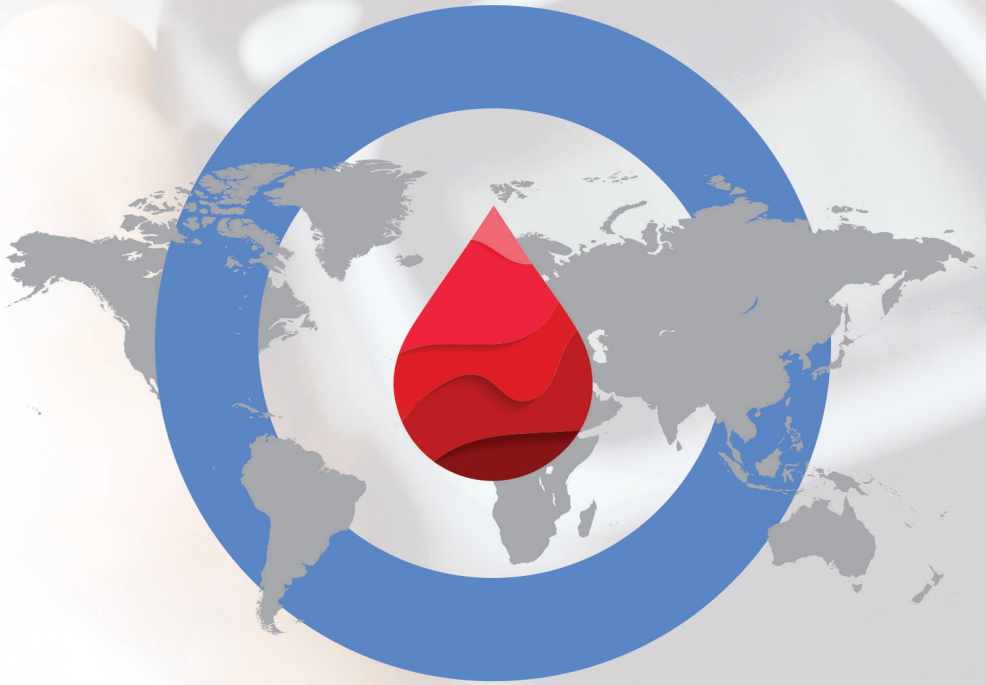
MODULE 1

IFDCD
INTERNATIONAL FEDERATION OF DIABETES AND CARDIOMETABOLIC DISORDERS

DISCIPLINE IS LIFE
DIABETIC ASSOCIATION OF BANGLADESH

CLINICAL EXCELLENCE PROGRAM FOR

Diabetes PRACTITIONERS *in* BANGLADESH



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PROGRAM OBJECTIVES

This clinical excellence program is an attempt to apprise participants on the concepts related to development of diabetes and its complications, together with updated recommendations on its diagnosis and management.

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APPROACH TO IDENTIFYING & DIAGNOSING COMPLICATIONS OF T2D – AN UPDATE

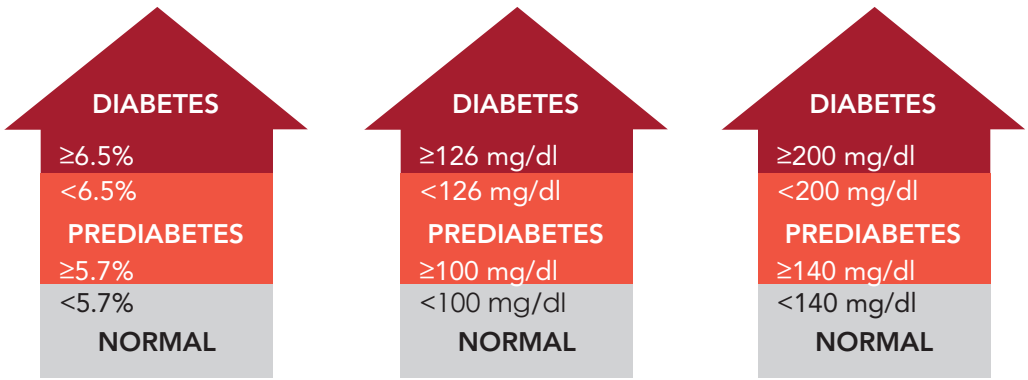
Broadcast Date: 10th July 2023
Broadcast Time: 09:00 PM (Bangladesh time)

Dr. W David Strain
FRCP, MD
Clinical Senior Lecturer and Honorary Consultant,
University of Exeter Medical School

The first webinar in the series forming part of the Clinical Excellence Program for Diabetes Practitioners in Bangladesh was conducted on 10th July, 2023, wherein Dr. W David Strain, Clinical Senior Lecturer and Honorary Consultant from the University of Exeter Medical School, navigated the participants through contemporary concepts related to understanding and practice of Diabetes especially with relevance to the sub-continent. The Webinar was moderated by Dr Jayanta Dey from Sun pharma. Following Dr David's presentation, there was a Q&A session that benefitted from the rich clinical experience of all the esteemed panelists, providing meaningful insights to the participants which would be of benefit in their real-world clinical practice.

Dr David started his presentation by highlighting the fact that diabetes is a much more complex disease than understood. The diagnosis of diabetes is the first step when approaching a symptomatic patient, and for this need, there are clear pre-defined criteria as shown in Figure 1. The criteria is applicable to persons without any other hematological problem. It is important to note here that the disease – diabetes – is a continuum, and patients may have pre-diabetes for many years before being clinically diagnosed for diabetes.

Figure 1: Diagnostic criteria for Diabetes



The management of diabetes has evolved in the past few years, founded on the growing understanding of the disease. Earlier, a three-pronged approach was used as shown in Figure 2; However, a significant change was later seen in the approach to identifying and managing diabetes with the introduction of the pathophysiological concept of "Ominous octet", which mentioned that hyperglycaemia is only a symptom of the disease affecting multiple organ systems (Figure 3). About three years ago, the concept was further modified with inclusion of the effects of the other mechanisms like microbiome dysregulation and inflammatory dysregulation, resulting in the pathophysiological construct of "Egregious Eleven" (Figure 4). Hence, diabetes is not one disease, and regulating glucose could not be the only therapeutic goal in patients with diabetes. Nevertheless, insulin resistance is the most common type of type 2 diabetes phenotype seen in patients. Besides, this component is also central to the inter-related Cardio-renal-metabolic (CRM) system, wherein dysregulation of the one system affects the functioning of the other two.

Figure 2: Historical approach to diabetes, 2007

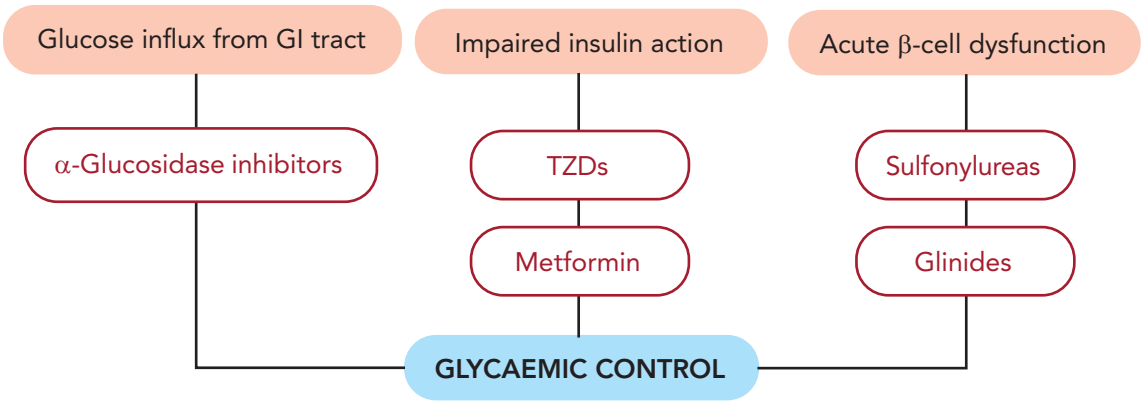


Figure 3: The "ominous octet" of pathophysiological defects underlying type 2 diabetes and individualised strategies

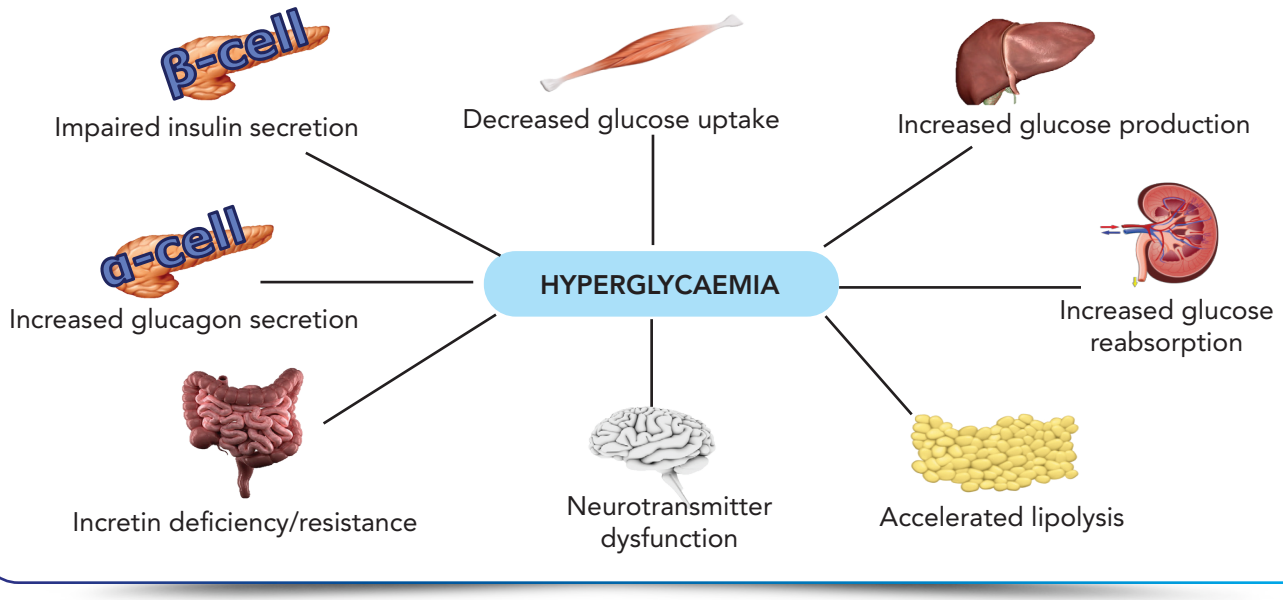
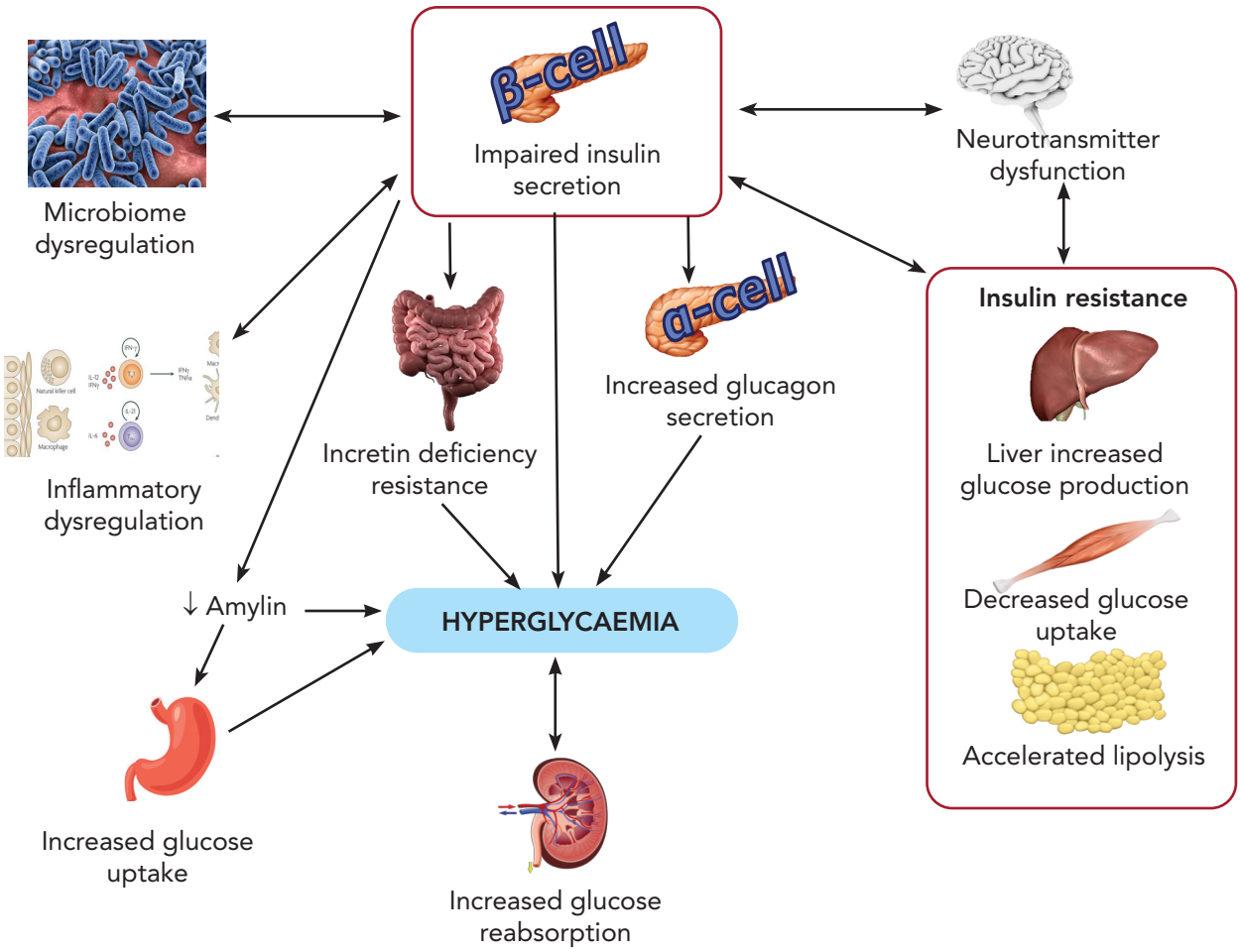


Figure 4: Moving on to the Egregious Eleven



Therefore, when encountering patients with diabetes, it is important to consider where do they fit in this entire continuum of CRM system (Figure 5). Furthermore, liver is now also emerging as an additional component that is affected in many of these patients. Herein, obesity is being identified as a key risk factor for all these inter-related comorbidities and complications (Figure 6), affecting several components of patients' well-being. It is therefore important to treat obesity early.

Figure 5: Diseases of the CRM systems share many of the same risk factors

Progression of interrelated diseases (T2D, CV disease, HF and CKD) can occur due to dysfunction of the CRM systems, which, in turn, may lead to an increased risk of CV death

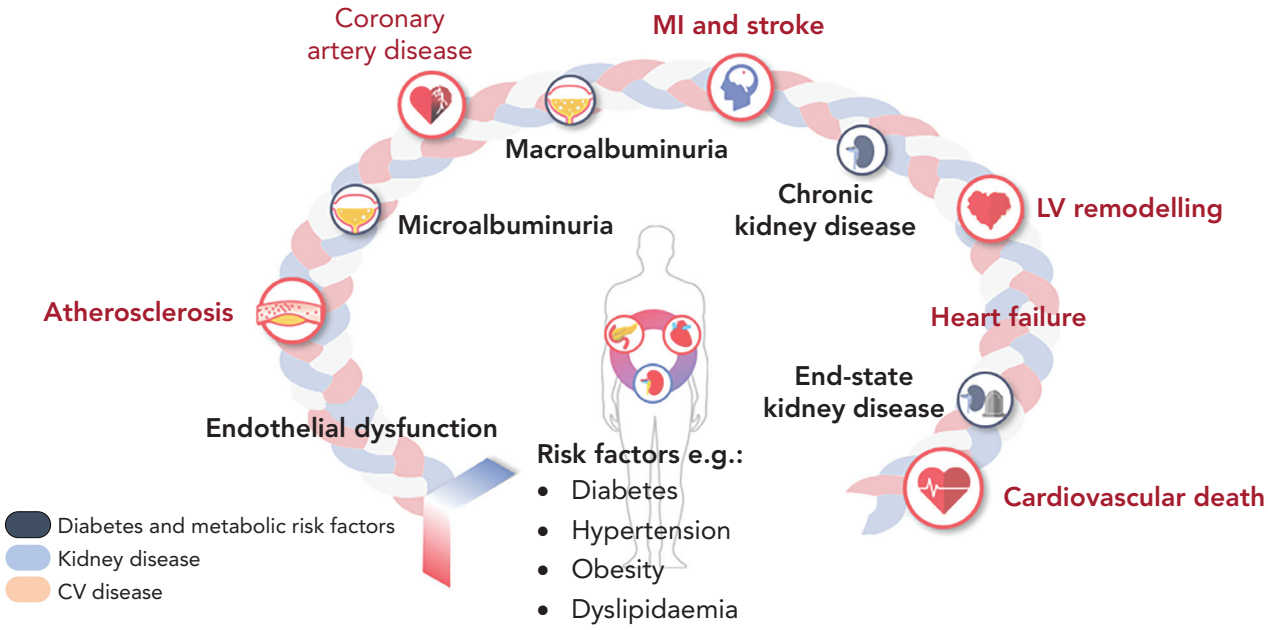
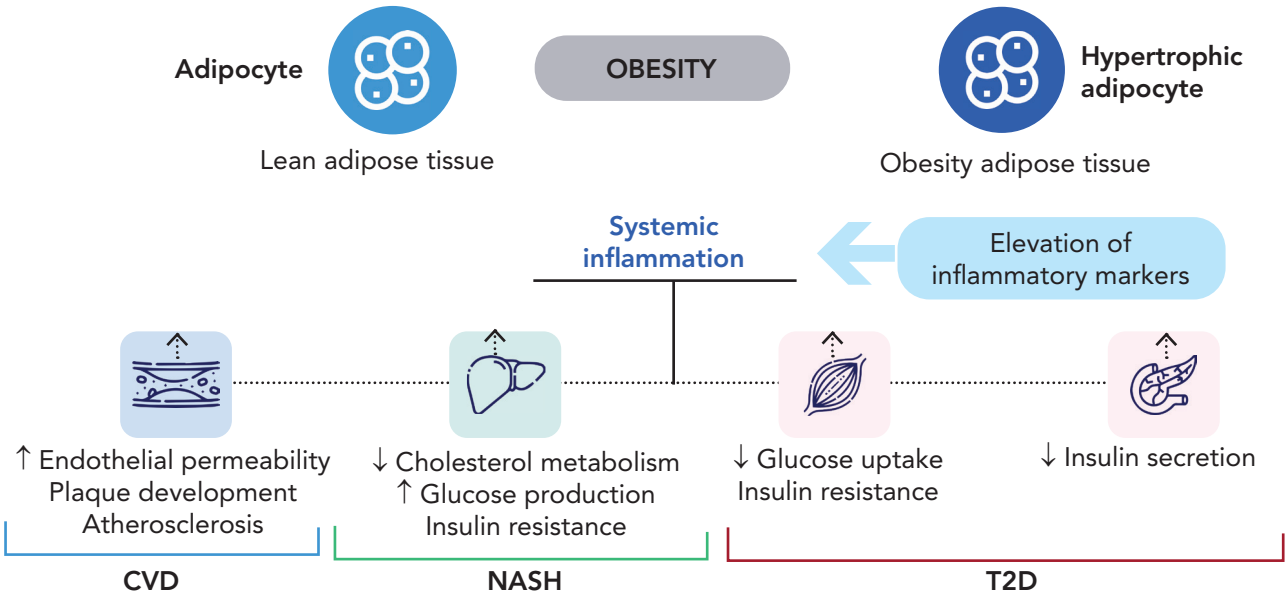


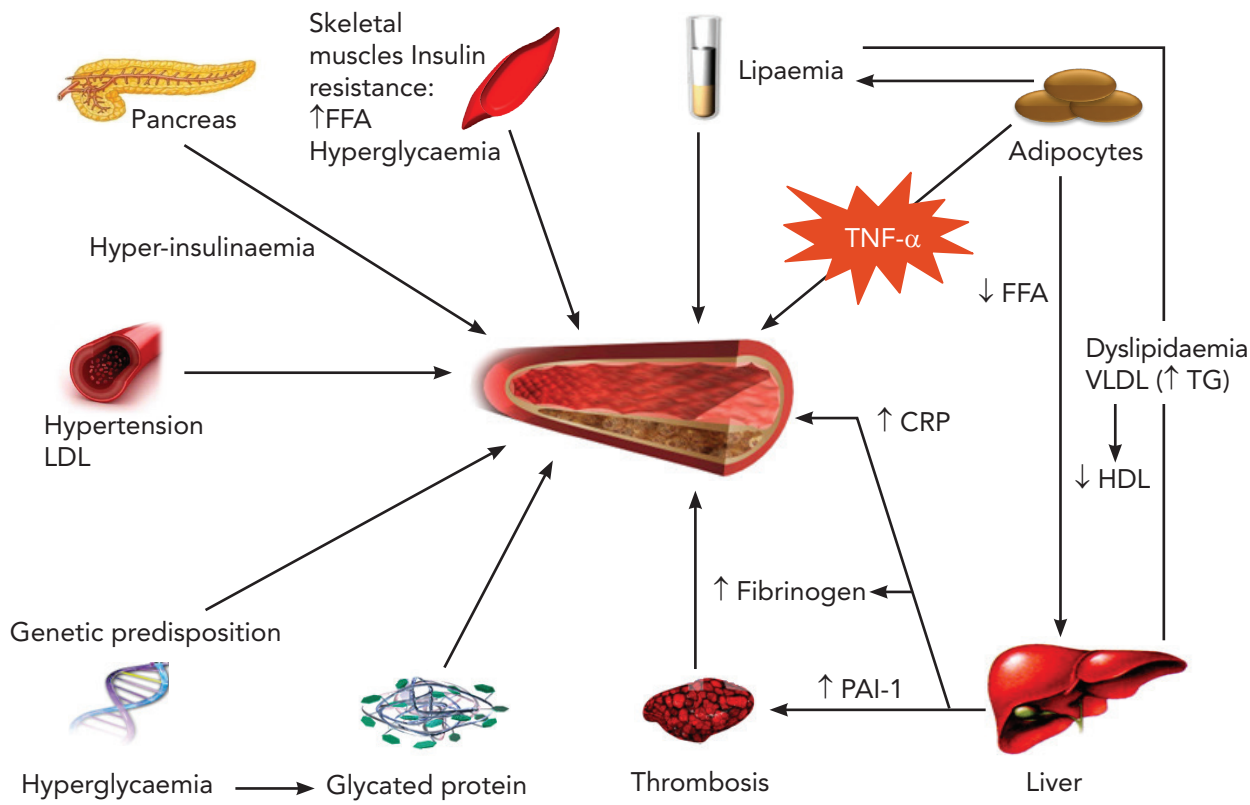
Figure 6: Pathophysiology of obesity related complications



CVD, cardiovascular disease; NASH, non-alcoholic steatohepatitis; T2D, type 2 diabetes

In patients with type 2 diabetes, albuminuria and reduced estimated glomerular filtration rate (eGFR) are associated with increased risk of cardiovascular (CV) death, though there are other factors also contributing to this increased CV risk (Figure 7). Monitoring patients is therefore important to identify these risk factors. For effect on the kidneys - when monitoring patients with diabetes - microalbuminuria might be a better early indicator than eGFR for disease progression.

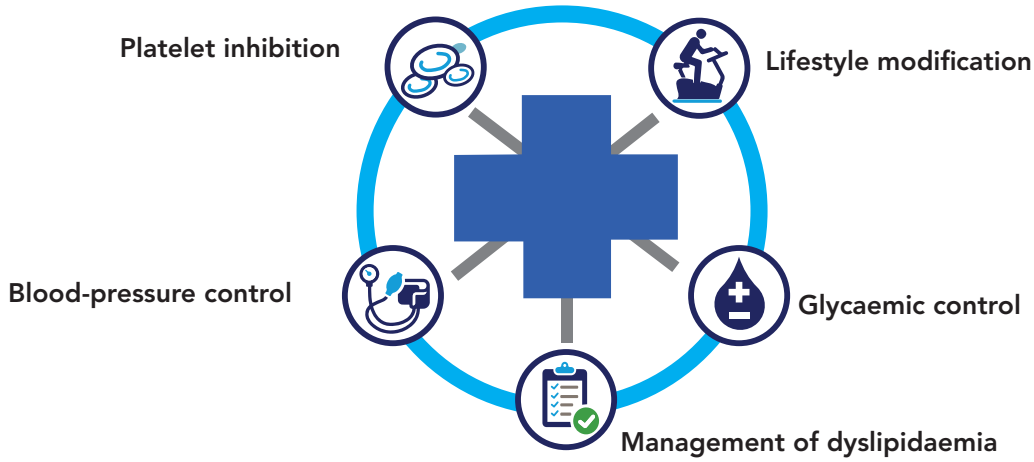
Figure 7: Many factors contribute to increased CV risk in T2D



CRP, C-reactive peptide; CV, cardiovascular; FFA, free fatty acid; HDL, high-density lipoprotein; PAI-1, plasminogen activator inhibitor-1; T2D, type 2 diabetes; TG, triglyceride; TNF-α, tumour necrosis factor-α; VLDL, very low-density lipoprotein

While myocardial infarction and stroke are well-known complications in patients with diabetes; heart failure remains an important under-recognised complication, which can prove fatal if not diagnosed early. In fact, concomitant diabetes can double the risk of death in people with chronic heart failure. It is therefore important to modify CV risk in patients with T2D (Figure 8). Herein, glycaemic control is a key therapeutic intervention that, when initiated early, can be of benefit in alleviating both micro- and macrovascular complications of diabetes. Multifactorial management of the CV risk factors is well-established as standard of care for patients with T2D (Figure 9).

Figure 8: How do we modify CV risk in T2D?



CV, cardiovascular; T2D, type 2 diabetes mellitus

Figure 9: Multifactorial management of the CV risk factors in patients with T2D

	Target	Treatment
Glucose control	Targets are individualised – for many patients HbA1c <7%	• Metformin, SGLT2 inhibitors, GLP-1 receptor agonists, DPP-4 inhibitors, sulphonylureas, thiazolidinediones, insulin
Blood pressure-lowering	For individuals with T2D and hypertension, a blood pressure target of: • <130/80 mmHg if at higher CV risk • <140/90 mmHg if at lower risk for CV disease	• RAAS blocker (ACEi/ARB), calcium channel blocker, thiazide-like diuretics • Dual therapy is recommended as first-line treatment
LDL cholesterol-lowering	• <1.8 mmol/l (<70 mg/dl) with LDL-C reduction of ≥50% if at high CV risk • <2.6 mmol/l (<100 mg/dl) if at moderate CV risk	Statins, ezetimibe or PCSK9 inhibitor
Individualised diet and lifestyle	Weight loss and smoking cessation	• Diet • Physical activity • Behavioural therapy

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; PCSK9, proprotein convertase subtilisin/kexin type 9; RAAS, renin-angiotensin-aldosterone system

Q1. WHAT TREATMENTS CAN BE GIVEN TO DIABETES PATIENTS WITH KIDNEY DISEASE?

A. In diabetes patients with kidney dysfunction, DDP-4 inhibitors can be used; Linagliptin is particularly well-tolerated at any GFR levels, and hence can be used in most such patients. ARBs and ACE inhibitors can be considered for both renal and cardiac protection. Furthermore, SGLT2 inhibitors have also been found to prevent progression of kidney disease in patients with diabetes.

Q2. WHAT IS THE CURRENT PERSPECTIVE REGARDING IN-CLINIC USAGE OF NEWER-GENERATION SULFONYLUREAS?

A. Newer-generation sulfonylureas are widely used in treatment of type 2 diabetes because of their easy accessibility, affordability and tolerability profile. These drugs work best at optimal dose, and can be used for years in patients without significant risk of hypoglycemia. Care should however be exercised in certain patients' groups like elderly, not because of the drug's effect but owing to potential consequences of an hypoglycemia event if that occurs.

Overall, newer-generation sulfonylureas seem to have a significant place, both as monotherapy and combination therapy, in management of patients with type 2 diabetes. The treatment needs to be individualized for every patient.

The contents of this booklet have been prepared based on the Webinar broadcasted on 10th July, 2023

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