#### 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
- Medications: 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**:

• ≥7 mmol (126 mg)

Impaired fasting glucose (IFG) [Prediabetes]:

• 5.6 to 6.9 mmol (100-125 mg)

# **Interpretation of A1c**



# 75-gram OGTT 2-hour plasma glucose interpretation



#### **Criteria for prediabetes**



# Why is prediabetes important?



Schlesinger S, et al. Diabetologia 2022;65(2):275

# 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

#### The New England Journal of Medicine

FEBRUARY 7, 2002	NUMBER 6
	FEBRUARY 7, 2002

#### 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  $\downarrow$  by **58%** 

Patients on Metformin



#### **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 ≥35 (51 & 53%)
- Metformin had no effect in patients age ≥60 years

# The DPP continued

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

Patients on lifestyle changes



Patients on Metformin

 $\mathbf{F}$  Risk of DM  $\downarrow$  by **18%** 

Nathan D et al. Lancet Diabetes Endocrinol 2015;3:866



Li G, et al. Lancet Diabetes Endocrinol 2014;2:474. Lindstorm J, et al. Lancet 2006;368:1673

#### **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)

Salas-Salvadó J, et al. Ann Intern Med 2014; 160:1. Bloomfield HE, et al. Ann Intern Med 2016; 165:491. Estruch R, Ros E, et al. N Engl J Med 2013;368:1279. Estruch R, Ros E, et al. N Engl J Med 2018;378:e34.

#### **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%

Chen Y, et al. JAMA Intern Med 2023;183(3):272. Luo M, et al. Br J Sports Med 2023;57(19):1257. Smith AD, et al. Diabetologia. 2016;59(12):2527.

## 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

Madsen KS, et al. Cochrane Database Syst Rev 2019; 12:CD008558.

# 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**

#### **<u>10-year direct medical cost:</u>**

Lifestyle changes \$29,164





Metformin



\$27,915





\$28,236

DPPOS study. Diabetes Care. 2012;35(4):723.

# **Cost effectiveness in** the **DPP**

#### **Quality-adjust life years:**

Lifestyle changes



6.81

Metformin

6.69

Placebo

6.67

DPPOS study. Diabetes Care. 2012;35(4):723.

Guidelines on the management of prediabetes

#### **Management of prediabetes**

#### 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 ≥35
  - Fasting glucose ≥6.1 mmol/L
  - HbA1c ≥6%
  - Previous history of gestational diabetes

 Endocrine society does not recommend Metformin for persons age ≥65 years

American Diabetes Association. Diabetes Care 2024;47 (suppl 1):S43 Endocrine Society guidelines. J Clin Endocrinol Metab 2019;104:1520

#### NICE guidelines for management of prediabetes

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

NICE guidelines 2017. nice.org.uk

# 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



- 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

#### For talks & educational materials:

# www.eledrisi.com Needs VPN in Libya

# الزبدة Easy Medicine

