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Bridging Evidence and Practice: A Consensus Statement from the Korean Diabetes Association on Diabetes Screening, Pharmacological Treatment and Severe Diabetes

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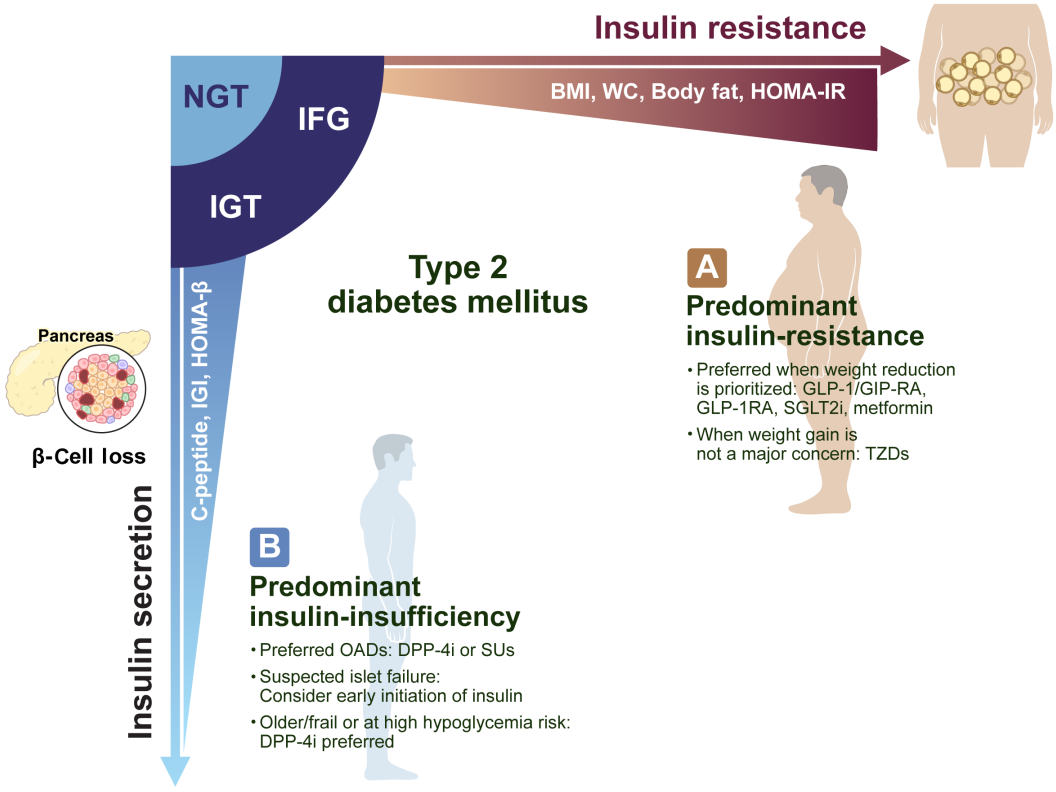

Highlights

- **Integrates screening, pharmacologic therapy, and severe diabetes into one framework.**
- **Recommends risk-aligned screening from age 35 or 19 with risk factors.**
- **Introduces pathophysiology- and comorbidity-guided drug selection framework.**
- **Defines hypercatabolic states and islet failure requiring prompt insulin use.**
- **Proposes severity-based Diabetes Grade–Stage Classification to match treatment intensity.**

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Bridging Evidence and Practice: A Consensus Statement from the Korean Diabetes Association on Diabetes Screening, Pharmacological Treatment and Severe Diabetes

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This Korean Diabetes Association (KDA) consensus statement bridges global evidence with the Korean clinical context, where large randomized and real-world data remain limited. Recommendations required ≥80% agreement by the committee of clinical practice guideline and approval by the board of directors. The statement comprises three domains: diabetes screening aligned with Korean epidemiology; pharmacologic management guided by pathophysiology and comorbidities; and a severity construct of "severe diabetes mellitus" that links complication-based staging with metabolic grading to match therapeutic intensity to disease complexity. Compared with prior KDA guidelines, this statement introduces substantive advances in three areas. First, screening recommendations are streamlined to emphasize risk-aligned, practical implementation rather than prescriptive test sequences. Second, pharmacologic management applies an individualized framework for drug selection that jointly considers pathophysiology and comorbidities. It operationalizes individualized selection by dominant pathophysiology (insulin resistance vs. insulin insufficiency) and coexisting conditions, and formalizes treatment dynamics—early combination, timely initiation of injectables, avoidance of overbasalization, and structured deintensification. It also prioritizes agents with proven cardiovascular and renal protection and elevates management of obesity and metabolic dysfunction-associated steatotic liver disease as central goals; clinically, insulin should be initiated promptly in hypercatabolic states or suspected islet failure, and technology-enabled care—including continuous glucose monitoring and automated insulin delivery—are integral across all stages. Third, the newly introduced severity construct underpins treatment-intensity decisions across domains without reiterating prescriptive algorithms. Collectively, these recommendations provide a coherent, context-appropriate framework for diabetes screening and management in Korea and identify priorities for future evidence generation.

Keywords: Consensus development conference; Diabetes mellitus; Drug therapy; Mass screening; Practice guideline

INTRODUCTION

Diabetes mellitus is one of the most prevalent chronic diseases worldwide, imposing significant clinical and socioeconomic burdens in Korea [1]. To provide evidence-based recommendations, the Korean Diabetes Association (KDA) has issued biennial clinical practice guidelines [2]. However, the applicability of global evidence in Korea may be limited due to the relative scarcity of large, randomized controlled trial (RCTs) and real-world data specific to the Korean population. To address areas with limited direct evidence, the KDA has initiated consensus statements, providing timely, context-sensitive guidance. These statements aim to bridge global evidence with local practice, reflecting Korea's healthcare delivery system, and patient characteristics. Recommendations were accepted when they achieved ≥80% agreement among members of the KDA Committee of Clinical Practice Guideline; items below this threshold were revised or excluded and re-evaluated until consensus was reached. Agreement rates for individual recommendations are provided in the Supplementary Table 1. The finalized set was subsequently reviewed and approved by the KDA board of directors.

In this inaugural consensus statement, the KDA addresses three domains where localized guidance is especially warranted: (1) Diabetes screening: target populations, testing modalities, and screening intervals relevant to Korea; (2) Pharmacological management of type 2 diabetes mellitus (T2DM), organized into three subthemes: management of hypercatabolic states and islet failure with prompt insulin initiation; glycemic management using a person-centered, pathophysiology-based and target-driven strategies; and comorbidity-oriented therapy; and (3) Severe diabetes: clarifying the concept in the Korean context, encompassing hypercatabolic states and islet failure, with emphasis on timely insulin initiation and the use of advanced diabetes technologies. By integrating the best available evidence with expert consensus and Korean clinical realities, this document provides practical, context-appropriate recommendations to support optimal diabetes care in Korea.

DIABETES SCREENING IN KOREAN ADULTS

As of 2022, the prevalence of diabetes among Korean adults aged ≥19 years was 12.5%, and 28.0% among those aged ≥65 years [1,3]. T2DM often develops insidiously, and many individuals remain undiagnosed until complications emerge. With increasing longevity, people are living longer with diabetes, and evidence for the legacy effect of early glycemic control underscores the importance of early detection and timely treatment [4]. The purpose of screening is to identify high-risk individuals and diagnose diabetes early to prevent complications and preserve long-term health and quality of life.

The criteria and methods for diabetes screening in Korea are

generally aligned with those of the American Diabetes Association (ADA) [5]. However, compared with many Western populations—where insulin resistance typically predominates—impaired insulin secretion plays a comparatively greater role in Koreans [6]. In fact, in a pooled analysis of four large Korean cohorts, the fasting plasma glucose (FPG) level corresponding to a 2-hour plasma glucose (2-hr PG) during 75-g oral glucose tolerance test (OGTT) plasma glucose level of 200 mg/dL was 110 mg/dL [7]. Thus, FPG, glycosylated hemoglobin (HbA1c), and 2-hr PG during 75-g OGTT thresholds are not fully concordant in Koreans, and reliance on a single test may miss isolated post-challenge hyperglycemia. In clinical practice, FPG and HbA1c are most commonly used owing to feasibility, whereas OGTT—though more burdensome—remains valuable when diagnostic certainty is needed or post-prandial dysglycemia is suspected, particularly in high-risk groups.

1. Target population for diabetes screening

Recommendation 1-1. All Korean adults aged ≥19 years with one or more risk factors (Table 1) should be screened for diabetes.

Recommendation 1-2. All Korean adults aged ≥35 years should be screened for diabetes regardless of risk factors.

The rising prevalence of prediabetes and diabetes—as well as general and abdominal obesity—among adults <40 years prompted the ADA to lower the initial screening age from 45 to 35 years [8]. In alignment, the KDA, incorporating analyses based on the Korea National Health and Nutrition Examination Survey 2016–2020 and the National Health Insurance Service sample cohort 2012–2017, has likewise lowered the recommended initiation age from 40 to 35 years since 2023 [9]. The KDA also recommends screening for all adults aged ≥19 years who have risk factors and has expanded the list of T2DM risk factors to include abdominal obesity (Table 1).

2. Initial screening testing

Recommendation 2-1. Screening for diabetes may be performed using FPG, HbA1c, or a 2-hr PG during 75-g OGTT.

Recommendation 2-2. For high-risk individuals or those with prior screening suggestive of prediabetes, combining two tests (e.g., FPG+HbA1c) may be considered to improve detection.

For asymptomatic individuals, screening can be conducted with FPG, HbA1c, or 2-hr PG during 75-g OGTT, all of which are also used for diagnosis [2]. Among these, the 2-hr PG during OGTT is more sensitive for detecting diabetes than FPG or HbA1c, but it has lower reproducibility, is more time-consuming, and may cause patient discomfort; therefore, FPG or HbA1c are most used in routine practice. In high-risk individuals, combining two tests (e.g., FPG+HbA1c) can improve detection accuracy, particularly when postprandial hyperglycemia is suspected, or prior results are discordant [10]. The diagnostic thresholds adopted by the KDA are the same as those of the ADA: prediabetes is defined as FPG 100–125 mg/dL or HbA1c 5.7%–6.4%, and diabetes as FPG ≥126 mg/dL or HbA1c ≥6.5% [8].

3. Screening interval after a normal result

Recommendation 3. Individuals with normal screening results, without evidence of prediabetes or diabetes, are recommended to undergo repeat screening every 1–2 years, depending on risk factors and previous test results.

Table 1. Risk factors for type 2 diabetes mellitus in Korean adults

No.	Risk factor
1	Overweight or obesity (body mass index ≥23 kg/m²)
2	Abdominal obesity (waist circumference ≥90 cm in men, ≥85 cm in women)
3	Family history of diabetes in a first-degree relative (parents or siblings)
4	History of impaired fasting glucose or impaired glucose tolerance
5	History of gestational diabetes mellitus or delivery of a macrosomic infant (≥4 kg)
6	Hypertension (blood pressure ≥140/90 mm Hg or use of antihypertensive medication)
7	Dyslipidemia (high-density lipoprotein cholesterol <35 mg/dL or triglycerides ≥250 mg/dL)
8	Evidence of insulin resistance (e.g., polycystic ovary syndrome, acanthosis nigricans)
9	History of cardiovascular disease (e.g., stroke, coronary artery disease)
10	Use of medications known to affect glucose metabolism (e.g., glucocorticoids, atypical antipsychotics)

The KDA recommends annual screening for adults at risk [2], although the optimal screening interval has not been firmly established. For those with normal prior results and no additional risk factors, a 2-year interval may be acceptable.

4. Additional testing and follow-up after a prediabetes result on FPG or HbA1c

Recommendation 4-1. If one screening test falls within the prediabetes range, one or more additional tests should be considered to improve diagnostic accuracy.

Recommendation 4-2. A 2-hr PG during 75-g OGTT should be considered in individuals with FPG 110–125 mg/dL or HbA1c 6.1%–6.4%.

Recommendation 4-3. Individuals confirmed to have prediabetes after screening are recommended to undergo repeat screening annually.

Even when FPG or HbA1c falls in the prediabetes range, relying on a single test risks misclassification due to biological variability (intra-/inter-day fluctuation), analytical error, acute illness or stress, medication effects (e.g., glucocorticoids), and known discordance among glycemic indices [10]. Accordingly, when a screening test suggests prediabetes, add one or more additional tests (e.g., HbA1c or OGTT after FPG; FPG or OGTT after HbA1c) to refine diagnostic accuracy and phenotype.

Several Korean studies have shown that the FPG and HbA1c levels corresponding to a 2-hr PG during 75-g OGTT of 200 mg/dL were approximately 110 mg/dL and 6.1%, respectively [11-13]. Therefore, individuals with FPG ≥110 mg/dL or HbA1c ≥6.1% are at particularly high risk and should undergo OGTT for confirmation. Moreover, the Korean Diabetes Prevention Study revealed that even individuals with FPG <100 mg/dL were sometimes diagnosed with diabetes through an OGTT, underscoring the importance of OGTT in those with a body mass index (BMI) ≥23 kg/m^2, even if FPG or HbA1c are only modestly elevated (Fig. 1) [14,15].

Individuals with prediabetes require at least annual follow-up. When diagnostic certainty is needed (e.g., discordant results or suspicion of postprandial hyperglycemia), combined testing (e.g., FPG+HbA1c or FPG+OGTT) should be considered. Earlier re-testing is also reasonable if risk status changes (e.g., weight gain, new risk factors, or exposure to hyperglycemia-inducing medications).

5. Diagnostic confirmation following abnormal screening results

For asymptomatic individuals whose screening result meets the diagnostic threshold for diabetes, confirmation should be obtained by either repeating the same test on a different day or performing an alternative diagnostic test; diabetes is confirmed if the result of repeat or alternative test also meets diagnostic criteria. If two different tests conducted on the same day both meet diagnostic thresholds, the diagnosis can be confirmed without repeat testing. When results are discordant, additional test, such as repeat testing or OGTT, may be considered if uncertainty persists. Although symptomatic individuals are not the primary target of screening, diabetes can be confirmed without repeat testing when it is clinically obvious (e.g., classic symptoms with random plasma glucose ≥200 mg/dL, or a hyperglycemic crisis). Once diabetes is confirmed, HbA1c should be measured if not already obtained, as it is essential for establishing baseline glycemic status and guiding decisions on treatment initiation and intensity.

6. Summary

Early detection of diabetes is essential for preventing complications and preserving quality of life. Therefore, screening should therefore be implemented in all Korean adults aged ≥35 years and in those aged ≥19 years with one or more risk factors. For individuals at high risk, appropriate use of multiple tests is recommended to minimize missed diagnoses. Further research is needed to refine the optimal screening interval, clarify the role of combined testing, define age-specific diagnostic thresholds, and develop tailored strategies for older adults.

PHARMACOLOGICAL MANAGEMENT OF T2DM

Pharmacological treatment of T2DM should be person-centered, with therapeutic decisions tailored to each individual's clinical characteristics, comorbidities, and preferences. Optimal outcomes are achieved when the pharmacologic profile of an agent is matched to the patient's context, including glycemic status, body weight, comorbidities, age, treatment acceptability, and social determinants of health. This approach is particularly important in Koreans, given their unique pathophysiology, characterized by an earlier decline in insulin secretory capacity compared with Western populations [16,17]. The diagnostic framework of diabetes has historically been linked to the onset of complications, such as retinopathy in the Pima Indians [18]. Building on this concept, the 2025 KDA Consensus Statement integrates global evidence with Korean data, which

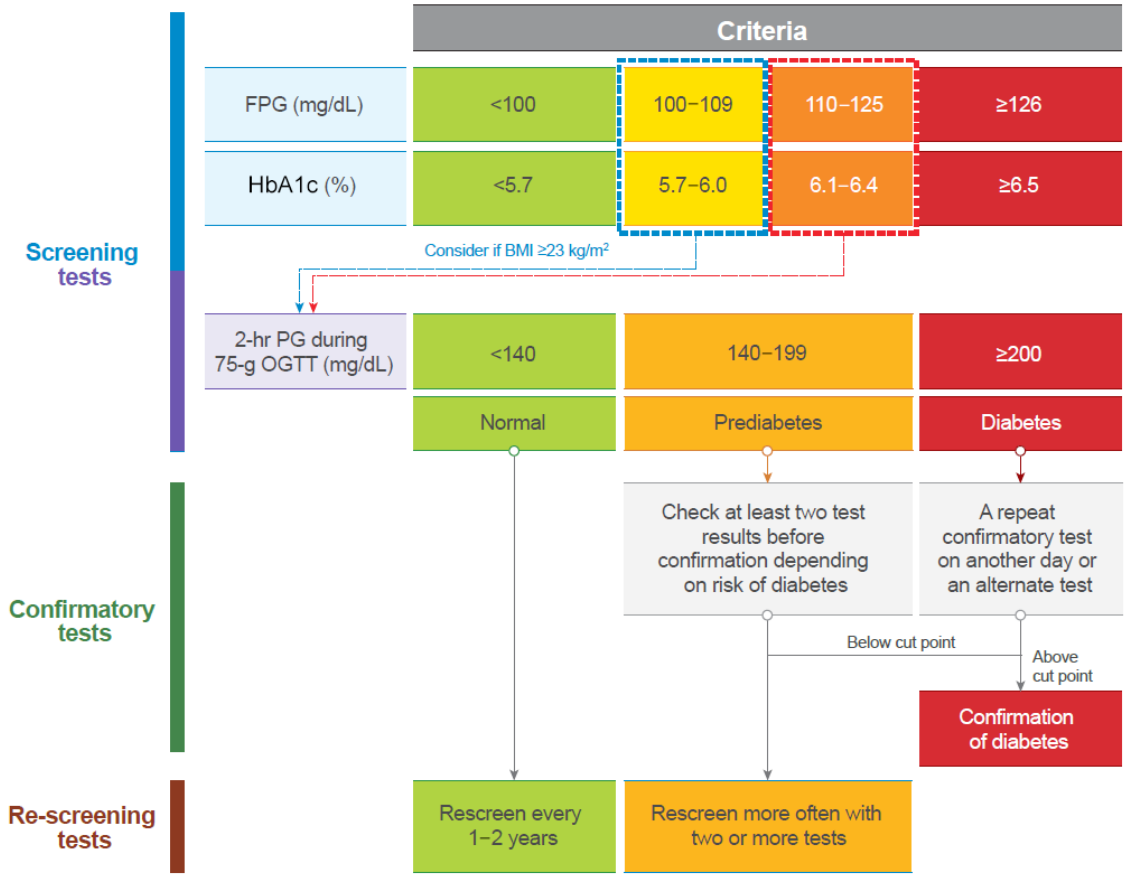

Fig. 1. Algorithm for diabetes screening, confirmatory testing, and rescreening in Korean adults. When to perform oral glucose tolerance test (OGTT): Recommend a 2-hour plasma glucose (2-hr PG) during 75-g OGTT when fasting plasma glucose (FPG) 110–125 mg/dL or glycosylated hemoglobin (HbA1c) 6.1%–6.4% (red dashed outline). Consider a 2-hr PG during 75-g OGTT when FPG 100–109 mg/dL or HbA1c 5.7%–6.0% and body mass index (BMI) ≥23 kg/m² (blue dashed outline). Confirmatory testing: To confirm diabetes, either repeat the same test on a different day and again meet the diagnostic threshold, or obtain two or more different tests on the same day that each meet diagnostic thresholds. Rescreening: Normal results → rescreen every 1–2 years; Prediabetes → at least annual follow-up, with combined tests considered in high-risk or discordant cases.

may be limited, and incorporates expert consensus to reflect the Korean clinical context. The consensus highlights three major pillars of pharmacological management: (1) management of hypercatabolic state or islet failure, (2) glycemic management, and (3) cardiovascular and renal risk management.

While RCT of intensive versus conventional glycemic control (e.g., United Kingdom Prospective Diabetes Study [UKPDS], Action to Control Cardiovascular Risk in Diabetes [ACCORD], Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation [ADVANCE]) showed no short-term mortality benefit, long-term follow-up has demonstrated a legacy effect, particularly in newly diagnosed patients [19-21]. By contrast, drug class-based trials have shown that sodium-glucose cotransporter 2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1RAs) reduce cardiovascular events and mortality within shorter time frames, underscoring the need to align therapy not only with glycemic targets but also with comorbidity profiles [22,23]. Meanwhile, in Korea, insulin remains underused despite its critical role [24]. Individuals presenting with hypercatabolic symptoms—such as unintended weight loss, polyuria, or polydipsia—may require insulin initiation even when HbA1c is not markedly elevated. Importantly, islet failure may occur not only in type 1 diabetes mellitus (T1DM) but also in

long-standing T2DM or other forms of diabetes, necessitating timely initiation of insulin therapy [25,26]. In addition, achieving glycemic targets without delay is a key determinant for preventing complications [19]; therefore, early combination therapy or the timely introduction of injectable agents should be considered whenever indicated [27-29].

1. Person-centered determinants in pharmacological treatment decision-making for T2DM

Recommendation 1-1. In determining whether to initiate pharmacologic therapy and which antidiabetic agents to select in individuals with T2DM, a comprehensive assessment should include: the presence of hypercatabolic symptoms; likelihood of islet failure; current glycemic status and glycemic target; body weight; comorbidities—especially cardiovascular and renal risks; the individual's dominant pathophysiologic phenotype of diabetes; life expectancy; physical and cognitive function; personal values and treatment acceptability; and social determinants of health.

Recommendation 1-2. Throughout all stages of pharmacologic treatment, lifestyle modification—including medical nutrition therapy, physical activity, smoking cessation, and psychosocial management—should be consistently integrated with diabetes self-management education and support (DSMES) to optimize clinical outcomes.

Recommendation 1-3. From the initiation of pharmacologic therapy through each stage of treatment, medication adherence should be regularly assessed, and treatment should be promptly intensified when individualized glycemic targets are not achieved, to minimize therapeutic inertia.

The initial choice and subsequent adjustment of pharmacologic therapy in T2DM should be individualized, adhering to the core principle that treatment be person-centered rather than uniform. Key considerations include comorbidities, individual's dominant pathophysiologic phenotype of diabetes, effects on body weight, hypoglycemia risk, and drug-specific safety profiles, which are addressed in detail in later sections. At every stage of diabetes management, lifestyle modification should be integrated with DSMES [30]. These non-pharmacologic interventions are essential components of effective therapy. Evidence consistently shows that combining lifestyle modification and DSMES with pharmacologic treatment enhances glycemic outcomes, reduces complications, and improves quality of life [31]. Overcoming therapeutic inertia is equally important. Clinical inertia and patient non-adherence remain major barriers to achieving glycemic goals. Clinicians should regularly reassess glycemic status, evaluate adherence, and intensify treatment without delay when individualized targets are not met [32]. Proactive strategies—including early use of combination therapy, timely initiation of injectable agents, and ongoing shared decision-making—are critical to prevent prolonged exposure to hyperglycemia and reduce long-term risk of complications.

2. Hypercatabolic state or islet failure

2-1. Initial treatment approach of hypercatabolic state

Recommendation 2-1-1. In individuals presenting with hypercatabolic symptoms attributable to diabetes—such as unintended weight loss, polyuria, and polydipsia—insulin therapy should be initiated promptly, including when the current blood glucose is not markedly elevated.

Recommendation 2-1-2. For individuals with mild hypercatabolic features who are clinically stable and able to take oral intake, basal insulin with or without oral antihyperglycemic agents may be initiated.

Recommendation 2-1-3. For individuals requiring more aggressive glycemic control—due to marked hyperglycemia or more prominent hypercatabolic features—intensive insulin regimens (basal-plus, premixed, or basal-bolus) may be initiated.

Recommendation 2-1-4. In cases with severe dehydration, altered mental status, or suspected diabetic ketoacidosis or hyperosmolar hyperglycemic state, the individual should be promptly hospitalized. Initial treatment should include intravenous insulin infusion and fluid resuscitation, followed by transition to multiple daily injections once stabilized and oral intake is possible.

Hypercatabolic states in diabetes are characterized by profound insulin deficiency, leading to increased hepatic glucose production, reduced peripheral glucose utilization, and enhanced lipolysis and proteolysis [33-35]. These processes result in unintended weight loss, polyuria, polydipsia, and, in some cases, ketonuria [36]. Unlike isolated hyperglycemia, this pathophysiology reflects systemic metabolic decompensation and requires prompt initiation of insulin therapy, even when the current glucose level is not markedly elevated (and all the more so when it is very high) [32,37]. This recommendation pertains to hypercatabolic states due to diabetes; non-diabetic causes of catabolism should be evaluated and managed accordingly.

For individuals with mild hypercatabolic features who remain clinically stable and can maintain oral intake, therapy may begin with basal insulin alone or in combination with oral antihyperglycemic agents. A typical starting dose is 10 units daily or 0.1–0.2 units/kg, with titration according to glycemic response. In cases with significantly elevated baseline glucose, higher starting doses of 0.3–0.4 units/kg may be considered,

with careful monitoring for hypoglycemia [38].

For those requiring more intensive control—owing to markedly elevated glucose levels or more prominent hypercatabolic features—a basal-bolus regimen is recommended. The usual starting total daily insulin dose is 0.4–0.5 units/kg, administered as approximately 50% basal and 50% divided among prandial doses before meals [39]. In older adults (≥70 years) or those with reduced renal function (estimated glomerular filtration rate [eGFR] <60 mL/min/1.73 m^2), a more conservative initiation of 0.2–0.3 units/kg is advised to minimize hypoglycemia risk [40].

When severe hyperglycemia is accompanied by dehydration, altered mental status, or suspicion of diabetes ketoacidosis (DKA)/hyperglycemic hyperosmolar state, prompt hospitalization is mandatory. Management includes intravenous insulin infusion and isotonic fluid resuscitation until metabolic stabilization is achieved. Once clinically stable and able to resume oral intake, therapy should be transitioned to multiple daily doses of insulin (MDI) for ongoing insulin replacement [26,37].

2-2. Treatment evaluation and adjustment in hypercatabolic state: intensification and deintensification strategies

Recommendation 2-2-1. After insulin initiation at hypercatabolic state, treatment response may be evaluated based on improvement in symptoms, glucose levels, and resolution of ketonuria.

Recommendation 2-2-2. If basal insulin alone (±oral antihyperglycemic drugs [OADs]) is insufficient to achieve glycemic targets—based on persistent hyperglycemia, inadequate symptom resolution, or ongoing ketonuria—intensification of insulin therapy should be considered. This may involve the addition of prandial insulin (e.g., basal-plus), transition to premixed insulin, or basal-bolus regimens depending on clinical needs and meal patterns.

Recommendation 2-2-3. Insulin dose reduction or discontinuation may be considered once metabolic stability is achieved, hypercatabolic symptoms have resolved, and glycemic control is maintained with declining insulin requirements.

Following the initiation of insulin therapy in individuals with a hypercatabolic state, close monitoring is essential until clinical stabilization is achieved. Treatment response should be assessed by improvement in hypercatabolic symptoms, stabilization of glucose levels, and resolution of ketonuria [32]. The frequency and intensity of monitoring should be tailored to the severity of the presentation and the care setting.

If glycemic targets are not achieved with optimized basal insulin, stepwise intensification should follow. Basal insulin can be titrated by approximately 2 units or 10% every 2–3 days, provided hypoglycemia does not occur. If persistent hyperglycemia remains despite basal optimization, a prandial dose may be added before the meal with the largest postprandial excursion (commonly starting at 4 units or 10% of the basal dose), with further titration as needed [32,37,41]. If targets remain unmet after 1–2 weeks of intensification, secondary causes of poor control—such as poor adherence, concurrent infection, or glucocorticoid use—should be carefully evaluated [42]. If control is still inadequate, therapy may be advanced to premixed insulin or a full basal-bolus regimen, depending on individual needs and meal patterns. Prompt reassessment is warranted if symptoms persist or if DKA is suspected [32,37,41].

Once metabolic stability has been achieved, deintensification—and even discontinuation—of insulin may be considered, provided that hypercatabolic features have resolved and glycemic control is maintained with declining insulin requirements. In this context, C-peptide measurement may be used as supportive information for assessing β-cell function, though it should not be considered a mandatory criterion. In case where insulin is discontinued, ongoing glucose surveillance is necessary to ensure continued stability, and insulin should be promptly reinstated if glycemic control deteriorates or hypercatabolic features recur [32,37,41].

2-3. Use and contraindications of oral antidiabetic drugs in hypercatabolic state

Recommendation 2-3-1. During insulin therapy in hypercatabolic state, the concomitant use of OADs may be considered if there are no specific contraindications.

Recommendation 2-3-2. SGLT2 inhibitors should be avoided in hypercatabolic states due to safety concerns, including the risk of euglycemic diabetic ketoacidosis. If SGLT2 inhibitors are indicated for comorbid conditions, initiation may be cautiously considered only after the hypercatabolic state has resolved and metabolic stability is confirmed.

In the hypercatabolic state, OADs may be combined with insulin to achieve additional glycemic control or provide cardiovascular and renal benefits. However, RCTs and meta-analyses have demonstrated that SGLT2 inhibitors have been associated with an approximately 2- to 3-fold increased risk of DKA [43,44], particularly in insulin-deficient states [45], and may exacerbate volume depletion through osmotic diuresis. Accordingly, caution is warranted during hypercatabolic states, and their use should be deferred until the condition has clearly resolved.

2-4. Management of islet failure: insulin strategies and technology-enabled care

Recommendation 2-4-1. In individuals with established islet failure (Table 2), intensive insulin therapy using MDI or insulin pump is the preferred treatment to optimize glycemic control and reduce hypoglycemia risk.

Recommendation 2-4-2. Diabetes technologies—including real-time continuous glucose monitoring (CGM), sensor-augmented pumps, or automated insulin delivery (AID) systems—should be actively considered for individuals capable of safe device use.

Recommendation 2-4-3. Given the complexity of insulin management in islet failure, individuals should receive structured education from trained diabetes educators. If this is not feasible, referral to specialized diabetes centers with adequate expertise and resources is recommended.

For managing diabetes with established islet failure, intensive insulin therapy using MDI or an insulin pump is recommended. Rapid-acting and long-acting insulin analogs are preferred for MDI [46], as multiple clinical trials have demonstrated that these regimens improve glycemic control and reduce the risk of nocturnal and postprandial hypoglycemia compared with those using intermediate-acting, regular, or premixed insulin [47,48].

In individuals with islet failure, routine use of real-time CGM is recommended to support optimal glycemic control and reduce the hypoglycemia risk [49,50]. When device use is feasible and safe, AID systems could be prioritized. If AID is not available or appropriate, alternatives include sensor-augmented pump with bolus calculators. Implementing these technology-based strategies alongside structured education for patients and caregivers maximized the benefits [46].

3. Glycemic management

3-1. Pathophysiology- and comorbidity-guided initial selection of antidiabetic drugs

Recommendation 3-1. At the initiation of pharmacological treatment, glucose-lowering agents should be selected based on the individual's underlying pathophysiology of diabetes or the presence of comorbidities.

Recommendation 3-1-1. In the absence of established end-organ damage comorbidities such as atherosclerotic cardiovascular disease (ASCVD), heart failure (HF), chronic kidney disease (CKD), or ischemic stroke, drugs should be selected primarily according to the person's dominant pathophysiologic phenotype (refer to subsection 3-3).

Recommendation 3-1-2. In individuals with established end-organ damage comorbidities such as ASCVD, HF, CKD, or ischemic stroke, agents with proven benefits for the relevant condition(s) should be prioritized when initiating pharmacologic therapy. (refer to subsection 4)

The initial choice and subsequent adjustment of pharmacologic therapy in newly diagnosed T2DM should be person-centered, reflecting not only glycemic needs but also underlying pathophysiology and comorbid conditions. This individualized framework enables more effective and sustainable management while minimizing risk.

In individuals without established end-organ damage, such as ASCVD, HF, CKD, or ischemic stroke, decisions should be

Table 2. Diagnostic criteria for islet failure and severe islet failure

Islet failure diabetes mellitus: Defined when both (A) and (B) are satisfied
A. One or more of the following:
1. Fasting C-peptide ≤0.6 ng/mL
2. Postprandial (within 5 hours after meal) C-peptide ≤1.8 ng/mL
3. 24-hour urinary C-peptide <30 μg/day
4. Spot urine C-peptide to creatinine ratio ≤0.6 nmol/mmol
B. Currently using a multiple daily doses of insulin (MDI) regimen including rapid-acting insulin or an insulin pump
Severe islet failure diabetes mellitus: Defined when both (A) and (B) are satisfied
A. One or more of the following:
1. Fasting C-peptide <0.24 ng/mL
2. Postprandial C-peptide <0.6 ng/mL
3. Spot urine C-peptide to creatinine ratio <0.2 nmol/mmol
B. Currently using an MDI regimen including rapid-acting insulin or an insulin pump

guided primarily by the dominant pathophysiologic phenotype. For those with insulin resistance and obesity, agents that improve insulin sensitivity and promote weight loss—such as glucose-dependent insulinotropic polypeptide/glucagon-like peptide-1 dual receptor agonist (GIP/GLP-1 dual agonist), GLP-1RAs, SGLT2 inhibitors, metformin, or thiazolidinediones (TZDs)—are preferred. Conversely, in individuals with impaired insulin secretion and relatively low BMI, agents that enhance insulin secretion, such as dipeptidyl peptidase-4 (DPP-4) inhibitors or sulfonylureas, may be considered (see subsection 3-3).

In contrast, individuals with established end-organ damage comorbidities therapeutic priorities should shift toward drug classes with demonstrated cardiovascular and renal benefits (see subsection 4). Large RCTs and meta-analyses show that SGLT2 inhibitors reduce hospitalization for HF, slow CKD progression, and lower cardiovascular mortality—particularly in HF/CKD populations—whereas GLP-1RAs consistently reduce major adverse cardiovascular events (MACE), especially in people with established ASCVD. In these cases, the presence of comorbidities should take precedence over pathophysiology alone when selecting initial therapy.

3-2. Glycemic target-based initial selection of treatment intensity and combination therapy

Recommendation 3-2. At the initiation of pharmacologic therapy, medications with sufficient glucose-lowering efficacy should be selected to achieve glycemic targets, considering the individual's current glycemic status and target goals.

Recommendation 3-2-1. If monotherapy is unlikely to achieve the glycemic target, initial combination therapy with two or three OADs with complementary mechanisms of action should be considered.

Recommendation 3-2-2. If the glycemic target is unlikely to be achieve with oral combination therapy, initiating injectable therapy—such as a GIP/GLP-1 dual agonist, a GLP-1RA, or insulin—should be considered.

Achieving glycemic targets early is critical for reducing glucotoxicity, preserving β-cell function, and lowering long-term complication risk [19,51,52]. Therefore, the initial pharmacologic regimen should provide sufficient efficacy to match the individual's baseline glycemic status and treatment goals. When monotherapy is unlikely to reach target, initial combination therapy with two or three oral agents that have complementary mechanisms should be considered. RCTs consistently show that early dual therapy—such as metformin combined with an SGLT2 inhibitor, a DPP-4 inhibitor, or other fixed-dose combinations—achieves greater HbA1c reduction, higher target-attainment rates, and faster improvement than monotherapy escalation, without a significant increase in hypoglycemia [27,53-55]. Trials of initial triple therapy have also demonstrated superior durability of glycemic control compared with stepwise escalation, while maintaining a favorable safety profile [56-58]. Where available, fixed-dose combinations can reduce pill burden and are consistently associated with better adherence and persistence in real-world practice; RCTs primarily demonstrate glycemic efficacy comparable or superior to standard comparators [59,60].

If glycemic targets are unlikely to be achieved with oral combination therapy alone, early initiation of injectables should be considered. Clinical trials consistently show that GLP-1RAs, GIP/GLP-1 dual agonist, and insulin provide greater glucose-lowering efficacy than oral agents, making them appropriate when more potent intervention is required. Selection among these injectables and integration with oral regimens are discussed in later sections.

3-3. Pathophysiology-based initial selection of antidiabetic drugs for Korean patients with T2DM

3-3-1. Predominant insulin resistance

Recommendation 3-3-1a. In adults with T2DM who are obese and considered to have an insulin resistance–dominant phenotype, GIP/GLP-1 dual agonist, GLP-1RAs, SGLT2 inhibitors, and metformin may be preferred options for both their insulin-sensitizing and weight-reducing effects.

Recommendation 3-3-1b. Although TZDs may cause modest weight gain, they effectively improve insulin resistance and can be beneficial for insulin resistance–dominant individuals. To minimize weight gain, combining TZDs with weight-reducing agents may be an effective strategy.

3-3-2. Predominant insulin insufficiency

Recommendation 3-3-2a. In adults with T2DM who are not obese and considered to have an insulin insufficiency–dominant phenotype, DPP-4 inhibitors or sulfonylureas can be considered as potential first-line oral agents.

Recommendation 3-3-2b. In older adults, frail individuals, or those with lower body weight, DPP-4 inhibitors are preferred due to weight neutrality and a low risk of hypoglycemia.

The pathophysiology of T2DM shows distinct patterns in East Asians, including Koreans, compared with Western popula-

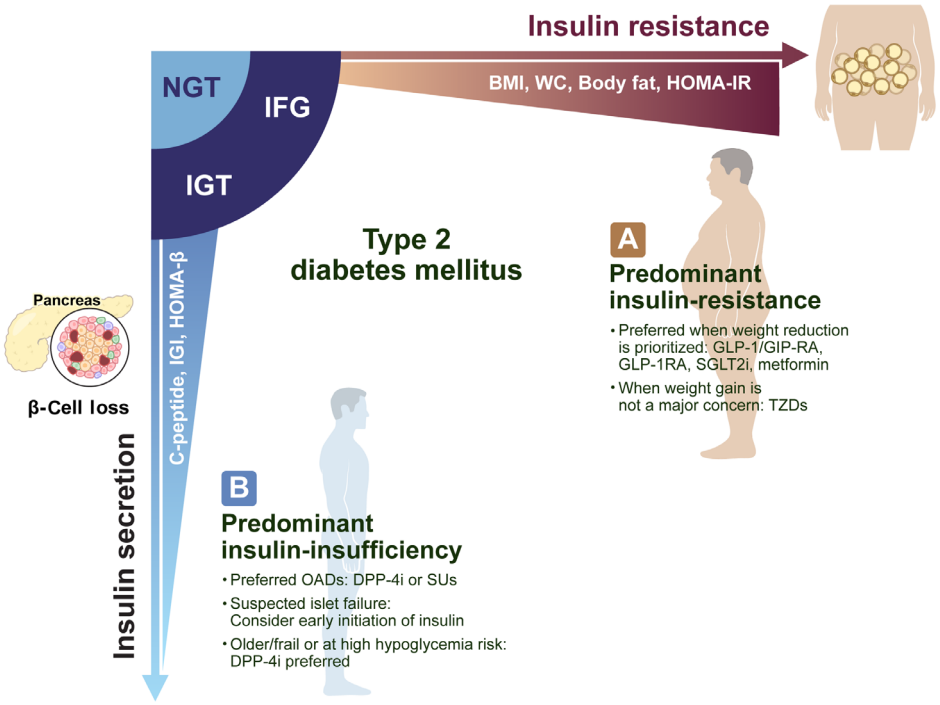

Fig. 2. Pathophysiology-oriented framework for treatment selection in type 2 diabetes mellitus. The schematic maps type 2 diabetes mellitus along two axes: insulin resistance (rightward gradient; indexed by body mass index [BMI], waist circumference [WC], body fat, homeostatic model assessment of insulin resistance [HOMA-IR]) and insulin secretion (downward gradient; indexed by C-peptide, insulinogenic index [IGI], homeostatic model assessment of β-cell function [HOMA-β]). Curves illustrate transitions from normal glucose tolerance (NGT) to impaired fasting glucose (IFG)/impaired glucose tolerance (IGT) as resistance increases and/or secretion declines. Two phenotypic poles guide therapy. (A) Predominant insulin resistance: Preferred when weight reduction is prioritized (glucose-dependent insulinotropic polypeptide [GIP]/glucagon-like peptide-1 [GLP-1] dual agonist, glucagon-like peptide-1 receptor agonists [GLP-1RAs], sodium-glucose cotransporter 2 inhibitor [SGLT2i], metformin); When weight gain is not a major concern (thiazolidinediones [TZDs]). (B) Predominant insulin insufficiency: Preferred oral antihyperglycemic drugs (OADs): dipeptidyl peptidase-4 inhibitor (DPP-4i) or sulfonylureas (SUs); insulin if secretion is inadequate; Older/frail or at high hypoglycemia risk: DPP-4i preferred; Suspected islet failure or high glycemic burden: consider early insulin. This figure is a conceptual aid, not a prescribing algorithm. The displayed indicators (e.g., BMI, waist circumference, body fat, HOMA-IR; C-peptide, IGI, HOMA-β) do not have absolute cutoffs and vary by assay, population, and clinical context; they should be interpreted as ranges and trends, not thresholds. Phenotypes may shift over time with disease progression or treatment, so reassessment is required. The schema is intended only to support drug selection when end-organ damage (e.g., atherosclerotic cardiovascular disease, heart failure, chronic kidney disease, stroke) is absent, by conceptually weighing insulin resistance versus insulin insufficiency. It does not supersede established indications for organ-protective therapy, nor does it override the need for prompt insulin in hypercatabolic states or suspected islet failure.

tions [61]. While insulin resistance is a key mechanism in obesity-driven diabetes [62], East Asians tend to exhibit an earlier and more pronounced decline in insulin secretory capacity [63-66]. In light of this pathophysiologic uniqueness, the 2023 Japan Diabetes Society statement had proposed selecting antidiabetic agents based on obesity status, as a means to assess insulin secretion or resistance [67].

In Korean adults with obesity, insulin resistance is often the predominant abnormality, which is relevant given recent increases in obesity and T2DM among younger adults in Korea [1,68]. Notably, East Asians often have a lower BMI than Western populations, yet central obesity (elevated waist circumference or increased visceral fat area) is common even at a normal BMI; therefore, careful assessment of obesity and insulin resistance is warranted. Accordingly, in individuals with obesity—particularly those with heightened insulin resistance—agents that improve insulin sensitivity and promote weight reduction (GIP/GLP-1 dual agonist, GLP-1RAs, SGLT2 inhibitors, and

metformin) are preferred [69-72]. TZDs also improve insulin resistance and can be beneficial, although their tendency to cause weight gain may be a consideration [73,74]. Combining TZDs with weight-reducing drugs, such as SGLT2 inhibitors or GLP-1RAs, may mitigate this drawback [75,76].

Conversely, in relatively older, non-obese adults with marked hyperglycemia, impaired insulin secretion often predominates over insulin resistance [63,66]. In these individuals, use of agents that cause marked weight loss—for example, high-potency GLP-1RAs (or GIP/GLP-1 dual agonist) and SGLT2 inhibitors—may be undesirable or potentially harmful. Significant weight loss can exacerbate sarcopenia by reducing lean mass and strength, leading to weakness or functional decline; therefore, these agents should be used with caution and individualized consideration in non-obese people with insulin insufficiency–dominant diabetes [77,78]. In these individuals, DPP-4 inhibitors or sulfonylureas may be more effective, with DPP-4 inhibitors generally preferred in older, frail, or low-weight patients because of low hypoglycemia risk and weight neutrality [79,80].

Taken together, treatment of Korean adults with T2DM should not follow a uniform approach but should be based on the dominant pathophysiologic phenotype. This framework enables selection of therapies that are effective for glycemic control (Fig. 2) and aligned with patient safety, comorbidity profiles, and long-term outcomes.

3-4. Intensification strategies in individuals already receiving glucose-lowering medications

3-4-1. Early intensification and combination therapy with oral agents

Recommendation 3-4-1a. Treatment should be promptly intensified to effectively achieve the glycemic target at an early stage, by uptitrating current medications to their maximum tolerated doses and/or by adding agents with different mechanisms of action, based on the individual's glycemic status and existing treatment regimen.

Recommendation 3-4-1b. If glycemic targets are not achieved despite triple OADs, and injectable treatment is not feasible, an up-to quadruple OADs regimen may be considered in limited situations—specifically when the individual does not exhibit symptoms of hypercatabolic states, has moderately elevated hyperglycemia (e.g., HbA1c <8.0%), and is not suspected to have significant islet failure.

Timely intensification is essential to avoid prolonged exposure to hyperglycemia and to minimize complication risk. Existing agents can be up-titrated to their maximally tolerated doses, and drugs with complementary mechanisms added when glycemic targets are not achieved. When control remains suboptimal despite three oral agents, and injectables are not feasible due to reasons such as refusal, poor vision, hand tremors, or other barriers, quadruple oral therapy could be considered as an alternative strategy. Recent Korean a meta-analysis evidence including real-world data, shows that quadruple OAD regimens can achieve meaningful HbA1c reductions of –1.1% to –1.3%, with a generally favorable safety profile and low risk of severe hypoglycemia [81]. Benefits have been observed across combinations such as adding SGLT2 inhibitors, DPP-4 inhibitors, or TZDs to existing triple therapy. This approach is best suited for individuals with moderately elevated glycemia (e.g., HbA1c <8.0%), without hypercatabolic features and without clinical suspicion of significant islet failure. In such cases, quadruple therapy can provide additional glycemic improvement while preserving adherence and delaying the need for injectables. However, patients require close monitoring, and if targets remain unmet, escalation to GLP-1RAs or insulin should not be delayed.

3-4-2. Early intensification of injectable therapy, prioritizing incretin-based agents

Recommendation 3-4-2a. If glycemic targets are not achieved despite appropriate oral combination therapy, injectable therapies should be initiated promptly.

Recommendation 3-4-2b. When selecting an injectable agent, GLP-1RAs (or GIP/GLP-1 dual agonist) are preferred over basal insulin in individuals without symptoms of hypercatabolic states and with low likelihood of islet failure.

Recommendation 3-4-2c. If glycemic targets are not achieved with either GLP-1RA (or GIP/GLP-1 dual agonist) or basal insulin, combination therapy using both agents should be considered.

Recommendation 3-4-2d. When combining GLP-1RA and basal insulin, fixed-ratio combination therapy may be considered to reduce injection frequency and improve adherence.

Injectable agents—including GLP-1RA, GIP/GLP-1 dual agonist, and insulin—generally provide greater glucose-lowering efficacy than OADs [28]. Therefore, in individuals who fail to achieve target glycemic control despite appropriate oral combination therapy, the transition to injectable therapy should be considered. In cases of hyperglycemia without evidence of islet failure or hypercatabolic symptoms, GLP-1RAs (or GIP/GLP-1 dual agonist) are preferred over basal insulin, given their greater efficacy, lower hypoglycemia risk, favorable effects on

body weight, and the availability of once-weekly formulations in some agents [82]. If glycemic targets remain unmet despite the use of either GLP-1RA (or GLP-1/GIP dual agonist) or basal insulin, combination therapy with both agents should be considered [83,84]. When both basal insulin and a GLP-1RA are required, fixed-ratio combinations can reduce injection burden, simplify treatment, and improve adherence, while delivering comparable efficacy to separate injections [85,86].

3-4-3. Avoiding overbasalization and transitioning to intensive insulin regimens

Recommendation 3-4-3a. In individuals receiving basal insulin therapy (±OADs) who experience frequent hypoglycemia and marked glycemic fluctuation, overbasalization should be suspected, and treatment should be intensified by reducing basal insulin and adding postprandial glucose-lowering strategies such as GLP-1RA (or GIP/GLP-1 dual agonist) or insulin intensification.

Recommendation 3-4-3b. If glycemic targets are not achieved despite combination therapy with GLP-1RA (or GIP/GLP-1 dual agonist) and basal insulin, intensive insulin therapy—such as basal-plus, premixed, or basal-bolus regimens—should be implemented.

In individuals already receiving basal insulin, the persistence of frequent hypoglycemia, significant glycemic variability, or the need for excessively high basal doses may suggest overbasalization [87]. This condition reflects inadequate postprandial glucose coverage rather than true basal insulin deficiency [88]. In such cases, intensification should focus on reducing the basal dose and adding postprandial glucose-lowering strategies, such as a GLP-1RA, a GIP/GLP-1 dual agonist, or prandial insulin [41,89]. This approach not only addresses postprandial hyperglycemia but also reduces the risk of hypoglycemia and excessive weight gain associated with higher basal insulin doses [90,91]. When glycemic targets remain unmet despite combination therapy with basal insulin and incretin-based injectables, transition to a more structured and intensive insulin regimen is warranted [41,92]. Options include basal-plus (addition of a single prandial injection before the largest meal), premixed insulin, or a full basal-bolus regimen. The choice depends on the individual's meal patterns, lifestyle, and the individual's ability to adhere to more complex regimens. Basal-plus is often an effective initial step for incremental intensification, whereas basal-bolus offers the most comprehensive control in those with marked postprandial excursions. This stepwise approach tailors insulin therapy to pathophysiologic needs and treatment burden while minimizing hypoglycemia and weight gain.

3-4-4. Optimizing combination therapy with injectables and oral agents

Recommendation 3-4-4a. In individuals on intensive insulin therapy, GLP-1RA (or GIP/GLP-1 dual agonist) may be added to provide additional clinical benefits, including weight loss, reduced insulin requirements, and improved management of cardiovascular, renal, and metabolic dysfunction-associated steatotic liver disease (MASLD)-related risks.

Recommendation 3-4-4b. In all people with T2DM receiving injectable therapy (GLP-1RA, basal insulin, or intensive insulin therapy), combination with OADs may be added to achieve additional clinical benefits, such as reduced insulin requirements, and cardiovascular and renal risk management. However, DPP-4 inhibitors should not be combined with GLP-1RA.

Recommendation 3-4-4c. In individuals receiving insulin therapy, any addition, withdrawal, or dose adjustment of GLP-1RA or oral agents should prompt reassessment of insulin dosing to ensure appropriateness.

In individuals on intensive insulin therapy, adding a GLP-1RA (or GIP/GLP-1 dual agonist) can yield additional glycemic benefits, facilitate weight reduction, and support cardiorenal and MASLD risk management [41,93]. Concomitant OADs are feasible in this setting; however, DPP-4 inhibitors should not be combined with GLP-1RAs because of overlapping mechanisms and lack of incremental glycemic benefit [94]. Although the evidence base is smaller than for GLP-1RA plus basal insulin, studies suggest that adding a GLP-1RA to intensive insulin regimens may further improve glycemia and reduce bolus insulin requirements [95-97]. When initiating insulin or intensifying basal-plus/premixed/basal-bolus regimens, clinicians should decide which existing OADs to continue, discontinue, or dose-adjust. Conversely, when adding or withdrawing oral or injectable agents in people already on insulin, the insulin dose should be re-evaluated and adjusted accordingly. Finally, for those using insulin, structured education on correct administration and ongoing adherence reinforcement are essential components of care.

3-5. Deintensification strategies after optimizing glycemic control

Recommendation 3-5-1. In individuals who have achieved stable glycemic control within target ranges through sustained lifestyle management and continued DSMES, stepwise deintensification of pharmacologic therapy may be considered—particularly in older adults and those with renal or cognitive impairment or polypharmacy—to reduce hypoglycemia, adverse drug reactions, and treatment burden.

Recommendation 3-5-2. Deintensification should be implemented gradually under close clinical monitoring, with the capacity to promptly re-intensify therapy if glycemic deterioration occurs.

Deintensification is a purposeful reduction or simplification of glucose-lowering therapy after durable achievement of individualized targets [98,99]. Its aim is to limit hypoglycemia, adverse effects, and treatment burden without compromising metabolic stability. Candidates include people who have maintained stable control for several months with sustained lifestyle measures and DSMES—particularly older adults, those with renal or cognitive impairment, and those on multiple medications [32,100-102]. Decisions should be person-centered, balancing the expected benefits of ongoing therapy (e.g., cardiorenal protection) against risks and burden.

Deintensification should proceed with clear guardrails. Agree in advance on the target range, monitoring plan, and explicit re-intensification triggers. Reduce one agent at a time, starting with drugs that confer the greatest hypoglycemia risk or treatment burden (e.g., sulfonylureas), and adjust basal insulin in small steps with close review of fasting and postprandial profiles. Drugs with proven organ-protective effects (e.g., SGLT2 inhibitors in CKD/HF or GLP-1RA with ASCVD/stroke benefit) should not be withdrawn solely based on HbA1c if their indication persists. When weight loss is undesirable (e.g., frailty or sarcopenia risk), prefer agents with weight neutrality and low hypoglycemia risk.

Monitoring is essential. Arrange early follow-up, reinforce blood glucose monitoring or CGM use to track fasting and postprandial glucose, and reassess HbA1c within 3 months. Define reversible thresholds for action (e.g., persistent fasting or postprandial values above the individualized range, or an HbA1c rise above target) at which therapy should be promptly re-intensified. In parallel, review nutrition, physical activity, and DSMES to sustain control, and screen for symptoms of hyperglycemia or functional decline.

Finally, simplify whenever possible—fewer daily doses, once-daily formulations, or fixed combinations—while keeping the regimen aligned with the person's capabilities, preferences, and comorbidities. Document the plan and educate that deintensification is iterative and reversible; the goal is to preserve safety and quality of life while maintaining glycemic stability.

4. Comorbidity management

4-1. Management of cardiovascular and renal risk with end-organ damage

4-1-1. Atherosclerotic cardiovascular disease

Recommendation 4-1-1. In cases of ASCVD, prioritize the use of GLP-1RAs or SGLT2 inhibitors with proven cardiovascular benefits.

4-1-2. Heart failure

Recommendation 4-1-2a. In adults with T2DM and HF, SGLT2 inhibitors with proven HF benefits are preferentially recommended regardless of HbA1c levels, and therapy should be continued unless contraindications or adverse effects are present.

Recommendation 4-1-2b. If SGLT2 inhibitors are contraindicated or cannot be used, certain GLP-1RA (e.g., semaglutide) with demonstrated benefits in HF with preserved ejection fraction (HFpEF) with obesity may be considered as an alternative.

4-1-3. Chronic kidney disease

Recommendation 4-1-3a. In cases of albuminuria or decreased eGFR, prioritize the use of SGLT2 inhibitors with proven renal benefits, regardless of HbA1c levels, and maintain therapy unless there are contraindications or side effects.

Recommendation 4-1-3b. If SGLT2 inhibitors are contraindicated or not tolerated, GLP-1RAs with renal benefit may be considered as an alternative.

4-1-4. Ischemic stroke or transient ischemic attack (TIA)

Recommendation 4-1-4. In adults with T2DM and a history of ischemic stroke or TIA, GLP-1RA or TZDs may be considered to reduce the risk of recurrent stroke.

Cardiovascular and renal complications represent the major causes of morbidity and mortality in people with T2DM. Recent cardiovascular outcome trials and renal outcome studies have demonstrated that SGLT2 inhibitors and GLP-1RAs provide significant benefits beyond glucose lowering. Therefore, in adults with T2DM and comorbid ASCVD, HF, CKD, or history of ischemic stroke/TIA, drug selection should be prioritized according to proven organ protection rather than glycemic efficacy.

In T2DM patients with established ASCVD, both GLP-1RAs and SGLT2 inhibitors are effective in reducing MACE. Liraglutide Effect and Action in Diabetes: Evaluation of cardiovascular outcome Results (LEADER) (liraglutide) reduced 3-point MACE by 13%, Trial to Evaluate Efficacy and Safety of Semaglutide in Subjects with Type 2 Diabetes (SUSTAIN)-6 (semaglutide) by 26%, and Researching Cardiovascular Events with

a Weekly INcretin in Diabetes (REWIND) (dulaglutide) by 12% [23,103,104]. SGLT2 inhibitors, including empagliflozin (Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients [EMPA-REG OUTCOME]) and dapagliflozin (Dapagliflozin Effect on CardiovascuLAR Events–Thrombolysis in Myocardial Infarction [DECLARE-TIMI58]), reduced cardiovascular events and demonstrated strong benefits in preventing HF hospitalization [22,105].

SGLT2 inhibitors consistently reduce the risk of HF hospitalization and cardiovascular death. EMPA-REG OUTCOME and DECLARE-TIMI58 showed empagliflozin and dapagliflozin significantly reduced HF hospitalization by 35% and 17%, respectively [22,105]. Subsequent dedicated HF trials in patients with reduced ejection fraction—including Dapagliflozin And Prevention of Adverse-outcomes in Heart Failure (DAPA-HF) (dapagliflozin) and Empagliflozin Outcome Trial in Patients With Chronic Heart Failure and a Reduced Ejection Fraction (EMPEROR-Reduced) (empagliflozin)—demonstrated 26% and 25% risk reductions, respectively, in the composite outcome of hospitalization for HF or cardiovascular death, regardless of diabetes status [106,107]. In contrast, subsequent studies in patients with HFpEF, namely Empagliflozin Outcome Trial in Patients with Chronic Heart Failure with Preserved Ejection Fraction (EMPEROR-Preserved) (empagliflozin) and Dapagliflozin Evaluation to Improve the Lives of Patients with Preserved Ejection Fraction Heart Failure (DELIVER) (dapagliflozin), also confirmed significant reductions in HF hospitalizations [108,109]. Thus, SGLT2 inhibitors are recommended as first-line therapy for T2DM patients with HF, irrespective of HbA1c levels. When SGLT2 inhibitors cannot be used, semaglutide has shown improvements in symptoms and physical limitations among patients with obesity-related HFpEF [110].

CKD substantially worsens outcomes in T2DM. The Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) trial (canagliflozin) reduced the risk of end stage kidney disease or renal death by 30% in patients with diabetic kidney disease [111]. Dapagliflozin And Prevention of Adverse outcomes in Chronic Kidney Disease (DAPA-CKD) (dapagliflozin) and The Study of Heart and Kidney Protection With Empagliflozin (EMPA-KIDNEY) (empagliflozin) also demonstrated robust renal benefits, including reductions in sustained eGFR decline and renal composite outcomes [112,113]. These effects were consistent regardless of glycemic status. GLP-1RAs such as liraglutide (LEADER), semaglutide (SUSTAIN-6), and dulaglutide (REWIND) have also shown renal protective effects, primarily by reducing albuminuria [23,103,104].

In people with prior ischemic stroke or TIA, GLP-1RAs significantly reduce the risk of recurrent stroke [114]. REWIND and SUSTAIN-6 both demonstrated risk reductions in nonfatal stroke [103,104]. TZDs, particularly pioglitazone, reduced recurrent stroke and cardiovascular events in The PROspective pioglitAzone Clinical Trial In macroVascular Events (PROactive) and The Insulin Resistance Intervention after Stroke (IRIS) trials, but should be avoided in patients with HF due to risk of edema and weight gain [115,116].

For adults with T2DM and cardiovascular or renal complications, therapy should prioritize drugs with proven cardiorenal benefits. SGLT2 inhibitors are preferred in HF and CKD, GLP-1RAs in ASCVD and stroke prevention, and TZDs may be considered selectively for secondary stroke prevention. These recommendations represent a paradigm shift from glucose-centric to organ-centric diabetes care.

4-2. Management of metabolic comorbidity without end-organ damage

4.2.1. Obesity

Recommendation 4-2-1. In adults with T2DM and comorbid obesity, anti-obesity pharmacotherapy—such as GIP/GLP-1 dual agonist (e.g., tirzepatide) or GLP-1RAs (e.g., semaglutide and liraglutide)—should be considered, regardless of glycemic status, when lifestyle intervention alone is insufficient.

4.2.2. Metabolic dysfunction-associated steatotic liver disease

Recommendation 4-2-2a. In adults with T2DM and MASLD, GIP/GLP-1 dual agonist (e.g., tirzepatide) or GLP-1RAs (e.g., semaglutide and liraglutide) may be considered to improve hepatic steatosis, and cardiometabolic risk factors, regardless of glycemic status.

Recommendation 4-2-2b. In cases where GIP/GLP-1 dual agonist or GLP-1RA are not tolerated, contraindicated, or unavailable, TZDs may be considered as an alternative option for improving insulin sensitivity and hepatic steatosis.

Obesity is one of the most prevalent and modifiable risk factors in people with T2DM. Lifestyle modification remains the cornerstone of management, but pharmacotherapy is recommended when lifestyle measures alone are insufficient. Incretin-based therapies, particularly GLP-1RAs (e.g., semaglutide and liraglutide) and the GIP/GLP-1 dual agonist (e.g., tirzepatide), have demonstrated substantial and durable weight reduc-

tion along with improvements in glycemic and cardiometabolic risk factors. The Semaglutide Treatment Effect in People with Obesity (STEP) trials confirmed that semaglutide 2.4 mg achieved about 15% mean weight in participants without diabetes, with consistent, though somewhat smaller, benefits observed in those with T2DM [117,118]. The Tirzepatide Development Program for Weight Management in Adults with Obesity (SURMOUNT)-1 trial demonstrated that tirzepatide achieved up to approximately 21% mean weight reduction at the highest dose over 72 weeks [119]. More recently, the STEP-11 trial in East Asian adults with obesity confirmed significant weight loss with semaglutide 2.4 mg [120]. These results establish GLP-1RAs and tirzepatide as first-line pharmacologic options for weight management in T2DM when lifestyle intervention is insufficient.

MASLD is highly prevalent in T2DM and closely linked with insulin resistance and obesity. Pharmacologic agents targeting incretin pathways have shown benefits in improving hepatic steatosis, weight, and cardiometabolic outcomes. Liraglutide improved histologic resolution of steatohepatitis compared with placebo [121], and semaglutide demonstrated significant improvement in metabolic dysfunction-associated steatohepatitis (MASH) resolution without worsening of fibrosis, with confirmatory results in later-phase study [122]. Tirzepatide has likewise reduced liver fat and improved steatohepatitis endpoints in biopsy-confirmed MASH in studies enrolling individuals with and without T2DM; reductions in liver fat have also been observed in T2DM subgroups using magnetic resonance imaging-based assessments [123]. Collectively, these data support prioritizing incretin-based therapies for MASLD management, irrespective of glycemic control.

When GLP-1–based options are unsuitable, pioglitazone can be considered to improve insulin sensitivity, hepatic steatosis, and histologic features of MASH, particularly in individuals with T2DM [124]. While TZDs can cause weight gain and fluid retention and carry a potential risk of HF exacerbation, these effects are generally manageable with appropriate patient selection, dose titration, and monitoring; avoid or use with great caution in symptomatic or advanced HF.

In T2DM with comorbid obesity or MASLD, pharmacologic approaches that target weight reduction and insulin sensitivity are effective strategies to improve metabolic health and long-term outcomes. GLP-1RAs and GIP/GLP-1 dual agonist are preferred for their robust effects on weight, liver health, and cardiometabolic risk reduction, while TZDs remain a reasonable alternative in selected cases.

5. Summary

Pharmacological management of T2DM should be person-centered and organ-protective, with therapeutic choices aligned to dominant pathophysiology, comorbidities, and clinical severity while ensuring sufficient early intensity to avoid therapeutic inertia. As operationalized in Fig. 3, practice proceeds along three coordinated tracks: (1) prompt management of hypercatabolic states or suspected islet failure through timely insulin initiation and structured adjustment; (2) target-driven glycemic management that employs initial combination therapy when indicated, timely transition to injectables, active avoidance of overbasalization, and stepwise deintensification once durable control is established; and (3) comorbidity-oriented risk modification that prioritizes organ-protective agents for ASCVD, HF, CKD, ischemic stroke, and metabolic conditions such as obesity and MASLD. When insulin resistance predominates—often with obesity—agents that improve insulin sensitivity and reduce body weight (GIP/GLP-1 dual agonist, GLP-1RAs, SGLT2 inhibitors, metformin, TZDs) should be prioritized; when insulin insufficiency is dominant, secretagogue-based options (DPP-4 inhibitors, sulfonylureas) or earlier insulin may be more appropriate. Across all phases of care, lifestyle intervention and DSMES are foundational; technology-enabled care (e.g., CGM and AID) should be leveraged when feasible. Ultimately, clinical success is judged not only by HbA1c but by sustained safety, organ protection, and quality of life through ongoing shared decision-making and periodic re-evaluation.

SEVERE DIABETES MELLITUS, NOT YET ESTABLISHED BUT NEEDS TO BE CLARIFED

Recommendation 1. In determining whether to initiate pharmacologic therapy and which antidiabetic agents to select in individuals with diabetes mellitus, a comprehensive assessment of disease severity should be made. This includes evaluating the degree of metabolic dysfunction and the complication burden.

The KDA has recently issued a separate consensus statement on severe diabetes mellitus; readers are referred to that article for detailed definitions, grading or staging criteria, and therapeutic pathways [125]. In this regard, the KDA defined severe diabetes mellitus as diabetes mellitus as a condition of high

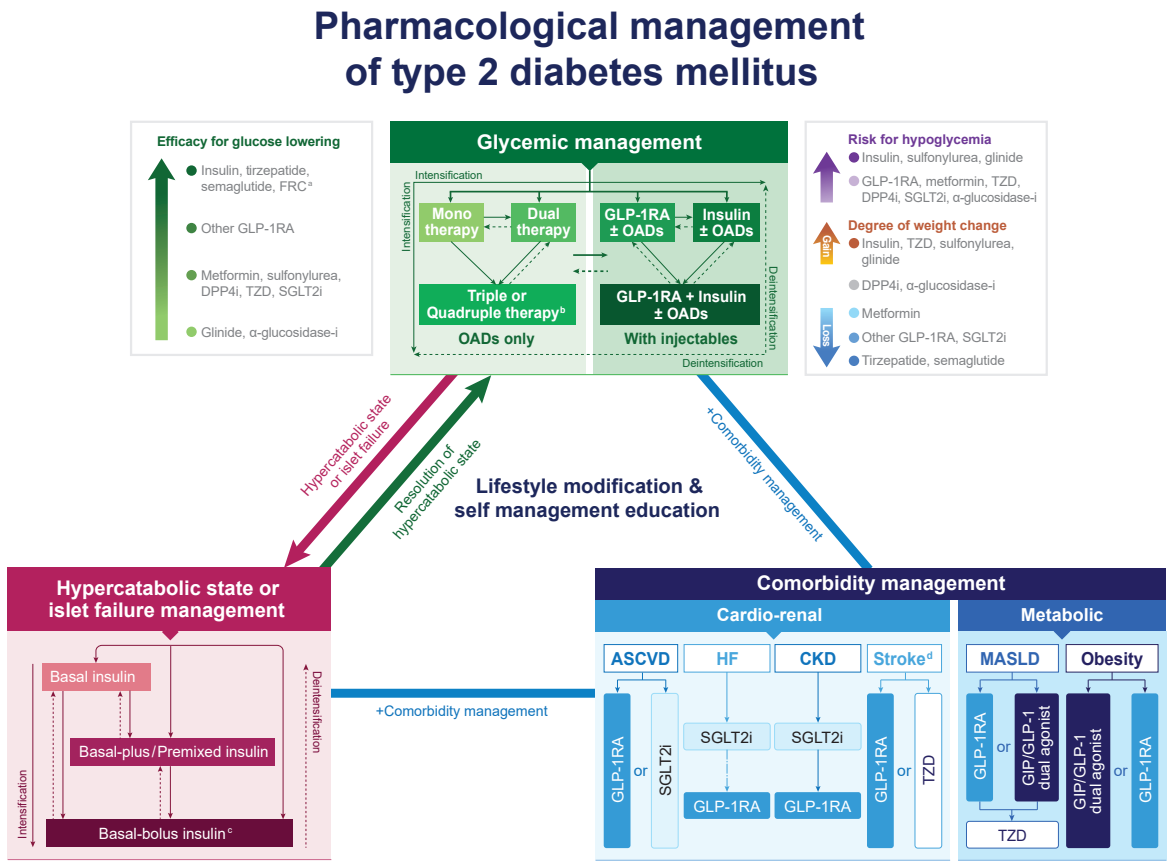

Fig. 3. Integrated algorithm for pharmacologic management of type 2 diabetes mellitus: hypercatabolic state/islet failure, glycemic management, and comorbidity management. The figure synthesizes three coordinated treatment tracks anchored in lifestyle modification and diabetes self-management education and support. The algorithm is a clinical guide, not a rigid rule set. Class selections are representative; final choices must be individualized to glycemic status and targets, hypoglycemia risk, weight goals, organ function, tolerability, access/coverage, and patient preferences, with shared decision-making. Left panel: Hypercatabolic state or islet failure management. Initiate basal insulin promptly; intensify to basal-plus/premixed or basal-bolus when needed, then deintensify as the hypercatabolic state resolves. Insulin therapy should not be delayed when hypercatabolic features or islet failure are present. Basal-bolus regimens can be delivered via multiple daily doses of insulin (MDI) or insulin pump. Center panel: Glycemic management. Pathways include oral antihyperglycemic drugs (OADs) only (mono → dual → triple/quadruple) and with injectables (glucagon-like peptide-1 receptor agonist [GLP-1RA] ± OADs, insulin ± OADs, or GLP-1RA+insulin ± OADs). Intensification and deintensification flows are depicted bidirectionally. Fixed-ratio combinations (FRCs) pair basal insulin+GLP-1RAs to reduce injection burden. The small insets summarize relative hypoglycemia risk (highest with insulin, sulfonylureas, glinides) and direction of weight change (loss with tirzepatide/semaglutide > GLP-1RA/sodium-glucose cotransporter 2 inhibitor [SGLT2i]; neutral with metformin; gain with insulin, thiazolidinedione [TZD], sulfonylureas, glinide). Right panel: Comorbidity management. Examples of agents with proven benefits available in Korea: atherosclerotic cardiovascular disease (ASCVD)—GLP-1RAs: semaglutide, liraglutide, dulaglutide; SGLT2i: dapagliflozin, empagliflozin. heart failure (HF)—SGLT2i: dapagliflozin, empagliflozin; GLP-1RA: semaglutide (HF with preserved ejection fraction with obesity). Chronic kidney disease (CKD)—SGLT2i: dapagliflozin, empagliflozin; GLP-1RAs: semaglutide, liraglutide, dulaglutide. Stroke (ischemic/transient ischemic attack; hemorrhagic excluded)—GLP-1RAs: semaglutide, dulaglutide; TZD: pioglitazone. Metabolic dysfunction-associated steatotic liver disease (MASLD)—GIP/GLP-1 dual agonist: tirzepatide; GLP-1RAs: semaglutide, liraglutide; TZD: pioglitazone. Obesity—glucose-dependent insulinotropic polypeptide (GIP)/glucagon-like peptide-1 (GLP-1) dual agonist: tirzepatide; GLP-1RAs: semaglutide, liraglutide. DPP-4i, dipeptidyl peptidase-4 inhibitor; CVD, cardiovascular disease. [a]FRC: basal insulin+GLP-1RA, [b]Insulin therapy should not be delayed, [c]Can be delivered via MDI or insulin pump, [d]Individuals with ischemic stroke, including transient ischemic attack, but excluding hemorrhagic stroke.

metabolic grade (3 or higher) or high complication stage (3 or higher). This underscores the need for a classification system that moves beyond traditional etiologic categories (such as T1DM and T2DM) to emphasize disease severity as a key determinant of prognosis and treatment. To address this, the KDA proposes a dual-axis framework, the Diabetes Grade–Stage Classification (DGSC), integrating both metabolic grading and complication staging. pathophysiology-based metabolic grading captures the severity of underlying metabolic dysfunction based on two core domains: insulin deficiency and insulin resistance. This metabolic grade ranges from grade 1 (mild dysfunction) to grade 4 (very severe dysfunction). In parallel, complication staging assesses cumulative organ damage across the cardiovascular, kidney, ocular, and nervous systems, ranging from stage 1 (at risk) to stage 4 (advanced). After classifying an individual as having severe diabetes mellitus using the DGSC, a secondary clinical evaluation is recommended to guide management intensity or specialist referral. This evaluation considers factors such as difficulty in glycemic control (e.g., persistent hyperglycemia, high glycemic variability, or hypoglycemia) and the rate of disease progression.

By integrating the stage–grade framework in clinical assessment, healthcare providers can more effectively stratify risk and individualize therapy for people with diabetes mellitus. This approach also facilitates standardized documentation for clinical decision-making, reimbursement, and research. Ultimately, adopting this integrated severity classification aims to improve outcomes by aligning therapeutic intensity with objective measures of disease complexity.

CONCLUSIONS

This consensus statement offers a comprehensive and practical approach to diabetes management in Korea, incorporating the latest scientific insights to optimize patient outcomes. By integrating three foundational pillars—targeted screening, person-centered pharmacotherapy, and a severity framework that aligns therapeutic intensity with disease complexity—we provide robust, actionable guidance for clinicians. For successful implementation, health systems should support ongoing clinician education, alignment with reimbursement and broader health policy, and consistent integration of these practices across diverse care settings. We further advocate the establishment of national registries and the conduct of pragmatic trials and real-world studies to validate and refine these recommendations in Korean populations. Priority areas include developing screening and treatment thresholds tailored to age and phenotypic characteristics, with particular attention to older or frail individuals.

SUPPLEMENTARY MATERIALS

Supplementary materials related to this article can be found online at https://doi.org/10.4093/dmj.2025.0978.

CONFLICTS OF INTEREST

Hyuk-Sang Kwon has been editor-in-chief of the *Diabetes & Metabolism Journal* since 2024. Seung-Hyun Ko has been the executive editor of the *Diabetes & Metabolism Journal* since 2022. Jae Hyun Bae has been a managing editor of the *Diabetes & Metabolism Journal* since 2024. Sang Yong Kim has been an associate editor of the *Diabetes & Metabolism Journal* since 2022. They were not involved in the review process of this article. Otherwise, there was no conflict of interest.

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Supplementary Table 1. Agreement rates for individual recommendations

	Recommendations	Agreement rate, %
Diabetes screening in Korean adults		
1. Target population for diabetes screening		
Recommendation 1-1.	All Korean adults aged ≥19 years with one or more risk factors should be screened for diabetes.	100
Recommendation 1-2.	All Korean adults aged ≥35 years should be screened for diabetes regardless of risk factors.	100
2. Initial screening testing		
Recommendation 2-1.	Screening for diabetes may be performed using FPG, HbA1c, or a 2-hr PG during 75-g OGTT.	100
Recommendation 2-2.	For high-risk individuals or those with prior screening suggestive of prediabetes, combining two tests (e.g., FPG+HbA1c) may be considered to improve detection.	96
3. Screening interval after a normal result		
Recommendation 3.	Individuals with normal screening results, without evidence of prediabetes or diabetes, are recommended to undergo repeat screening every 1–2 years, depending on risk factors and previous test results.	96
4. Additional testing and follow-up after a prediabetes result on FPG or HbA1c		
Recommendation 4-1.	If one screening test falls within the prediabetes range, one or more additional tests should be considered to improve diagnostic accuracy.	96
Recommendation 4-2.	A 2-hr PG during 75-g OGTT should be considered in individuals with FPG 110–125 mg/dL or HbA1c 6.1%–6.4%.	100
Recommendation 4-3.	Individuals confirmed to have prediabetes after screening are recommended to undergo repeat screening annually.	96
Pharmacological management of T2DM		
1. Person-centered determinants in pharmacological treatment decision-making for T2DM		
Recommendation 1-1.	In determining whether to initiate pharmacologic therapy and which antidiabetic agents to select in individuals with T2DM, a comprehensive assessment should include: the presence of hypercatabolic symptoms; likelihood of islet failure; current glycemic status and glycemic target; body weight; comorbidities—especially cardiovascular and renal risks; the individual's dominant pathophysiologic phenotype of diabetes; life expectancy; physical and cognitive function; personal values and treatment acceptability; and social determinants of health.	92
Recommendation 1-2.	Throughout all stages of pharmacologic treatment, lifestyle modification—including medical nutrition therapy, physical activity, smoking cessation, and psychosocial management—should be consistently integrated with diabetes self-management education and support (DSMES) to optimize clinical outcomes.	96
Recommendation 1-3.	From the initiation of pharmacologic therapy through each stage of treatment, medication adherence should be regularly assessed, and treatment should be promptly intensified when individualized glycemic targets are not achieved, in order to minimize therapeutic inertia.	100
2. Hypercatabolic state or islet failure		
2-1. Initial treatment approach of hypercatabolic state		
Recommendation 2-1-1.	In individuals presenting with hypercatabolic symptoms attributable to diabetes—such as unintended weight loss, polyuria, and polydipsia—insulin therapy should be initiated promptly, including when the current blood glucose is not markedly elevated.	96
Recommendation 2-1-2.	For individuals with mild hypercatabolic features who are clinically stable and able to take oral intake, basal insulin with or without oral antihyperglycemic agents may be initiated.	88
Recommendation 2-1-3.	For individuals requiring more aggressive glycemic control—due to marked hyperglycemia or more prominent hypercatabolic features—intensive insulin regimens (basal-plus, premixed, or basal-bolus) may be initiated.	88

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Supplementary Table 1. Continued

	Recommendations	Agreement rate, %
Recommendation 2-1-4.	In cases with severe dehydration, altered mental status, or suspected diabetic ketoacidosis (DKA) or hyperosmolar hyperglycemic state, the individual should be promptly hospitalized. Initial treatment should include intravenous insulin infusion and fluid resuscitation, followed by transition to multiple daily doses of insulin (MDI) once stabilized and oral intake is possible.	88
2-2. Treatment evaluation and adjustment in hypercatabolic state: intensification and deintensification strategies		
Recommendation 2-2-1.	After insulin initiation at hypercatabolic state, treatment response may be evaluated based on improvement in symptoms, glucose levels, and resolution of ketonuria.	84
Recommendation 2-2-2.	If basal insulin alone (±OADs) is insufficient to achieve glycemic targets—based on persistent hyperglycemia, inadequate symptom resolution, or ongoing ketonuria—intensification of insulin therapy should be considered. This may involve the addition of prandial insulin (e.g., basal-plus), transition to premixed insulin, or basal-bolus regimens depending on clinical needs and meal patterns.	96
Recommendation 2-2-3.	Insulin dose reduction or discontinuation may be considered once metabolic stability is achieved, hypercatabolic symptoms have resolved, and glycemic control is maintained with declining insulin requirements.	92
2.3. Use and contraindications of OADs in hypercatabolic state		
Recommendation 2-3-1.	During insulin therapy in hypercatabolic state, the concomitant use of OADs may be considered if there are no specific contraindications.	88
Recommendation 2-3-2.	SGLT2 inhibitors should be avoided in hypercatabolic states due to safety concerns, including the risk of euglycemic DKA. If SGLT2 inhibitors are indicated for comorbid conditions, initiation may be cautiously considered only after the hypercatabolic state has resolved and metabolic stability is confirmed.	96
2.4. Management of islet failure: insulin strategies and technology-enabled care		
Recommendation 2-4-1.	In individuals with established islet failure, intensive insulin therapy using MDI or insulin pump is the preferred treatment to optimize glycemic control and reduce hypoglycemia risk.	96
Recommendation 2-4-2.	Diabetes technologies—including real-time continuous glucose monitoring, sensor-augmented pumps, or automated insulin delivery systems—should be actively considered for individuals capable of safe device use.	92
Recommendation 2-4-3.	Given the complexity of insulin management in islet failure, individuals should receive structured education from trained diabetes educators. If this is not feasible, referral to specialized diabetes centers with adequate expertise and resources is recommended.	100
3. Glycemic management		
3.1. Pathophysiology- and comorbidity-guided initial selection of antidiabetic drugs		
Recommendation 3-1.	At the initiation of pharmacological treatment, glucose-lowering agents should be selected based on the individual's underlying pathophysiology of diabetes or the presence of comorbidities.	96
Recommendation 3-1-1.	In the absence of established end-organ damage comorbidities such as atherosclerotic cardiovascular disease (ASCVD), heart failure (HF), chronic kidney disease (CKD), or ischemic stroke, drugs should be selected primarily according to the person's dominant pathophysiologic phenotype (refer to subsection 3-3).	84
Recommendation 3-1-2.	In individuals with established end-organ damage comorbidities such as ASCVD, HF, CKD, or ischemic stroke, agents with proven benefits for the relevant condition(s) should be prioritized when initiating pharmacologic therapy (refer to subsection 4).	100

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Supplementary Table 1. Continued

Recommendations		Agreement rate, %
3.2. Glycemic target-based initial selection of treatment intensity and combination therapy		
Recommendation 3-2.	At the initiation of pharmacologic therapy, medications with sufficient glucose-lowering efficacy should be selected to achieve glycemic targets, considering the individual's current glycemic status and target goals.	96
Recommendation 3-2-1.	If monotherapy is unlikely to achieve the glycemic target, initial combination therapy with two or three OADs with complementary mechanisms of action should be considered.	100
Recommendation 3-2-2.	If the glycemic target is unlikely to be achieve with oral combination therapy, initiating injectable therapy—such as a GLP-1/GIP dual agonist, a GLP-1RA, or insulin—should be considered.	96
3.3. Pathophysiology-based initial selection of antidiabetic drugs for Korean patients with T2DM		
3.3.1. Predominant insulin resistance		
Recommendation 3-3-1a.	In adults with T2DM who are obese and considered to have an insulin resistance–dominant phenotype, GLP-1/GIP dual agonists, GLP-1RAs, SGLT2 inhibitors, and metformin may be preferred options for both their insulin-sensitizing and weight-reducing effects.	84
Recommendation 3-3-1b.	Although TZDs may cause modest weight gain, they effectively improve insulin resistance and can be beneficial for insulin resistance–dominant individuals. To minimize weight gain, combining TZDs with weight-reducing agents may be an effective strategy.	88
3.3.2. Predominant insulin insufficiency		
Recommendation 3-3-2a.	In adults with T2DM who are not obese and considered to have an insulin insufficiency–dominant phenotype, DPP-4 inhibitors or sulfonylureas can be considered as potential first-line oral agents.	80
Recommendation 3-3-2b.	In older adults, frail individuals, or those with lower body weight, DPP-4 inhibitors are preferred due to weight neutrality and a low risk of hypoglycemia.	84
3.4. Intensification strategies in individuals already receiving glucose-lowering medications		
3.4.1. Early intensification and combination therapy with oral agents		
Recommendation 3-4-1a.	Treatment should be promptly intensified to effectively achieve the glycemic target at an early stage, by uptitrating current medications to their maximum tolerated doses and/or by adding agents with different mechanisms of action, based on the individual's glycemic status and existing treatment regimen.	100
Recommendation 3-4-1b.	If glycemic targets are not achieved despite triple OADs, and injectable treatment is not feasible, an up-to quadruple OADs regimen may be considered in limited situations—specifically when the individual does not exhibit symptoms of hypercatabolic states, has moderately elevated hyperglycemia (e.g., HbA1c <8.0%), and is not suspected to have significant islet failure.	100
3.4.2. Early intensification of injectable therapy, prioritizing incretin-based agents		
Recommendation 3-4-2a.	If glycemic targets are not achieved despite appropriate oral combination therapy, injectable therapies should be initiated promptly.	100
Recommendation 3-4-2b.	When selecting an injectable agent, GLP-1RAs (or GLP-1/GIP dual agonist) are preferred over basal insulin in individuals without symptoms of hypercatabolic states and with low likelihood of islet failure.	92
Recommendation 3-4-2c.	If glycemic targets are not achieved with either GLP-1RA (or GLP-1/GIP dual agonist) or basal insulin, combination therapy using both agents should be considered.	100
Recommendation 3-4-2d.	When combining GLP-1RA and basal insulin, fixed-ratio combination therapy may be considered to reduce injection frequency and improve adherence.	96

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Supplementary Table 1. Continued

Recommendations		Agreement rate, %
3.4.3. Avoiding overbasalization and transitioning to intensive insulin regimens		
Recommendation 3-4-3a.	In individuals receiving basal insulin therapy (±OADs) who experience frequent hypoglycemia and marked glycemic fluctuation, overbasalization should be suspected, and treatment should be intensified by reducing basal insulin and adding postprandial glucose-lowering strategies such as GLP-1RA (or GLP-1/GIP dual agonist) or insulin intensification.	92
Recommendation 3-4-3b.	If glycemic targets are not achieved despite combination therapy with GLP-1RA (or GLP-1/GIP dual agonist) and basal insulin, intensive insulin therapy—such as basal-plus, premixed, or basal-bolus regimens—should be implemented.	100
3.4.4. Optimizing combination therapy with injectables and oral agents		
Recommendation 3-4-4a.	In individuals on intensive insulin therapy, GLP-1RA (or GLP-1/GIP dual agonist) may be added to provide additional clinical benefits, including weight loss, reduced insulin requirements, and improved management of cardiovascular, renal, and metabolic dysfunction-associated steatotic liver disease (MASLD)-related risks.	100
Recommendation 3-4-4b.	In all people with T2DM receiving injectable therapy (GLP-1RA, basal insulin, or intensive insulin therapy), combination with OADs may be added to achieve additional clinical benefits, such as reduced insulin requirements, and cardiovascular and renal risk management. However, DPP-4 inhibitors should not be combined with GLP-1RA.	100
Recommendation 3-4-4c.	In individuals receiving insulin therapy, any addition, withdrawal, or dose adjustment of GLP-1RA or oral agents should prompt reassessment of insulin dosing to ensure appropriateness.	96
3.5. Deintensification strategies after optimizing glycemic control		
Recommendation 3-5-1.	In individuals who have achieved stable glycemic control within target ranges through sustained lifestyle management and continued DSMES, stepwise deintensification of pharmacologic therapy may be considered—particularly in older adults and those with renal or cognitive impairment or polypharmacy—to reduce hypoglycemia, adverse drug reactions, and treatment burden.	96
Recommendation 3-5-2.	Deintensification should be implemented gradually under close clinical monitoring, with the capacity to promptly re-intensify therapy if glycemic deterioration occurs.	96
4. Comorbidity management		
4.1. Management of cardiovascular and renal risk with end-organ damage		
4.1.1. Heart failure		
Recommendation 4-1-1a.	In adults with T2DM and HF, SGLT2 inhibitors with proven HF benefits are preferentially recommended regardless of HbA1c levels, and therapy should be continued unless contraindications or adverse effects are present.	100
Recommendation 4-1-1b.	If SGLT2 inhibitors are contraindicated or cannot be used, certain GLP-1RA (e.g., semaglutide) with demonstrated benefits in HF with preserved ejection fraction with obesity may be considered as an alternative.	92
4.1.2. Chronic kidney disease		
Recommendation 4-1-2a.	In cases of albuminuria or decreased eGFR, prioritize the use of SGLT2 inhibitors with proven renal benefits, regardless of HbA1c levels, and maintain therapy unless there are contraindications or side effects.	100
Recommendation 4-1-2b.	If SGLT2 inhibitors are contraindicated or not tolerated, GLP-1RAs with renal benefit may be considered as an alternative.	100

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Supplementary Table 1. Continued

Recommendations		Agreement rate, %
4.1.3. Atherosclerotic cardiovascular disease		
Recommendation 4-1-3.	In cases of ASCVD, prioritize the use of GLP-1RAs or SGLT2 inhibitors with proven cardiovascular benefits.	96
4.1.4. Ischemic stroke		
Recommendation 4-1-4.	In adults with T2DM and a history of ischemic stroke or transient ischemic attack, GLP-1RA or TZDs may be considered to reduce the risk of recurrent stroke.	96
4.3. Management of metabolic comorbidity without end-organ damage		
4.3.1. Morbid obesity		
Recommendation 4-2-1.	In adults with T2DM and comorbid obesity, anti-obesity pharmacotherapy—such as GLP-1/GIP dual agonist (e.g., tirzepatide) or GLP-1RAs (e.g., semaglutide and liraglutide)—should be considered, regardless of glycemic status, when lifestyle intervention alone is insufficient.	96
4.3.2. Metabolic dysfunction-associated steatotic liver disease		
Recommendation 4-2-2a.	In adults with T2DM and MASLD, GLP-1/GIP dual agonist (e.g., tirzepatide) or GLP-1RAs (e.g., semaglutide and liraglutide) may be considered to improve hepatic steatosis, and cardiometabolic risk factors, regardless of glycemic status.	84
Recommendation 4-2-2b.	In cases where GLP-1/GIP dual agonist or GLP-1RA are not tolerated, contraindicated, or unavailable, TZDs may be considered as an alternative option for improving insulin sensitivity and hepatic steatosis.	92
Severe diabetes mellitus, not yet established but needs to be clarifed		
Recommendation 1.	In determining whether to initiate pharmacologic therapy and which antidiabetic agents to select in individuals with severe T2DM, a comprehensive assessment should be made of the following: a high complication stage, indicating substantial target organ damage; a high metabolic grade, reflecting severe insulin deficiency, marked insulin resistance, and uncontrolled or highly variable glycemia; or both.	80

FPG, fasting plasma glucose; HbA1c, glycosylated hemoglobin; 2-hr PG, 2-hour plasma glucose; OGTT, oral glucose tolerance test; T2DM, type 2 diabetes mellitus; OAD, oral antihyperglycemic drug; SGLT2, sodium-glucose cotransporter 2; GLP-1, glucagon-like peptide-1; GIP, glucose-dependent insulinotropic polypeptide; GLP-1RA, glucagon-like peptide-1 receptor agonist; TZD, thiazolidinedione; DPP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration rate.