inconsistency between total population and population summed for individual variable was because of missing information. †Based on Poisson assumption. §Based on Cox proportional hazards regression with adjustment for geographic area, urbanization status, clinical risk factors for depression, and diabetes complications. ‖Based on Cox proportional hazards regression with adjustment for geographic area, urbanization status, clinical risk factors for depression, diabetes complications, and age. ¶Based on Cox proportional hazards regression with adjustment for geographic area, urbanization status, clinical risk factors for depression, diabetes complications, age, and sex.

A later investigation indicated that the elevated risk was found in treated diabetic patients but not in those untreated (17). In our analyses, the diabetic group was identified from claims records, likely consisting of a relatively large proportion of patients with severe diabetes who were more likely to seek health care and be treated.

In a meta-analysis report (9), investigators suggested that the relationship between diabetes and incidence of depression may differ by age and sex. Indeed, we found that diabetes was mostly associated with subsequent depression in female subjects <45 years of age and in male patients <35 years of age, and the association weakened in those that were older. A cross-sectional study supported our observation, indicating that the odds ratios for depression associated with diabetes were much higher in individuals 20–39 years of age than in those 40–64 years of age (3). The age difference may partly explain the modest association observed in previous studies, most of which did not include young adults.

Several potential explanations for the age differences have been proposed. First, the association between diabetes and depression among the elderly may be masked because of a greater burden of competing risks for depression in this age-group. Second, evidence has shown that older adults were less likely to endorse the symptoms of depression (27). The nondifferential misclassification of depression could bias the association toward null. Third, previous studies reported that type of treatment, severity of the disease, and its impact on physical and psychological conditions may vary between the diabetic patients of various ages (28). Younger diabetic patients tended to respond negatively to their disease

Table 3—*Demographic data of the depressive and control subjects*

	Control group		Depression group	
	n	%	*n*	%
Sex				
Male	2,355	40.4	2,355	40.4
Female	3,480	59.6	3,480	59.6
Age (years)				
<35	1,897	32.4	1,897	32.4
35–44	1,317	22.5	1,317	22.5
45–54	1,034	17.7	1,034	17.7
55–64	677	11.6	677	11.6
>64	922	15.8	922	15.8
Mean age (SD)	44.4	(17.7)	44.5	(17.6)
Urbanization of residential area				
Urban	2,597	44.4	2,607	44.6
Satellite	1,695	29.0	1,685	28.8
Rural	1,529	26.2	1,522	26.0
Geographic location of residential area				
North	3,026	51.8	2,982	51.0
Center	1,051	18.0	972	16.6
South	1,640	28.1	1,753	30.0
East	130	2.2	140	2.4
Overall*	5,847	100.0	5,847	100.0

*Inconsistency between total population and population summed for individual variable was because of missing information.

Table 4—*Overall and age- and sex-specific relative hazards of diabetes in association with depression*

Variables	Control group			Depression group			
	No. patients	No. events	ID (per 1,000 PY) (95% CI)†	No. patients	No. events	ID (per 1,000 PY) (95% CI)†	Adjusted HR (95% CI) in association with depression group
Men (years)							
<35	765	20	3.02 (1.69–4.35)	769	64	10.46 (7.90–13.03)	3.46 (2.37–5.04)§
35–44	531	56	12.94 (9.55–16.33)	503	102	27.55 (22.20–32.89)	2.13 (1.51–3.00)§
45–54	416	93	28.80 (22.93–34.67)	384	104	40.17 (32.45–47.89)	1.41 (1.03–1.91)§
55–64	272	61	30.25 (22.64–37.86)	251	73	44.91 (34.61–55.22)	1.49 (0.99–2.23)§
>64	371	105	47.05 (38.08–56.02)	448	116	48.57 (39.73–57.40)	1.03 (0.73–1.46)§
Total	2,355	335	18.25 (16.29–20.20)	2,355	459	27.95 (25.39–30.51)	1.83 (1.56–2.16)‖
Women (years)							
<35	1,128	28	2.91 (1.84–3.98)	1,125	94	10.40 (8.29–12.50)	3.50 (2.47–4.97)§
35–44	784	62	9.44 (7.10–11.78)	811	132	21.17 (17.56–24.78)	2.21 (1.54–3.18)§
45–54	616	118	24.45 (20.03–28.87)	648	176	37.58 (32.03–43.14)	1.50 (1.10–2.05)§
55–64	403	89	28.51 (22.58–34.44)	424	157	57.15 (48.21–66.09)	1.94 (1.33–2.83)§
>64	549	130	35.20 (29.14–41.26)	472	138	49.87 (41.55–58.19)	1.42 (0.95–2.11)§
Total	3,480	427	15.27 (13.82–16.72)	3,480	697	27.36 (25.33–29.39)	2.23 (1.89–2.62)‖
Overall*	5,847	762	16.45 (15.28–17.62)	5,847	1,156	27.59 (26.00–29.18)	2.02 (1.80–2.27)¶

The *P* value for depression-age interaction is <0.0001 for both sexes. The *P* value for depression-sex interaction is 0.0721. *Inconsistency between total population and population summed for individual variable was because of missing information. †Based on Poisson assumption. §Based on Cox proportional hazard regression with adjustment for geographic area and urbanization status. ‖Based on Cox proportional hazard regression with adjustment for geographic area, urbanization status, and age. ¶Based on Cox proportional hazard regression with adjustment for geographic area, urbanization status, age, and sex.

and have more trouble in undergoing complex treatments and intensive health monitoring, which could lead to greater psychological burden (3).

A greater risk of depression in women has been well documented previously (14,29). The sex difference was also observed in patients with diabetes (30). In line with these studies, our observations revealed greater IDs of depression in women than in men in both the diabetic and control groups. However, the test for an interaction effect between sex and diabetes was not statistically significant, suggesting that the relationship between diabetes and risk depression did not differ between men and women. This result was consistent with the finding of Engum (1), which indicated that sex did not modify the diabetes effect on onset of depression and anxiety.

The link between depression and diabetes

The results of studies linking depression to the risk of developing diabetes were consistent (5–9). Potential mechanisms have been elaborated, involving factors on a psychological, socioeconomic, and biological level (7,17). Different from the analyses for diabetes predicting depression, an increased risk of diabetes in patients with depression was observed in all age-groups, with the exception of men ≥55 years of age and women >64 years of age in this study. Our analyses showed that the adjusted HR reduced as age increased, consistent with the results of the subgroup analysis of the meta-analysis (9). The RR derived from studies including subjects with a mean (or median) age of <50 years was 1.96, higher than that from studies consisting of individuals with a mean (or median) age of ≥50 years (RR 1.50). In older patients with depression, a competing risk of death from other causes may increase, precluding the observation of diabetes. In addition, a misclassification of depression to no depression due to the difficulty in detecting the condition in the elderly may result in an underestimation of HR in this group.

Studies reporting stratified analyses on sex for depression predicting diabetes showed controversial findings. Some studies found greater risk in men (9,31,32), but other reports, similar to our analysis, revealed that sex did not significantly modify the relation between depression and diabetes (1,5). We observed a slightly greater HR in women than in men. A possible explanation is our use of claims data to identify depression and diabetes. It has been suggested that women were more likely to seek medical consultations (33). Women with depression may seek health care even more frequently, and thus their diabetes is more likely to be detected. Further studies are needed to clarify this issue.

Strengths and limitations

A strength of this study is that it included a large, population-based sample that is highly representative, leaving little room for selection bias. The large sample size also made it possible to perform age- and sex-specific analyses without comprising the required sample size. There are also limitations to this study. First, the exposure and outcome in this study were both diagnosed depression and diabetes, as we relied solely on claims data that do not cover those who went undiagnosed. The misclassification for both conditions could lead to biased estimation on the association. Second, the claims data do not contain BMI, diet, and lifestyle information, which are important risk factors of diabetes. However, previous studies have suggested that these factors explained partially, but not all, of the association between depression and diabetes (17,18). Third, surveillance bias might occur in this study, as both patients with diabetes and depression are more likely than their control counterparts to seek medical care. To address this issue, we calculated the frequency of medical visits for each study subject and adjusted this variable in the multivariate regression model. The annual average number of outpatient visits was approximately twofold higher in the patient groups than in the control groups at baseline (i.e., the year 2000). After adjusting for the

number of outpatient visits, the overall HR of depression onset reduced from 1.43 (95% CI 1.16–1.77) to 1.25 (1.21–1.30), and HR of diabetes incidence decreased from 2.02 (1.80–2.27) to 1.72 (1.53–1.94), suggesting a small magnitude of surveillance bias in our analysis. Fourth, because the NHIRD dataset covers the claims only beginning from 1997, we were unable to obtain each study subject's lifetime information on the diagnoses of diabetes and depression.

Implications

Given that diabetes is a serious, chronic disease that is usually accompanied by various life-threatening complications and that depression is a complex condition characterized by distraction in all facets of life, including physiological, behavioral, and psychosocial impacts, it is crucial to both public and medical professionals to be aware of the bidirectional relationship between the two conditions. This study, focused on identifying groups at high risk, could help target prevention efforts and priorities. In this study, the association between diabetes and depression was particularly strong in adults <45 years of age, who should be the objects of further attention.

To address the public health impact, we further calculated the overall population-attributable risk percentage associated with diabetes and depression, respectively. According to the NHI statistics (34), the prevalence rate of treated diabetes and depression in 2010 was 6,541 and 4,685 per 10^5, respectively. Together with the RR estimated from this current study, we estimated that 2.74% of depression was attributable to diabetes. On the other hand, ~4.65% of diabetes was attributable to depression. Given the increasing incidences of both diabetes and depression, efforts on preventing both conditions may help decrease the population-attributable risk percentage associated with these two conditions.

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P.-C.C. designed the study, researched data, and drafted the manuscript. Y.-T.C. contributed to statistical analyses and drafted the manuscript. H.-F.C. designed the study, research data, and contributed to the discussion. M.-C.K. designed the study and reviewed and revised the manuscript. C.-Y.L. obtained the research grant, designed the study, and reviewed and edited the manuscript. C.-Y.L. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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