

Diabetes Mellitus and the Elderly individual with I/DD

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Brief Early History

- 400 B.C.
 - Hindus described “honeyed urine”
- 17th Century
 - This is the period marked with the discovery of the sweetness of urine (by Oxford Physician Thomas Willis) and glycosuria itself but the reason behind it was not established
- 19th Century
 - The concept of excessive glucose production was that of Frenchman Claude Bernard
 - Czech researcher Pavlov discovers the link between the nervous system and gastric secretion
 - In 1869 German student Paul Langerhans was studying the pancreas and preliminarily found what later became known as the Islets of Langerhans
 - 1889 Austrians von Mering and Minkowski determined the effect that removing the pancreas has on digestion



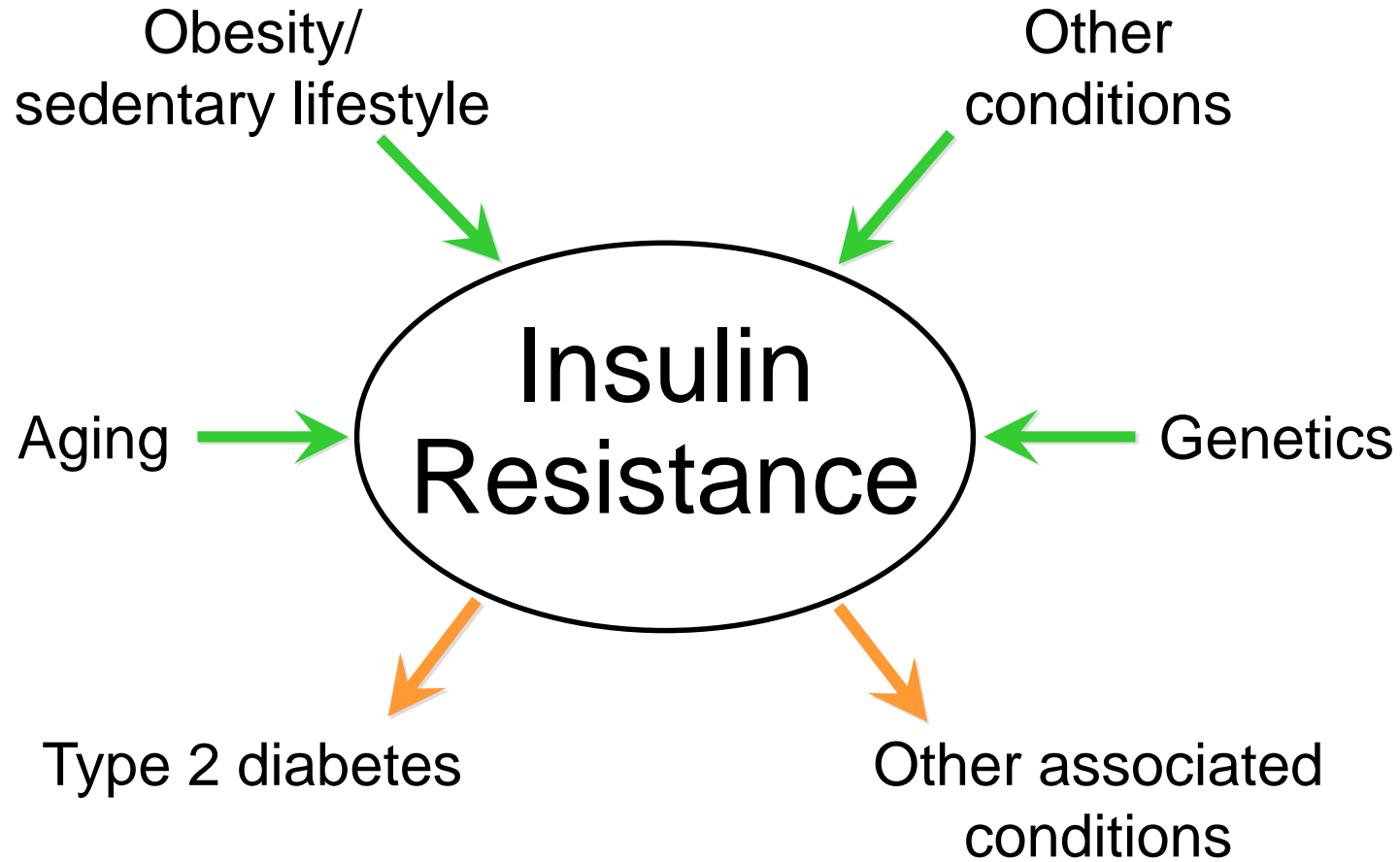
Later Foundations

- Canada 1921
 - Frederick Banting and Charles Best discovered insulin
 - Britain 1936
 - Sir Harold Himsworth proposed theory of insulin insensitivity
 - Britain 1955
 - Frederick Sanger discovered the structural formula of insulin
 - USA 1957
 - Rosalind Yalow and Solomon Berson discovered technique of immunoassay
 - Britain 1969
 - Dorothy Hodgkin elucidated the physical structure of insulin
-
- Watkins PJ. ABC of diabetes. BMJ Publishing. 1998
 - Salteil AR. J Clin Investigation 2000;106:163-4.

Diabetes Overview

- Insulin resistance
 - Metabolic syndrome
 - Definitions
 - Etiology
 - Epidemiology
 - Risk factors, diagnoses and tests
- Complications
 - Treatment and management goals
 - Pharmacologic agents
 - Future advances
 - Summary

Insulin Resistance

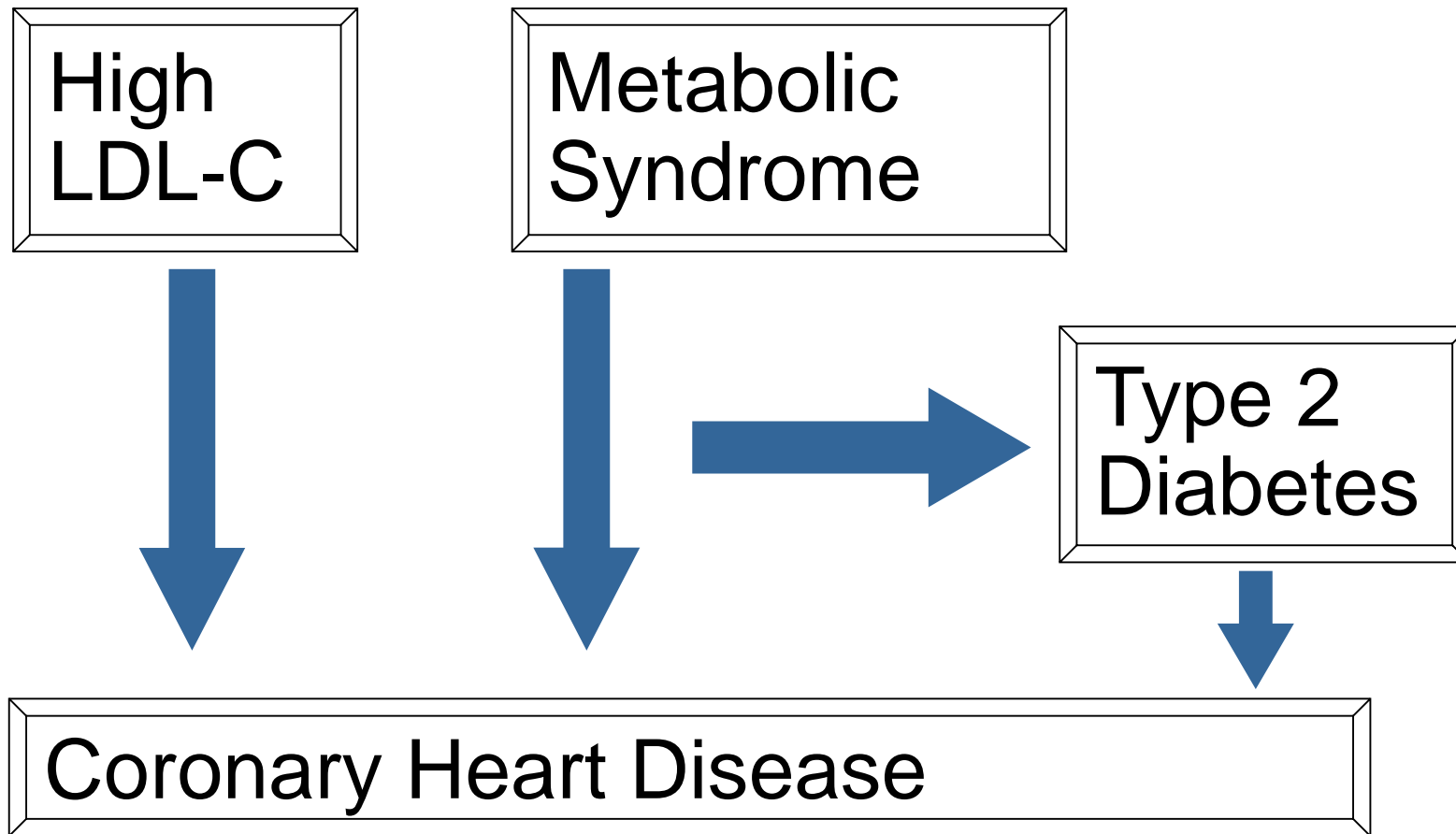


Olefsky JM. In: Endocrinology. 2nd ed. 1989:1369-88.

Reaven GM. Clinical Diabetes. 1994;12:32-6.

Seely BL, Olefsky JM. In: Insulin Resistance. 1993:187-252.

Metabolic Syndrome Increases Risk for CHD and Type 2 Diabetes



ATP III: Metabolic Syndrome

Diagnosis is established when ≥ 3 of these risk factors are present

Risk Factor	Defining Level
Abdominal obesity (Waist circumference) Men Women	 >102 cm (>40 in) >88 cm (>35 in)
Triglycerides	≥ 150 mg/dL
HDL-C Men Women	 <40 mg/dL <50 mg/dL
Blood pressure	$\geq 130/\geq 80$ mm Hg*
Fasting glucose	≥ 110 mg/dL

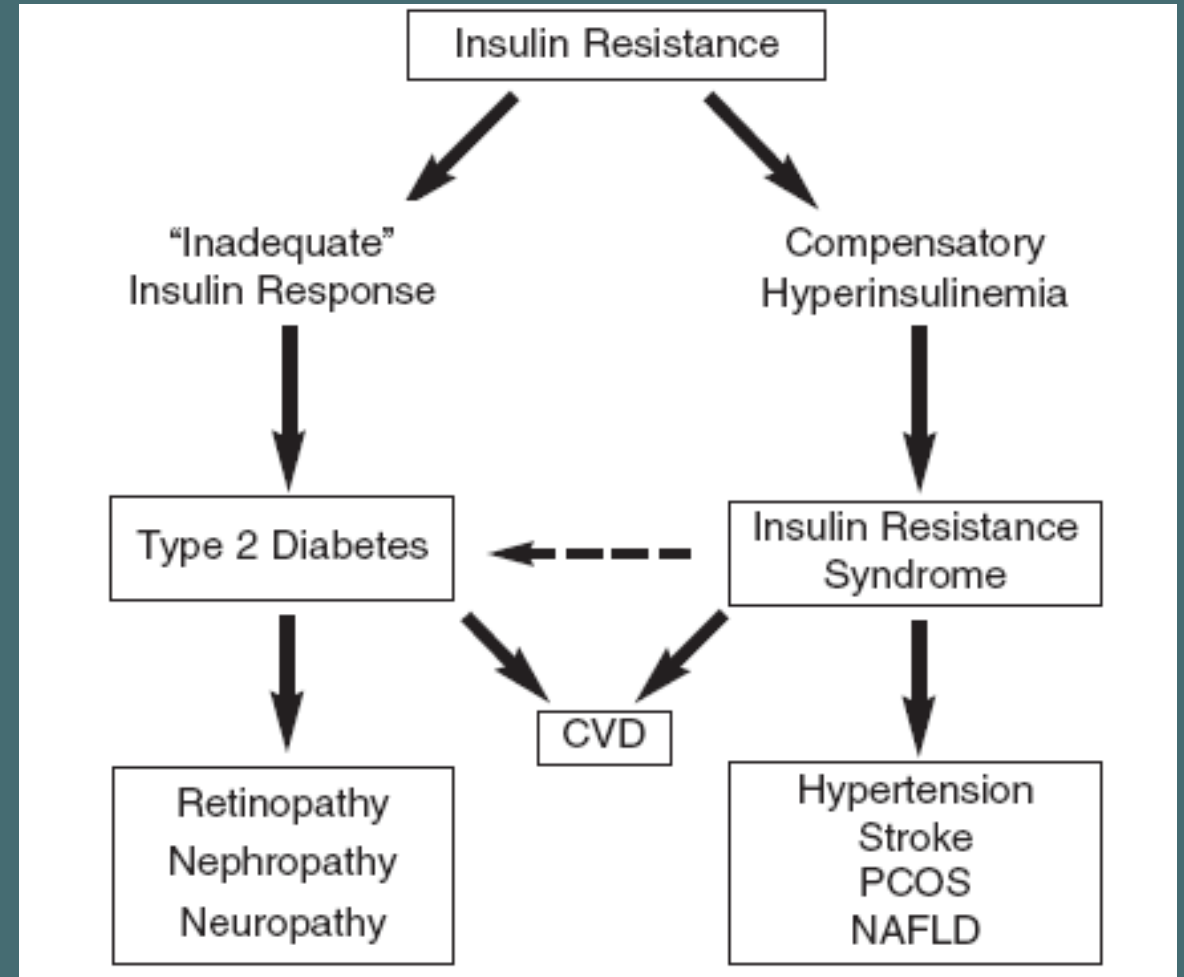
WHO Definition of Metabolic Syndrome

- Insulin resistance
 - Type 2 diabetes, impaired fasting glucose (IFG) or impaired glucose tolerance (IGT)
- Plus any 2 of the following:
 - Elevated blood pressure (>140/90 and/or medication)
 - Plasma triglycerides ≥ 150 mg/dL
 - HDL <35 mg/dL (men); <40 mg/dL (women)
 - BMI >30
 - Urinary albumin >20 mcg/min; Alb/Cr >30 mcg/mL

IFG and IGT is considered serum blood glucose of 100 mg/dL - 125 mg/dL

Diabetes Differentiation

- AACE Position Statement on the Insulin Resistance Syndrome. Endocr Prac 2003;9:240-52.

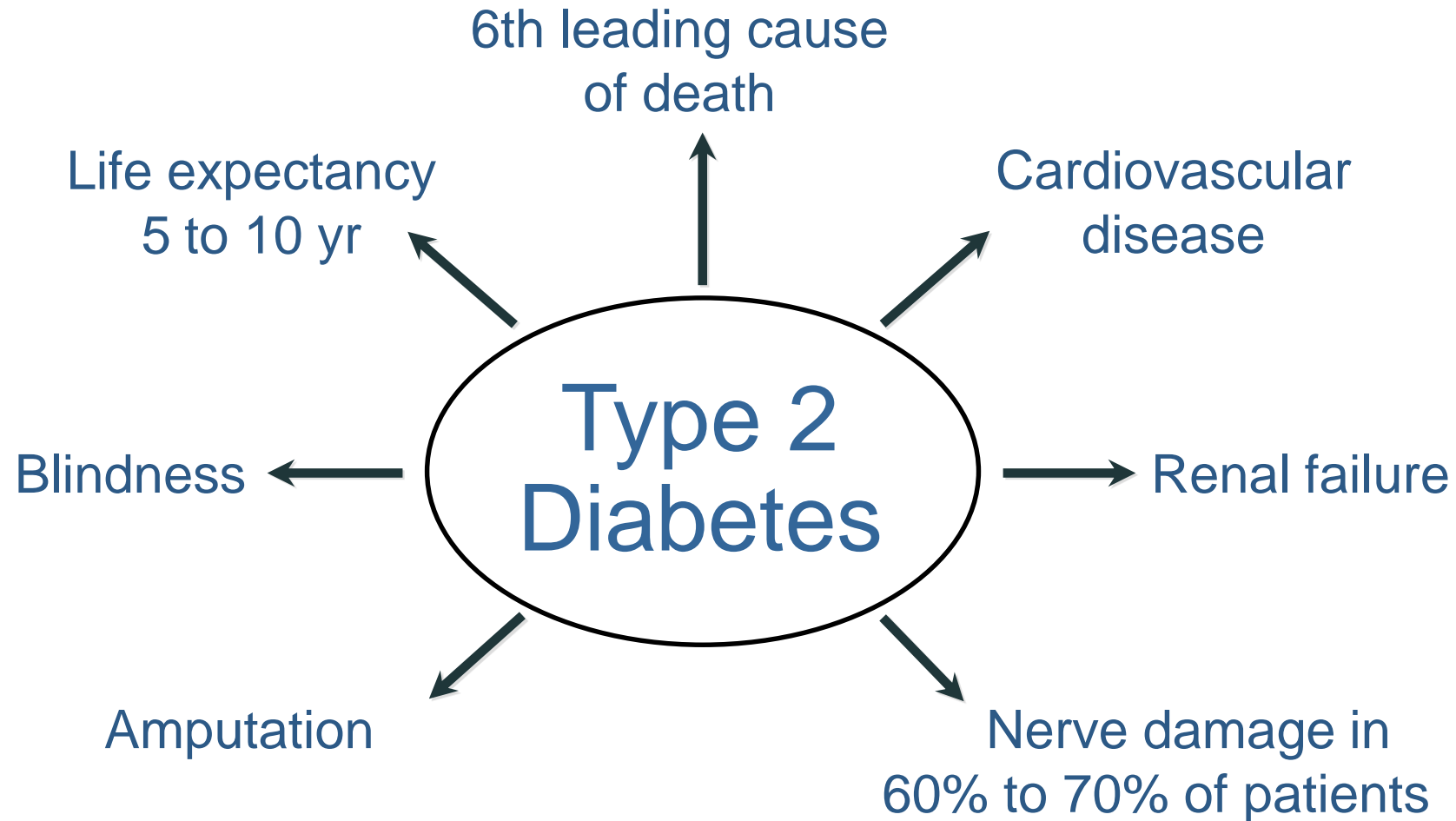


Definition of Diabetes

- “A metabolic disorder characterized by chronic hyperglycemia with disturbances in carbohydrate, fat and protein metabolism caused by defects in insulin secretion, insulin action, or both.”

Report of a WHO Consultation, Part 1: Diagnosis and Classification of Diabetes Mellitus,. 1999. Geneva

Diabetes Mellitus in the US: Health Impact of the Disease



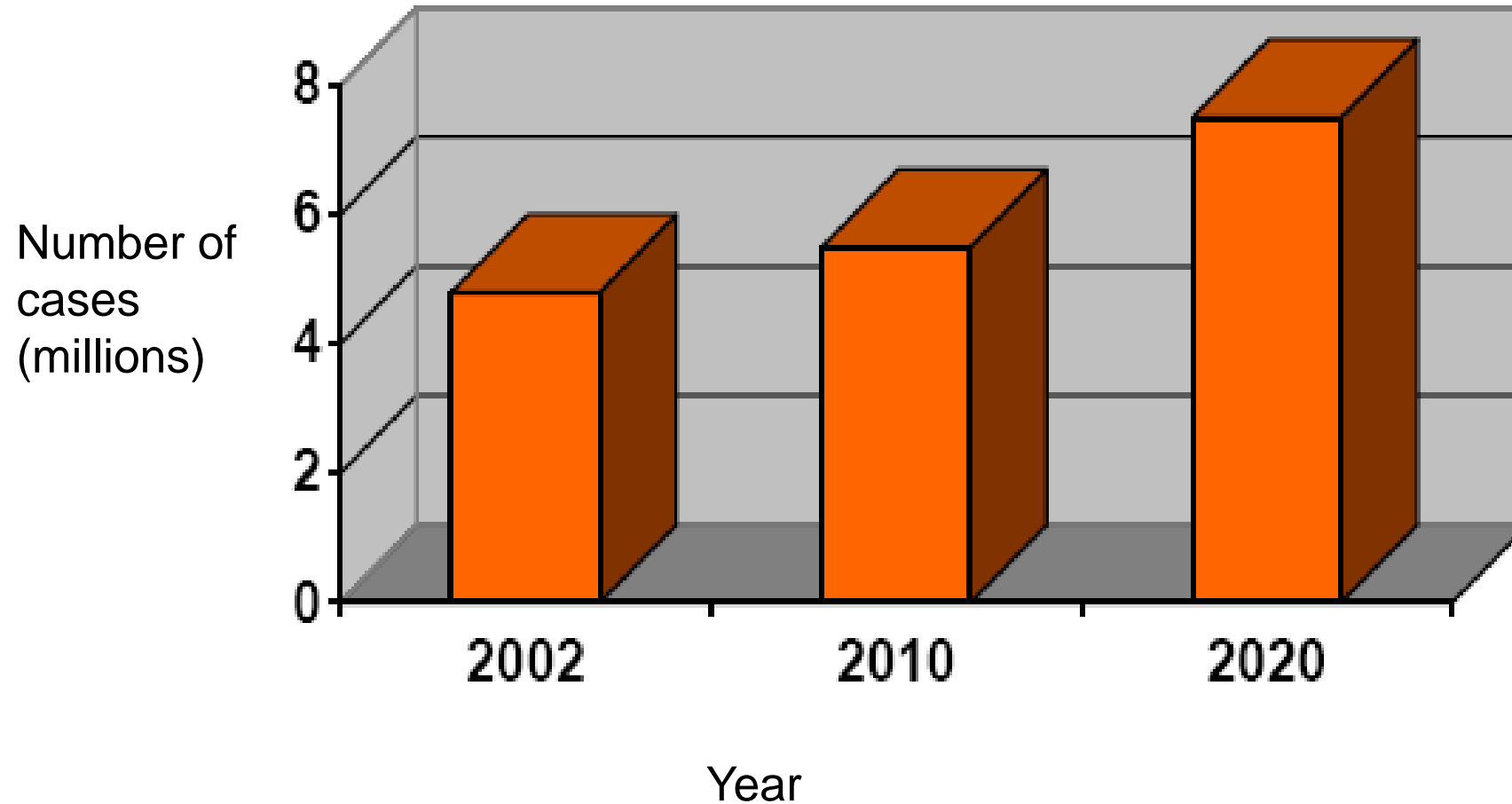
Diabetes Facts

- ~13 million people in the U.S. are diagnosed with diabetes
- 60 million people in the U.S. have metabolic syndrome
- 1.3 million (≥ 20 years) newly diagnosed cases of diabetes each year
- 90-95% of those with diabetes are type 2
- Sixth leading cause of death in U.S. in 2001
- ~ 80% of people with type 2 diabetes are overweight

Diabetes Facts In Elderly Settings

- 25% of residents in nursing homes have diabetes
- In long-term care residents with diabetes:
 - 80% have cardiovascular disease
 - 69% have 2 or more chronic conditions
 - 56% have hypertension
 - 39% have senile dementia
 - 33% have impaired vision
 - 6% are blind
 - 2.8% have kidney failure

Diabetes Incidence in the Elderly (≥ 65 years)



Types of Diabetes

- Pre-Diabetes
 - Impaired fasting glucose (100 – 125 mg/dL)
 - Impaired glucose tolerance (100 – 125 mg/dL)
 - 20.1 million Americans
- Type 1 Diabetes
 - Affects 5 to 10% of people with diabetes
- Type 2 Diabetes
 - Affects 90 to 95% of people with diabetes
- Gestational Diabetes
 - Affects 7% of pregnant women (more than 200,000 cases per year)

Type 1 Versus Type 2 Diabetes

	Type 1	Type 2
Clinical	Onset typically < 20 years Normal weight Anti-islet cell antibodies Ketoacidosis common Decreased blood insulin	Onset typically > 30 years Often overweight No anti-islet cell antibodies Ketoacidosis rare Normal or increased blood insulin
Genetics	50% concordance in twins HLA-D linked	90%-100% concordance in twins No HLA association About 40% chance of inheriting from a first degree relative
Pathogenesis	Autoimmunity, immunopathologic mechanisms Severe insulin deficiency due to pancreatic failure	Insulin resistance Relative insulin deficiency
Islet Cells	Inflammatory reaction early Marked atrophy and fibrosis β -cell depletion and/or failure	No inflammatory reaction Focal atrophy and amyloid deposits Mild β -cell depletion

Latent Autoimmune Diabetes of Adulthood

- Adult at diagnosis -- usually over 25 years of age
- Initial presentation -- non-obese type 2 diabetes
- Initially controlled with diet with/without diabetes medications
- Insulin dependency within a short period
- Presence of pancreatic antibodies
- Low C-peptide levels
- Unlikely to have a family history of type 2 diabetes

Etiologic Classification

- Genetic defects of beta-cell function
- Genetic defects in insulin action
- Diseases of the exocrine pancreas
- Endocrinopathies
- Drug- or chemical-induced
- Physiologic stress (e.g., infection)
- Uncommon forms of immune-mediated diabetes
- Other genetic syndromes sometimes associated with diabetes

Type 1 Diabetes

GENETIC PREDISPOSITION

HLA-linked genes and
other genetic loci



Immune response
against
normal beta-cells
AND/OR
Immune response
against
altered beta cells



AUTOIMMUNE ATTACK

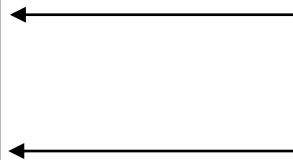
Beta-cell destruction



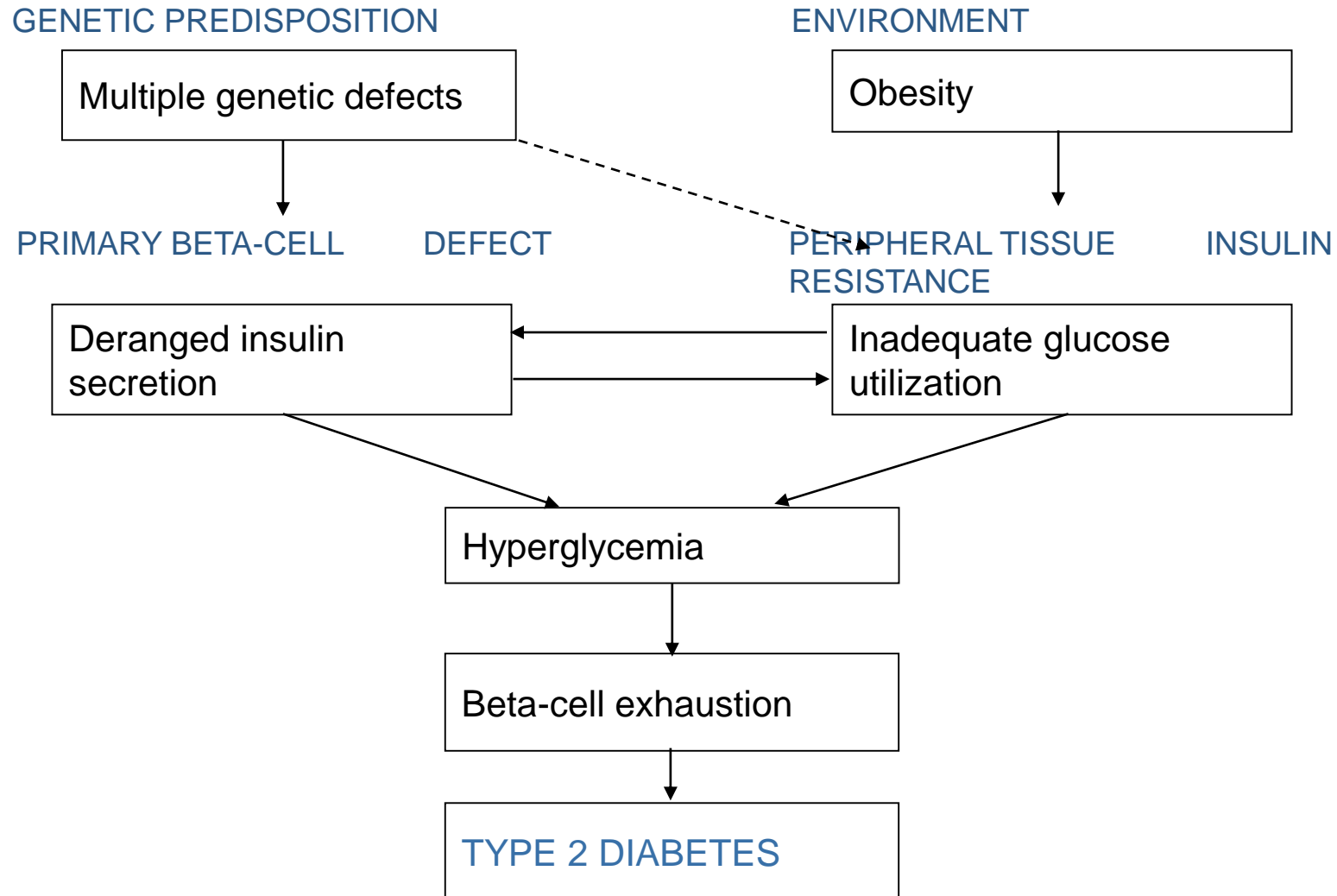
TYPE 1 DIABETES

ENVIRONMENTAL INSULT

Viral Infection:
Molecular mimicry
by viral antigen
evokes autoimmune attack
of similar beta-cell antigen
AND/OR
Damage to β -cells



Type 2 Diabetes



Risk Factors for Type 2 Diabetes

NONMODIFIABLE

- Genetic factors
- Age
- Ethnicity
- Family history
- Gestational diabetes
- Delivery of baby > 9lbs
- Polycystic ovarian disease
- Previous impaired glucose tolerance

MODIFIABLE

- Obesity (BMI > 25 kg/m²)
- Physical activity
- Hypertension (\geq 140/90 mm Hg)
- Increased triglycerides and/or low cholesterol

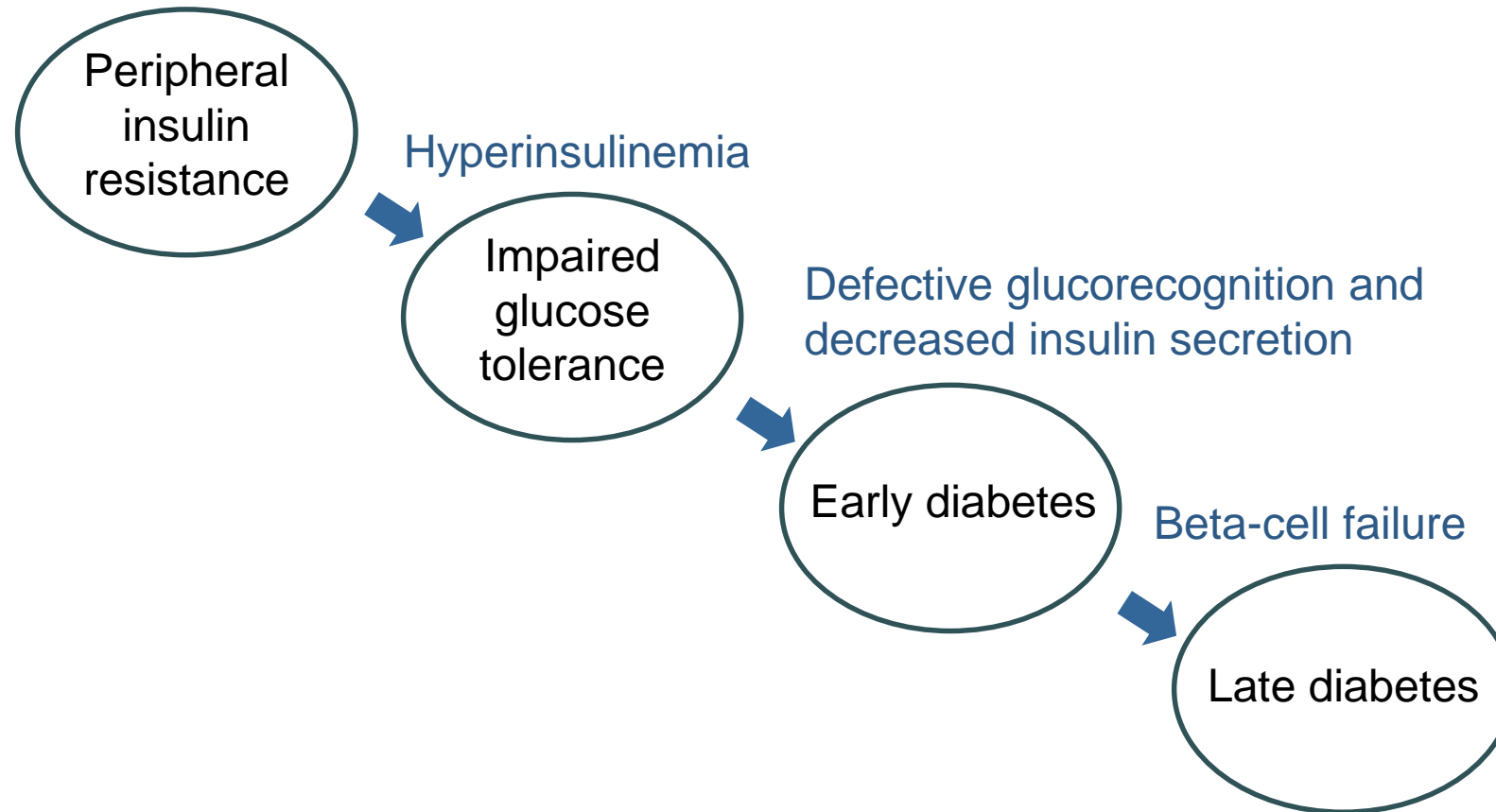
ADA. Screening for Type 2 diabetes. Diabetes Care. 2004;27:S11-14

Matrex, International Diabetes Center. Type 2 diabetes practice guidelines 2000

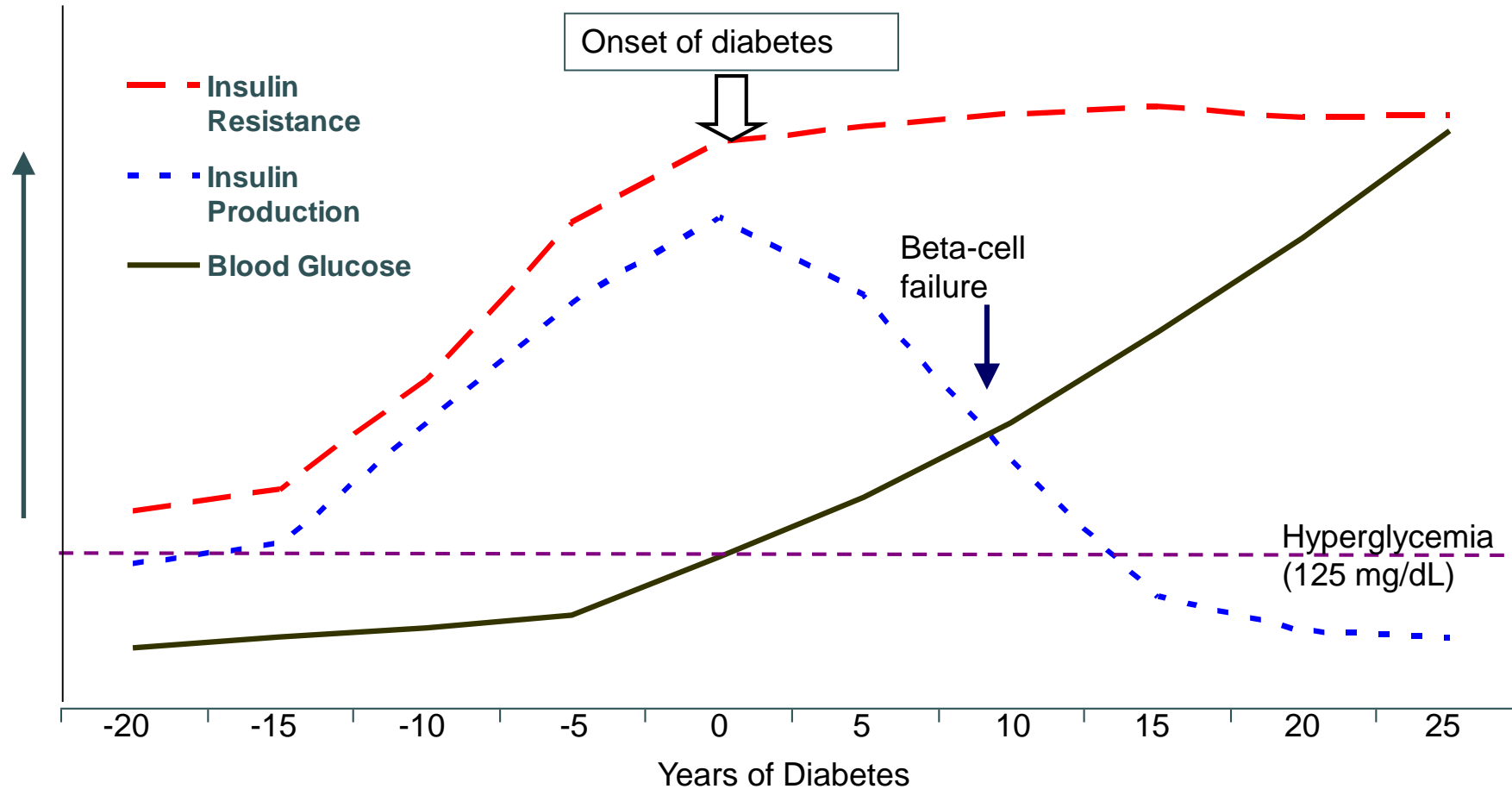
AACE. Consensus conference on guidelines for glycemic control. Endocr Prac 2001

Metabolic Staging of Type 2 Diabetes

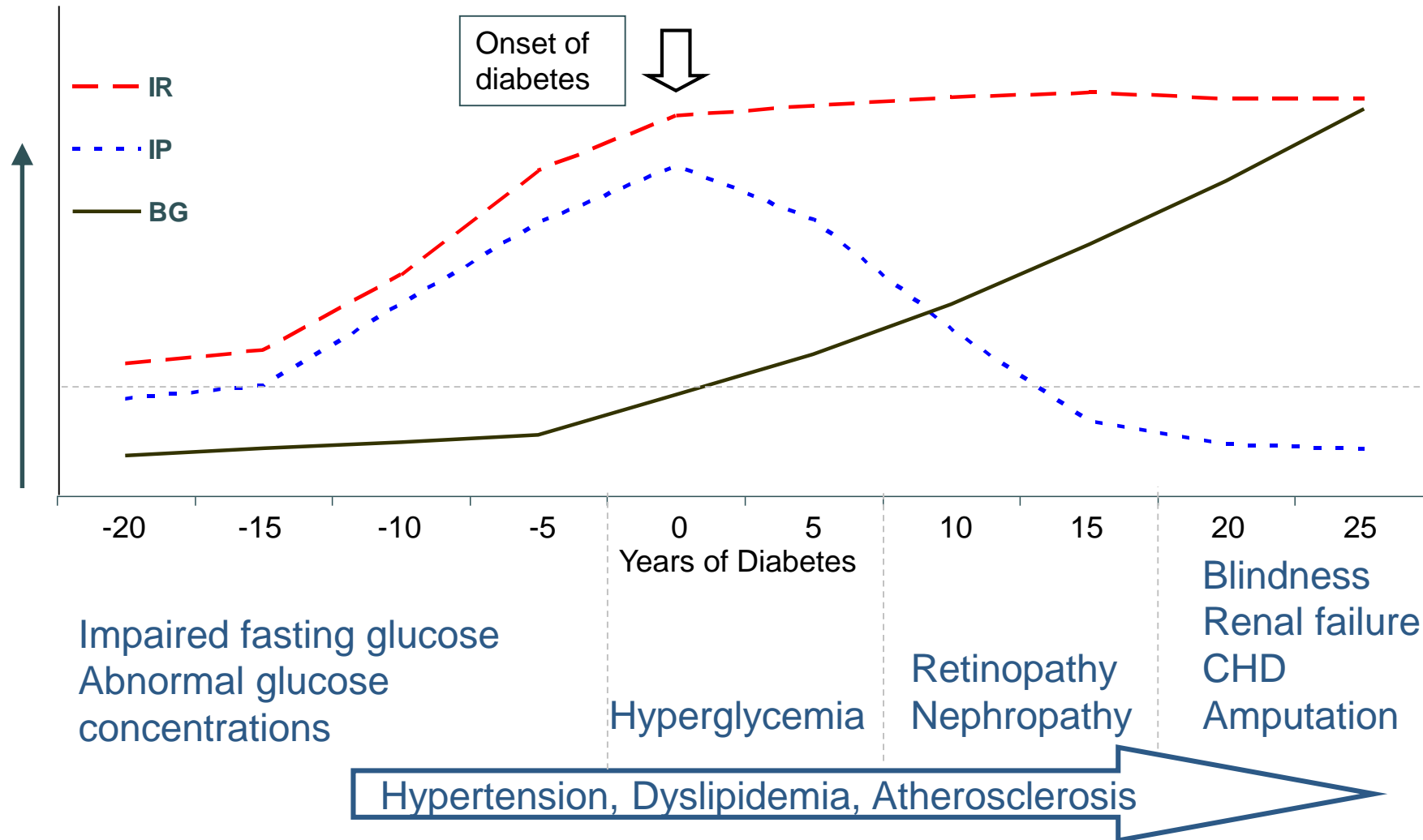
Obesity



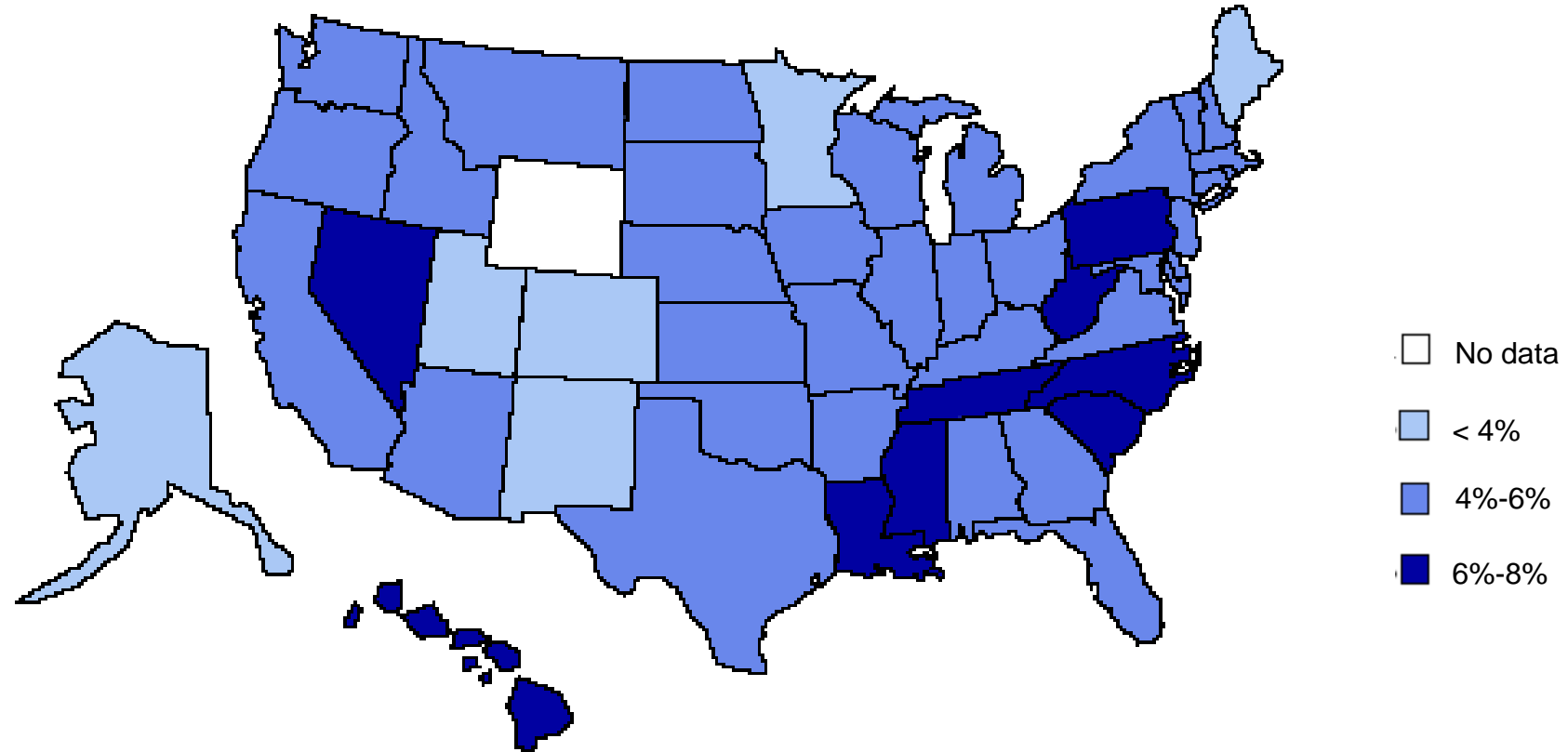
Insulin Resistance and Hyperinsulinemia



Insulin Resistance and Hyperinsulinemia (cont'd)

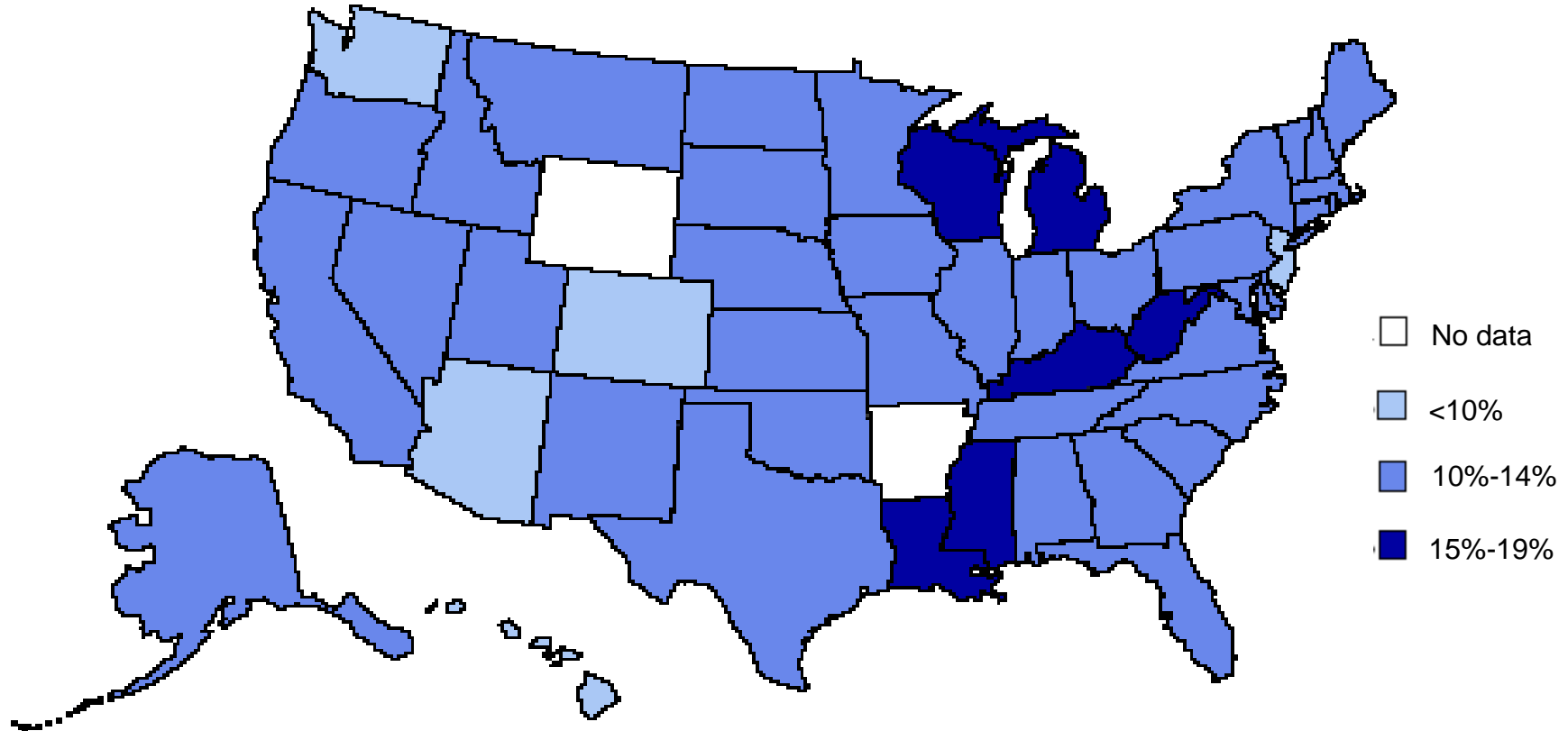


Diabetes Trends in Adults in the US 1992

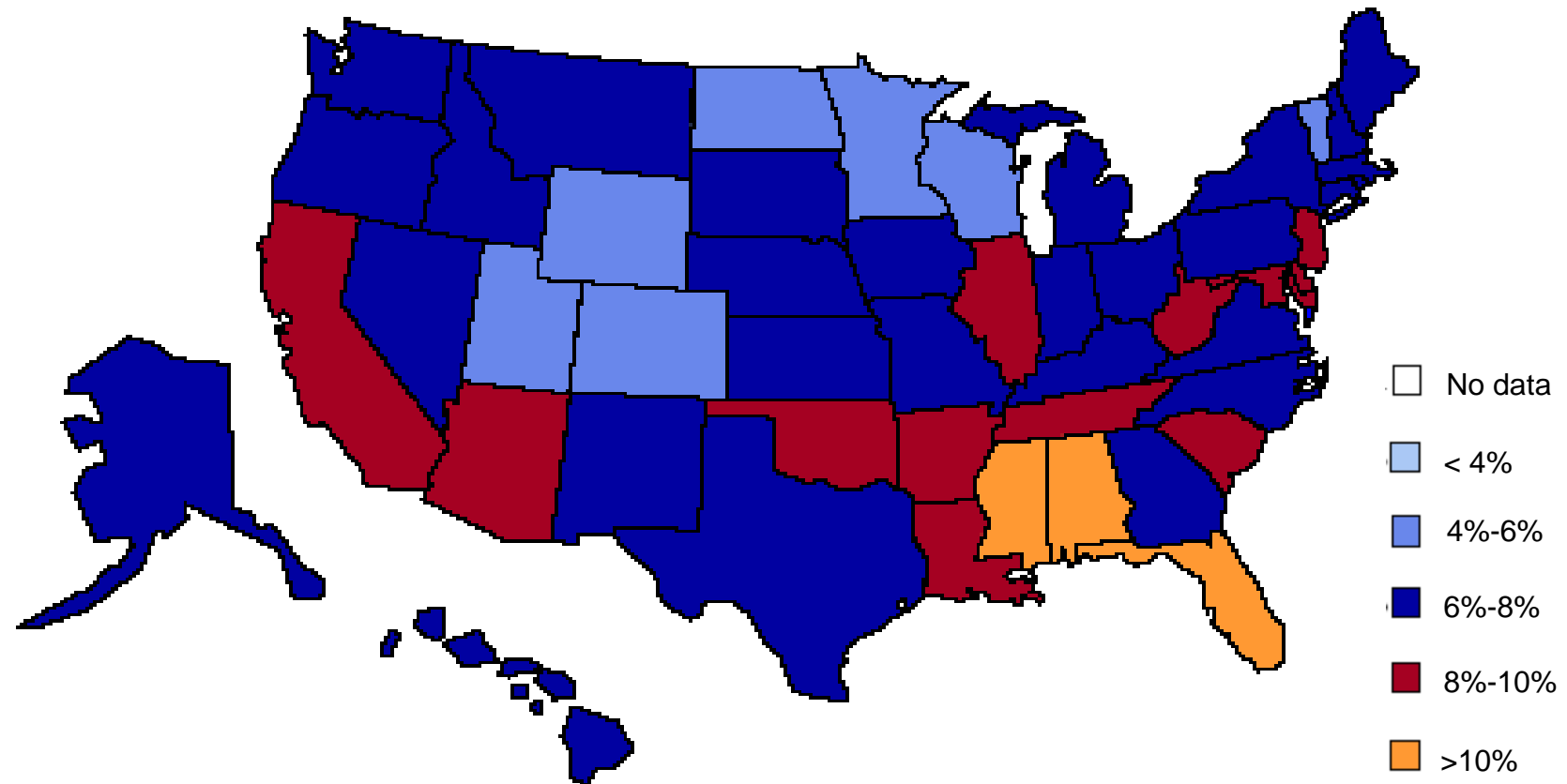


Mokdad AH et al. JAMA 2003;1:289
Haines ST. Pharmacotherapy 2003;23:1227-31

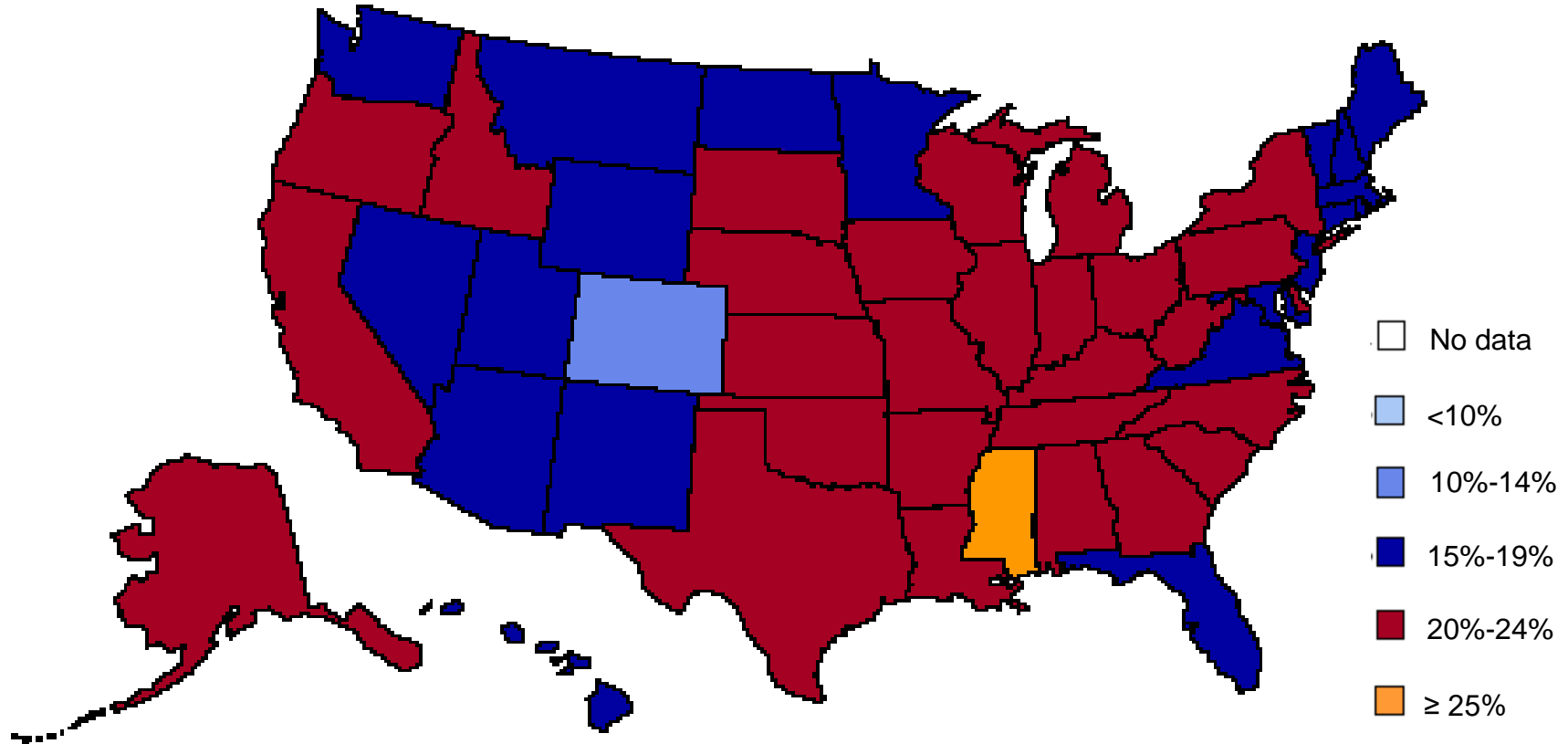
Obesity Trends in Adults in the US 1992



Diabetes Trends in Adults in the US 2001



Obesity Trends in Adults in the US 2001



Clinical Diagnosis

- **Signs**
 - Polyuria
 - Polydipsia
 - Polyphagia
 - Slow healing wounds
 - Weight loss
 - Recurrent infections
 - Hyperglycemia
- **Symptoms**
 - Blurred vision
 - Fatigue
 - Itching

Haines ST. Pharmacotherapy 2003;23:1227-31
National Diabetes Information Clearing House.
National Diabetes Statistics 2003

Tests for Diabetes

- Fasting Plasma Glucose (FPG)
 - Preferred in clinical settings
 - Easiest and fastest to perform
 - Most accurate and the least expensive
 - If < 126 mg/dL with suspicion of diabetes then OGTT should be performed
 - Fasting defined as no consumption of food/beverage (other than water) for at least 8 hours before testing
- Oral Glucose Tolerance Test (OGTT)
 - Plasma glucose levels following a 75 gm anhydrous glucose load
- Casual Plasma Glucose (non-fasting)
 - Any time of day without regard to time since last meal
 - If < 200 mg/dL perform FPG and/or OGTT

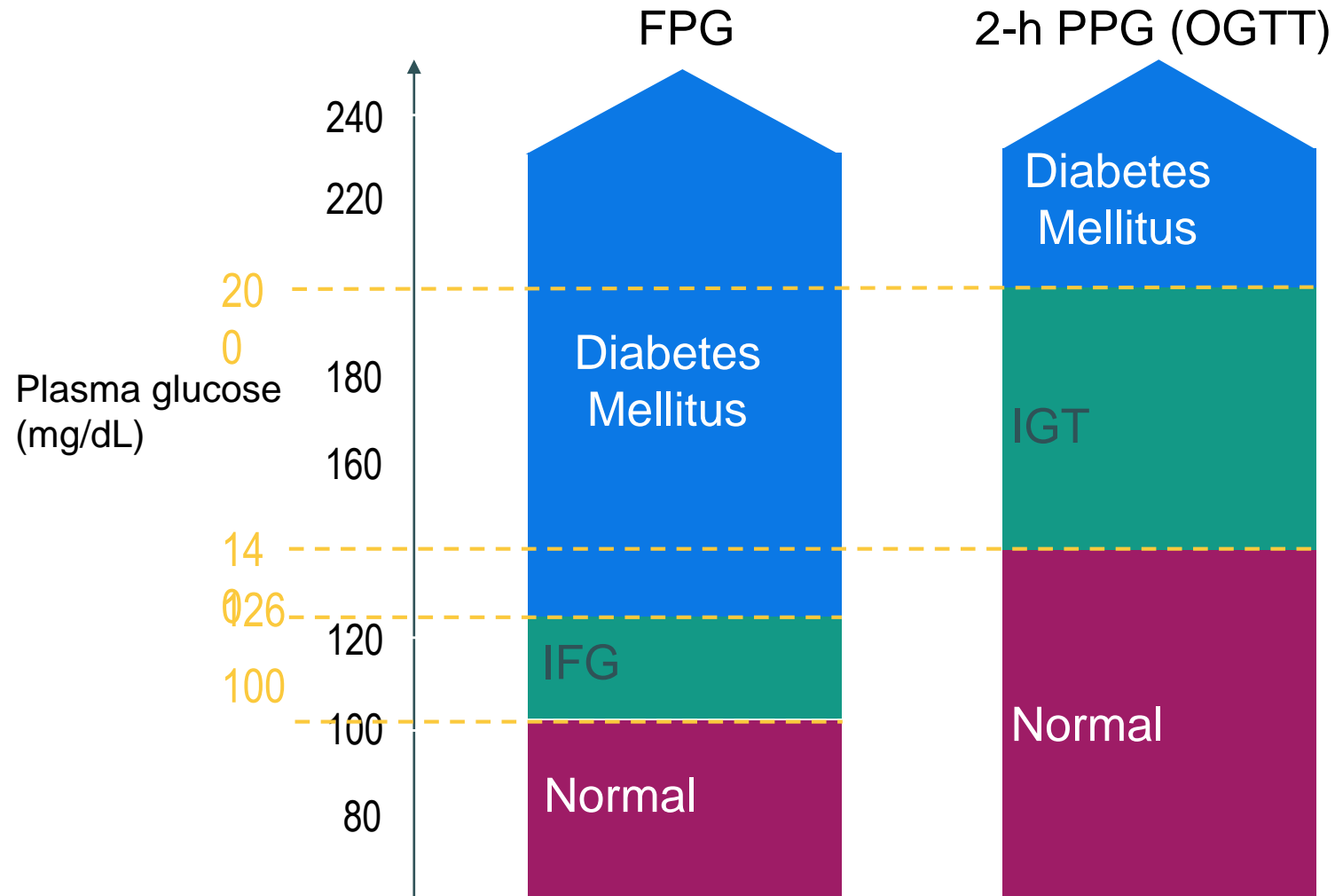
Criteria for Diagnosis

Stage of Glycemic Control	Plasma Glucose Level (mg/dL)		
	Fasting Plasma Glucose	OGTT (2-hr Postload Glucose)	Casual Plasma Glucose
Normal	<100	<140	< 200
IFG or IGT	$\geq 100 < 126$	$\geq 140 < 200$	unknown
Diabetes	≥ 126	≥ 200	>200 + symptoms of diabetes

IFG=impaired fasting glucose

IGT=impaired glucose tolerance

Glucose Tolerance Categories

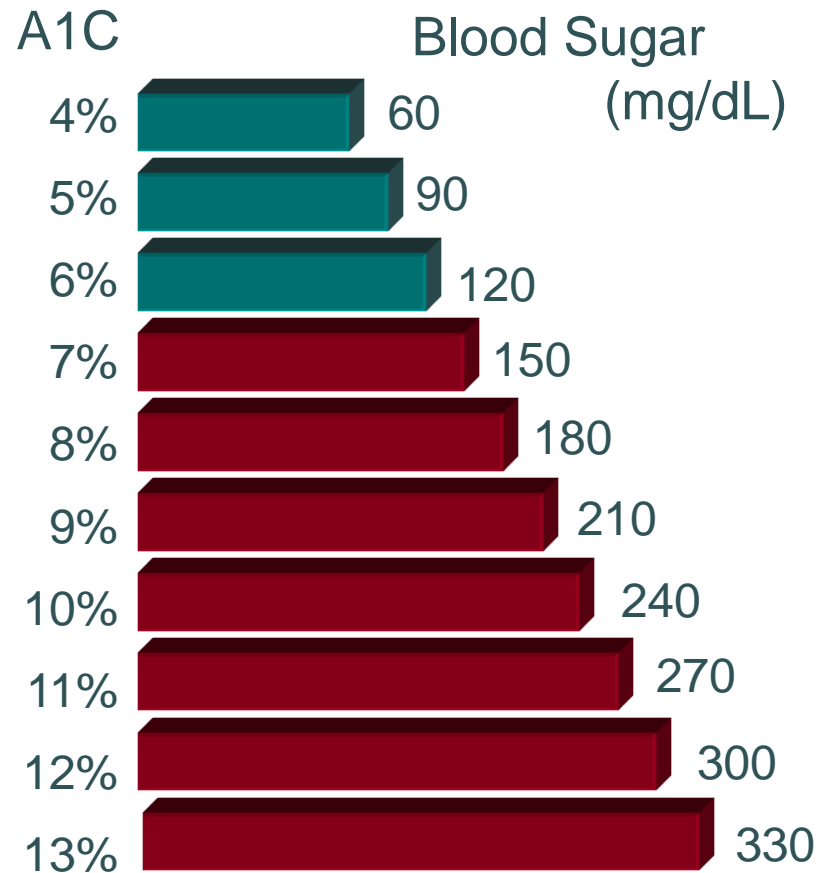


A1C test

- % glycosylation of hemoglobin related to the concentration of blood glucose in contact with RBC over their 120 day lifespan
- Average blood glucose control for past 2 to 3 months
- Not used for diagnosis
- Necessary for monitoring blood glucose and affect of treatment
- Minimum 2 times yearly, more if poor control or start of new medication
- Measure of overall control

A1C Levels and Corresponding Plasma Glucose Levels

How to Compare

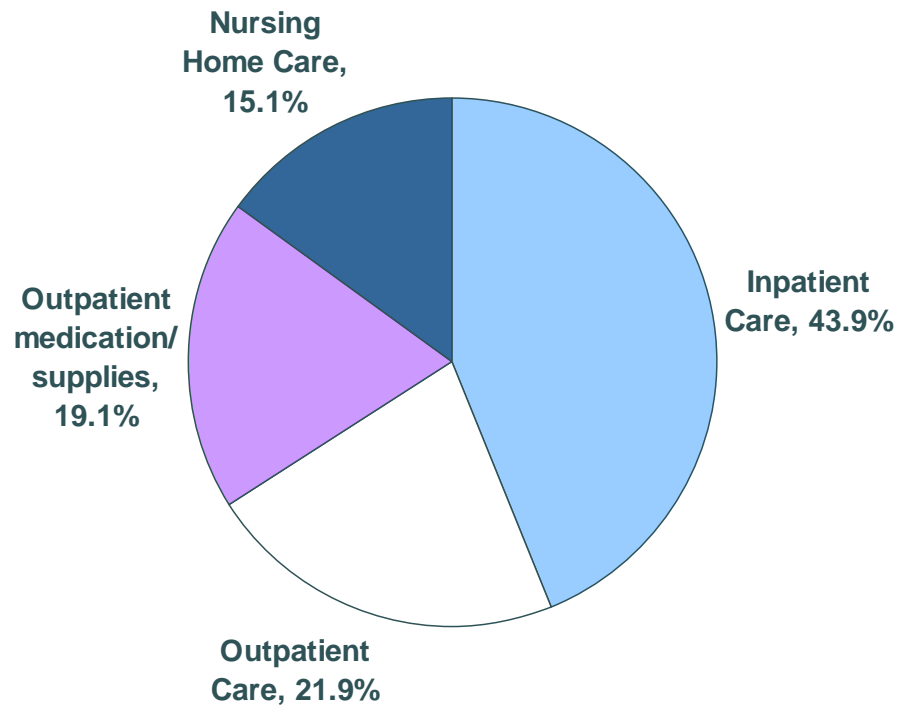


Plasma Glucose Versus Whole Blood Glucose Goals

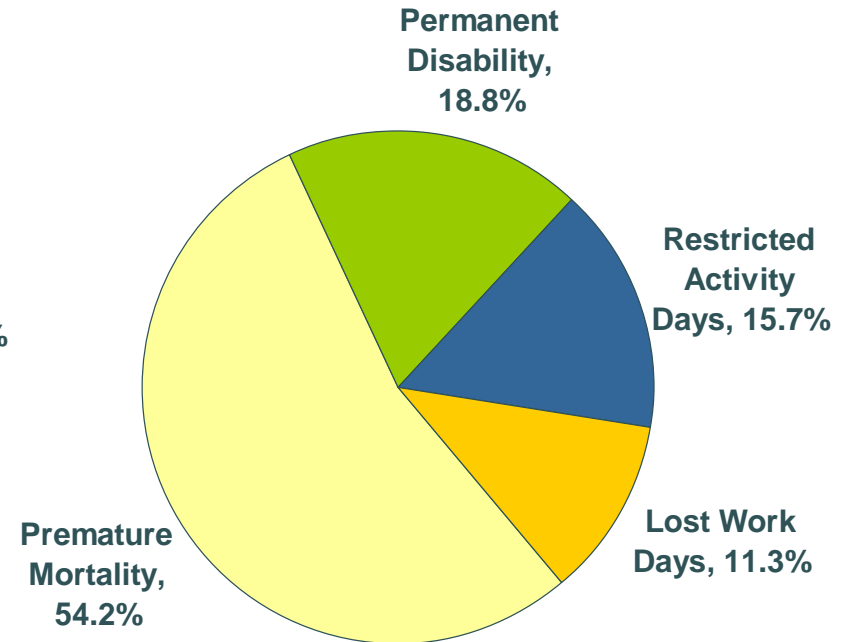
- These values are for nonpregnant adults with diabetes. Treatment goals should be individualized. Patients with comorbid disease, the very young, the elderly, and others with unusual conditions or circumstances may warrant different treatment goals.

	Normal	Goal	Action suggested when:
A1C (%)	< 6	< 7	> 8
Plasma values (mg/dL) – values calibrated to plasma glucose			
Average preprandial glucose	< 110	90-130	< 90 or > 150
Average bedtime glucose	< 120	110 - 150	< 110 or > 180
Whole blood values (mg/dL) – measurement of capillary blood glucose			
Average preprandial glucose	< 100	80 - 120	< 80 or > 140
Average bedtime glucose	< 110	100 - 140	< 100 or > 160

Health Care Costs of Diabetes

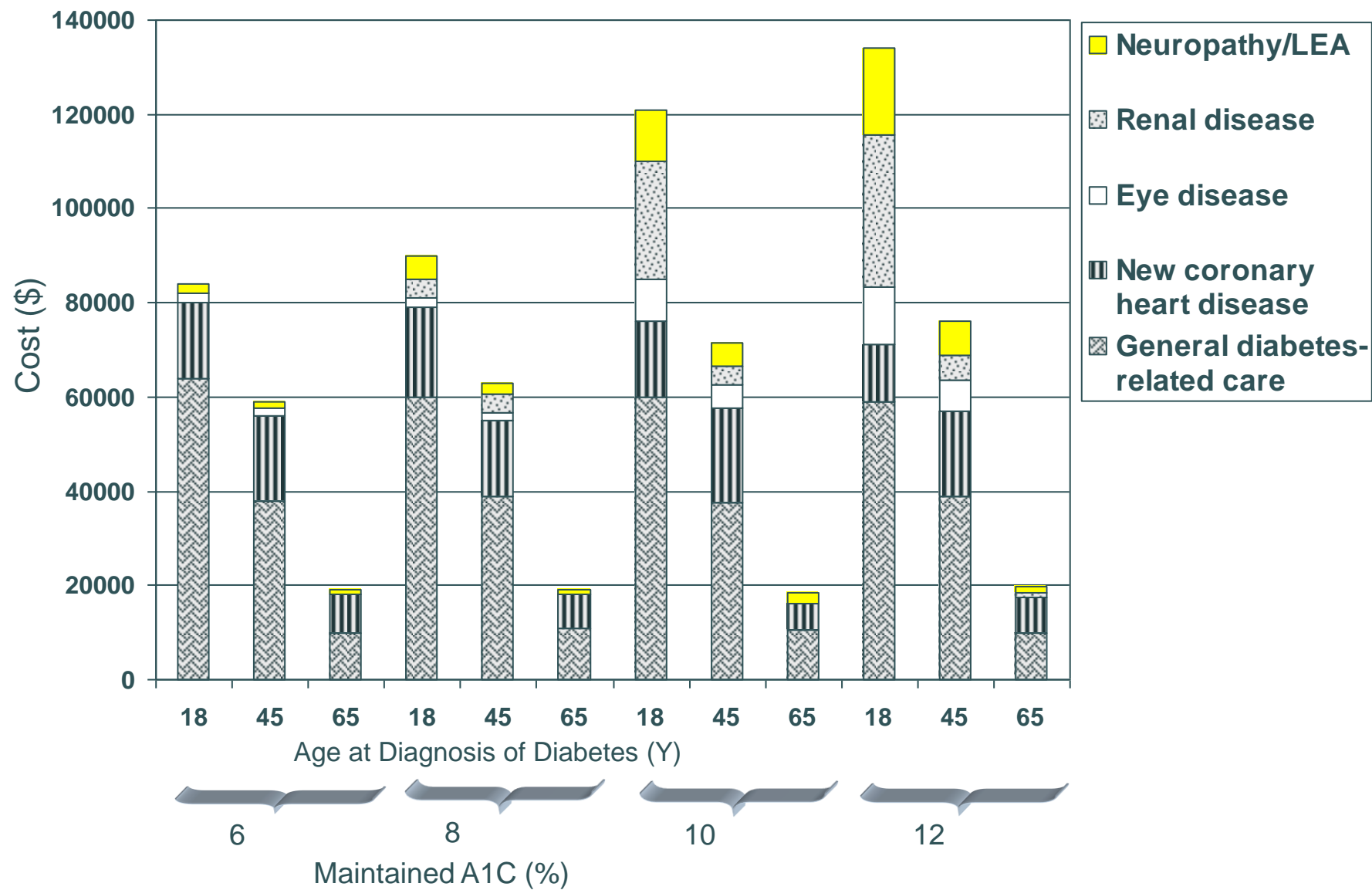


DIRECT COSTS:
\$92 Billion



INDIRECT COSTS:
\$40 Billion

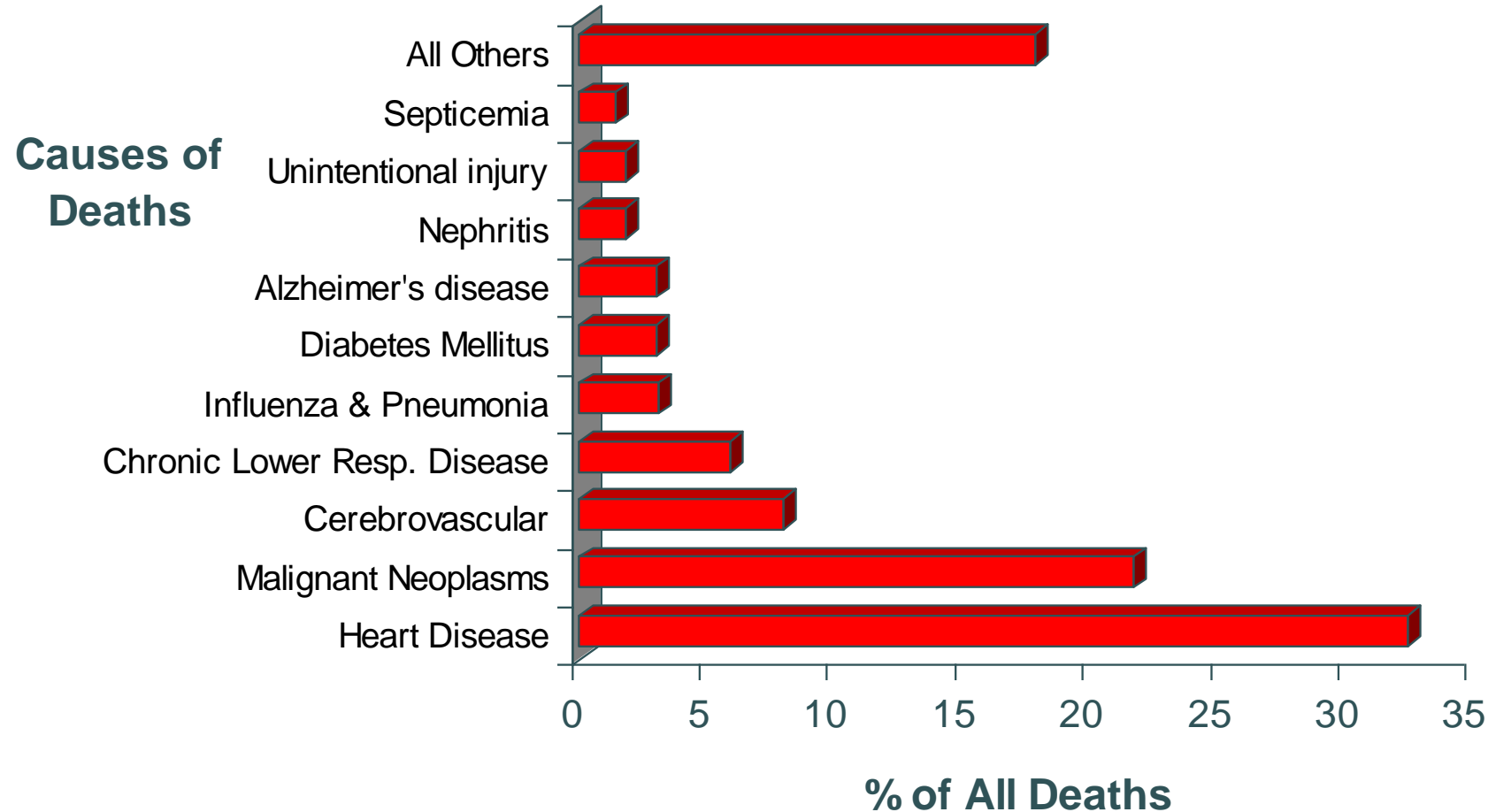
Lifetime Costs of Diabetes



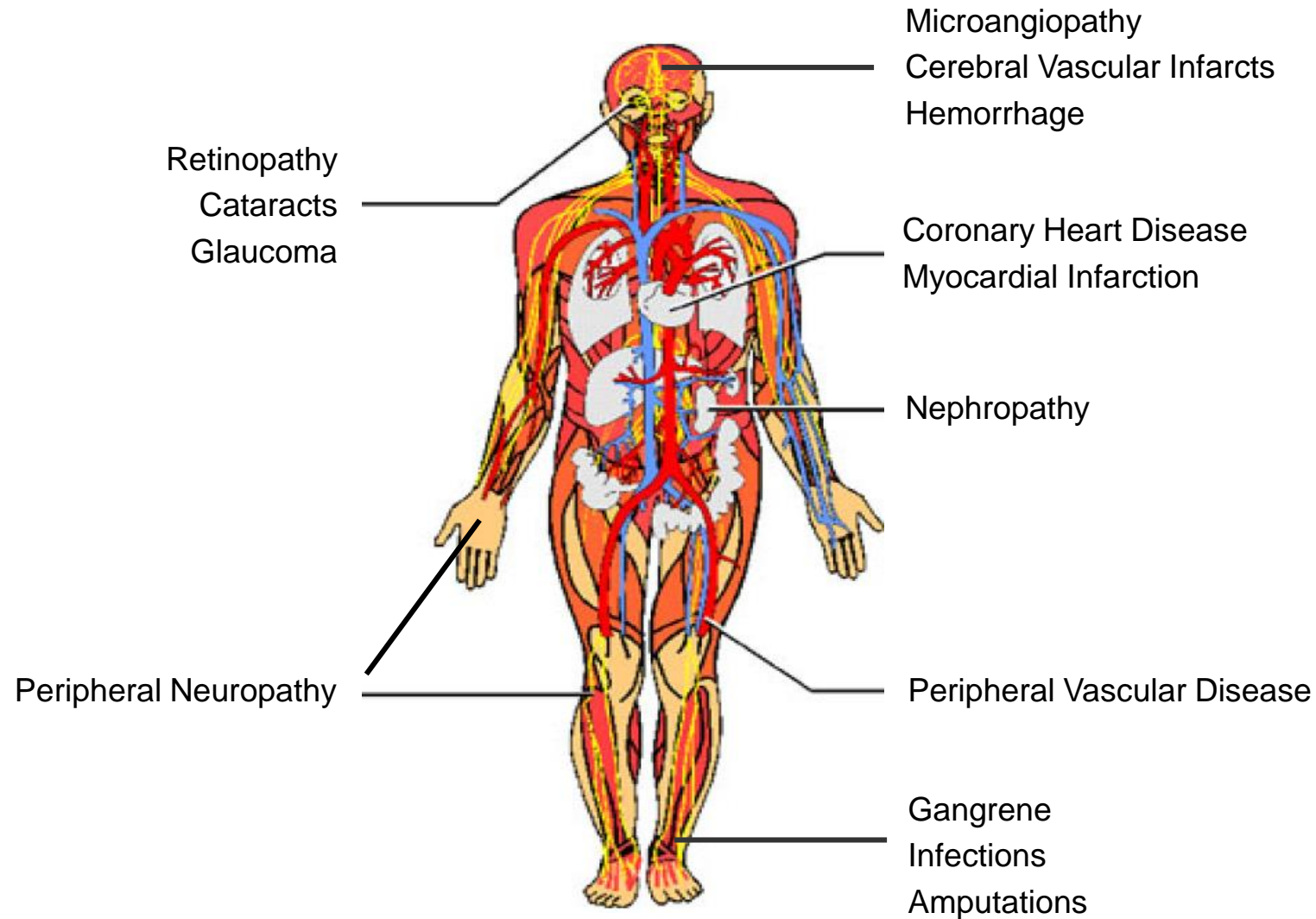
Select Diabetes Interventions: Cost- effectiveness

	Intervention		
	Intensive glycemic control	Intensive hypertension control	Reduction in serum cholesterol
Standard treatment (\$)	10,785	11,030	10,756
Cost of intervention (\$)	12,213	3,708	15,942
Cost of complications (\$)	33,271	28,902	36,505
Total cost (\$)	56,270	43,641	63,204
Incremental cost effectiveness ratio (\$)	41,384	-1,959	51,889

Leading Causes of Death in the US, 2001



Long-Term Complications of Diabetes

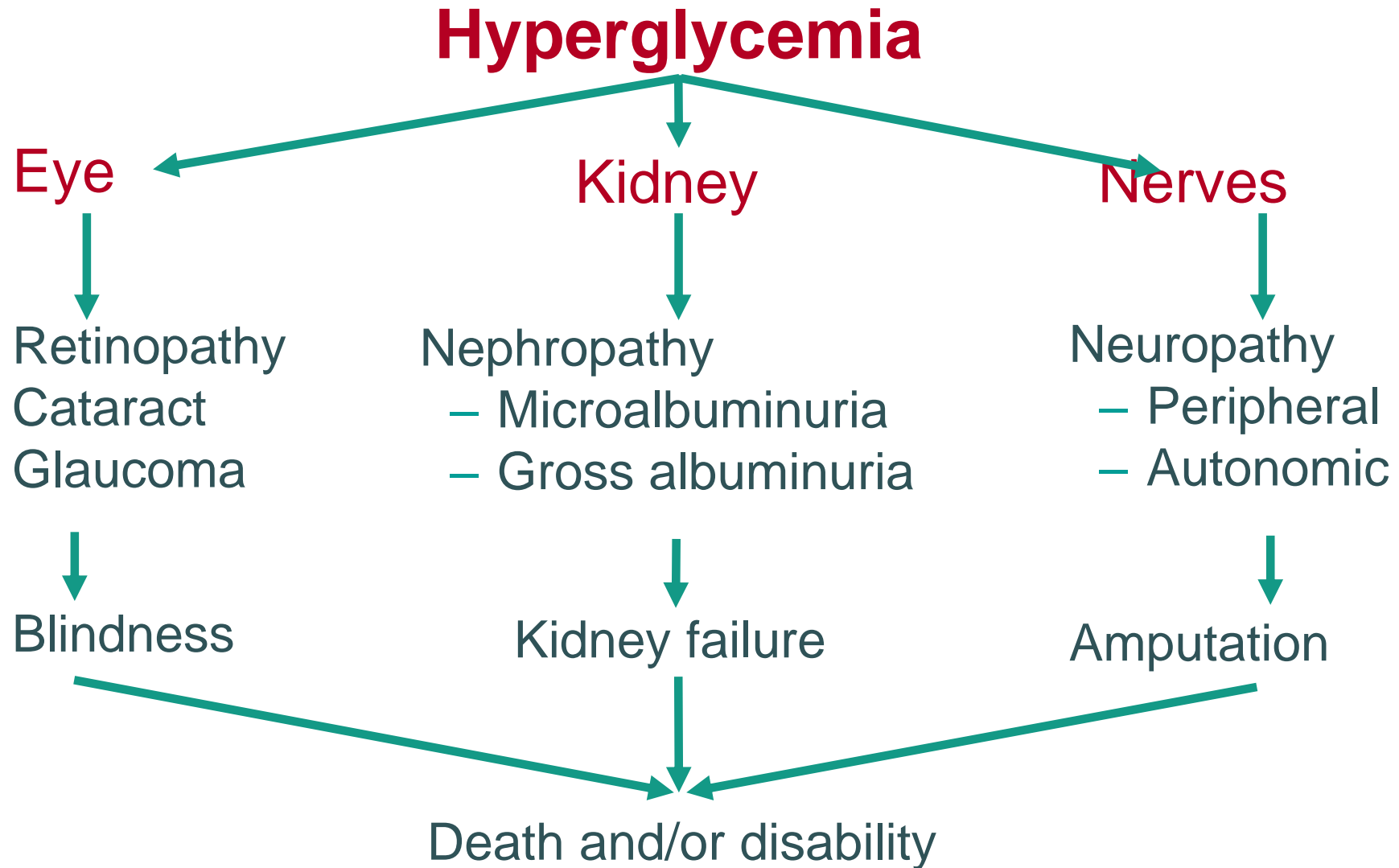


Complications of Diabetes

- Adapted from: Baker DE. Management of type 2 diabetes. Clin Pharm Newswatch 1997;4:1-8
- ADA. Standards of medical care for patients with diabetes mellitus. Diabetes Care 2003;26:S33-S50

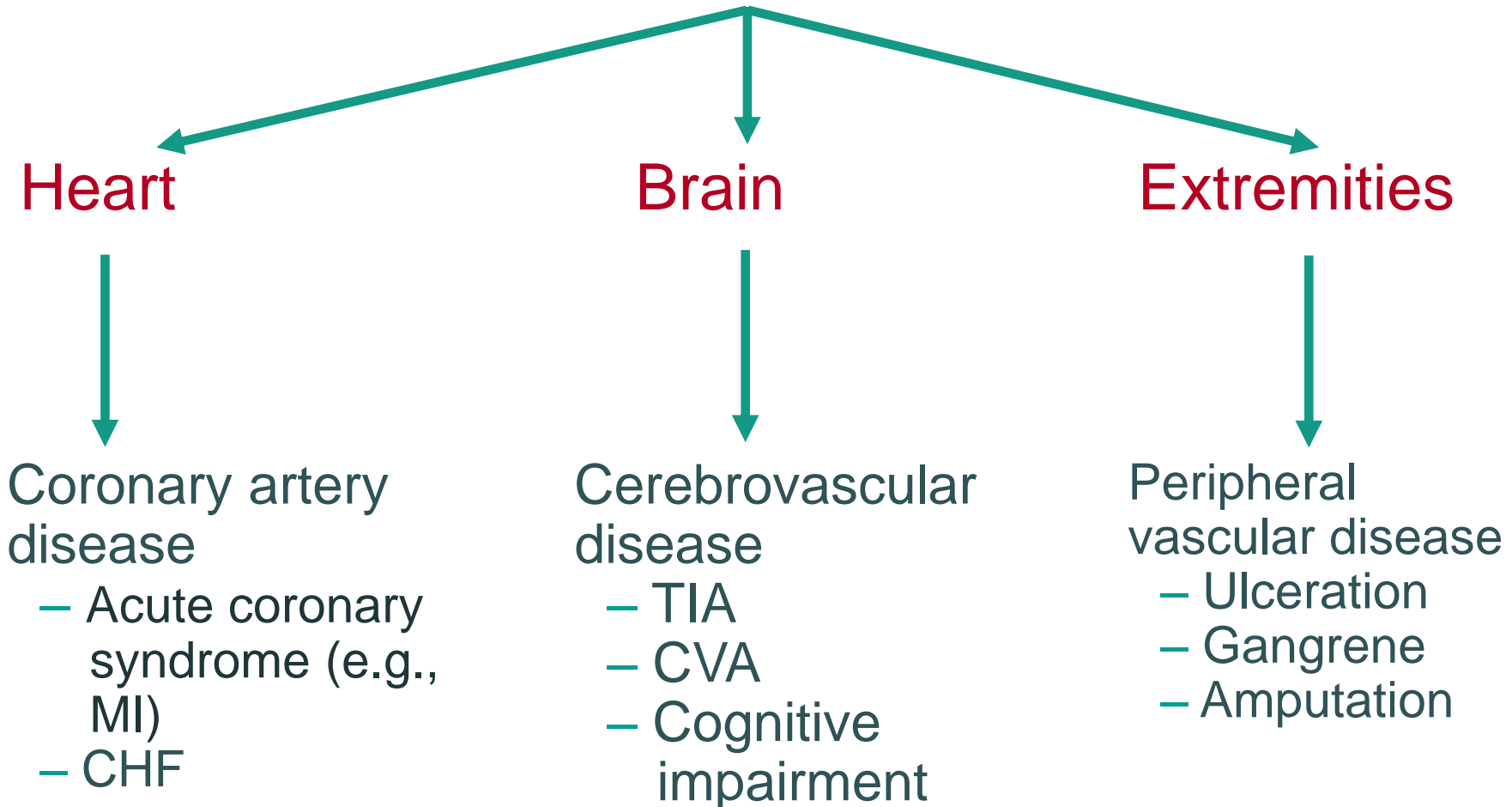
Complications	Comments
Cardiovascular Disease	Leading cause of diabetes related deaths
Stroke	Risk is increased by two to four times
Dyslipidemia	97% have lipid abnormalities contributing to higher rates of cardiovascular disease
High Blood Pressure	Incidence is 73%
Blindness	Retinopathy is the leading cause of new blindness in adults aged 20-74 years
Kidney Disease	Nephropathy is the leading cause of end stage renal disease (44% of new cases)
Nervous System Disease	60% to 70% have mild to severe form of damage
Amputations and Peripheral Neuropathy	Leading nontraumatic cause of lower limb amputations and foot ulcerations
Acute-Life Threatening Events	Diabetic ketoacidosis, hyperosmolar nonketonic coma, more susceptible to infections (e.g. pneumonia and influenza)

Microvascular Complications



Macrovascular Complications

Metabolic injury to large vessels



Questions?
