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REVIEW ARTICLE

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Standards of medical care for type 2 diabetes in China 2019

Weiping Jia[1] | Jianping Weng[2] | Dalong Zhu[3] | Linong Ji[4] | Juming Lu[5] | Zhiguang Zhou[6] | Dajin Zou[7] | Lixin Guo[8] | Qiuhe Ji[9] | Li Chen[10] | Liming Chen[11] | Jingtao Dou[5] | Xiaohui Guo[12] | Hongyu Kuang[13] | Ling Li[14] | Qifu Li[15] | Xiaoying Li[16] | Jing Liu[17] | Xingwu Ran[18] | Lixin Shi[19] | Guangyao Song[20] | Xinhua Xiao[21] | Liyong Yang[22] | Zhigang Zhao[23] | On behalf of Chinese Diabetes Society

[1] Shanghai Diabetes Institute, Shanghai Clinical Center for Diabetes, Shanghai Key Laboratory of Diabetes Mellitus, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China

[2] Department of Endocrinology, the First Affiliated Hospital, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, China

[3] Department of Endocrinology, Drum Tower Hospital Affiliated to Nanjing University Medical School, Nanjing, China

[4] Department of Endocrinology and Metabolism, Peking University People's Hospital, Beijing, China

[5] Department of Endocrinology, Chinese People's Liberation Army General Hospital, Beijing, China

[6] Institute of Metabolism and Endocrinology, Key Laboratory of Diabetes Immunology, Ministry of Education, National Clinical Research Center for Metabolic Diseases, The Second Xiangya Hospital and the Diabetes Center, Central South University, Changsha, China

[7] Department of Endocrinology, Changhai Hospital, Second Military Medical University, Shanghai, China

[8] Department of Endocrinology, Beijing Hospital, Beijing, China

[9] Department of Endocrinology, Xijing Hospital, Xi'an, China

[10] Department of Endocrinology, Qilu Hospital of Shandong University, Ji'nan, China

[11] Tianjin Metabolic Diseases Hospital & Tianjin Institute of Endocrinology, Tianjin Medical University, Tianjin, China

[12] Department of Endocrinology, Peking University First Hospital, Beijing, China

[13] Department of Endocrinology, The First Affiliated Hospital of Harbin Medical University, Harbin, China

[14] Department of Endocrinology, Shengjing Hospital, China Medical University, Shenyang, China

[15] Department of Endocrinology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China

[16] Department of Endocrinology and Metabolism, Zhongshan Hospital, Fudan University, Shanghai, China

[17] Department of Endocrinology, Gansu Provincial Hospital, Lanzhou, China

[18] Department of Endocrinology and Metabolism, West China Hospital, Sichuan University, Chengdu, China

[19] Department of Endocrinology, Affiliated Hospital of Guizhou Medical University, Guizhou, China

[20] Department of Endocrinology, Hebei General Hospital, Shijiazhuang, China

[21] Department of Endocrinology, Peking Union Medical College Hospital, Beijing, China

[22] Department of Endocrinology, The First Affiliated Hospital of Fujian Medical University, Fuzhou, China

[23] Department of Endocrinology, Yihe Hospital of Zhengzhou, Zhengzhou, China

Abbreviations: 2hPG, 2-Hour plasma glucose; 24hMG, 24-Hour mean glucose; ABI, Ankle-brachial index; ADL, Activities of daily living; ACEI, Angiotensin-converting enzyme inhibitor; ARB, Angiotensin II receptor blocker; ASCVD, Atherosclerotic cardiovascular disease; BMI, Body mass index; CDC, Chinese Center for Disease Control and Prevention; CDS, Chinese Diabetes Society; CGM, Continuous glucose monitoring; CKD, Chronic kidney disease; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CSII, Continuous subcutaneous insulin infusion; CVD, Cardiovascular diseases; DCCT, Diabetes Control and Complications Trial; DMRR, Diabetes/Metabolism Research and Reviews; DKD, Diabetic kidney disease; DPN, Diabetic peripheral neuropathy; DPP-4, Dipeptidyl peptidase 4; DSPN, Distal symmetric polyneuropathy; eGFR, Estimated glomerular filtration rate; FPG, Fasting plasma glucose; GA, Glycated albumin; GDM, Gestational diabetes mellitus; GLP-1, Glucagon-like peptide-1; HbA1c, Haemoglobin A1c; HDL-C, High-density lipoprotein cholesterol; HOT, Hypertension Optimal Treatment; ICU, Intensive care unit; IFG, Impaired fasting glucose; IGT, Impaired glucose tolerance; LDL-C, Low-density lipoprotein cholesterol; LEAD, Lower extremity arterial disease; MDRD, Modification of Diet in Renal Disease; MetS, Metabolic syndrome; MODY, Maturity onset diabetes of the young; OGTT, Oral glucose tolerance test; PCOS, Polycystic ovarian syndrome; PGDM, Pregestational diabetes mellitus; SGLT2, Sodium-glucose cotransporter 2; SMBG, Self-monitoring of blood glucose; T1DM, Type 1 diabetes mellitus; T2DM, Type 2 diabetes mellitus; TCM, Traditional Chinese medicines; TG, Triglycerides; TZDs, Thiazolidinediones; UACR, Urinary albumin/creatinine ratio; VEGF, Vascular endothelial growth factor; UKPDS, United Kingdom Prospective Diabetes Study; WHO, World Health Organization

Correspondence
Weiping Jia, Shanghai Diabetes Institute, Shanghai Clinical Center for Diabetes, Shanghai Key Laboratory of Diabetes Mellitus, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China.
Email: wpjia@sjtu.edu.cn

Jianping Weng, Department of Endocrinology, the First Affiliated Hospital, Division of Life Sciences and Medicine, University of Science and Technology of China, 17 Lujiang Road, Hefei, China.
Email: wengjp@vip.163.com

Dalong Zhu, Department of Endocrinology, Drum Tower Hospital Affiliated to Nanjing University Medical School, Nanjing, China.
Email: zhudalong@nju.edu.cn

Summary

The prevalence of diabetes in China has increased rapidly from 0.67% in 1980 to 10.4% in 2013, with the aging of the population and westernization of lifestyle. Since its foundation in 1991, the Chinese Diabetes Society (CDS) has been dedicated to improving academic exchange and the academic level of diabetes research in China. From 2003 to 2014, four versions of Chinese diabetes care guidelines have been published. The guidelines have played an important role in standardizing clinical practice and improving the status quo of diabetes prevention and control in China. Since September 2016, the CDS has invited experts in cardiovascular diseases, psychiatric diseases, nutrition, and traditional Chinese medicine to work with endocrinologists from the CDS to review the new clinical research evidence related to diabetes over the previous 4 years. Over a year of careful revision, this has resulted in the present, new version of guidelines for prevention and care of type 2 diabetes in China. The main contents include epidemiology of type 2 diabetes in China; diagnosis and classification of diabetes; primary, secondary, and tertiary diabetes prevention; diabetes education and management support; blood glucose monitoring; integrated control targets for type 2 diabetes and treatments for hyperglycaemia; medical nutrition therapy; exercise therapy for type 2 diabetes; smoking cessation; pharmacologic therapy for hyperglycaemia; metabolic surgery for type 2 diabetes; prevention and treatment of cardiovascular and cerebrovascular diseases in patients with type 2 diabetes; hypoglycaemia; chronic diabetic complications; special types of diabetes; metabolic syndrome; and diabetes and traditional Chinese medicine.

KEYWORDS

guideline, medical care, type 2 diabetes

1 | INTRODUCTION

Over the last 40 years, the prevalence of diabetes in China has increased rapidly from 0.67% in 1980 to 10.4% in 2013, with the aging of the population and westernization of lifestyle. Since its foundation in 1991, the Chinese Diabetes Society (CDS) has been dedicated to improving academic exchange and the academic level of diabetes research in China. And because of ethnic differences in pathogenic and clinical features of diabetes between East Asians and Caucasians such as different blood glucose profiles,[1] it is important to have country-specific guidelines for the management of diabetes. This has been previously highlighted in other treatment algorithms for the management of diabetes such as the "The A1C and ABCD of glycaemia management in type 2 diabetes."[2] The guidelines proposed by the CDS suggest tools for medical doctors in China and worldwide to appropriately face diabetes in Chinese people.[3] Thus, CDS has been actively involved in the development and dissemination of Chinese diabetes care standards, guidelines, and related documents for over 15 years based on update of medical research evidence from China. From 2003 to 2014, four versions of Chinese diabetes care guidelines have been published. The last English version of standards of care for type 2 diabetes in China was published in 2016 in Diabetes/Metabolism Research and Reviews (DMRR).[4] It has played an important role in standardizing clinical practice and improving the status quo of diabetes prevention and control in China. With 3 years passing, the mission of developing this guideline is to adhere to the principle of combination of diabetes prevention and treatment based on medical evidence from China, with a focus on the applicability of clinical application and practical value. Since the September of 2016, CDS has invited experts in cardiovascular diseases, psychiatric diseases, nutrition, and traditional Chinese medicine to work with endocrinologists from the CDS over a year of careful revision to review recent clinical research in diabetes over the past 4 years to develop this new version of type 2 diabetes prevention and care guideline of China. The main contents include epidemiology of type 2 diabetes in China; diagnosis and classification of diabetes; primary, secondary, and tertiary diabetes prevention; diabetes education and management support; blood glucose monitoring; integrated control targets for type 2 diabetes and treatments for hyperglycaemia; medical nutrition therapy; exercise therapy for type 2 diabetes; smoking cessation; pharmacologic therapy for hyperglycaemia; metabolic surgery for type 2 diabetes; prevention and treatment of cardiovascular and cerebrovascular

diseases in patients with type 2 diabetes; hypoglycaemia; chronic diabetic complications; special types of diabetes; metabolic syndrome; and diabetes and traditional Chinese medicine. This document is an official CDS position, is authored by the CDS, and provides all of the current clinical practice recommendations of the CDS.

2 | SUMMARY OF REVISIONS IN THE 2019 STANDARDS

1. In the current revision, recommendations and evidence levels are provided at the beginning of each chapter. The evidence is categorized as A, B, and C levels according to the quality of evidence, clinical significance, universality, applicability, etc.

Level of Evidence	Description
A	Evidence obtained from multiple randomized clinical trials or meta-analysis
B	Evidence obtained from single randomized clinical trial or multiple nonrandomized controlled studies
C	Evidence from expert consensus and/or small-scale studies, retrospective studies, and registry

2. The target of blood pressure has been changed from <140/80 to <130/80 mmHg (1 mmHg = 0.133 kPa).
3. The algorithm for antihyperglycaemic treatment was updated to incorporation of monotherapy, dual therapy, triple therapy, and multiple insulin injections.
4. The current recommendation for the use of aspirin as primary prevention is no longer limited to men >50 years old and women >60 years old, but expanded to both men and women aged ≥50 years.
5. The current recommended standard for the estimated glomerular filtration rate (eGFR) is to be calculated with equations from the studies of Modification of Diet in Renal Disease (MDRD) or Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI).
6. Among the indications for metabolic surgery, the recommendation changed the cutoff point of body mass index (BMI) from 28.0 to 27.5 kg/m^2.
7. A new recommendation was added on stratified therapeutic goals for glycaemia, blood pressure and dyslipidaemia in older adults with diabetes.
8. A new section on diabetes and traditional Chinese medicines (TCMs) was added to the standards for the first time.

3 | EPIDEMIOLOGY OF TYPE 2 DIABETES IN CHINA

3.1 | Epidemiology of diabetes in China

The prevalence of diabetes has been rising substantially over the past three decades in China. In 1980, an epidemiological survey that included 300 000 individuals from 14 provinces and municipalities nationwide showed that the prevalence of diabetes was 0.67%.[5] An epidemiological survey that included 210 000 individuals from 19 provinces and municipalities in 1994 to 1995 found that the prevalence of diabetes was 2.28% in people aged 25 to 64 years old.[6] A national nutrition and health survey in 2002 showed that the prevalence of diabetes was 4.5% in urban residents and 1.8% in rural residents aged 18 years and older.[7] In 2007 to 2008, the CDS performed an epidemiological survey in 14 provinces and municipalities in China, which showed that the prevalence of diabetes was 9.7% in Chinese adults aged 20 years and over.[8] In 2010, the Chinese Center for Disease Control and Prevention (CDC) and the Chinese Society of Endocrinology conducted a survey in Chinese populations aged 18 years and over, which showed that the prevalence of diabetes was 9.7%.[9] In 2013, the China Chronic Disease and Risk Factors Surveillance study found that the prevalence of diabetes and prediabetes was 10.4% and 16.6% in individuals aged 18 years and over, respectively (Table 1).[10,11]

The epidemiological characteristics of diabetes in China are as follows:

1. The overall proportion of patients who were aware of their diabetes condition was 38.6%.[11]
2. The prevalence of diabetes was significantly higher in urban than rural areas (12.0% vs 8.9%) and among men than women (11.1% vs 9.6%).[10]
3. Genetic susceptibility including several susceptibility loci, such as PAX4 and NOS1AP, has been identified to increase the risk of type 2 diabetes mellitus (T2DM) by 5% to 25% in Chinese populations.[12-14]

4 | DIAGNOSIS AND CLASSIFICATION OF DIABETES

4.1 | Recommendations

- Fasting plasma glucose (FPG), random plasma glucose, or oral glucose tolerance test (OGTT) 2-hour plasma glucose (2hPG) can be used to diagnose diabetes. Individuals with no typical symptoms of diabetes must be retested to confirm the diagnosis (A).
- Diabetes is aetiologically classified into four types: type 1 diabetes mellitus (T1DM), T2DM, other specific types of diabetes, and gestational diabetes mellitus (GDM) (A).

4.2 | Diagnosis of diabetes

This standard adopts the World Health Organization (WHO) (1999) criteria for diagnosis and classification of diabetes. Tables 2 and 3 summarize the diagnostic criteria for diabetes and the classification of metabolic status.[15]

In 2011, WHO recommended that wherever conditions permit, countries and regions may consider adopting the haemoglobin A1c

TABLE 1 Summary of seven nationwide epidemiological surveys of diabetes in China

Year of Survey (Diagnostic Criteria)	Number of Surveyed People (×10 000)	Age, y	Prevalence of Diabetes, %	Prevalence of IGT, %	Screening Method
1980[a] (Lanzhou standard)	30	Entire population	0.67	-	Urine glucose +2hPG (steamed bread tolerance test) for screening high-risk subjects
1986 (WHO 1985)	10	25-64	1.04	0.68	2hPG (steamed bread tolerance test) for screening high-risk subjects
1994 (WHO 1985)	21	25-64	2.28	2.12	2hPG (steamed bread tolerance test) for screening high-risk subjects
2002 (WHO 1999)	10	≥18	4.5 (Urban), 1.8 (rural)	1.6 (IFG 2.7)	FPG screening of the high-risk group
2007-2008 (WHO 1999)	4.6	≥20	9.7	15.5[b]	OGTT
2010 (WHO 1999)	10	≥18	9.7	-	OGTT
2013 (WHO 1999)[c]	17	≥18	10.4	16.6	OGTT

Note. Blood glucose 1 mmol/L = 18 mg/dL.

Abbreviations: WHO, World Health Organization; OGTT, oral glucose tolerance test; IGT, impaired glucose tolerance; IFG, impaired fasting glucose; FPG, fasting plasma glucose; 2hPG, 2-hour postprandial plasma glucose; -, no data available.

[a]Diagnostic criteria: FPG ≥ 130 mg/dL and/or 2hPG ≥ 200 mg/dL and/or more than three items on the OGTT curve that are above the diagnostic criteria [0′125, 30′190, 60′180, 120′140, 180′125, wherein 0′, 30′, 60′, 120′, and 180′ were time points (min); 30′ and 60′ is one time point; 125, 190, 180, and 140 were blood glucose values (mg/dL); the glucose measurement uses the o-toluidine method with 100 g of glucose].

[b]Prediabetes, including IFG, IGT, or both (IFG/IGT).

[c]The 2013 survey included Han and ethnic minority populations in China.

TABLE 2 Values for diagnosis of diabetes mellitus and other categories of hyperglycaemia (WHO 1999)

Categories of Hyperglycaemia	Venous Plasma Glucose (mmol/L)	
	FPG	OGTT 2hPG
IFG	≥6.1, <7.0	<7.8
IGT	<7.0	≥7.8, <11.1
Diabetes	≥7.0	≥11.1

Note. Both IFG and IGT are considered impaired glucose regulation, also known as prediabetes. For epidemiological or population screening purposes, the fasting or 2hPG during 75 g OGTT may be used alone.

TABLE 3 Diagnostic criteria for diabetes

1. Typical symptoms of diabetes (polydipsia, polyuria, polyphagia, and weight loss) plus random plasma glucose ≥11.1 mmol/L

or

2. FPG ≥ 7.0 mmol/L[a]

or

3. OGTT 2hPG ≥ 11.1 mmol/L[a]

Note. Fasting is defined as no caloric intake for at least 8 hours. Random blood glucose refers to the blood glucose level at any time of day regardless of the time of the last meal, which cannot be used to diagnose IFG or IGT.

[a]No typical symptoms of diabetes, venous FPG, or OGTT 2hPG must be retested on a different day to confirm diabetes.

(HbA1c) ≥6.5% as the cutpoint for diabetes diagnosis.[16] Although the standardization of HbA1c test has improved in China, it has not been sufficiently characterized to support routine adoption. Thus, this standard does not recommend the use of HbA1c for diagnosis of diabetes in China. Nevertheless, medical facilities are encouraged to conduct studies to investigate the feasibility of HbA1c as the basis for diagnosis of diabetes. Several studies have shown that the optimal cut-off value for HbA1c is 6.3% to diagnose diabetes in Chinese adults.

4.3 | Classification

This standard adopts the classification of diabetes aetiology proposed by the WHO (1999) that divides diabetes into four categories: T1DM, T2DM, other specific types of diabetes, and GDM.

Mitochondrial DNA 3243 mutation diabetes and maturity onset diabetes of the young (MODY) are common types of monogenic diabetes in Chinese population. Table 4 summarizes the most common types and clinical features of MODY in the Chinese population.

5 | PRIMARY, SECONDARY, AND TERTIARY DIABETES PREVENTION

5.1 | Recommendations

- Screening should be undertaken in high-risk populations to enable early detection of diabetes (B).
- Individuals with abnormal FPG or random blood glucose but who have not reached the diagnostic criteria of diabetes should undergo OGTT (A).
- Prediabetes should receive lifestyle interventions to reduce the risk of diabetes (A).

TABLE 4 Common types and clinical features of maturity onset diabetes of the young (MODY) in the Chinese population

Type of MODY	Gene	Clinical features
1	Hepatocyte nuclear factor-4α (HNF-4α)	Progressive impaired insulin secretion during adolescence or early adulthood; high birth weight and transient hypoglycaemia in newborns; sensitivity to sulfonylureas
2	Glucokinase (GCK)	Stable, nonprogressive FPG elevation, usually not requiring pharmacotherapy; microvascular complications are rare; OGTT 2hPG slightly higher than FPG (difference < 3 mmol/L)
3	Hepatocyte nuclear factor-1α (HNF-1α)	Progressive impairment in insulin secretion in adolescence or early adulthood; decreased renal glucose threshold; OGTT 2hPG significantly higher than FPG (difference > 5 mmol/L); sensitivity to sulfonylureas
5	Hepatocyte nuclear factor-1β (HNF-1β)	Elevated blood glucose with renal developmental disorder (renal cyst); genitourinary abnormalities; pancreatic atrophy; hyperuricaemia; gout
10	Insulin (INS)	Deficiency of insulin secretion, usually requiring insulin treatment
13	Potassium channel Kir6.2 (KCNJ11)	Deficiency of insulin secretion; sensitivity to sulfonylureas

- Controlling blood glucose, lowering blood pressure, adjusting lipids, and aspirin therapy are recommended to prevent diabetic cardiovascular and microvascular diseases in patients with T2DM with cardiovascular risk factors (A).
- Diabetes with severe complications should be referred to specialists.

5.2 | Goals for primary, secondary, and tertiary prevention of type 2 diabetes

The goal of primary prevention is to reduce risk factors and prevent the occurrence of T2DM. The goal of secondary prevention is early detection, as well as early diagnosis and treatment of T2DM to prevent diabetic complications in individuals with T2DM. Tertiary prevention aims to delay the progression of diabetic complications, reduce morbidity and mortality, and improve the patients' quality of life.

5.3 | Primary prevention

Primary prevention of T2DM includes health education in the general population to raise public awareness of diabetes prevention and treatment and promote a healthy lifestyle, including healthy diet, weight control, physical activity, salt restriction, smoking cessation, alcohol restriction, and social and psychological well-being.

Multiple randomized and controlled studies have shown that appropriate lifestyle interventions (moderate physical activity and weight management) can delay or prevent progression to T2DM among people with impaired glucose tolerance (IGT). In a study conducted in Daqing, China, those in the lifestyle intervention group were asked to increase vegetable intake and reduce intake of alcohol and monosaccharides. Those who were defined as overweight or obese (BMI >25 kg/m^2) were encouraged to lose weight and to increase physical activity by performing at least 20 minutes of moderately intense activity per day. After a 6-year lifestyle intervention, the cumulative incidence of T2DM risk for the subsequent 14 years decreased by 43%.[17] The lifestyle intervention groups in the Finnish Diabetes Prevention Study[18] and the American Diabetes Prevention Program[19] also demonstrated that lifestyle intervention could significantly reduce the risk of developing T2DM among patients with IGT.

This standard recommends that individuals with prediabetes should be encouraged to adopt healthy diet and increase physical activity to reduce the risk of diabetes. They should also receive regular follow-up that provides psychosocial support to encourage long-term adherence to a healthy lifestyle, regular monitoring of blood glucose levels, regular monitoring of cardiovascular risk factors (such as smoking, hypertension, and dyslipidaemia), and appropriate intervention measures.[4] Specific objectives for prevention among those with prediabetes are (1) among overweight or obese individuals, lowering of BMI to approximately 24 kg/m^2 or weight loss of at least 7%, (2) reduction in total daily caloric intake by at least 400 to 500 kcal (1 kcal = 4.184 kJ), (3) reduction in saturated fatty acid intake to less than 30% of total fatty acid intake, and (4) moderate-intensity physical activity for at least 150 min/week.

5.4 | Secondary prevention

Secondary prevention of T2DM includes diabetes screening and intervention in high-risk populations, chronic complication screening, and comprehensive control of blood glucose, blood pressure, and lipid in patients with diabetes.

Those in high-risk populations (Table 5) may be screened by resident health records and opportunistic screening (eg, screening that occurs during routine physical examinations or during treatment of other diseases).

For adults in the high-risk group, diabetes screening should be performed as early as possible. For children and adolescents in high-risk groups, screening should begin at age 10; however, for individuals with an earlier onset of puberty, screening should start at puberty. Those whose initial screening results are normal are recommended to undergo screening again at least once every 3 years.[4]

FPG is a simple diabetes screening method that should be used for routine screening, albeit there is risk of missed diagnosis. Individuals with abnormal FPG or random blood glucose but who have not

TABLE 5 Definition of high-risk populations

Adults (>18 y) with at Least One of the Following Diabetes Risk Factors
1. Age ≥ 40 years
2. History of prediabetes (IGT and/or IFG)
3. Overweight (BMI ≥ 24 kg/m^2) or obesity (BMI ≥ 28 kg/m^2) and/or central obesity (waist circumference ≥90 cm in men and ≥85 cm in women)
4. Sedentary lifestyle
5. First-degree relatives with T2DM
6. History of GDM (for women)
7. Hypertension (systolic blood pressure ≥ 140 mmHg [1 mmHg = 0.133 kPa] and/or diastolic blood pressure ≥ 90 mmHg) or receiving antihypertensive therapy
8. Dyslipidaemia (high-density lipoprotein cholesterol [HDL-C] ≤ 0.91 mmol/L and/or triglycerides [TG] ≥ 2.22 mmol/L) or receiving lipid-lowering therapy
9. Atherosclerotic cardiovascular disease (ASCVD)
10. A transient history of steroid diabetes
11. Polycystic ovary syndrome (PCOS) or clinical conditions associated with insulin resistance (such as acanthosis nigricans)
12. Long-term use of antipsychotics and/or antidepressants and statins

reached criteria for diagnosis of diabetes should undergo OGTT. Chronic complications screening should be initiated once diabetes is diagnosed.

The United Kingdom Prospective Diabetes Study (UKPDS) showed that among patients in the early stage of diabetes, intensive glucose control can significantly reduce the risk of diabetic microvascular and macrovascular diseases.[20,21] The Hypertension Optimal Treatment (HOT) showed that intensive blood pressure control reduced the risk of cardiovascular diseases (CVD) in diabetic patients without significant vascular complications.[22] Several studies indicated that the use of statins to lower low-density lipoprotein cholesterol (LDL-C) could reduce the risk of CVD in diabetic patients without significant vascular complications.[23,24] A systematic review of multiple clinical trials demonstrated a protective effect of aspirin against CVD among individuals with T2DM and CVD risk factors.[25]

For those with T2DM without significant diabetic vascular complications but with risk factors for cardiovascular diseases, controlling blood glucose, lowering blood pressure, adjusting lipids (mainly to reduce LDL-C), and aspirin therapy are all useful methods to prevent CVD and diabetic microvascular diseases.[4]

5.5 | Tertiary prevention

The tertiary prevention aims to delay the progression of diabetic complications, reduce morbidity and mortality, and improve the patients' quality of life. The standard recommends that patients be referred to specialists for treatment promptly following identification of severe chronic diabetic complications.

6 | DIABETES EDUCATION AND SELF-MANAGEMENT SUPPORT

Diabetes is a long-term chronic disease. Therefore, healthy lifestyle and self-management are keys to successful diabetic control. For patients with diabetes, self-management education provides patients with the knowledge and skills necessary for disease self-care. Counselling or tailoring according to individual needs, goals, and life experiences helps to improve engagement in care plans and, thereby, clinical outcomes while also reducing costs. Diabetes self-management education should be patient-centred. That is, it should respect and reflect the patient's personal preferences, needs, and values which should also be the basis for clinical decisions. Diabetes educators who have received standard training should provide patients with diabetes self-management education. Health care professionals should provide patients with diabetes with individualized diabetes self-management education at a proper time, promptly after diagnosis and then repeated as individuals' care plan and circumstances change over the course of the disease.[26,27]

7 | BLOOD GLUCOSE MONITORING

Blood glucose monitoring is one of the important components in diabetes management. It is essential to determine the degree of glucose metabolic disturbance, develop an effective hypoglycaemic plan, evaluate therapeutic effects, and guide the adjustments of hypoglycaemic regimens. At present, blood glucose is monitored based on capillary blood glucose including self-monitoring of blood glucose (SMBG) and bedside blood glucose testing, continuous glucose monitoring (CGM), HbA1c, or glycated albumin (GA).

7.1 | Capillary blood glucose monitoring

SMBG is an integral component of comprehensive diabetes management and education and is recommended for all patients with diabetes. The frequency of SMBG should be determined according to the patient's condition, taking into consideration both effectiveness and convenience. Principles include the following:

1. Monitoring blood glucose four to seven times daily or as needed for patients who are hospitalized because of poor glycaemic control or with severe conditions.
2. Monitoring blood glucose as needed to assess the effect of diet and exercise on blood glucose for patients with lifestyle interventions.

3. Testing FPG or 2hPG two to four times per week for patients with oral hypoglycaemic agents.
4. Monitoring blood glucose according to the insulin treatment plan in patients with insulin therapy.
5. Blood glucose monitoring should be individualized according to the basic principles stated above in special populations, including perioperative patients, patients with high risk of hypoglycaemia, elderly patients, T1DM, patients with GDM, etc.

7.2 | Haemoglobin A1c

Haemoglobin A1c (HbA1c) has become a gold standard for the assessment of glycaemic control over the previous 2 to 3 months and the basis for the adjustments of treatment regimens. The normal reference range is 4% to 6% with the standard HbA1c assay, which is recommended to be tested every 3 months during initial treatment and every 6 months once treatment targets are reached. However, the HbA1c value is not reliable in patients with anaemia or haemoglobin disorders. The HbA1c assay should be traceable to the Diabetes Control and Complications Trial (DCCT) reference assay.

7.3 | Glycated albumin

GA reflects the average glucose level over the previous 2 to 3 weeks, and the normal reference range is 11% to 17%.[28,29] In addition, GA can be used for differential diagnosis of stress-induced hyperglycaemia caused by acute stress. However, the GA value is not reliable in patients with conditions that affect the rate of albumin renewal, such as nephrotic syndrome and cirrhosis.

7.4 | Continuous glucose monitoring

Continuous glucose monitoring (CGM) continuously monitors interstitial glucose levels using a subcutaneous glucose sensor, which provides more comprehensive information regarding the blood glucose level and the basis for individualized diabetes care. Retrospective CGM is mainly applicable for use in the following patients or situations:

1. T1DM.
2. T2DM requiring intensive insulin therapy.
3. Patients with T2DM who use hypoglycaemic treatment under SMBG guidance, but still encounter one of the following situations: (1) unexplained severe or recurrent hypoglycaemia, asymptomatic hypoglycaemia, or nocturnal hypoglycaemia; (2) refractory hyperglycaemia, especially when fasting; (3) large blood glucose excursions; (4) state of hyperglycaemia maintained by individuals because of fear of hypoglycaemia.
4. GDM or diabetes in pregnancy.
5. Patients who need diabetes education.

Retrospective CGM data can be also used to evaluate the results of clinical studies as needed.[30-33] Real-time CGM data are indicated in children and adolescents with T1DM who have achieved HbA1c levels below 7.0%, children and adolescents with T1DM who have HbA1c levels more than 7.0% but are able to use the device on a daily basis, adult patients with T1DM who can use the device on a daily basis, nonintensive care unit inpatients with T2DM receiving insulin treatment,[34] and perioperative patients with T2DM.

Table 6 shows the normal reference values for CGM in a Chinese population aged 20 to 69 years.[35,36] The 24-hour mean glucose (24hMG) is strongly correlated with HbA1c and can be calculated with the following formula: 24hMG = 1.198 × HbA1c − 0.582. Thus, when HbA1c were 6.0%, 6.5%, and 7.0%, the calculated 24hMG were 6.6, 7.2, and 7.8 mmol/L, respectively.[37] In addition, the standard "three-step" analysis is recommended for interpretation of the CGM profile and data. For analysis of data from 3-day monitoring, step 1 is to analyse nocturnal blood glucose, step 2 is to analyse preprandial glucose, and step 3 is to analyse postprandial glucose. During each step, hypoglycaemia is checked before hyperglycaemia, and reasons for it are identified so as to adjust the treatment plan. For data from 14-day monitoring, step 1 is to check on-target time, step 2 is to check glucose fluctuations, and step 3 is to check hypoglycaemia.

8 | OBJECTIVES OF INTEGRATED TYPE 2 DIABETES CONTROL AND TREATMENT OPTIONS FOR HYPERGLYCAEMIA

8.1 | Recommendations

- For most nonpregnant adults with T2DM, reasonable control targets include HbA1c < 7% (A), blood pressure < 130/80 mmHg, LDL-C < 2.6 mmol/L (without atherosclerotic cardiovascular disease (ASCVD)) or <1.8 mmol/L (with ASCVD), and BMI < 24 kg/m^2.

TABLE 6 Normal reference for continuous glucose monitoring (CGM) in Chinese adults (24 h)

Index Type	Index Name	Normal Reference
Glucose level	Mean glucose level	<6.6 mmol/L
	Percentage time and duration of blood glucose ≥7.8 mmol/L	<17% (4 h)
	Percentage time and duration of blood glucose ≤3.9 mmol/L	<12% (3 h)
Glucose fluctuations	Standard deviation (SD) of blood glucose	<1.4 mmol/L

- Lifestyle intervention is the basis for diabetes care, and drug therapy should be initiated in the event of uncontrolled blood glucose (HbA1c $\geq$ 7.0%) (A).
- Metformin, α-glucosidase inhibitors, or insulin secretagogues could be options for monotherapy (A).
- In the event of no response to monotherapy, dual therapy, triple therapy, or multiple daily insulin injections may be prescribed (B).

8.2 | Objectives of comprehensive type 2 diabetes control

The ideal comprehensive control of T2DM varies according to the age, comorbidities, and complications of patients (Table 7). A treatment that does not achieve the control targets should not be viewed as a failure because any improvement in the control indicators confers benefits to the patient and reduces the risks associated with complications. For example, reductions in HbA1c are closely correlated with reductions in microvascular complications and neuropathy.

The primary principle for determining the targets for integrated T2DM control is individualized management, which should comprehensively consider age, disease duration, life expectancy, severity of complications, or comorbidities.[4]

HbA1c is one of the main indicators reflecting long-term glucose control. The reasonable HbA1c goal for most nonpregnant adult is <7%. This goal of HbA1c $\geq$7% can generally be used as the criterion for initiating clinical treatment or adjusting the treatment plan for T2DM. More stringent HbA1c targets (such as <6.5%, or even close to the normal reference value) are indicated in patients with T2DM with a short duration of disease, long life expectancy, no complications, and no significant CVD, without significant hypoglycaemia or other adverse effects of treatment. Less stringent HbA1c goals (such as <8.0%) are indicated in patients with a history of severe hypoglycaemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, long-standing diabetes in whom the goal is difficult to achieve despite comprehensive treatment including diabetes self-management education, appropriate glucose monitoring, and effective doses of multiple glucose-lowering agents (including insulin).[38]

TABLE 7 Targets for the integrated control of type 2 diabetes in China

Indicator	Target Value
Blood glucose (mmol/L)[a]	
Fasting	4.4-7.0
Nonfasting	<10.0
HbA1c (%)	<7.0
Blood pressure (mmHg)	<130/80
Total cholesterol (mmol/L)	<4.5
HDL-C (mmol/L)	
Male	>1.0
Female	>1.3
TG (mmol/L)	<1.7
LDL-C (mmol/L)	
No atherosclerotic cardiovascular disease	<2.6
With atherosclerotic cardiovascular disease	<1.8
BMI (kg/m^2)	<24.0

Note. 1 mmHg = 0.133 kPa.

[a]Capillary blood glucose.

8.3 | Type 2 diabetes blood glucose control strategy and treatment options

T2DM is a progressive disease. Blood glucose tends to increase gradually as disease duration increases; therefore, the intensity of hyperglycaemia control treatment should be increased accordingly. Lifestyle intervention is the basis for T2DM treatment and should be applied throughout the diabetes treatment process. When lifestyle change alone is unable to reach blood glucose target, monotherapy should be initiated. The preferred drug for T2DM is metformin, which should remain part of the diabetes treatment regimen if no contraindications are present. Patients who could not take metformin may use α-glucosidase inhibitors or insulin secretagogues. When metformin alone is unable to achieve blood glucose target, dual therapy should utilize insulin secretagogues, α-glucosidase inhibitors, dipeptidyl peptidase IV (DPP-4) inhibitors or thiazolidinediones (TZDs), sodium-glucose cotransporter 2 (SGLT2) inhibitors, insulin, or glucagon-like peptide-1 (GLP-1) receptor agonists. A combination of three types of drugs may be initiated when dual therapy is still unable to achieve a blood glucose target. Patients with uncontrolled blood glucose after triple therapy should proceed to multiple daily insulin injections (basal + prandial insulin or multiple daily injections of premixed insulin) as needed. When treating with multiple insulin injections, insulin secretagogue use should be discontinued. Figure 1 shows the treatment pathways for hyperglycaemia in T2DM.

9 | MEDICAL NUTRITION THERAPY

Patients with diabetes or prediabetes require individualized medical nutrition therapy, which should be provided by the guidance of a dietician who is familiar with diabetes treatment or a comprehensive integrated diabetes management team (including a diabetes educator). To achieve the metabolic control objectives for patients and satisfy their dietary preferences, reasonable quality objects should be established. In order to control the total energy intake and distribute various nutrients in a reasonable and balanced manner, the nutrition status should be evaluated before setting quality objectives.

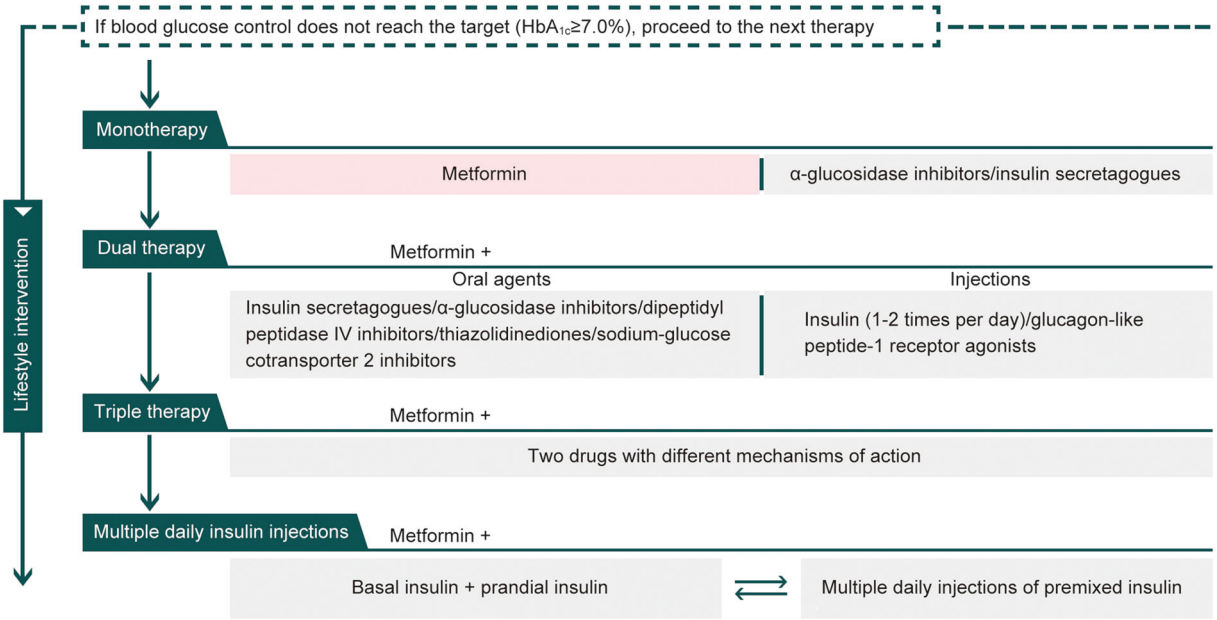

FIGURE 1 The treatment algorithm for high blood glucose in type 2 diabetes. Note: HbA1c: glycated hemoglobin; Metformin is the preferred drug for monotherapy treatment. It may be given to obese patients receiving multiple daily insulin injections. Figure 1 reflects the primary drug treatments paths recommended based on clinical evidence of the drug's efficacy and safety, health and economic benefits and the national conditions in China

The objectives of medical nutrition therapy include the following[38,39]:

1. Maintaining a proper body weight: The weight loss goal for overweight/obese patients is 5% to 10% of body weight in 3 to 6 months. People who are underweight should recover and maintain an ideal body weight over the long term via a sound nutrition plan.
2. Providing balanced nutrition to meet the needs of patients for micronutrients.
3. Achieving and maintaining ideal blood glucose levels and reducing the HbA1c level.
4. Reducing risk factors for cardiovascular disease, including control of blood lipids and blood pressure.

9.1 | Nutrients

Patients with prediabetes or diabetes mellitus should follow individualized energy balance plans, with the goal of achieving or maintaining ideal body weight and meeting nutritional needs. Dietary energy provided by fat should account for 20% to approximately 30% of total calorie intake, and carbohydrate should account for 50% to approximately 65% of total calorie intake. In diabetic patients with normal renal function, protein intake should account for 15% to approximately 20% of the total calorie intake. The recommended protein intake is about 0.8 g/kg/day. Excessive protein intake (eg, >1.3 g/kg/day) is associated with increased proteinuria, decreased renal function, increased cardiovascular, and mortality risk. Protein intake below 0.8 g/kg/day does not delay the progression of diabetic nephropathy. Patients receiving dialysis can increase protein intake appropriately. Drinking alcohol is not recommended for diabetic patients. Energy from alcohol intake should be calculated in the total energy for patients who do drink alcohol. For women, no more than 15 g of alcohol per day should be consumed. For men, no more than 25 g (15 g of alcohol is equivalent to 350 mL of beer, 150 mL of wine, or 45 mL of distilled alcohol) should be consumed.

Increasing dietary fibre intake is beneficial to health. The recommended daily intake of dietary fibre for diabetic patients is 10 to 14 g/1000 kcal. Salt intake is limited to 6 g per day, and sodium intake is no more than 2000 mg per day. Diabetic patients are prone to lack B vitamins, vitamin C, vitamin D, chromium, zinc, selenium, magnesium, iron, manganese, and other micronutrients, which can be supplemented according to the results of nutritional assessment. Different eating patterns should be designed by professionals, with consideration of patients' metabolic goals and personal preferences (eg, customs, culture, religion, health concepts, economic status, etc).

10 | EXERCISE THERAPY FOR TYPE 2 DIABETES

Exercise plays an important role in the comprehensive management of T2DM. Regular exercise helps control blood glucose, reduces cardiovascular risk factors, reduces weight, and improves overall well-being. Moreover, exercise has a substantial primary preventive effect on populations at high risk of diabetes. Epidemiological studies have shown that regular exercise of more than 8 weeks reduced HbA1c level by 0.66% and that mortality is significantly reduced among those with diabetes who adhered to regular exercise for 12 to 14 years. The key points of exercise therapy include the following:

1. Adults with T2DM should engage in moderate-intensity aerobic activity for at least 150 minutes per week.
2. Adults with T2DM are encouraged to take more daily physical activities and reduce sedentary time.[40,41]
3. Exercise may be contraindicated in patients with extremely poor glucose control, acute complications, or severe chronic complications.

11 | SMOKING CESSATION

Every diabetic smoker should be advised to stop smoking or using tobacco products and reduce second-hand smoke exposure. Patients' smoking status and the extent of nicotine dependence should be assessed. Brief consultations and hotlines for quitting should be provided, and if necessary, medications should be prescribed to help patients quit smoking. Individuals should be educated regarding the synergistic risks of smoking in diabetes, especially for cardiovascular disease. The authority of the clinician should be used to make clear that smoking cessation is as important as any other part of the treatment plan. Standard advice for quitting smoking includes the following: (1) recognize that abstinence is the objective because reducing the rate of smoking places individual at risk for return to previous levels, (2) set a quite date, (3) identify circumstances likely to encourage relapse and make specific plans for dealing with them, (4) enlist the cooperation of family members and friends, and (5) remain vigilant for 6 to 12 months until nonsmoking has been well established. Given its importance, clinicians should continue to monitor smoking status and praise maintained nonsmoking.

12 | PHARMACOLOGIC THERAPY FOR HYPERGLYCAEMIA

12.1 | Oral hypoglycaemic agents

Medical nutrition therapy and exercise treatment are basic for glucose control in T2DM. When diet and exercise cannot effectively control blood glucose levels, pharmacologic therapy, should be provided in a timely manner.

T2DM is a progressive disease. During the natural course of T2DM, the reliance on exogenous glycaemic control measures gradually increases. Clinical treatment often requires the use of oral medication or a combination of oral medication and injectable antidiabetic medications (eg, insulin and GLP-1 receptor agonists).

12.1.1 | Metformin

Metformin hydrochloride is the primary biguanide medication currently used in medical practice. The major pharmacological effect of biguanides is lowering blood glucose by reducing the hepatic glucose output and improving peripheral insulin resistance. The diabetes treatment guidelines of many countries and international organizations recommend metformin as the basic medication among the first-line medications and combinations for control of hyperglycaemia in T2DM. Meta-analyses of clinical trials have shown that metformin can reduce HbA1c levels by 1.0% to 1.5% versus placebo and can also reduce body weight.[4] Clinical trials in Chinese patients with T2DM have shown that metformin can decrease HbA1c by 0.7% to 1.0%.[42,43] However, no significant difference was observed in glucose control between metformin alone and low-dose metformin plus DPP-4 inhibitors.[44,45] The UKPDS study results showed that metformin also decreased the likelihood of cardiovascular events and death in obese patients with T2DM.[46] In China, randomized controlled clinical trials have been conducted to investigate the effect of metformin and sulfonylureas on recurrent cardiovascular events in patients with T2DM combined with coronary heart disease, and the results showed that metformin treatment was correlated with a significant reduction of major cardiovascular events.[47] Metformin alone did not cause hypoglycaemia, but the combination of metformin and insulin or insulin secretagogues increased the risk of hypoglycaemia.

The main adverse effects of metformin are gastrointestinal reactions. Starting with a small dose and gradually increasing the dosage were effective ways to reduce adverse reactions. Biguanides are contraindicated in patients with renal insufficiency (serum creatinine >132.6 μmol/L [1.5 mg/dL] for men or >123.8 μmol/L [1.4 mg/dL] in women or an estimated glomerular filtration rate [eGFR] < 45 mL/min/(1.73 m^2)), liver dysfunction, severe infection, or hypoxia, or in patients undergoing major surgery. The dose of metformin should be reduced if eGFR is 45 to 59 mL/min/(1.73 m^2). Moreover, metformin should be temporarily discontinued for patients undergoing angiography with iodinated contrast agents. The relationship between metformin and lactic acidosis risk is uncertain. Long-term use of metformin may cause vitamin B12 deficiency.

12.1.2 | Sulfonylureas

Sulfonylureas are insulin secretagogues whose main pharmacological effect is increasing insulin levels by stimulating insulin secretion from pancreatic β cells and therefore lowering blood glucose levels. Sulfonylureas can reduce HbA1c level by 1.0% to 1.5%.[48] Prospective and randomized clinical studies have shown that the use of sulfonylureas was associated with a reduced risk of diabetic microvascular and macrovascular diseases.[21,49] Currently, the main commercially available sulfonylureas in China are gliburide, glimepiride, gliclazide, glipizide, and gliquidone. Sulfonylureas, if used improperly, can lead to hypoglycaemia, particularly in elderly patients and in those with liver and kidney dysfunctions. Sulfonylureas may also cause weight gain. Patients with mild renal insufficiency should use gliquidone. Xiao Ke Wan is a fixed dose combination drug containing glyburide and various TCMs that have the antihyperglycaemic effect similar to that of glyburide. Compared with glyburide alone, Xiao Ke Wan carries a lower risk of hypoglycaemia.[50]

12.1.3 | Thiazolidinediones

TZDs decrease blood glucose primarily by increasing the target cells' sensitivity to the action of insulin. Currently, the main commercially available TZDs in China are rosiglitazone and pioglitazone. Clinical trials in Chinese patients with T2DM have shown that TZDs can decrease HbA1c by 0.7% to 1.0%.[51-53]

TZDs do not cause hypoglycaemia when used alone, but they may increase the risk of hypoglycaemia when used in combination with insulin or insulin secretagogues. Weight gain and oedema are common adverse effects of TZDs, and these adverse effects are more remarkable when TZDs are used in combination with insulin. TZD use has been correlated with increased risk of fractures and heart failure. Contraindications for TZDs are heart failure (New York Heart Association heart function classification class II and above), active liver disease, transaminase elevations exceeding 2.5 times the upper limit of normal, and severe osteoporosis and fractures.

12.1.4 | Glinides

Glinides are nonsulfonylurea insulin secretagogues. The currently available glinides in China are repaglinide, nateglinide, and mitiglinide. This class of medications reduces postprandial blood glucose by stimulating insulin secretion in the early phase. They can lower HbA1c by 0.5% to 1.5%.[54] These medicines must be taken immediately before a meal and can be used separately or in combination with other antidiabetic medications. For newly diagnosed patients with T2DM, combination therapy using repaglinide with metformin reduced HbA1c more significantly than repaglinide alone but with a significantly increased risk of hypoglycaemia.[55]

Common adverse effects of glinides are hypoglycaemia and weight gain, but the risk and degree of hypoglycaemia are lower with glinides than with sulfonylureas. Glinides can be used in patients with renal insufficiency.[54]

12.1.5 | α-Glucosidase inhibitors

α-Glucosidase inhibitors reduce postprandial blood glucose by inhibiting carbohydrate absorption in the upper small intestine. They are suitable for patients who consume carbohydrates as their main food ingredient and experience postprandial hyperglycaemia. Commercially available α-glucosidase inhibitors in China include acarbose, voglibose, and miglitol. Clinical studies in Chinese patients with T2DM showed that for newly diagnosed patients with diabetes, acarbose 300 mg/day demonstrated a similar hypoglycaemic effect to that of metformin 1500 mg/day.[56] α-Glucosidase inhibitors can be used in combination with biguanides, sulfonylureas, TZDs, or insulin.

Common adverse reactions to α-glycosidase inhibitors are gastrointestinal reactions, such as abdominal distension and flatulence. Starting with a small dose and gradually increasing the dose are effective ways to reduce adverse effects. The risk of hypoglycaemia is very low when α-glycosidase inhibitors are used alone. When patients using α-glucosidase inhibitors manifest hypoglycaemia, glucose or honey can be used as treatments; dietary sucrose and starchy foods have a poor ability to correct hypoglycaemia.

12.1.6 | Dipeptidyl peptidase 4 inhibitors

DPP-4 inhibitors increase the endogenous level of GLP-1 by reducing the deactivation of GLP-1 in vivo through inhibition of DPP-4. GLP-1 enhances insulin secretion and inhibits glucagon secretion in a glucose-dependent manner. Commercially available DPP-4 inhibitors in China include sitagliptin, saxagliptin, vildagliptin, linagliptin, and alogliptin. Clinical trials in patients with T2DM in China have shown that DPP-4 inhibitors reduce HbA1c level by 0.4% to 0.9%.[42,43,57-71] The use of DPP-4 inhibitors alone does not increase the risk of hypoglycaemia and includes a neutral or mild effect on weight gain.[57] Sitagliptin, saxagliptin, and alogliptin do not increase the risk of cardiovascular disease. If sitagliptin, saxagliptin, alogliptin, or vildagliptin are prescribed for patients with renal dysfunction, the dosage must be reduced according to the instructions accompanying the medication. Dosage adjustments are unnecessary when using linagliptin in patients with liver or renal insufficiency.[57] Clinical studies in China have shown that HbA1c levels can be further reduced after glimepiride, gliclazide, repaglinide, or acarbose is added to the combination therapy with metformin and sitagliptin.

12.1.7 | Sodium-glucose cotransporter 2 inhibitors

SGLT2 inhibitors reduce glucose levels by inhibiting renal tubular SGLT2 responsible for glucose reabsorption from urine, reducing the renal glucose threshold and promoting urinary glucose excretion.[72,73] Commercially available SGLT2 inhibitors in China include dapagliflozin, empagliflozin, and canagliflozin. SGLT2 inhibitors can reduce HbA1c levels by approximately 0.5% to 1.0%, reduce body weight by 1.5 to 3.5 kg, and lower systolic blood pressure by 3 to 5 mmHg. SGLT2 inhibitors reduce the risk of major cardiovascular adverse events, renal events, and hospitalization rates for heart failure.[74] SGLT2 inhibitors do not increase the risk of hypoglycaemia when used alone. The dose of SGLT2 inhibitors should be reduced in patients with moderate renal impairment and discontinued in severe renal impairment. Common adverse effects of SGLT2 inhibitors are genitourinary tract infections. Rare adverse reactions include increased risk of ketoacidosis, acute kidney injury, bone fracture, and need for toe amputation (canagliflozin).[73,75-77]

12.2 | Glucagon-like peptide-1 receptor agonists

GLP-1 receptor agonists reduce blood glucose by activating the GLP-1 receptors. They enhance insulin secretion and inhibit glucagon secretion in a glucose-dependent manner, delay gastric emptying, thus reducing food intake via central appetite suppression. Commercially available GLP-1 receptor agonists in China include exenatide, liraglutide, lixisenatide, and beinaglutide,[78-81] all of which require

subcutaneously injection. GLP-1 receptor agonists effectively lower blood glucose and also significantly reduce body weight and improve triglycerides and blood pressure. GLP-1 receptor agonists alone do not significantly increase the risk of hypoglycaemia. GLP-1 receptor agonists may be used alone or in combination with other hypoglycaemic agents. Several clinical studies have shown that the addition of GLP-1 receptor agonists is effective after failure of an oral hypoglycaemic agent (metformin, sulfonylureas). Common adverse effects of GLP-1 receptor agonists are gastrointestinal symptoms (eg, nausea and vomiting) that occur mainly in the initial stage of treatment and gradually diminish as treatment time is increased. Studies have shown that liraglutide, lixisenatide, and exenatide exert protective effects in patients with T2DM with a history of cardiovascular disease or cardiovascular risk factors.[82-84]

12.3 | Insulin

12.3.1 | Recommendations

- Patients with T2DM who are not achieving glycaemic goals with lifestyle intervention and oral hypoglycaemic agents should initiate insulin therapy as soon as possible, ideally within 3 months of recognition of failure of lifestyle intervention and other combination of oral medication therapies (A).
- Insulin therapy may start with one to two daily injections in patients with T2DM (A).
- Multiple daily insulin injections (two to four injections per day) or continuous subcutaneous insulin infusion (CSII) are available for insulin therapy (A).
- Short-term (2 weeks to 3 months) intensive insulin treatment may be implemented in newly diagnosed patients with T2DM with HbA1c-9.0% or FPG ≥ 11.1 mmol/L and symptomatic hyperglycaemia (A).

Insulin therapy is an important approach for glucose control. Patients with T1DM require insulin to sustain life, control blood glucose, and reduce the risk of diabetic complications. Insulin is also needed in patients with T2DM who do not respond to or are contraindicated for oral hypoglycaemic agents to control blood glucose and reduce the risk of diabetic complications.

Depending on the source and chemical structure, insulin can be divided into animal insulin, human insulin, and insulin analogues. According to the pharmacokinetic properties, insulin can also be classified into rapid-acting insulin analogues, regular (short-acting) insulin, intermediate-acting insulin, long-acting insulin, long-acting insulin analogues, premixed insulin, and premixed insulin analogues. The insulin treatment paths for T2DM are shown in Figure 2.

13 | METABOLIC SURGERY FOR TYPE 2 DIABETES

Obesity commonly accompanies T2DM. Obesity and T2DM significantly increase the risk of CVD. Clinical evidence shows that bariatric surgery significantly improves glucose control in obese patients with T2DM. Moreover, bariatric surgery significantly reduces the risk of diabetic macrovascular and microvascular complications and improves obesity-related conditions.[85-89] Accordingly, it has recently been termed "metabolic surgery."

13.1 | Indications for metabolic surgery

Patients with T2DM who are 18 to 60 years old, who are generally in good health, who have a low surgical risk, in whom disease control or control of comcomitant conditions is difficult to achieve (HbA1c > 7.0%) after lifestyle interventions and various drug treatments, and who meet the following conditions may consider metabolic surgery[90]:

1. Indications: Metabolic surgery is feasible if the patient with T2DM has BMI ≥ 32.5 kg/m^2, with or without diabetic complications.[91]

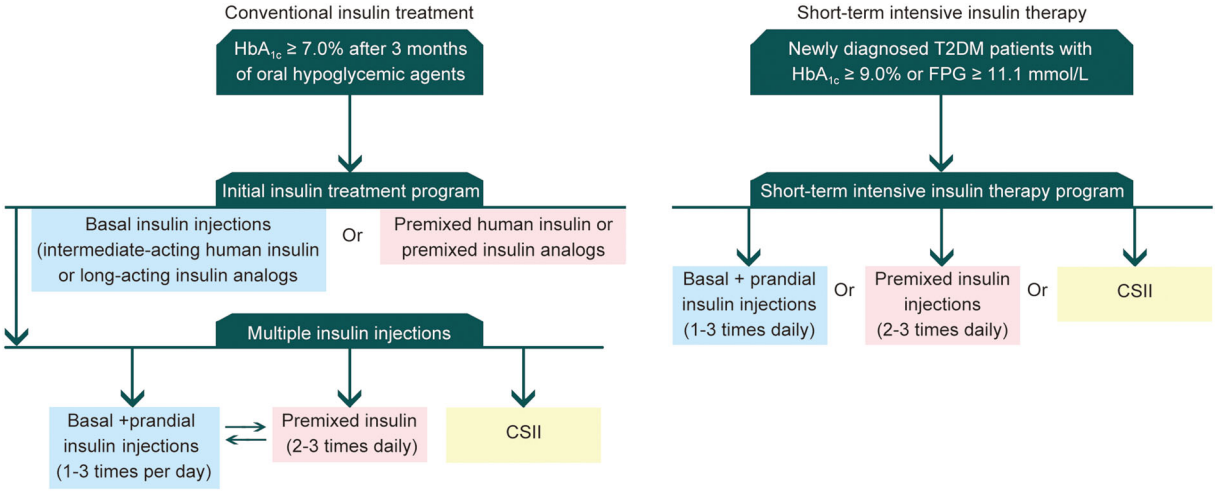

FIGURE 2 Insulin treatment paths for type 2 diabetes. HbA1c, glycated haemoglobin; FPG, fasting plasma glucose; CSII, continuous subcutaneous insulin infusion

2. Precautions: Metabolic surgery could be considered with caution for patients with T2DM with 27.5 kg/m^2 ≤ BMI < 32.5 kg/m^2, particularly in the presence of other cardiovascular risk factors.[92]
3. Not recommended: Patients with T2DM with 25.0 kg/m^2 ≤ BMI < 27.5 kg/m^2, but metabolic surgery may be considered if central obesity (waist circumstance ≥90 cm in men and ≥ 85 cm in women) is present along with at least two additional metabolic syndrome components: high triglycerides (TGs), low high-density lipoprotein cholesterol (HDL-C), or hypertension. Metabolic surgery should be regarded as purely for clinical research and must be approved by the Medical Ethics Committee in advance. Currently, evidence is insufficient, and surgery is not recommended as a routine clinical treatment. Surgery should be conducted in strict accordance with study protocol with the patient's informed consent.

13.2 | Contraindications for metabolic surgery[93]

1. Patients who abuse drugs, are addicted to alcohol, or have a mental illness that is difficult to control, and who lack the ability to understand the risks, benefits, and expected consequences of metabolic surgery.
2. Patients with confirmed, diagnosed T1DM.
3. Patients with T2DM who have a clear failure of pancreatic β cell function.
4. Contraindications for surgery.
5. Patients with BMI < 25 kg/m^2.
6. Patients with GDM and other specific types of diabetes.

13.3 | Efficacy evaluation of metabolic surgery

Remission of T2DM is defined as HbA1c ≤ 6.5% with lifestyle intervention alone after operation.

13.4 | Management of metabolic surgery

Metabolic surgery requires multidisciplinary teams for comprehensive preoperative, intraoperative, and postoperative management.[94-96] Life-long follow-up should be provided to patients after surgery, and micronutrients and nutritional status should be routinely monitored and evaluated.

14 | PREVENTION AND TREATMENT OF CARDIOVASCULAR AND CEREBROVASCULAR DISEASES IN PATIENTS WITH TYPE 2 DIABETES

Diabetes is an independent risk factor for cardiovascular and cerebrovascular diseases. FPG and postprandial hyperglycaemia are correlated with an increased risk of cardiovascular and cerebrovascular diseases, even when they do not reach the diagnostic criteria for diabetes. Diabetic patients often present with other important risk factors for cardiovascular and cerebrovascular diseases, such as hypertension and dyslipidaemia.

Clinical evidence suggests that strict glycaemic control in patients with T2DM has a limited effect on reducing the risks of cardiovascular and cerebrovascular diseases and death from those causes, particularly among patients with a longer disease duration, who are older, and who have a history of cardiovascular diseases or multiple cardiovascular risk factors. However, the comprehensive management of multiple risk factors can significantly decrease the risk of cardiovascular and cerebrovascular diseases and death from those causes in patients with diabetes. Therefore, the prevention of diabetic vascular diseases requires the comprehensive assessment and control of cardiovascular disease risk factors (ie, high blood glucose, hypertension, and dyslipidaemia) and appropriate antiplatelet therapy.

At present, the incidence of cardiovascular risk factors is high among patients with T2DM in China, and they are insufficiently controlled. Among outpatients with T2DM, only 5.6% achieved all triple therapeutic goals for HbA1c, blood pressure, and total cholesterol. The use of aspirin has also been low.[4] Clinically, more active screening and treatment of cardiovascular risk factors and an increased prescription or recommendation of aspirin therapy are recommended.

14.1 | Screening

The risk factors of CVD should be assessed at least annually following the diagnosis of diabetes, including the present and past history of CVD, age, risk factors for CVD (smoking, hypertension, dyslipidaemia, obesity, especially abdominal obesity, family history of young-onset cardiovascular disease), kidney injury (increased urinary albumin excretion rate, etc), and atrial fibrillation (which can cause stroke).

14.2 | Cardiovascular disease risk factor control

14.2.1 | Antihypertensive treatment

1. The blood pressure target is <130/80 mmHg in most diabetic patients with hypertension.[97,98] A less stringent blood pressure target may apply (<140/90 mmHg) in elderly patients and those with severe coronary heart disease.[99]
2. Antihypertensive treatment may be considered in diabetic patients with blood pressure ≥ 140/90 mmHg. Patients with blood pressure ≥ 160/100 mmHg or 20/10 mmHg above the target should initiate immediately with single-agent treatment or multiple-drug therapy.[97,100]
3. Five types of antihypertensive agents [angiotensin-converting enzyme inhibitor (ACEI), angiotensin II receptor blocker (ARB), diuretics, calcium antagonists, β-blockers] may be used in patients with diabetes, with ACEI and ARB preferred.[101-105]

4. Lifestyle intervention should be initiated in diabetic patients with blood pressure ≥ 120/80 mmHg to prevent hypertension.

14.2.2 | Lipid-lowering therapy

1. The primary goal is to reduce LDL-C to the target (very high risk of ASCVD: <1.8 mmol/L, high risk of ASCVD: <2.6 mmol/L).[106]
2. Statins are the preferred lipid-lowering drugs. Lipid-lowering therapy should start with a moderate-intensity statin, and the dose should be adjusted according to individual response to medication and tolerability. Other types of lipid-lowering drugs may be added if statins are unsuccessful in controlling cholesterol.
3. LDL-C reduction by ≥50% may be used as an alternative target in the event of high baseline LDL-C and failure to reduce LDL-C to the target after 3 months of standard lipid-lowering therapy.
4. TG-lowering drugs should be given first to prevent acute pancreatitis if fasting TG is ≥5.7 mmol/L.[106]

14.2.3 | Antiplatelet therapy

1. Aspirin (75-150 mg/day) should be used as secondary prevention in patients with diabetes and ASCVD.
2. Clopidogrel (75 mg/day) should be used as secondary prevention in patients with ASCVD with documented aspirin allergy.
3. Aspirin (75-100 mg/day) may be considered as primary prevention in patients with diabetes who are at risk for cardiovascular disease, including patients aged ≥50 years with at least one additional major risk factor (family history of young-onset ASCVD, hypertension, dyslipidaemia, smoking, albuminuria).[107-110]

15 | HYPOGLYCAEMIA

During treatment, patients may experience hypoglycaemia, which may cause discomfort and can be life-threatening. Hypoglycaemia poses a major obstacle to reaching blood glucose targets and warrants special attention.

15.1 | Classification of hypoglycaemia

1. Hypoglycaemia alert value: blood glucose ≤3.9 mmol/L.
2. Clinically significant hypoglycaemia: blood glucose <3.0 mmol/L.
3. Severe hypoglycaemia: no specific glucose threshold but severe cognitive impairment that requires external assistance for recovery.[38]

15.2 | Hypoglycaemia treatment

An individualized treatment plan should be developed to reach maximum glucose control with minimal risk of hypoglycaemia in patients with diabetes. The treatment plan should include monitoring the

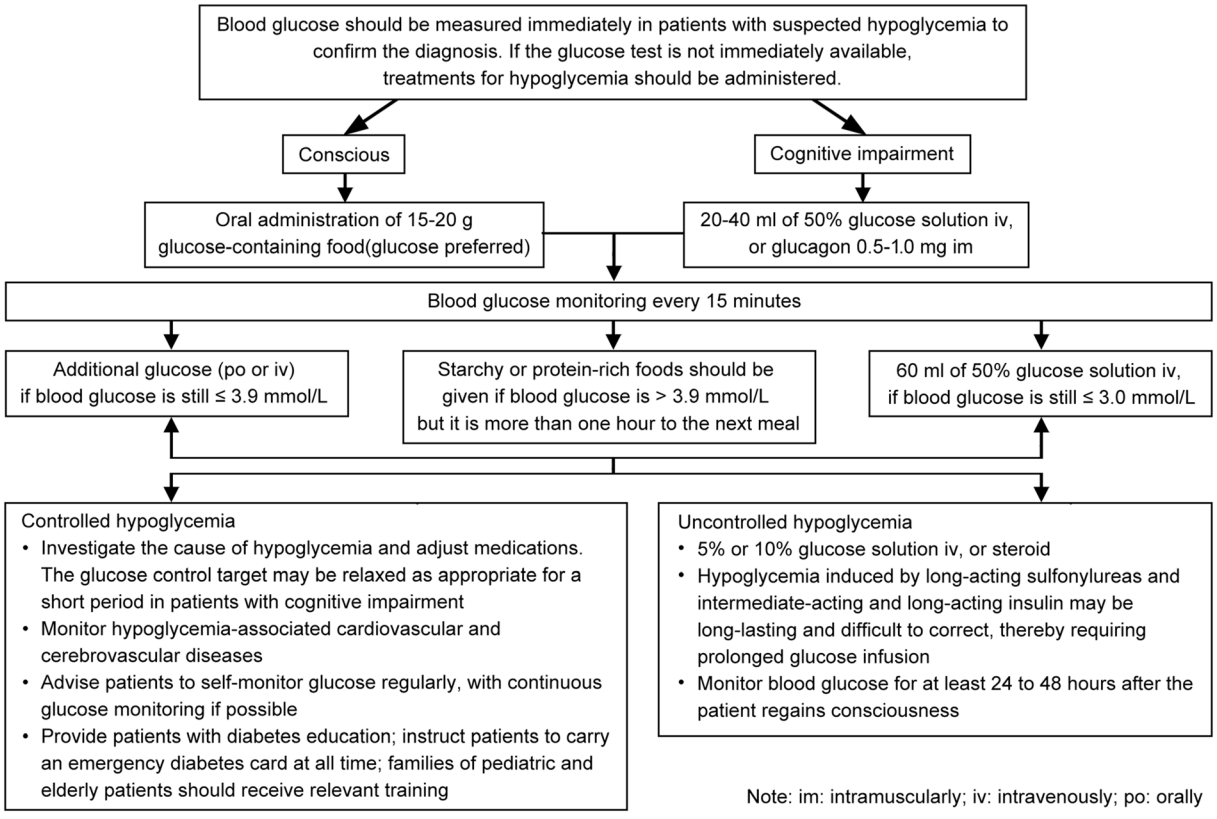

FIGURE 3 The treatment algorithm for hypoglycaemia

causes or antecedents of hypoglycaemia, timely and appropriate response to antecedents, and prompt treatment in response to hypoglycaemia.

Glucose or glucose-containing foods should be given when blood glucose is ≤3.9 mmol/L in patients with diabetes. For severe hypoglycaemia, proper care and monitoring should be given according to the patient's cognitive function and blood glucose level (Figure 3).

16 | CHRONIC DIABETIC COMPLICATIONS

16.1 | Diabetic kidney disease

16.1.1 | Recommendations

- It is recommended that patients with T2DM have urinary albumin/creatinine ratio (UACR) and eGFR evaluated at least once a year (B).
- Effective hypoglycaemic therapy and blood pressure management delay the development and progression of diabetic kidney disease (A).
- ACEIs or ARBs are preferred treatments in patients with diabetes with hypertension and UACR >300 mg/g, or eGFR <60 mL/min/1.73 m^2 (A).
- ACEIs or ARBs are preferred treatments in patient with diabetes with hypertension and UACR of 30 to 300 mg/g (B).
- Recommended protein intake should be approximately 0.8 g/kg/day in patients with diabetic kidney disease. It may be slightly higher in patients on dialysis (B).
- Renal replacement therapy should be given in patients with eGFR <30 mL/min/1.73 m^2 (A).

16.1.2 | Definition

Chronic kidney disease (CKD) is defined as chronic abnormalities of kidney structure and function. Diabetic kidney disease (DKD) refers to CKD that is specific to diabetes. Approximately 20% to 40% of diabetic patients suffer from diabetic kidney disease in China, which is the main cause of CKD and end-stage renal failure in patients with diabetes.[111,112]

16.1.3 | Screening

Once diagnosed, patients with T2DM should have an initial screening as soon as possible and at least once a year thereafter, including urine routine, urinary albumin/creatinine ratio (UACR), and serum creatinine (for eGFR).

16.1.4 | Diagnosis and classification

DKD is diagnosed by elevated urinary albumin excretion and reduced eGFR in the absence of other primary causes of kidney damage. Those with the following symptoms should be considered as possibly having nondiabetic kidney disease and referred to a nephrologist: abnormal urinary sediment (hematuria, proteinuria with hematuria, and tubular urine), rapid decline in eGFR, no retinopathy (especially T1DM), rapid urine increase of UACR within a short period, or nephrotic syndrome. The pathological diagnosis is the gold standard of DKD. The pathological examination of kidney biopsy is feasible when it is difficult to identify the cause, but it is not recommended as routine examination in diabetic patients.

Spot urine sample is recommended to assess UACR. The diagnostic value of 24-hour urinary albumin is equal to UACR. Albuminuria is confirmed if at least two of three tests are abnormal after an additional ACR measurement within 3 to 6 months and in the absence of urinary tract infection. Albuminuria is defined as albumin/creatinine ratio of 30 mg/g or more, microalbuminuria as albumin/creatinine ratio between 30 and 300 mg/g, and macroalbuminuria as albumin/creatinine ratio > 300 mg/g. The eGFR should be calculated using MDRD or CKD-EPI formula (http://www.nkdep.nih.gov). The stages of chronic kidney disease are shown in Table 8.

16.1.5 | Treatment

1. Lifestyle changes mainly include reasonable weight control, healthy diet adhering to dietary guidelines under medical nutrition therapy, smoking cessation, and proper exercise.
2. Recommended protein intake is approximately 0.8 g/kg/day in patients with diabetic kidney disease.
3. Well-control blood glucose, blood pressure, and dyslipidaemia may delay the development and progression of kidney dysfunction.
4. Dialysis therapy and transplantation should be considered in patients with eGFR <30 mL/min/1.73 m^2.

TABLE 8 Stages of renal function in chronic kidney disease (CKD)

CKD Stage		Feature Description	eGFR [mL/min/1.73 m^2]
1		Increased GFR or normal GFR with kidney damage[a]	≥90
2		Slightly decreased GFR with kidney damage[a]	60-89
3	3a	Mild to moderate GFR decrease	45-59
	3b	Moderate to severe GFR decrease	30-44
4		Severe GFR decrease	15-29
5		Kidney failure	<15 or dialysis

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate.

[a]Kidney injury is defined as albuminuria (UACR ≥ 30 mg/g) or as an abnormality in pathological, urine, blood or imaging examinations.

16.2 | Diabetic retinopathy

16.2.1 | Recommendations

- Once diagnosed, patients with T2DM should have an initial comprehensive eye exam. Patients with T1DM should have a comprehensive eye exam within 5 years of diagnosis. Patients with no diabetic retinopathy should have a comprehensive eye exam at least every 1 to 2 years, and the frequency should increase in patients with diabetic retinopathy (B).
- Well-controlled blood glucose, blood pressure, and blood lipids may prevent or delay the progression of diabetic retinopathy (A).
- Patients with moderate or severe nonproliferative retinopathy identified during screening should be referred to an ophthalmologist.

16.2.2 | Definition

Diabetic retinopathy is characterized by gradually progressive alterations in the retinal microvasculature, leading to a series of typical lesions caused by diabetes. It is one of the most common diabetic microvascular complications and the leading cause of preventable blindness in working-aged people[113]

16.2.3 | Screening and follow-up

Patients with T2DM should have an initial comprehensive eye examination at the time of or as soon as possible following diagnosis, including visual acuity and retinal examination. Patients with T1DM should have a comprehensive eye exam within 5 years of diagnosis.

In the absence of comprehensive eye screening by ophthalmologists, the nonmydriatic retinal photography of at least two posterior pole photographs at 45 ocular angles is a feasible screening method for diabetic retinopathy.[114] Patients with moderate or severe nonproliferative retinopathy identified during screening should follow-up with an ophthalmologist.

Diabetic patients without retinopathy are recommended to undergo follow-up check-up once every 1 to 2 years; patients with mild retinopathy should be checked once a year, and patients with moderate retinopathy should be checked once every 3 to 6 months. Patients with severe retinopathy should be checked once every 3 months. Eye examinations should occur before pregnancy or in the first trimester after which patients should be monitored every 3 months postpartum and for 1 year postpartum as indicated by the degree of retinopathy.

16.2.4 | Diagnosis and classification

Diabetic retinopathy has to be graded according to the international clinical grading standard for diabetic retinopathy (2002), in which macular oedema is included (Tables 9 and 10).[115]

TABLE 9 International diabetic retinopathy disease severity scale (2002)

Proposed Disease Severity Level	Findings Observable on Dilated Ophthalmoscopy
No apparent retinopathy	No abnormality
NPDR	
Mild	Microaneurysms only
Moderate	More than just microaneurysms but less than severe nonproliferative diabetic retinopathy
Severe	Any of the following, but no signs of proliferative retinopathy 1. More than 20 intraretinal haemorrhages in each of four quadrants. 2. Definite venous beading in two or more quadrants. 3. Prominent intraretinal microvascular abnormalities in one or more quadrants.
Proliferative diabetic retinopathy	One or more of the following: neovascularization, vitreous/preretinal haemorrhage

Abbreviation: NPDR, nonproliferative diabetic retinopathy.

TABLE 10 Diabetic macular oedema disease severity scale

Proposed Disease Severity Level	Findings Observable on Dilated Ophthalmoscopy
Diabetic macular oedema apparently absent	No apparent retinal thickening or hard exudates in posterior pole
Diabetic macular oedema apparently present	Some apparent retinal thickening or hard exudates in posterior pole
Mild	Some retinal thickening or hard exudates in posterior pole but distant from the centre of the macula
Moderate	Retinal thickening or hard exudates approaching the centre of the macula but not involving the centre
Severe	Retinal thickening or hard exudates involving the centre of the macula

16.2.5 | Treatment

1. Good control of blood glucose, blood pressure, and lipids may prevent or delay the progression of diabetic retinopathy.[21,116,117]
2. Patients with sudden blindness or retinal detachment require an immediate referral to an ophthalmologist. Diabetic patients with any degree of macular oedema, severe nonproliferative diabetic retinopathy, or any proliferative diabetic retinopathy should be referred to an experienced ophthalmologist for the diagnosis and treatment of diabetic retinopathy.
3. Laser photocoagulation therapy is the main treatment for high-risk proliferative diabetic retinopathy and severe nonproliferative diabetic retinopathy.[118,119]

4. Intravitreal injection of antivascular endothelial growth factor (VEGF) is suitable for vision-threatening diabetic macular oedema.[120]
5. Corticosteroids can also be used locally to treat vision-threatening diabetic retinopathy and macular oedema.
6. Retinopathy is not a contraindication to aspirin therapy. Aspirin therapy does not increase the risk of retinal haemorrhage.

16.3 | Diabetic neuropathy

16.3.1 | Recommendations

- A complete neurologic evaluation should be started 5 years after the diagnosis of T1DM and at the time of T2DM diagnosis, followed up at least once a year thereafter (B).
- Neurologic testing including temperature sensation, pinprick sensation, vibration perception, pressure sensation, and ankle reflexes are recommended for screening of distal symmetric polyneuropathy (DSPN) (B).
- Well-controlled blood glucose delays the progression of diabetic neuropathy (B).

16.3.2 | Definition

Diabetic neuropathy is one of the most common chronic complications of diabetes. Neuropathy may affect the central nervous system or, more commonly, the peripheral nerves. Diabetic central neuropathy is the damage of brain, cerebellum, brainstem, motor neurons of the spinal cord, and nerve fibres, as well as the injury of sensory nerve fibres in the spinal cord. Diabetic peripheral neuropathy (DPN) refers to peripheral nerve dysfunction, including spinal nerves, cranial nerves, and autonomic neuropathy. DSPN is a typical diabetic neuropathy.

16.3.3 | Screening

A complete neurologic evaluation should be started 5 years after the diagnosis of T1DM and at the time of diagnosis of T2DM, and re-evaluated at least once a year thereafter.

Neurologic testing included thermal sensitivity, pinprick sensation, vibration perception, and pressure sensation, and ankle reflexes are recommended for the screen of DSPN. For epidemiologic surveys or primary medical care units, the use of 128-Hz tuning fork (for large fibre function) and 10-g monofilament testing are recommended to identify the risk of foot ulcers and amputations.

16.3.4 | Diagnosis and classification

16.3.4.1 | Diagnosis

Patients with typical symptoms are easy to detect and diagnose, and asymptomatic patients need to be diagnosed by physical examination or neuroelectrophysiological examination. The diagnosis should be made after excluding the following conditions: other causes of neuropathy such as cervical and lumbar disease (nerve root compression, spinal stenosis, cervical and lumbar degeneration), cerebral infarction, Green Bali syndrome, severe arteriovenous venereal disease changes (venous embolism, lymphangiogenesis), neurotoxicity of drugs, especially chemotherapeutic drugs, and damage to the nerves by the metabolic toxicants caused by renal insufficiency. If the above examinations cannot be confirmed, differential diagnosis is needed and can be done by electromyography.[4,121,122] The diagnostic flowchart of DPSN is shown in Figure 4.[123-126]

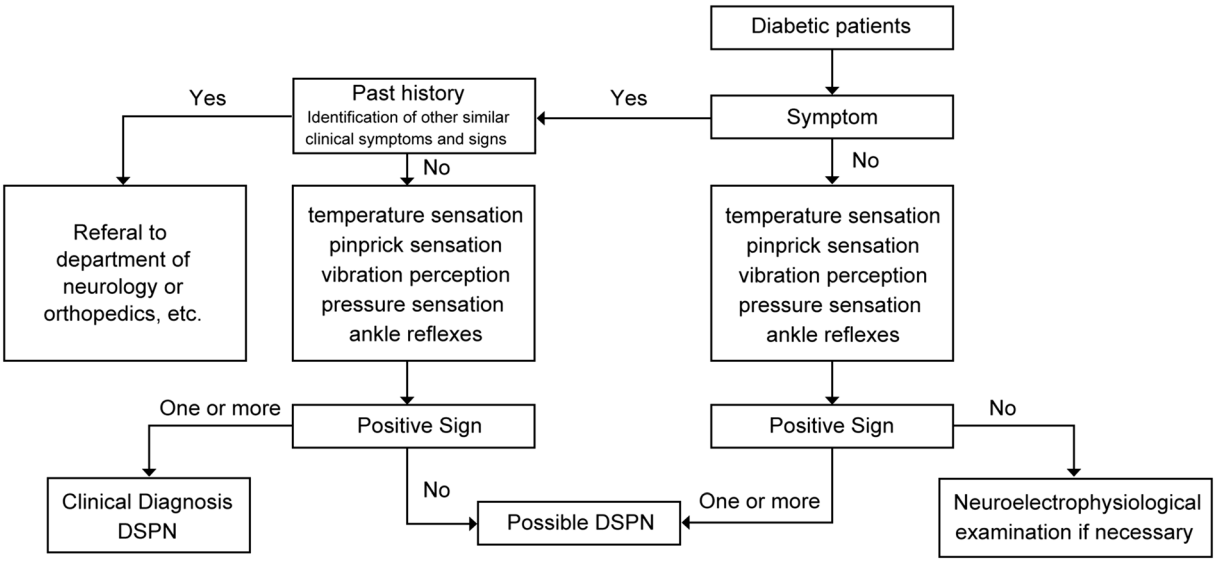

FIGURE 4 Diagnostic flowchart of distal symmetric polyneuropathy (DPSN)

16.3.4.2 | Diagnosis of diabetic autonomic neuropathy

1. Cardiac autonomic neuropathy can be screened by heart rate variability testing, postural hypotension testing, and ambulatory blood pressure monitoring.
2. Gastrointestinal neuropathies can be screened by scintigraphy and lectrogastrography.
3. Bladder dysfunction and erectile dysfunction: Ultrasound can be used to determine bladder volume and residual urine volume to determine bladder dysfunction.
4. Others: including ahidrosis, heat intolerance, dry skin, and hyperhidrosis.

16.3.5 | Treatment

1. Well-controlled blood glucose may delay the progression of diabetic neuropathy.
2. Symptomatic treatment: Medications for the treatment of painful diabetic neuropathy include anticonvulsants (pregabalin, gabapentin, valproate, and carbamazepine), antidepressants (duloxetine, amitriptyline, imipramine, and citalopram), opioids (tramadol and oxycodone), and capsaicin, etc.
3. Other treatments: nerve repair (such as methylcobalamin and growth factors), antioxidant stress (such as lipoic acid),[4,127] and improved microcirculation (prostaglandin E1, beraprost natriuretic peptide, cilostazol, pentoxifylline, pancreatic kallikrein, calcium antagonists, and blood circulation-promoting TCM).[128]

16.4 | Lower extremity arterial disease

16.4.1 | Definition

Lower extremity arterial disease (LEAD) is a component of peripheral artery disease that manifests as lower extremity arterial stenosis or occlusion.[129]

16.4.2 | Screening[130,131]

For patients with diabetes over the age of 50 years, LEAD screening should be conducted routinely. Patients with diabetes with LEAD-associated risk factors (eg, cardiovascular disease, dyslipidaemia, hypertension, smoking, or duration of diabetes of more than 5 years) should be screened at least once a year.

In patients with diabetes with foot ulcers and gangrene, regardless of their age, a comprehensive examination and evaluation of arterial disease should be conducted.

16.4.3 | Diagnosis and classification[132]

1. If the patient has a resting ankle-brachial index (ABI) $\leq$0.90, regardless of the presence of lower limb discomfort, a LEAD diagnosis should be considered.
2. For a patient who experiences discomfort upon moving and has a resting ABI $\geq$0.90: If ABI decreases by 15% to 20% after a treadmill test, a LEAD diagnosis should be considered.
3. If the patient has a resting ABI <0.40, or ankle arterial pressure <50 mmHg or toe arterial pressure <30 mmHg, a critical limb ischaemia diagnosis should be considered.

16.4.4 | Treatment

The therapeutic approach to LEAD includes the prevention of progression of systemic atherosclerotic disease, the prevention of cardiovascular events, the prevention of ischaemia-induced ulcers and gangrene, the prevention of amputation or the reduction of the amputation level, and the improvement of the functional status of patients with intermittent claudication.[131]

16.5 | Diabetic foot

16.5.1 | Recommendations

- Diabetic patients should have a comprehensive foot exam once every year (B).
- Diabetic patients should receive comprehensive education on foot self-care (B).
- Multidisciplinary collaboration is required for diagnosing and treating diabetic foot ulcers (B).

16.5.2 | Definition

Diabetic foot refers to foot ulcers, infections, and (or) deep tissue destruction associated with distal extremity nerve abnormalities and varying degrees of peripheral vascular lesions.

16.5.3 | Screening

Patient with diabetes should have a comprehensive foot exam once every year. During the exam, detailed information on the history of macroangiopathy and microangiopathy is collected, and current symptoms of neuropathy (pain, burning, numbness) and vascular disease in the lower extremities (fatigue, limping) are evaluated to determine the risk of ulcer and amputation.

The food exam should include the appearance of the foot (deformity, skin, fissures, infection, ulcer, amputation), neurological evaluation (10-g nylon monofilament test, prick or vibration test, or ankle

tendon reflexes), and vascular evaluation (vascular pulsation of the lower limbs and feet).

16.5.4 | Diagnosis and classification

Once diabetic foot disease is diagnosed, it should be evaluated within clinical classification. At present, the most widely accepted classification methods are Wagner grading (Table 11) and Texas grading (Table 12).[133]

16.5.5 | Treatment

A multidisciplinary approach is recommended to diagnose and treat diabetic foot ulcers.

1. Assess the severity of ulcers before treatment.
2. Antibiotic therapy: Antibiotics can be empirically selected before the results of bacterial culture and drug sensitivity tests.
3. Control of blood glucose.
4. Local treatment included debridement and hyperbaric oxygen therapy.
5. Referral to special units in the following situations: rapid changes in skin colour, exacerbation of local pain with redness and swelling, newly developed ulcers, deterioration of the original ulcers and involvement of soft tissue and/or bone tissue, disseminated cellulitis, signs of systemic infection, osteomyelitis, etc.

TABLE 11 The Wagner grading for diabetic foot

Grading	Clinical Manifestation
0	There are risk factors for foot ulcers, but there are no ulcers.
1	Superficial ulcers, no signs of infection, manifested as nerve ulcers
2	Deeper ulcers, often associated with soft tissue infection, without osteomyelitis or deep abscess
3	Deep ulcers with abscesses or osteomyelitis
4	Localized necrosis (toe, heel, or forefoot) characterized by ischemic gangrene, usually associated with neuropath
5	Full foot necrosis

TABLE 12 The Texas grading for diabetic foot

Grading	Characteristic	Classification	Characteristic
0	History of foot ulcers	A	No infection and ischemia
1	Superficial ulcers	B	With infection
2	Ulcers involve tendon	C	With ischemia
3	Ulcers involve bone and joints	D	With infection and ischemia

17 | SPECIAL TYPES OF DIABETES

17.1 | Diabetes in pregnancy

17.1.1 | Recommendations

- Patients with diabetes should carefully plan for pregnancy. Glucose control and chronic complications should be evaluated before pregnancy (B).
- It is recommended that patients with diabetes should not become pregnant until HbA1c is <6.5% in order to reduce the risk of congenital anomalies (B).
- Pregnant nondiabetic women should have one-step 75-g OGTT screening at 24 to 28 weeks of gestation (A).
- Patients should self-monitor blood glucose (FPG and postprandial glucose), with the frequency and schedule adjusted according to individual condition in order to facilitate glucose control and prevent hypoglycaemia (B).
- Lifestyle intervention is an essential component for diabetes care during pregnancy, and medications should be added in the event of uncontrolled glucose (A).
- Insulin is the preferred treatment for diabetes in pregnancy, as all oral agents lack long-term safety data (A).

17.1.2 | Diagnostic criteria

Diabetes in pregnancy included the following three types.

1. Gestational diabetes mellitus (GDM)
   GDM refers to glucose metabolic disorders of different severities during pregnancy, but the level of blood glucose has not reached that of overt diabetes. It accounts for 80% to 90% of all diabetes cases during pregnancy. GDM is diagnosed if 75-g OGTT at any time during pregnancy shows 5.1 mmol/L $\leq$ FPG < 7.0 mmol/L, OGTT 1hPG $\geq$ 10.0 mmol/L, or 8.5 mmol/L $\leq$ OGTT 2hPG < 11.1 mmol/L.[134]
2. Overt diabetes mellitus in pregnancy
   Overt diabetes in pregnancy is diagnosed if the glucose test at any time during pregnancy meets the diagnostic criteria of diabetes in nonpregnant population: FPG $\geq$ 7.0 mmol/L, OGTT 2hPG $\geq$ 11.1 mmol/L, or random plasma glucose $\geq$11.1 mmol/L.[134]
3. Pregestational diabetes mellitus (PGDM)
   PGDM refers to confirmed type 1, type 2, or special types of diabetes before pregnancy.

17.1.3 | Screening for diabetes during pregnancy

1. Screening in high-risk population
   People at risk for diabetes during pregnancy include women with a history of GDM, a history of macrosomia, obesity, polycystic ovarian syndrome (PCOS), family history of diabetes in first-degree relatives,

TABLE 13 Framework for considering treatment goals for glycaemia, blood pressure, and dyslipidaemia in older adults with diabetes[38]

Patient Characteristics/Health Status	Rationale	Reasonable HbA1c Goal, %[a]	Fasting or Preprandial Glucose, mmol/L	Bedtime Blood Glucose, mmol/L	Blood Pressure, mmHg	Blood Lipids
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.5	5.0-7.2	5.0-8.3	<140/90	Statins, unless contraindicated or not tolerated
Complex/intermediate (multiple coexisting chronic illnesses[b] or 2+ instrumental ADL Impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycaemia vulnerability, fall risk	<8.0	5.0-8.3	5.6-10.0	<140/90	Statins, unless contraindicated or not tolerated
Very complex condition/poor health (LTC or end-stage chronic illnesses[c] or moderate-to-severe cognitive impairment or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain	<8.5	5.6-10.0	6.1-11.1	<150/90	Consider likelihood of benefit with statin (secondary prevention more so than primary)

Note. This represents a consensus framework for considering treatment goals for glycaemia, blood pressure, and dyslipidaemia in older adults with diabetes. The patient characteristic categories are general concepts. Not every patient will clearly fall into a particular category. Consideration of patient and caregiver preferences is an important aspect of treatment individualization. Additionally, a patient's health status and preferences may change over time. A1C of 8.5% (69 mmol/mol) equates to an estimated average glucose of 200 mg/dL (11.1 mmol/L). Looser A1C targets above 8.5% (69 mmol/mol) are not recommended as they may expose patients to more frequent higher glucose values and the acute risks from glycosuria, dehydration, hyperglycaemic hyperosmolar syndrome, and poor wound healing. 1 mmHg = 0.133 kPa.

Abbreviation: ADL, activities of daily living.

[a]A lower A1C goal may be set for an individual if achievable without recurrent or severe hypoglycaemia or undue treatment burden.

[b]Coexisting chronic illnesses are conditions serious enough to require medications or lifestyle management and may include arthritis, cancer, congestive heart failure, depression, emphysema, falls, hypertension, incontinence, stage 3 or worse chronic kidney disease, myocardial infarction, and stroke. By "multiple," we mean at least three, but many patients may have five or more.

[c]The presence of a single end-stage chronic illness, such as stage 3 to 4 congestive heart failure or oxygen-dependent lung disease, chronic kidney disease requiring dialysis, or uncontrolled metastatic cancer, may cause significant symptoms or impairment of functional status, and significantly reduce life expectancy.

fasting urinary glucose positive during the first trimester, a history of unexplained recurrent spontaneous miscarriage, a history of intrauterine fetal demise, and a history of delivering a baby with neonatal respiratory distress syndrome. Blood glucose should be screened during the first maternity visit and repeated on a different day (within 2 weeks) in asymptomatic patients with FPG $\geq$ 7.0 mmol/L and/or random blood glucose $\geq$11.1 mmol/L, or 75 g OGTT 2hPG $\geq$ 11.1 mmol/L to confirm overt diabetes during pregnancy. Patients at risk for GDM with normal blood glucose during the first maternity visit should complete a 75-g OGTT at 24 to 28 weeks of gestation, which may be repeated during the third trimester if needed.

2. Screening in nonhigh-risk populations
   It is recommended that all pregnant women should have 75-g OGTT during 24 to 28 weeks of gestation (if not already done before) to evaluate glucose metabolism.

17.1.4 | Treatment

Lifestyle intervention is the essential component of diabetes care during pregnancy, and drug therapy should be added in the event of uncontrolled glucose. Insulin is the preferred treatment for diabetes during pregnancy. Since long-term safety data are lacking for oral hypoglycaemic agents, the standards advise against the use of oral hypoglycaemic agents during pregnancy.

17.2 | Diabetes in older adults

17.2.1 | Recommendations

- Elderly patients with diabetes should undergo comprehensive evaluation, including general health status, and be guided to set an

TABLE 14 Treatment targets in metabolic syndrome

Indicator	Target Value
Weight loss	7% to 10% in 1 year to achieve normal BMI and waist circumference
Blood pressure	<130/80 mmHg for diabetes patients <140/90 mmHg for nondiabetic patients
LDL-C	<2.60 mmol/L
TG	<1.70 mmol/L
HDL-C	$\geq$1.0 mmol/L (40 mg/dL)
FPG	<6.1 mmol/L
OGTT 2hPG	<7.8 mmol/L
HbA1c	<7.0%

individualized glucose control target, drug treatment, and monitoring plan (A).

- Health education and lifestyle interventions are the basis for diabetes care in elderly patients. An effective and safe hypoglycaemic treatment plan should be developed to prevent hypoglycaemia. Attention should be paid to prevent interactions among hypoglycaemic drugs (A).
- Elderly patients with diabetes commonly have multiple risk factors for ASCVD, multiple comorbidities and complications, geriatric syndrome, and muscle atrophy, and a high risk of osteoporosis and bone fracture, which require comprehensive management (A).
- It is recommended that patients with diabetes aged 65 years and above be screened for depression and cognitive function annually (B).

17.2.2 | Definition

Diabetes in older adults is defined as diabetes in patients aged ≥60 years regardless of whether diabetes is diagnosed before or after the age of 60 years. The goal of treatment is to reduce the disability and premature death associated with acute and chronic complications, improve quality of life, and extend expected survival.

17.2.3 | Treatment of senile diabetes

A comprehensive evaluation of the health status of diabetes in older adults is the basis for individualized glucose control targets and treatment strategies, as well as individualized blood lipids and blood pressure targets (Table 13).[38] Senile diabetes requires treatments with many considerations. It requires more humanistic care, and the benefits of treatment should be carefully weighed against potential risks after comprehensive evaluation.

18 | METABOLIC SYNDROME

Metabolic syndrome (MetS) is a clustering of medical conditions including obesity, hyperglycaemia (diabetes or impaired glucose regulation), hypertension, and dyslipidaemia (high TG and/or low HDL-C levels).

18.1 | Definitions for metabolic syndrome

MetS was defined as three or more of the following abnormalities[106,135]:

1. Abdominal obesity (central obesity): waist circumstance ≥90 cm in men or ≥85cm in women.[136]
2. Hyperglycaemia: FPG ≥ 6.1 mmol/L or OGTT 2hPG ≥ 7.8 mmol/L and/or confirmed diabetes that is under treatment,
3. Hypertension: blood pressure ≥130/85 mmHg and/or diagnosed and on antihypertensive therapy.
4. Fasting TG ≥ 1.70 mmol/L.
5. Fasting HDL-C < 1.04 mmol/L.

18.2 | The prevention and treatment of metabolic syndrome

The prevention and treatment goal for MetS is to prevent clinical CVD and T2DM and to prevent recurrence of cardiovascular events in patients with CVD. In principle, lifestyle intervention should be implemented first, and proper drug therapy should be added for patients with uncontrolled metabolic situations. The treatment targets are shown in Table 14.

19 | DIABETES AND TCM

Ancient TCM doctors regarded diabetes as Xiao Ke a kind of consumptive thirsty disease with typical manifestations including polydipsia, polyuria, polyphagia, and weight loss.

In TCM, the natural course of diabetes includes four stages: stagnation, heat, deficiency, and injuring. The stagnation stage is close to prediabetes whereas the heat stage is close to the early period of DM. The deficiency stage can be identified as the middle period of DM whereas the injuring stage can be recognized as the period of DM with appreciable complications.[137]

Multiple randomized and controlled clinical trials in patients with T2DM have shown that Chinese medicine including Jinlida granules, Gegen Huangqin Huanglian Decoction, and Da Chaihu Decoction are effective in lowering blood glucose and improving diabetic symptoms.[138-140]

CONFLICT OF INTEREST

All authors declare no conflict of interests.

AUTHOR CONTRIBUTIONS

All authors have discussed, read, and approved the manuscript. W. J. wrote and revised the paper. J. W. and D. Z. participated in the discussion and revision of the paper.

ORCID

Weiping Jia https://orcid.org/0000-0002-6244-2168

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