Chinese Expert Consensus on the Diagnosis and Treatment of Diabetes Comorbid with Depression (Postprint)

Authors: Psychosomatic Endocrinology Collaborative Group, Psychosomatic Medicine Branch, Chinese Medical Association, Professional Committee for Diabetes Prevention and Control, Chinese Preventive Medicine Association

Date: 2025-09-15T16:00:01+00:00

Abstract

Comorbidity of diabetes and depression represents a relatively common phenomenon in clinical practice, characterized by a significant bidirectional relationship between the two conditions. This comorbid state not only exacerbates disease burden and increases treatment complexity, but also substantially impairs patients' quality of life and long-term prognosis. The shared pathophysiological mechanisms may encompass multiple factors, including neuroendocrine dysregulation, chronic inflammatory responses, and unhealthy lifestyle patterns. The principal challenges currently confronting clinical practice include insufficient awareness of this comorbidity among healthcare professionals, resulting in frequent underrecognition or misdiagnosis of depressive symptoms; inadequate interdisciplinary collaboration, which constrains the implementation of integrated management; and the absence of specialized diagnostic and therapeutic guidelines for this comorbidity both domestically and internationally, leading to a lack of standardized protocols in clinical practice. To address these issues, the Psychosomatic Endocrinology Collaborative Group of the Psychosomatic Medicine Branch of the Chinese Medical Association, in conjunction with experts from diverse fields including endocrinology and metabolism, psychiatry, neurology, psychology, psychosomatic medicine, and traditional Chinese medicine, has formulated the inaugural "Chinese Expert Consensus on the Diagnosis and Treatment of Depression Comorbid with Diabetes." This consensus systematically delineates the clinical features, pathophysiological mechanisms, assessment instruments, and intervention strategies for depression comorbid with diabetes, explicitly emphasizes the critical importance of multidisciplinary collaborative management, proposes standardized screening and diagnostic pathways, and offers specific recommendations for coordinated treatment. The publication of this consensus will provide clinicians with evidence-based, actionable diagnostic

and therapeutic guidance, facilitate enhanced recognition and intervention efficacy for the comorbidity, and promote comprehensive health management and improved prognostic outcomes for patients with diabetes.

Full Text

Preamble

Chinese Expert Consensus on the Diagnosis and Treatment of Diabetes Comorbid with Depression

Psychosomatic Endocrinology Coordination Group of the Psychosomatic Medicine Society of the Chinese Medical Association, Diabetes Prevention and Control Committee of Chinese Preventive Medicine Association

Corresponding authors:
TAO Hong, Department of Endocrinology and Metabolism, Beijing Anzhen Hospital, Capital Medical University; E-mail: vivientao@126.com
YUAN Yonggui, Department of Psychosomatic and Psychiatry, Zhongda Hospital, Southeast University; E-mail: yygylh2000@sina.com
LU Wei, Department of Psychosomatic Medicine, Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University; E-mail: luwei@vip.sina.com

Abstract The comorbidity of diabetes and depression is relatively common in clinical practice, with a significant bidirectional association between the two conditions. This comorbid state not only increases disease burden and treatment complexity but also severely impacts patients' quality of life and long-term prognosis. Shared pathophysiological mechanisms may involve neuroendocrine dysregulation, chronic inflammation, and unhealthy lifestyle factors. Currently, clinical management faces several major challenges: insufficient awareness among healthcare providers often leads to underdiagnosis of depression; lack of effective interdisciplinary collaboration hampers integrated care; and the absence of specific diagnostic and treatment guidelines results in nonstandardized clinical practice. To address these issues, the Psychosomatic Endocrinology Collaboration Group of the Psychosomatic Medicine Branch of the Chinese Medical Association, together with experts from endocrinology, psychiatry, neurology, psychology, psychosomatic medicine, and traditional Chinese medicine, has developed the first Chinese Expert Consensus on the Diagnosis and Treatment of Diabetes Comorbid with Depression.

This consensus systematically elaborates on the clinical features, pathophysiological mechanisms, assessment tools, and intervention strategies for this comorbidity, underscores the importance of multidisciplinary collaboration, proposes a standardized screening and diagnostic pathway, and provides specific recommendations for collaborative care. The release of this consensus aims to offer scientific and practical clinical guidance, improve recognition and management of this comorbidity, and ultimately enhance overall patient care and long-term

outcomes.

[**Key words**] Diabetes mellitus; Depression; Comorbidity; Diagnosis; Treatment; Expert consensus; Guidebook

---

1. Concepts and Epidemiology

Diabetes mellitus is a group of metabolic diseases characterized by chronic hyperglycemia resulting from defects in insulin secretion and/or action. Long-term disturbances in carbohydrate, fat, and protein metabolism can cause multisystem damage, leading to chronic progressive lesions and functional decline in eyes, kidneys, nerves, heart, and blood vessels. Based on etiological evidence, diabetes is classified into four types: type 1 diabetes (T1DM), type 2 diabetes (T2DM), specific types of diabetes, and gestational diabetes mellitus [1]. T2DM accounts for over 90% of diabetic populations.

Depression manifests as low mood, loss of interest, insufficient energy, and is often accompanied by attention difficulties, decreased appetite, insomnia, pain, and other somatic symptoms. Patients may have suicidal ideation and exhibit cognitive, behavioral, and social functional abnormalities. Commonly used clinical concepts include depressive mood, depressive state, and depressive disorder.

1.1 Depressive Mood

Depressive mood is a normal human emotional response that arises when individuals feel powerless or frustrated when facing certain situations. The degree of low mood varies, is time-limited, usually short-term, and does not affect basic social functioning. It can typically be relieved through self-regulation and generally requires no special medical intervention.

1.2 Depressive State or Depressive Syndrome

A depressive state is a common clinical condition characterized by a cluster of symptoms with obvious depressive mood as the main feature. It presents as pathological emotions, cognition, behavior, and various somatic discomforts, with duration significantly longer than normal physiological depressive mood. When symptoms reach sufficient severity or impair social functioning, professional medical evaluation and intervention are required.

1.3 Depressive Disorder

Depressive disorder refers to a group of mental illnesses characterized by significant and persistent low mood and lack of interest, lasting more than two weeks, accompanied by varying degrees of changes in thinking and behavior, and may include psychotic symptoms such as hallucinations and delusions. It significantly impacts social functioning, and severe cases may have suicidal ideation

and behavior. Most patients have a recurrent tendency, with most episodes being remitting, though some may have residual symptoms or become chronic. When patients meet clinical diagnostic criteria, diagnosis must be made by mental health professionals based on structured assessment, followed by active treatment. Depressive disorders include depressive episodes, recurrent depressive disorder, persistent mood disorder, other mood disorders, and unspecified mood disorders.

1.4 Major Depressive Disorder (MDD)

Major depressive disorder is the most common type of depressive disorder, presenting as single or recurrent episodes with significant emotional, cognitive, and somatic symptoms during episodes, with symptom remission between episodes [2]. Given that MDD accounts for the highest proportion within the depressive disorder spectrum, has the most extensively studied comorbidity mechanisms with chronic physical diseases like diabetes, and represents the most well-established clinical entity with an evidence-based treatment system, this consensus focuses on standardized MDD diagnosis and treatment pathways under the DSM-5/ICD-11 framework. It emphasizes a diagnostic assessment system based on symptom dimensions (emotional/cognitive/somatic) and severity stratification, as well as evidence-based treatment for diabetes comorbid with MDD.

Both diabetes and depression have become global public health issues. The global adult prevalence of diabetes is 11.1%, while the global prevalence of depression is approximately 5% [3]. In China, the adult prevalence of diabetes has reached 12.4%, with about 140 million diabetic patients [1]. The prevalence of depressive disorders in China is 6.8%, with MDD at 3.4% [4], making it the most common mood disorder. Depression is extremely prevalent among diabetic patients. Foreign studies show that compared with non-diabetic populations, the prevalence of depression is three times higher in T1DM patients and twice as high in T2DM patients [5-6]. Fourteen percent of diabetic patients have depression, while the prevalence of clinically significant depressive symptoms is as high as 32.4% [5]. A bidirectional Mendelian randomization study analyzing the causal relationship between T2DM and depression showed that depression increases the risk of developing T2DM by 26% [7]. The U.S. National Ambulatory Medical Care Survey (NAMCS) revealed a 12.4% prevalence of depression among diabetic patients, with female diabetic patients having higher rates than non-diabetic females and diabetic males (15.4%, 13.7%, and 9.1%, respectively) [8].

Chinese data show similar trends. One study using the CHARLS database explored the bidirectional relationship between clinically significant depressive symptoms and T2DM, finding that T2DM patients had a 15% increased risk of depressive symptoms, while those with depressive symptoms had a 33% increased risk of developing T2DM [9]. Another study found that individuals with depressive symptoms had a 19% increased risk of T2DM, and patients

with depression had a 31% increased risk [10].

[**Expert Consensus 1**] There is a significant bidirectional risk-increasing relationship between diabetes and depression. This mutual influence cannot be ignored and warrants high clinical attention.

2. Serious Consequences of Comorbidity

2.1 Increased Risk of Diabetes Complications

A systematic review and meta-analysis of longitudinal studies showed that comorbid depression increases the risk of macrovascular complications by 38% and microvascular complications by 33% in diabetic patients [11]. A large prospective cohort study demonstrated that depression in T1DM and T2DM patients is associated with an increased risk of chronic kidney disease development [12]. Adolescents with T1DM and comorbid depression or anxiety had significantly prolonged hospitalization for ketoacidosis [13]. A meta-analysis of 11 cross-sectional and prospective cohort studies indicated that depression is significantly associated with increased incidence of diabetic retinopathy in T2DM patients [14]. However, it remains unclear whether a causal relationship exists between these conditions.

The underlying mechanisms may be related to behavioral changes in depressed patients, including decreased self-care ability, reduced medication adherence, increased smoking, decreased physical activity, prolonged sedentary time, and increased intake of high-calorie foods. These adverse behaviors may affect metabolic indicators such as blood glucose and increase the risk of diabetes complications.

2.2 Increased Mortality Risk and Deteriorated Long-term Survival

A large prospective cohort study in the UK showed that during a median follow-up of 6.8 years, the all-cause mortality risk, cancer-related mortality risk, and other mortality risks in patients with both diabetes and depression exceeded the sum of risks from diabetes and depression alone, demonstrating a synergistic effect on all-cause mortality [15]. Compared with diabetic patients alone, comorbid depression significantly increases all-cause mortality risk [16-17]. In elderly T2DM patients, the negative impact of comorbid depression is particularly significant, including worse activities of daily living and higher mortality risk [18-19].

2.3 Deterioration of Health-related Quality of Life

Research from the U.S. National Health and Nutrition Examination Survey (NHANES), based on the Patient Health Questionnaire-9 (PHQ-9) (with PHQ-9 score $ $10 defining depression), showed that the negative impact of diabetes and depression comorbidity on health-related quality of life (HRQoL) presents a significant synergistic effect [20]. The risk of HRQoL deterioration increased

2.49-fold and 2.44-fold in patients with diabetes and depression, respectively, while patients with both conditions had a more than 5-fold increased risk. Moreover, patients with diabetes and comorbid depression experienced more severe physical function impairment and significantly increased healthcare utilization needs.

2.4 Increased Healthcare Utilization and Economic Burden

Diabetic patients with comorbid depression have increased healthcare service utilization frequency and overall medical costs [21]. Depressive symptoms also significantly increase the all-cause hospitalization risk in diabetic patients and are associated with poor prognosis. This may be due to accompanying burnout reducing self-care ability, leading to declining physical and mental health, increased healthcare utilization frequency, and reduced adherence to medication regimens [22-24]. Recent studies show that even after adjusting for medication discontinuity, age, and other potential confounders, depression is still associated with increased risks of all-cause and cardiovascular disease-related hospitalization in T2DM patients, suggesting that diabetic patients should be regularly assessed for depression and receive active treatment [25].

2.5 Increased Suicide Risk

Diabetic patients have significantly increased risks of suicidal ideation, suicide attempts, and suicide death compared with the general population. Among patients with both diabetes and depression, over 20% report a history of suicide attempts [26].

[Expert Consensus 2] Diabetes comorbid with depression can lead to serious consequences. Recognition and diagnosis of the comorbidity should be strengthened, and active treatment should be provided to improve prognosis and reduce medical economic burden.

3. Etiology and Pathogenesis of Comorbidity

The bidirectional association between diabetes and depression may involve shared biological mechanisms, behavioral-socio-psychological factors, and genetic factors. The specific causes and mechanisms are not fully understood but involve multiple systems and pathways that interact with each other, including hypothalamic-pituitary-adrenal (HPA) axis dysfunction, monoamine theory, immune and inflammatory responses, insulin resistance, gut microbiota dysbiosis, genetic susceptibility, etc. [27-28]. Additionally, both conditions share common behavioral pathogenic mechanisms and environmental and social factors.

3.1 HPA Axis Dysfunction

The HPA axis plays a key role in stress response. Patients with diabetes and comorbid depression exhibit HPA axis hyperactivity and circadian rhythm disturbances, manifested by elevated corticotropin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH), and cortisol levels. Long-term exposure to high glucocorticoids can inhibit hippocampal neurogenesis and damage synaptic plasticity, induce neuronal atrophy, and enhance amygdala activity, thereby disrupting emotional regulation [28]. The mechanism involves abnormalities in the hippocampal-paraventricular nucleus regulatory circuit: reduced and abnormally phosphorylated glucocorticoid receptor expression in the paraventricular nucleus impairs negative feedback inhibition, leading to persistent HPA axis activation [28-29]. HPA rhythm disturbances also weaken autophagy inhibition in nerve cells, disrupting regulation of circadian blood glucose variations [30]. Hyperinsulinemia further exacerbates HPA axis hyperactivity, leading to stress response system dysregulation associated with depression occurrence. Impaired negative feedback regulation of HPA axis function is a hallmark of major depressive disorder [31-32]. Similarly, HPA axis hyperactivity in depressed patients worsens diabetes metabolism by inhibiting insulin secretion and promoting peripheral tissue insulin resistance.

3.2 Central Monoamine Neurotransmitter Dysfunction

Neurotransmitter imbalance is a core pathological mechanism of depression. Diabetes may affect neurotransmitter synthesis, release, and metabolism through metabolic disorders and inflammation. Serotonin (5-HT) in the central nervous system plays important roles in mood, cognition, learning and memory, eating, sleep-wake cycles, and social behavior. Its decreased level is associated with mood disorders and neurogenesis damage, affecting depression occurrence through multiple receptor pathways [33-35]. In diabetes, metabolic imbalance of 5-HT precursor tryptophan leads to reduced 5-HT synthesis. Persistent hyperglycemia and insulin resistance can further reduce 5-HT activity. Insulin may improve depressive symptoms in diabetic mice by reducing brain monoamine oxidase activity and decreasing 5-HT decomposition [36].

The locus coeruleus-norepinephrine system participates in stress response, energy metabolism, and synaptic plasticity. Chronic stress such as diabetes may lead to norepinephrine transporter consumption and decreased norepinephrine concentration, resulting in downregulated brain excitability and affecting mood. In patients with diabetes and comorbid depression, impaired mesolimbic dopamine pathway function may lead to reward system dysregulation, while abnormal activity in limbic system regions such as the amygdala contributes to low mood [30].

3.3 Chronic Inflammation and Oxidative Stress

Diabetes and depression are closely associated with chronic low-grade inflammation, manifested by elevated serum inflammatory factors such as interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) [37]. These pro-inflammatory factors affect different levels of the HPA axis, leading to increased CRH, ACTH, and plasma cortisol concentrations, which exacerbate hyperglycemia and insulin resistance and worsen depressive symptoms [32]. Inflammatory factors can cross the blood-brain barrier and affect brain regions regulating emotion, such as the hippocampus and prefrontal cortex [38]. Chronic inflammation may reduce synthesis of neurotransmitters such as serotonin and dopamine, leading to depressive symptoms. Diabetic patients typically have elevated oxidative stress levels, producing large amounts of free radicals that not only damage neurons but also activate inflammatory pathways, worsening depressive symptoms. Increased oxidative stress is also associated with neurodegenerative changes, particularly in brain regions involved in memory and emotion such as the hippocampus and prefrontal cortex.

3.4 Insulin Resistance

Insulin resistance plays an important bridging role in the comorbidity of diabetes and depression. It impairs neuronal energy metabolism and structure in key brain regions such as the hippocampus and prefrontal cortex, leading to abnormalities in emotional regulation and cognitive function [39]. Simultaneously, insulin resistance causes neurotransmitter imbalance in the brain, manifested by decreased dopamine and serotonin levels, which are closely related to core depressive symptoms such as low mood and anhedonia [40]. Additionally, insulin resistance activates the nuclear factor- B (NF- B) pathway, triggering a chronic low-grade inflammatory state where pro-inflammatory factors such as IL-6 and TNF-α exacerbate peripheral and central insulin resistance while activating microglia to trigger neuroinflammatory cascades [41-42]. Insulin resistance also affects neurotransmitter metabolism, such as reducing transport of serotonin precursor tryptophan and interfering with dopamine synthesis and release [43].

3.5 Gut Microbiota and Brain-Gut Axis

Gut microbiota dysbiosis is associated with both diabetes and depression. Impaired intestinal barrier function in diabetic patients leads to elevated blood endotoxin levels, promoting insulin resistance and pro-inflammatory phenotypes of central microglia, triggering hippocampal and hypothalamic inflammation, causing oxidative stress and neuronal apoptosis, and worsening depressive symptoms [30,44]. Tryptophan metabolism disorders in depressed patients may be closely related to gut microbiota dysbiosis [45]. Gut microbiota participates in neurotransmitter synthesis and regulation by secreting short-chain fatty acids and other metabolites, playing an important role in the comorbidity mechanism between diabetes and depression by affecting the HPA axis negative feedback regulation mechanism and influencing stress response and metabolic status

[44,46].

3.6 Brain Structural and Functional Reorganization

Patients with both diabetes and depression show reduced brain volume on neuroimaging, particularly in the anterior cingulate cortex and orbital frontal regions. Magnetization transfer techniques show reduced magnetization transfer ratios in specific brain areas, indicating impaired neuroplasticity. Hyperglycemia is neurotoxic, affecting neuronal subpopulations and inhibiting the limbic system; it also damages microvasculature, leading to loss of microstructure in supplied brain regions. Insulin resistance affects neuronal energy utilization, causing hippocampal volume reduction [30,47].

3.7 Personal Behavior, Personality Traits, and Psychosocial Factors

Unhealthy lifestyles and high neuroticism personality traits may trigger both diabetes and depression. Individuals with high neuroticism are more prone to negative emotions and have strong psychological and physiological responses to stress, which may promote the development of diabetes and depression by enhancing inflammatory responses and altering HPA axis function [48]. Factors such as poverty, low birth weight, childhood adversity, chronic stress, and low socioeconomic status may increase the risk of both diseases [49]. Depressed patients with lack of social support and poor stress coping ability often have difficulty adhering to diabetes management due to lack of motivation, exacerbating blood glucose control difficulties; while diabetes management difficulties and complication risks can worsen patients' depressive mood, forming a bidirectional vicious cycle.

3.8 Genetic Susceptibility and Epigenetics

Bidirectional Mendelian randomization studies have confirmed a significant causal relationship between depression and T2DM (OR=1.26, 95%CI=1.11~1.44) [7]. Multi-phenotype GWAS analyses have identified multiple genetic loci, including key genes regulating insulin resistance (such as FTO), inflammatory response (such as IL-6R), and neurotransmitter metabolism (such as SLC6A4), which are closely related to pathways such as HPA axis dysfunction, chronic inflammation, and metabolic disorders [7,50]. Epigenetic regulation (DNA methylation/histone modification) mediates gene-environment interactions between hyperglycemic environment and depression susceptibility, forming a metabolic-neural bidirectional regulatory network [51].

[Expert Consensus 3] The etiology and pathogenesis of diabetes comorbid with depression are complex and diverse, involving multifactorial interactions including HPA axis dysfunction, monoamine system alterations, oxidative stress and inflammatory responses, insulin resistance, gut microbiota dysbiosis, brain structural and functional reorganization, genetics, and personal behavioral and

psychosocial factors. In-depth research on comorbidity mechanisms provides theoretical support for early clinical diagnosis and treatment.

4. Clinical Features and Screening

4.1 Clinical Features

4.1.1 Main Clinical Characteristics of Depression Depression comprises emotional, somatic, and cognitive symptoms [52]. When diabetic patients present with the following three categories of clinical manifestations, clinicians should be alert to possible depression:

[**Expert Consensus 4**] If diabetic patients present with emotional symptom clusters (significant low mood, loss of interest/pleasure, slowed responses, pessimism and hopelessness), emotion-related cognitive symptoms (poor concentration or memory), and unexplained somatic symptom clusters (significant fatigue, unexplained pain, weight loss, insomnia, appetite reduction, gastrointestinal dysfunction, general discomfort), and relevant clinical laboratory and imaging examinations show no clear organic etiology, the possibility of comorbid depression should be highly suspected and further evaluated.

(1) **Emotional symptoms**: Core symptoms of depression include low mood, low self-evaluation, feeling hopeless about life, easily feeling wronged, and even crying easily. Interest in everything declines, and patients no longer want to engage in previously enjoyable activities. Family members or caregivers may notice they are "very sensitive to trivial matters." In severe cases, some patients may express thoughts that "life is meaningless."

(2) **Somatic symptoms**: Manifestations include lack of energy, fatigue, weight loss, insomnia, pain, palpitations, general discomfort, migratory skin numbness, blood pressure instability, decreased appetite, gastrointestinal dysfunction, and sexual dysfunction. Patients may repeatedly seek medical care in various departments of general hospitals without finding organic diseases that can explain their symptoms. Sleep problems are also very common in diabetic patients with comorbid depression, presenting as difficulty falling asleep, frequent dreams, easy awakening, early awakening, and fatigue after waking; a few patients may have hypersomnia.

(3) **Cognitive symptoms**: Diabetic patients often have cognitive impairment. Depressed patients also have reduced speech, slowed thinking and activity, poor concentration, memory decline, difficulty making decisions, and indifference to external matters.

4.1.2 Suicidal Ideation, Attempts, and Suicide Due to low mood and low self-evaluation, patients easily develop inferiority, self-blame, and hopelessness, leading to persistent and recurrent suicidal ideation. Driven by these thoughts, some patients may develop suicide plans or attempts. Therefore, for patients

with past suicidal ideation or attempts, high vigilance is required, and physicians should repeatedly remind family members and caregivers to prioritize suicide prevention.

4.2 Screening for Depression

4.2.1 History Taking For diabetic patients highly suspected of having comorbid depression, detailed history inquiry and symptom recording are essential during consultations. The interview should include: (1) the main reason for consultation (emotional, cognitive, psychotic symptoms, etc.) and social functional impairment; (2) history of physical diseases and personal history, including detailed psychosocial assessment such as personality characteristics, social support system deficits (social isolation/poor family support), lack of hobbies, stressful life events, unhealthy lifestyle, and substance abuse; (3) previous antidepressant use history, including efficacy, adherence, and adverse reactions; (4) family history of mental disorders, including mental illness, personality abnormalities, self-harm/suicide history, and consanguineous marriage in family members [54].

4.2.2 Depression Screening

(1) **Screening scale selection**: The 2-item Patient Health Questionnaire (PHQ-2, Table 1) or the "90-second 4-question assessment" (Table 2) are recommended for initial depression screening. If PHQ-2 score is $ $3 or all four questions in the 90-second assessment are positive, further assessment with the 9-item Patient Health Questionnaire (PHQ-9) (Table 3) is recommended [54-56].

PHQ-9 is a commonly used self-rated depression scale in clinical practice for screening and assessing depression in the past two weeks. In recent years, PHQ-9 has been widely used for depression screening in diabetic patients. A total PHQ-9 score $ $10 is generally considered the optimal cutoff for screening diagnosis, with sensitivity and specificity both at 88% [57]. This consensus recommends a PHQ-9 total score $ $10 as the screening diagnostic threshold. Some studies suggest that when using PHQ-9 for depression screening in diabetic patients, the overlap between chronic disease-related somatic symptoms (such as fatigue, sleep disturbance) and scale items should be considered, and recommend adjusting the diagnostic threshold to $ $12 to reduce false positive rates [58-59]. In summary, PHQ-9 is an efficient screening tool, but its optimal cutoff may need adjustment for different target populations and requires further validation.

(2) **Screening scope and frequency**: In risk stratification for depression in diabetic patients, the following clinical characteristics indicate high-risk groups [49]: Demographic risk factors: female, adolescent, elderly (especially those with limited mobility and $ $2 comorbidities), low socioeconomic status, and insufficient social support; Chronic exposure to stressors: those who have experienced recent major life events (such as bereavement, unemployment) or chronic stress; Diabetes duration $ $5

years, poor glycemic control [glycated hemoglobin (HbA1c) >7%], established chronic diabetes complications, or multiple chronic disease comorbidities.

Based on these high-risk groups, standardized depression screening should be initiated at key time points (such as initial diagnosis, complication onset, or 1-3 months after treatment adjustment). PHQ-9 is recommended, with routine reassessment every 6-12 months. Those with $ $2 risk factors should have screening intervals shortened to 3-6 months. Evidence shows that targeted psychological intervention can reduce depression incidence and improve glycemic target achievement rates [49].

(3) **Other depression symptom scales**: In clinical practice, multiple validated standardized depression symptom scales are widely used to assess symptom severity in suspected depression patients, including the Beck Depression Inventory (BDI), Zung Self-Rating Depression Scale (SDS), Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR), and Hospital Anxiety and Depression Scale (HADS). These scales have proven effective in screening depressive symptoms and can provide preliminary assessment of symptom severity. In addition to these self-rated scales, psychiatrists can also use observer-rated scales such as the Hamilton Depression Rating Scale (HAMD) and Montgomery-Åsberg Depression Rating Scale (MADRS) when assessing depressive symptoms. Comprehensive use of these scales enables physicians to thoroughly evaluate patients' depressive symptom severity and provide important basis for clinical diagnosis and treatment [52,54].

4.2.3 Physical Examination, Laboratory, and Imaging Investigations
Comprehensive physical examination is crucial for distinguishing between physical disease and depressive symptoms. The following investigations should be selected based on specific circumstances: (1) Routine laboratory tests: including blood routine, liver and kidney function, blood glucose, blood lipids, thyroid function, and myocardial markers, which provide general health information and identify physiological abnormalities related to depressive symptoms; (2) Special examinations based on differential diagnosis needs, such as endocrine hormone measurement to exclude depression caused by endocrine system diseases, and infectious markers screening (hepatitis B, hepatitis C, syphilis, HIV, etc.) to exclude depression caused by infectious diseases; (3) Imaging assessment should be symptom-oriented: for palpitations, chest tightness, or chest pain, chest CT, pulmonary CTA, echocardiography, 24-hour dynamic electrocardiogram, or coronary CT angiography can be selected to differentiate coronary heart disease, arrhythmia, pulmonary embolism, etc.; for cognitive decline, neurological imaging and electroencephalography can differentiate cerebrovascular disease and neurodegenerative diseases such as Parkinson' s disease and Alzheimer' s disease; for digestive symptoms, weight loss, and fatigue, abdominal ultrasound or CT can be selected. If positive findings are detected, further examination or

referral to relevant departments is warranted.

[Expert Consensus 5] PHQ-2 and PHQ-9 scales are recommended for depression symptom screening. Detailed history taking, physical examination, and laboratory investigations must be conducted simultaneously to exclude diabetes-related organic diseases and avoid missed diagnosis. This consensus recommends a PHQ-9 total score $ $10 as the screening diagnostic threshold; for diabetic patients with PHQ-9 total score <10 but with depressive symptoms, regular follow-up and reassessment are recommended.

5. Diagnosis and Differential Diagnosis

5.1 Depression Diagnosis

For diabetic patients with initial PHQ-9 score $ $10, diagnosis of depression should be made by psychiatric or psychological professionals based on ICD-11 diagnostic criteria, referencing previous guidelines and literature [60].

5.1.1 Symptom Criteria At least five characteristic symptoms should be present simultaneously for most of the day, almost daily, for a minimum of two weeks, with at least one symptom from the emotional symptom cluster. Main manifestations include:

(1) **Emotional symptom cluster**: Depressed mood, either self-reported or observed by others; Markedly diminished interest or pleasure in activities, especially those previously considered interesting, including loss of libido.

(2) **Cognitive-behavioral symptom cluster**: Decreased ability to concentrate or marked indecisiveness; Low self-esteem or excessive/inappropriate guilt; Hopelessness about the future; Recurrent thoughts of death, recurrent suicidal ideation, or evidence of suicide attempts.

(3) **Autonomic nervous system symptom cluster**: Significant sleep disturbance (difficulty falling asleep, increased nighttime awakenings, or early morning awakening) or hypersomnia; Significant appetite or weight changes; Psychomotor agitation or retardation; Decreased energy or fatigue.

5.1.2 Course Criteria

(1) **Single episode**: Only one previous or current episode, lasting at least two weeks; (2) **Recurrent**: At least two episodes with several months of no obvious mood disturbance between them, with the current episode lasting at least two weeks. Neither situation includes manic, mixed, or hypomanic episodes.

5.1.3 Severity Grading of Depression Depression severity depends on the number of symptoms, their severity, and resulting social functional impairment. Based on current episode severity (mild, moderate, severe) and presence or absence of psychotic symptoms, depression can be further classified. If psychotic symptoms are present, the depression severity is at least moderate (Table 4).

5.2 Differential Diagnosis

5.2.1 Diabetes Distress When diabetic patients have low mood, diabetes distress needs to be differentiated. Diabetes distress (DD) is a diabetes-specific emotional adjustment disorder, referring to multidimensional emotional responses triggered by disease management complexity. It is characterized by persistent emotional distress ($ $3 months) related to diabetes, essentially forming an emotional-cognitive negative feedback loop during disease coping [61]. Among T2DM patients, the prevalence of diabetes-related distress is 18%-45%, with 38%-48% incidence over 18 months. The Diabetes Distress Scale (DDS) is recommended for quantitative assessment, which can effectively differentiate diabetes distress from depression [62-64]. The Chinese version of DDS [65] is suitable for self-assessment in adult diabetic patients and can identify main sources of distress through different dimensions (Table 5).

Diabetes distress is an emotional response triggered by specific negative or frustrating stressors (such as long-term disease management, complication risks), while depression is a comprehensive manifestation of symptoms usually lacking specific etiological direction. Diabetes distress more reflects patients' emotional coping with diabetes and its long-term management demands, whereas depression is an independent mental illness. Although there may be some overlap in emotional manifestations, such as fatigue and low mood, their psychological mechanisms and intervention strategies differ. Precise differentiation is crucial for developing personalized psychological interventions.

Once diabetes distress is diagnosed, patients should receive diabetes self-management education and support (DSMES) to address diabetes self-management ability problems causing distress and affecting clinical treatment outcomes. Cognitive behavioral therapy, problem-solving therapy, and mindfulness combined with self-compassion training can improve both diabetes distress and depressive emotions [66-68]. Diabetes distress is closely related to anxiety, depression, and reduced health-related quality of life. Therefore, if diabetes distress does not improve after receiving personalized diabetes education, patients should be referred for careful assessment and treatment by mental health professionals.

5.2.2 Diabetic Autonomic Neuropathy Diabetic autonomic neuropathy (DAN) often coexists or overlaps with depressive clinical symptoms, making differential diagnosis difficult. Typical DAN clinical manifestations mainly involve four target organ systems: (1) Cardiovascular system (orthostatic hypotension, resting tachycardia); (2) Gastrointestinal tract (gastroparesis, gastroesophageal

reflux, constipation, diarrhea); (3) Urogenital system (bladder dysfunction such as urinary retention, erectile dysfunction); (4) Sweat gland regulation (anhidrosis or hyperhidrosis). Notably, depression in diabetic patients often presents with atypical somatization symptoms, including diffuse pain, blood pressure fluctuations, functional gastrointestinal disorders, and peripheral sensory abnormalities. Given the high symptomatic overlap, clinical diagnosis should be based on patient symptoms, and when necessary, cardiovascular autonomic function reflex tests, gastrointestinal motility assessment, bladder residual urine and urodynamic examinations, and quantitative sudomotor axon reflex testing should be performed for differential diagnosis [53], combined with depression scales (PHQ-9, etc.) for systematic differentiation.

5.2.3 Differentiation from Other Mental Disorders

(1) **Anxiety disorders**: Diabetic patients often have comorbid anxiety or anxiety disorders along with depression. Depression is characterized by low mood as the core symptom, while anxiety is characterized by fear, worry, and apprehension. Differentiation through scale screening (such as Generalized Anxiety Disorder scale) is relatively easy. Unless anxiety symptoms meet independent diagnostic criteria, when depression diagnosis is met, depression should be prioritized according to hierarchical diagnostic principles; when unrelated, comorbid diagnosis can be made.

(2) **Bipolar affective disorder**: In addition to the core depressive symptoms, this disease also has emotional instability. If there is a history of $ $1 manic/hypomanic episodes in addition to depressive episodes, bipolar affective disorder should be diagnosed. For patients without manic/hypomanic episodes but with early onset age, family history of bipolar disorder, sudden and frequent depressive episodes, mood instability, irritability, agitation, or obvious mood elevation during adequate antidepressant treatment, careful attention and regular follow-up assessment for possible manic episodes are needed, with timely correction of diagnosis and referral [69].

(3) **Schizophrenia**: Negative symptoms of schizophrenia such as emotional blunting, slowed thinking, and reduced spontaneous movements and speech need to be differentiated. The former has a more chronic course, and besides emotional blunting, mainly includes psychotic symptoms with incoordination among cognition, emotion, and volitional activity, affecting social functioning; while the core symptom of depression is low mood without incoordination among cognition, emotion, and volitional activity.

(4) **Secondary depressive disorder**: Brain organic diseases, other physical diseases, certain medications, and psychoactive substances can all cause secondary depressive disorders, requiring comprehensive assessment of patients' physical conditions.

5.3 Referral Recommendations

In general hospitals and community primary care institutions, after screening and the above assessments, if patients meet any of the following conditions, doctors should promptly communicate with patients and their families, clearly inform them of the necessity for standardized treatment, and recommend referral to psychiatric hospitals or specialized clinics for further treatment [54]. Specific indications include: (1) Suicidal behavior or ideation; (2) Presence of psychotic symptoms; (3) Multiple comorbid physical diseases; (4) Recurrent or worsening symptoms; (5) Current treatment failure requiring further treatment; (6) Intolerable adverse drug reactions; (7) Poor treatment adherence; (8) Self-neglect. Patients with recent suicidal behavior, strong suicidal ideation, self-blame and guilt, consciousness disturbance after medication, or severe adverse reactions such as abnormal liver function should be urgently referred to psychiatric institutions for standardized treatment.

The screening and diagnostic pathway for depression in diabetic patients is shown in Figure 1 [Figure 1: see original paper].

[**Expert Consensus 6**] Diagnosis of diabetes comorbid with depression should be based on comprehensive clinical assessment, including detailed history taking (focusing on emotional, cognitive, and somatic symptoms), physical examination, and necessary laboratory and imaging investigations. Depressive symptoms should be identified, diagnosed, and severity-graded according to current diagnostic criteria (ICD-11), forming the basis for individualized management plans.

[**Expert Consensus 7**] For patients diagnosed with or suspected of having severe depressive episodes, psychotic symptoms, or suicidal ideation/behavior, immediate referral to psychiatric institutions is mandatory, while fully informing family members or primary caregivers of disease risks and monitoring responsibilities.

6. Treatment

Treatment of diabetes comorbid with depression should address both psychological and physical health. Depression intervention should be implemented on the basis of routine diabetes treatment. The primary goals are to prevent suicide and relieve depressive symptoms until remission; secondary goals include improving health-related quality of life, restoring social functioning, more positively accepting diabetes, improving diabetes self-management ability, and forming healthy lifestyles.

Currently, a stepped, stratified treatment strategy for depression based on severity is recommended, implementing a collaborative care model to standardize diagnosis and treatment. For mild depression, psychotherapy or traditional Chinese medicine can be used alone based on education and lifestyle intervention; for moderate to severe depression, combined psychotherapy and medication is

recommended. If mild depression patients show no response to psychotherapy alone after 6 weeks or incomplete symptom remission after 12 weeks, medication should be added.

6.1 Lifestyle Intervention

Lifestyle intervention mainly includes healthy diet, appropriate exercise, increased light exposure, improved sleep, smoking cessation, and alcohol limitation [1,54], with weight control for overweight or obese patients. However, lifestyle intervention is rarely used alone for treating diabetes comorbid with depression, and is mostly combined with psychotherapy.

6.1.1 Dietary Management In dietary management for diabetes comorbid with depression, the Mediterranean diet is recommended as the core intervention model [70]. It is plant-based (fresh vegetables, fruits, whole grains, legumes, seeds), rich in monounsaturated fatty acids (olive oil, nuts) and omega-3 fatty acids (deep-sea fish), and limits red meat, processed foods, and refined sugar. It improves glucose metabolism and mental health through multiple mechanisms including anti-inflammatory, antioxidant, and gut microbiota regulation. Studies confirm that following this diet for 3-6 months can reduce HbA1c by 0.4%-0.5% [71] and significantly relieve depressive symptoms [72]. Other healthy dietary patterns such as the Dietary Approaches to Stop Hypertension (DASH) diet (emphasizing low sodium, high potassium) or low glycemic index diet can also be used as supplementary options, adjusted according to individual needs. Specific nutrients (such as vitamins D, B-complex, zinc, chromium, magnesium, and selenium) should be ensured for adequate intake to support neurotransmitter synthesis and glucose metabolism homeostasis, with optional probiotic or fish oil supplementation to enhance efficacy [73]. Clinical practice should develop individualized plans based on metabolic characteristics, cultural preferences, and comorbidity severity, integrating multidisciplinary collaboration among nutrition, psychology, and endocrinology to achieve dual benefits for metabolic and mental health.

6.1.2 Exercise Therapy Exercise therapy is also a fundamental intervention for patients with diabetes comorbid with depression. Exercise can improve multiple metabolic abnormalities in T2DM patients including blood glucose, insulin resistance, blood lipids, blood pressure, weight, and body fat percentage [74]. For mild to moderate depression, exercise can effectively improve depressive symptoms and physical health. When combined with cognitive behavioral therapy (CBT), it can synergistically reduce depression scale scores (PHQ-9 or BDI) and HbA1c, demonstrating the necessity of multimodal intervention [75-77]. Depressed patients are recommended to engage in moderate-intensity aerobic exercise (such as brisk walking, swimming) 2-3 times/week for 45-60 minutes/session, or combined with resistance training (such as elastic bands, dumbbells, or fixed equipment) to simultaneously improve cardiopulmonary function and neuroplasticity [78]. Studies on resistance training alone for depression

treatment are limited. It should be emphasized that exercise programs should be implemented under the guidance of physiotherapists or professional coaches to ensure safety and improve adherence.

[**Expert Consensus 8**] For patients with diabetes comorbid with depression, the core lifestyle interventions recommended are the Mediterranean diet and regular moderate-intensity exercise, combined with psychotherapy to achieve synergistic benefits for metabolic and mental health.

6.2 Glycemic Control

6.2.1 Glycemic Control Targets HbA1c combined with self-monitoring of blood glucose (SMBG) and continuous glucose monitoring (CGM) can optimize glycemic management. The HbA1c target for non-pregnant adults is typically <7%, with SMBG fasting glucose target of 4.4-7.0 mmol/L, postprandial glucose target <10.0 mmol/L, and CGM time-in-range (TIR) >70% [1]. However, targets should be adjusted based on individual patient conditions. For diabetic patients with comorbid depression, hypoglycemia risk, treatment adherence, and psychological status need to be evaluated. If patients have severe depressive symptoms or impaired hypoglycemia awareness, targets can be appropriately relaxed to HbA1c <7.5%-8.0% to reduce psychological stress and hypoglycemia risk from strict glycemic control [1].

6.2.2 Selection of Antidiabetic Medications Currently, randomized controlled trial (RCT) evidence on the effects of antidiabetic drugs on depression is limited. In patients with diabetes comorbid with depression, antidiabetic drug selection should comprehensively consider metabolic control, potential for improving depressive symptoms, and drug safety. Recent studies suggest that some antidiabetic drugs may have additional effects on depressive symptoms through metabolic regulation or neuroprotection, and clinical decisions should be based on individualized treatment principles. Additionally, depressed patients may have difficulty adhering to complex treatment regimens. Therefore, selecting simple antidiabetic regimens with low hypoglycemia risk and no weight gain is crucial for improving glycemic control and depressive symptoms.

(1) **Metformin**: Multiple studies support the positive role of metformin in improving depressive symptoms in T2DM patients, and continuous metformin use and combination regimens including metformin are associated with reduced depression incidence [79-81]. Cohort studies show that metformin users have significantly lower new-onset depression risk compared with insulin or sulfonylurea (SU) patients (HR=0.85, 95%CI=0.76-0.95). Case-control studies further support this finding, showing long-term metformin use is associated with reduced depression risk (OR=0.82, 95%CI=0.71-0.94). The mechanism may be related to metformin' s anti-inflammatory, anti-apoptotic, and antioxidant properties, as well as its neuromodulatory effects on neurotrophic factors and axonal regeneration pathways related to depression. Recent animal

studies found metformin can restore brain monoamine neurotransmitter 5-HT synthesis and metabolism by regulating gut microbiota [82]. Given its good safety profile and potential cardiovascular protective effects, this consensus recommends metformin as first-line treatment for T2DM patients with comorbid depression.

(2) **Thiazolidinediones**: Recent studies suggest thiazolidinediones may improve depressive symptoms through anti-inflammatory mechanisms. Meta-analysis indicates pioglitazone can relieve depressive symptoms, possibly by reducing pro-inflammatory factors (IL-6, TNF-α) rather than through glucose or insulin resistance improvement [83]. Animal experiments show pioglitazone can inhibit microglial activation and reduce hippocampal inflammation, exerting neuroprotective effects. However, pioglitazone-induced weight gain (average 2-4 kg) may offset psychological benefits, and risks of edema and heart failure limit its widespread use in patients with comorbid depression [79]. It is recommended only for diabetic patients with comorbid depression who have significant insulin resistance and no cardiovascular risk factors.

(3) **Insulin and sulfonylureas**: Previous studies suggest insulin and sulfonylurea use is associated with increased depression risk, possibly related to hypoglycemia and increased treatment complexity worsening mood fluctuations [81][84]. Depressed patients are more likely to discontinue antidiabetic medications, especially among young patients (<45 years) and those using non-metformin antidiabetic drugs (including multiple drug therapies combined with insulin) [85]. The GRADE study randomized T2DM patients with inadequate glycemic control on metformin monotherapy to four groups: basal insulin (glargine), sulfonylurea (glimepiride), dipeptidyl peptidase-4 (DPP-4) inhibitor (sitagliptin), and glucagon-like peptide-1 (GLP-1) receptor agonist (liraglutide), comparing the efficacy and safety of these four different mechanisms. Recent sub-study results on emotional distress [80] showed that during one-year follow-up, all treatments reduced depression symptom scores and diabetes distress, with glargine showing better improvement in diabetes distress than glimepiride and sitagliptin. These results suggest there should be no "psychological insulin resistance," and insulin should be actively initiated when clinically indicated.

(4) **GLP-1 receptor agonists (GLP-1RAs)**: In recent years, the potential antidepressant effects of GLP-1RAs have attracted attention. Studies show GLP-1RAs exhibit antidepressant effects by regulating neurotransmitters, promoting hippocampal neurogenesis, reducing systemic inflammation, and improving synaptic function. A meta-analysis including five RCTs and one prospective cohort study showed that adult depression scale scores were significantly reduced in patients receiving GLP-1RA treatment (exenatide or liraglutide), supporting the beneficial effect of GLP-1RAs on depressive symptoms [86]. A simulated target trial based on U.S. Medicare data showed that for T2DM patients $ $66 years, GLP-1RAs reduced

depression risk compared with DPP-4 inhibitors, but showed no significant difference versus sodium-glucose cotransporter 2 (SGLT2) inhibitors. The study suggests GLP-1RAs may be preferred over DPP-4 inhibitors in elderly patients at risk for depression, but individual treatment goals including weight and cardiovascular protection should be considered comprehensively [87].

(5) **SGLT2 inhibitors**: In addition to glucose-lowering and improving cardiometabolic indicators (such as weight, blood pressure), SGLT2 inhibitors may relieve depressive symptoms by inhibiting brain monoamine oxidase activity and improving mitochondrial function. A nationwide population-based cohort study from Denmark analyzed the association between T2DM, specific antidiabetic drugs, and depression [81]. The study showed that T2DM patients had increased depression risk; compared with T2DM patients treated with lifestyle intervention alone, those using insulin, sulfonylureas, and high-dose metformin (>2 g/d) had increased depression risk, while those using low-dose metformin ($ $2 g/d), DPP-4 inhibitors, GLP-1RAs, and SGLT2 inhibitors had reduced depression risk, with SGLT2 inhibitor users having the lowest depression risk, even lower than non-diabetic individuals. A T2DM patient cohort propensity score-matched study [88] found that compared with DPP-4 inhibitor use, SGLT2 inhibitors significantly reduced new-onset depression risk (HR=0.52, 95%CI=0.35-0.77).

(6) **DPP-4 inhibitors**: Although DPP-4 inhibitors lack direct evidence for depression improvement and clinical research evidence, their low hypoglycemia risk, high convenience, and good adherence make them suitable for glycemic management in elderly diabetic patients with mild depression [79].

[**Expert Consensus 9**] Individualized glycemic treatment is emphasized for patients with diabetes comorbid with depression. Metformin is recommended as first-line antidiabetic medication, while drugs that significantly increase weight or hypoglycemia risk should be used with caution.

6.3 Psychotherapy

Psychotherapy can be categorized by treatment method and medium into individual therapy, group therapy, offline psychotherapy, and online psychotherapy based on internet, email, or telephone. Research suggests that almost all psychotherapy methods help improve emotional states in patients with diabetes comorbid with depression, but not all can reduce blood glucose levels [89]. Online psychotherapy is convenient and economical [90], effectively reducing depressive symptoms but showing no significant efficacy in glycemic control [91-92]. Psychotherapy methods include cognitive behavioral therapy (CBT), mindfulness, interpersonal therapy (IPT), psychoeducation, and motivational interviewing, among which suitable methods can be selected based on patient characteristics.

(1) **Cognitive Behavioral Therapy (CBT)**: This is the most extensively studied treatment method with robust clinical evidence, proven to effectively relieve depressive and anxiety symptoms and improve cognitive function [60]. Its core is correcting cognition and changing behavior. For patients with diabetes comorbid with depression who have incorrect understanding of their disease, economic pressure from long-term medical costs, and functional impairment leading to irrational beliefs and negative emotions, CBT can help them readjust cognitive patterns about reality, change negative thinking, reduce negative emotions and behaviors, and enhance confidence. Studies show that CBT can effectively reduce patients' depressive and anxiety emotions, lower fasting blood glucose, and improve treatment adherence and quality of life [93-95]. CBT combined with lifestyle intervention has sustained effects on improving depressive/anxiety emotions and HbA1c levels, and can improve patients' self-care behavior and medication adherence [75]. Internet-based CBT (i-CBT) via telephone and email is also an optional convenient treatment method that can relieve depressive and anxiety emotions, but has no obvious effect on blood glucose regulation, with its adherence and long-term efficacy requiring further research [90].

(2) **Mindfulness therapy**: Aims to focus attention on the present moment, experiencing psychological or physical symptoms in a purposeful, non-judgmental way, ultimately reducing distress. Mindfulness-based therapy can reduce depressive and anxiety emotions in diabetic patients [96]. However, CBT based on mindfulness shows no obvious advantage over CBT alone in treating depressive emotions and blood glucose in diabetic patients [97].

(3) **Interpersonal Therapy (IPT)**: Aims to relieve symptoms by improving interpersonal problems related to symptoms. The American Diabetes Association' s position statement on psychosocial care in diabetes suggests that for depression treatment in diabetic patients, referral to therapists with CBT, IPT, or other evidence-based treatment experience is recommended, in collaborative care with the patient' s diabetes treatment team [63]. Small-sample clinical studies show IPT has comparable effects to the antidepressant sertraline in improving emotions in patients with diabetes comorbid with depression, but has no obvious effect on blood glucose [98].

(4) **Psychoeducation**: Mainly includes depression symptom recognition, diabetes treatment, the relationship between diabetes and depression, and self-management content, which can reduce depressive and anxiety emotions, improve self-efficacy, and enhance self-care ability and quality of life in mild patients [99-100].

(5) **Other psychotherapies** such as motivational interviewing, positive psychotherapy, and behavioral activation techniques can improve emotional states in diabetic patients [101-103], but their clinical efficacy in patients with diabetes comorbid with depression has not been fully studied.

[Expert Consensus 10] Psychotherapy is the first choice for non-pharmacological treatment of diabetes comorbid with depression, with CBT having the most robust evidence. Mindfulness therapy, IPT, and psychoeducation also have certain therapeutic effects. Lifestyle intervention can be combined with psychotherapy, requiring individualized treatment selection.

6.4 Physical Therapy

Modified electroconvulsive therapy, transcranial direct current stimulation, and repetitive transcranial magnetic stimulation (rTMS) are common treatment methods for depressive disorders. rTMS is proven to have definite efficacy for depression and can improve cognitive function [60]. However, no studies have reported rTMS treatment for diabetes comorbid with depression, so it is not recommended.

6.5 Antidepressant Medication Treatment

6.5.1 Principles of Medication Use Antidepressants should be started at small doses and gradually increased, using the lowest effective dose to minimize adverse reactions. Medications generally take effect in about two weeks, with efficacy rates showing a linear relationship with time. If treatment remains ineffective after 6-8 weeks at adequate doses, medication change should be considered, either to another drug of the same class or to a different mechanism. If still ineffective, referral to psychiatry is recommended. When treatment continues for more than three months, medication duration and discontinuation timing should be determined based on disease condition.

6.5.2 Antidepressant Selection for Diabetes Comorbid with Depression This consensus follows a methodological framework for evidence grading and recommendation formation: referring to the WHO Guidelines Development Handbook and AGREE Collaboration principles, combined with Chinese clinical practice, using the 2009-updated AGREE II tool as the methodological quality evaluation standard. Specific evidence level and recommendation grading standards [49] are shown in Table 6 . This consensus reviewed literature from 1995-2024 in CNKI and PubMed on antidepressant use in diabetic patients, providing recommendations based on evidence levels.

Multiple antidepressant options are available for patients with diabetes comorbid with depression, with different classes described below:

(1) **Selective Serotonin Reuptake Inhibitors (SSRIs)**: Representative drugs include escitalopram, fluoxetine, sertraline, paroxetine, and fluvoxamine. They are generally well-tolerated and safe. Studies show SSRIs benefit glycemic control in patients with diabetes comorbid with depression, can reduce HbA1c [98,104-105], and may help reduce weight and improve insulin resistance through metabolic improvement [106-109]. Specific drug RCTs show: citalopram and fluoxetine improve depressive sever-

ity while reducing fasting blood glucose and HbA1c in T2DM patients [110]; sertraline reduces HbA1c levels [111]; short-term paroxetine reduces depression severity and helps better control HbA1c and improve quality of life [112]; evidence for fluvoxamine in diabetes comorbid with depression is insufficient, but case reports show increased fasting blood glucose after 5 days of treatment, returning to normal after discontinuation [113]. Notably, among SSRIs, escitalopram and sertraline have weak inhibitory effects on cytochrome P450 (CYP) isoenzymes 3A4 and 2D6 with low drug interaction risk; while fluoxetine, paroxetine, and fluvoxamine inhibit CYP isoenzyme complexes, thus requiring dose adjustment of antidiabetic drugs metabolized by CYP enzymes, especially insulin.

(2) **Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)**: Duloxetine and venlafaxine improve depressive severity in patients with diabetes comorbid with depression, with venlafaxine being more effective than citalopram in improving HbA1c [114]. Duloxetine is approved as first-line treatment for diabetic peripheral neuropathic pain, with some guidelines recommending venlafaxine as second-line [115-116]. Milnacipran also reduces HbA1c and fasting blood glucose after 6 months of treatment [117]. Although theoretically norepinephrine reuptake inhibitors may disrupt glucose homeostasis, current research generally supports their use in treating depression in diabetic patients [118].

(3) **Noradrenergic and Specific Serotonergic Antidepressants (NaSSA)**: Mirtazapine may cause weight gain [119], but studies show it doesn' t affect fasting insulin levels or HbA1c [120-122]. Some studies show reduced HbA1c after 6 months of mirtazapine treatment, but with small sample sizes [123]. To date, no studies have confirmed the long-term effects of mirtazapine on glucose metabolism.

(4) **Triazolopyridine antidepressants**: Trazodone reduces HbA1c in patients with diabetes comorbid with depression, with more obvious glucose-lowering effects than citalopram [114].

(5) **Norepinephrine-Dopamine Reuptake Inhibitors (NDRI)**: Bupropion reduces depressive severity and HbA1c after 34 weeks of treatment [124], but lacks large-sample RCT confirmation.

(6) **Melatonergic antidepressants**: Agomelatine can be used in patients with diabetes comorbid with depression to improve depressive severity. Studies show that in patients aged 27-49, HbA1c and BMI were not significantly different between agomelatine and paroxetine/fluoxetine groups, but in patients aged 50-70, agomelatine significantly reduced HbA1c and BMI [125].

(7) **Tricyclic Antidepressants (TCAs)**: These typically have obvious adverse reactions that are poorly tolerated by diabetic patients, such as increased appetite, weight gain, elevated blood glucose, worsening diabetes, and increased carbohydrate craving, thus are not recommended [106].

(8) **Monoamine Oxidase Inhibitors (MAOIs)**: These also have obvious adverse reactions, with risks of hypoglycemia episodes and weight gain, and are irreversible, thus are not recommended [126].

For the new specific serotonergic antidepressant vortioxetine, there is insufficient research in diabetes comorbid with depression, and it is not currently recommended.

Depressed patients have higher risk of developing T2DM, making it challenging to distinguish whether poor glycemic control results from metabolic effects of depression or effects of antidepressants on blood glucose [127-129]. Antidepressant dose and duration are additional considerations. Studies show that populations receiving medium-to-high dose antidepressant treatment have increased diabetes risk, and patients taking antidepressants for >2 years have significantly increased diabetes risk [127,129-130]. Therefore, antidepressant-induced diabetes risk may not be mechanism-specific but more related to individual susceptibility [131].

Antipsychotic medications can be effective augmentation strategies for treating severe depression. Large-scale meta-analysis evidence shows these drugs are associated with significantly increased T2DM risk, with substantial differences among medications. Olanzapine and clozapine have the highest risks, while cariprazine and haloperidol also show significantly elevated risks. These drugs not only cause weight gain but also worsen glycemic control in diabetic patients. In contrast, aripiprazole has the lowest diabetes risk [132-134].

[Expert Consensus 11] For diabetes comorbid with depression, SSRIs and SNRIs are recommended; duloxetine has both antidepressant and diabetic peripheral neuropathic pain relief effects. Caution is needed for CYP450 enzyme-mediated drug interactions when combined with antidiabetic drugs. If antipsychotic combination is needed, aripiprazole is preferred to minimize adverse effects on glucose metabolism and weight. TCAs and MAOIs should be avoided.

6.6 Traditional Chinese Medicine Treatment

Traditional Chinese medicine (TCM) is a commonly used treatment for diabetes comorbid with depression. Syndrome differentiation and treatment is the basic guiding principle. After clear diagnosis, interventions including Chinese herbs, patent medicines, acupuncture, and exercise therapy can be selected. This consensus refers to the Expert Consensus on Integrated Traditional Chinese and Western Medicine Diagnosis and Treatment of Depression [137], Guidelines for Integrated Prevention and Treatment of Adolescent Depressive Disorders with Traditional Chinese and Western Medicine [138], Guidelines for Integrated Disease-Syndrome Diagnosis and Treatment of Type 2 Diabetes [139], and Clinical Terminology of Traditional Chinese Medicine: Part 2 - Syndromes (Standard No.: GB/T 16751.2-2021) to develop TCM syndrome differentiation for diabetes comorbid with depression.

6.6.1 TCM Syndrome Differentiation

(1) **Liver Depression and Spleen Deficiency Syndrome**: Clinical manifestations: low mood, sentimentality, fatigue, rib-side pain, abdominal bloating, poor appetite, loose stools. Tongue and pulse: pale and swollen tongue, white or greasy coating, wiry and slow pulse.

(2) **Phlegm-Qi Stagnation Syndrome**: Clinical manifestations: low mood, foreign body sensation in throat that cannot be swallowed or coughed out, chest and rib-side fullness, obesity, oily complexion, heavy body, fatigue, sticky mouth, excessive phlegm. Tongue and pulse: pale red tongue, white greasy coating, wiry and slippery pulse.

(3) **Damp-Heat Accumulation Syndrome**: Clinical manifestations: restlessness, low mood, inability to sit still, irritability, dizziness, headache, fever not pronounced, thirst without desire to drink much, obesity, sticky and unsmooth stools, short and yellow urine. Tongue and pulse: red tongue, yellow greasy coating, slippery and rapid pulse.

(4) **Heart-Spleen Deficiency Syndrome**: Clinical manifestations: low mood, overthinking, palpitations, forgetfulness, poor sleep with many dreams, shortness of breath, timidity, sallow complexion, poor appetite, weight loss, abdominal bloating, loose stools. Tongue and pulse: pale tongue, white coating, thin and weak pulse.

(5) **Qi-Yin Deficiency Syndrome**: Clinical manifestations: low mood, fatigue, shortness of breath, reluctance to speak, dry mouth and throat, thirst with desire to drink, afternoon malar flush, scanty urine, dry stools. Tongue and pulse: thin tongue body, scanty and dry coating, weak and rapid pulse.

(6) **Liver-Kidney Yin Deficiency Syndrome**: Clinical manifestations: low mood, irritability, dizziness, tinnitus, dry mouth worse at night, five-center heat, low fever with malar flush, rib-side pain, lumbar and knee weakness, dry skin, night blindness, frequent and turbid urine like paste. Tongue and pulse: red tongue with scanty coating, thin and rapid pulse.

(7) **Yin-Yang Deficiency Syndrome**: Clinical manifestations: low mood, fatigue, cold limbs, lower limb edema or even generalized edema, frequent urination with increased nocturia, turbid urine like fat paste or even drinking one and urinating one, palpitations, sore waist, five-center heat, dry mouth and throat, withered ear helix, dark complexion, impotence. Tongue and pulse: pale tongue with scanty fluid, weak and rapid pulse.

6.6.2 Chinese Herbal Medicine Treatment Clinical medication selection follows syndrome differentiation principles: Liver Depression and Spleen Deficiency Syndrome can use Xiao Yao San; Phlegm-Qi Stagnation Syndrome can

use Ban Xia Hou Po Tang combined with Wu Ling San; Damp-Heat Accumulation Syndrome can use Huang Lian Wen Dan Tang combined with San Ren Tang; Heart-Spleen Deficiency Syndrome can use Gui Pi Tang; Qi-Yin Deficiency Syndrome can use Yi Guan Jian combined with Yu Ye Tang/Yu Quan Wan; Liver-Kidney Yin Deficiency Syndrome can use Zi Shui Qing Gan Yin or Qi Ju Di Huang Wan; Yin-Yang Deficiency Syndrome can use Jin Gui Shen Qi Wan.

Chinese herbal medicine combined with Western medicine based on syndrome differentiation has proven superior to Western medicine alone in improving HbA1c, TCM syndrome scores, SDS, and HAMD scores [140].

6.6.3 Patent Chinese Medicine Treatment Patent medicines also follow syndrome differentiation principles: Liver Depression and Spleen Deficiency Syndrome can use Shu Gan Jie Yu Capsule or Xiao Yao Wan; Heart-Spleen Deficiency Syndrome can use Gui Pi Wan; Qi-Yin Deficiency Syndrome can use Jia Wei Xiao Yao Wan combined with Tian Qi Jiang Tang Capsule/Yu Quan Wan; Liver-Kidney Yin Deficiency Syndrome can use Qi Ju Di Huang Oral Liquid; Yin-Yang Deficiency Syndrome can use Jin Gui Shen Qi Wan, etc.

6.6.4 TCM Non-pharmacological Therapies TCM non-pharmacological therapies including acupuncture, massage, cupping, and Baduanjin exercise are also widely used clinically for diabetes comorbid with depression. Acupuncture therapy has been proven to improve fasting blood glucose, 2-hour postprandial blood glucose, HbA1c, HAMD scores, and SDS scores, with efficacy superior to conventional drugs [141]. Back cupping combined with massage rubbing method shows equivalent effects to fluoxetine hydrochloride in improving HAMD and SDS scores [142]. Baduanjin exercise can relieve anxiety and depression in patients with diabetes comorbid with emotional disorders (including depression) and reduce HbA1c levels [143]. Small-sample studies also show that auricular acupuncture combined with Chinese herbs can improve HAMD scores and fasting and 2-hour postprandial blood glucose levels, with efficacy superior to fluoxetine [144]; traditional music therapy can improve HAMD and SDS scores, with efficacy superior to psychological intervention [145].

[Expert Consensus 12] Chinese herbs, acupuncture, and other TCM therapies are recommended as interventions for diabetes comorbid with depression. For mild to moderate patients, TCM therapy can be used alone; for severe patients, integrated Chinese and Western medicine can be adopted.

7. Patient-centered Collaborative Management

Diabetes comorbid with depression requires patient-centered, close collaboration among clinical departments, forming a stepped, multidisciplinary collaborative model based on risk assessment. Endocrinologists in primary care need to recognize diabetes distress, be alert to characteristic clues of depression, understand

diagnostic criteria for depression, skillfully use screening assessment tools, master good communication skills, apply diabetes self-management education and psychoeducation, and provide consultation and referral when necessary. Mental health professionals have professional advantages in managing depression, including disease recognition, doctor-patient relationship, guidance on psychological intervention and medication treatment. After risk assessment grading based on healthcare resource consumption, functional impairment degree, and doctor-patient relationship, appropriate stepped diagnosis and treatment should be implemented: patients with diabetes distress receive psychoeducation guidance based on different dimensional problems; mild depression patients are regularly followed up by endocrinologists; moderate depression patients are managed by endocrinologists with psychiatric consultation for psychological and/or pharmacological treatment, with functional improvement, symptoms, and treatment effects evaluated according to treatment plans; severe depression patients are transferred to psychiatry for further treatment while receiving regular diabetes management follow-up in endocrinology. Specific implementation of the multidisciplinary collaborative model still requires exploration.

[**Expert Consensus 13**] Diabetes comorbid with depression should implement patient-centered, stepped diagnosis and treatment based on risk assessment and symptom grading, leveraging multidisciplinary advantages to provide integrated psychosomatic services to maximize functional improvement and quality of life.

8. Follow-up Management

Diabetes comorbid with depression has high incidence and recurrence rates, is a chronic disease requiring long-term follow-up and management. Referencing previous guidelines, expert consensus, and literature, follow-up and management content should include the following aspects [54,63,146]:

8.1 Lifestyle Management

Lifestyle management for patients with diabetes comorbid with depression should include diabetes diet, medication, and self-monitoring of blood glucose management, as well as depression lifestyle management including health behavior promotion, exercise, good sleep hygiene, reduced coffee consumption, and reduced tobacco, alcohol, and other harmful substance exposure.

8.2 Treatment Adherence Management

Both diabetes and depression are chronic diseases requiring good treatment adherence. The initial two weeks of depression treatment are crucial; some patients need to adapt to early adverse reactions of antidepressants. Patients and families should be informed in advance that reactions are temporary and medication should be continued if tolerable to enhance patient confidence. Symptomatic drugs can be used short-term to relieve and prevent possible adverse reactions. If treatment reactions are severe, obvious, and intolerable, patients should be

informed to seek medical help promptly. For patients who have achieved treatment response, they should be informed that medication needs to be adequate and of sufficient duration, and they should not reduce or discontinue medication without authorization. Only standardized and reasonable treatment can effectively prevent relapse and recurrence.

8.3 Safety Risk Management

Patients with diabetes and comorbid depression often have other chronic disease comorbidities and take multiple medications simultaneously. In addition to paying attention to drug toxicology and metabolic characteristics in treatment selection, patients' weight, blood routine, liver and kidney function, electrolytes, thyroid function, electrocardiogram, and echocardiogram should be regularly monitored to observe for medication-related abnormalities, allowing timely treatment adjustments to avoid risks.

8.4 Caregiver Education Management

Family members and caregivers should be educated that depression is a disease that can be effectively treated with standardized treatment. When possible, regular health education for patients and caregivers should be conducted on how to observe disease conditions and assess suicide risk at home.

8.5 Patient Healthcare Accessibility Management

Specialized clinics for diabetes comorbid with depression and online consultation channels should be established to facilitate patient access to care.

[Expert Consensus 14] Diabetes comorbid with depression requires long-term comprehensive follow-up, standardized lifestyle and medication use, strengthened risk monitoring, coordinated caregiver involvement, and optimized healthcare services to improve prognosis.

Writing Group of the Chinese Expert Consensus on Diagnosis and Treatment of Diabetes Comorbid with Depression

Consensus Steering Committee: YUAN Yonggui (Department of Psychosomatic and Psychiatry, Zhongda Hospital, Southeast University), WANG Yuping (Department of Neurology, Xuanwu Hospital, Capital Medical University), JIANG Ronghuan (Department of Medical Psychology, First Medical Center, Chinese PLA General Hospital)

Writing Committee Members (in alphabetical order): AO Yutian (Department of Psychosomatic Medicine, Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University), BAO Bingnan (Department of Endocrinology and Metabolism, Beijing Anzhen Hospital, Capital Medical University), CHEN Huiling (Department of Geriatric Endocrinology, Xiangya Hospital,

Central South University), CHEN Luwen (Department of Geriatric Endocrinology and Metabolism, Guangxi Zhuang Autonomous Region People' s Hospital), CHEN Yanna (Department of Endocrinology, Huai' an First People' s Hospital), CUI Limei (Department of Endocrinology, Beijing Chuiyangliu Hospital), GUO Rongjuan (Department of Encephalopathy, Dongfang Hospital, Beijing University of Chinese Medicine), HAN Yajuan (Department of Endocrinology, Guangzhou Eighth People' s Hospital, Guangzhou Medical University), HE Qing (Department of Endocrinology, Tianjin Medical University General Hospital), HONG Xia (Department of Psychological Medicine, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences), JIANG Molin (Department of Psychosomatic Medicine, Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University), LI Songbo (Beijing Sport University), LI Wei (Department of Endocrinology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences), LI Yang (Department of Psychosomatic Medicine, Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University), LI Yuxiu (Department of Endocrinology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences), LIAO Qiuhong (Department of Endocrinology, Beijing Shunyi District Hospital), LIN Shanshan (Department of Endocrinology, Beijing Shijingshan Hospital), LU Wei (Department of Psychosomatic Medicine, Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University), LU Zheng (Department of Psychiatry, Tongji Hospital, Tongji University), MA Mingfu (Department of Endocrinology, Qinghai Fifth People' s Hospital), MA Xiaojing (Department of Endocrinology and Metabolism, Shanghai Sixth People' s Hospital), PAN Qi (Department of Endocrinology, Beijing Hospital, National Center for Gerontology, Institute of Geriatrics, Chinese Academy of Medical Sciences), PEI Yu (Department of Endocrinology, First Medical Center, Chinese PLA General Hospital), QI Lin (Department of Endocrinology, Beijing Yanhua Hospital), QIAO Hong (Department of Endocrinology, Second Affiliated Hospital of Harbin Medical University), SHI Dai (Department of Endocrinology, Second Affiliated Hospital of Guizhou University of Traditional Chinese Medicine), SONG Lulu (Department of Endocrinology, China-Japan Friendship Hospital), SUN Xiuqin (Department of Endocrinology, Peking University Shougang Hospital), TAO Hong (Department of Endocrinology and Metabolism, Beijing Anzhen Hospital, Capital Medical University), WANG Zhihong (Department of Endocrinology, First Affiliated Hospital of Chongqing Medical University), XIANG Qian (Department of Endocrinology and Metabolism, Fifth Affiliated Hospital of Kunming Medical University), XU Wen (Department of Endocrinology and Metabolism, Third Affiliated Hospital of Sun Yat-sen University), YAN Caifeng (Department of Endocrinology, Northern Jiangsu People' s Hospital), YANG Xiaohui (Beijing Anzhen Hospital, Capital Medical University; Beijing Office for Cardiovascular Disease Prevention), YANG Ying (Department of Endocrinology, Xiangyang Central Hospital, Hubei Province), ZHANG Hua (Department of General Neurology, Beijing Anzhen Hospital, Capital Medical University), ZHANG Songjun (Department of Endocrinology, Second Hospital of Hebei Medical University), ZHEN Donghu (Department of Endocrinology, First

Hospital of Lanzhou University), ZHOU Yaru (Department of Endocrinology, Third Hospital of Hebei Medical University), ZHOU Yingsheng (Department of Endocrinology and Metabolism, Beijing Anzhen Hospital, Capital Medical University)

Lead Writers: TAO Hong, LU Wei, ZHANG Hua, LIN Shanshan, LIAO Qiuhong, LI Yang, AO Yutian, JIANG Molin

Declaration of Conflicts of Interest: All authors declare no conflicts of interest.

[References]

[1] Chinese Diabetes Society, ZHU Dalong, GUO Lixin. Chinese Guidelines for the Prevention and Treatment of Diabetes (2024 Edition) [J]. Chinese Journal of Diabetes Mellitus, 2025, 17(1): 16-
[2] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders [M]. 5th ed. Arlington VA: American Psychiatric Association, 2013.
[3] HERRMAN H, PATEL V, KIELING C, et al. Time for united action on depression: a lancet-world psychiatric association commission [J]. Lancet, 2022, 399(10328): 957-1022. DOI: 10.1016/S0140-6736(21)02141-3.
[4] HUANG Y Q, WANG Y, WANG H, et al. Prevalence of mental disorders in China: a cross-sectional epidemiological study [J]. Lancet Psychiatry, 2019, 6(3): 211-224. DOI: 10.1016/S2215-0366(18)30511-X.
[5] GAVARD J A, LUSTMAN P J, CLOUSE R E. Prevalence of depression in adults with diabetes. An epidemiological evaluation [J]. Diabetes Care, 1993, 16(8): 1167-1178. DOI: 10.2337/diacare.16.8.1167.
[6] ROY T, LLOYD C E. Epidemiology of depression and diabetes: a systematic review [J]. J Affect Disord, 2012, 142 Suppl: S8-21. DOI: 10.1016/S0165-0327(12)70004-6.
[7] MAINA J G, BALKHIYAROVA Z, NOUWEN A, et al. Bidirectional mendelian randomization and multiphenotype GWAS show causality and shared pathophysiology between depression and type 2 diabetes [J]. Diabetes Care, 2023, 46(9): 1707-1714. DOI: 10.2337/dc22-2373.
[8] CHIEH A, CHU J, WALLACE L A, et al. Depression prevalence, screening, and treatment in adult outpatients with type 1 and type 2 diabetes: a nationally representative cross-sectional study (National Ambulatory Medical Care Survey 2014-2019) [J]. J Affect Disord, 2025, 368: 471-476. DOI: 10.1016/j.jad.2024.09.088.
[9] ZHAO F, PAN A, YANG X, et al. Bidirectional association between depressive symptoms and type 2 diabetes mellitus: The China Health and Retirement Longitudinal Study [J]. J Diabetes Complications, 2019, 33(10): 107387. DOI: 10.1016/j.jdiacomp.2019.05.018.
[10] MENG R W, LIU N, YU C Q, et al. Association between major depressive episode and risk of type 2 diabetes: a large prospective cohort study in Chinese adults [J]. J Affect Disord, 2018, 234: 59-66. DOI: 10.1016/j.jad.2018.02.052.
[11] NOUWEN A, ADRIAANSE M C, VAN DAM K, et al. Longitudinal

associations between depression and diabetes complications: a systematic review and meta-analysis [J]. Diabet Med, 2019, 36(12): 1562-1572. DOI: 10.1111/dme.14054.
[12] NOVAK M, MUCSI I, RHEE C M, et al. Increased risk of incident chronic kidney disease, cardiovascular disease, and mortality in patients with diabetes with comorbid depression [J]. Diabetes Care, 2016, 39(11): 1940-1947. DOI: 10.2337/dc16-0048.
[13] MUNOZ F A, CHIN C, KOPS S A, et al. Increased length of stay and hospital charges in adolescents with type 1 diabetes and psychiatric illness [J]. J Pediatr Endocrinol Metab, 2020, 34(2): 183-186. DOI: 10.1515/jpem-2020-0373.
[14] ZOU Y W, YOU W J, WANG J, et al. Depression and retinopathy in patients with type 2 diabetes mellitus: a meta-analysis [J]. Psychosom Med, 2021, 83(3): 239-246. DOI: 10.1097/PSY.0000000000000924.
[15] PRIGGE R, WILD S H, JACKSON C A. Depression, diabetes, comorbid depression and diabetes and risk of all-cause and cause-specific mortality: a prospective cohort study [J]. Diabetologia, 2022, 65(9): 1450-1460. DOI: 10.1007/s00125-022-05723-9.
[16] PARK M, KATON W J, WOLF F M. Depression and risk of mortality in individuals with diabetes: a meta-analysis and systematic review [J]. Gen Hosp Psychiatry, 2013, 35(3): 217-225. DOI: 10.1016/j.genhosppsych.2013.01.006.
[17] TU Q, HYUN K, LIN S L, et al. Individual and joint effects of diabetes and depression on incident cardiovascular diseases and all-cause mortality: Results from a population-based cohort study [J]. J Diabetes Complications, 2024, 38(11): 108878. DOI: 10.1016/j.jdiacomp.2024.108878.
[18] SODHI B, MALIK M, AGARWAL P, et al. The prevalence and predictors of depression and disability in older adults and elderly patients with Diabetes in India: Cross-sectional analysis from the Longitudinal Study on Ageing [J]. Diabetes Metab Syndr, 2023, 17(4): 102765. DOI: 10.1016/j.dsx.2023.102765.
[19] LIMONGI F, NOALE M, CREPALDI G, et al. Prevalence of diabetes and depressive symptomatology and their effect on mortality risk in elderly Italians: The Italian Longitudinal Study on Aging [J]. Diabetes Metab, 2014, 40(5): 373-378. DOI: 10.1016/j.diabet.2014.05.001.
[20] HSIEH H M, LIN C H, WENG S F, et al. Health-related quality of life, medical resource use and physical function in patients with diabetes mellitus and depression: a cross-sectional analysis from the National Health and Nutrition Examination Survey [J]. J Affect Disord, 2023, 327: 93-100. DOI: 10.1016/j.jad.2023.02.011.
[21] HUANG C J, LIN C H, HSIEH H M, et al. A longitudinal study of healthcare utilisation and expenditure in people with type 2 diabetes mellitus with and without major depressive disorder [J]. Gen Hosp Psychiatry, 2019, 57: 50-58. DOI: 10.1016/j.genhosppsych.2018.09.007.
[22] CIECHANOWSKI P S, KATON W J, RUSSO J E. Depression and diabetes: impact of depressive symptoms on adherence, function, and costs [J]. Arch Intern Med, 2000, 160(21): 3278-3285. DOI: 10.1001/archinte.160.21.3278.
[23] LIN E H B, KATON W, VON KORFF M, et al. Relationship of depression

and diabetes self-care, medication adherence, and preventive care [J]. Diabetes Care, 2004, 27(9): 2154-2160. DOI: 10.2337/diacare.27.9.2154.
[24] FRANK P, BATTY G D, PENTTI J, et al. Association between depression and physical conditions requiring hospitalization [J]. JAMA Psychiatry, 2023, 80(7): 690-699. DOI: 10.1001/jamapsychiatry.2023.0777.
[25] TARDIF I, GUÉNETTE L, ZONGO A, et al. Depression and the risk of hospitalization in type 2 diabetes patients: a nested case-control study accounting for non-persistence to antidiabetic treatment [J]. Diabetes Metab, 2022, 48(4): 101334. DOI: 10.1016/j.diabet.2022.101334.
[26] MYERS A K, GRANNEMANN B D, LINGVAY I, et al. Brief report: depression and history of suicide attempts in adults with new-onset Type 2 Diabetes [J]. Psychoneuroendocrinology, 2013, 38(11): 2810-2814. DOI: 10.1016/j.psyneuen.2013.06.013.
[27] HUANG Yanjing, DONG Hui, TANG Yueheng, et al. Research progress on biological mechanisms of diabetes comorbid with depression [J]. Chinese Journal of Diabetes, 2020, 28(11): 870-873.
[28] JOSEPH J J, GOLDEN S H. Cortisol dysregulation: the bidirectional link between stress, depression, and type 2 diabetes mellitus [J]. Ann N Y Acad Sci, 2017, 1391(1): 20-34. DOI: 10.1111/nyas.13217.
[29] LI S X, YANG D, ZHOU X H, et al. Neurological and metabolic pathophysiologies and treatment of comorbid diabetes with depression [J]. CNS Neurosci Ther, 2024, 30(4): e14497. DOI: 10.1111/cns.14497.
[30] CUI L L, LI S, WANG S M, et al. Major depressive disorder: hypothesis, mechanism, prevention and treatment [J]. Signal Transduct Target Ther, 2024, 9: 30. DOI: 10.1038/s41392-024-01738-y.
[31] WILSON J B, EPSTEIN M, LOPEZ B, et al. The role of neurochemicals, stress hormones and immune system in the positive feedback loops between diabetes, obesity and depression [J]. Front Endocrinol (Lausanne), 2023, 14: 1224612. DOI: 10.3389/fendo.2023.1224612.
[32] MOSILI P, MKHIZE B C, SIBIYA N H, et al. Review of the direct and indirect effects of hyperglycemia on the HPA axis in T2DM and the co-occurrence of depression [J]. BMJ Open Diabetes Res Care, 2024, 12(1): e003218. DOI: 10.1136/bmjdrc-2022-003218.
[33] ZHU Le, LIAO Shuying, ZENG Yan, et al. Role of serotonin system in stress-induced hippocampal neurogenesis injury [J]. Chinese Journal of Pathophysiology, 2024, 40(5):
[34] MONCRIEFF J, COOPER R E, STOCKMANN T, et al. The serotonin theory of depression: a systematic umbrella review of the evidence [J]. Mol Psychiatry, 2023, 28(8): 3243-3256. DOI: 10.1038/s41380-022-01661-0.
[35] CORREIA A S, CARDOSO A, VALE N. Oxidative stress in depression: the link with the stress response, neuroinflammation, serotonin, neurogenesis and synaptic plasticity [J]. Antioxidants (Basel), 2023, 12(2): 470. DOI: 10.3390/antiox12020470.
[36] DERKACH K V, BONDAREVA V M, CHISTYAKOVA O V, et al. The effect of long-term intranasal serotonin treatment on metabolic parameters and hormonal signaling in rats with high-fat diet/low-dose streptozotocin-

induced type 2 diabetes [J]. Int J Endocrinol, 2015, 2015: 245459. DOI: 10.1155/2015/245459.
[37] DANTZER R, O' CONNOR J C, FREUND G G, et al. From inflammation to sickness and depression: when the immune system subjugates the brain [J]. Nat Rev Neurosci, 2008, 9(1): 46-56. DOI: 10.1038/nrn2297.
[38] MILLER A H, RAISON C L. The role of inflammation in depression: from evolutionary imperative to modern treatment target [J]. Nat Rev Immunol, 2016, 16(1): 22-34. DOI: 10.1038/nri.2015.5.
[39] BIESSELS G J, REAGAN L P. Hippocampal insulin resistance and cognitive dysfunction [J]. Nat Rev Neurosci, 2015, 16(11): 660-671. DOI: 10.1038/nrn4019.
[40] KULLMANN S, HENI M, FRITSCHE A, et al. Insulin action in the human brain: evidence from neuroimaging studies [J]. J Neuroendocrinol, 2015, 27(6): 419-423. DOI: 10.1111/jne.12254.
[41] HOTAMISLIGIL G S, ERBAY E. Nutrient sensing and inflammation in metabolic diseases [J]. Nat Rev Immunol, 2008, 8(12): 923-934. DOI: 10.1038/nri2449.
[42] PERRY R J, PENG L, BARRY N A, et al. Acetate mediates a microbiome-brain-β-cell axis to promote metabolic syndrome [J]. Nature, 2016, 534(7606): 213-217. DOI: 10.1038/nature18309.
[43] OWENS M J, NEMEROFF C B. Role of serotonin in the pathophysiology of depression: focus on the serotonin transporter [J]. Clin Chem, 1994, 40(2): 288-295.
[44] MÁZALA-DE-OLIVEIRA T, SILVA B T, CAMPELLO-COSTA P, et al. The role of the adrenal-gut-brain axis on comorbid depressive disorder development in diabetes [J]. Biomolecules, 2023, 13(10): 1504. DOI: 10.3390/biom13101504.
[45] GAO X H, CAO Q H, CHENG Y, et al. Chronic stress promotes colitis by disturbing the gut microbiota and triggering immune system response [J]. Proc Natl Acad Sci USA, 2018, 115(13): E2960-E2969. DOI: 10.1073/pnas.1720696115.
[46] DE PALMA G, COLLINS S M, BERCIK P, et al. The microbiota-gut-brain axis in gastrointestinal disorders: stressed bugs, stressed brain or both [J]. J Physiol, 2014, 592(14): 2989-2997. DOI: 10.1113/jphysiol.2014.273995.
[47] LI Zhoule, ZHAO Lianping, HUANG Gang, et al. Brain function study of T2DM comorbid with depression based on resting-state centrality [J]. Chinese Journal of Magnetic Resonance Imaging, 2022, 13(2): 37-41.
[48] KOTOV R, GAMEZ W, SCHMIDT F, et al. Linking "big" personality traits to anxiety, depressive, and substance use disorders: a meta-analysis [J]. Psychol Bull, 2010, 136(5): 768-821. DOI: 10.1037/a0020327.
[49] DIABETES CANADA CLINICAL PRACTICE GUIDELINES EXPERT WORKING GROUP, ROBINSON D J, HANSON K, et al. Diabetes and mental health [J]. Can J Diabetes, 2023, 47(4): 308-344. DOI: 10.1016/j.jcjd.2023.04.009.
[50] POSTOLACHE T T, DEL BOSQUE-PLATA L, JABBOUR S, et al. Co-shared genetics and possible risk gene pathway partially explain the

comorbidity of schizophrenia, major depressive disorder, type 2 diabetes, and metabolic syndrome [J]. Am J Med Genet B Neuropsychiatr Genet, 2019, 180(3): 186-203. DOI: 10.1002/ajmg.b.32712.
[51] KLENGEL T, BINDER E B. Epigenetics of stress-related psychiatric disorders and gene × environment interactions [J]. Neuron, 2015, 86(6): 1343-1357. DOI: 10.1016/j.neuron.2015.05.036.
[52] LI Lingjiang, MA Xin. Chinese Guidelines for the Prevention and Treatment of Depressive Disorders [M]. 2nd ed. Beijing: Chinese Medical Multimedia Press, 2015: 45-98.
[53] Neuropathy Group of Chinese Diabetes Society, Primary Diabetes Prevention and Management Office of National Basic Public Health Service Project, SHI Lixin, et al. National Primary Diabetes Neuropathy Diagnosis and Treatment Guidelines (2024 Edition) [J]. Chinese Journal of Diabetes Mellitus, 2024, 16(5): 496-511. DOI: 10.3760/cma.j.cn115791-
[54] Chinese Medical Association, Chinese Medical Association Magazine Publishing House, General Practice Branch of Chinese Medical Association, et al. Guidelines for Primary Care of Depression (2021) [J]. Chinese Journal of General Practitioners, 2021, 20(12): 1249-1260. DOI: 10.3760/cma.j.cn114798-
[55] MANEA L, GILBODY S, MCMILLAN D. Optimal cut-off score for diagnosing depression with the patient health questionnaire (PHQ-9): a meta-analysis [J]. CMAJ, 2012, 184(3): E191-E196. DOI: 10.1503/cmaj.110829.
[56] GOLDEN S H, SHAH N, NAQIBUDDIN M, et al. The prevalence and specificity of depression diagnosis in a clinic-based population of adults with type 2 diabetes mellitus [J]. Psychosomatics, 2017, 58(1): 28-37. DOI: 10.1016/j.psym.2016.08.003.
[57] KROENKE K, SPITZER R L, WILLIAMS J B. The PHQ-9: validity of a brief depression severity measure [J]. J Gen Intern Med, 2001, 16(9): 606-613. DOI: 10.1046/j.1525-1497.2001.016009606.x.
[58] ZHANG Ling, WANG Gang. Diagnosis, assessment and treatment of diabetes comorbid with depression [J]. Chinese Journal of Diabetes Mellitus, 2016, 8(4): 195-198. DOI: 10.3760/cma.j.issn.1674-5809.2016.04.002.
[59] REDDY P, PHILPOT B, FORD D, et al. Identification of depression in diabetes: the efficacy of PHQ-9 and HADS-D [J]. Br J Gen Pract, 2010, 60(575): e239-45. DOI: 10.3399/bjgp10X502128.
[60] Behavioral Medicine Branch of Chinese Medical Association, Cognitive Behavioral Therapy Group of Behavioral Medicine Branch of Chinese Medical Association, WANG Changhong, et al. Expert recommendations on depression treatment and management (2022) [J]. Chinese Journal of Behavioral Medicine and Brain Science, 2023, 32(3): 193-202. DOI: 10.3760/cma.j.cn371468-20220921-00563.
[61] NICOLUCCI A, BURNS K K, HOLT R G, et al. Diabetes attitudes, wishes and needs second study (DAWN2™): cross-national benchmarking of diabetes-related psychosocial outcomes for people with diabetes [J]. Diabet Med, 2013, 30(7): 767-777. DOI: 10.1111/dme.12245.
[62] FISHER L, HESSLER D M, POLONSKY W H, et al. When is diabetes distress clinically meaningful: establishing cut points for the Diabetes Distress

Scale [J]. Diabetes Care, 2012, 35(2): 259-264. DOI: 10.2337/dc11-1572.
[63] YOUNG-HYMAN D, DE GROOT M, HILL-BRIGGS F, et al. Psychosocial care for people with diabetes: a position statement of the American diabetes association [J]. Diabetes Care, 2016, 39(12): 2126-2140. DOI: 10.2337/dc16-2053.
[64] POLONSKY W H, FISHER L, EARLES J, et al. Assessing psychosocial distress in diabetes: development of the diabetes distress scale [J]. Diabetes Care, 2005, 28(3): 626-631. DOI: 10.2337/diacare.28.3.626.
[65] YANG Qing, LIU Xueqin. Reliability and validity evaluation of the Chinese version of Diabetes Distress Scale [J]. Journal of Nursing Science, 2010, 17(17): 8-10. DOI: 10.16460/j.issn1008-9969.2010.17.023.
[66] YANG Yanxiaoxiao, SUN Zilin, YUAN Yonggui. Progress in psychological intervention techniques in diabetes education [J]. Chinese Journal of Diabetes Mellitus, 2014, 6(6): 417-420. DOI: 10.3760/cma.j.issn.1674-5809.2014.06.014.
[67] FRIIS A M, JOHNSON M H, CUTFIELD R G, et al. Kindness matters: a randomized controlled trial of a mindful self-compassion intervention improves depression, distress, and HbA1c among patients with diabetes [J]. Diabetes Care, 2016, 39(11): 1963-1971. DOI: 10.2337/dc16-0416.
[68] WEISSBERG-BENCHELL J, SHAPIRO J B, BRYANT F B, et al. Supporting teen problem-solving (STEPS) 3 year outcomes: preventing diabetes-specific emotional distress and depressive symptoms in adolescents with type 1 diabetes [J]. J Consult Clin Psychol, 2020, 88(11): 1019-1031. DOI: 10.1037/ccp0000608.
[69] LU Lin. Shen Yucun' s Psychiatry [M]. 6th ed. Beijing: People' s Medical Publishing House,
[70] BASIRI R, SEIDU B, RUDICH M. Exploring the interrelationships between diabetes, nutrition, anxiety, and depression: implications for treatment and prevention strategies [J]. Nutrients, 2023, 15(19): 4226. DOI: 10.3390/nu15194226.
[71] MARTÍN-PELÁEZ S, FITO M, CASTANER O. Mediterranean diet effects on type 2 diabetes prevention, disease progression, and related mechanisms. a review [J]. Nutrients, 2020, 12(8): 2236. DOI: 10.3390/nu12082236.
[72] PARLETTA N, ZARNOWIECKI D, CHO J, et al. A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: a randomized controlled trial (HELFIMED) [J]. Nutr Neurosci, 2019, 22(7): 474-487. DOI: 10.1080/1028415X.2017.1411320.
[73] BASIRI R, SEIDU B, CHESKIN L J. Key nutrients for optimal blood glucose control and mental health in individuals with diabetes: a review of the evidence [J]. Nutrients, 2023, 15(18): 3929. DOI: 10.3390/nu15183929.
[74] National Center for Gerontology, Chinese Diabetes Society, Chinese Sports Science Society. Chinese Guidelines for Exercise Therapy in Type 2 Diabetes (2024 Edition) [J]. Chinese Journal of Sports Medicine, 2024, 43(6): 419-452. DOI: 10.3969/j.issn.1000-6710.2024.06.001.
[75] CUMMINGS D M, LUTES L D, LITTLEWOOD K, et al. Randomized trial of a tailored cognitive behavioral intervention in type 2 diabetes with comorbid depressive and/or regimen-related distress symptoms: 12-month

outcomes from COMRADE [J]. Diabetes Care, 2019, 42(5): 841-848. DOI: 10.2337/dc18-1011.
[76] VAN DER FELTZ-CORNELIS C, ALLEN S F, HOLT R I G, et al. Treatment for comorbid depressive disorder or subthreshold depression in diabetes mellitus: Systematic review and meta-analysis [J]. Brain Behav, 2021, 11(2): e01981. DOI: 10.1002/brb3.1981.
[77] DE GROOT M, SHUBROOK J H, JR W G H, et al. Program ACTIVE II: outcomes from a randomized, multistate community-based depression treatment for rural and urban adults with type 2 diabetes [J]. Diabetes Care, 2019, 42(7): 1185-1193. DOI: 10.2337/dc18-2400.
[78] STUBBS B, VANCAMPFORT D, HALLGREN M, et al. EPA guidance on physical activity as a treatment for severe mental illness: a meta-review of the evidence and Position Statement from the European Psychiatric Association (EPA), supported by the International Organization of Physical Therapists in Mental Health (IOPTMH) [J]. Eur Psychiatry, 2018, 54: 124-144. DOI: 10.1016/j.eurpsy.2018.07.004.
[79] KESSING L V, RYTGAARD H C, EKSTRØM C T, et al. Antidiabetes agents and incident depression: a nationwide population-based study [J]. Diabetes Care, 2020, 43(12): 3050-3060. DOI: 10.2337/dc20-1561.
[80] GONZALEZ J S, BEBU I, KRAUSE-STEINRAUF H, et al. Differential effects of type 2 diabetes treatment regimens on diabetes distress and depressive symptoms in the glycemia reduction approaches in diabetes: a comparative effectiveness study (GRADE) [J]. Diabetes Care, 2024, 47(4): 610-619. DOI: 10.2337/dc23-2459.
[81] WIUM-ANDERSEN I K, OSLER M, JØRGENSEN M B, et al. Diabetes, antidiabetic medications and risk of depression–A population-based cohort and nested case-control study [J]. Psychoneuroendocrinology, 2022, 140: 105715. DOI: 10.1016/j.psyneuen.2022.105715.
[82] XIE X X, LI W W, XIONG Z, et al. Metformin reprograms tryptophan metabolism via gut microbiome-derived bile acid metabolites to ameliorate depression-Like behaviors in mice [J]. Brain Behav Immun, 2025, 123: 442-455. DOI: 10.1016/j.bbi.2024.09.014.
[83] MOULTON C D, HOPKINS C W P, ISMAIL K, et al. Repositioning of diabetes treatments for depressive symptoms: a systematic review and meta-analysis of clinical trials [J]. Psychoneuroendocrinology, 2018, 94: 91-103. DOI: 10.1016/j.psyneuen.2018.05.010.
[84] BAI X S, LIU Z M, LI Z S, et al. The association between insulin therapy and depression in patients with type 2 diabetes mellitus: a meta-analysis [J]. BMJ Open, 2018, 8(11): e020062. DOI: 10.1136/bmjopen-2017-020062.
[85] LUNGHI C, MOISAN J, GRÉGOIRE J P, et al. The association between depression and medication nonpersistence in new users of antidiabetic drugs [J]. Value Health, 2017, 20(6): 728-735. DOI: 10.1016/j.jval.2016.09.2399.
[86] CHEN X D, ZHAO P Y, WANG W H, et al. The antidepressant effects of GLP-1 receptor agonists: a systematic review and meta-analysis [J]. Am J Geriatr Psychiatry, 2024, 32(1): 117-127. DOI: 10.1016/j.jagp.2023.08.010.
[87] TANG H L, LU Y, DONAHOO W T, et al. Glucagon-like peptide-1

receptor agonists and risk for depression in older adults with type 2 diabetes: a target trial emulation study [J]. Ann Intern Med, 2025, 178(3): 315-326. DOI: 10.7326/ANNALS-24-01347.
[88] MUI J V, LI L F, CHOU O H I, et al. Comparing sodium-glucose cotransporter 2 inhibitors and dipeptidyl peptidase-4 inhibitors on new-onset depression: a propensity score-matched study in Hong Kong [J]. Acta Diabetol, 2023, 60(7): 917-927. DOI: 10.1007/s00592-023-02063-6.
[89] XIE J, DENG W Q. Psychosocial intervention for patients with type 2 diabetes mellitus and comorbid depression: a meta-analysis of randomized controlled trials [J]. Neuropsychiatr Dis Treat, 2017, 13: 2681-2690. DOI: 10.2147/NDT.S116465.
[90] NEWBY J, ROBINS L, WILHELM K, et al. Web-based cognitive behavior therapy for depression in people with diabetes mellitus: a randomized controlled trial [J]. J Med Internet Res, 2017, 19(5): e157. DOI: 10.2196/jmir.7274.
[91] VARELA-MORENO E, CARREIRA SOLER M, GUZMÁN-PARRA J, et al. Effectiveness of eHealth-based psychological interventions for depression treatment in patients with type 1 or type 2 diabetes mellitus: a systematic review [J]. Front Psychol, 2022, 12: 746217. DOI: 10.3389/fpsyg.2021.746217.
[92] FRANCO P, GALLARDO A M, URTUBEY X. Web-based interventions for depression in individuals with diabetes: review and discussion [J]. JMIR Diabetes, 2018, 3(3): e13. DOI: 10.2196/diabetes.9694.
[93] LI C, XU D, HU M Y, et al. A systematic review and meta-analysis of randomized controlled trials of cognitive behavior therapy for patients with diabetes and depression [J]. J Psychosom Res, 2017, 95: 44-54. DOI: 10.1016/j.jpsychores.2017.02.006.
[94] PETRAK F, HERPERTZ S, ALBUS C, et al. Cognitive behavioral therapy versus sertraline in patients with depression and poorly controlled diabetes: the diabetes and depression (DAD) study: a randomized controlled multicenter trial [J]. Diabetes Care, 2015, 38(5): 767-775. DOI: 10.2337/dc14-1599.
[95] SAFREN S A, GONZALEZ J S, WEXLER D J, et al. A randomized controlled trial of cognitive behavioral therapy for adherence and depression (CBT-AD) in patients with uncontrolled type 2 diabetes [J]. Diabetes Care, 2014, 37(3): 625-633. DOI: 10.2337/dc13-0816.
[96] MEDINA W L, WILSON D, DE SALVO V, et al. Effects of mindfulness on diabetes mellitus: rationale and overview [J]. Curr Diabetes Rev, 2017, 13(2): 141-147. DOI: 10.2174/15.
[97] TOVOTE K A, SCHROEVERS M J, SNIPPE E, et al. What works best for whom? Cognitive Behavior Therapy and Mindfulness-Based Cognitive Therapy for depressive symptoms in patients with diabetes [J]. PLoS One, 2017, 12(6): e0179941. DOI: 10.1371/journal.pone.0179941.
[98] GOIS C, DIAS V V, CARMO I, et al. Treatment response in type 2 diabetes patients with major depression [J]. Clin Psychol Psychother, 2014, 21(1): 39-48. DOI: 10.1002/cpp.1817.
[99] PENCEKOFER S M, FERRANS C, MUMBY P, et al. A psychoeducational intervention (SWEEP) for depressed women with diabetes [J]. Ann Behav Med, 2012, 44(2): 192-206. DOI: 10.1007/s12160-012-9377-2.

[100] YANG Dan, ZHANG Yan, HUI Rong, et al. Effects of structural and psychological empowerment health education model on blood glucose, psychological status and self-efficacy in elderly type 2 diabetic patients with depression [J]. International Journal of Psychiatry, 2024, 51(1): 314-317. DOI: 10.13479/j.cnki.jip.2024.01.046.
[101] NAIK A D, HUNDT N E, VAUGHAN E M, et al. Effect of telephone-delivered collaborative goal setting and behavioral activation vs enhanced usual care for depression among adults with uncontrolled diabetes: a randomized clinical trial [J]. JAMA Netw Open, 2019, 2(8): e198634. DOI: 10.1001/jamanetworkopen.2019.8634.
[102] WANG Hongyan, ZHANG Yunqiu, XI Jiayu, et al. Application effect of positive psychological intervention based on PCI model in elderly type 2 diabetic patients with depressive state [J]. Modern Clinical Medicine, 2024, 50(3): 165-168, 172.
[103] HARVEY J N. Psychosocial interventions for the diabetic patient [J]. Diabetes Metab Syndr Obes, 2015, 8: 29-43. DOI: 10.2147/DMSO.S44352.
[104] DHAVALE H S, PANIKKAR V, JADHAV B S, et al. Depression and diabetes: impact of antidepressant medications on glycaemic control [J]. J Assoc Physicians India, 2013, 61(12):
[105] MARKOWITZ S M, GONZALEZ J S, WILKINSON J L, et al. A review of treating depression in diabetes: emerging findings [J]. Psychosomatics, 2011, 52(1): 1-18. DOI: 10.1016/j.psym.2010.11.007.
[106] GOODNICK P J, HENRY J H, BUKI V M. Treatment of depression in patients with diabetes mellitus [J]. J Clin Psychiatry, 1995, 56(4): 128-136.
[107] VAN TILBURG M A, MCCASKILL C C, LANE J D, et al. Depressed mood is a factor in glycemic control in type 1 diabetes [J]. Psychosom Med, 2001, 63(4): 551-555. DOI: 10.1097/00006842-200107000-00005.
[108] LUSTMAN P J, FREEDLAND K E, GRIFFITH L S, et al. Fluoxetine for depression in diabetes: a randomized double-blind placebo-controlled trial [J]. Diabetes Care, 2000, 23(5): 618-623. DOI: 10.2337/diacare.23.5.618.
[109] NICOLAU J, RIVERA R, FRANCÉS C, et al. Treatment of depression in type 2 diabetic patients: Effects on depressive symptoms, quality of life and metabolic control [J]. Diabetes Res Clin Pract, 2013, 101(2): 148-152. DOI: 10.1016/j.diabres.2013.05.009.
[110] KHAZAIE H, RAHIMI M, TATARI F, et al. Treatment of depression in type 2 diabetes with fluoxetine or citalopram [J]. Neurosciences (Riyadh), 2011, 16(1): 42-45.
[111] LUSTMAN P J, CLOUSE R E, NIX B D, et al. Sertraline for prevention of depression recurrence in diabetes mellitus: a randomized, double-blind, placebo-controlled trial [J]. Arch Gen Psychiatry, 2006, 63(5): 521-529. DOI: 10.1001/archpsyc.63.5.521.
[112] PAILE-HYVÄRINEN M, WAHLBECK K, ERIKSSON J G. Quality of life and metabolic status in mildly depressed patients with type 2 diabetes treated with paroxetine: a double-blind randomized placebo controlled 6-month trial [J]. BMC Fam Pract, 2007, 8: 34. DOI: 10.1186/1471-2296-8-34.
[113] OSWALD P, SOUERY D, MENDLEWICZ J. Fluvoxamine-induced

hyperglycaemia in a diabetic patient with comorbid depression [J]. Int J Neuropsychopharmacol, 2003, 6(1): 85-87. DOI: 10.1017/S1461145703003262.
[114] GAGNON J, LUSSIER M T, MACGIBBON B, et al. The impact of antidepressant therapy on glycemic control in Canadian primary care patients with diabetes mellitus [J]. Front Nutr, 2018, 5: 47. DOI: 10.3389/fnut.2018.00047.
[115] SAŁAT K. Chemotherapy-induced peripheral neuropathy-part 2: focus on the prevention of oxaliplatin-induced neurotoxicity [J]. Pharmacol Rep, 2020, 72(3): 508-527. DOI: 10.1007/s43440-020-00106-1.
[116] HERSHMAN D L, LACCHETTI C, DWORKIN R H, et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline [J]. J Clin Oncol, 2014, 32(18): 1941-1967. DOI: 10.1200/JCO.2013.54.0914.
[117] ABRAHAMIAN H, HOFMANN P, PRAGER R, et al. Diabetes mellitus and co-morbid depression: treatment with milnacipran results in significant improvement of both diseases (results from the Austrian MDDM study group) [J]. Neuropsychiatr Dis Treat, 2009, 5: 261-266. DOI: 10.2147/ndt.s5421.
[118] HALL J A, WANG F J, OAKES T M, et al. Safety and tolerability of duloxetine in the acute management of diabetic peripheral neuropathic pain: analysis of pooled data from three placebo-controlled clinical trials [J]. Expert Opin Drug Saf, 2010, 9(4): 525-537. DOI: 10.1517/14740338.2010.484418.
[119] WEBER-HAMANN B, GILLES M, SCHILLING C, et al. Improved insulin sensitivity in 51 nondiabetic depressed inpatients remitting during antidepressive treatment with mirtazapine and venlafaxine [J]. J Clin Psychopharmacol, 2008, 28(5): 581-584. DOI: 10.1097/JCP.0b013e31818582ef.
[120] CHEN Y C, LIN W W, CHEN Y J, et al. Antidepressant effects on insulin sensitivity and proinflammatory cytokines in the depressed males [J]. Mediators Inflamm, 2010, 2010: 573594. DOI: 10.1155/2010/573594.
[121] HIMMERICH H, FULDA S, SCHAAF L, et al. Changes in weight and glucose tolerance during treatment with mirtazapine [J]. Diabetes Care, 2006, 29(1): 170. DOI: 10.2337/diacare.29.1.170.
[122] LAIMER M, KRAMER-REINSTADLER K, RAUCHENZAUNER M, et al. Effect of mirtazapine treatment on body composition and metabolism [J]. J Clin Psychiatry, 2006, 67(3): 421-424. DOI: 10.4088/jcp.v67n0313.
[123] SONG H R, WOO Y S, WANG H R, et al. Does mirtazapine interfere with naturalistic diabetes treatment [J]. J Clin Psychopharmacol, 2014, 34(5): 588-594. DOI: 10.1097/JCP.0000000000000183.
[124] LUSTMAN P J, WILLIAMS M M, SAYUK G S, et al. Factors influencing glycemic control in type 2 diabetes during acute- and maintenance-phase treatment of major depressive disorder with bupropion [J]. Diabetes Care, 2007, 30(3): 459-466. DOI: 10.2337/dc06-1769.
[125] LIANG Z H, JIA Y B, ZHAO L Z, et al. Agomelatine might be more appropriate for elderly, depressed, type 2 diabetes mellitus patients than paroxetine/fluoxetine [J]. Aging (Albany NY), 2021, 13(19): 22934-22946. DOI: 10.18632/aging.203586.
[126] GOODNICK P J. Use of antidepressants in treatment of comorbid diabetes mellitus and depression as well as in diabetic neuropathy [J]. Ann Clin

Psychiatry, 2001, 13(1): 31-41. DOI: 10.1023/a:1009012815127.
[127] ANDERSOHN F, SCHADE R, SUISSA S, et al. Long-term use of antidepressants for depressive disorders and the risk of diabetes mellitus [J]. Am J Psychiatry, 2009, 166(5): 591-598. DOI: 10.1176/appi.ajp.2008.08071065.
[128] FAGIOLINI A, FRANK E, SCOTT J A, et al. Metabolic syndrome in bipolar disorder: findings from the bipolar disorder center for pennsylvanians [J]. Bipolar Disord, 2005, 7(5): 424-430. DOI: 10.1111/j.1399-5618.2005.00234.x.
[129] KIVIMÄKI M, HAMER M, BATTY G D, et al. Antidepressant medication use, weight gain, and risk of type 2 diabetes: a population-based study [J]. Diabetes Care, 2010, 33(12): 2611-2616. DOI: 10.2337/dc10-1187.
[130] WANG Y Q, LIU D B, LI X Z, et al. Antidepressants use and the risk of type 2 diabetes mellitus: a systematic review and meta-analysis [J]. J Affect Disord, 2021, 287: 41-53. DOI: 10.1016/j.jad.2021.03.023.
[131] BARNARD K, PEVELER R C, HOLT R I G. Antidepressant medication as a risk factor for type 2 diabetes and impaired glucose regulation: systematic review [J]. Diabetes Care, 2013, 36(10): 3337-3345. DOI: 10.2337/dc13-0560.
[132] MITCHELL A J, VANCAMPFORT D, SWEERS K, et al. Prevalence of metabolic syndrome and metabolic abnormalities in schizophrenia and related disorders—a systematic review and meta-analysis [J]. Schizophr Bull, 2013, 39(2): 306-318. DOI: 10.1093/schbul/sbr148.
[133] VANCAMPFORT D, CORRELL C U, GALLING B, et al. Diabetes mellitus in people with schizophrenia, bipolar disorder and major depressive disorder: a systematic review and large scale meta-analysis [J]. World Psychiatry, 2016, 15(2): 166-174. DOI: 10.1002/wps.20309.
[134] PILLINGER T, MCCUTCHEON R A, VANO L, et al. Comparative effects of 18 antipsychotics on metabolic function in patients with schizophrenia, predictors of metabolic dysregulation, and association with psychopathology: a systematic review and network meta-analysis [J]. Lancet Psychiatry, 2020, 7(1): 64-77. DOI: 10.1016/S2215-0366(19)30416-X.
[135] David M. Taylor, Thomas R.E. Barnes, Allan H. Young, authors; SI Tianmei, chief translator. Maudsley Prescribing Guidelines in Psychiatry [M]. Beijing: People' s Medical Publishing House, 2024: 280-290.
[136] YU Dongshan, GE Maohong, SU Hailing. Handbook of Rational Drug Use in Psychiatry [M]. 4th ed. Nanjing: Jiangsu Phoenix Science and Technology Press, 2020: 215-344.
[137] GUO Weifeng, CAO Xiaolan, SHENG Lei, et al. Expert consensus on integrated traditional Chinese and Western medicine diagnosis and treatment of depression [J]. Chinese Journal of Integrated Traditional and Western Medicine, 2020, 40(2): 141-148. DOI: 10.7661/j.cjim.20191222.421.
[138] Writing Group of Guidelines for Integrated Prevention and Treatment of Adolescent Depressive Disorders with Traditional Chinese and Western Medicine, Psychosomatic Medicine Branch of China Association of Chinese Medicine, Psychosomatic Medicine Branch of Chinese Medical Association. Guidelines for integrated prevention and treatment of adolescent depressive disorders with traditional Chinese and Western medicine [J]. Journal of Beijing University of Traditional Chinese Medicine, 2024, 47(6): 874-888. DOI:

10.3969/j.issn.1006-2157.2024.06.019.
[139] PANG Guoming, NI Qing, ZHANG Fang. Guidelines for integrated disease-syndrome diagnosis and treatment of type 2 diabetes [J]. Journal of Traditional Chinese Medicine, 2021, 62(4): 361-368. DOI: 10.13288/j.11-2166/r.2021.04.019.
[140] GUO Qiang, ZHAO Huan, ZHU Yuxia, et al. Meta-analysis of efficacy of Yimu Futu method in treating type 2 diabetes mellitus with depression [J]. Shandong Medical Journal, 2015, 55(26):
[141] LIU Meijun, LIU Zhicheng, XU Bin, et al. Meta-analysis of acupuncture treatment for type 2 diabetes mellitus with depression [J]. Journal of Zhejiang Chinese Medical University, 2016, 40(1): 54-59. DOI: 10.16466/j.issn1005-5509.2016.01.016.
[142] HE Lingna, DU Ping, SHEN Zhifu, et al. Observation on therapeutic effect of Hechelu cupping combined with rubbing method on post-diabetes depression [J]. Chinese Acupuncture & Moxibustion, 2016, 36(3): 245-249. DOI: 10.13703/j.0255-2930.2016.03.005.
[143] LUO X W, ZHAO M X, ZHANG Y L, et al. Effects of Baduanjin exercise on blood glucose, depression and anxiety among patients with type II diabetes and emotional disorders: a meta-analysis [J]. Complement Ther Clin Pract, 2023, 50: 101702. DOI: 10.1016/j.ctcp.2022.101702.
[144] ZHANG Zhenfeng, XU Jianghong. Clinical observation of auricular acupuncture combined with Chinese herbs on type 2 diabetes with depression [J]. Chinese Archives of Traditional Chinese Medicine, 2014, 32(1): 114-116. DOI: 10.13193/j.issn.1673-7717.2014.01.038.
[145] LI Hui, ZHU Tianmin. Clinical study on traditional Chinese music therapy for diabetes with depression [J]. Liaoning Journal of Traditional Chinese Medicine, 2011, 38(5): 929-931. DOI: 10.13192/j.ljtcm.2011.05.132.lih.042.
[146] Dual Heart Group of Cardiovascular Physicians Branch of Chinese Medical Doctor Association, Beijing Medical Association Heart-Mind Branch, LIU Meiyan. Consensus on primary care for stable coronary artery disease with psychological problems (2023) [J]. Chinese Journal of General Practitioners, 2023, 22(12):

Received date: 2025-05-10; Revised date: 2025-08-20
Edited by: ZHAO Yuecui

Note: Figure translations are in progress. See original paper for figures.