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GUIDELINES

Recommendations for Early and Comprehensive Management of Type 2 Diabetes and Its Related Cardio-Renal Complications

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ABSTRACT

Type 2 diabetes (T2D) is a global health problem accompanied by an elevated risk of complications, the most common being cardiac and renal diseases. In Lebanon, the prevalence of T2D is estimated at 8–13%. Local medical practice generally suffers from clinical inertia, with gaps in the yearly assessment of clinical manifestations and suboptimal screening for major complications. The joint statement presented here, endorsed by five Lebanese scientific medical societies, aims at providing physicians in Lebanon with a tool for early, effective, and comprehensive care of patients with T2D. Findings from major randomized clinical trials of antidiabetic medications with cardio-renal benefits are presented, together with recommendations from international medical societies. Optimal care should be multidisciplinary and should include a multifactorial risk assessment, lifestyle modifications, and a regular evaluation of risks, including the risks for cardiovascular (CV) and renal complications. With international guidelines supporting a shift in T2D management from glucose-lowering agents

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to disease-modifying drugs, the present statement recommends treatment initiation with metformin, followed by the addition of sodium-glucose cotransporter 2 inhibitors or glucagon-like peptide-1 receptor agonists due to their CV and renal protection properties, whenever possible. In addition to the selection of the most appropriate pharmacological therapy, efforts should be made to provide continuous education to patients about their disease, with the aim to achieve a patient-centered approach and to foster self-management and adherence to the medical plan. Increasing the level of patient engagement is expected to be associated with favorable health outcomes. Finally, this statement recommends setting an achievable individualized management plan and conducting regular follow-ups to monitor the patients' glycemic status and assess their risks every 3–6 months.

Keywords: Type 2 diabetes; Early management; Diabetic complications; Glycemic control; Chronic kidney disease; Nephropathy risk; Cardiovascular risk; Treatment

Key Summary Points

Local medical practice regarding type 2 diabetes (T2D) management in Lebanon suffers from clinical inertia, with serious gaps in the initial and periodic assessments for major complications.

Cardiac and renal diseases are two main T2D complications, and these can be as challenging to treat and as life-threatening as the disease itself.

The management of T2D has shifted from glucose-lowering agents to disease-modifying drugs, such as sodium-glucose cotransporter type 2 inhibitors (SGLT2i) and glucagon-like peptide-1 receptor agonists (GLP-1 RA).

SGLT2i and GLP-1 RA have become pillars in the management of T2D due to their cardiovascular and renal protective properties.

The Lebanese consortium, in this joint statement based on international recommendations, endorses evidence-based practice, collaborative care, and patient engagement and empowerment for early T2D management in order to achieve optimal outcomes on a long-term basis.

INTRODUCTION

Diabetes, particularly type 2 (T2D), is a worldwide health problem with a major burden of disease that entails 10% of total global adult healthcare expenditure [1]. In Lebanon, reports on the prevalence of diabetes mellitus vary, with figures ranging from 8% to 13% [2–4]. Patients with T2D are at high risk of serious complications, with the most frequent of these being cardiac and renal diseases. These complications have an early onset although they generally remain under-recognized [5]. The

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importance of early prevention is all the more accentuated by the cardiac and renal risks that develop along a risk continuum over several years [6]. The objective of this joint statement is to provide Lebanese physicians with a tool to support the early, effective, and comprehensive care of patients with T2D, with the ultimate aim to achieve optimal outcomes. It was developed by a multidisciplinary panel of physicians involved in T2D care, representative of the Lebanese Society of Endocrinology, Diabetes and Lipids, the Lebanese Society of Cardiology, the Lebanese Society of Nephrology and Hypertension, the Lebanese Society of Internal Medicine, and the Lebanese Society of General Practice. This article outlines a strategy for a comprehensive approach to T2D care in Lebanon, including assessment for and management of risk factors, with a focus on the selection of anti-hyperglycemic agents conferring cardiac and renal protection and benefits, and on collaborative patient-centered care, based on the latest global recommendations and emerging scientific evidence.

T2D BURDEN: THE CARDIO-RENAL-METABOLIC INTERACTION

The management of T2D has shifted from glucose-lowering agents, mainly insulin, metformin, and sulfonylureas, to disease-modifying drugs (DMDs) [7]. Studies applying the international requirements to confirm the cardiovascular (CV) safety of antidiabetics [8] and dipeptidyl peptidase-4 inhibitors (DPP-4i) showed CV safety of these drugs but did not show any CV superiority [9–11]. The most commonly used DMDs are sodium-glucose cotransporter type 2 inhibitors (SGLT2i) and glucagon-like peptide-1 receptor agonists (GLP-1 RA), which currently constitute the major pillars in the management of T2D due to their CV and renal protection properties [12–14].

Studies underline that the main focus of local clinical management of T2D is glycated hemoglobin (HbA1c) control, with delays in treatment intensification despite suboptimal levels of control, lack of patients' awareness on the importance of self-monitoring of blood glucose, negligence or gaps in the yearly assessment of clinical manifestations, and suboptimal screening and diagnosis of major complications, such as CV and renal conditions [15–17]. T2D remains uncontrolled in many patients, i.e., HbA1c > 7%, even with improvements in the screening for complications over the years [18]. This, along with the high occurrence of T2D in Lebanon, highlights a dire need for practical local guidelines to design a comprehensive approach for an optimal management of patients with T2D. Major elements for optimal care are summarized in Fig. 1 and will be outlined in detail in this joint statement.

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

CARDIAC, RENAL, AND METABOLIC RISK FACTORS ASSESSMENT

Although reaching glycemic control is at the heart of T2D management, optimal care should tackle all risk factors and clinical manifestations beyond HbA1c. HbA1c levels play a primordial role in predicting T2D complications [19] and should be continuously monitored. The management plan must then be reassessed in accordance with these results, based on patients' life expectancy, duration of diabetes, presence of microvascular and macrovascular complications, comorbid conditions, risk of hypoglycemia, and the patients' social, psychological, and economic status. Because T2D is often complicated by microvascular, macrovascular, and multiple cardio-renal-metabolic conditions, optimal care for patients should translate into multifactorial risk assessment, counseling to guide lifestyle modifications, and a regular evaluation for major complications, mainly CV, renal, neurological, ophthalmological, and peripheral arterial disease. Lifestyle management is an important component in reducing the risk of T2D-associated complica-

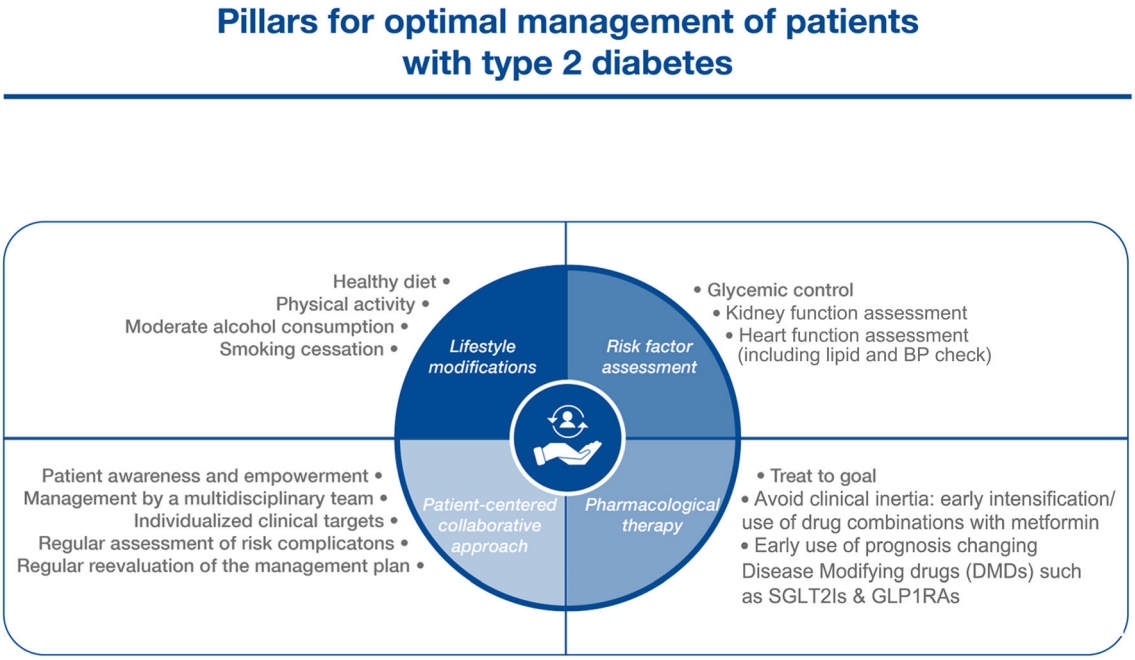

Fig. 1 Pillars for optimal management of patients with type 2 diabetes. *BP* Blood pressure, *DMDs* Disease modifying drugs, *GLP-1 RA* glucagon-like peptide-1 receptor agonists, *SGLT2i* sodium-glucose cotransporter type 2 inhibitors

tions and comorbidities. In Lebanon, the prevalence of overweight among adults is reported to be around 40% and that of obesity to range from 26.1% to 28.2% [20, 21]. Those obesity figures increase in patients with T2D to reach a prevalence of 48.4% [15]. Health hygiene practices include weight loss for overweight patients, increased physical activity to more than 150 min per week, limited sedentary time, a healthy diet, moderate alcohol consumption, and smoking cessation. Lifestyle modifications should be applied by the patients in a timely manner and be sustained over the long term, in parallel with pharmacological treatment, in support of the three pillars of T2D clinical care: glycemic control, heart function assessment, and kidney function assessment.

Glycemic Control

An HbA1c goal of 7% is considered appropriate for many adults; however, it could be fine-tuned and individualized based on the patient's profile and according to the treating physician's opinion. Setting and controlling individualized glycemic targets, especially early on in the course of T2D, has shown persistent CV and microvascular benefits, including a reduction or a delay in myocardial infarction and nephropathy onset [22, 23]. Hence, when therapeutic targets are not met, timely adjustments in the treatment regimen of patients with T2D are recommended to avoid clinical inertia, for optimal control of glycemia, and prevention of both microvascular and macrovascular complications [24]. In Lebanon, a recent report showed a delay in treatment intensification for patients with T2D, highlighting suboptimal management of the disease. This report should motivate healthcare providers on the importance of early intervention and on the adoption of a more proactive and aggressive approach for a timely and optimal control of T2D and prevention of related complications [16]. Glycemic control is usually unsustainable over time with monotherapy; therefore, dual or triple therapy is required to attain it. Hence, early combination therapies (dual or triple) are recommended

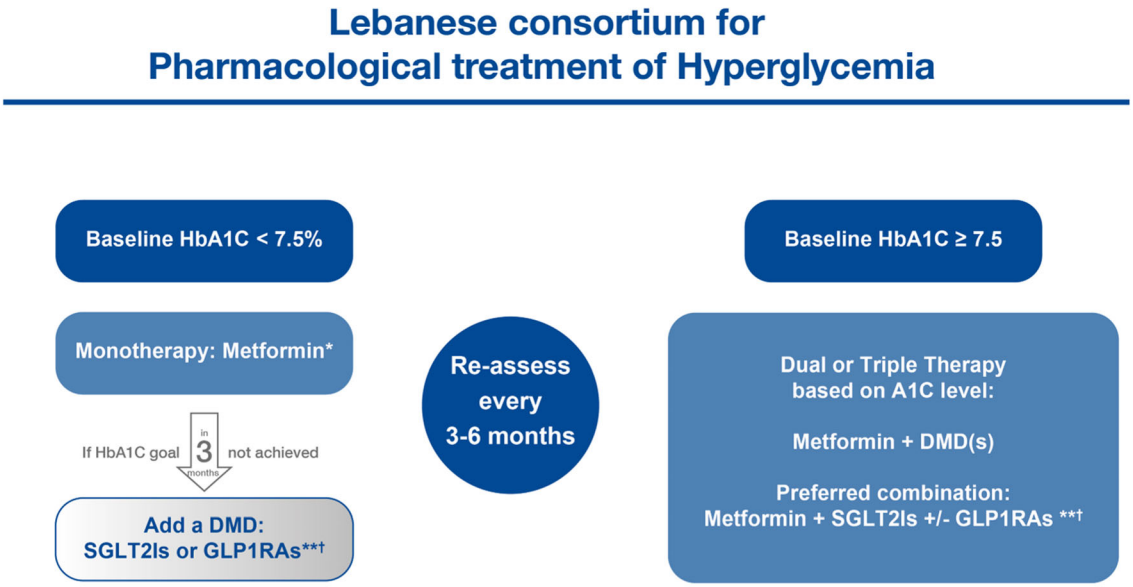

Fig. 2 Lebanese consortium for pharmacological treatment of hyperglycemia recommendation. Single asterisk: For patients at high risk (e.g., atherosclerotic cardiovascular disease, multiple risk factors, HF, or chronic kidney disease) or if treatment with metformin is contraindicated, DMDs could be initiated first. Double asterisks: For patients with established HF or CKD, SGLT2i remain the DMD with the highest proven benefit. Dagger: For patients who cannot tolerate or afford DMDs, then other antidiabetic medications (dipeptidyl peptidase-4 inhibitor, thiazolidinediones, sulfonylureas or insulin) remain viable options for effective glycemic control, although they do not offer cardio-renal protection. *HbA1c* Glycated hemoglobin A1

to achieve HbA1c goals and prevent treatment failure.

In addition, reaching glycemic control does not necessarily imply treatment de-intensification, especially in patients expected to live for a long time with T2D and who are at low risk for hypoglycemia. This is even less of a challenge with novel anti-hyperglycemic agents that do not increase the risk of hypoglycemia, namely GLP-1 RA and SGLT2i, which confer additional CV and renal benefits beyond glycemic management. Figure 2 summarizes the pharmacological treatments applied to reach glycemic control.

Heart Function Assessment

Worldwide, cardiovascular disease (CVD) is the most common cause of death in patients with T2D [25]. In addition to the increased risk of CVD by T2D itself, common T2D-associated conditions, such as hypertension and dyslipidemia, also increase the CVD risk. Therefore, regular monitoring of CV risk factors is required for an optimal management of T2D, especially in light of studies showing that addressing several risk factors simultaneously with an intensive treatment reduces the risk of all-cause deaths and CV-related deaths among patients with T2D [26]. These risk factors include elevated blood pressure (BP) and low-density lipoprotein (LDL)-cholesterol, low HDL levels, heart failure (HF), and atherosclerotic CVD. HF is the leading complication in patients with T2D, and it is currently widely acknowledged that the incidence of hospitalization due to HF in this patient population is twice as high as that in non-T2D subjects. Indeed, HF occurs more often than other CV complications and has an early onset in patients with T2D [5, 27]. Evidence from randomized trials demonstrates that HF, in addition to being common in patients with T2D and clinically relevant, is also preventable and treatable [28]. This finding is of a particular clinical importance because HF has

long been ignored when the focus was mainly on glycemic control and the prevention of ischemic macrovascular complications [28, 29]. Early assessment and management of HF risk, i.e., 5 years post T2D diagnosis, is crucial because HF represents a substantial global burden with significant unmet needs in terms of morbidity and mortality. Screening and diagnostic tests for HF include an electrocardiography (ECG), an echocardiography (ECHO), and assessment of biomarkers, such as B-type natriuretic peptide (BNP) or its N-terminal prohormone (NT-proBNP), where possible.

Kidney Function Assessment

Screening for nephropathy is one of the pillars of the management of T2D. Diabetic kidney disease (DKD) occurs in up to 40% of patients with T2D [30], prompting the need for regular screening that should be done by measuring both the urinary albumin to creatinine ratio (UACR) and serum creatinine coupled with automatic laboratory reporting of the estimated glomerular filtration rate (eGFR) using an appropriate formula, such as that of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), annually. Periodic monitoring is needed with more frequent testing if the UACR exceeds 300 mg/g and/or the eGFR is $<$ 60 mL/min/1.73 m^2. Current recommendations, in particular those of the Kidney Disease Global Improved Outcomes (KDIGO), endorse testing both UACR and eGFR since an abnormality in one of these markers can be an indicator for DKD. A heat map for assessment of risk progression of chronic kidney disease (CKD), included in the recent American Diabetes Association (ADA)/KDIGO 2022 consensus report for diabetes management in CKD [31], is based on both UACR and eGFR. A higher UACR coupled with low eGFR carries a significant risk of progression to end-stage kidney disease (ESKD), hence the importance of regular checks of these parameters in patients with already established DKD and timely intervention [32]. A study carried out in the USA in 2014 showed that although physicians generally agree with the definition of CKD and albuminuria testing, a large proportion seemed to recognize that low levels of eGFR could be lone indicators of CKD while a smaller proportion agreed that UACR could also be an indicator for CKD even when eGFR values are normal [33]. At the local clinical level, a recent study on T2D management and patient quality of life and treatment satisfaction in Jordan and Lebanon showed suboptimal screening for diabetic kidney complications [15]. It is common practice to have urine albumin measured without simultaneous urine creatinine measurement, which does not allow the calculation of UACR and, consequently, does not achieve the aim of the testing. The Lebanese Consortium for Early and Comprehensive Management of T2D (LCECMD) attributed the suboptimal follow-up in part to a lack of knowledge of treating physicians and recommended that the clinical laboratories automatically provide standardized UACR and eGFR calculations, which can be used to optimize the collaborative multidisciplinary care of each patient. This recommendation is supported by other studies underlining the lack of awareness in physicians regarding the development and monitoring of CKD [34]. However, CKD imposes a heavy burden on patients with T2D, especially in that renal and CV complications are connected and the worsening of renal function negatively impacts the CV outcomes [35, 36]. In addition, and besides the risk of ESKD, DKD is associated with or can exacerbate several other conditions, such as hypertension, volume overload, electrolyte abnormalities, metabolic acidosis, anemia, malnutrition, and metabolic bone disease.

ANTIDIABETICS WITH CARDIO-RENAL BENEFITS

While DPP-4 inhibitors have not been shown to reduce hospitalization for HF or CV events in patients with T2D [11, 37–39], novel antidiabetic agents like SGLT2i and GLP-1 RA have been proven to have cardio-renal benefits in robust evidence-based clinical trials. However, unlike SGLT2i, GLP-1 RA has been shown to have a neutral effect on hospitalization due to HF. Tables 1 and 2 summarize evidence from

Table 1 Summary of randomized clinical trials of the major sodium-glucose cotransporter type 2 inhibitor and glucagon-like peptide-1 receptor agonists classes available in Lebanon and with cardiovascular benefits in patients with type 2 diabetes

Antidiabetic agent	Randomized clinical trial[a]	Enrolled patients	Comparator	CV outcomes (HR)
SGLT2i				
Dapagliflozin	DECLARE [49]	17200	Placebo	[b]CV death or hHF: 4.9% vs. 5.8% (0.83)
Empagliflozin	EMPA-REG [14]	7000	Placebo	[b]Death from CV causes, nonfatal MI, or nonfatal stroke: 10.5% vs. 12.1% (0.86)
				[c]Lower risk of hHF (0.65)
Canagliflozin	CANVAS [50]	10100	Placebo	[b]Death from CV causes, nonfatal MI, or nonfatal stroke: 26.9 vs. 31.5 participants per 1000 patient-years (0.86)
				[d]hHF: 5.5 vs. 8.7 participants per 1000 patient-years (0.67)
	CREDENCE [46]	4400	Placebo	[d]CV death or hHF: 31.5 vs. 45.4 participants per 1000 patient-years (0.69)
Ertugliflozin	VERTIS CV [51]	8200	Placebo	[d]Death from CV causes or hHF: 8.1% vs. 9.1% (0.88)
				[d]hHF: 2.5% vs. 3.6% (0.70)
GLP-1 RA				
Liraglutide	LEADER [12]	9300	Placebo	[b]First occurrence of death from CV causes, nonfatal MI, or nonfatal stroke: 13.0% vs. 14.9% (0.87)
				[c]hHF: 4.7% vs. 5.3% (0.87)
Semaglutide	SUSTAIN-6 [52]	3300	Placebo	[b]First occurrence of CV death, nonfatal MI, or nonfatal stroke: 6.6% vs. 8.9% (0.74)
Dulaglutide	REWIND [53]	9900	Placebo	[b]First occurrence of non-fatal MI, non-fatal stroke, or death from CV causes: 12.0% vs. 13.4% (0.88)

CV Cardiovascular, *GLP-1 RA* glucagon-like peptide-1 receptor agonist, *hHF* hospitalization due to heart failure, *HR* hazard ratio, *MI* myocardial infarction, *SGLT2i* sodium-glucose transport protein 2 inhibitor

[a]CANVAS, Canagliflozin Cardiovascular Assessment Study; CREDENCE, Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation; DECLARE, Dapagliflozin Effect on Cardiovascular Events; ELIXA, Evaluation of Lixisenatide in Acute Coronary Syndrome; EMPA-REG, Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients; EXSEL, Exenatide Study of Cardiovascular Event Lowering; LEADER, Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results; *PIONEER-6* Peptide Innovation for Early Diabetes Treatment; REWIND, Researching Cardiovascular Events with a Weekly Incretin in Diabetes; SUSTAIN-6, Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with Type 2 Diabetes-6; VERTIS CV, Evaluation of Ertugliflozin Efficacy and Safety Cardiovascular Outcomes Trial

[b]Primary outcome

[c]Exploratory outcome

[d]Secondary outcome

Table 2 Summary of randomized clinical trials of the major sodium-glucose cotransporter type 2 inhibitor and glucagon-like peptide-1 receptor agonists classes with renal benefits in patients with type 2 diabetes

Antidiabetic agent	Randomized clinical trial[a]	Enrolled patients	Comparator	Composite renal outcomes (HR)
SGLT2i				
Dapagliflozin	DECLARE [49]	17200	Placebo	[b]Sustained ≥ 40% reduction in eGFR, new ESRD, or death from renal causes: 1.5% vs. 2.8% (0.5)
Empagliflozin	EMPA-REG [13]	7000	Placebo	[c]Incident or worsening nephropathy: 12.7% vs. 18.8%, relative risk reduction: 39%
Canagliflozin	CANVAS [50]	10100	Placebo	[b]Sustained 40% reduction in eGFR, need for renal-replacement therapy, or death from renal causes: 5.5 vs. 9.0 participants per 1000 patient-years (0.6)
	CREDENCE [46]	4400	Placebo	[d]ESRD, doubling of the serum creatinine level, or death from renal causes: 34% reduction (0.7)
Ertugliflozin	VERTIS CV [54]	8200	Placebo	[c]Sustained 40% reduction in eGFR, chronic kidney dialysis/transplant or renal death: 2.1% vs. 3.09% (0.7)
GLP-1 RA				
Liraglutide	LEADER [55]	9300	Placebo	[b]New-onset persistent macroalbuminuria, persistent doubling of the serum creatinine level, ESRD, or death due to renal disease: 5.7% vs. 7.2% (0.8)
Semaglutide	SUSTAIN-6 [52]	3300	Placebo	[b]New or worsening nephropathy: 3.8% vs. 6.1% (0.6)
Dulaglutide	REWIND [56]	9900	Placebo	[e]New macroalbuminuria, a sustained decline in eGFR of 30% or more, or chronic renal replacement therapy: 17.1% vs. 19.6% (0.9)

eGRF Estimated glomerular filtration rate, *ESRD* end-stage renal disease
[a]See footnote to Table 1 for complete name of trials
[b]Secondary outcome
[c]Pre-specified outcome
[e]Exploratory outcome
[d]Primary outcome

T2D-dedicated randomized clinical trials that show beneficial effects of those therapeutic classes on CV and renal outcomes, with a reduction of hospitalization due to HF. In particular, the benefits of dapagliflozin and empagliflozin in lowering the risks of CV events, hospitalization due to HF, and all-cause mortality in patients with T2D have also been evidenced through real-world studies in routine clinical care [40–42]. Interestingly, the cardio-renal benefits of these two agents extend beyond the risks of T2D, as they are now indicated for the management of HF [43, 44] regardless of the patient's T2D status. In addition, dapagliflozin is indicated for the management of CKD regardless of the patient's T2D status [45], while canagliflozin is indicated for the management of CKD in patients with T2D

[46]. And although not approved as anti-hypertensive agents, SGLT2i have shown to significantly reduce systolic BP by 4 to 10 mmHg [47, 48].

COMPREHENSIVE CARE: TARGETS FOR OPTIMUM MANAGEMENT AND SELECTION OF THERAPY

Clinical Targets

The management strategy of T2D should be comprehensive and address all risks. A number of targets should be set and periodically reassessed to ensure goals are effectively achieved. In the last decade, the care of T2D was established beyond glycemic control, and the evaluation and follow-up of metabolic, cardiac, and renal risks are required, motivating the role of a multidisciplinary panel of experts from different specialties. Table 3 shows the recommendations that should be aimed for by physicians for a controlled T2D. These general recommendations are in line with international ones [57, 58] and can be fine-tuned on a case-by-case basis according to the patient's profile and characteristics.

Target achievement must be evaluated every 3–6 months, and adjustments to treatment must be made if the goal(s) are not met, in order to reduce complications.

Tailoring Treatment of T2D to Improve Cardio-Renal Outcomes

Use of Guideline-Directed Medical Therapy

Local guidance in the management of T2D relies on recommendations from major international societies, such as the ADA, the American Association of Clinical Endocrinologists (AACE)/American College of Endocrinology (ACE), the European Association for the Study of Diabetes (EASD), the European Society of Cardiology (ESC), and the KDIGO organization. Table 4 summarizes treatment recommendations laid down by these societies.

Local Lebanese Consortium Guidance

Along with lifestyle modifications, patients diagnosed with T2D should initiate treatment with metformin and continue this treatment as long as it is tolerated and not contraindicated, since it is a cost-effective agent with significant data supporting efficacy and safety, especially for patients with DKD or HF. For patients not reaching their clinical targets, treatment intensification should not be delayed and is recommended to be applied within 3 months. The timely introduction of second-line treatments and the early use of therapeutic combinations are crucial steps in avoiding clinical inertia, a major burden in the management of T2D in Lebanon [16]. Therefore, in case of intolerance to metformin or if metformin alone did not yield target achievement within 3 months of treatment initiation, the preferred class of medications to be given alone or in combination with metformin should confer CV and renal benefits. The choice of pharmacological agents should be guided by a patient-centered approach that takes into account, besides efficacy, the risks of CVD, DKD, hypoglycemia, weight loss, and other adverse effects, in addition to cost, access to medication, and patient preference. A local study showed a preference for oral medication among Lebanese patients compared to injectable medication [15]. Another study emphasized the importance of the choice of agents with low risk of hypoglycemia in the Lebanese diabetic population that has a relatively high rate of hypoglycemia [66]. Therefore, to meet individualized patient goals, and to prevent treatment failure, it is crucial to initiate an oral combination therapy at the primary care level [67]. Indeed, treatment with a single glucose-lowering agent does not provide adequate glycemic control in many cases, and initial combination therapy should be considered if the HbA1c level is moderately elevated, i.e., HbA1c $> 7.5\%$. Treatment intensification using a range of antidiabetic agents early on in the course of therapy reduces morbidity and premature mortality associated with T2D [68]. According to most recent international guidelines, the two most recommended DMD classes for second-line therapy are GLP-1 RA and SGLT2i [62, 69]. These two agents have

Table 3 Recommendations for the management of major clinical manifestations of type 2 diabetes

Targets	Recommendations
Lifestyle	
Diet	Balanced and healthy diet, moderate alcohol consumption, smoking cessation
Physical activity	Weight loss for overweight patients, increased physical activity to more than 150 min per week, limited sedentary time
Glycemia	More or less stringent targets may be individually appropriate
HbA1c	< 7.0% (53 mmol/mol)
Blood lipids	
LDL-C levels [59]	< 100 mg/dL or < 70 mg/dL if very high risk or < 55 mg/dL if extreme risk
Blood pressure [60, 61]	SBP < 130 mmHg and DBP < 80 mmHg
	SBP 130–139 mmHg in patients older than 65 years
Cardiac function	An ECG, ECHO with or without NT-proBNP or BNP biomarker tests, 5 years post T2D diagnosis to screen for heart failure
	Other cardiac tests could be ordered for a complete heart health assessment based on the patient condition
Renal function	Normal eGFR is ≥ 90 mL/min/1.73 m^2
UACR	Normal UACR is < 30 mg/g
eGFR	eGFR declines with age, even in people without kidney disease
	Assess eGFR and UACR together at the initial visit and every 6 months[a]

BNP B-type natriuretic peptide, *DBP* diastolic blood pressure, *ECG* electrocardiography, *ECHO* echocardiography, *HbA1c* glycated hemoglobin, *LDL-C* low-density lipoprotein cholesterol, *NT-proBNP* N-terminal prohormone of BNP, *SBP* systolic blood pressure, *T2D* type 2 diabetes, *UACR* urine albumin to creatinine ratio

[a]With evidence of kidney impairment and if UACR ≥ 300 mg/g or eGFR < 60 mL/min/1.73 m^2 more frequent testing is recommended; i.e., every 3 months

shown benefit not only with regards to glycemic control, but also in terms of CV and renal protection, as well as supporting weight control and preventing hypoglycemia episodes [70]. In patients at high risk or with established HF or CKD, SGLT2i remain the medications with the highest proven benefit. However, if patients cannot tolerate or afford DMDs, other antidiabetic medications (DPP-4i, thiazolidinediones, sulfonylureas or insulin) remain viable options for effective glycemic control, although these do not offer cardiac or renal protection.

Once the decision is made to initiate any medication, physicians should be prompted to monitor any adverse event that might occur. The most common adverse events associated with the SGLT2i drug class are an increased rate of genital/urinary infections (mostly genital infections) and diabetic ketoacidosis, a rarer but serious adverse event [71]. Regarding treatment with GLP-1 RA, the most common adverse events are predictably gastrointestinal in nature, notably nausea, vomiting, and diarrhea [72].

Table 4 Summary of the main recommendations of major global societies/organizations regarding the pharmacological treatment of type 2 diabetes

Society/organization[a]	Pharmacological treatment recommendations
ADA, 2022 [62] ADA/KDIGO, 2022 [31, 63]	For patients with established ASCVD or indicators of high CV risk, established kidney disease, or heart failure, a SGLT2i and/or GLP-1 RA with demonstrated CVD benefit are recommended as part of the glucose-lowering regimen and comprehensive CV risk reduction independent of baseline HbA1c, individualized HbA1c target, or metformin use
	A SGLT2i with proven kidney or cardiovascular benefit is recommended for patients with T2D, CKD, and eGFR $\geq$ 20 mL/min/1.73 m^2; once initiated, the SGLT2i can be continued at lower levels of eGFR
	A GLP-1 RA with proven cardiovascular benefit is recommended for patients with T2D and CKD who do not meet their individualized glycemic target with metformin and/or an SGLT2i or who are unable to use these drugs
AACE/ACE, 2020 [64]	Independently of glycemic control, if established ASCVD or high risk ASCVD, CKD, or HFrEF, start LA-GLP-1 RA or SGLT2i with proven efficacy
ESC/EASD, 2019 [65]	SGLT2i or GLP-1 RA are recommended prior to metformin in drug-naïve patients with T2D and established ASCVD or at high/very high CV risk
	Empagliflozin, canagliflozin, dapagliflozin, liraglutide, semaglutide or dulaglutide are recommended in patients with T2D and CVD or at high/very high CV risk to reduce CV events
	Empagliflozin is recommended in patients with T2D and CVD to reduce the risk of death
	Liraglutide is recommended in patients with T2D and CVD or at very high/high CV risk to reduce the risk of death

ASCVD atherosclerotic cardiovascular disease, *CKD* chronic kidney disease, *CVD* cardiovascular disease, *HfrEF* heart failure with reduced ejection fraction

[a]AACE/ACE, American Association of Clinical Endocrinologists/American College of Endocrinology; ADA, American Diabetes Association; ESC/EASD, European Society of Cardiology/European Association for the Study of Diabetes; KDIGO, Kidney Disease Improving Global Outcomes

Regardless of the clinical decisions, all treatment plans should be re-evaluated continuously, preferably every 3–6 months. To avoid therapeutic inertia, modification of therapeutic strategies should be considered regularly.

PATIENT ENGAGEMENT AND EMPOWERMENT

A successful evaluation of T2D and a successful management of its comorbidities and risk factors rely heavily on the interaction between patients and clinicians. Most recent international guidelines recommend a patient-centered collaborative care approach to the management of T2D that involves patient education to foster self-management and adherence to the medical plan. Daily self-management is essential for those patients to reach healthy glucose levels, minimize the impact of the disease on their health and daily life, and reduce the risk of complications [73]. In addition to pharmacological therapies, key elements of T2D self-management include maintaining a healthy diet, regular physical activity, foot care, and

blood glucose monitoring. Patient engagement and empowerment can be defined as the level of knowledge, skills, and confidence someone has that is needed for adequate self-management of a chronic disease. Advanced patient engagement allows patients to better manage their disease, actively take part in decision-making, and engage in the self-management behaviors needed for health and daily performance improvement. Additionally, higher levels of patient engagement have been found to be associated with favorable health outcomes and cost-saving in T2D or other chronic conditions [74]; in contrast, in this same study, lower levels of patient engagement correlated with unhealthy behavior (e.g., physical inactivity) and less favorable health outcomes (e.g., higher glucose levels).

The Lebanese consortium of experts recommends investing efforts in the continuous education of patients on their disease, its complications, management goals, the importance of adopting a healthy lifestyle and diet and adhering to medications, and regularly following up with their treating physician every 3–6 months to assess goal attainment and readjust their management plan as required. The supportive role of healthcare staff, added to an effective educational program, increase patients' levels of self-confidence, leading to healthful behavioral change and improvement of outcomes. In addition, Lebanese medical societies rely in part on the social media platforms to support awareness campaigns, as the increase in social media use has given T2D care and education specialists a new route to reach people with T2D. Social media can promote engaging and informative T2D education content while also fostering a support network for people with T2D. Several local societies and healthcare companies have initiated T2D education over their social media channels [75, 76].

COLLABORATIVE MULTIDISCIPLINARY CARE

Diabetes is a chronic and complex disease that imposes a heavy economic burden on patients and healthcare systems alike, and requires lifestyle modifications and pharmacotherapy. Hence, a multidisciplinary collaborative care approach may be more effective in allowing some people to cope with the demands of controlling this complex disease [77].

Multidisciplinary collaborative care usually involves at least two care providers working together with patients and their caregivers, with the overall aim to achieve shared goals within and across settings that provide coordinated, high-quality patient-centered care and improve clinical and humanistic outcomes [78]. A patient with T2D should preferably be followed by a diabetes expert if this is possible. This expert might then refer the patient to another specialist when it is medically appropriate. Since T2D is frequently associated with overweight, DKD, hypertension, and CVD, accurate referrals should be based on comorbidity priority order. For instance, if diabetic retinopathy is evident on screening, prompt referral to an ophthalmologist is recommended. In addition, and per KDIGO 2012 guidelines on CKD management and the recent 2022 consensus statement addressing diabetic patients in particular, patients should be referred for evaluation by a nephrologist if they have an eGFR < 30 mL/min/1.73 m^2, or UACR consistently > 300 mg/g, or if there is uncertainty about the etiology of kidney disease, difficulty in the management of renal issues, or rapid progression of kidney disease. Similarly, patients with risk factors or symptoms placing them at high risk for CVD should be referred to a cardiologist. Such conditions include but are not limited to difficulty in controlling high BP or dyslipidemia, shortness of breath, chest pain, and fatigue. In all these scenarios, close collaboration between different specialists and the patient should be at the heart of decision-making.

FOLLOW-UP AND MONITORING

After assessing patient characteristics, such as age, HbA1c levels, body mass index (BMI), comorbidities, lifestyle habits, and social and psychological status, the clinical team and the patient should come up with a shared decision on the implementation of a specific,

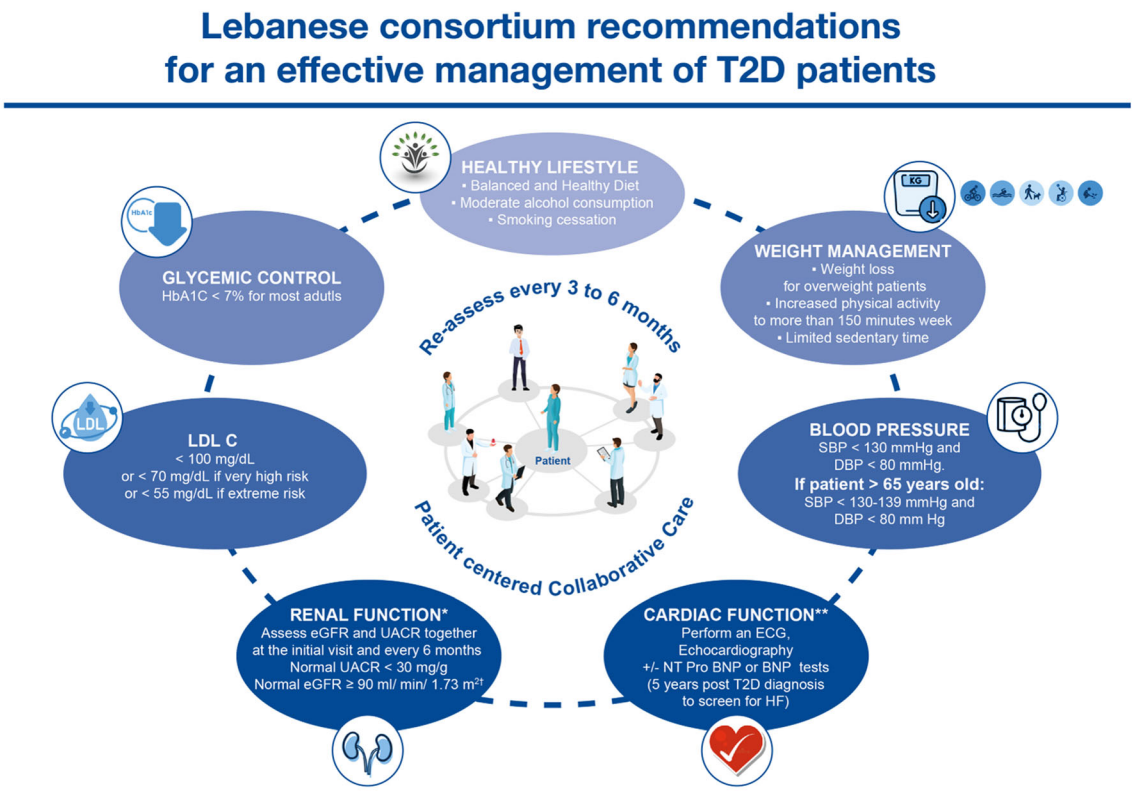

Fig. 3 Lebanese consortium recommendations for an effective management of T2D patients. Single asterisk: With evidence of kidney impairment and if UACR $\geq$ 300 mg/g or eGFR $<$ 60 mL/min/1.73 m^2, testing is recommended every 3 months. Double asterisks: Other cardiac tests could be ordered for a complete heart health assessment based on the patient condition. Single cross: eGFR declines with age, even in people without kidney disease. *BNP* Brain natriuretic peptide, *DBP* diastolic blood pressure, *ECG* electrocardiography, *LDL-C* low-density-lipoprotein-cholesterol, *NT-ProBNP* N-terminal prohormone of BNP, *SBP* systolic blood pressure, *T2D* type 2 diabetes, *UACR* urinary albumin to creatinine ratio

measurable, achievable, realistic, and time-limited management plan. The patient should then be followed up regularly to monitor glycemic status, CV and renal risks, tolerability to medication, weight changes, lipid profile, BP, and emotional well-being, every 3–6 months. Figure 3 summarizes the Lebanese consortium recommendations for an effective management of T2D patients.

CONCLUSION

Type 2 diabetes is a complex disease that is primarily diagnosed by elevated levels of blood glucose and HbA1c, entailing various related morbidities, poor quality of life, and increased risk of premature death. However, recent medical advances have rendered T2D a manageable chronic disease, mostly illustrated by a shift in treatment paradigm from hypoglycemic agents to DMDs. In this paper we outline strategic recommendations for the early, effective, and comprehensive management of T2D and its related cardio-renal complications in Lebanon. To achieve optimal control, adequate and continuous education should be offered both to patients and all healthcare professionals involved in the management of the disease. Treatment for T2D should not solely aim to control glycemia, because underlying T2D comorbidities can be as challenging and life

threatening as the disease itself. Patients with T2D are at great risk of developing CVD or DKD, which drives the need to control risk factors, such as overweight, hypertension, dyslipidemia, kidney disease, HF, and others. Early initiation of combination medications is critical to overcome clinical inertia, to break glucotoxicity, and to support HbA1c goal achievement, while offering cardiac, renal, and metabolic benefits to prevent or slow down diabetes complications.

Treatment strategies need to revolve around a patient-centered approach. In addition, a multidisciplinary collaboration translating into timely referral is sometimes essential in patients with comorbid conditions requiring the expertise of a specialist. The choice of pharmacological treatment should be adjusted on a regular basis to properly address clinical inertia, taking into consideration the patient's clinical profile, risk factors, personal preferences, and access to medication. Therefore, effective therapies target the shared pathways of diabetes, CVD, and kidney disease, and a comprehensive approach will improve outcomes for patients with T2D.

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