Diabetes complications

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- I do not have any relevant financial relationships to disclose

- Learning Objectives:
  - Describe the pathophysiology, early signs, and diagnostic approaches to diabetic complications
  - Identify current guidelines and evidence-based practices to manage and prevent diabetic complications

- Type 2 diabetes mellitus is characterized by hyperglycemia, insulin resistance, and relative impairment in insulin secretion

- Pathogenesis is only partially understood but is heterogeneous and both genetic factors affecting insulin release and responsiveness and environmental factors, such as obesity, are important.

- Given the marked increase in childhood obesity, there is concern that the prevalence of diabetes will continue to increase substantially

- Global data appear to substantiate this concern as the worldwide incidence rate of type 2 diabetes among adolescents and young adults (aged 15 to 39 years) rose from 117 to 183 per 100,000 population between 1990 and 2019

The prevalence of diabetes is higher in certain populations:

- Using data from a national survey for people aged 20 years or older, the prevalence of diagnosed type 2 diabetes in the United States (2018) was 7.5% in non-Hispanic White Americans, 9.2% in non-Hispanic Asian Americans, 12.5% in Hispanic Americans, 11.7 % in non-Hispanic Black Americans, and 14.7% in Native Americans/Alaska Natives

- Outside the United States, type 2 diabetes is most prevalent in Polynesia and other Pacific islands (approximately 25%) with similarly high rates in the Middle East and South Asia (Kuwait and Pakistan, in particular)

- In China, the most populous country in the world, an estimated 13 percent of the adult population has diabetes, with approximately one-half undiagnosed

Acute complications

- Hypoglycemia
- Diabetes Ketoacidosis
- Hyperosmolar Hyperglycemic State

Hypoglycemia

- Most common acute complication of glucose-lowering therapy and is associated with poor outcomes and quality of life

- Specific medication classes (eg, insulin, sulfonylureas, or meglitinides)

- **Symptoms/signs**
  - Autonomic neurogenic symptoms- tremors, palpitations, anxiety, sweating, hunger, paresthesia

  - Neuroglycopenic symptoms- dizziness, weakness, drowsiness, confusion, delirium, seizure, coma

  - Profound, prolonged hypoglycemia can cause brain death if unwitnessed and left untreated, but the vast majority of episodes are reversed after the glucose level is raised

- In patients with diabetes, the onset of symptoms of hypoglycemia may occur at glucose levels <70 mg/dl, although the specific value varies between and within individuals over time

- The glycemic thresholds for neurogenic and neuroglycopenic responses shift to higher plasma glucose concentrations in patients with chronic hyperglycemia and to lower plasma glucose concentrations in patients with repeated episodes of hypoglycemia, which may be caused by intensive diabetes treatment

- Impaired awareness of hypoglycemia: likely results from reduced sympathoadrenal (predominantly sympathetic neural) responses

- Health-related outcomes: Mortality, cardiovascular disease, cognitive impairment, dementia, falls and fractures

Treatment

- Immediate ingestion of concentrated carbohydrate sources- sugar, juice, soda, candy, honey (15 grams of carb, check blood sugar in 15 minutes)
- Glucagon- IM, SQ, Intranasal
- IV glucose

Reducing the risk of hypoglycemia

- patient education and empowerment
- frequent blood glucose monitoring (fingerstick measurements or continuous glucose monitoring [CGM])
- individualized glycemic goals
- flexible and rational insulin (and other drug) regimens
- ongoing professional guidance and support.

- Intensive treatment of blood glucose is associated with an increased risk of hypoglycemia, as well as accompanying burdens of polypharmacy, additional side effects, and cost

Severe Hypoglycemia EMERGENCY CARE

THE MORE YOU KNOW

Hypoglycemia occurs when the amount of glucose (sugar) in the blood is lower than it should be. Very low blood glucose that isn't treated can result in serious health effects, including seizures or coma. It can even lead to death. Severe hypoglycemia is more common in patients with diabetes who take insulin or certain medicines like sulfonylureas. According to the CDC, hypoglycemia is the cause of about **300,000 emergency department visits each year.** This is why it is vital to take steps to prevent hypoglycemia and to be prepared to take quick action to treat it.

Early signs and symptoms of hypoglycemia may include:

- Shakiness or dizziness
- Headache
- Fast, pounding heart rate
- Sweating or cold, clammy skin

KNOW WHEN TO GIVE GLUCOSE

When signs of hypoglycemia are present and a person cannot consume a fast-acting source of sugar orally, a glucose injection should be given. Severe hypoglycemia often requires the assistance of a family member, friend, or bystander to administer rescue glucose. Glucose is the only way to increase blood sugar in an emergency situation.

It is important to **KNOW** the signs of hypoglycemia.

KNOW what actions to take.

KNOW how to use a glucagon kit in an emergency.

REMEMBER SEVERE HYPOGLYCEMIA IS PREVENTABLE!

EARLY EMERGENCY CARE

KNOW the first signs of hypoglycemia:

- Check blood glucose (sugar).
- Use a fast-acting sugar source to help raise blood glucose levels, such as glucose tablets or gel. Other sugar sources include: Fruit juice, regular soda, table sugar, honey, corn syrup, or hard candies.
- Check blood glucose level again after 15 minutes of eating the fast-acting sugar.

EMERGENCY KIT

Carry an emergency kit. KNOW what it should contain:

- Emergency contact information
- Instructions for administering emergency glucagon
- Blood glucose meter and test strips (including extra batteries)
- Glucose tablets (to be used only if you are conscious)
- Emergency glucagon

Keep this resource in your emergency kit and share with your friends and loved ones.

KNOW HOW TO USE AN EMERGENCY GLUCAGON KIT

Remove contents from kit and check label for expiration.

Choose injection site and expose skin.

Push needle into skin releasing all liquid into the body.

Turn person on their side.

PREPARE:

- Check the label to make sure the medicine hasn't expired.
- Remove the contents from the kit along with any covers or caps.
- Find a spot on the person's thigh or arm.

INJECT:

Is it an auto-injection?

- Push down on the skin and hold for 5 seconds.
- Wait for window to turn red.

Is it a manual injection?

- Mix the saline and the powder. Gently swirl or roll the vial until the liquid looks clear.
- Insert the needle into the vial and draw back all of the liquid into the syringe.
- Inject the needle into the body.

ASSIST:

- Turn the person on their side.
- Wait up to 15 minutes for them to wake up.
- If they are still unresponsive, inform a provider or emergency services.

Moving patients from educated to engaged, visit endocrine.org/patient-engagement!

Diabetic Ketoacidosis (DKA)

Symptoms and Signs

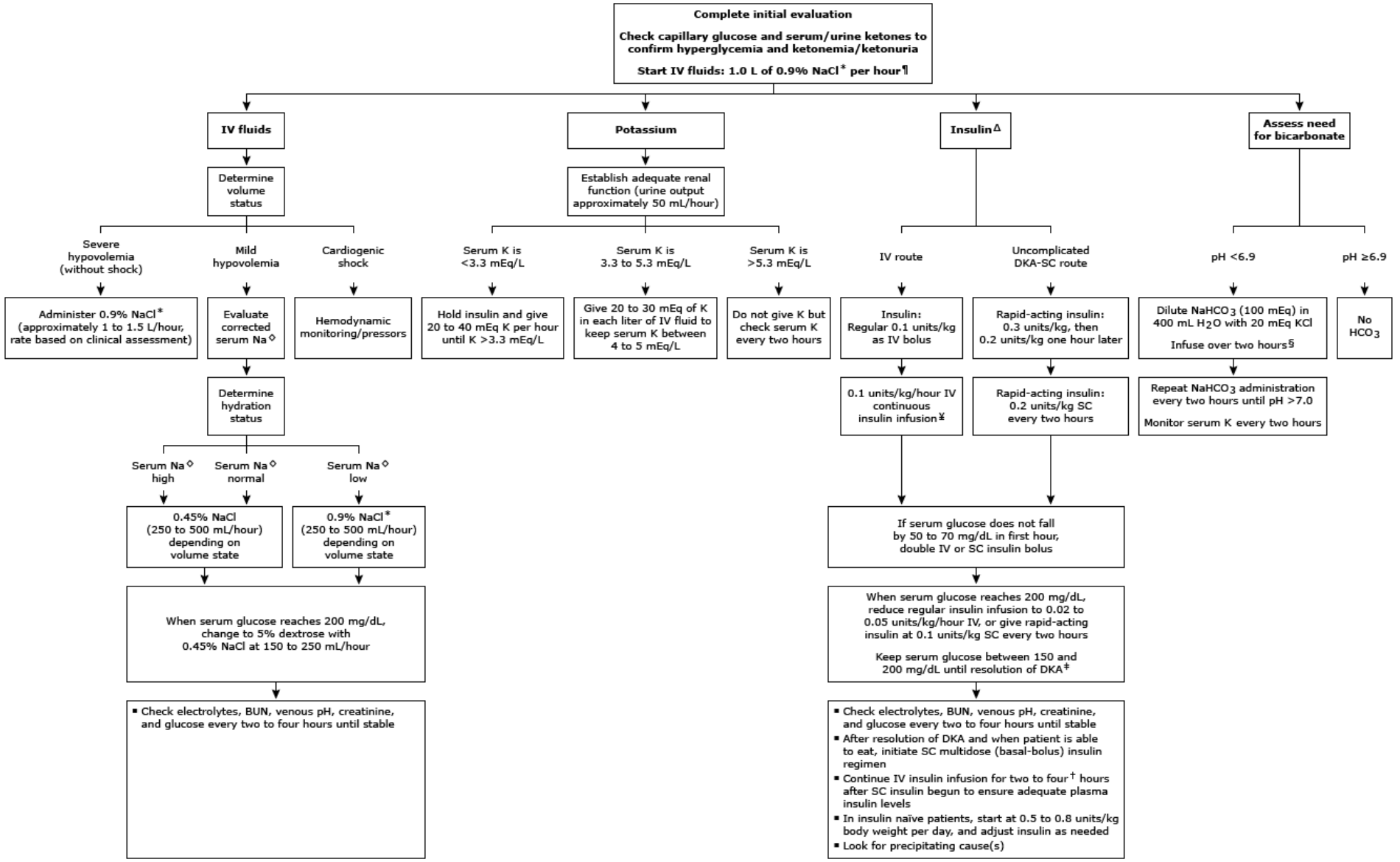
- Polyuria, polydipsia, nausea, vomiting, abdominal pain, generalized weakness, altered mental status, characteristic smell (acetone in breath)
- Dehydration, Hypotension, Tachycardia
- Hypokalemia
- Pseudohyponatremia

3 Major metabolic derangements

- Hyperglycemia
- Ketonemia
- Anion gap metabolic acidosis

DKA treatment

- Fluid resuscitation
- Correction of electrolyte imbalance
- Insulin
- Clinical and laboratory monitoring
- Treatment of precipitating events



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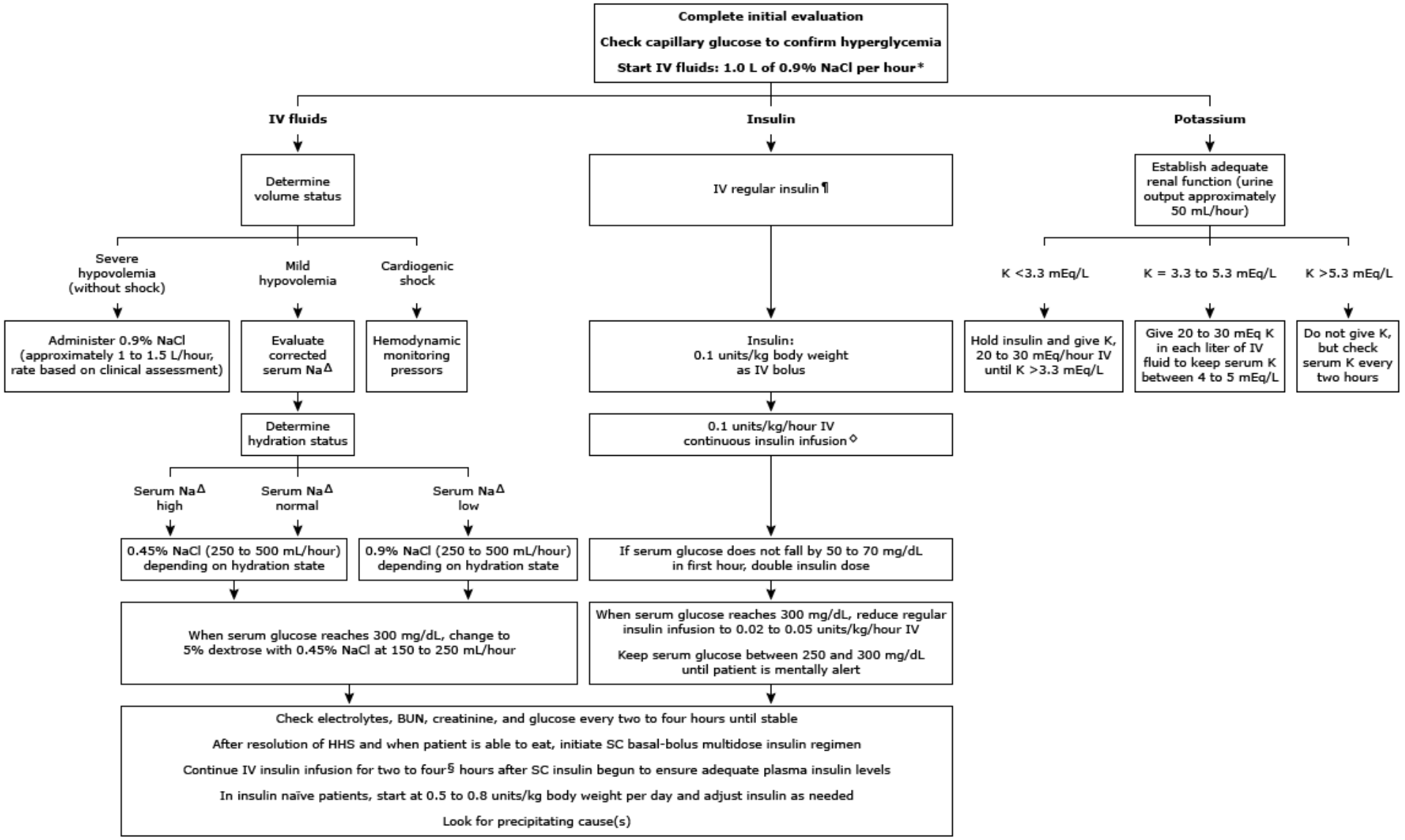
Hyperosmolar Hyperglycemic State

Clinical features:

- Severe hyperglycemia
- Severe dehydration
- Increased Osmolality
- Little or no ketoacid accumulation
- Neurological abnormalities are frequently present including coma



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Chronic complications

Microvascular complications

- Neuropathy- Peripheral and Autonomic
- Nephropathy
- Retinopathy

- The importance of intensive glycemic management for protection against microvascular and cardiovascular disease (CVD) in diabetes was established for type 1 diabetes in the Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications (EDIC) study

- The benefit of glycemic management on microvascular disease in type 2 diabetes was documented in the United Kingdom Prospective Diabetes Study (UKPDS), Action in Diabetes and Vascular Disease (ADVANCE), and Action to Control Cardiovascular Risk in Diabetes (ACCORD) trials

- A systematic review of studies in patients with type 2 diabetes shows that maintaining a higher TIR as assessed by continuous glucose monitoring (CGM) is associated with a reduced risk of diabetes-related microvascular complications including retinopathy, nephropathy, and neuropathy

Peripheral Neuropathy

- Pain, tingling, and burning
- Numbness and loss of feeling
- Muscle weakness (amyotrophy)
- Skin ulcers (open sores)

- About half of people with DPN might not have symptoms, except for losing feeling in their feet. Because of this feeling of loss, they could injure their feet and not know it
- Untreated foot injuries can lead to ulcers and infection and, sometimes, amputation

Patient education:

- Good blood glucose control may prevent further nerve damage but usually can't reverse the damage that's already happened

- Avoiding smoking and limiting alcoholic beverages can also help

- Protect your feet by:

- Always wearing shoes (or slippers) and clean, dry socks
- Choosing shoes that are comfortable and fit well
- Wash and dry feet and check them every day. Choose a regular time, such as after shower in the morning
- Look for blisters, calluses, bruises, redness, swelling, cracked skin, sores, or cuts
- Cut nails once a week or as needed
- Put lotion on dry skin but not between toes
- Seeing a podiatrist regularly for foot care

Autonomic Neuropathy

- Postural hypotension
- Hyper/Hypo-hidrosis
- Impaired genitourinary function– paralytic bladder, incomplete voiding, Impotence, Retrograde ejaculation
- Digestive system problems – Gastric atony, bloating, nausea, vomiting, diarrhea, constipation
- Cranial nerve involvement- Extraocular nerve paralysis, impaired pupillary responses

Retinopathy

- Retinopathy affects approximately one-third of adults with diabetes and represents the leading cause of blindness in these individuals

- Non-Proliferative Retinopathy
- Proliferative Retinopathy
- Macular edema

- Also, at high risk of developing cataract and glaucoma

- Establish regular follow up with Ophthalmology

Diabetes Nephropathy

- Diabetes is the most common cause of ESRD

Macrovascular complications

- Coronary Artery Disease (CAD)
- Cerebrovascular Disease (CVA)
- Peripheral Artery Disease (PAD)
- CVD is a major cause of death and disability among people with diabetes
- 2 to 4, fold higher risk of hospitalization for major CVD events and CVD-associated clinical procedures compared with those without diabetes

- Epidemiologic analyses (observational studies or secondary analyses of trials) suggest a correlation between higher rates of cardiovascular disease (CVD) and chronic hyperglycemia

- Most randomized clinical trials have not been of sufficient duration and size to demonstrate a beneficial effect of intensive therapy on macrovascular outcomes in type 2 diabetes

- Only long-term follow-up of several large clinical trials (UKPDS and VADT) has demonstrated a macrovascular benefit with intensive therapy in patients with type 2 diabetes

- In meta-analyses including UKPDS, VADT, ACCORD, and ADVANCE, there was a reduction in the risk for coronary heart disease (eg, RR 0.89 [95% CI 0.81-0.96]) and nonfatal myocardial infarction (RR 0.84 [95% CI 0.75-0.94]) with intensive glucose-lowering versus standard treatment. However, intensive treatment did not significantly affect stroke, all-cause, or cardiovascular mortality

- The **most effective approach** for the prevention of macrovascular complications appears to be **multifactorial risk factor reduction** (**glycemic management, smoking cessation, aggressive blood pressure management, treatment of dyslipidemia, and, for secondary prevention, daily aspirin**)

- For patients with CVD, the actual type of glucose-lowering medication used has a more substantive effect on CVD risk than might be expected from the degree of glucose-lowering alone

- Specifically, the sodium-glucose cotransporter 2 **(SGLT2) inhibitors** and the glucagon-like peptide 1 **(GLP-1) receptor agonists**, and, perhaps to a lesser extent, the **thiazolidinedione** (Pioglitazone), have been associated with reduced incidence of major adverse cardiovascular events, mainly in individuals with preexisting CVD.

- The **SGLT2 inhibitors** also reduce adverse heart failure outcomes and the progression of chronic kidney disease, in those both **with and without CVD**

- these effects appear to be **independent of the effect of these agents on A1C**

Infections

- Immunocompromised state- altered PMN function(adherence, chemotaxis, phagocytosis) ,vascular disease, neuropathies,
- Higher risk of infections
- Soft tissue infections of extremities- folliculitis, abscess, carbuncle, Fournier's gangrene
- Post-operative wound infections
- Osteomyelitis
- UTI and Pyelonephritis
- Candidal infection of the skin and mucous membranes
- Dental caries, periodontal disease
- Tuberculosis

Pregnancy complications

- Premature birth
- Congenital malformations
- Polyhydramnios
- IUGR
- IUFD
- Preeclampsia
- Neonatal Macrosomia
- Neonatal Hypoglycemia

Others

- Bone disease in Diabetes Mellitus- high risk of fracture
- Depression and Anxiety
- Anemia
- Sleep Apnea
- NAFLD, NASH, Cirrhosis
- Increased risk of cancer
- Physical and cognitive Disability

Thank you