PREDIABETES

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PREDIABETES STATISTICS

Intermediate state of glucose dysregulation

Precedes type 2 diabetes

In 2021 affected 720 million individuals worldwide

By 2045, estimated 1 billion people

In the US, ~ 10% of people progress to type 2 DM annually

Criteria	American Diabetes Association (2023)	World Health Organization (2006)	International Expert Committee (2009)
Fasting plasma glucose, mg/dL	100-125	110-125	NA
2-h Postload plasma glucose (75-g oral glucose tolerance test), mg/dL	140-199	140-199	NA
Hemoglobin A_{1c}, %	5.7-6.4	NA	6.0-6.4

DIAGNOSTIC CRITERIA

DIFFER BY ORGANIZATION

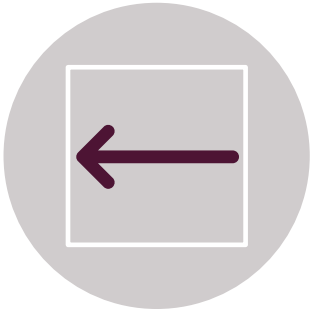
SCREENING RECOMMENDATIONS

- ADA: universal screening every 3 years for all adults 35 years or older regardless of risk factors
- **Screening tests**:
  - Fasting plasma glucose
  - HbA1C
  - 2-hour post-glucose challenge
- 2 abnormal screening test results either from the same sample or 2 separate test samples
- If pre-DM diagnosed, annual monitoring is recommended for progression to DM

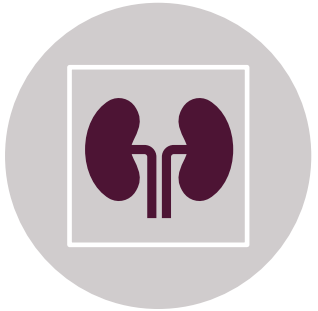
PATHOPHYSIOLOGY

Liver insulin resistance → higher or "inappropriate" glucose production by the liver → lower ability of glucose to stimulate its own uptake by the tissues

Pancreatic beta cell dysfunction

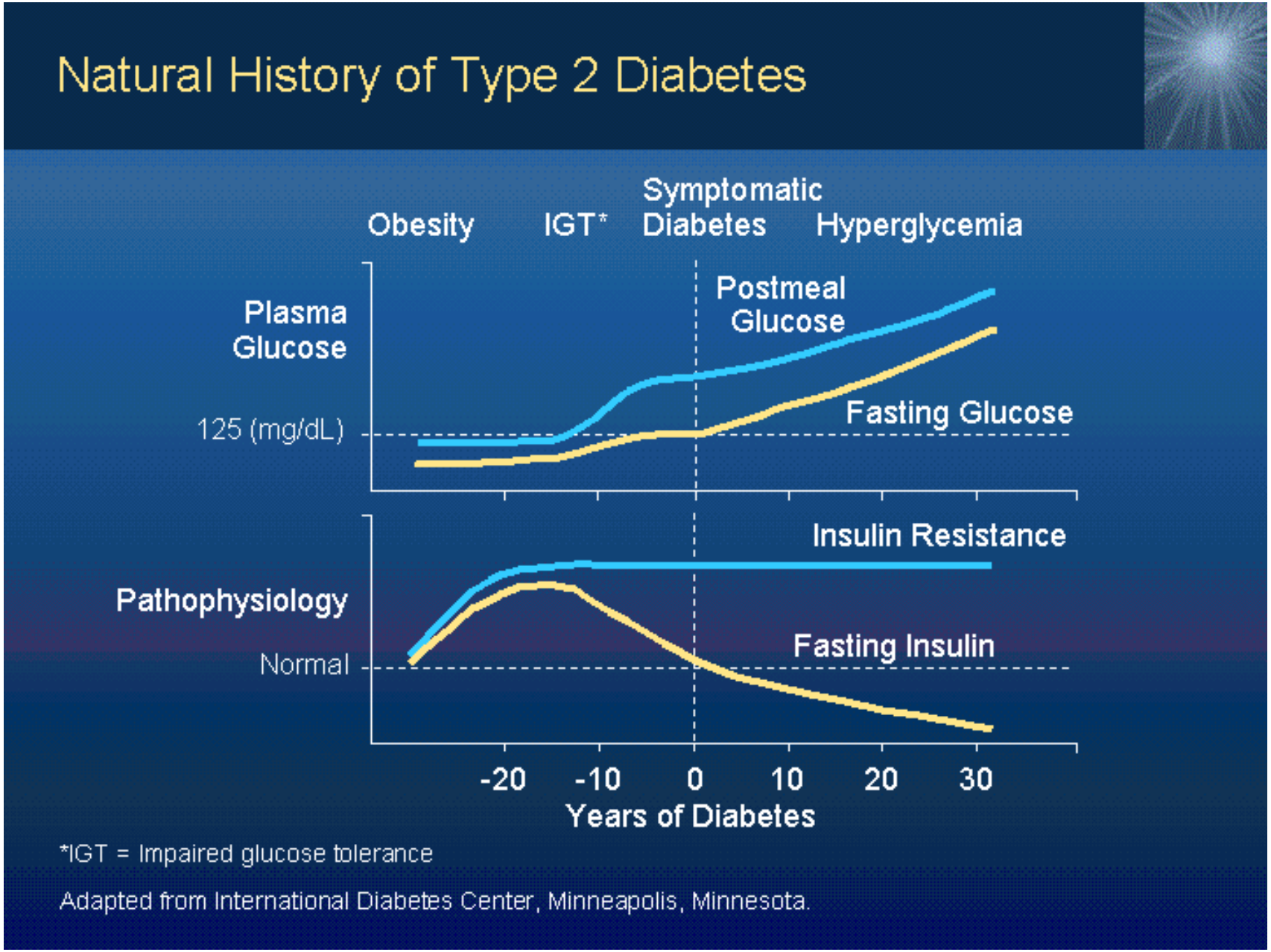


Muscle insulin resistance



Impaired fasting glucose, impaired glucose tolerance, or both

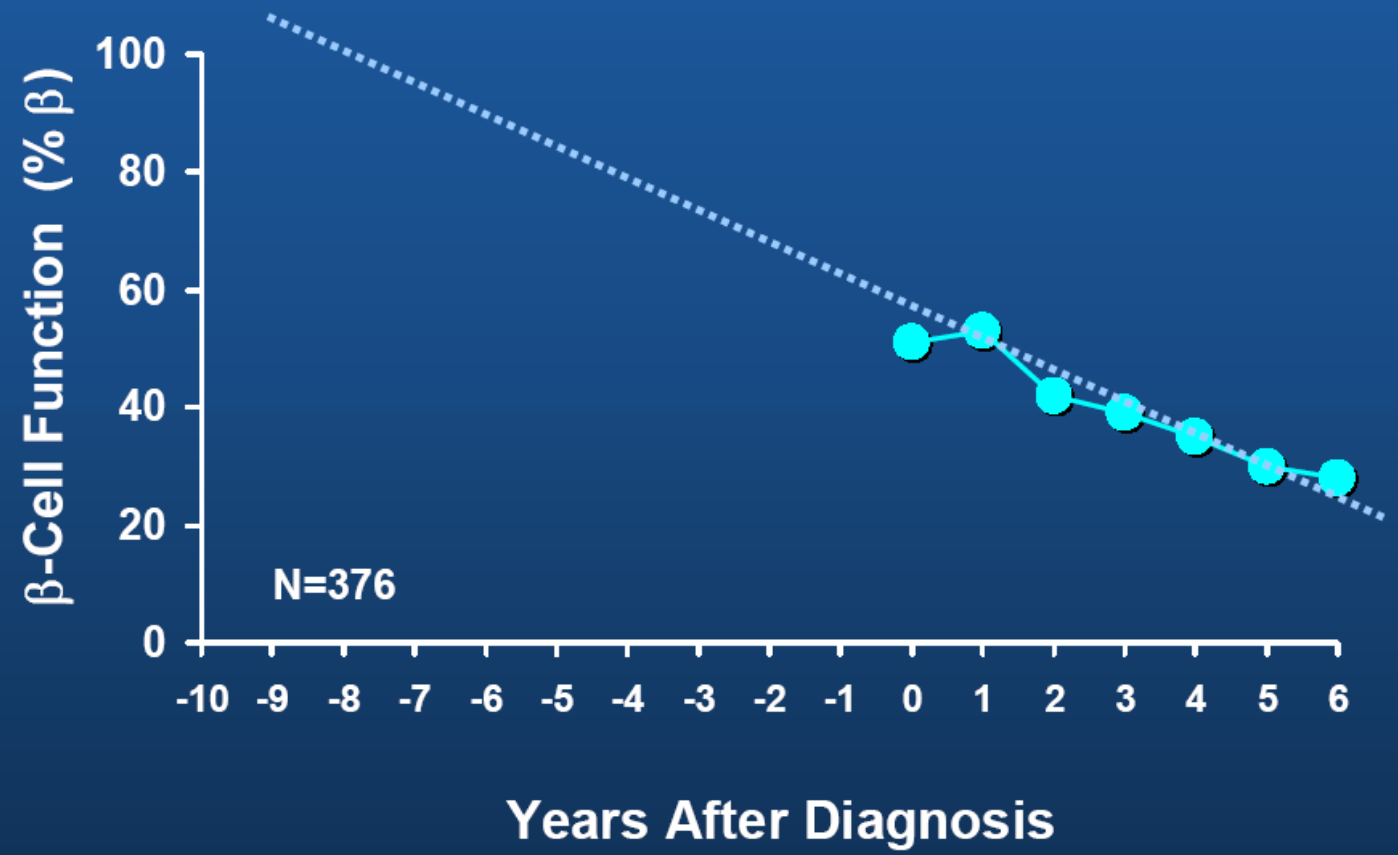
Natural History of Type 2 Diabetes



*IGT = Impaired glucose tolerance

Adapted from International Diabetes Center, Minneapolis, Minnesota.

UKPDS: β-Cell Function for the Patients Remaining on Diet for 6 Years



Adapted from UKPDS Group. *Diabetes.* 1995; 44:1249-1258.

~ 40% RELATIVE DECREASE IN BETA CELL FUNCTION IN INDIVIDUALS WITH PRE-DM

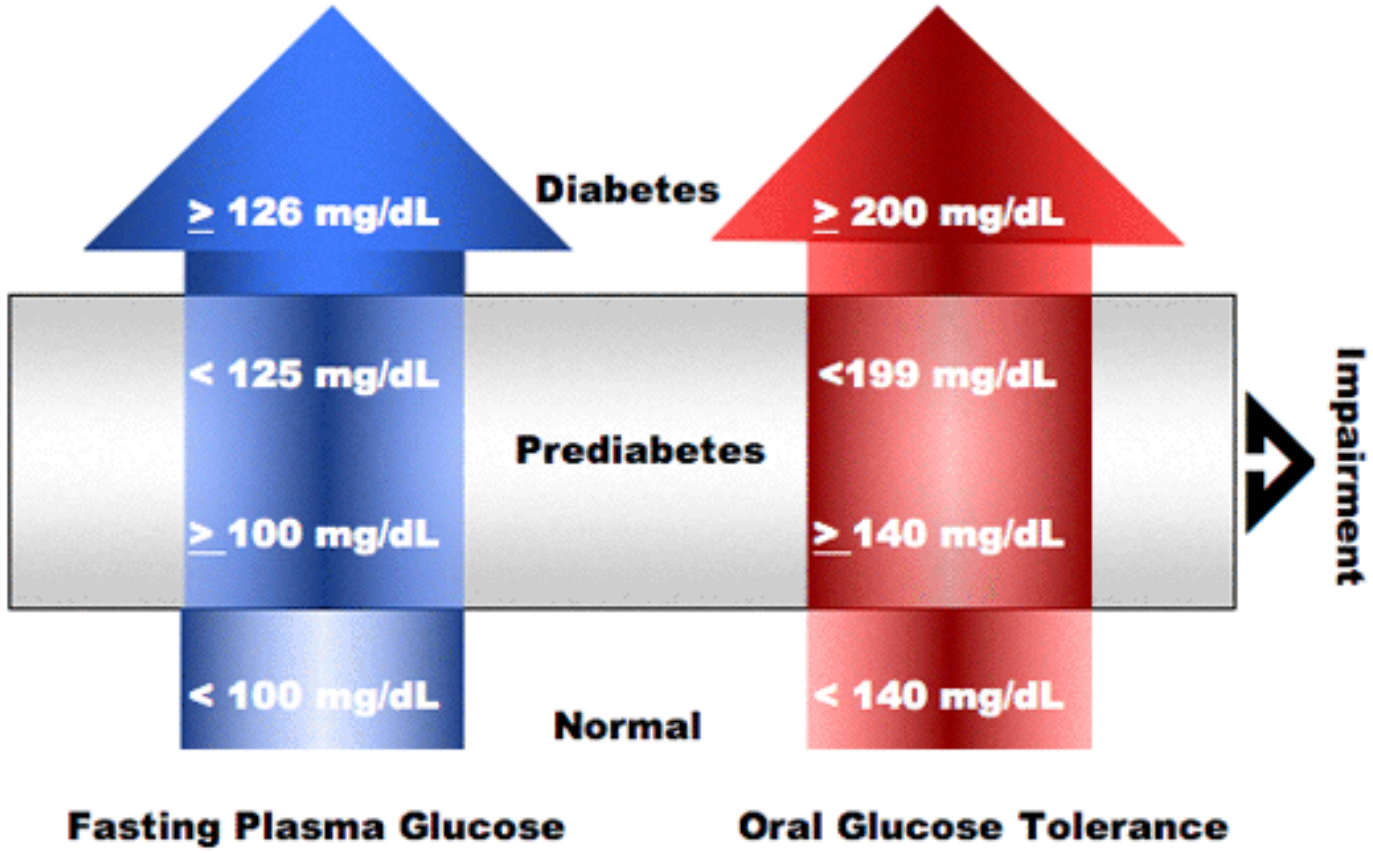
MAJOR RISK FACTORS FOR PREDIABETES

- BMI (weight in kg : height in meters squared) > 25
- Older age
- Physical inactivity
- Unhealthy diet
- Genetic predisposition

IFG

IGT

Categories of Prediabetes



COMPLICATIONS OF PREDIABETES

PREDIABETES TO DIABETES

Progression to Diabetes:

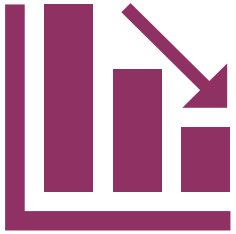
Age of pre-DM onset and higher A1C (6-6.4%)

Cumulative incidence of DM – 31% for IFG during 12 years and 41% for IGT

Higher in individuals with both IGT and IFG

Richter B, Hemmingsen B, Metzendorf MI, Takwoingi Y. Development of type 2 diabetes mellitus in people with intermediate hyperglycaemia. Cochrane Database Syst Rev. 2018

MACRO- AND MICROVASCULAR COMPLICATIONS

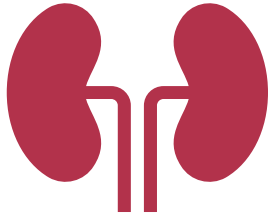


Macrovascular

Higher CVD risk than individuals without prediabetes

Higher rates of hospitalizations

Higher rates of mortality compared to normoglycemia



Microvascular (retinopathy, neuropathy, nephropathy)

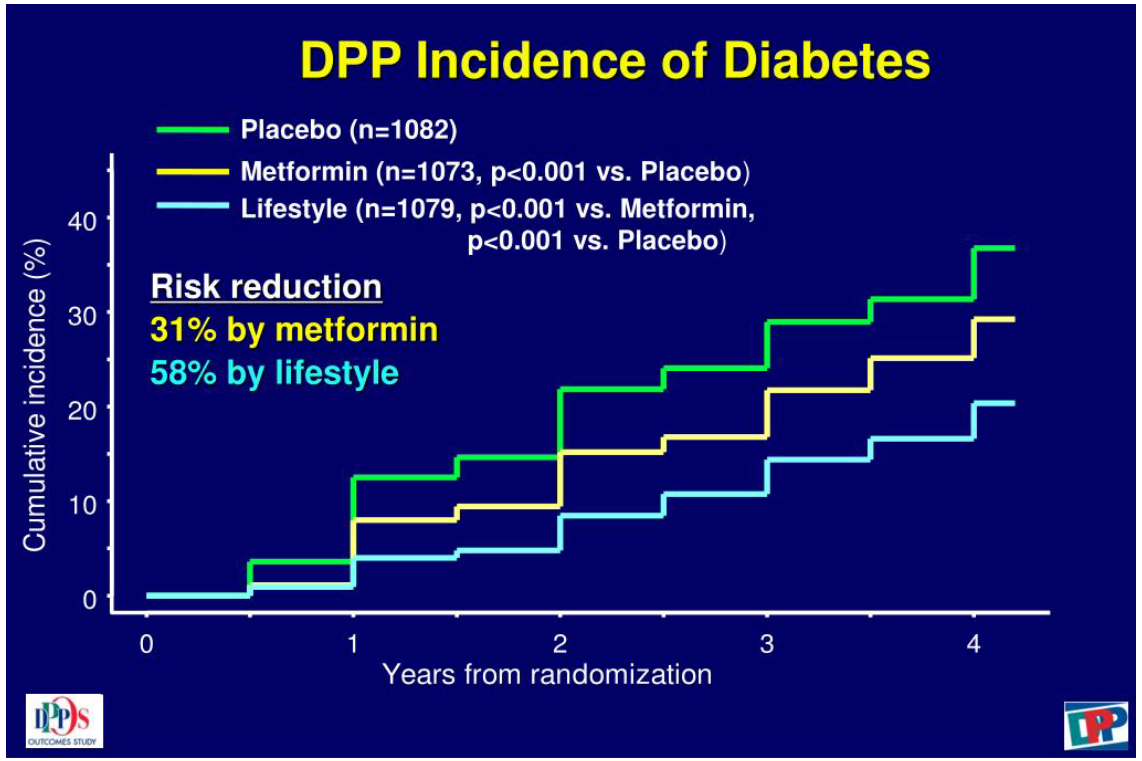
Proportion of patients who have neuropathy 7.5-16%

Retinopathy 7.9% (DPP study)

CKD 9.7%

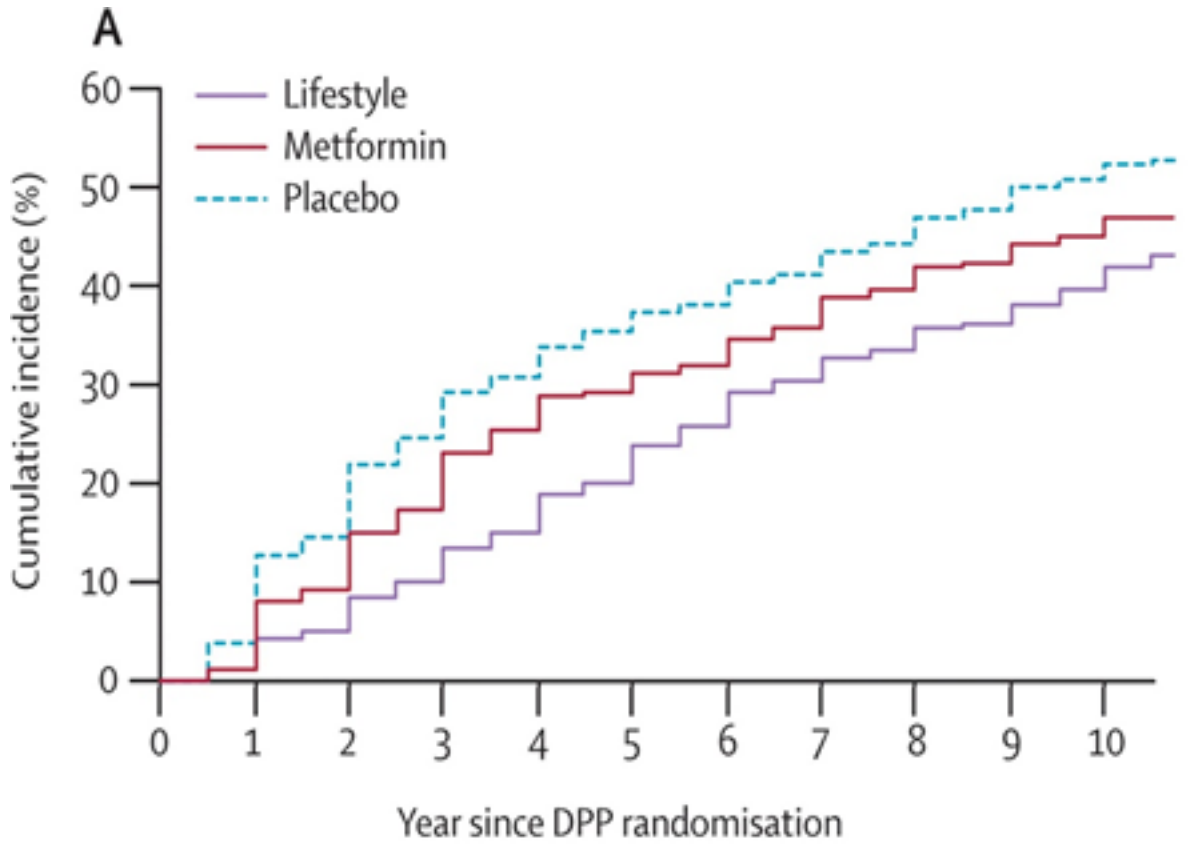
TREATMENT OF PREDIABETES

- **DPP Trial**
- Patients with IGT randomized to:
- Lifestyle modification program: healthy eating and physical activity
  - 16 individual core sessions during the fist 6 months
  - Twice monthly in person maintenance sessions with phone calls in between
- Metformin
- placebo



Knowles et al, NEJM, 2002, Ramachadran et al, Diabetologia 2006

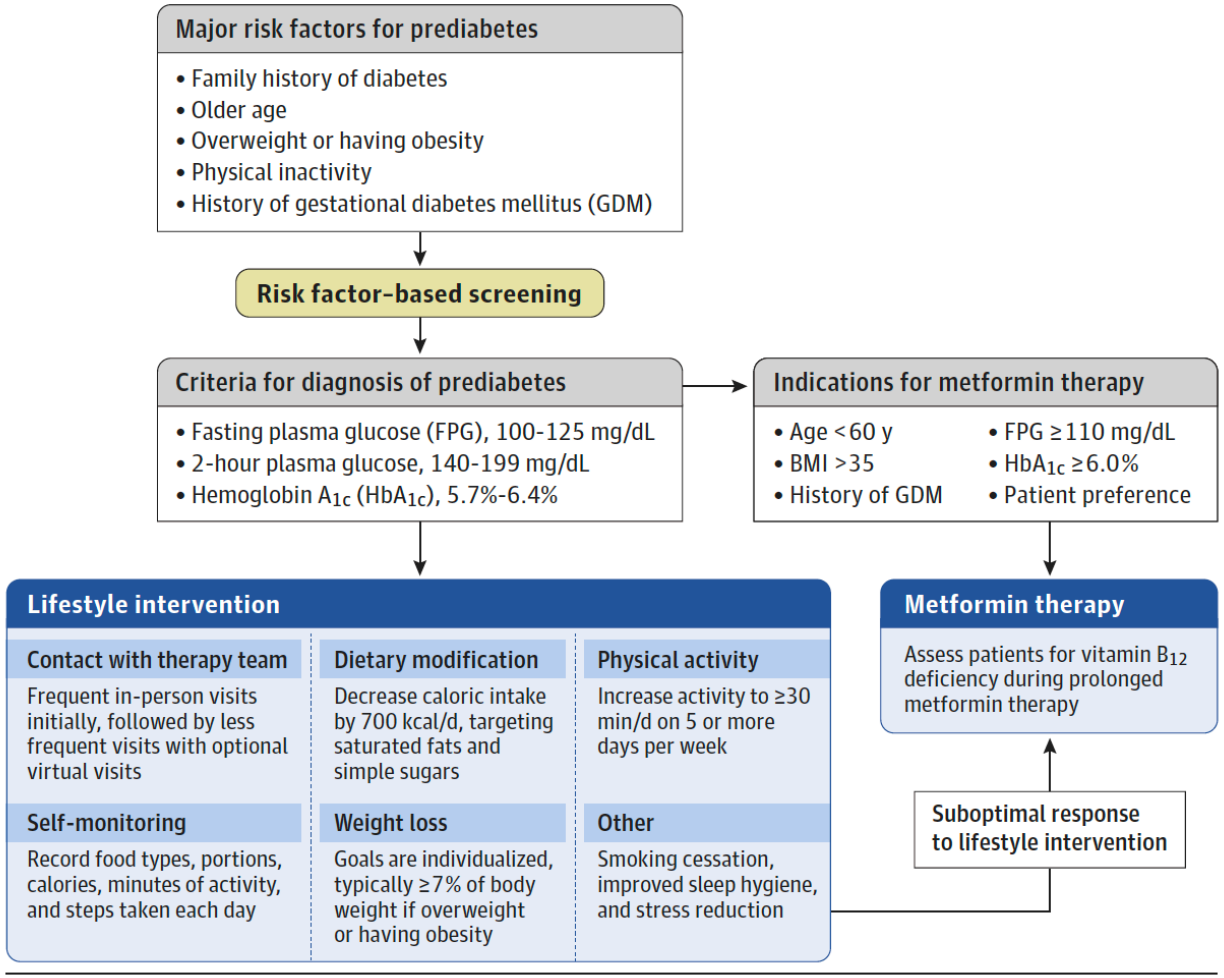
DPP 10 YEARS LATER



10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. The Lancet 2009;374:1677-1686

- **Keyes for success**:
  - Weight loss
  - Reduction in total calories
  - Achieving 150 min of of activity each week

APPROACH TO PREDIABETES



Lifestyle modification is the preferred initial approach after a diagnosis of prediabetes. BMI is calculated as weight in kilograms divided by height in meters squared. This specific algorithm has not been tested in randomized clinical trials.

CONCLUSIONS

- **Prediabetes is associated with increased risk of**:
  - Diabetes
  - Cardiovascular events
  - Mortality
- **First line therapy:**
- Lifestyle modification (largest benefit) with weight loss and exercise
- Metformin