

# TYPE 2 DIABETES MELLITUS

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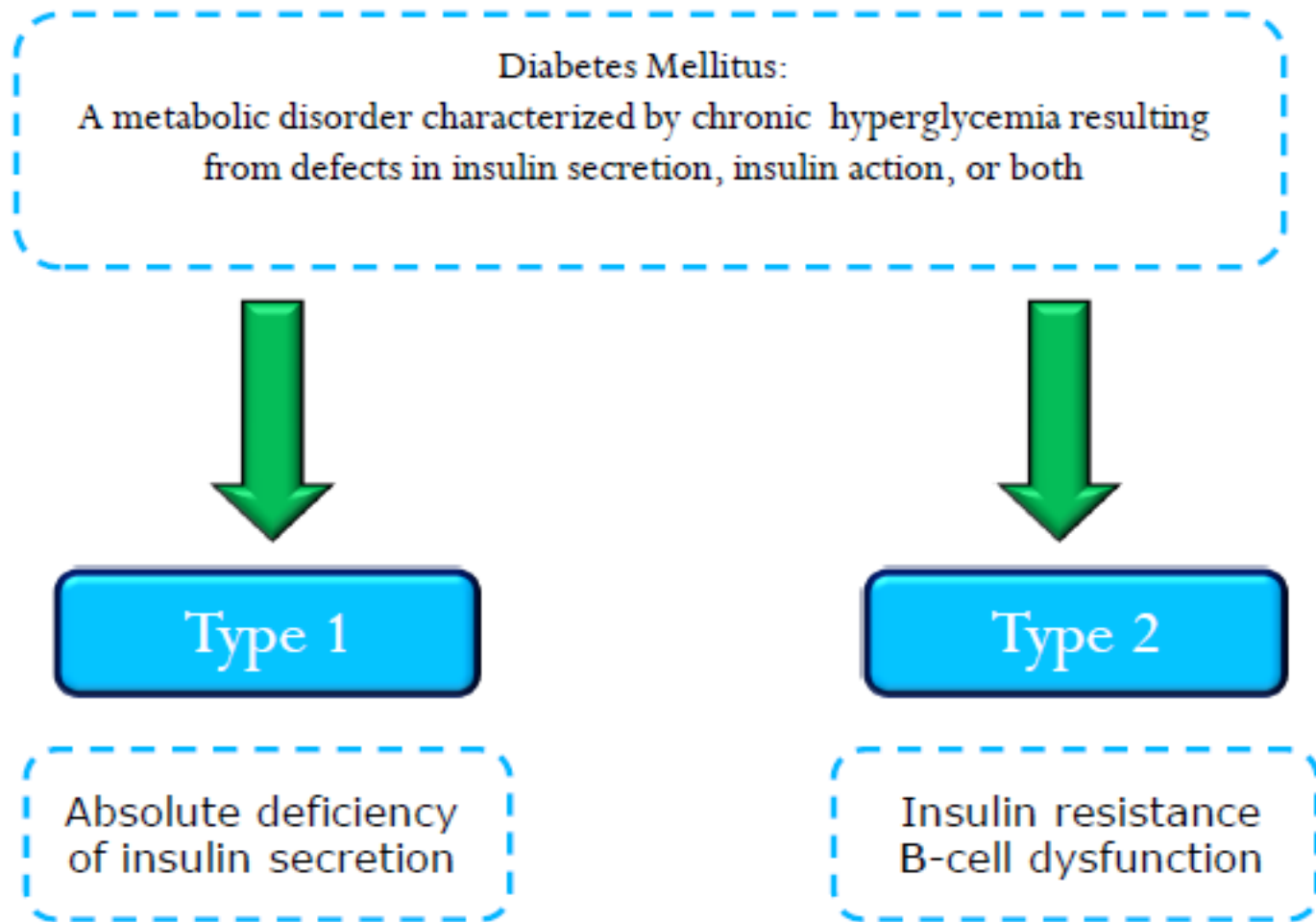
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# OUTLINE

- Introduction
- Pathophysiology
- Clinical manifestations
- Diagnosis
- Complications
- Management of DM
- Take home message

# What is diabetes?



# Introduction...

- Diabetes mellitus has been known for over 3000 years.
- **Diabetes**, a greek word means passing through; **a large discharge of urine**,
- **Mellitus** means pleasant tasting, **honey**.
- T2 DM is by far the most common type of diabetes in adults
- predisposes to cardiovascular diseases
- In the US, DM is the leading cause of end-stage renal disease, nontraumatic lower extremity amputations, and adult blindness.
- Etiology involves complex interactions between environmental and genetic factors

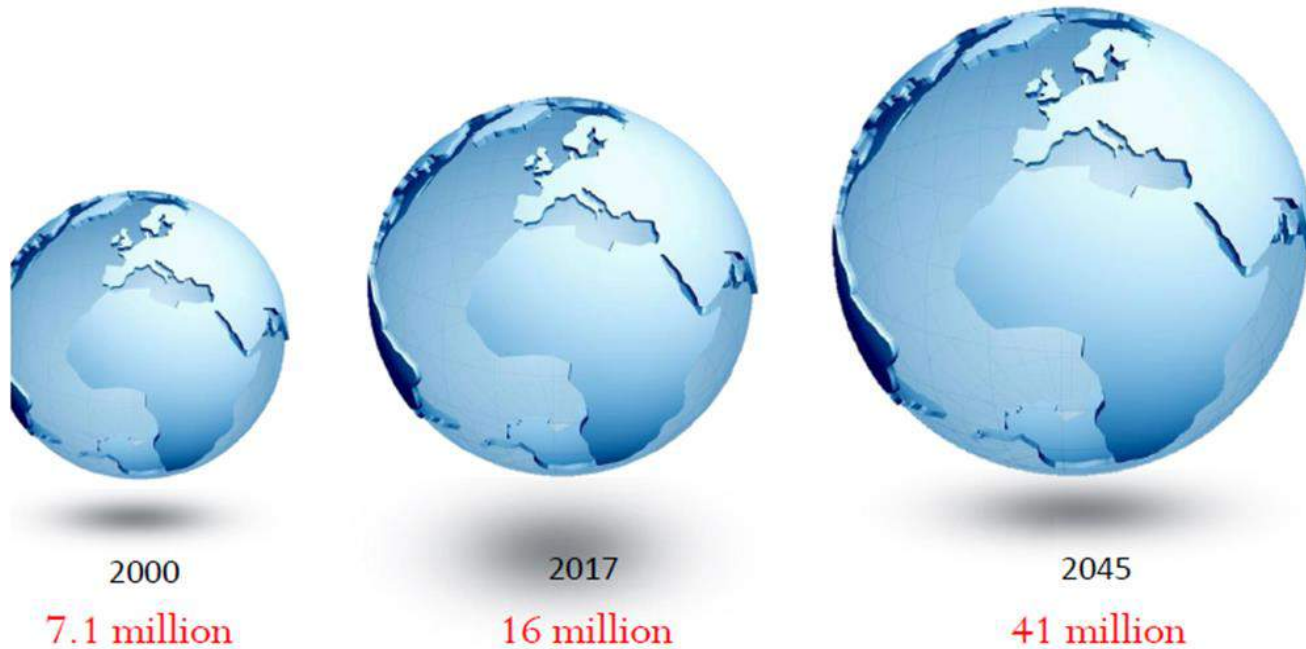
# Epidemiology



**FIGURE 417-2 Worldwide prevalence of diabetes mellitus.** Global estimate is 382 million individuals with diabetes. Regional estimates of the number of individuals with diabetes (20–79 years of age) are shown (2013). (Used with permission from the *IDF Diabetes Atlas, the International Diabetes Federation, 2013.*)

# Diabetes prevalence in Africa

Estimated prevalence according to IDF Atlas



IDF Diabetes Atlas 8<sup>th</sup> Ed. 2017  
Wild et al. Diabetes Care 2004;27(5):1047-1053

At least 80% of people in Africa with diabetes are undiagnosed, and many in their 30s to 60s will die from diabetes there.

The greatest percentage increase in rates of diabetes will occur in Africa over the next 20 years.

# Major risk factors

- Age > 45 years (may occur in young individuals)
- Obesity (BMI  $\geq 25$  kg/m<sup>2</sup> or ethnically relevant definition for overweight)
- Physical inactivity
- Family history of type 2 diabetes in a first-degree relative (eg, parent or sibling)
- Race: panick, Native American, **African American**, Asian American, or Pacific Islander descent.
- History of previous impaired glucose tolerance (IGT) or impaired fasting glucose (IFG)

# Major risk factors cont...

- **Hypertension (>140/90 mm Hg) or dyslipidemia (HDL cholesterol level < 40 mg/dL or triglyceride level >150 mg/dL)**
- History of gestational diabetes mellitus or of delivering a baby with a birth weight of over 4kg
- Polycystic ovarian syndrome (which results in insulin resistance)
- History of cardiovascular disease

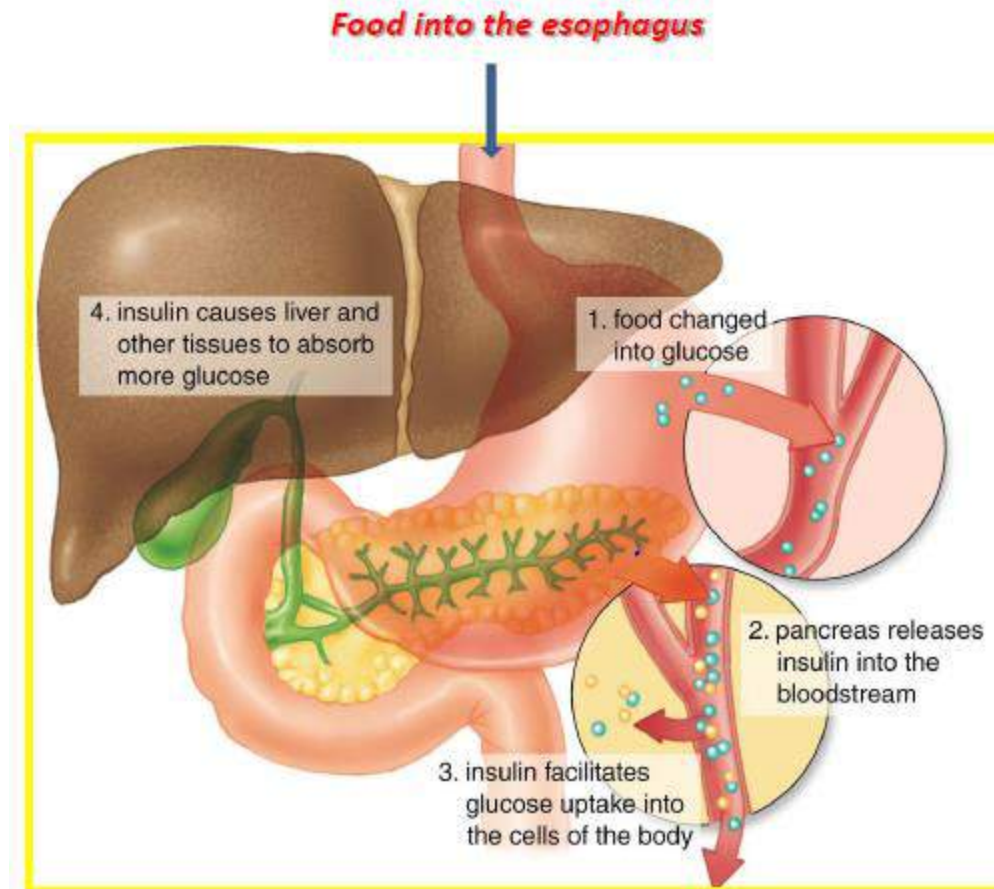


# Pathogenesis: glucose metabolism

*The pancreas releases insulin after eating to lower blood glucose.*

*The actions of insulin are:*

- (1) promotes glucose uptake by target cells (muscle, brain,...) and provides for glucose storage as glycogen,
- (2) prevents fat and glycogen breakdown and inhibits gluconeogenesis,
- (3) Increases protein synthesis



# Pathogenesis of Type 2 Diabetes Mellitus



Insulin Resistance: Receptor and Postreceptor Defects

Increased glucose production

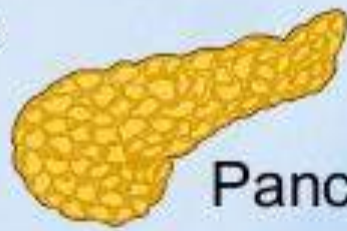
Insufficient glucose disposal

**Hyperglycemia / Type 2 DM**

X



Liver



Pancreas



Peripheral tissues (skeletal muscle)

Impaired insulin secretion



# Effects of insulin deficiency

## Metabolic defects

### **Carbohydrate Metabolism**

1. Diminished uptake of glucose by tissues such as muscle, adipose tissue and liver
2. Overproduction of glucose (via glycogenolysis and glyconeogenesis) by the liver

### **Protein Metabolism**

1. Diminished uptake of amino and diminished synthesis of protein
2. Increased proteolysis

### **Fat Metabolism**

1. Increased lipolysis
2. Decreased lipogenesis
3. Increased production of triglycerides
4. Decreased removal of ketones and increased ketone production

## Chemical abnormalities

Hyperglycemia

Negative nitrogen balance

Elevated levels of branch chain amino acids

Elevated blood urea nitrogen level

Elevated potassium level

Elevated plasma fatty acids level

Elevated plasma glycerol level

Hypertriglyceridemia

Elevated plasma and urine ketones

## Clinical abnormalities

Polyuria, polydipsia, polyphagia  
Blurred vision,  
Diminished mental alertness

Loss of muscle mass  
Weakness

Loss of adipose tissue

Exudative xanthoma  
Lipemia retinalis  
Pancreatitis (abdominal pain)  
Hyperventilation  
metabolic acidosis

# SYMPTOMS OF DIABETES



# Criteria for the Diagnosis of Diabetes Mellitus

Symptoms of diabetes plus random blood glucose concentration  $\geq 11.1$  mmol/L (200 mg/dL),

**Or**

Fasting plasma glucose  $\geq 7.0$  mmol/L (126 mg/dL)

**Or,**

Hemoglobin A1c  $\geq 6.5\%$

**Or,**

2-h plasma glucose  $\geq 11.1$  mmol/L (200 mg/dL) during an oral glucose tolerance test

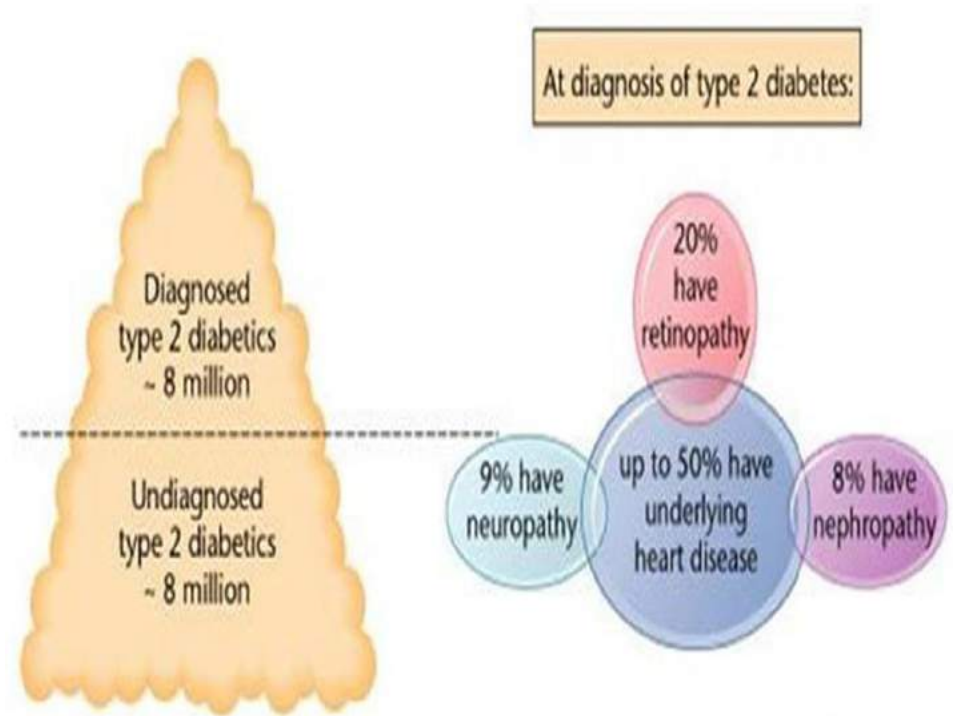


# Screening

- a large number of individuals with DM are asymptomatic
- type 2 DM may be present for up to a decade before diagnosis,
- complications at the time of their diagnosis,
- treatment of type 2 DM may favorably alter the natural history of DM

The ADA recommends screening all individuals:

- >45 years every 3 years
- Early if overweight (BMI >25 kg/m<sup>2</sup>) and have **one** additional risk factor for diabetes



# Complications

- Poorly controlled type 2 diabetes is associated with an array of complications.
- Diabetic complications:
  - Acute: diabetic ketoacidosis (DKA), hyperglycemic hyperosmolar state(HHS), hypoglycemia
  - Longterm complications:
    - Microvascular: Retinopathy, Nephropathy (DKD), Neuropathy / diabetic foot
    - Macrovascular: Coronary, cerebral, and peripheral arterial disease

# Hypoglycemia

As plasma glucose falls:

- **↑** glucagon/epinephrine → **↑** CV stress
- **↓** K<sup>+</sup> → Qt prolongs → **↑** Arrhythmia
- Endothelial dysfunction/ **↑** PLT activation/ **↑** blood viscosity → **↑** Thrombosis
- **↓** brain fuel x 5-6 hrs → **↑** Neuronal death

**Outcomes are (much) worse with HYPOglycemia**

50% **↑** mortality among outpatients with lowest Hgb A1c <6.5% vs A1c 7.5%



# ADA Diagnostic Criteria for DKA and HHS

Parameter	DKA			HHS
	Mild	Moderate	Severe	
Plasma glucose, mg/dL	>250	>250	>250	>600
Arterial pH	7.25-7.3	7.0-7.24	<7.0	>7.30
Serum bicarbonate, mmol/L	15-18	10 to <15	<10	>15
Serum ketones <sup>†</sup>	Positive	Positive	Positive	Small
Urine ketones <sup>†</sup>	Positive	Positive	Positive	Small
Effective serum osmolality,* mOsm/kg	Variable	Variable	Variable	>320
Alteration in sensoria or mental obtundation	Alert	Alert/drowsy	Stupor/coma	Stupor/coma

\*Calculation:  $2[\text{measured Na}^+ (\text{mEq/L})] + \text{glucose (mg/dL)}/18$ .

<sup>†</sup> Nitroprusside reaction method.

# Macrovascular and microvascular complications.

## *Retinopathy*

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Leading cause of blindness in adults.

Accounts for ~ 24,000 cases of blindness every year.

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## *Nephropathy*

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Leading cause of end-stage renal disease (ESRD) in the United States.

Accounts for ~ 28,000 cases of ESRD every year.

Diabetes accounts for 1 of 3 patients with ESRD in the United States.

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## *Myocardial Infarction and Stroke*

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Increased 2 to 4 fold.

Accounts for 60% to 70% of all diabetes-related deaths.

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## *Peripheral Vascular Disease*

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Leading cause of nontraumatic amputations.

Accounts for ~ 67,000 limbs lost per year.

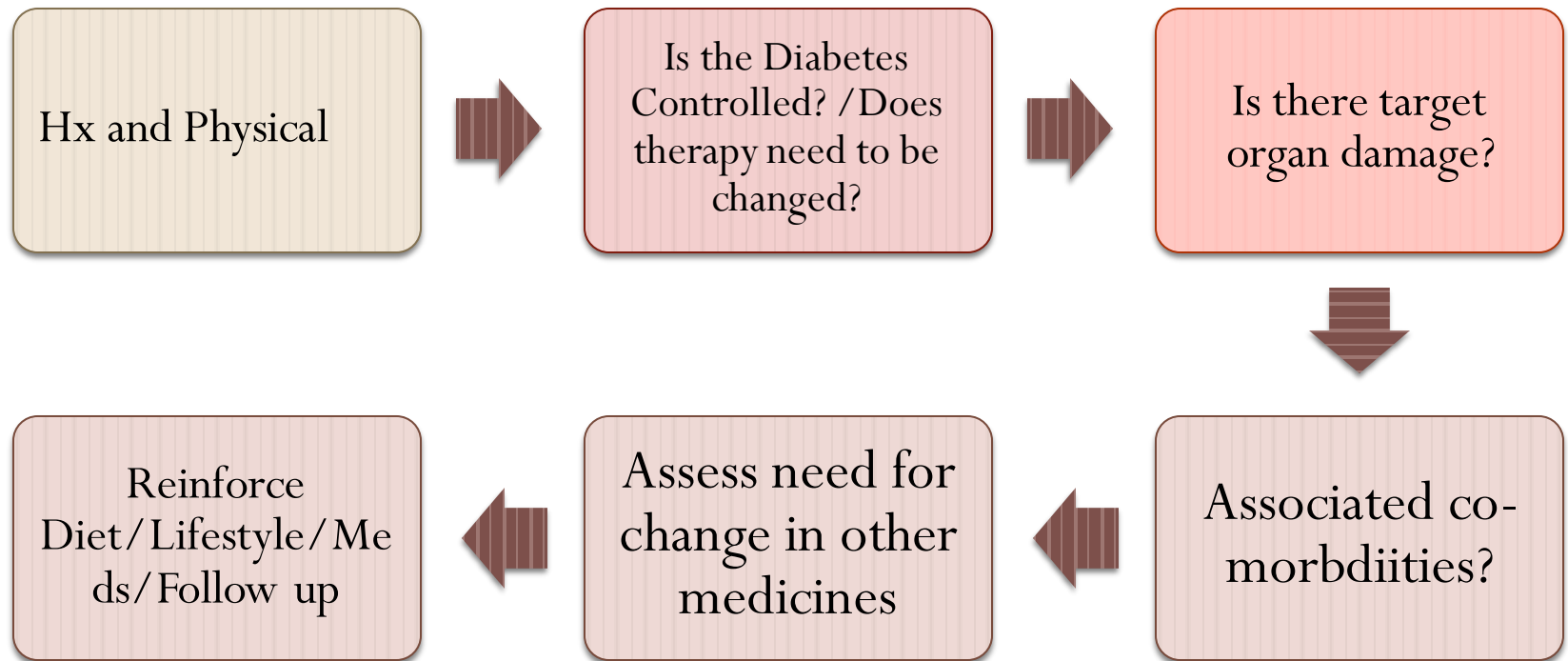
Three year survival is ~ 50%.

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# MANAGEMENT OF T2DM

# Patient Exam



# The goals of therapy

- (1) eliminate symptoms related to hyperglycemia,
- (2) reduce or eliminate the long-term microvascular and macrovascular complications of DM
- (3) allow the patient to achieve as normal a lifestyle as possible.

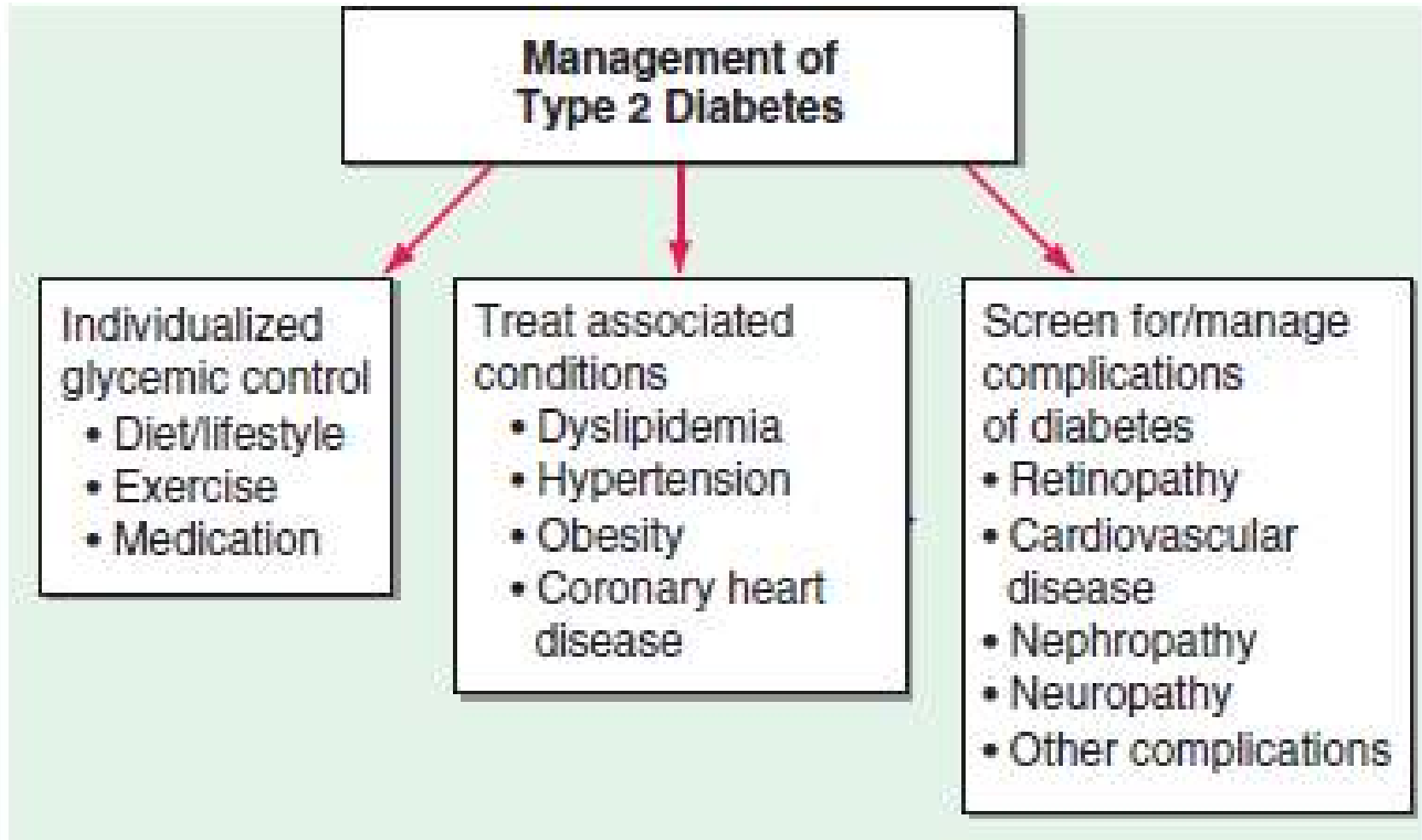
*Symptoms of diabetes usually resolve when the plasma glucose is  $<11.1 \text{ mmol/L}$  ( $200 \text{ mg/dL}$ ).*

# Glycemic goals for Nonpregnant Adults with Diabetes :ADA/EASD

- **A1C : <7.0%**
- **Preprandial capillary plasma glucose: 80–130 mg/dL (4.4–7.2 mmol/L)**
- **Peak postprandial capillary plasma glucose: <180 mg/dL (<10.0 mmol/L)**



Essential elements in comprehensive care of type 2 diabetes.



# Diabetes self-management education(DSME) and support (DSMS).

- DSME/S are ways to improve the patient's knowledge, skills, and abilities necessary for diabetes self-care
- Four critical time points for DSME/S delivery:
  - At diagnosis
  - Annually for assessment of education, nutrition, and emotional needs
  - When new complicating factors arise that influence self-management; and
  - When transitions in care occur



# DSME/S

Education topics important for optimal diabetes care include:

- self-monitoring of blood glucose; urine ketone monitoring
- insulin administration;
- guidelines for diabetes management during illnesses;
- prevention and management of hypoglycemia
- foot and skin care;
- diabetes management before, during, and after exercise; and risk factor–modifying activities.

# Medical nutrition therapy

- preventing or delaying the onset of type 2 DM in high-risk individuals (obese or with prediabetes) by promoting weight reduction. Medical treatment of obesity
- preventing or delaying diabetes-related complications in diabetic individuals by improving glycemic control.
- managing diabetes-related complications.
  
- the components of optimal MNT are similar for individuals with type 1 or type 2 DM and similar to those for the general population (fruits, vegetables, fiber-containing foods, and low fat)
- Weight loss and exercise improve insulin resistance.

# Estimation of Food Portion Sizes

Your hands can be very useful in estimating portions. They're always with you, and they're always the same size! When planning a meal, the Canadian Diabetes Association suggests using these portion sizes as a guide:

## How many vegetables?

Choose as much as you can hold in both hands



## How much grains & starches?

Choose an amount up to the size of your fist.



## How much meat & alternatives

Choose an amount the size of your palm and the thickness of your little finger.



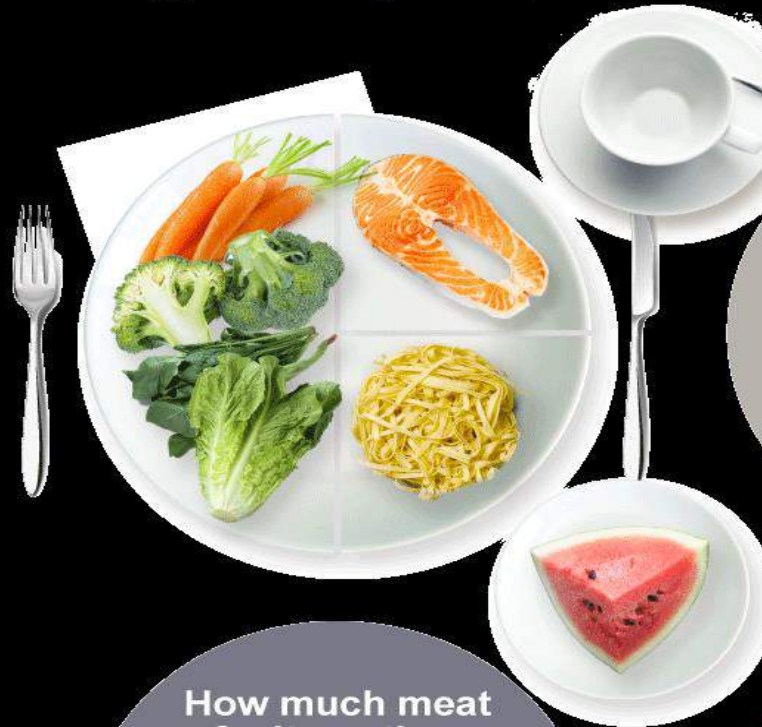
## How much milk?

Drink up to 1 cup or 250 ml of low-fat milk with a meal.



## How much fruit?

Choose an amount up to the size of your fist.



# Physical activity

- Children with diabetes/prediabetes: at least 60 min/day physical activity.
- Adults:
  - 150+ min/wk of moderate-to-vigorous activity over at least 3 nonconsecutive days/week
  - perform resistance training in 2-3 sessions/week on nonconsecutive days



# Lifestyle change

- smoking cessation : Advise all patients not to use cigarettes, other tobacco products or e-cigarettes.
- Psychosocial care should be provided to all people with diabetes,
- Emotional well-being is an important part of diabetes care and self-management .

# IDF treatment algorithm update

Lifestyle measures

■ Usual approach  
■ Alternative approach

Then, at each step, if not to target (generally  $HbA_{1c} < 7.0\%$ )

Consider first line

Metformin

Sulfonylurea or  
 $\alpha$ -glucosidase

Consider second line

Sulfonylurea

Metformin (if not first line)

or

$\alpha$ -gluc or DPP-4  
or TZD

Consider third line

Basal insulin or pre-mix insulin

or

$\alpha$ -gluc or DPP-4  
or TZD

or

GLP-1 agonist

Consider fourth line

Basal + mealtime insulin



Basal or pre-mix  
(later basal+mealtime)

# ADA/EASD Position Statement 2015

## Initial monotherapy

Not at target HbA<sub>1c</sub> after ~3 months

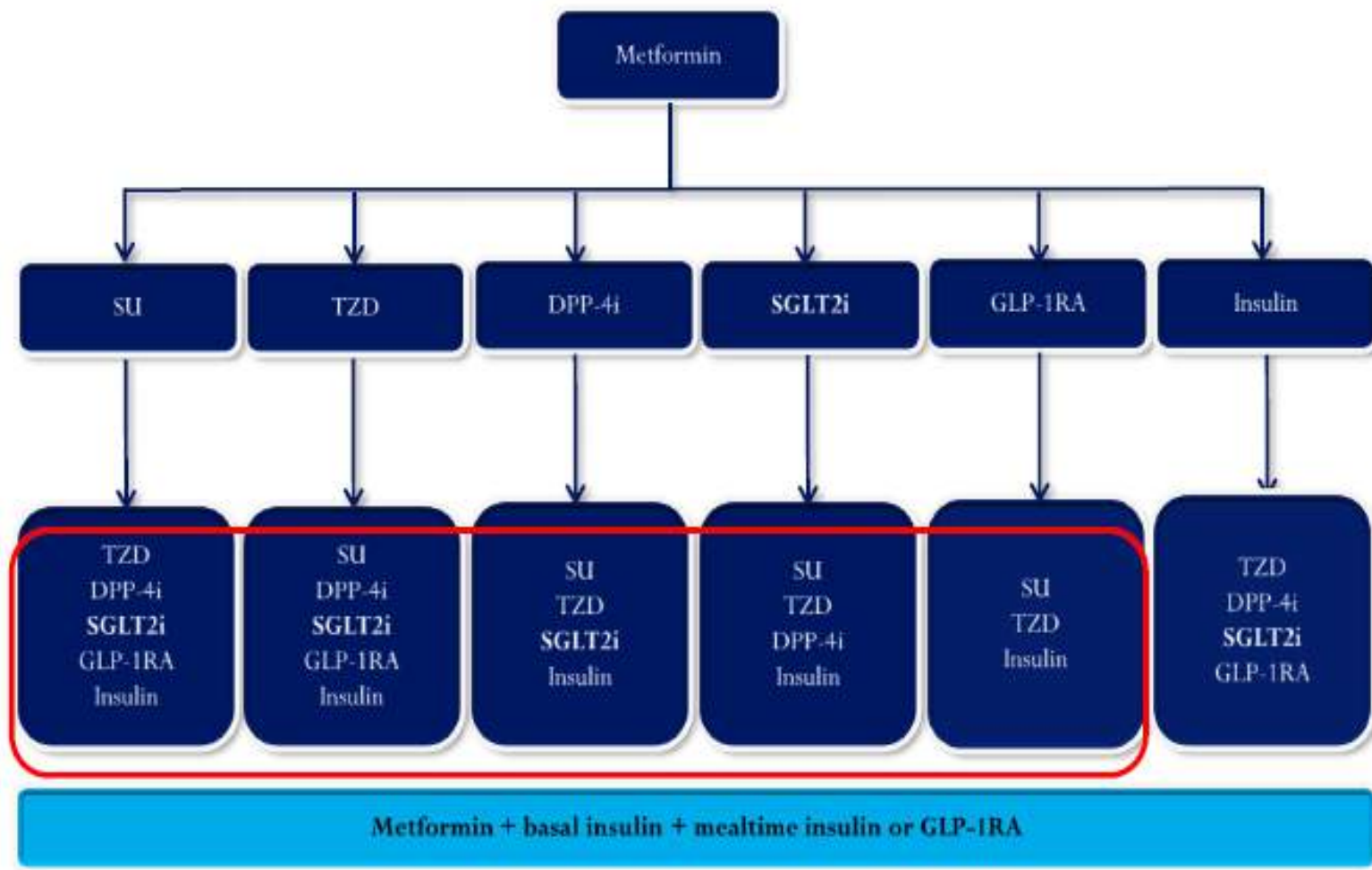
## Two-drug combinations

Not at target HbA<sub>1c</sub> after ~3 months

## Three-drug combinations

Not at target HbA<sub>1c</sub> after ~3 months

## Combination injectable therapy



Disease progression

<i>Patient characteristics</i>	<i>Estimated total daily dose (units per kg)</i>
Normal weight	0.4
Stage IV chronic kidney disease not on dialysis	0.25
Underweight, older age, or hemodialysis	0.3
Overweight	0.5
Obese, insulin resistant, or taking systemic glucocorticoids	≥ 0.6

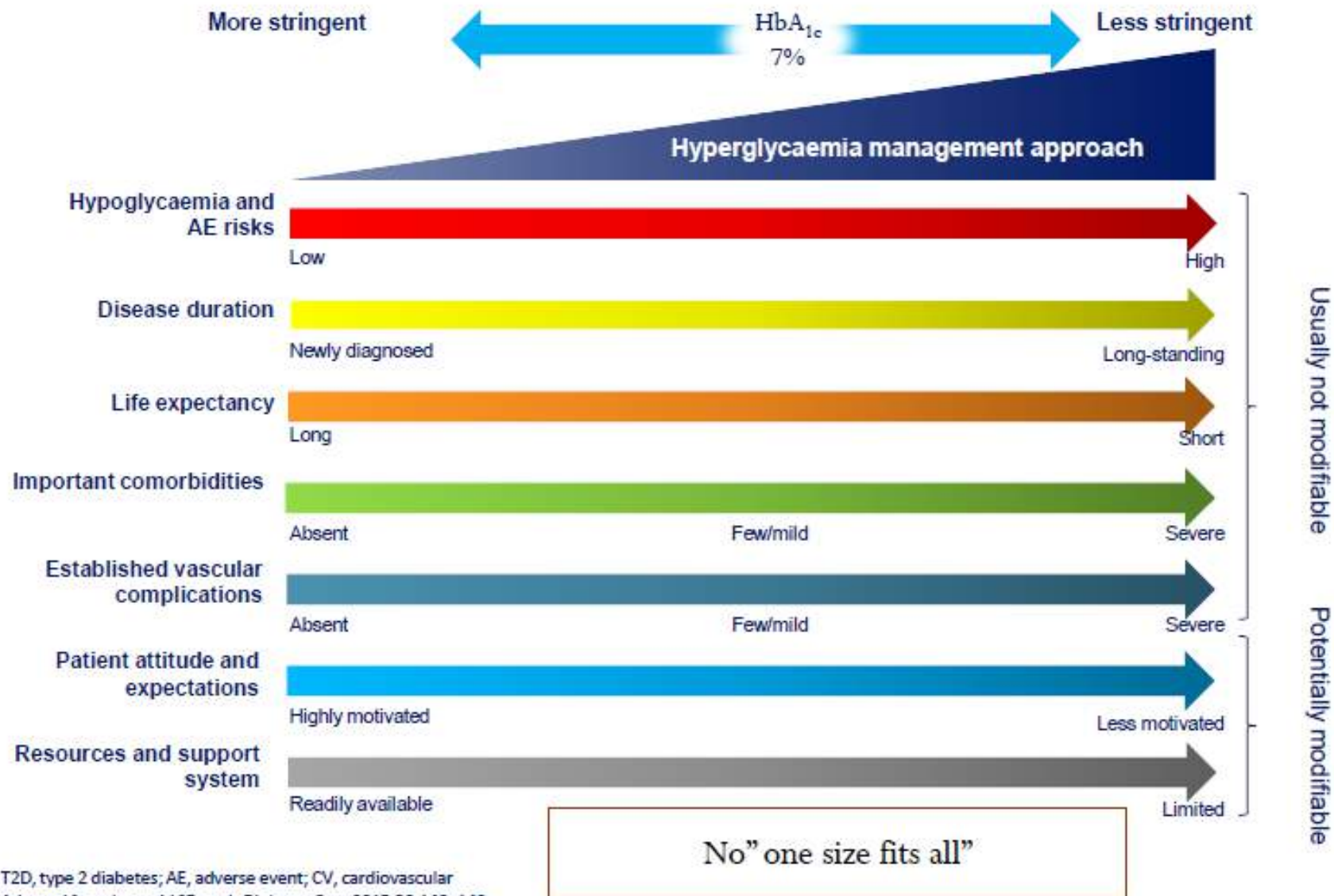
NOTE: *Glargine (Lantus) and detemir (Levemir) are the preferred agents, and glargine is favored because of its longer duration and once-per-day administration.*<sup>30</sup>

*Information from references 7 and 30.*





# Diabetes management considerations for individualized treatment: ADA/EASD Position Statement 2015



# Action to Control Cardiovascular Risk in Diabetes (ACCORD)

## Hypertension/ Blood Pressure Control

- Patients with diabetes should be treated to a blood pressure <140/90 mmHg.
- Lower targets, such as <130/80 mmHg, may be appropriate for certain individuals at high risk of CVD, if they can be achieved without undue treatment burden.

## Lifestyle intervention including:

- Weight loss if overweight
- healthy diet
- Moderation of alcohol intake
- Increased physical activity

# HTN...

- Treatment for hypertension should include
- ACE inhibitor
- Angiotensin II receptor blocker (ARB)
- Thiazide-like diuretic
- Dihydropyridine calcium channel blockers

Multiple drug therapy (two or more agents at maximal doses) generally required to achieve BP targets.

# Lipid Management

In adults a screening lipid profile is reasonable:

- At diabetes diagnosis
- At the initial medical evaluation
- And every 5 years, or more frequently if indicated

To improve lipid profile:

- Weight loss (if indicated)
- Reduction of saturated fat, trans fat, cholesterol intake
- Increase of  $\omega$ -3 fatty acids, viscous fiber, plant stanols/sterols
- Increased physical activity

**Table 9.1—Recommendations for statin and combination treatment in people with diabetes**

Age	Risk factors	Recommended statin intensity*
<40 years	None	None
	ASCVD risk factor(s)**	Moderate or high
	ASCVD	High
40–75 years	None	Moderate
	ASCVD risk factors	High
	ASCVD	High
	ACS and LDL cholesterol $\geq 50$ mg/dL (1.3 mmol/L) or in patients with a history of ASCVD who cannot tolerate high-dose statins	Moderate plus ezetimibe
>75 years	None	Moderate
	ASCVD risk factors	Moderate or high
	ASCVD	High
	ACS and LDL cholesterol $\geq 50$ mg/dL (1.3 mmol/L) or in patients with a history of ASCVD who cannot tolerate high-dose statins	Moderate plus ezetimibe

\*In addition to lifestyle therapy. \*\*ASCVD risk factors include LDL cholesterol  $\geq 100$  mg/dL (2.6 mmol/L), high blood pressure, smoking, chronic kidney disease, albuminuria, and family history of premature ASCVD.

# Antiplatelet therapy

- men or women with diabetes age  $\geq 50$  years who have at least one additional major risk factor, including:
  - Family history of premature ASCVD
  - Hypertension
  - Smoking
  - Dyslipidemia
  - Albuminuria
- Consider aspirin therapy (75–162 mg/day)
- As a primary prevention strategy in those with type 1 or type 2 diabetes at increased cardiovascular risk

# Diabetic Retinopathy

- Prevent with good glycemic Control
- Exam at diagnosis, then every 2 years if normal
- If not normal: at least annually per ophthalmologist
- Classified into Proliferative and non proliferative
- Laser photocoagulation therapy is indicated to reduce the risk of vision loss in patients with high-risk PDR and, in some cases, severe NPDR.
- Retinopathy is not a contraindication to aspirin therapy for cardioprotection, as it does not increase the risk of retinal hemorrhage.

# Diabetic kidney disease

- Defined by albuminuria or decreased GFR in absence of other cause of kidney disease
- Albuminuria: spot albumin: creatinine ratio
- Screening: Yearly
- Prevent Progression
  - **ACE I or ARB** strongly recommended for patients w/ urinary albumin excretion  $\geq 300$  mg/g creatinine and/or eGFR  $< 60$  ,
  - Control BP and Glycemia
- patients have eGFR  $< 30$ , refer for evaluation for renal replacement treatment



# Diabetic neuropathies

- =are a family of nerve disorders caused by diabetes.
- People with diabetes can, over time, develop nerve damage throughout the body.
- May be asymptomatic,
- Others may have symptoms such as pain, tingling, or numbness—loss of feeling—in the hands, arms, feet, and legs.
- Nerve problems can occur in every organ system, including the digestive tract, heart, and sex organs.
- Life time risk of **diabetic foot is 25%**

# Diabetic neuropathies: Patient education

- Avoid smoking, walking barefoot.
- The feet should be inspected daily, looking between and underneath the toes and at pressure areas for skin breaks, blisters, swelling, or redness
- may be prevented with good glycemic control.
- It can be treated with gabapentin and/or amitriptyline, along with pain medicines.

# Foot care

All patients with diabetes should have their feet inspected at every visit.

Provide general foot self-care education to all patients with diabetes.

A multidisciplinary approach is recommended for individuals with foot ulcers and high-risk feet.



# Mental Health and DM

- Dementia
  - ↑73% risk of all dementia, esp vascular dementia (↑127%)
- Increased risk of Anxiety
  - Worries about injecting, hypo/hyper glycemia
- Increased risk of Depression
  - Chronic Illness, stress
- Patients with schizophrenia high risk of T2DM
  - Screen yearly

# Take home message

- T2 DM is by far the most common type of diabetes in adults
- Rates of diabetes are increasing worldwide
- The greatest percentage increase in rates of diabetes will occur in Africa over the next 20 years.
- T2DM results from a combination of peripheral insulin resistance and inadequate insulin secretion by pancreatic beta cells.
- Usually asymptomatic, need of screening.
- Poorly controlled T2DM is associated with an array of complications including end-stage renal disease, nontraumatic lower extremity amputations, and adult blindness.

# Take home message

- The goal of therapy is to eliminate symptoms related to hyperglycemia, reduce or eliminate the long-term microvascular and macrovascular complications of DM, allow the patient to achieve as normal a lifestyle as possible
- Multi-disciplinary approach to address complications
- No one size fits all; individualized approach

END

THANK YOU