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Bidirectional association between depressive symptoms and type 2 diabetes mellitus: The China Health and Retirement Longitudinal Study

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ABSTRACT

Objective: To prospectively examine the bidirectional relationship between depressive symptoms and type 2 diabetes mellitus (T2DM) among middle-aged and elderly Chinese.
Methods: Participants were enrolled in 2011–2012 (Wave 1) and followed up in 2013–2014 (Wave 2) and 2015–2016 (Wave 3) in the China Health and Retirement Longitudinal Study. Depressive symptoms were evaluated by the Chinese language version of 10-item Center for Epidemiological Studies Depression Scale (CESD-10) at three waves. T2DM was assessed by biochemical biomarkers at Wave 1 and reported physician-diagnosis at Wave 2 and 3. Cox proportional hazards regression was applied to calculate hazard ratio (HR) and 95% confidence intervals (CIs) for the bidirectional association.
Results: Participants with baseline depressive symptoms were 1.33 times as likely to develop T2DM (HR, 1.33; 95% CI: 1.06, 1.66), compared to their counterparts after adjusting for demographic characteristics and T2DM risk factors. The risk of T2DM increased linearly with higher severity of depression as determined by a higher CESD-10 score (P for trend $\ll 0.001$). In addition, baseline T2DM was associated with increased risk of incident depressive symptoms (1.15; 1.00, 1.31) and persistent depressive symptoms (1.35; 1.03, 1.77).
Conclusion: There is a positive bidirectional association between depressive symptoms and T2DM in middle-aged and elderly Chinese.

1. Introduction

Both diabetes and depressive disorders are leading causes of disability-adjusted life years worldwide. 8.8% of adults aged 20–79 years (425 million) had diabetes in 2017,[1] while global point prevalence and annual incidence of major depressive disorder were estimated to be 4.7% and 3.0%.[2] In China, a national survey showed that about 10.9% of Chinese adults had diabetes and another 35.7% had prediabetes in 2013.[3] The 1-month prevalence of major depressive disorder reached up to 2.1% in a large study in four provinces of China in 2001–2005.[4] The burden of diabetes and depression may continue to increase in China, given the demographic and social transitions due to rapid aging,[5] urbanization[6] and lifestyle change.[7]

Mounted epidemiological evidence suggests that depression may be a risk factor for the development of diabetes in addition to being a consequence of diabetes.[8,9] The pooled relative risk was estimated to be 1.60 (95% confidence interval [CI], 1.37, 1.88) for depression leading to T2DM in a meta-analysis of 13 cohort studies, and 1.15 (1.02, 1.30) for T2DM leading to depression in a meta-analysis of 7 cohort studies.[9] However, the bidirectional association was only examined in the same population in a limited number of original studies,[10–14] most of which were conducted in Western populations. Our previous study using the China Kadoorie Biobank data demonstrated that both major depressive episode and depressive symptoms increased the risk of T2DM among 0.5 million Chinese during a follow-up of 3291,908 person-years.[15] Since prospective studies on this topic are still sparse in Chinese and none of them ever examined the reciprocal association in the same population in Chinese mainland, it is still relevant to revisit the prospective bidirectional association in Chinese adults.

The China Health and Retirement Longitudinal Study (CHARLS) is a nationally representative longitudinal survey in Chinese aged 45 years or older that aims to provide high-quality databases for scientific and policy research on aging-related issues.[16] Capitalizing on

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this data resource, we aimed to prospectively evaluate the bidirectional association between depressive symptoms and T2DM in middle-aged and elderly Chinese. In addition, we examined whether the bidirectional association differed in subgroups defined by different characteristics.

2. Material and methods

2.1. Study population

The CHARLS collected high quality data from a national representative sample of Chinese residents aged 45 and above from 28 provinces, municipal cities and autonomous regions. Details of the study design were described elsewhere.[16] Based on a multistage stratified sampling design, a total of 17,708 participants were enrolled in the first wave (W1) in 28 of the overall 32 provinces in China between June 2011 and March 2012. 18,612 people, including 2458 newly enrolled participants, were interviewed in the second wave (W2) between 2013 and 2014. The third wave (W3) was conducted between 2015 and 2016. Trained staff interviewed participants using face-to-face laptop-based questionnaires and explained each question to the participants. The CHARLS was approved by the Biomedical Ethics Review Committee of Peking University, and informed consent was obtained from all participants.

2.2. Assessment of depression symptoms

Depressive symptoms were assessed at each wave using the Chinese language version of 10-item Center for Epidemiologic Studies Depression Scale (CESD-10), which has been validated and used to measure depressive symptoms in Chinese older adults.[17,18] The scale covered items related to major components of depression, such as the feeling of loneliness, hopelessness and unhappiness, attention deficit disorder and sleep disorder. Participants were assessed for each item on a scale from 0 to 3 based on their feeling during the past week: 1) rarely or none of the time (≪1 day); 2) some of time (1–2 days); 3) occasional or a moderate amount of the time (3–4 days); and 4) most or all of the time (5–7 days). The total score ranges from 0 to 30, with a higher score indicating higher level of depressive symptoms. A cut-off point of 10 showed high sensitivity and specificity for the diagnosis of depressive symptoms,[19] and a cut-off point of 21 was also recommended to defined major depression.[20] We thus used the cut-off point of 10 to dichotomize participants in our primary analysis, and graded depressive symptoms into no (0–9), moderate, and severe levels (≥21) in sensitivity analyses. Incident and persistent depressive symptoms were estimated only for participants with a CESD-10 score ≪10 at W1: incident depressive symptoms were defined as having a CESD-10 score ≥10 at W2 or W3, while persistent depressive symptoms as having a CESD-10 score ≥10 at both W2 and W3.

2.3. Assessment of T2DM

Baseline diabetes was determined by self-reported physician diagnosis or glucose measures (FBG ≥ 126 mg/dL or HbA1c ≥ 6.5%).[21] Incident cases of T2DM were identified as participants without baseline diabetes who reported physician-diagnosed diabetes during two follow-up surveys conducted 2 (2013–2014) and 4 (2015–2016) years later. Study participants were asked the question in two follow-up surveys, "*have you been diagnosed with diabetes mellitus by a doctor in the last two years?*"

2.4. Assessment of covariates

Covariates were obtained by interviewer-administered structural questionnaires at baseline, including demographic characteristics (age, sex, education level, and residence) and T2DM risk factors (body mass index [BMI], cigarette smoking, alcohol drinking, hypertension, and dyslipidemia). Education level was graded as illiterate, primary school, and middle school or above. Cigarette smoking and alcohol drinking were categorized into two groups (yes and no). Anthropometric measurements such as height and weight were measured using standard device according pre-specified protocols. 8-mL blood samples were collected for bioassays such as fasting blood glucose, total cholesterol (TC), high-density lipoprotein cholesterol (HDL—C), low high-density lipoprotein cholesterol (LDL-C), and triglycerides (TGs) at the Youanmen Center for Clinical Laboratory of Capital Medical University. Participants were classified into two categories based on self-reported hypertension or blood pressure measurements (systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg). We defined dyslipidemia as TC/HDL-C ≫ 5.0 or self-report dyslipidemia to avoid the influence of lipid-lowering drugs.[22] Participants self-reported dyslipidemia through answering the question, *have you been diagnosed with the dyslipidemia (elevation of LDL-C, TGs, and TC, or a low HDL—C) by a doctor?*

3. Statistical analysis

We used two different sets of research populations for two analytical purposes. To examine the impact of depressive symptoms on risk of T2DM, we excluded 1) participants without baseline socio-demographic information; 2) participants without baseline health information; 3) participants with erroneous age information; 4) participants without baseline depression information; and 5) participants with baseline diabetes (Supplementary Fig. 1). 12,030 participants free of diabetes were included in final analyses.

To examine the impact of T2DM on risk of depressive symptoms, we excluded 1) participants without baseline socio-demographic information; 2) participants without baseline health information; 3) participants with erroneous age information; 4) participants without baseline depression information; and 5) participants with baseline depressive symptoms (Supplementary Fig. 2). 7786 participants free of depressive symptoms were included in final analyses.

Baseline characteristics were presented as mean (standard deviation, SD) for continuous variables and percentage (%) for categorical variables, and compared using *t*-test (for continuous variable) and Chi square test (categorical variable), respectively. Cox proportional hazards regression was applied to calculate hazard ratios (HRs) and 95% CIs for examining the bidirectional association between depressive symptoms and T2DM. We adjusted for covariates in three models in a stepwise manner. The first multivariable model included age (continuous, years), sex (female and male), education (illiterate, primary school, and middle school or above), and residence (urban and rural). The second multivariable model included BMI (continuous, kg/m^2), cigarette smoking (yes and no), alcohol drinking (yes and no), and other covariates in the first model. The third multivariable model included prevalent hypertension (yes and no), prevalent dyslipidemia (yes and no) and other covariates in the second model. Adjusted HRs were estimated in major subgroups stratified by sex (female and male), age (≪60 and ≥60 years), residence (urban and rural), education level (illiterate, primary school, and middle school or above), BMI (≪24 and ≥24 kg/m^2), cigarette smoking (yes and no), alcohol drinking (yes and no), prevalent hypertension (yes and no) and prevalent dyslipidemia (yes and no). Potential effect modifications by these variables were examined by adding a product term of the stratifying variable and the exposure of interest (depressive status or diabetes depending on the analytical purpose) to the final model, and determined by comparing the two models using the likelihood ratio test. All analyses were performed using Stata 14 (StataCorp LLC, College Station, Texas, US). All *P* values were two-sided, and statistical significance was defined as $P \ll 0.05$.

Table 1
Baseline characteristics of study participants for the association between depressive symptoms and risk of T2DM in the CHARLS ($N = 12030$).

Characteristics	Total (%)	Depressive status		*P* values
		Yes (%)	No (%)	
Total	12030 (100)	4342 (36.09)	7688 (63.91)	–
Age (years)[a]	58.57 (9.58)	59.62 (9.71)	57.98 (9.45)	≪0.001
BMI (kg/m^2)[a]	23.36 (3.74)	22.88 (3.73)	23.63 (3.71)	≪0.001
Sex				≪0.001
Male	5865 (48.75)	1729 (39.82)	4136 (53.80)	
Female	6165 (51.25)	2613 (60.18)	3552 (46.20)	
Education level				≪0.001
Illiterate	3140 (26.10)	1450 (33.39)	1690 (21.98)	
Primary school	4984 (41.43)	1933 (44.52)	3051 (39.69)	
Middle school or above	3906 (32.47)	959 (22.09)	2947 (38.33)	
Residence				≪0.001
Rural	9778 (81.28)	3797 (87.45)	5981 (77.80)	
Urban	2252 (18.72)	545 (12.55)	1707 (22.20)	
Cigarette smoking				≪0.001
No	7137 (59.33)	2761 (63.59)	4376 (56.92)	
Yes	4893 (40.67)	1581 (36.41)	3312 (43.08)	
Alcohol drinking				≪0.001
No	8910 (74,06)	3437 (79.16)	5473 (71.19)	
Yes	3120 (25.94)	905 (20.30)	2215 (28.81)	
Hypertension				0.20
No	7450 (61.93)	2656 (61.17)	4794 (62.36)	
Yes	4580 (38.07)	1686 (38.83)	2894 (37.64)	
Dyslipidemia				0.31
No	7688 (63.91)	3616 (83.28)	6347 (82.56)	
Yes	4342 (36.09)	726 (16.72)	1341 (17.44)	

Abbreviation: BMI: body mass index; CHARLS: China Health and Retirement Longitudinal Study; T2DM: type 2 diabetes mellitus.
[a] Presented as mean (standard deviation).

4. Results

4.1. Depressive symptoms and risk of T2DM

4.1.1. Baseline characteristics

Of 12,030 individuals without baseline diabetes, 48.75% were male and mean age was 58.57 (standard deviation: 9.58) years. 26.10% were illiterate, and 81.28% were from rural areas. 4342 (36.09%) participants showed depressive symptoms as defined by CESD-10 of 10 or higher at baseline. Compared to their counterparts, participants with depressive symptoms were older, had lower BMI, and were more likely to be female and living in rural areas but less likely to be smokers and drinkers (Table 1).

4.1.2. Association between depressive symptoms and incident T2DM

A total of 328 participants developed T2DM during the whole 4-year follow-up, including 141 and 187 in two follow-up surveys respectively (Table 2). The incidence rate was 9.03 per 1000 person years in participants with depressive symptoms versus 7.13 per 1000 person years among those without depressive symptoms. Participants with baseline depressive symptoms were 1.33 times as likely to develop T2DM (HR: 1.33; 95%CI: 1.06, 1.66), compared to those without depressive symptoms after adjusting for age, sex, educational level, residence, BMI, cigarette smoking, alcohol drinking, prevalent hypertension and dyslipidemia. There was a linear association between the severity of depression and risk of T2DM (*P* for trend ≪ 0.001); one SD increase of the CESD-10 score was associated with a 21% increase in risk of incident T2DM (1.21; 1.09, 1.34). No heterogeneity in effect estimates were observed in subgroups as defined by sex, age, residence, education level, BMI, cigarette smoking, alcohol drinking, prevalent hypertension and dyslipidemia (Supplementary Fig. 3). Despite no statistical significance, HRs were higher in female than male participants (1.36 versus 1.24), in participants aged 60 years or above than those below 60 years (1.45 versus 1.21), and in participants with BMI below 24 kg/m^2 than those with BMI of 24 kg/m^2 or higher (1.61 versus 1.18). Besides, seemingly stronger associations were also observed in non-smokers, participants without hypertension, and participants without dyslipidemia.

4.2. T2DM and risk of depressive symptoms

4.2.1. Baseline characteristics

Of 7786 participants without depressive symptoms, 53.28% were male and mean age was 58.67 (standard deviation: 9.37) years (Table 3). 22.81% were illiterate, and 77.18% were from rural areas. 981 (12.60%) participants had prevalent diabetes at baseline. Compared to their counterparts, participants with diabetes were older, had higher BMI, and were more likely to live in urban areas and have prevalent hypertension and dyslipidemia but less likely to be drinkers.

4.2.2. Association between T2DM and risk of depressive symptoms

During a 4-year follow-up, 2036 and 432 cases of incident and persistent depressive symptoms were documented, respectively. Compared with participants without baseline T2DM, those with baseline T2DM had a 15% increased risk of incidence depressive symptoms (HR 1.15, 95%CI: 1.00, 1.31; Table 4). In addition, baseline T2DM was associated with a 35% (HR 1.35, 95%CI: 1.03, 1.77) increase in the risk of persistent depressive symptoms after adjusting for established or potential confounders (Table 5). No heterogeneity in effect estimates were observed in major subgroups (Supplementary Fig. 4). Despite no statistical significance, HRs seemed to be higher in urban than rural residents (1.30 versus 1.11), in non-drinkers than drinkers (1.19 versus 1.02), and in participants with than without dyslipidemia (1.24 versus 1.08).

Table 2
Association between depressive status and risk of incident T2DM in the CHARLS ($N = 12030$).

Depressive status	Cases/person years	Model 1	Model 2	Model 3	Model 4	*P* values
		HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	
Depressive symptoms						
No (≪10)	191/26796	1	1	1	1	
Yes (≥10)	137/15171	1.27 (1.02, 1.58)	1.24 (0.99, 1.59)	1.33 (1.06, 1.67)	1.33 (1.06, 1.66)	0.02
Depressive symptom groups						
No (≪10)	191/26796	1	1	1	1	≪0.001[a]
Moderate (10–20)	111/13057	1.16 (0.91, 1.47)	1.18 (0.93, 1.49)	1.26 (0.99, 1.60)	1.26 (0.99, 1.60)	
Severe (≥21)	26/2114	1.77 (1.23, 1.54)	1.68 (1.11, 2.55)	1.81 (1.19, 2.74)	1.77 (1.16, 2.68)	
Per 1 SD change	328/41967	1.18 (1.06, 1.30)	1.17 (1.05, 1.30)	1.21 (1.08, 1.34)	1.21 (1.09, 1.34)	≪0.001

Abbreviation: CHARLS: China Health and Retirement Longitudinal Study. CI: confidence interval; HR: hazard ratio; T2DM: type 2 diabetes mellitus.
Model 1: Non-adjusted.
Model 2: Adjusted for age (continuous, years), sex (male and female), education (illiterate, primary school, and middle school or above), and residence (urban and rural).
Model 3: Adjusted for the variables in Model 1 and body mass index (continuous, kg/m^2), cigarette smoking (yes and no), and alcohol drinking (yes and no).
Model 4: Adjusted for the variables in Model 2 and prevalent hypertension (yes and no) and dyslipidemia (yes and no).
[a] *P* for trend was estimated from a likelihood ratio test comparing the model with CESD-10 categories as an ordered categorical variable with the model without it.

Table 3
Baseline characteristics of study participants for the association between T2DM and risk of depressive symptoms in the CHARLS ($N = 7786$).

Characteristics	Total (%)	Diabetes		*P* values
		Yes (%)	No (%)	
Total	7786 (100)	981 (12.60)	6805 (87.40)	–
Age (years)[a]	58.67 (9.37)	60.17 (9.17)	57.98 (9.45)	≪0.001
BMI (kg/m^2)[a]	23.73 (3.76)	25.04 (3.65)	23.55 (3.74)	≪0.001
Sex				0.07
Male	4148 (53.28)	496 (50.56)	3652 (53.67)	
Female	3638 (46.72)	485 (49.44)	3153 (46.33)	
Education level				0.67
Illiterate	1776 (22.81)	217 (22.12)	1559 (22.91)	
Primary school	3045 (39.11)	378 (38.53)	2667 (39.19)	
Middle school or above	2965 (38.08)	386 (39.35)	2579 (37.90)	
Residence				≪0.001
Rural	6009 (77.18)	685 (69.83)	5324 (78.24)	
Urban	1777 (22.82)	296 (30.17)	1481 (21.76)	
Cigarette smoking				0.12
No	4447 (57.12)	583 (59.43)	3864 (56.78)	
Yes	3339 (42.88)	398 (40.57)	2941 (43.22)	
Alcohol drinking				0.05
No	5625 (72,25)	735 (74.92)	4890 (71.86)	
Yes	2161 (27.75)	246 (25.08)	1915 (28.14)	
Hypertension				≪0.001
No	4671 (59.99)	425 (43.32)	4246 (62.40)	
Yes	3115 (40.01)	556 (56.68)	2559 (37.60)	
Dyslipidemia				≪0.001
No	6061 (77.84)	520 (53.01)	5541 (81.43)	
Yes	1725 (22.16)	461 (46.99)	1264 (18.57)	

Abbreviation: BMI: body mass index; CHARLS: China Health and Retirement Longitudinal Study; T2DM: type 2 diabetes mellitus.
[a] Presented as mean (standard deviation).

5. Discussion

To the best of our knowledge, this current study was the first to assess the bidirectional relationship between depressive symptoms and T2DM in the same population-based cohort in China. Our study showed a positive bidirectional association between depressive symptoms and T2DM independent of established or potential confounders, which was consistent with findings from previous meta-analyses.[8,9] Our findings demonstrate a close link between depression and diabetes that can be used to inform the population-based control and prevention of these two major health challenges.

In our study, participants with depressive symptoms were 1.33 times more likely to develop T2DM compared to those without. Our finding is consistent with results from a comprehensive meta-analysis (pooled relative risk, 1.60)[9] and a more recent meta-analysis of only longitudinal studies (pooled relative risk, 1.41).[23] In the current study, there was a 21% increased risk of incident diabetes associated with each SD increase in addition to increased risk with higher severity of depression. The increasing trend was fairly consistent with our previous findings in the China Kadoorie Biobank among 0.5 million Chinese in 2018, which showed an HR of 1.32 for major depressive episode versus 1.19 for depressive symptoms only.[15] Direct comparison was not possible between the two studies because the modified Chinese language version of Composite International Diagnostic Interview Short-Form was used in the previous one. In the Atherosclerosis Risk in Communities study among 11,615 participants, an increasing trend was also observed across the quartiles of depression scores as defined by the 42-point Vital Exhaustion Scale.[24] Thus we believe that a higher risk of diabetes may exist for depression in a dose-response manner. Our two studies in China together with supporting evidence from other populations reflect that depression may be a reliable risk factor for diabetes in Chinese adults.

We found a statistically significant, though modest, elevation in the risk of incident depressive symptoms associated with T2DM (multivariable-adjusted HR of 1.15), which was lower than that reported in a recent meta-analysis of longitudinal studies (pooled relative risk: 1.33) on this topic.[25] Of note, the review contained studies (except one in Korea and one in Chinese Taiwan) mostly conducted in European and North American populations. The only one Chinese study was conducted in about 16,957 pairs of cases and controls in Taiwan residents that reported a HR of 1.43.[14] In addition, a weakened association between diabetes and subsequent depression was observed in older participants compared with those younger than 45 years old in that study. The moderate difference between our findings and those in this study might be partly explained by the age difference as our study did not include individuals aged younger than 45 years. We also observed a strong relation for persistent depressive symptoms (HR, 1.35) in addition to that for incident symptoms, which indicates that diabetes can also predict lasting depressive symptoms that has rarely been evaluated in literature. Our findings thus demonstrate that T2DM can be a reliable independent risk factor for depression in the Chinese population.

Although the mechanisms underlying the link between depression and T2DM are still uncertain, it is hypothesized that increased release of counterregulatory hormones due to hyperactivity of hypothalamic-pituitary-adrenal axis and sympathetic nervous system in depression leads to abdominal adiposity and insulin resistance.[15,26] On the other hand, diabetes may increase the risk of depression mainly because of long-term stress that is link to awareness of negative consequences of diabetes, suffering from chronic complications such as cardiovascular disease, and lifestyle change and inconvenience.[27] The reciprocal relation between depression and diabetes may also because they share predisposing unhealthy lifestyle factors such as physical inactivity and smoking.[15]

Our study is one of the only few prospective studies to examine the bidirectional association between depressive symptoms and T2DM in the same population. It has advantages such as large representative sample, detailed information on demographic and potential confounders, and prospective study design. However, certain limitations should be acknowledged. First, we did not use a diagnostic tool for depression ascertainment, which may cause misclassification of depression. In particular, the prevalence of depressive symptoms based on the screening scale, CESD-10 was higher than reported in a study in four provinces in China (17.5%).[4] However, depression screening scales

Table 4
Association between T2DM and risk of incident depressive symptoms in the CHARLS ($N = 7786$).

Group	Cases/person-years	Model 1	Model 2	Model 3	Model4	*P* values
		HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	
Total	2036/25569	–	–	–	–	–
Non-diabetic	1766/22438	1	1	1	1	
Diabetic	270/3131	1.11 (0.98, 1.26)	1.12 (0.99, 1.28)	1.15 (1.01, 1.31)	1.15 (1.00, 1.31)	0.05

Abbreviation: CESD-10: 10-item Center for Epidemiological Studies Depression Scale; CHARLS: China Health and Retirement Longitudinal Study. CI: confidence interval; OR: odds ratio; T2DM: type 2 diabetes mellitus.
Model 1: Non-adjusted.
Model 2: Adjusted for age (continuous, years), sex (male and female), education (illiterate, primary school, and middle school or above), and residence (urban and rural).
Model 3: Adjusted for the variables in Model 1 and body mass index (continuous, kg/m^2), cigarette smoking (yes and no), and alcohol drinking (yes and no).
Model 4: Adjusted for the variables in Model 2 and prevalent hypertension (yes and no) and dyslipidemia (yes and no).

Table 5
Association between T2DM and risk of persistent depressive symptoms in the CHARLS ($N = 7786$).

Group	Cases/person-years	Model 1	Model2	Model 3	Model4	*P* values
		HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	
Total	432/26783	–	–	–	–	–
Non-diabetic	363/23496	1	1	1	1	
Diabetic	69/3287	1.35 (1.04, 1.75)	1.37 (1.06, 1.78)	1.39 (1.07, 1.81)	1.35 (1.03, 1.77)	0.03

Abbreviation: CESD-10: 10-item Center for Epidemiological Studies Depression Scale; CHARLS: China Health and Retirement Longitudinal Study. CI: confidence interval; OR: odds ratio; T2DM: type 2 diabetes mellitus.
Model 1: Non-adjusted.
Model 2: Adjusted for age (continuous, years), sex (male and female), education (illiterate, primary school, and middle school or above), and residence (urban and rural).
Model 3: Adjusted for the variables in Model 1 and body mass index (continuous, kg/m^2), cigarette smoking (yes and no), and alcohol drinking (yes and no).
Model 4: Adjusted for the variables in Model 2 and prevalent hypertension (yes and no) and dyslipidemia (yes and no).

were highly frequently used in similar population studies[23,25] and our analyses using continuous CESD-10 scores and multiple categories in addition to a depression/non-depression binary definition consistently showed increased risk with higher severity of depression. Second, since CESD-10 only measures the depressive status in the past week, the measured depression may be only transient. In the analyses for the effect of T2DM on depressive symptoms, we tried to additionally use a definition of persistent depressive symptoms to consolidate their association. Third, the exact information of anti-depressant medication use was not fully available in our study, and whether anti-depressant use could explain the observed association between depression and incident diabetes needs further investigation. Finally, incident T2DM was ascertained by self-reported physician diagnosis at two follow-up surveys. The lack of biochemical markers and clinical evaluation may cause under-reporting of diabetes cases that do not present to health care providers.[28] This may potentially obscure the association between depression and diabetes if the underreporting did not occur randomly among the depressed and non-depressed.

In conclusion, we found a positive bidirectional relationship between depressive symptoms and diabetes in middle-aged and elderly Chinese. More precisely, the risk of diabetes can be increased as the consequence of depression, and as a predisposing factor diabetes also increases the risk of depression, especially of persistent depressive condition. Future studies are still needed to confirm our findings in the Chinese population and explore the potential mechanisms underlying this association. Clinical trials are also necessitated to test whether screening for depression or treatment of diabetes can reduce the risk of the counterpart of the link.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jdiacomp.2019.05.018.

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