Frontiers in DIABETES

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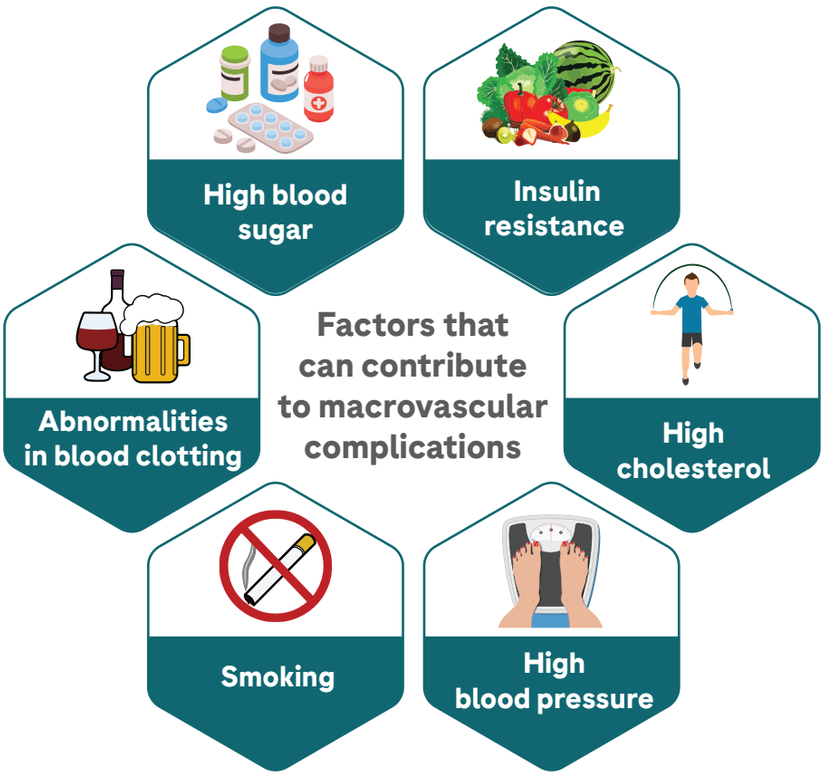
Knowledge+

Diabetes and macrovascular complications

Macrovascular diabetes complications are diseases and conditions of the large blood vessels caused by diabetes. These complications can occur in blood vessels in any part of the body.[1,2]

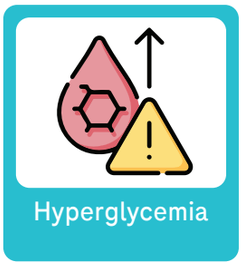


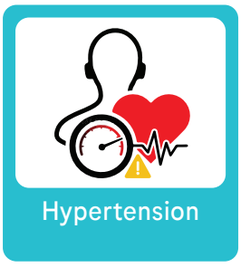
Macrovascular complications associated with diabetes include:

1. Cardiovascular

- Cardiovascular disease (CVD) is two to four times more common in those with diabetes than in people without the condition.

The main risk factors for developing coronary heart disease (CHD):





Lowering the risk for macrovascular complications remains complex and involves more than lowering glucose levels.

The goal is prevention; however, aggressive management of risk factors are vital.[1,2]

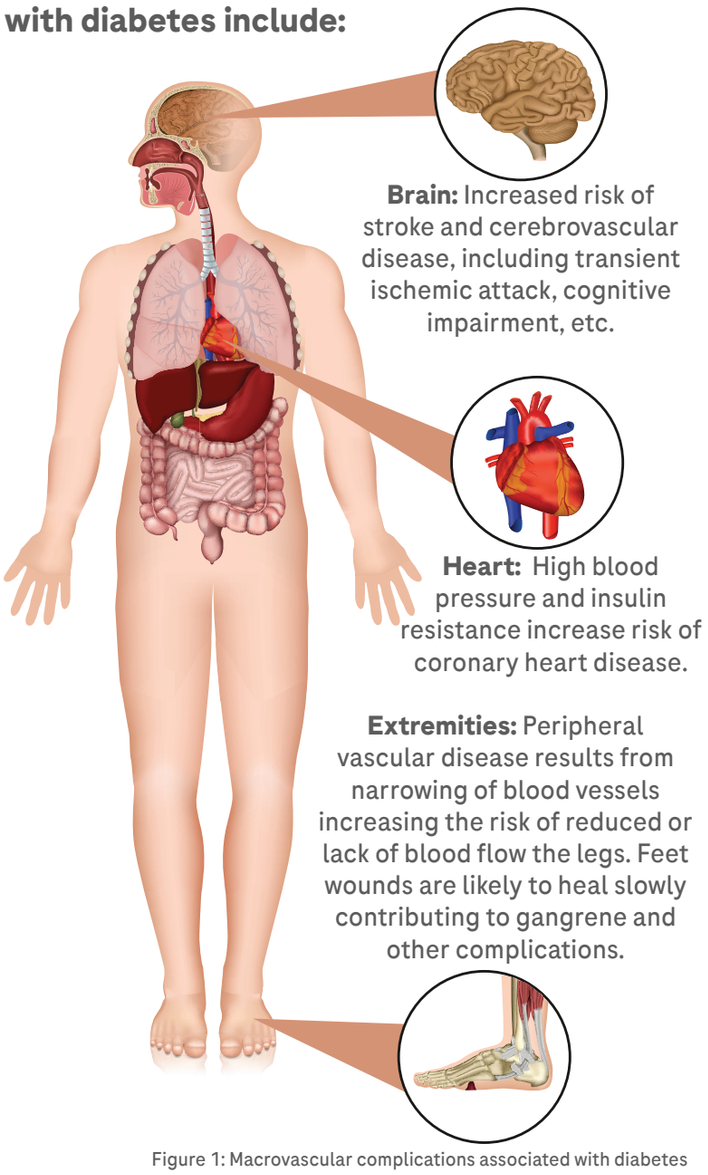
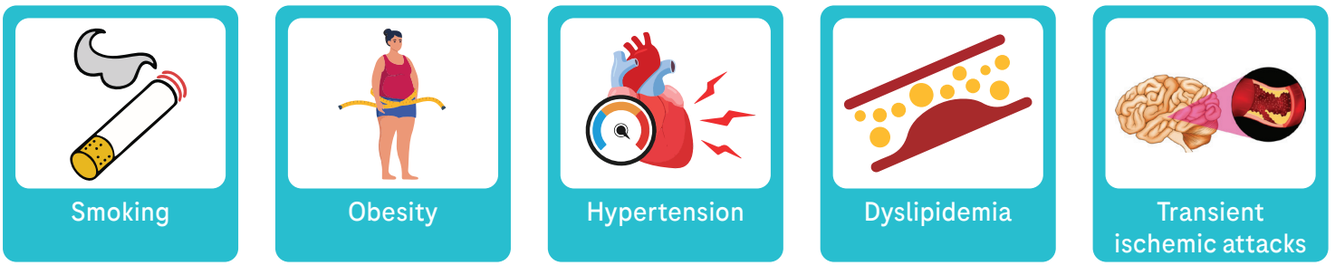


Figure 1: Macrovascular complications associated with diabetes

2. Cerebrovascular

- The word "cerebrovascular disease" refers to a broad range of conditions affecting the central nervous system's blood vessels.
- These conditions are caused by either haemorrhage into the parenchyma or subarachnoid space of the central nervous system (CNS) or insufficient blood supply to the brain (cerebral ischemia).
- Cerebrovascular events have been referred to by several names.
- For example, the clinical condition known as transient ischemic attack (TIA) refers to a patient's sudden focal neurologic deficit, which may manifest as blindness, aphasia, slurred speech, or weakness or paralysis of a limb.
  - These symptoms appear quickly and remain from 15 minutes to even 24 hours but there won't be any residual neurological deficit.
  - Like a transient ischemic attack (TIA), a reversible ischemic neurologic impairment improves over a maximum of 72 hours but may not fully disappear.
- **Cerebral Infarction** refers to ischemic stroke, which occurs when blood flow to the brain is blocked or reduced, often due to a clot or narrowing of blood vessels.
- Blood can leak from arteries into the brain and its surrounding structures and this condition is called **cerebral haemorrhage.**
- Sudden confusion, loss of coordination, unilateral weakness, and numbness are warning signs of a cerebrovascular event.

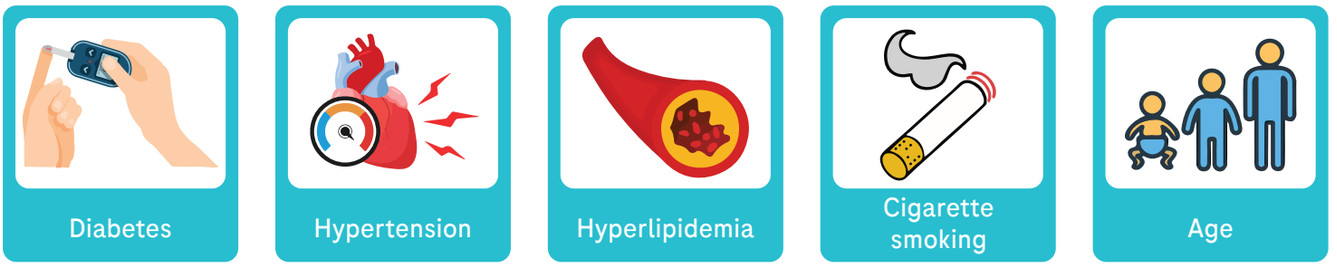
Major risk factors



3. Peripheral arterial disease (PAD)

- It is the main cause of risk for amputations of the lower extremities.
- Patients with diabetes mellitus have a three- to four-fold increased chance of developing PAD.[1,2]

Major risk factors



Practitioners must support quitting smoking, managing diabetes, hypertension, and cholesterol, encouraging physical activity and foot care, starting antiplatelet treatment, and treating symptoms to manage PAD.[1,2]

Pathophysiological mechanisms of macrovascular complications in diabetes

➤ Numerous intricate pathophysiological processes contribute to macrovascular difficulties in diabetes; at least 12 pathophysiological abnormalities—also referred to as "the dirty dozen of diabetes"—are known to exist, and further unidentified disease causes are being researched.[3]

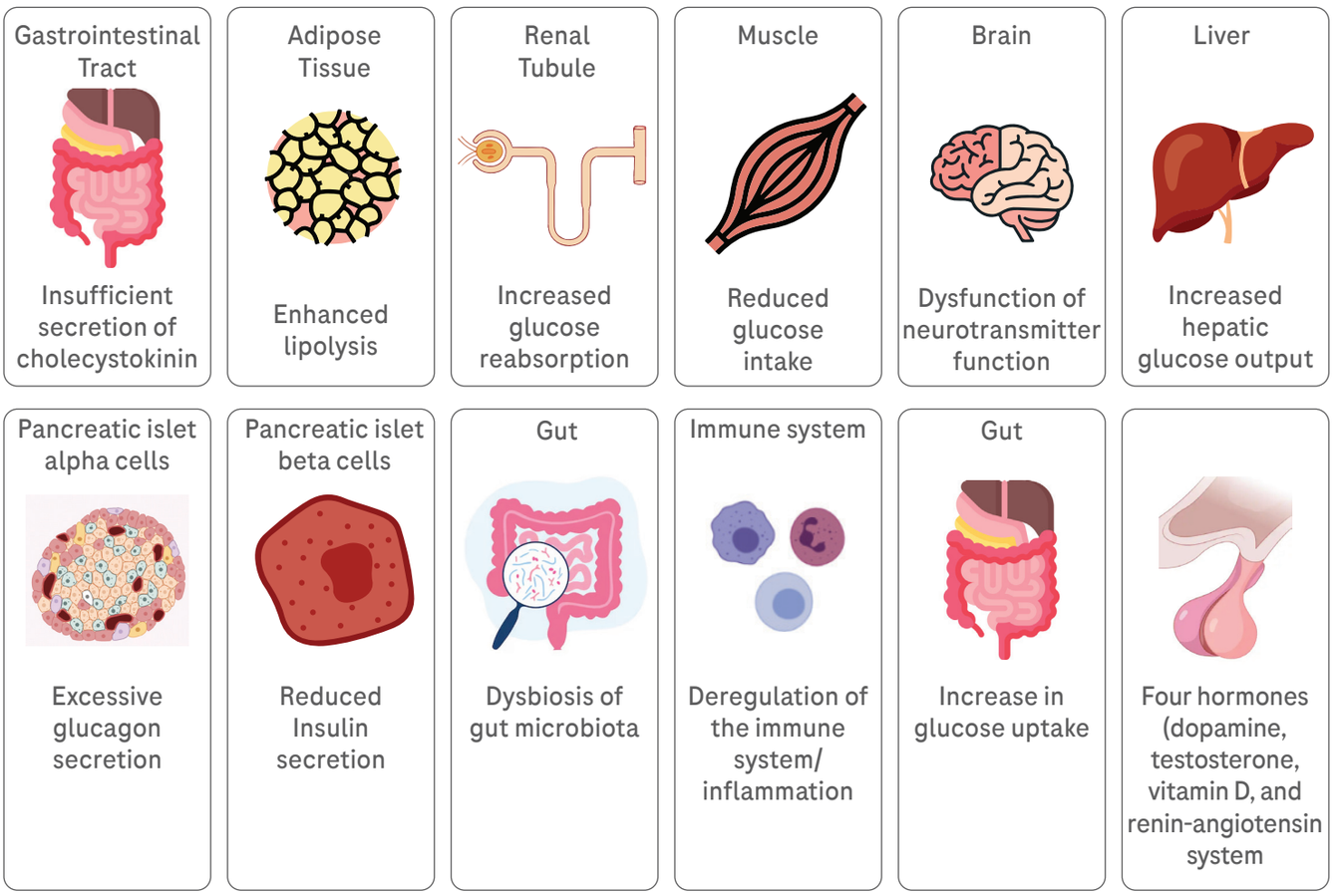


Figure 2: The dirty dozen of diabetes

Adapted from: Guan H et al 2024.

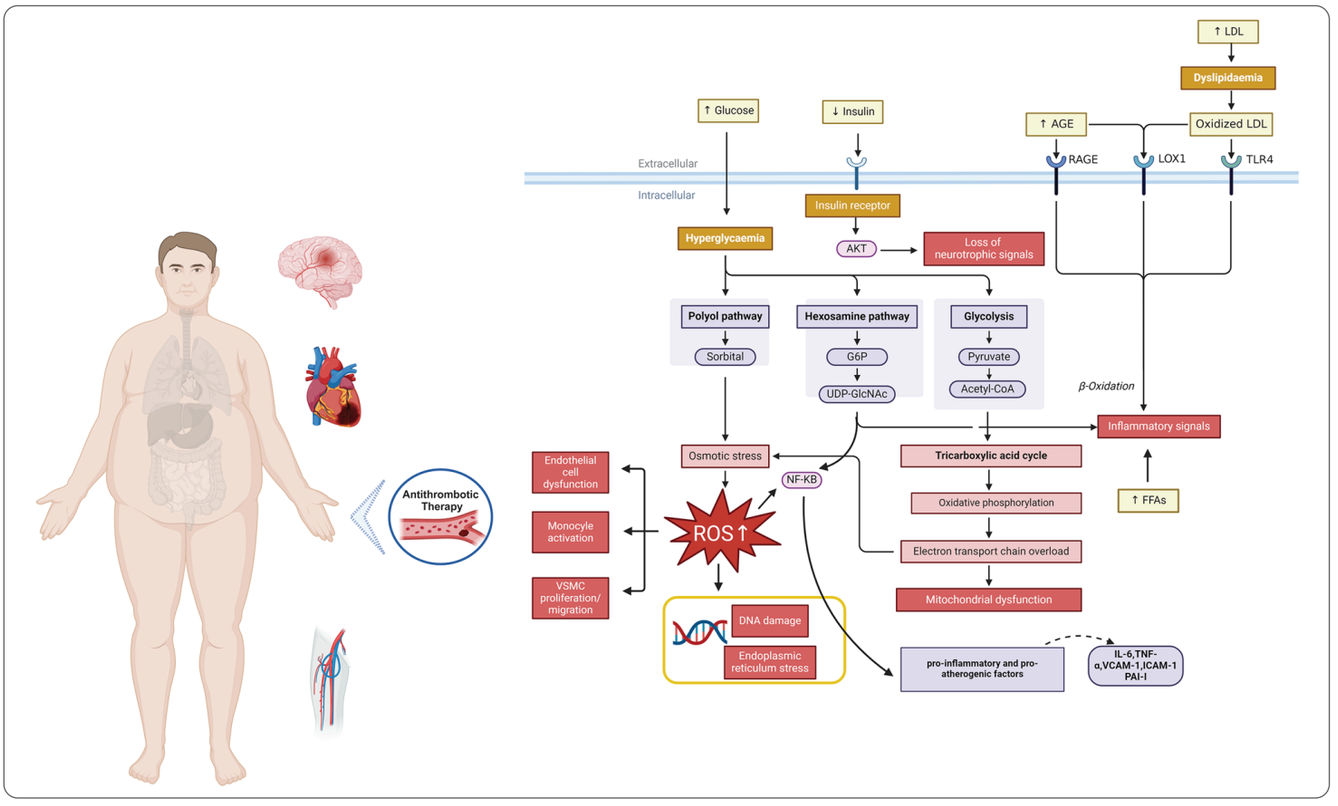


Figure 3: Pathophysiological mechanisms of diabetes and its complications

Adapted from: Guan H et al 2024.

RAGE, receptor for advanced glycation end product; LOX1, Lectin-like oxidized low-density lipoprotein receptor-1; TLR4,Toll-like receptor 4; LD, low-density lipoprotein; AKT, protein kinase; G6P,Glucose 6-phosphate; CoA,coenzyme A; FFA, Free fatty acids; NF-KB, nuclear factor kappa B ; DNA, deoxyribonucleic acid; ROS, Reactive oxygen species; iL-6,Interleukin-6; TNF-α, Tumor necrosis factor α; VCAM-1, Vascular cell adhesion molecule-1; ICAM-1,Intercellular adhesion molecule-1; PAI-1, Plasminogen activator inhibitor-1

The pathophysiology is primarily due to persistent hyperglycemia, insulin resistance, and dyslipidemia.

Toxic metabolites from glucose metabolism contribute to the formation of atherosclerotic lesions and plaques, worsening endothelial dysfunction and oxidative stress. Long-term diabetes, poor glycemic control, genetic factors, and comorbidities all heighten the risk of macrovascular complication.

Additionally, conditions like hypertension and obesity can further disrupt intracellular glucose levels, leading to biochemical reactions that worsen vascular damage.

Preventing macrovascular complications

➤ A recent study found that macrovascular complications in patients at high risk can be reduced through a multifactorial approach (involving behaviour modification and pharmacological therapy targeting hyperglycemia, hypertension, dyslipidemia and microalbuminuria, plus low-dose aspirin).[4]

Lifestyle measures

Dietary modification, regular exercise and smoking cessation are recommended to help prevent cardiovascular disease.

Treating hypertension

Individual antihypertensives may also be selected because of their effects in specific situations, such as β-blockers after myocardial infarction, and angiotensin-converting enzyme inhibitors and diuretics in congestive cardiac failure.

Control of dyslipidemia

Statin therapy is the mainstay of treatment.

Control of hyperglycemia

Intensive control of hyperglycemia can be beneficial in preventing macrovascular complications in people with diabetes

Aspirin

Low-dose aspirin therapy can be considered in people with diabetes and other risk factors, such as hypertension.

Macrovascular risk factors – Goals

➤ Glycemic control is associated with a reduced risk for macrovascular complications of diabetes.

➤ Treatment of CVD risk factors, especially dyslipidemia, is associated with a reduced risk for CVD events.[5]

Risk Factor	Goal of Therapy
Hyperlipidemia	
LDL Cholesterol	LDL <70 mg/dl
Diabetes and ASCVD risk	LDL <55 mg/dL
Triglyceride	<150 mg/dL
HDL	>40 mg/dl
Hypertension	BP <130/80 mmHg
Hyperglycemia	HbA1c <7%
Overweight (BMI 25-29 Kg/m^2) Obese (BMI ≥30 kg/m^2)	Decrease BMI to healthy weight
Physical Inactivity	Exercise prescription depending upon patient's status
Cigarette smoking	Complete cessation

Table 1: Goals for managing CVD risk factors in patients with diabetes

Adapted from: Diabetes care. Diabetes Care.2024;47(1): S1-S225.

Benefit and ease of modifying risk factors for macrovascular complications[5,6]

Risk factor	Ease of modification	Macrovascular disease
Blood glucose	Relatively hard to reduce Target reached (HbA1c <7%) in long-term therapy	Benefit marginal in randomised controlled trial, except with metformin in overweight people
Blood pressure	Target reached (<130/80 mmHg) in 50-60% of multiple agents often required	Significant benefits from even a modest reduction
Smoking	Difficult	Probable benefit
Dyslipidemia	Target reached (non-HDL cholesterol <130 mg/dL; triglyceride <150 mg/dL) in 30-50%	Significant benefit

HbA1c, glycosylated haemoglobin; BP, blood pressure

Adapted from: 1. Diabetes care. Diabetes Care.2024;47(1): S1-S225. 2. O'Flynn S. 2022;27(8):1.

For every 1-unit reduction in HbA1c after self-monitoring of blood glucose (SMBG), complications are reduced by:[7]

Adopting **structured SMBG** can greatly enhance glucose management, addressing a key factor in lowering the risk of both microvascular and macrovascular complications. Additionally, by effectively reducing postprandial glucose spikes, individuals can take significant steps towards decreasing their cardiovascular risk.[8]

- **It is vitally important to prevent and treat macrovascular problems in people with diabetes.**
- **Diabetes-related morbidity and mortality could result from the consequences of not receiving proper treatment.**
- **Managing diabetes requires a diverse approach.**
- **Nurses play a crucial role in preventing diabetes related complications in the community by providing education, early detection, and rehabilitation services to improve patient outcomes and quality of life.**

The tool

Telemedicine-assisted structured self-monitoring helps to achieve glycemic control and reduce hypoglycaemia

Telemedicine is a very promising method for providing individualised self-monitoring of blood glucose (SMBG) and healthcare wherever it is needed.[9]

Study Objective	To evaluate the effectiveness of telemedicine-assisted structured self-monitoring of blood glucose on glycemic control and diabetes management of Chinese patients.
Study Design	Open-label randomised (1:1) trial
Study Population	N=418 T2DM adult patients with suboptimal glycemic control (7% ≤ HbA1c ≤ 11%); randomised to intervention group (n = 212) or the control group (n = 206)

Method:

- The structured monitoring consisted of six points (before each meal and 2 h after eating) if three main meals were consumed daily and whenever there was a risk of hypoglycaemia, especially at night (i.e., the time of the highest risk of hypoglycaemia).
- However, only the BGM given to the patients in the intervention group was connected to the telemedicine system through Bluetooth and the SMBG data were transmitted to the telemedicine system in realtime.

Results:

- At six months, the intervention group showed a significant reduction in mean HbA1c levels to 7.38% from a baseline of 7.9 ± 0.9, while the control group had a mean HbA1c of 7.98%, down slightly from a baseline of 8.0 ± 0.9 ($P < 0.001$).
- The SMBG with telemedicine support improved diabetes self-care behaviour and reduced hypoglycaemia risk as evidenced by substantial changes in the group's 6-month outcomes on the Low Blood Glucose Index (LBGI) and the Diabetes Self-Management Questionnaire (DSMQ).
- Ultimately, following six months, the intervention group demonstrated a noteworthy decline in both total triglycerides and the number of visits to specialists.

Structured SMBG with telemedicine supports patients reach a target level of glycemic control and reduces the risk of hypoglycaemia.

Tips for you

Minimising risk for cardiovascular diseases

- It is crucial to conduct a comprehensive assessment of the patient's risk factors, including obesity/overweight, hypertension, dyslipidemia, smoking history, family history of premature coronary disease, chronic kidney disease (CKD), and presence of albuminuria.
- It is important to note that individuals with diabetes are at a significantly higher risk of myocardial infarction (MI), especially when compared to those without diabetes.
- Coronary artery disease poses a significant risk in diabetes cases, and MIs may present as "silent" or atypical due to autonomic neuropathy.
- Identifying and evaluating these risk factors is pivotal in developing a personalised care plan and determining appropriate management strategies.
- Patient education plays a crucial role in empowering individuals to take an active role in managing risk factors and promoting better control to reduce the likelihood of developing macrovascular complications.
- Regular monitoring of blood pressure and advocating lifestyle modifications are essential steps in risk management.
- It is also important to ensure people with diabetes are adhering to prescribed medications for managing hypertension, hyperlipidemia, and diabetes, as pharmacologic interventions are often necessary to achieve optimal control of blood pressure, lipid levels, and glucose management.
- Furthermore, it is recommended to administer antiplatelet therapy with aspirin for secondary prevention in individuals with diabetes and a history of atherosclerotic cardiovascular disease.
- Regular monitoring and assessment of blood glucose levels are crucial, especially in patients with symptoms suggestive of acute diabetic complications.
- Lastly, promoting adherence to statin therapy for lipid management, particularly in individuals with atherosclerotic cardiovascular disease or high cardiovascular risk, is vital for comprehensive risk reduction.[10]

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