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Depression, anxiety, and prevalent diabetes in the Chinese population: Findings from the China Kadoorie Biobank of 0.5 million people

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Abstract

Objective—Despite previous investigation, uncertainty remains about the nature of the associations of major depression (MD) with type 2 diabetes mellitus (T2DM), particularly in adult Chinese, and the relevance of generalized anxiety disorder (GAD) for T2DM.

Methods—Cross-sectional data from the China Kadoorie Biobank Study, a sample of approximately 500,000 adults from 10 geographically defined regions of China, were analyzed. Past year MD and GAD were assessed using the Composite International Diagnostic Inventory. T2DM was defined as either having self-reported physician diagnosis of diabetes at age 30 or later (“clinically-identified” cases) or having a non-fasting blood glucose ≥ 11.1 mmol/L or fasting blood glucose ≥ 7.0 mmol/L but no prior diagnosis of diabetes (“screen-detected” cases). Logistic

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regression was used to assess the relationship between MD and GAD with clinically-identified and screen-detected T2DM, adjusting for demographic characteristics and health behaviors.

Results—The prevalence of T2DM was 5.3% (3.2% clinically-identified and 2.1% screen-detected). MD was significantly associated with clinically-identified T2DM (Odds ratio [OR]: 1.75, 95% Confidence Interval (CI): 1.47 – 2.08), but not with screen-detected T2DM (OR: 1.18, 95% CI: 0.92 – 1.51). GAD was associated with both clinically-identified (OR: 2.14, 95% CI: 1.60 – 2.88) and screen-detected (OR: 1.44, 95% CI: 0.99 – 2.08) T2DM. The relationship between MD and GAD with T2DM was moderated by obesity.

Conclusion—MD is associated with clinically-identified, but not screen-detected T2DM. GAD is associated with both clinically-identified and screen-detected T2DM. The relationship between MD and T2DM is strongest among those who are not obese.

Keywords

anxiety; culture; depression; epidemiology; type 2 diabetes

INTRODUCTION

Major depression (MD) often co-occurs with chronic medical conditions such as type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD) [1-3]. Prospective studies indicate that the relationship between MD and T2DM is likely bi-directional, although the mechanisms underlying their relationship are largely unknown. There is recent evidence that undiagnosed T2DM is not strongly associated with MD, suggesting that the risk of MD subsequent to T2DM is likely driven by factors related to clinical treatment and self-management rather than hyperglycemia or related physiologic changes per se [4, 5].

MD often co-occurs with anxiety disorders, particularly generalized anxiety disorder (GAD) [6], and twin studies have indicated that part of the comorbidity between MD and GAD results from shared genetic liability [7]. However, relatively few studies have addressed the relationship between anxiety disorders and medical comorbidity [8]. In several cross-sectional reports and a recent meta-analysis, GAD and other anxiety disorders were modestly associated with T2DM [8-12], but a recent longitudinal study found no association between common anxiety disorders (e.g., GAD, panic disorder, agoraphobia, social phobia) and T2DM incidence [13]. These findings contrast with the fairly robust relationship between MD and T2DM, suggesting that different biological or psychological processes may underlie the co-occurrence of chronic conditions like T2DM with MD versus GAD.

China is undergoing rapid urbanization and modernization, with significant increases over the last few decades in the incidence of major chronic non-communicable diseases such as obesity, T2DM, and CVD [14, 15]. For example, the prevalence of T2DM in China has increased from 2.6% in 2000 to 9.7% in 2010 [16]. Parallel increases in the prevalence of MD have also been reported [17,18], with the lifetime risk for MD projected to be over 20 times greater for young adults compared with previous generations [19]. However, this increase in the prevalence of MD is likely confounded by improved awareness and detection of MD in the Chinese population [17, 20]. In addition, the relationships between psychiatric and medical conditions may be population-specific. There is evidence that people with depressive symptoms tend to have higher body mass index in Western non-Hispanic white populations, but the opposite is generally seen in Asian populations, supporting the so-called 'jolly fat' hypothesis (i.e., an inverse relationship between depressive symptoms and weight) [21-25]. Since obesity is a strong risk factor for T2DM, it is therefore possible that the relationship of MD, and related psychiatric conditions, with T2DM may differ between Chinese and Western populations.

To date only a few studies have examined the relationship between mood and anxiety disorders and T2DM in Asian populations, and the findings from these reports are mixed, partly due to limited sample sizes and the use of symptom scales rather than diagnostic instruments to assess psychiatric symptomology [26 – 29]. Moreover, most such studies were based on clinical data and thus have limited generalizability to the general population.

We report a detailed analysis of cross-sectional data from the China Kadoorie Biobank, a population-based study of 0.5 million people enrolled from 10 geographically defined regions of China. The aims of this study were to (1) examine the comorbidity between T2DM with MD and GAD, and further (2) to assess whether these relationships differ between clinically-identified versus undiagnosed diabetes.

METHODS

Sample

Data come from the baseline interview of the China Kadoorie Biobank (CKB) Study, a population-based study of 10 geographically defined regions interviewed between 2004 and 2008 [30]. The 10 regions were selected to provide approximately equal coverage of rural (Gansu, Henan, Sichuan, Hunan, and Zhejiang) and urban (Harbin, Qingdao, Suzhou, Liuzhou, and Haikou) provinces. Details of the study design and sample characteristics are described elsewhere [32]. Briefly, potential participants were approached in person by community leaders or health workers, and over 99% of those who consented to the baseline survey completed all assessments. In total, 512,891 adults aged 30 – 79 (representing approximately 30% of the total population of the 10 regions sampled) completed the interviewer-administered laptop-based questionnaire and clinic visit, and 98.4% completed a non-fasting blood spot test for glucose. During the clinic visit, a range of physical measurements were completed, including height and weight (used to calculate body mass index (BMI)), hip and waist circumference, bioimpedance, systolic and diastolic blood pressure (mmHg) and lung function. Participants with a non-fasting blood glucose level between 7.8mmol/L and <11.1mmol/L (N=29,636) were invited back to have a fasting blood glucose test, of which 13,289 (44.8%) completed the fasting draw. As shown by Supplemental Table 1, those who completed the fasting draw differed from those who were invited but did not complete the draw in terms of gender, marital status, education, socioeconomic status, province, smoking status, and physical activity (although in most cases the absolute amount of difference was small, but due to the large sample size still statistically significant). However, importantly, those who completed the fasting draw did not differ in terms of age ($F=1.85$, $p=0.173$), MD status ($X^2=0.86$, $p=0.354$) or GAD status ($X^2=0.270$, $p=0.604$). This analysis was restricted to participants who had valid non-fasting blood glucose measures (N=504,548).

Measures

Exposures—Past year major depression (MD) and generalized anxiety disorder (GAD) were assessed using the Chinese version of computerized Composite International Diagnostic Inventory –Short form (CIDI-SF) using face-to-face interview by trained health workers at the study clinic. The CIDI is a fully-structured diagnostic instrument based on criteria from the Diagnostic and Statistical Manual of Mental Disorders – IV (DSM-IV) and has moderate concordance with clinical psychiatric interviews [31, 32]; the Chinese version of the CIDI (calibrated as part of the World Mental Health Surveys) produces similar population estimates of MD to the Structured Clinical Interview for DSM (SCID) [33, 34]. MD was indicated by the presence of dysphoria and/or anhedonia accompanied by a clustering of somatic, cognitive, and behavioral disturbances, including appetite or weight change, sleeping problems, feelings of guilt or worthlessness, psychomotor changes, fatigue,

concentration problems, and thoughts of suicide that lasted two weeks or more. GAD was indicated by the presence of excessive anxiety or worry for at least six months accompanied by the presence of irritability, muscle tension, sleep disturbances, difficulty concentrating, tiring easily, and feelings of restlessness.

Outcomes—Two diabetes outcomes were examined: clinically-identified T2DM and screen-detected T2DM. Clinically-identified T2DM was defined as self-report of physician diagnosis of diabetes with an onset of age 30 or later; the age criteria was applied in order to exclude most cases of type 1 diabetes which tends to onset in adolescence. Screen-detected T2DM was defined according to the American Diabetes Association guidelines as either: (a) non-fasting blood glucose ≥ 11.1 mmol/L or (b) fasting blood glucose ≥ 7.0 mmol/L [35], plus no report of physician diagnosis of diabetes at the baseline survey. Overall, 20,502 individuals completed both a fasting and non-fasting blood draw (Supplemental Table 1). Of those who had a non-fasting blood glucose ≥ 11.1 mmol/L, 51.9% reported a physician diagnosis of diabetes. Sensitivity analyses restricting the undiagnosed diabetes cases to those with fasting glucose levels were conducted.

Other covariates—Demographic characteristics including age, sex, marital status (categorized as married, widowed/separated/divorced, and never married), and education (categorized as no formal schooling, primary school, middle school, high school, and college/university graduate) were assessed as part of the face-to-face interview. Two indicators of high socioeconomic status (SES) were considered in order to capture the diversity of SES across the rural and urban regions: (1) annual household income of $\geq 20,000$ Yuan, and (2) presence of a flushing toilet in the home. Province was included as a nine-level dummy variable with Gansu as the reference category. Health behaviors were assessed by self-report and included smoking status (categorized as never, former, and current regular smoker), alcohol use (categorized as consuming alcohol at least once per week vs. less because alcohol use is less common in China than in western nations), and total physical activity calculated as metabolic equivalent task hours (MET-hours/day) spent on work, transportation, housework, and non-sedentary recreation and sedentary leisure time was quantified as hours per day.

The CKB study was approved by the Institutional Review Boards at Oxford University and the China National Center for Disease Control (IRB ethics approval number X101222001 issued by the Chinese Academy of Medicine). All participants provided informed consent.

Analysis

Initially, comparisons between respondents with clinically-identified, screen-detected, and no T2DM were made using chi-squared tests for categorical variables and one-way Analysis of Variance (ANOVA) F-tests for continuous variables. The comorbidity between MD, GAD and physician diagnosis of neurasthenia was assessed using tetrachoric correlation coefficients. Next, a series of logistic regression models were fit to assess the relationships between MD and GAD with T2DM. Four nested logistic models were fit: (1) unadjusted, (2) adjusted for demographic and socioeconomic characteristics and region, (3) additionally adjusted for health behaviors smoking and alcohol use, and physical activity, and (4) additionally adjusted for health indicators BMI and systolic blood pressure. In order to assess whether the relationship between these mental health predictors and diabetes status was influenced by whether or not the T2DM had been clinically-identified, these analyses were repeated separately for (a) clinically-identified diabetes and (b) screen-detected T2DM. For the analyses predicting clinically-identified T2DM, those participants with screen-detected diabetes were excluded ($N = 10,528$, resulting in an analytic sample of 494,020), and similarly for the analyses predicting screen-detected T2DM those participants with

clinically-identified T2DM were excluded (N=15,981, resulting in an analytic sample of 488,567). Finally, given the impact that the ‘jolly fat’ hypothesis may have on the relationship between these mental health indicators and T2DM, analyses were repeated within strata of BMI defined according to World Health Organization (WHO) categories: underweight (BMI <18.5 kg/m²), normal (18.5 kg/m² ≤ BMI < 25 kg/m²), overweight (25 kg/m² ≤ BMI < 30 kg/m²) and obese (BMI ≥ 30 kg/m²).

Analyses were conducted using SAS 9.3 statistical software (SAS Institute, Cary NC) and all p-values refer to two-tailed tests. Statistical significance was set of p<0.05.

RESULTS

Baseline participant characteristics stratified by diabetes status are shown in Table 1. The overall prevalence of T2DM was 5.3% (3.2% clinically-identified and 2.1% screen-detected), and T2DM (both clinically-identified and screen-detected) was more common in urban provinces than in rural ones (7.2% versus 3.7%). The proportion of T2DM cases that were clinically-identified ranged from 78% in Zhejiang province to 39% in Gansu province (both rural provinces), with a median of 57%. For those with clinically-identified T2DM the mean (SD) age of diagnosis was 53.4 (9.3) years. Of the 3,198 individuals with past year MD, 471 (14.7%) also met criteria for GAD (terachoric correlation (r^2) = 0.75, SE = 0.01), and of the 1,147 individuals with past year GAD, 471 (41.1%) also met criteria for MD. MD was significantly more common among those with clinically-identified T2DM compared with those with screen-detected T2DM (0.9% vs. 0.6%, respectively) or without diabetes (0.6% and 1.1%). However, GAD was only marginally more common among the clinically-identified T2DM group.

Past year MD was significantly associated with prevalent T2DM, but this relationship was largely driven by the association with clinically-identified cases (Table 2). In fully-adjusted models, MD was associated with 1.75 times greater likelihood of having clinically-identified T2DM (95% Confidence Interval (CI): 1.47 – 2.08), but was only modestly associated with screen-detected T2DM (Odds Ratio (OR): 1.18, 95% CI: 0.92 – 1.51). In contrast, GAD was associated with more than two-fold higher likelihood of clinically-identified T2DM (OR: 2.14, 95% CI: 1.60 – 2.88), and a marginally significant 44% greater likelihood of screen-detected T2DM (OR: 1.44, 95% CI: 0.99 – 2.08). Adjustment for health behaviors and indicators (Table 2, Models 3 and 4, respectively) did not substantially alter the strength of the association between MD and GAD with diabetes status from Model 2 (adjusted for demographic characteristics only), indicating that these factors did not mediate the association between these disorders and T2DM. Sensitivity analyses restricting the screen-detected T2DM cases to those identified by fasting blood glucose measures only produced similar results (Supplemental Table 2).

There was an expected strong positive association of BMI with prevalence of T2DM; with each one-unit increase in kg/m² the odds of T2DM increased 13% (95% CI: 1.12 – 1.13). In contrast, there was an inverse association of BMI with prevalence of MD (data not shown). As shown by Table 3, the strength of the relationship between MD and any T2DM became attenuated with increasing BMI, which persisted when restricting the outcome to clinically-identified T2DM. BMI moderated the relationship between GAD and T2DM in a curvilinear manner, depending on whether the outcome was clinically-identified or screen-detected T2DM. The strength of the association between GAD and clinically-identified T2DM tended to increase with higher BMI, while higher BMI attenuated the relationship between GAD and screen-detected T2DM. However, we note that these analyses were based on relatively few cases of GAD.

Several other factors were also positively associated with prevalence of clinically-identified T2DM, including age (OR_(per year): 1.04, 95% CI: 1.04 – 1.05), female gender (OR: 1.48, 95% CI: 1.40 – 1.56), and systolic blood pressure (OR_(per mmHg): 1.01, 95% CI: 1.01 – 1.01). On the other hand, clinically-identified T2DM was inversely associated with household income (OR: 0.96, 95% CI: 0.92 – 0.99), having a flushing toilet in the home (OR: 0.84, 95% CI: 0.80 – 0.88), regular consumption of alcohol (OR: 0.54, 95% CI: 0.51 – 0.58), and higher levels of physical activity (OR: 0.98, 95% CI: 0.98 – 0.98). These relationships were similar in magnitude, but not always statistically significant, for screen-detected T2DM. Lower levels of education were significantly associated with increased likelihood of screen-detected T2DM but had no apparent association with clinically-identified T2DM.

DISCUSSION

In the largest study to date of the relationship between common mental disorders and prevalent T2DM in the Chinese population, we found that MD was significantly associated with increased likelihood of clinically-identified, but not screen-detected, T2DM. GAD was also significantly associated with higher prevalence of clinically-identified T2DM, and marginally associated with screen-detected T2DM. MD was inversely related to BMI, and the relationship between MD and T2DM was attenuated by increasing BMI. Our findings add to the growing body of research indicating that the relationship between MD, GAD, and T2DM is bi-directional, and suggest that the relationship between T2DM and mental health is not uniform across mood and anxiety disorders in this population.

Several reasons may help explain why the relationship with T2DM may differ between MD and GAD. The present analysis is based on cross-sectional data, and the information on MD and GAD pertain only to past-year, not lifetime, diagnoses. Therefore, it is not possible to establish whether the onset of MD or GAD occurred before or after T2DM; however, comparing the results from the clinically-identified and screen-detected T2DM cases provides some leverage for understanding these relationships. MD was only associated with clinically-identified T2DM, which is consistent with previous research that the relationship between T2DM and subsequent depressive symptoms is largely driven by diabetes-related distress and the behavior changes needed to effectively self-manage this condition [4, 5]. In contrast, GAD was associated with greater likelihood of both clinically-identified and screen-detected T2DM, although the magnitude of this relationship was stronger for the former. This indicates that processes other than diabetes self-management may contribute to this relationship, including possibly biological mechanisms not shared with MD. For example, a recent study of relaxation training showed changes in expression of genes related to energy metabolism and insulin function post-intervention, suggesting that anxiety symptoms may have direct effects on these systems [36]; more research is needed to understand the potential biological mechanism linking anxiety to metabolic disorders. It is also worth noting that because of the diagnostic criteria for GAD require symptom duration of at least six months, whereas those for MD specify only a period of two weeks, the cases of GAD identified in this study are necessarily more chronic in nature than the MD cases, which may contribute to their disparate relationship with screen-detected T2DM.

Consistent with so-called ‘jolly fat’ hypothesis, we found that the prevalence of MD was inversely associated with BMI and that the relationship between MD and T2DM is particularly strong among individuals who are not obese. These results are inconsistent with the hypothesis that BMI mediates the relationship between MD and T2DM (e.g., appetite and weight gain are symptoms of MD, which would in turn increase risk of T2DM), at least in the Chinese population. Other symptoms of MD unrelated to weight (e.g., sleeping disturbances, fatigue) may be more relevant to T2DM risk [37]. Alternatively, T2DM may

only be a risk factor for MD among individuals at otherwise low risk of this disease (e.g., individuals at normal weight), although due to the cross-sectional nature of this data we are not able to explore this hypothesis directly.

These findings have clinical implications regarding screening and diagnosis of T2DM. Consistent with previous research [4, 5] our results suggest that the relationship between T2DM and subsequent MD and GAD is related to the process of clinical diagnosis and self-management rather than hyperglycemia as a disease state per se. Self-management of T2DM can be a challenging, particularly for individuals with limited social and economic resources. Some factors that influence T2DM prognosis are under an individual's control (e.g., health-related behaviors) while others are not (e.g., access to affordable healthcare, genetic liability), and the process of self-management in and of itself can become a chronic stressor as individuals try, on a daily basis, to meet clinical recommendations for dietary intake, physical activity, and glycemic control [38]. A recent international study found that about 40% of individuals with clinically-identified diabetes had significant diabetes-related distress (in China specifically this estimate was approximately 50%) [38]. However, only one-third of individuals reported that they had been asked about feelings of depression or anxiety by their healthcare provider in the past year. Although there are various recommendations for screening for depression in the context of diabetes, there is no consensus as to which tools would be most appropriate nor how frequently such screening should occur for individuals with T2DM [39].

These findings should be interpreted in light of study strengths and limitations. The use of both fasting and non-fasting blood samples to determine undiagnosed T2DM status is another limitation; however, our sensitivity analysis among those with screen-detected T2DM determined by fasting glucose measurements was consistent with the results reported here. Finally, without additional clinical information we cannot definitively know that all the cases of diabetes examined here were type 2; however, over 95% of diabetes cases in the general adult population are T2DM. This study also has a number of strengths. The large, population-based sample mitigates the influence of selection bias and enhances the generalizability of the findings. MD and GAD were assessed using laptop-based validated structured diagnostic interviews with very complete data collection. Finally, in our analytic models we were able to adjust for a number of important confounding health behaviors and characteristics, including smoking, alcohol use, and BMI.

In summary, despite potential cultural differences in the expression of depressive and anxiety symptoms, this study demonstrates that MD and GAD are associated with clinically-identified T2DM in the Chinese population and suggests that there may be different biological and behavior pathways linking MD and GAD with T2DM. The role of culture in potentially modulating the relationship between psychiatric conditions with metabolic disorders such as T2DM requires further research. Populations in the midst of rapid social and economic change may provide a unique setting to understand how these factors influence the relationship between mental and physical health, and the regular resurvey and continuing follow up of the CKB participants for a wide of range of health-related outcomes should soon allow for their relationships to be investigated prospectively.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Appendix

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Author contributions B. Mezuk developed the idea for the study and wrote the first draft of the manuscript. Canqing Yu conducted the data analysis and Yiping Chen supervised the data analysis. Kenneth S. Kendler, Zhengming Chen, Yu Guo, Zheng Bian, Rory Collin, Junshi Chen, Zengchang Pang, Huijun Wang, Richard Peto, Xiangsan Que, Hui Zhang, Zhongwen Tan, and Liming Li edited and critiqued drafts of the manuscript. All authors approved the final version of the manuscript for submission.

Competing interest statement The authors have no completing interests to report.

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Table 1

Descriptive characteristics of participants by type 2 diabetes status

	Type 2 diabetes			F/Chi ² , p-value
	Clinically-identified (N= 15981)	Screen-detected (N= 10528)	No diabetes (N=478039)	
Socio-demographic characteristics				
Age in years (Mean, SD)	59.11 (9.1)	56.25 (9.9)	51.19 (10.6)	5401.70, <.0001
Female	9905 (62.0)	6218 (59.1)	281614 (58.9)	60.25, <.0001
Marital status				
Married	13820 (86.5)	9194 (87.3)	433918 (90.8)	616.45, <.0001
Widowed/Separated/Divorced	2104 (13.2)	1276 (12.1)	40528 (8.5)	
Never married	57 (0.4)	58 (0.6)	3593 (0.8)	
Education				
No formal school	3145 (19.7)	2245 (21.3)	86760 (18.2)	
Primary School	5068 (31.7)	3598 (34.2)	153853 (32.2)	
Middle School	4143 (25.9)	2658 (25.3)	136253 (28.5)	300.60, <.0001
High School	2353 (14.7)	1467 (13.9)	73209 (15.3)	
College/University	1272 (8.0)	560 (5.3)	27964 (5.9)	
Socioeconomic status				
Household income >= 20,000 Yuan/year	7424 (46.5)	4077 (38.7)	204167 (42.7)	159.64, <.0001
Have flushing toilet in home	10182 (63.7)	5494 (52.2)	239555 (50.1)	1155.43, <.0001
Province				
Qingdao	1853 (11.6)	954 (9.1)	32210 (6.7)	
Harbin	3538 (22.1)	1799 (17.1)	52150 (10.9)	5360.29, <.0001
Haikou	1160 (7.3)	694 (6.6)	27828 (5.8)	
Suzhou	1422 (8.9)	1057 (10.0)	50776 (10.6)	
Liuzhou	2503 (15.7)	1212 (11.5)	46458 (9.7)	
Sichuan	894 (5.6)	1183 (11.2)	49903 (10.4)	
Gansu	620 (3.9)	967 (9.2)	48449 (10.1)	
Henan	1490 (9.3)	1333 (12.7)	60533 (12.7)	

	Type 2 diabetes		F/Chi ² , p-value
	Clinically-identified (N= 15981)	Screen-detected (N= 10528)	
Socio-demographic characteristics			
Zhejiang	1367 (8.6)	417 (4.0)	52048 (10.9)
Hunan	1134 (7.1)	912 (8.7)	57684 (12.1)
Health behaviors			
Smoking status			
Never	10388 (65.0)	6414 (60.9)	296178 (62.0)
Former	2557 (16.0)	1455 (13.8)	54435 (11.4)
Current regular	3036 (19.0)	2659 (25.3)	127426 (26.7)
Consumes alcohol weekly	1474 (9.2)	1685 (16.0)	71119 (14.9)
Total physical activity (Mean, SD)	18.46 (10.4)	21.62 (12.2)	25.84 (13.6)
Mental health indicators			
Major depression	139 (0.9)	67 (0.6)	2992 (0.6)
Generalized anxiety disorder	49 (0.3)	29 (0.3)	1069 (0.2)
Health indicators			
Age of diabetes diagnosis (Mean, SD)	53.41 (9.3)	-	-
BMI in kg/m ² (Mean, SD)	24.93 (3.5)	25.24 (3.7)	23.59 (3.4)
Waist circumference in cm (Mean, SD)	85.85 (9.7)	86.52 (10.1)	80.00 (9.6)
Systolic BP in mmHg (Mean, SD)	141.85 (22.6)	141.78 (22.6)	130.55 (21.0)
			3580.23, <.0001

Values are N (%) unless otherwise specified. P-value refers to comparison across three diabetes categories (clinically-identified, screen-detected, and no diabetes).

Table 2
Relative odds of type 2 diabetes associated with major depression, generalized anxiety disorder, and neurasthenia

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 4 OR (95% CI)
Exposure: CIDI MD				
Any diabetes (N=504,548)				
Never MD	1.0	1.0	1.0	1.0
Past year MD	1.24 (1.08 – 1.43)	1.47 (1.27 – 1.69)	1.42 (1.23 – 1.65)	1.52 (1.31 – 1.75)
Clinically-identified T2DM (N=494,020)				
Never MD	1.0	1.0	1.0	1.0
Past year MD	1.40 (1.18 – 1.66)	1.71 (1.44 – 2.04)	1.65 (1.38 – 1.96)	1.75 (1.47 – 2.08)
Screen-detected T2DM (N=488,567)				
Never MD	1.0	1.0	1.0	1.0
Past year MD	1.02 (0.80 – 1.30)	1.12 (0.88 – 1.43)	1.11 (0.87 – 1.42)	1.18 (0.92 – 1.51)
Exposure: CIDI GAD				
Any diabetes (N=504,548)				
Never GAD	1.0	1.0	1.0	1.0
Past year GAD	1.32 (1.05 – 1.66)	1.78 (1.41 – 2.25)	1.74 (1.38 – 2.21)	1.82 (1.44 – 2.30)
Clinically-identified T2DM (N=494,020)				
Never GAD	1.0	1.0	1.0	1.0
Past year GAD	1.37 (1.03 – 1.83)	2.11 (1.57 – 2.82)	2.05 (1.53 – 2.75)	2.14 (1.60 – 2.88)
Screen-detected T2DM (N=488,567)				
Never GAD	1.0	1.0	1.0	1.0
Past year GAD	1.23 (0.85 – 1.78)	1.39 (0.96 – 2.01)	1.38 (0.95 – 2.00)	1.44 (0.99 – 2.08)

Values are odds ratio (95% confidence interval). Model 1: unadjusted. Model 2: Adjusted for age, sex, marital status, household income, education, presence of a flushing toilet in the home, and province. Model 3: Model 2 plus adjustment for smoking history, alc ohol use, and physical activity. Model 4: Model 3 plus adjustment for BMI and systolic blood pressure

Table 3

Relative odds of type 2 diabetes associated with major depression and generalized anxiety disorder stratified by body mass index

BMI categories	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Exposure: CIDI MD			
Any type of T2DM			
Underweight	1.89 (1.05 – 3.40)	2.21 (1.22 – 4.01)	2.12 (1.17 – 3.85)
Normal weight	1.24 (1.02 – 1.51)	1.49 (1.22 – 1.82)	1.49 (1.21 – 1.82)
Overweight	1.36 (1.07 – 1.72)	1.48 (1.16 – 1.89)	1.50 (1.18 – 1.92)
Obesity	1.25 (0.73 – 2.16)	1.41 (0.81 – 2.54)	1.41 (0.81 – 2.64)
Clinically-identified T2DM			
Underweight	2.12 (0.99 – 4.53)	2.32 (1.07 – 5.00)	2.15 (0.99 – 4.66)
Normal weight	1.43 (1.14 – 1.81)	1.77 (1.40 – 2.45)	1.75 (1.38 – 2.14)
Overweight	1.49 (1.12 – 2.00)	1.72 (1.28 – 2.32)	1.73 (1.28 – 2.33)
Obesity	1.22 (0.59 – 2.51)	1.55 (0.74 – 3.24)	1.51 (0.72 – 3.18)
Screen-detected T2DM			
Underweight	1.64 (0.67 – 4.01)	2.05 (0.83 – 5.06)	2.01 (0.81 – 4.98)
Normal weight	0.91 (0.63 – 1.33)	1.03 (0.71 – 1.50)	1.05 (0.72 – 1.58)
Overweight	1.16 (0.79 – 1.70)	1.18 (0.80 – 1.74)	1.21 (0.82 – 1.79)
Obesity	1.30 (0.60 – 2.80)	1.33 (0.61 – 2.88)	1.35 (0.62 – 2.94)
Exposure: CIDI GAD			
Any type of T2DM			
Underweight	2.97 (1.19 – 7.44)	3.40 (1.34 – 8.64)	3.18 (1.24 – 8.13)
Normal weight	1.15 (0.81 – 1.62)	1.53 (1.08 – 2.17)	1.56 (1.10 – 2.22)
Overweight	1.35 (0.93 – 1.97)	1.80 (1.23 – 2.64)	1.82 (1.24 – 2.67)
Obesity	2.43 (1.15 – 5.13)	3.20 (1.50 – 6.86)	3.21 (1.49 – 6.90)
Clinically-identified T2DM			
Underweight	1.13 (0.16 – 8.20)	1.13 (0.16 – 8.31)	0.96 (0.13 – 7.17)
Normal weight	1.34 (0.90 – 1.99)	1.98 (1.32 – 2.97)	2.02 (1.34 – 3.03)
Overweight	1.39 (0.96 – 2.24)	2.18 (1.34 – 3.56)	2.19 (1.34 – 3.56)
Obesity	2.46 (0.96 – 6.36)	3.89 (1.47 – 10.30)	3.77 (1.41 – 10.07)
Screen-detected T2DM			
Underweight	4.99 (1.80 – 13.86)	6.55 (2.30 – 18.65)	6.29 (2.21 – 17.95)
Normal weight	0.82 (0.43 – 1.59)	0.93 (0.48 – 1.80)	0.97 (0.50 – 1.87)
Overweight	1.30 (0.73 – 2.33)	1.41 (0.79 – 2.52)	1.44 (0.80 – 2.57)
Obesity	2.40 (0.95 – 6.83)	2.63 (0.92 – 7.53)	2.66 (0.92 – 7.66)

Model 1: unadjusted. Model 2: Adjusted for age, sex, marital status, household income, education, presence of a flushing toilet in the home, and province. Model 3: Model 2 plus adjustment for smoking history, alcohol use, and physical activity and systolic blood pressure.

Values are odds ratio (OR) and 95% Confidence Intervals (95% CI).