

Table 2. Summary of Studies Assessing the Association Between Depression and Diabetes Incidence

Study (N), Design	Depression Definition	Estimate; Time Period	Impact of Depression on Comorbidity ^a	
			Presence of Depression	Depression Recurrence/Severity ^b
Diabetes Only				
Atasoy et al 2018 ³¹ (MONICA/ KORA) (N=9,340) Prospective cohort	DEEX score ≥ 10/12, men/women	HR (95% CI) for developing T2DM; mean 15.4-year follow-up ^c	Overall: 1.16 (1.06 to 1.02); P=.02 Normal weight, depressed: 1.30 (0.90 to 1.91) Overweight: 3.11 (2.30 to 4.21); P<.0001 Obese: 8.05 (5.90 to 10.98); P<.0001	NR
Brown et al 2005 ³² (N=9,340) Retrospective case-control	ICD codes	OR (95% CI) history of depression and incident T2DM; 3-year exposure period ^d	Overall: 1.47 (1.14 to 1.90); P=.002 Age 20–50 years: 1.23 (1.10 to 1.37) Age ≥ 51 years: 0.92 (0.84 to 1.00)	NR
Campayo et al 2010 ³³ (ZARADEMP) (N=3,521) Prospective cohort	GMS-AGECAT (details NR)	HR (95% CI) depression as predictor of diabetes; 5-year follow-up ^e	Overall: 1.65 (1.02 to 2.66); P=.04 First episode: 1.59 (0.96 to 2.64); P=.07 Baseline only: 1.43 (0.79 to 2.58); P=.24 Untreated: 1.83 (1.11 to 2.99); P=.02 Treated: 0.823 (0.23 to 2.98); P=.77	Nonsevere: 1.66 (1.01 to 2.75); P=.048 Severe: 1.57 (0.55 to 4.44); P=.39 Previous episode: 2.06 (0.73 to 5.79); P=.17 Baseline + follow-up: 2.09 (1.06 to 4.14); P=.03
Eriksson et al 2008 ³⁴ (Stockholm Diabetes Prevention Program) (N=5,227) Prospective cohort	Patient questionnaire	OR (95% CI) depression quartile at baseline (low, middle, and high) and T2DM at 8- to 10-year follow-up ^f	NR	<u>Men</u> Middle vs low: 1.3 (1.0 to 1.7) High vs low: 1.6 (0.6 to 4.3) <u>Women</u> Middle vs low: 1.0 (0.7 to 1.3) High vs low: 0.7 (0.3 to 1.6)
Farmer et al 2008 ³⁵ (N=2,430) Retrospective case-control	DSM-IV or ICD recurrent MDD criteria using SCAN 2.1	OR (95% CI) for T2DM in cases with recurrent depression vs controls; lifetime history assessed ^g	NR	2.06 (0.84 to 5.04); P=NS
Karakus and Patton 2011 ³⁶ (Health and Retirement Study) (N=3,645) Prospective cohort	8-item CES-D score ≥ 3	OR (95% CI) depression at baseline as predictor of diabetes; 12-year follow-up ^h	Overall: 1.50 (1.01 to 2.24); P=.04 Including excessive alcohol drinking: 1.505; P=.044	NR
Kivimäki et al 2010 ³⁷ (N=59,940) Retrospective case-control	ICD codes	Study 1: OR (95% CI) for incident T2DM, depression vs no depression; 4-year follow-up ⁱ Study 2: HR (95% CI) for incident T2DM associated with antidepressant use; mean 4.75-year follow-up ⁱ	Untreated: 1.05 (0.55 to 2.04) Antidepressant use: 2.76 (1.93 to 3.94) 200–399 defined daily doses/year: 1.53 (1.25 to 1.87) ≥ 400 defined daily doses/year: 2.00 (1.51 to 2.66) P trend <.0001	Severe: 1.42 (1.01 to 1.99) NR
Mallon et al 2005 ³⁸ (N=1,187) Prospective cohort	Self-report	RR (95% CI) new diabetes according to depression at baseline; 12-year follow-up ^j	Women: 1.0 (0.3 to 3.2)/0.9 (0.3 to 2.9) Men: 0.6 (0.2 to 2.0)/1.3 (0.4 to 3.6) ^k	NR
Mezuk et al 2008a ²⁸ (Baltimore ECA) (N=3,481) Prospective cohort	DIS; details NR	HR (95% CI) risk of T2DM according to lifetime MDD; 24-year follow-up ^l	1981–2005: 1.62 (1.03 to 2.55); P<.05 1993–2005: 2.04 (1.09 to 3.81); P<.05	NR
Mezuk et al 2015 ³⁹ (SALT) (N=37,043) Cross-sectional	DSM-IV MDD using CIDI-SF	HR (95% CI) lifetime MDD predicting T2DM; 4-year follow-up ^m	Overall: 1.07 (0.91 to 1.26) Age 40–55 years All: 1.32 (1.00 to 1.80) Women: 1.74 (1.09 to 2.79) Men: 1.08 (0.70 to 1.67) Age ≥ 55 years All: 1.00 (0.83 to 1.21) Women: 0.92 (0.72 to 1.18) Men: 1.17 (0.87 to 1.57)	NR
Nichols and Moler 2011 ⁴⁰ (N=58,056) Retrospective cohort	ICD codes	RR (95% CI) risk of T2DM according to depression; follow-up ≤ 5 years ⁿ	1.10 (1.02 to 1.20)	NR
Pan et al 2010 ⁴¹ (Nurses' Health Study) (N=65,381) Prospective cohort	Self-report; MHI-5 score ≤ 52 or with clinical depression	RR (95% CI) incident T2DM according to depressive symptom status; 10-year follow-up ^o	Any depressed mood: 1.17 (1.05 to 1.30) Physician-diagnosed, untreated: 1.05 (0.85 to 1.30) Physician-diagnosed, with antidepressants: 1.25 (1.10 to 1.41) Single MDD: 0.5 (0.13 to 1.88)	<u>By MHI-5 score</u> 86–100: reference 76–85: 1.07 (0.97 to 1.17) 53–75: 1.13 (1.02 to 1.26); P trend=.002 ≤ 52: 1.04 (0.83 to 1.31) Recurrent MDD: 3.20 (1.10 to 9.33); P<.05
Windle and Windle 2013 ⁴² (N=557) Prospective cohort	DSM-IV MDD criteria using CIDI	OR (95% CI) lifetime MDD predicting T2DM; 5-year follow-up ^p	Single MDD: 0.5 (0.13 to 1.88)	Recurrent MDD: 3.20 (1.10 to 9.33); P<.05
Diabetes as a Component of Metabolic Syndrome				
Block et al 2016 ⁴³ (SHIP-0; SHIP-TREND-0) (N=8,040) Cross-sectional	DSM-IV MDD criteria using CID-S or M-CIDI	OR (95% CI) MDD and elevated glucose or antidiabetic medication; 4-year follow-up ^q	<u>Women</u> SHIP-0: 1.49 (0.92 to 2.41) SHIP-TREND-0: 0.96 (0.70 to 1.32) MDD lifetime: 0.85 (0.58 to 1.23) <u>Men</u> SHIP-0: 0.94 (0.50 to 1.78) SHIP-TREND-0: 1.21 (0.89 to 1.65) MDD lifetime: 1.23 (0.87 to 1.75)	<u>Recurrent MDD</u> Women: 0.73 (0.47 to 1.12) Men: 1.25 (0.81 to 1.93)
Goldbacher et al 2009 ⁴⁴ (SWAN) (N=429) Prospective cohort	DSM-IV MDD criteria using SCID-IV	HR (95% CI) depression as a predictor of high fasting glucose; 7-year follow-up ^r	Overall: 1.22 (0.75 to 2.92)	NR
Meta-Analyses				
Cosgrove et al 2008 ²⁷ 14 studies (N=NR)	Any assessment of MDD or raised depression score on a validated scale	Pooled RR (95% CI) risk of developing T2DM associated with depression	<u>Fixed/random effects model</u> Depression score or DIS for diagnosis: 1.33 (1.19 to 1.46)/1.17 (1.05 to 1.29) Depression scales for diagnosis: 1.42 (1.18 to 1.66)/1.25 (1.02 to 1.48)	NR
Mezuk et al 2008b ⁴⁵ 20 studies (N=NR)	NR	Pooled RR (95% CI) incident T2DM in people with depression	Overall: 1.60 (1.37 to 1.88) Age < 50 years: 1.96; P<.001 Age ≥ 50 years: 1.50; P<.001 Women: 1.26 (0.95 to 1.67) Men: 1.57 (1.24 to 1.99)	NR
Rotella and Mannucci 2013 ²⁹ 23 studies (N=424,557)	Any method included	Pooled HR (95% CI) incident diabetes in people with vs without depression	Overall: 1.379 (1.227 to 1.550); P<.001 Use of antidepressant: 1.68 (1.17 to 2.40); P=.005 Depression diagnosis, untreated: 1.56 (0.92 to 2.65); P=.09	NR
Vancampfort et al 2015 ³⁰ 17 studies (N=158,834)	Interview-defined MDD according to the DSM or ICD	Pooled RR (95% CI) risk of T2DM in people with MDD	1.49 (1.29 to 1.72); P<.001	NR

^aWhen multiple levels of covariate adjustment were reported, the model with the greatest level of adjustment is reported here. Unless otherwise specified, the effect estimate is for the comparison of depression vs no depression. Statistically significant differences (P < .05) are shown in bold; P values are reported when available.

^bFor the "Depression Recurrence/Severity" category, certain studies evaluated the association of certain subtypes of depression such as recurrent depression or certain severity levels depression on the risk or severity of comorbid disease.

^cAdjusted for age, sex, survey, lifestyle risk factors (smoking, alcohol consumption, physical inactivity), and metabolic risk factors (hypertension, dyslipidemia)

^dAdjusted for age as a continuous and quadratic variable, sex, and number of physician visits (≥ 5).

^eAdjusted for age, sex, living situation, educational level, BMI, hypertension, statin use, current smoking, family history, functional disability, alcohol consumption, antidepressant treatment, and antipsychotic treatment.

^fAdjusted for age, BMI, family history of diabetes, smoking, physical activity, and socioeconomic position. Middle quartiles were combined into a single group

^gAdjusted for age, sex, and BMI.

^hAdjusted for age at baseline, sex, race, marital status, education level, BMI, cigarette smoking, functional limitations index, self-report of limited ability to work, and household income.

ⁱStudy 1: adjusted for sex, hypertension, CHD, cerebrovascular disease, and cancer; Study 2: adjusted for sex. Participants in Study 2 did not have a clear diagnosis of depression, only antidepressant medication use (treatment for > 6 months).

^jAdjusted for age, marriage status, living alone, hypertension, obesity, smoking, alcohol use, snoring, and sleep difficulty (difficulties initiating sleep; difficulties maintaining sleep) or sleep duration (≤ 5 h and ≥ 9 h).

^kSignificant at a lower level of adjustment only.

^lAdjusted for age, sex, ethnicity, education, smoking status, alcohol use, antidepressant use, and social network size (1981–2005 analysis); additionally adjusted for BMI, family history of diabetes, stairs climbed per day, frequency of eating balanced meals or social network size, and frequency of social contact with relatives (1993–2005 analysis).

^mAdjusted for age, sex, and genetic risk.

ⁿAdjusted for age, sex, BMI, fasting glucose, SBP, triacylglycerol, HDL cholesterol, smoking, and the presence of the other conditions (CVD, heart failure, chronic kidney disease).

^oAdjusted for family history of diabetes, marital status, alcohol consumption, smoking status, physical activity level, coffee, whole grain, red/processed meat, and soft drinks.

^pAdjusted for baseline age, CVD, education, BMI, alcohol use, cigarette use, lifetime anxiety disorder, and stressful events.

^qAdjusted for age categories, marital status, education, employee status, smoking, physical inactivity, and risky alcohol consumption.

^rAdjusted for baseline age and race.

Abbreviations: AGECAT = Automated Geriatric Examination for Computer Assisted Taxonomy; BMI = body mass index; CES-D = Center for Epidemiologic Studies-Depression; CHD = coronary heart disease; CIDI = Composite International Diagnostic Interview; CIDI-SF = Composite International Diagnostic Interview-Short Form; CID-S = Composite International Diagnostic Screener; CVD = cardiovascular disease; DEEX = DEpression and EXhaustion subscale; DIS = Diagnostic Interview Schedule; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; ECA = Epidemiologic Catchment Area; GMS = Geriatric Mental State; HDL = high-density lipoprotein; HR = hazard ratio; ICD = International Classification of Diseases; KORA = Cooperative Health Research in the Region of Augsburg; M-CIDI = Munich-Composite International Diagnostic Interview; MDD = major depressive disorder; MHI-5 = 5-item Mental Health Inventory; MONICA = Monitoring of Trends and Determinants in Cardiovascular Disease Augsburg; NR = not reported; NS = not significant; OR = odds ratio; RR = risk ratio; SALT = Screening Across the Lifespan Twin; SBP = systolic blood pressure; SCAN = Schedules for the Clinical Assessment of Neuropsychiatry; SCID-IV = Structured Clinical Interview for DSM-IV disorders; SHIP = Study of Health In Pomerania; SWAN = Study of Women's Health Across the Nation; T2DM = type 2 diabetes mellitus; ZARADEMP = Zaragoza Dementia and Depression.