

Diabetes definition, guidelines and diagnosis of diabetes

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Disclosure

Daisuke Yabe, MD, PhD

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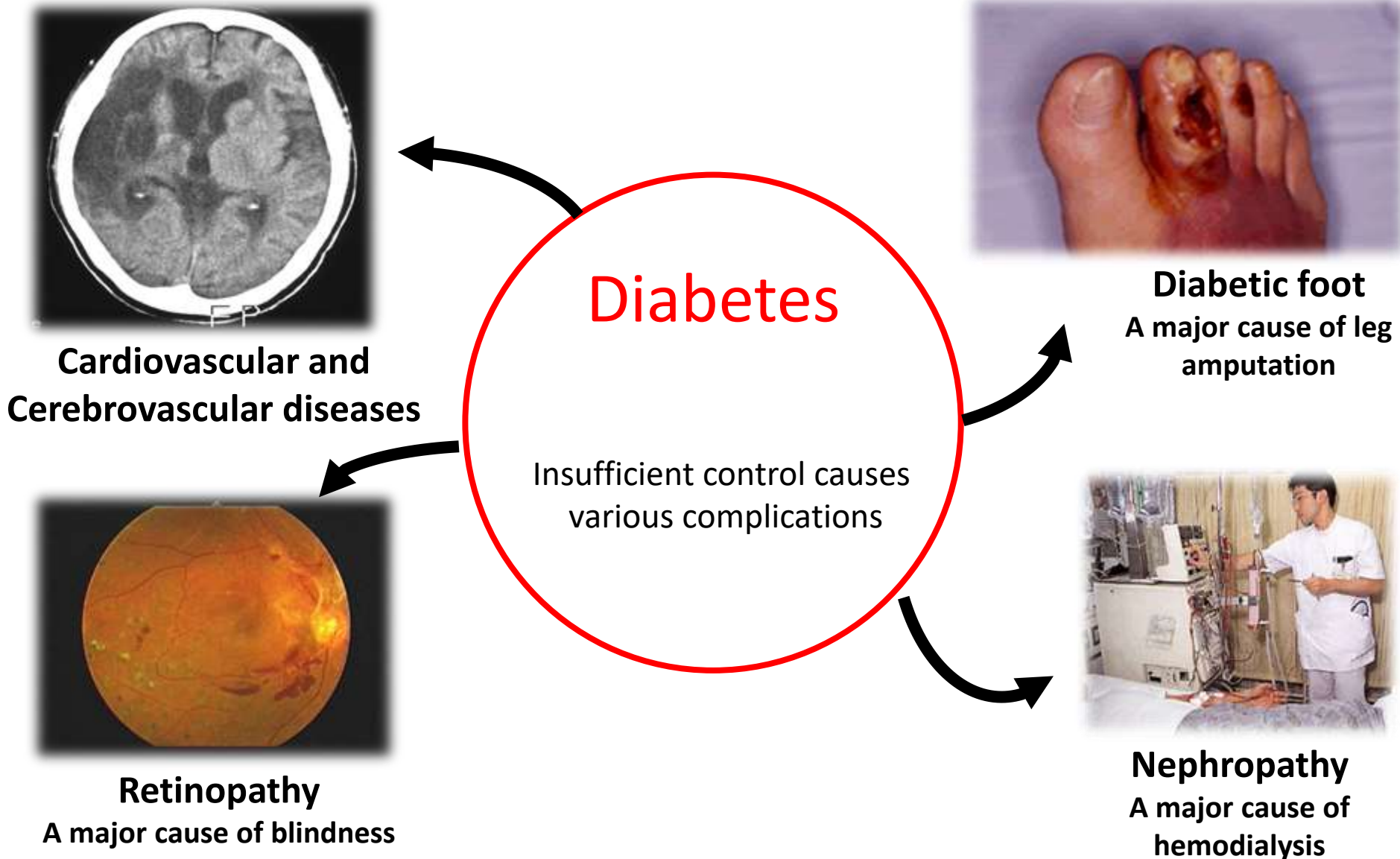
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Definition: What is diabetes?

Diabetes is a chronic condition that occurs when the body cannot produce enough insulin or cannot use insulin¹, and is diagnosed by observing raised levels of glucose in the blood. Insulin is a hormone produced in the pancreas; it is required to transport glucose from the bloodstream into the body's cells where it is used as energy. The lack, or ineffectiveness, of insulin in a person with diabetes means that glucose remains circulating in the blood. Over time, the resulting high levels of glucose in the blood (known as hyperglycaemia) causes damage to many tissues in the body, leading to the development of disabling and life-threatening health complications.



Threat of Diabetes: Diabetes and Complications



Necessity for diagnosis of diabetes at early stage

Maintenance of a quality of life (QOL) no different from that of non-diabetics

Prevention of onset and deferment of diabetic microvascular complications (retinopathy, nephropathy, neuropathy) **and atherosclerotic diseases** (ischemic heart disease, cerebrovascular disease, arteriosclerosis obliterans)

Maintenance of good control of blood glucose, body weight, blood pressure and serum lipid levels

Etiological classification of diabetes

Type 1

Due to autoimmune β -cell destruction, usually leading to absolute insulin deficiency

Type 2

Due to a progressive loss of β -cell insulin secretion frequently on the background of insulin resistance

Gestational

Diabetes diagnosed in the 2nd or 3rd trimester of pregnancy that was not clearly overt diabetes prior to gestation

Others

Monogenic diabetes syndromes (e.g., neonatal diabetes and MODY) and drug- or chemical-induced diabetes (e.g., glucocorticoid use, HIV/AIDS treatment and organ transplantation)

Pathophysiology of type 2 diabetes

Genetic Predisposition

Aging

Environmental Factors

(e.g., unhealthy diet and exercise)



β -cells

Impaired insulin secretion



Muscles



Fats



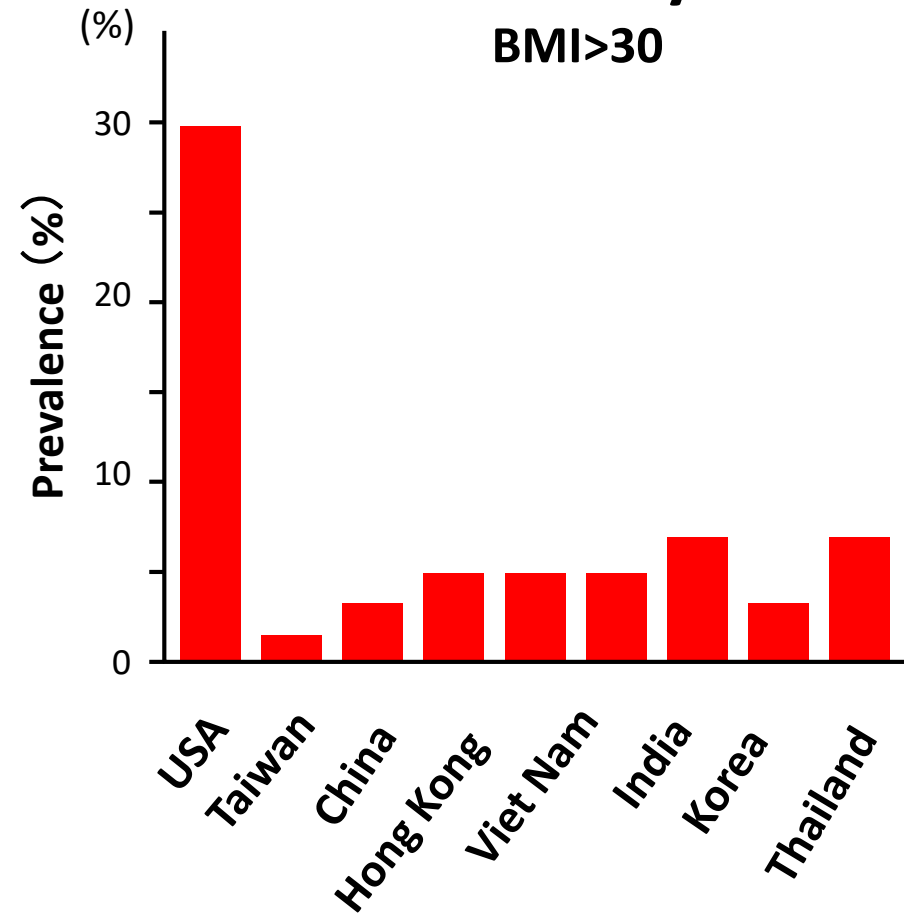
Liver

Decreased insulin sensitivity

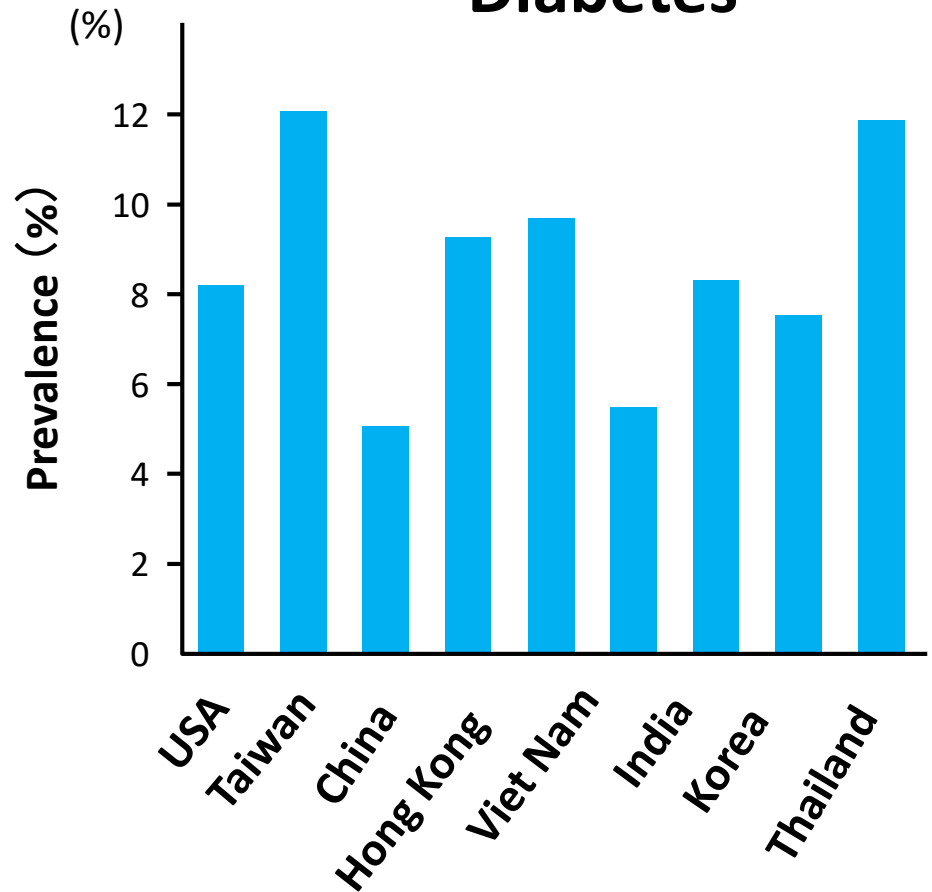
Type 2 Diabetes

Proportion of Adult Obesity and Diabetes Prevalence in Selected Countries

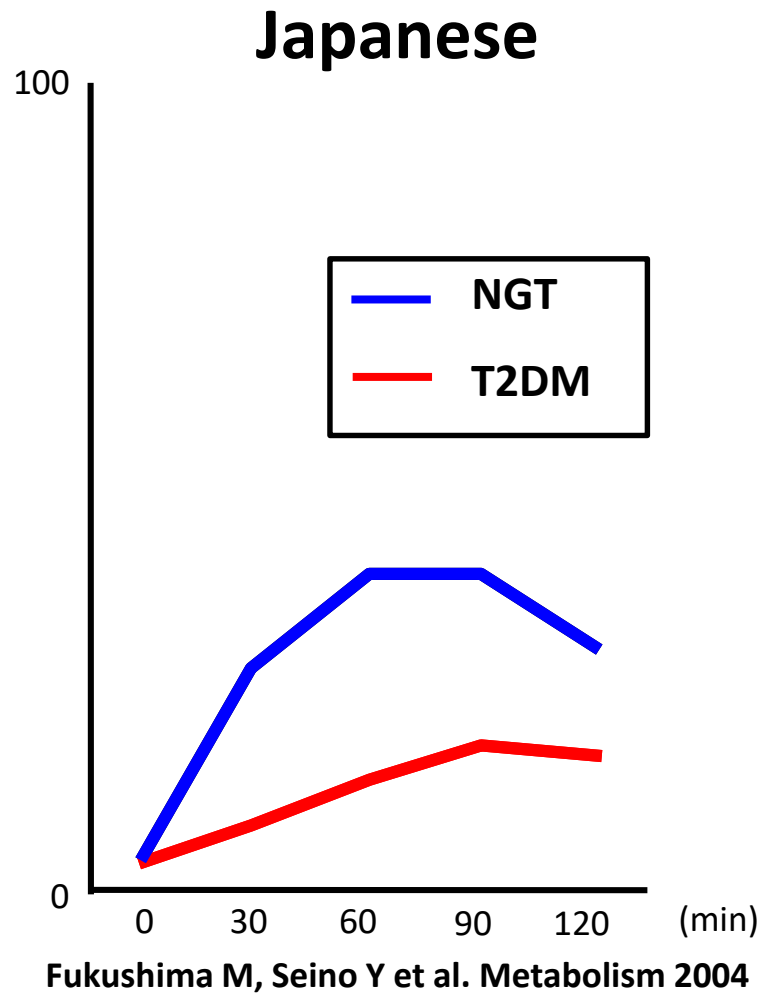
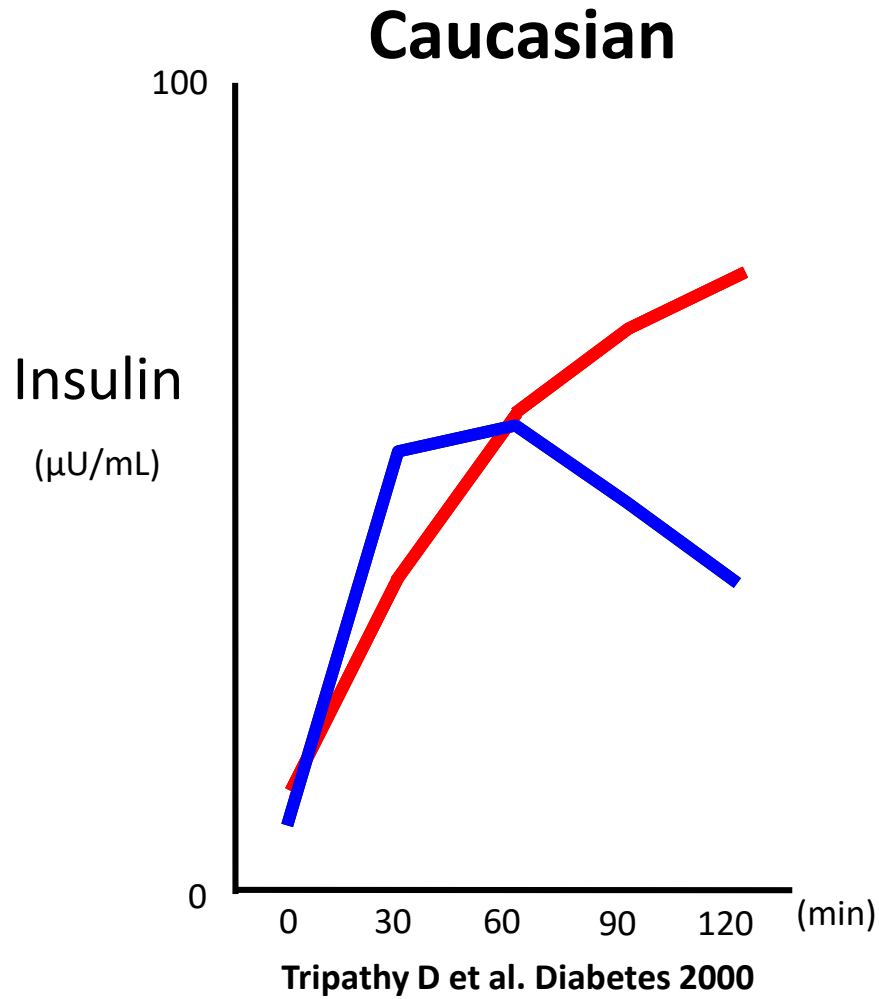
Obesity BMI>30



Diabetes



Insulin response after ingestion of glucose: Comparison of Caucasian and Japanese

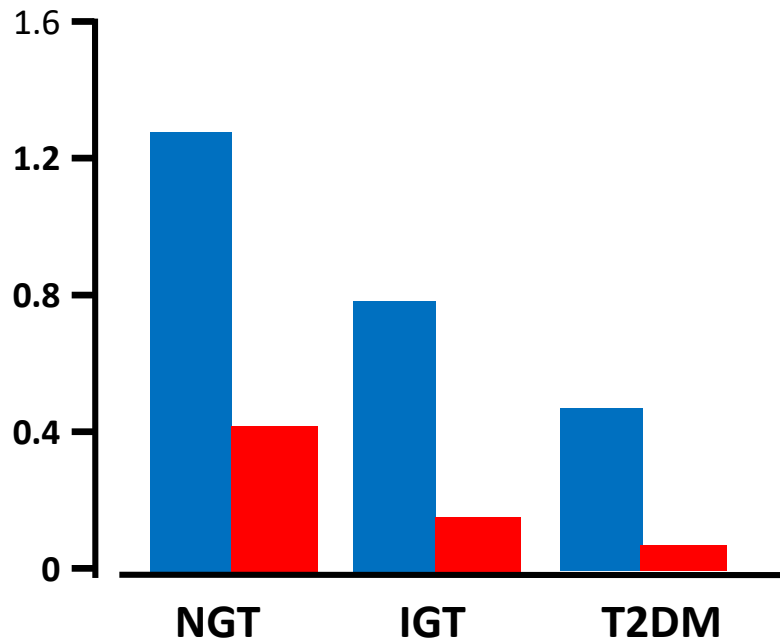


Early phase of insulin response in Japanese IGT and T2DM are reduced

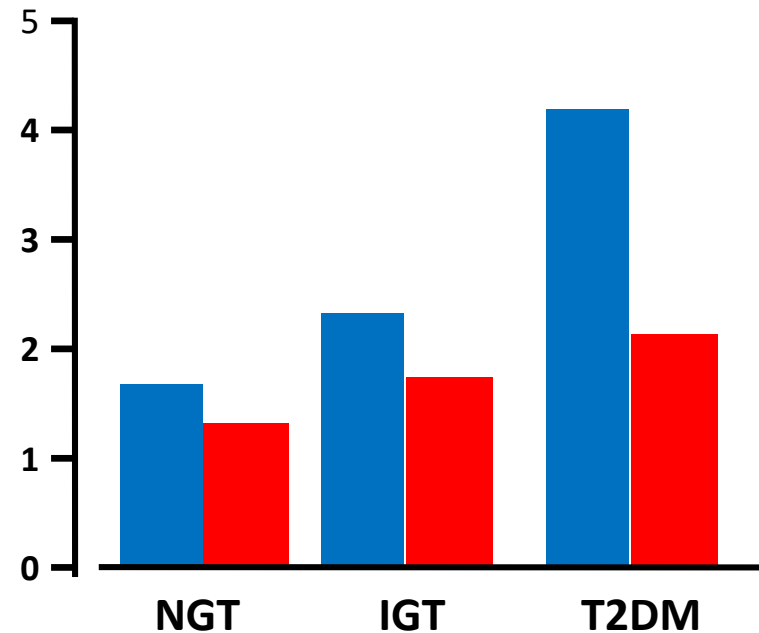
Insulin secretion and function: comparison of Caucasian and Japanese



Insulinogenic Index

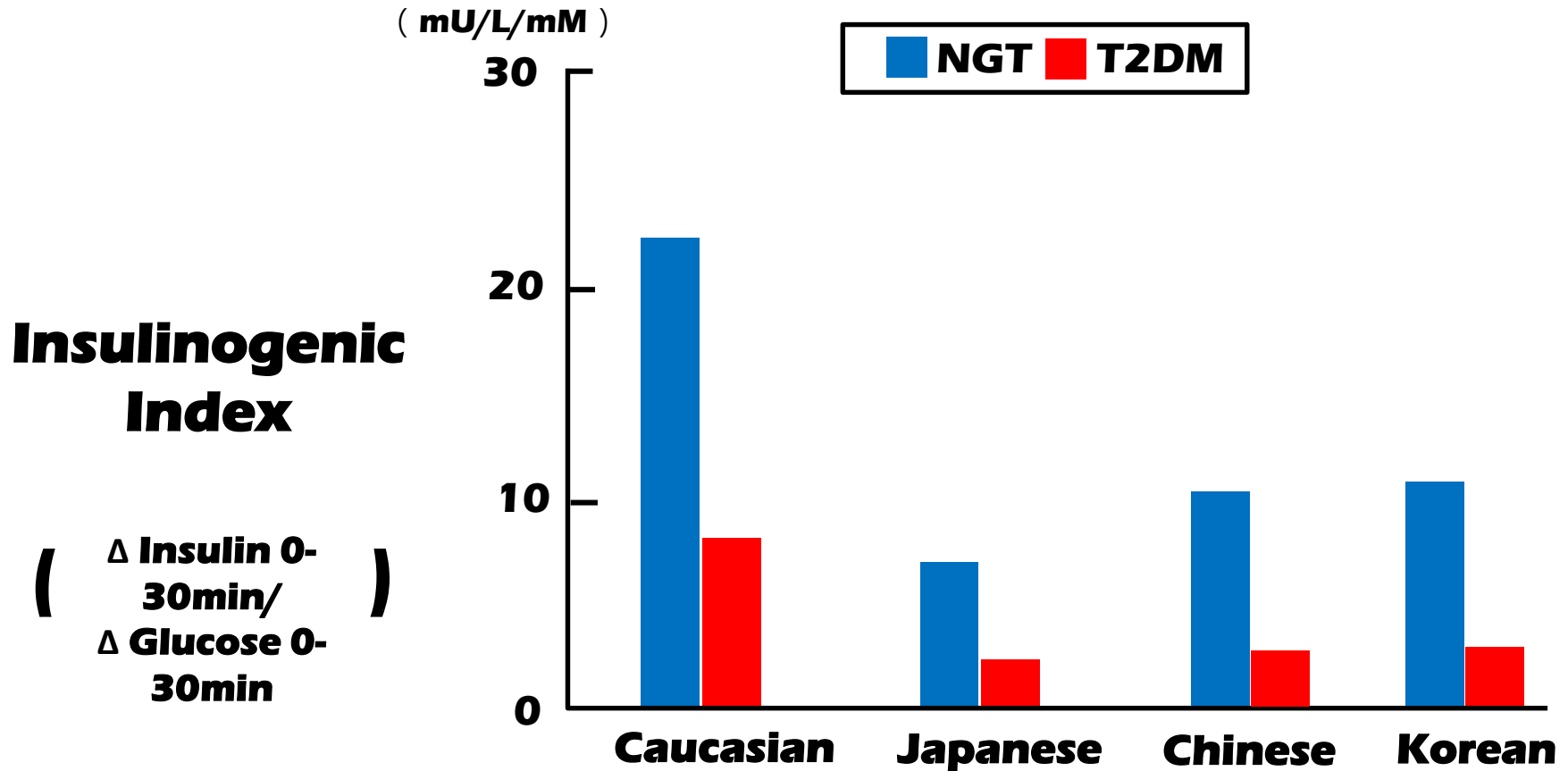


HOMA-IR



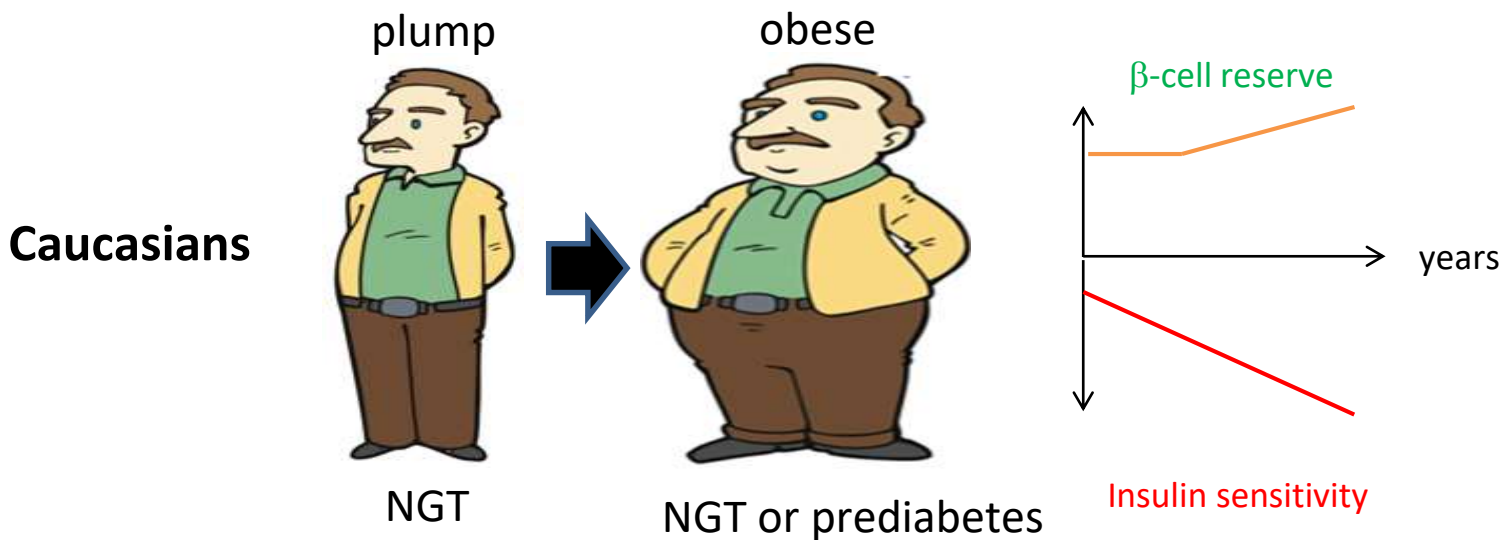
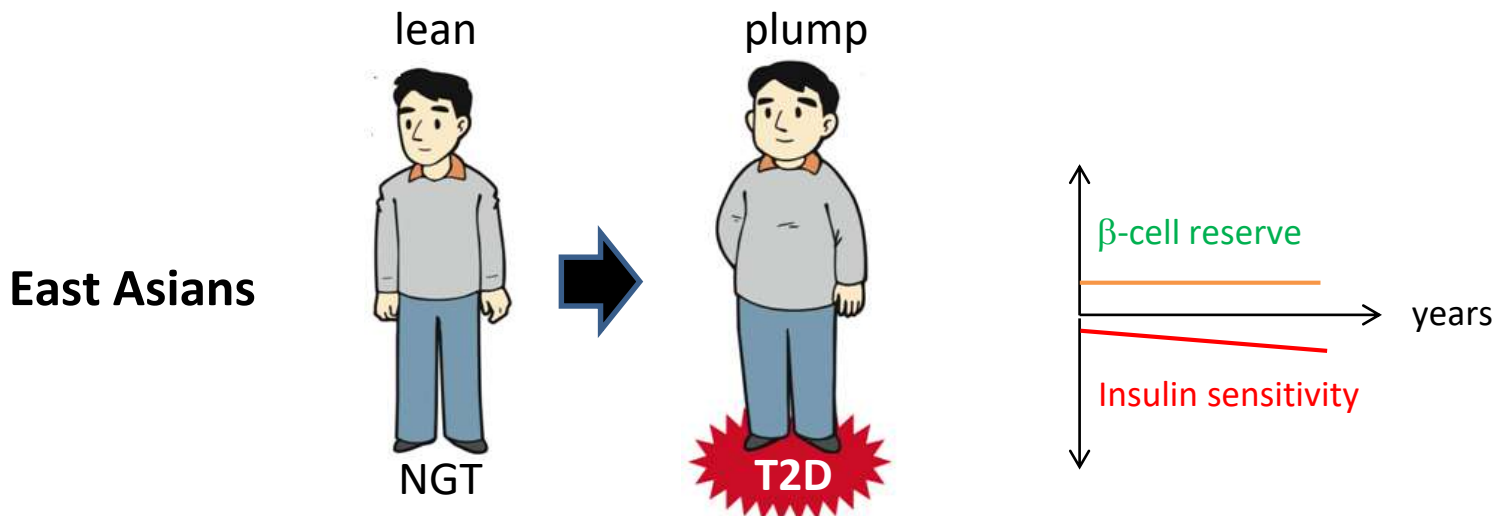
Japanese type 2 diabetes is characterized by reduced early phase insulin secretion with less insulin resistance

Insulin secretion among Caucasian and East Asians

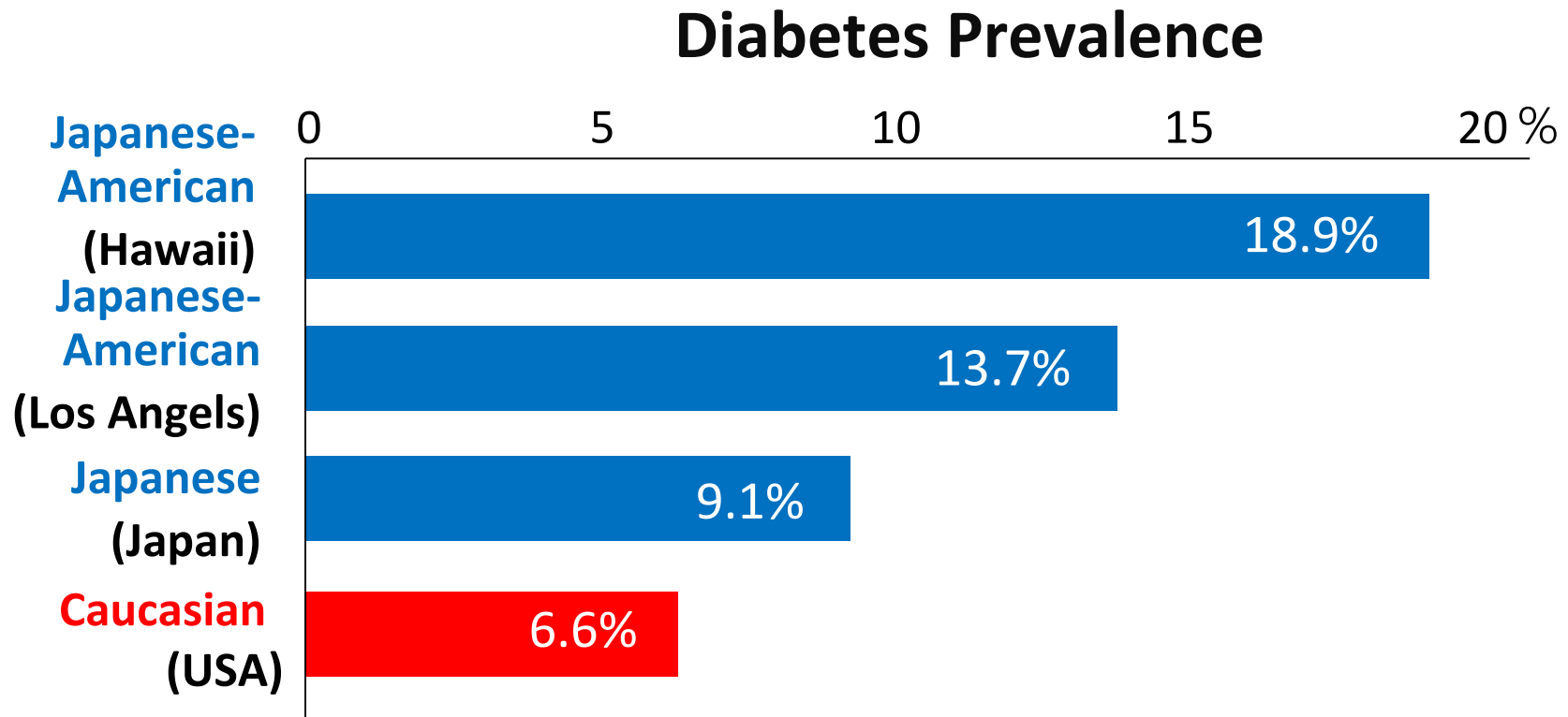


Reduced early phase insulin secretion is commonly observed among East Asians

Contributions of β -cell dysfunction and insulin resistance in pathophysiology of diabetes

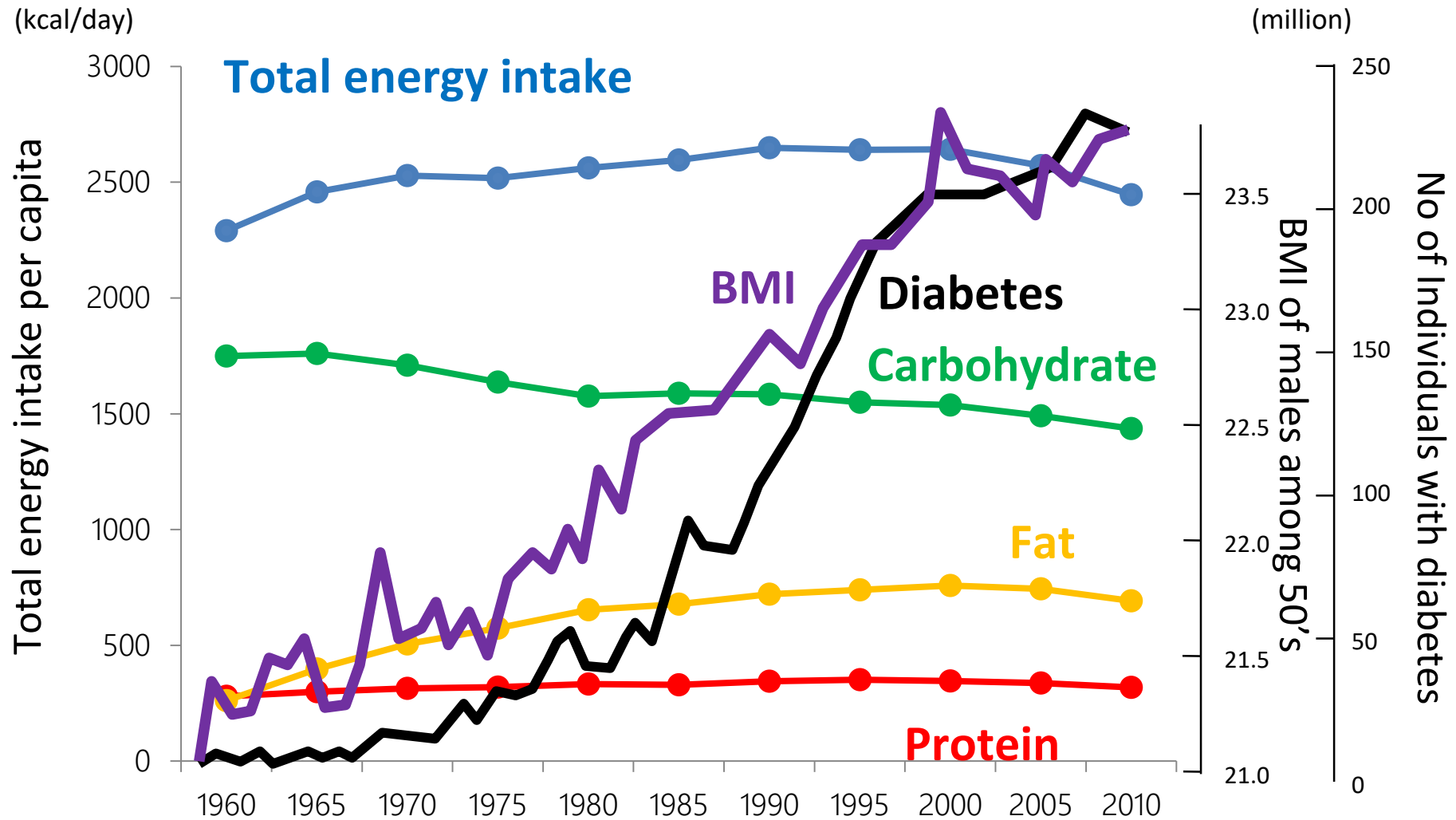


Comparison of diabetes prevalence of Japanese with those of Japanese American and Caucasian in USA



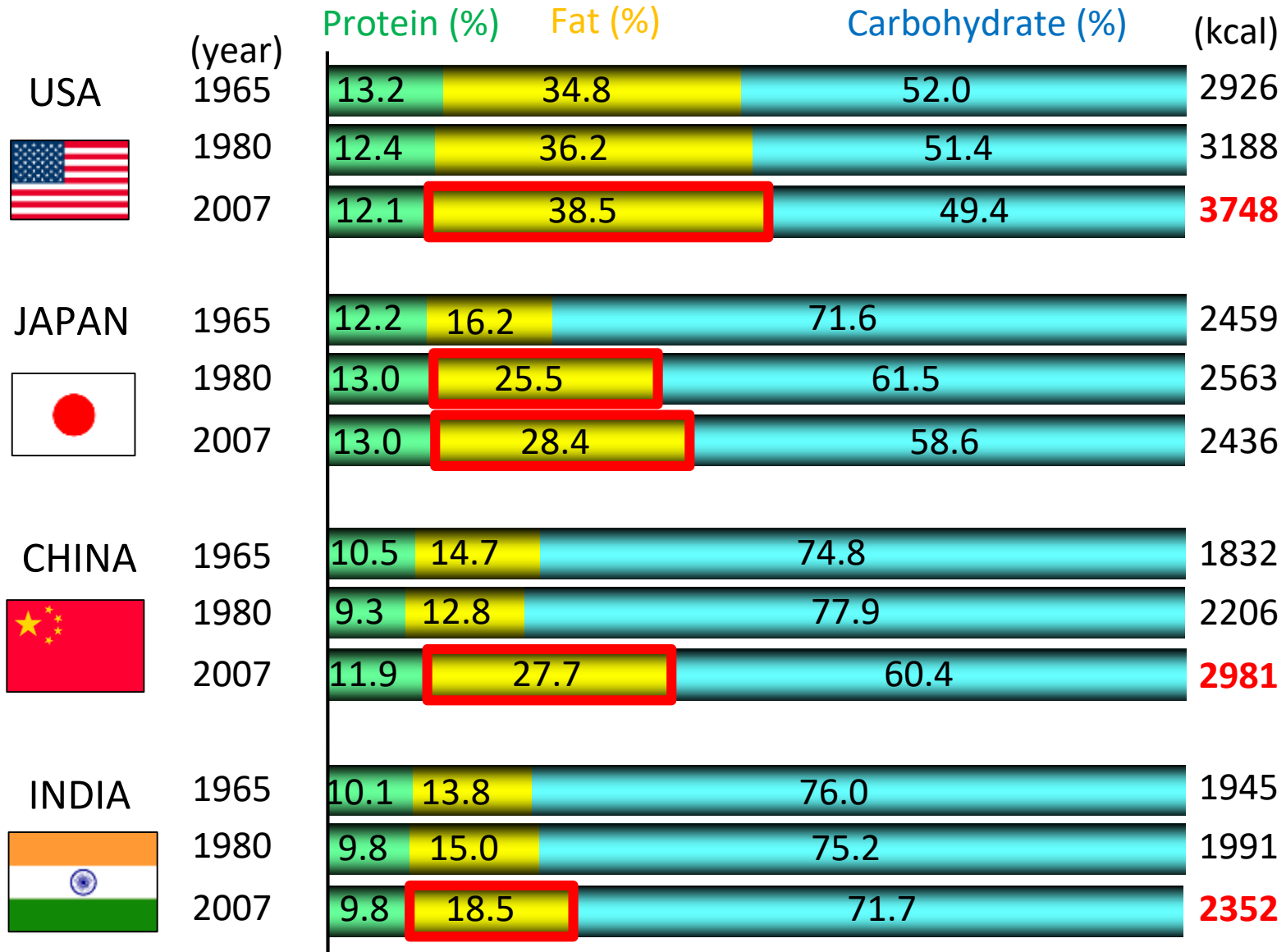
Japanese Americans who adopted western dietary habits including higher consumption of animal fat showed higher rates of diabetes

Changes in nutritional trends and rapid increase of diabetes in Japan



Pandemic of diabetes in Asia is partly due to changes in dietary habits, especially increased consumption of animal fats, which results in rapid increase of diabetes

Changes in nutritional trends in selected countries



Such alteration of dietary habits are found in Asian countries where diabetes is rapidly increasing.

Diagnosis: WHO Criteria 2006

Diabetes

Fasting plasma glucose	≥7.0mmol/l (126mg/dl)
2-h plasma glucose*	or ≥11.1mmol/l (200mg/dl)

Impaired Glucose Tolerance (IGT)

Fasting plasma glucose	<7.0mmol/l (126mg/dl)
2-h plasma glucose*	and ≥7.8 and <11.1mmol/l (140mg/dl and 200mg/dl)

Impaired Fasting Glucose (IFG)

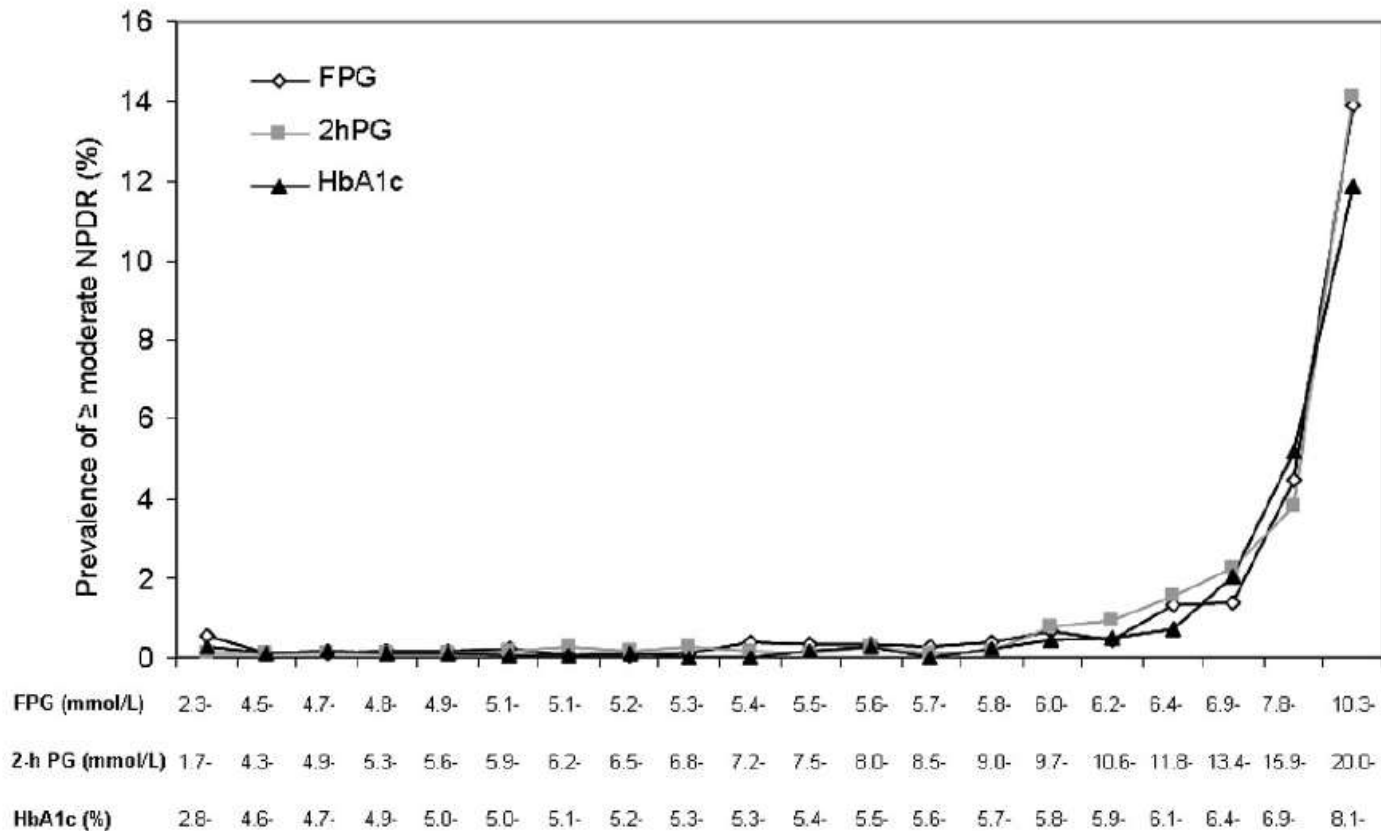
Fasting plasma glucose	6.1 to 6.9mmol/l
2-h plasma glucose*	(110mg/dl to 125mg/dl) and (if measured) <7.8mmol/l (140mg/dl)

* Venous plasma glucose 2-h after ingestion of 75g oral glucose load

* If 2-h plasma glucose is not measured, status is uncertain as diabetes or IGT cannot be excluded

- Despite the limitations with the data from which the diagnostic criteria for diabetes are derived, the current criteria distinguish a group with significantly increased premature mortality and increased risk of microvascular and cardiovascular complications.

Prevalence of diabetes-specific retinopathy (\geq moderate non-proliferative retinopathy) by vigintiles of distribution fo FPG, 2-h PG and HbA1c from DETECT-2



- HbA1c can be used as a diagnostic test when stringent quality assurance tests are in place and assays are standardized to criteria aligned to the international references, and there are no conditions present which preclude its accurate measurement.
- HbA1c 6.5 is recommended as the cut point for diagnosing diabetes. A value of $<6.5\%$ does not exclude diabetes diagnosed using glucose tests.

Factors influencing HbA1c and its measurement

1. Erythropoiesis

Increased HbA1c: iron, vitamin B12 deficiency, decreased erythropoiesis.

Decreased HbA1c: administration of erythropoietin, iron, vitamin B12, reticulocytosis, chronic liver disease.

2. Altered Haemoglobin

Genetic or chemical alterations in haemoglobin: haemoglobinopathies, HbF, methaemoglobin, may increase or decrease HbA1c.

3. Glycation

Increased HbA1c: alcoholism, chronic renal failure, decreased intra-erythrocyte pH.

Decreased HbA1c: aspirin, vitamin C and E, certain haemoglobinopathies, increased intra-erythrocyte pH.

Variable HbA1c: genetic determinants.

4. Erythrocyte destruction

Increased HbA1c: increased erythrocyte life span: Splenectomy.

Decreased A1c: decreased erythrocyte life span: haemoglobinopathies, splenomegaly, rheumatoid arthritis or drugs such as antiretrovirals, ribavirin and dapsone.

5. Assays

Increased HbA1c: hyperbilirubinaemia, carbamylated haemoglobin, alcoholism, large doses of aspirin, chronic opiate use.

Variable HbA1c: haemoglobinopathies.

Decreased HbA1c: hypertriglyceridaemia.

- In addition to above problematic factors, costs and availability of HbA1c measurements are major obstacles to implement HbA1c in diagnostic criteria.

Association of HbA1c with FPG and OGTT2hr among Japanese

FPG (mg/dl)

126

HbA1c(NGSP)(%)

6.5

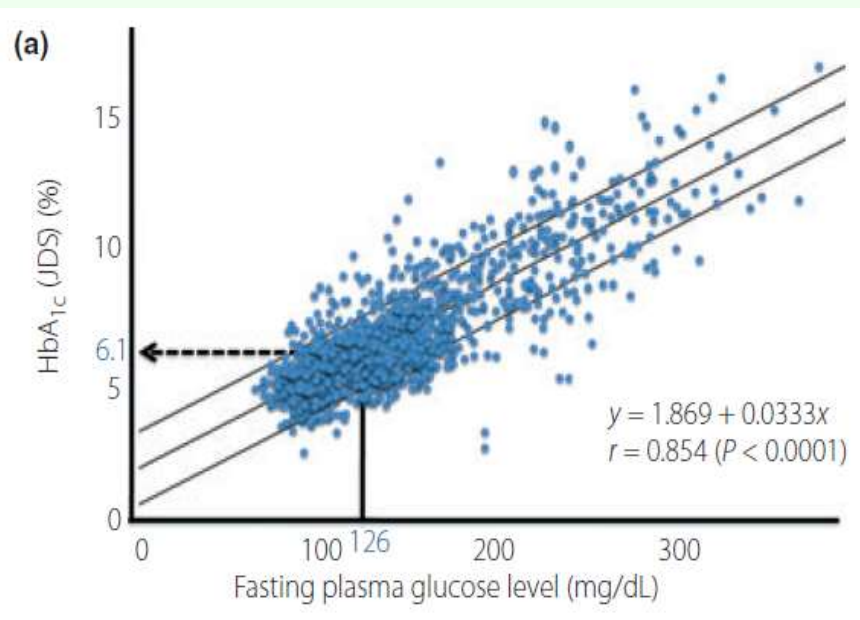
OGTT2hr (mg/dl)

200

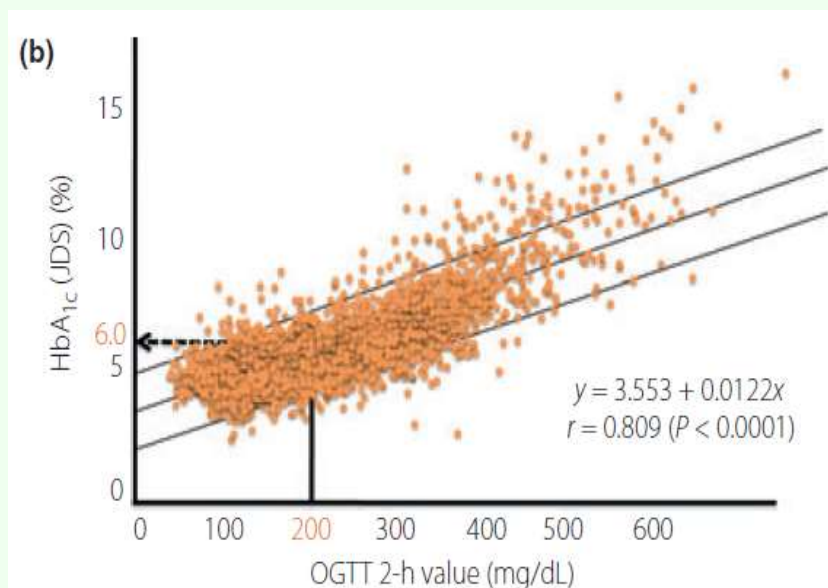
HbA1c(NGSP)(%)

6.4

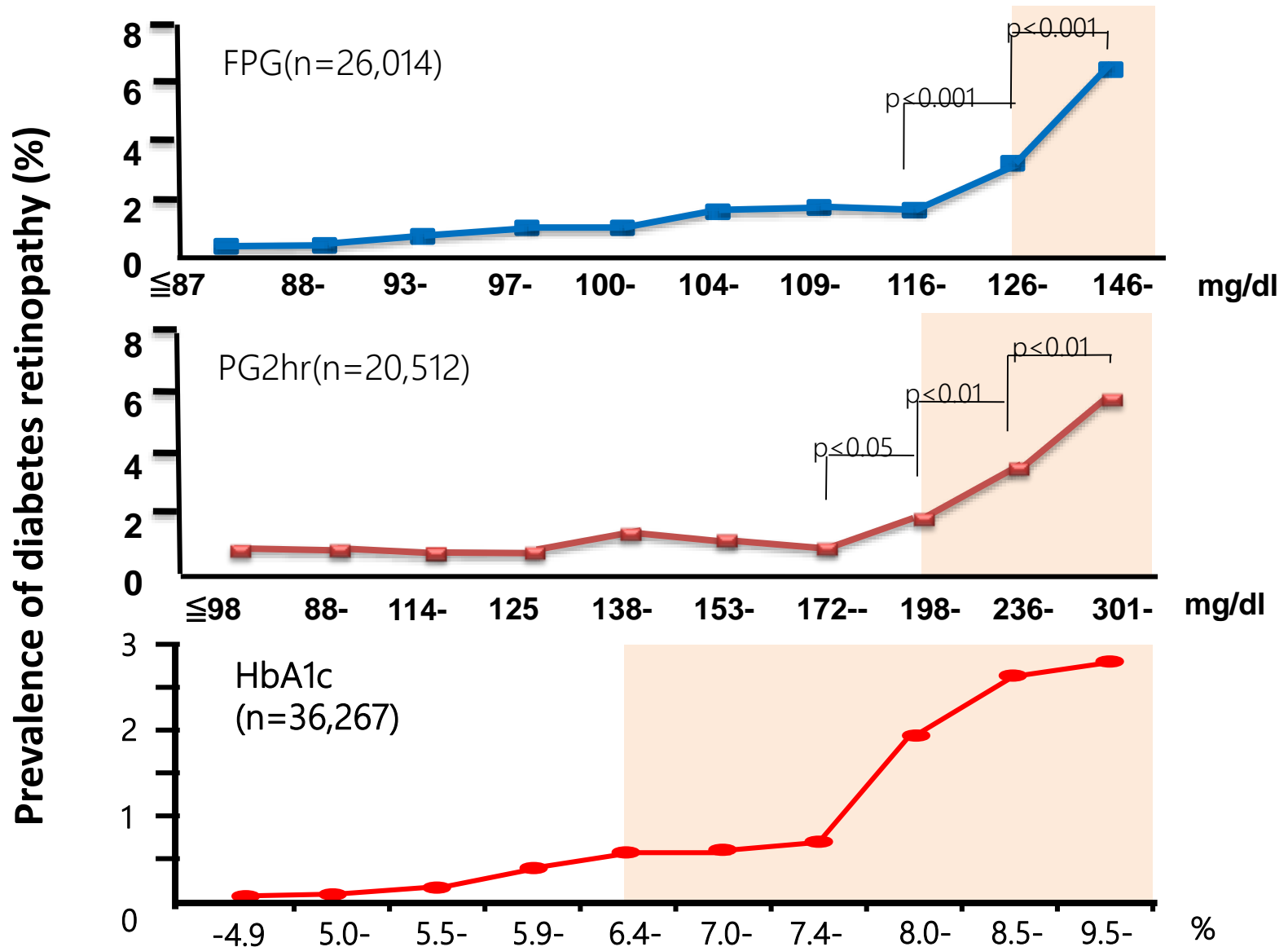
FPG and HbA1c(JDS)



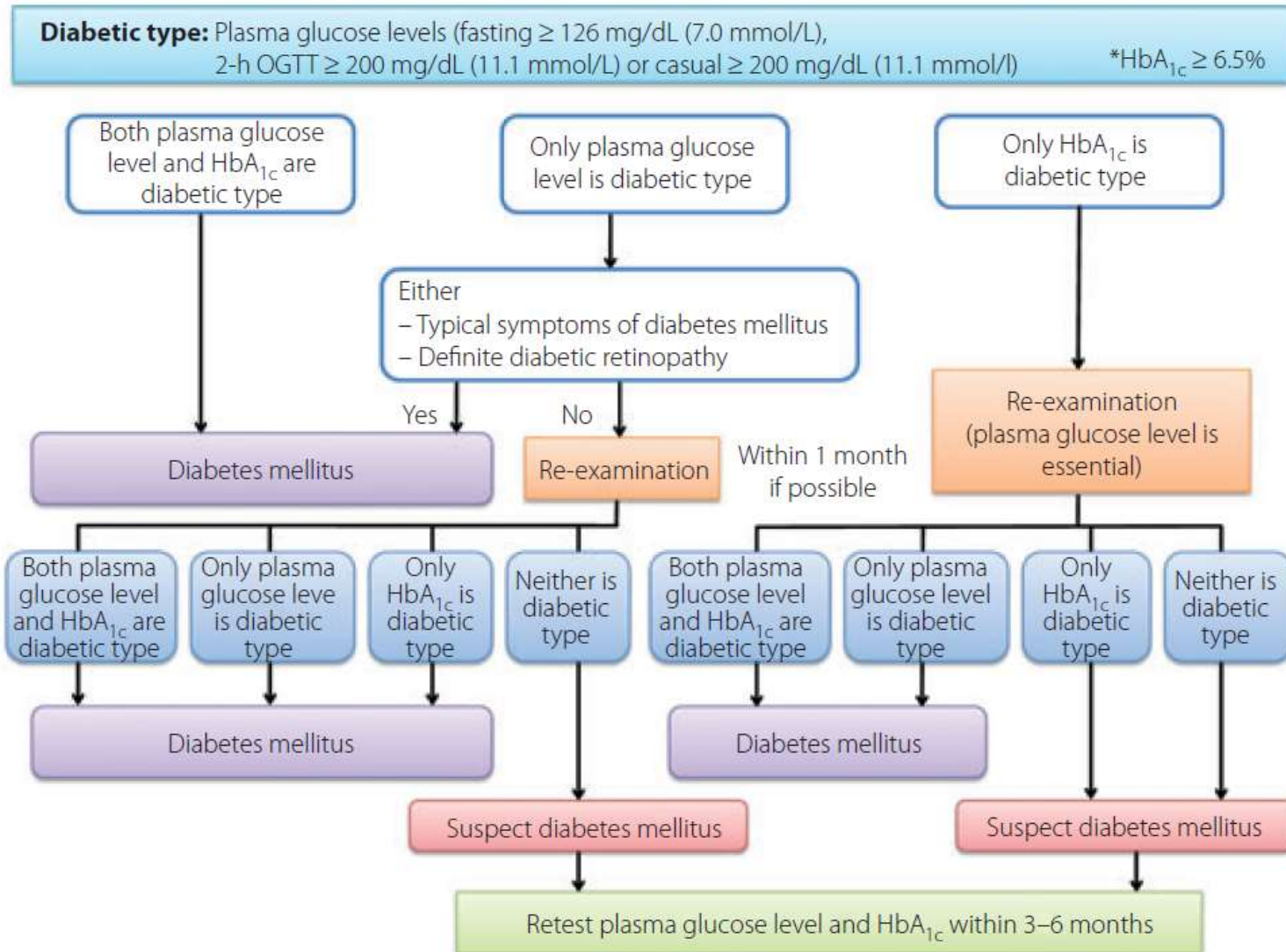
OGTT2hr and HbA1c(JDS)



Prevalence of diabetic retinopathy and FPG, PG2hr, and HbA1c among Japanese



Diagnosis: Japanese criteria



Diagnosis: American criteria

FPG \geq 126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

OR

2-h PG \geq 200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*

OR

A1C \geq 6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose \geq 200 mg/dL (11.1 mmol/L).

*In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.

- Unless there is a clear clinical diagnosis (e.g., patient in a hyperglycemic crisis or with classic symptoms of hypercemia and a random plasma glucose \geq 200 mg/dL), a second test is required confirmation.

Diagnosis: Korean criteria

A diagnosis of diabetes can be made from any one of the following four criteria:

1. FPG \geq 126 mg/dL
2. 2-hour PG \geq 200 mg/dL during the oral glucose tolerance test^a
3. Classic symptoms of hyperglycemia or hyperglycemic crisis, a random^b PG level \geq 200 mg/dL
4. HbA1c \geq 6.5%

Normal activity should be maintained for at least three days before sampling. In the absence of unequivocal hyperglycemia, blood sampling should be repeated.

FPG, fasting plasma glucose. "Fasting" means no caloric intake for at least 8 hours; PG, plasma glucose.

^aGlucose load containing the equivalent of 75 g of anhydrous glucose dissolved in water, ^b"Random" is defined as without regard to the time since the last meal.

- Most commercial laboratories in Korea are certified by Designated Comparison Methods, and accuracy-based proficiency tests are underway for HbA1c measurement. Based on this background, HbA1c was included as a diagnostic criterion in Korean clinical practice guidelines in 2011.

Diagnosis: Chinese criteria

Diagnostic methods	Venous plasma glucose level (mmol/L)
(1) Typical symptoms of diabetes (polydipsia, polyuria, polyphagia and weight loss) plus random blood glucose testing	≥ 11.1
or	
(2) Fasting plasma glucose	≥ 7.0
or	
(3) 2 h after the glucose load test Individuals who do not present diabetes symptoms should be re-tested on a separate day.	≥ 11.1

The fasting state refers to not eating for at least 8 h. Random blood glucose refers to the blood glucose level at any time of day regardless of the time of the last meal, which cannot be used to diagnose impaired fasting glucose or impaired glucose tolerance.

- Given the HbA1c test is not yet commonly applied in China, the insufficient degree of standardization, and the fact that the instruments are quality control for measuring HbA1c are currently unable to meet the current diagnostic standard for diabetes, this guide line does not recommend the use of HbA1c for diagnosis of diabetes in China.

Screening of diabetes: Nationwide Health Check-up and Health Guidance Program in Japan (2008-Present)

Purpose;

Aimed at extending the healthy lives of people according to their individual situation through a national health promotion campaign, with the **focus on preventive measures**, efforts will be made to create a healthy nation through reviewing the role of the family, enhancing local communities, and innovative new technologies and systems

Target population;

All Japanese **aged 40-74 years** old should have annual health check-ups and screened for guidance program

Examination includes;

- 1) Questionnaire survey: medication, smoking history, etc
- 2) Height, weight, **waist circumference** measurement
- 3) **Blood pressure**
- 4) Blood tests: AST, ALT, gamma-GTP
Triglycerides, HDL-cholesterol, LDL-cholesterol
Fasting plasma glucose or HbA1c
- 7) Urinalysis (glucose, protein)

Criteria for testing for diabetes or prediabetes in asymptomatic adults: American guidelines

1. Testing should be considered in overweight or obese (BMI ≥ 25 kg/m² or ≥ 23 kg/m² in Asian Americans) adults who have one or more of the following risk factors:
 - A1C $\geq 5.7\%$ (39 mmol/mol), IGT, or IFG on previous testing
 - first-degree relative with diabetes
 - high-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
 - women who were diagnosed with GDM
 - history of CVD
 - hypertension ($\geq 140/90$ mmHg or on therapy for hypertension)
 - HDL cholesterol level < 35 mg/dL (0.90 mmol/L) and/or a triglyceride level > 250 mg/dL (2.82 mmol/L)
 - women with polycystic ovary syndrome
 - physical inactivity
 - other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans).
2. For all patients, testing should begin at age 45 years.
3. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results (e.g., those with prediabetes should be tested yearly) and risk status.

Screening of diabetes: Korean criteria for screening of type 2 diabetes

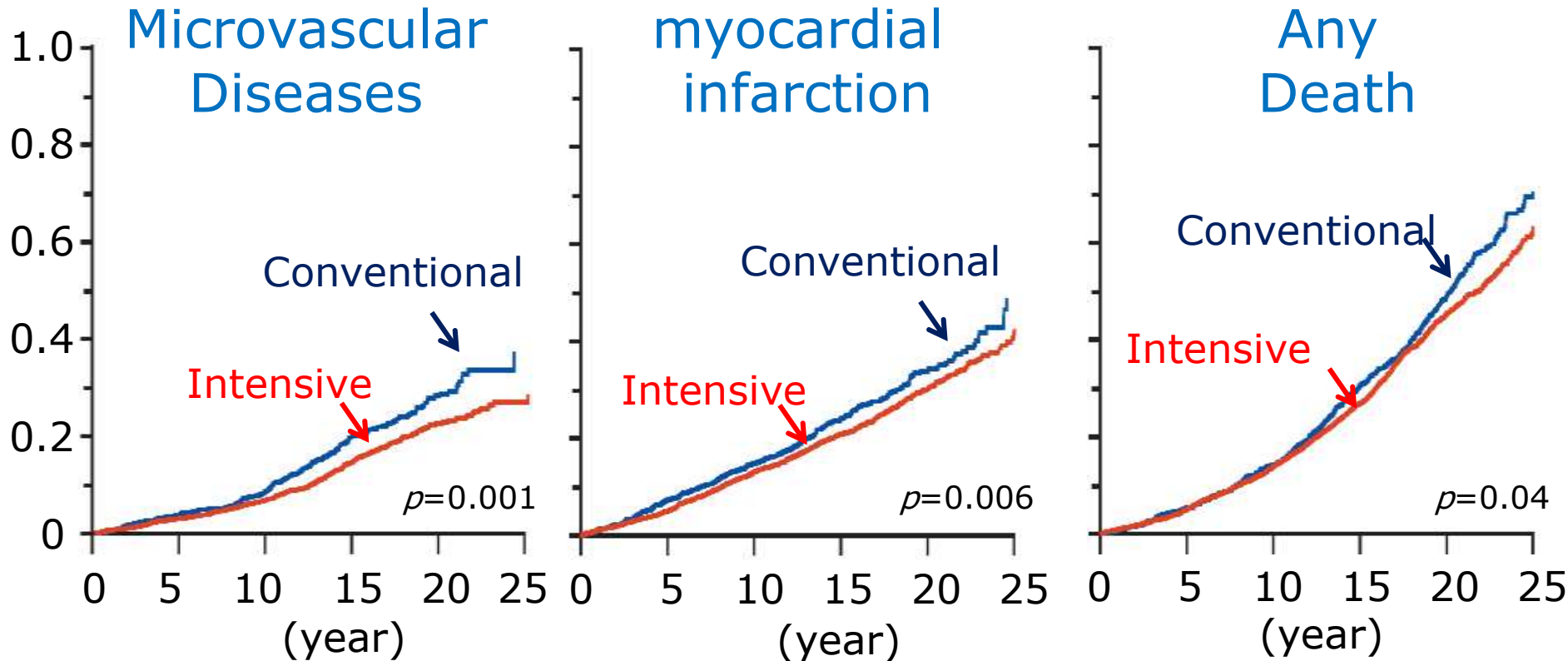
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1. FPG, 75 g OGTT, or HbA1c can be used as screening tests
 2. Annual screening should begin at age 40 years or adults >30 years who have risk factors
 3. If FPG or HbA1c are as follows, an additional test should be considered

Stage 1: If FPG is in the range of 100 to 109 mg/dL or HbA1c is 5.7% to 6.0%, annual FPG and HbA1c should be repeated annually

Stage 2: If FPG is in the range of 110 to 125 mg/dL or HbA1c is 6.1% to 6.4%, oral GTT should be performed

OGTT, oral glucose tolerance test; FPG, fasting plasma glucose.

Benefits of early intensive glucose control: UKPDS80



Benefits of early intensive glucose control to prevent diabetes complications were sustained for up to 10 years

Summary

- Diabetes is a chronic condition that occurs due to insufficient insulin secretion and/or insulin action. The resulting high glucose levels over time cause diabetes-related micro- and macrovascular complications.
- East Asians is characterized by less insulin secretion, which makes them vulnerable to development of type 2 diabetes in response to changes in dietary habits.
- Diagnosis of diabetes by practical and reliable methodologies should be made in order to initiate appropriate treatment strategies to prevent onset and progression of diabetes-related complication.