

# Management of prediabetes

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# Case presentation

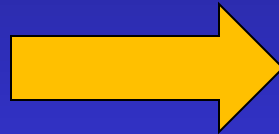
- A 55-year-old man with hypertension diagnosed 2 years ago
- Irregular exercise, no smoking, no alcohol
- Lisinopril, Amlodipine
- Examination: BMI 29.4. normal exam.
- Fasting plasma glucose 6.5 mmol/L (117 mg/dL)
- A1c 6.2%
- Serum electrolytes, ALT: normal
- **How would you manage his glucose?**

# Fasting plasma glucose

- **Normal:**
  - $<5.6$  mmol (100 mg) [some countries use 110 mg]
- **Diabetes:**
  - $\geq 7$  mmol (126 mg)
- **Impaired fasting glucose (IFG) [Prediabetes]:**
  - 5.6 to 6.9 mmol (100-125 mg)

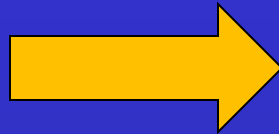
# Use of A1c to diagnose DM

Diabetes



$\geq 6.5$

Prediabetes



5.7- 6.4

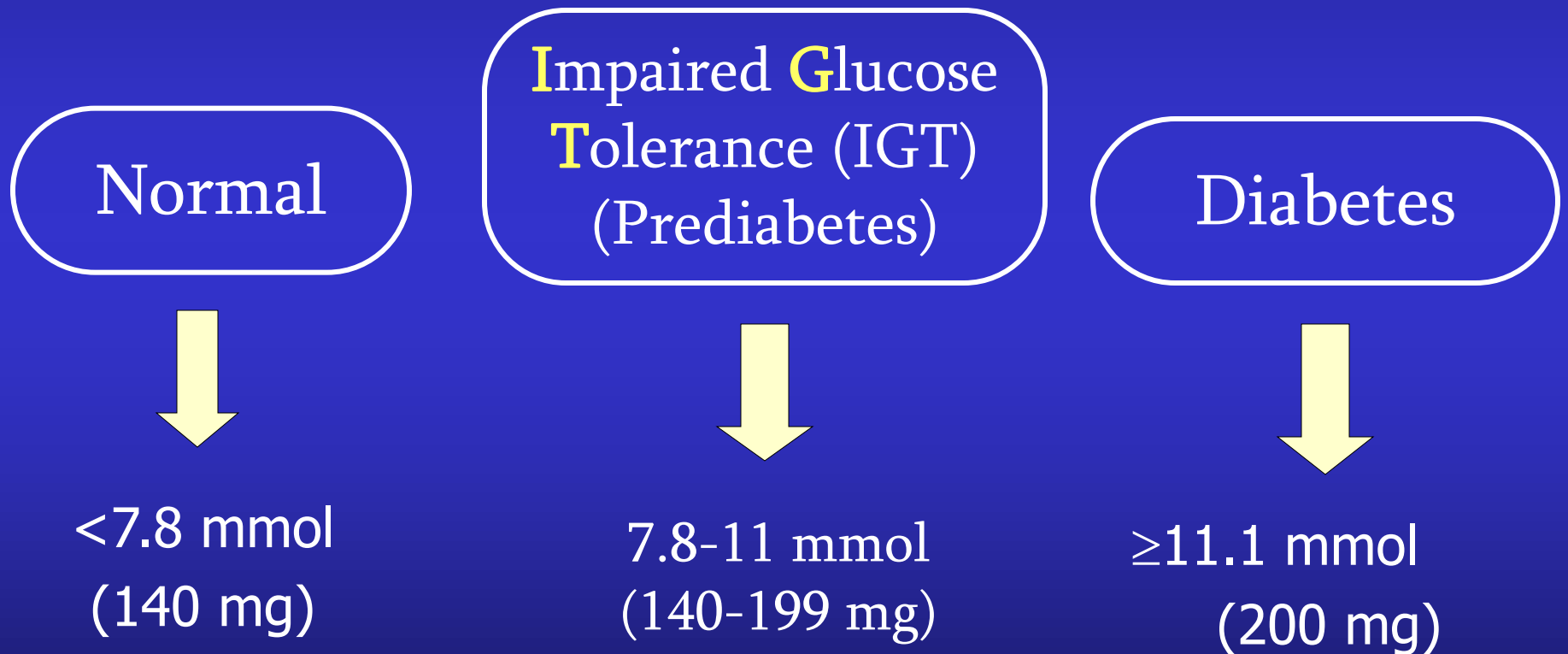
Normal



$< 5.7$

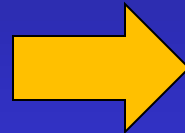
# 75-gram OGTT

## 2-hour plasma glucose interpretation



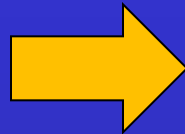
# Criteria for prediabetes

**Fasting glucose**



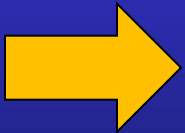
**5.6-6.9 mmol  
(100-125 mg)**

**HbA1c**



**5.7-6.4%**

**2-hour  
post 75-OGTT**



**7.8-11 mmol  
(140-199 mg)**

# Why is prediabetes important?

**DM 2**

**Cardiovascular  
disease**

**Neuropathy**

**Heart failure**

**Atrial fibrillation**

**Chronic kidney disease**

**Dementia**

**Cancers (liver, breast)**

**Mortality**

# Goals of management of prediabetes

- Prevention or delay of type 2 diabetes
- Prevention or delay of cardiovascular disease
- Prevention or delay of microvascular complications
- Reduction of the cost



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REDUCTION IN THE INCIDENCE OF TYPE 2 DIABETES WITH LIFESTYLE  
INTERVENTION OR METFORMIN

DIABETES PREVENTION PROGRAM RESEARCH GROUP\*

## **Diabetes prevention program**

# Diabetes prevention program

3234 persons with prediabetes  
randomized to:

Intensive lifestyle  
changes

Standard  
lifestyle  
changes  
+  
Metformin

Standard  
lifestyle  
changes  
+  
Placebo

# Diabetes Prevention Program

- **Intensive lifestyle changes:**

- Weight loss of at least 7% (low calorie, low fat)
- Structured exercise program  
[moderate intensity such as brisk walking]  
for at least 150 min./week

## **Metformin:**

- Dose of 850 mg twice daily

# Results of Diabetes Prevention Program

After 2.8 years (terminated 1 year earlier)  
Compared to standard lifestyle changes:

Patients on lifestyle changes



Risk of DM ↓ by **58%**

Patients on Metformin



Risk of DM ↓ by **31%**

# Other findings from the DPP

- Intensive lifestyle changes & Metformin had the same effect in patients age 25-44 years (48 & 44%)
- Intensive lifestyle changes & Metformin had the same effect in patients with gestational DM (53 & 50%)
- Intensive lifestyle changes & Metformin had the same effect in patients with BMI  $\geq 35$  (51 & 53%)
- Metformin had no effect in patients age  $\geq 60$  years

# The DPP continued!

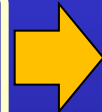
- DPP study continued for a total of 15 years (so far)

Patients on lifestyle changes



Risk of DM ↓ by **27%**

Patients on Metformin



Risk of DM ↓ by **18%**

# Other trials on diabetes prevention

## Effect of intensive lifestyle changes

	<u>F/U</u>	<u>Effect</u>
Da Qing (China) →	23 y	Risk of DM ↓ by <b>45%</b>
DPS (Finland) →	7 y	Risk of DM ↓ by <b>43%</b>

# Dietary intervention in the management of prediabetes

- **Mediterranean diet:**

- A reduction in the incidence of DM by 31%
- This was independent on weight loss & exercise  
(in 1 study with small number of events)



# Dietary intervention in the management of prediabetes

- **Low carbohydrate diet:**
  - Few studies with limited number of patients
  - Short duration of follow up
  - There was improvement of glucose levels

Kirsten S, et al. JAMA Netw Open 2022;5(10):e2238645.

Saslow LR, et al. PLoS One 2014;9(4):e91027.

Saslow LR, et al. Nutr Diabetes 2017;7(12):304.

# Role of exercise in the management of prediabetes

- A large number of studies showed benefit
- A program of 150 min/week of brisk exercise decreased the risk of DM by 26%
- A program of 300 min/week decreased the risk of DM by 36%

# Metformin for management of prediabetes

- A metaanalysis showed:
  - Compared with standard lifestyle changes, Metformin reduced the risk of DM by 50%
  - No difference between Metformin and intensive lifestyle changes

# Other medications for management of prediabetes

- Shorter duration of study compared to Metformin and to consider side effects and cost:
  - Pioglitazone
  - Rosiglitazone
  - Liraglutide
  - Semaglutide
  - Orlistat
  - Acarbose
  - Insulin Glargine

DREAM Trial Investigators. Lancet 2006; 368:1096; DeFronzo RA, et al. N Engl J Med 2011; 364:1104.

ORIGIN Trial Investigators. N Engl J Med 2012; 367:319; le Roux CW, et al. Lancet 2017; 389:1399.

Torgerson JS, et al. Diabetes Care 2004; 27:155; Heymsfield SB, et al. Arch Intern Med 2000; 160:1321.

Chiasson JL, et al. Lancet 2002; 359:2072; Perreault L, et al. Diabetes Care 2022; 45:2396.

# Cost effectiveness in the DPP

## 10-year direct medical cost:

Lifestyle changes → \$29,164

Metformin → \$27,915

Placebo → \$28,236

# Cost effectiveness in the DPP

## Quality-adjusted life years:

Lifestyle changes	➔	6.81
Metformin	➔	6.69
Placebo	➔	6.67

# **Guidelines on the management of prediabetes**

# Management of prediabetes

## 1) Lifestyle changes:

- Refer to lifestyle change behavior program
- Aim for weight loss of at least 7% of body weight
- Physical activity:
  - Moderate intensity (such as brisk walking)
  - Duration: at least 150 minutes/week (over 3-5 days)



# Dietary intervention in the management of prediabetes

- Plan is individualized based on assessment of current eating patterns, preferences, and metabolic goals
- Reduction of total dietary fat and calories
- Mediterranean and low-carbohydrate diets (interventional studies)
- Vegetarian, plant-based and DASH diets (observational studies )

# Management of prediabetes

- Screen & treat CVD risk factors:
  - Hypertension
  - Dyslipidemia
  - Smoking
- Self-management education & support
- Monitor glucose (fasting or A1c) annually

# Metformin for prediabetes

- Metformin for age 25-59 years (especially for):
  - **BMI  $\geq 35$**
  - **Fasting glucose  $\geq 6.1$  mmol/L**
  - **HbA1c  $\geq 6\%$**
  - **Previous history of gestational diabetes**
- Endocrine society does not recommend Metformin for persons age  $\geq 65$  years

# NICE guidelines for management of prediabetes

- 1) Metformin for fasting plasma glucose (5.6 to 6.9 mmol/L] or A1c (6 to 6.5%) who are:
  - A) Unable to participate in lifestyle interventions
  - or
  - B) If FPG or A1c values deteriorate despite participation in a lifestyle intervention program
- 2) Orlistat if BMI >28 when FPG or A1c show deterioration

# Back to the case

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# Case management

- Advise lifestyle changes
  - Weight loss of at least 7%
  - Physical activity (150 min/week of moderate exercise)
  - Self-management education support
- Monitor glucose (FPG or A1c) in 6-12 months
- If no improvement in glucose levels, consider  
Metformin

# Summary

- Lifestyle changes reduces the progression to DM
- Metformin reduces the progression to DM
- Metformin is as effective as lifestyle changes in:
  - ◆ Age 25-44 years, GDM, BMI  $\geq 35$
- Metformin did not work for age  $\geq 60$  years
- Lifestyle changes & Metformin are cost effective