

MODULE 2.2

Prediabetes

Prediabetes is an intermediate form of dysglycemia, defined by measures of impaired glucose control that range from just above normal levels to just below the threshold for outright diabetes.¹ Laboratory assessment values for prediabetes are:

- Hemoglobin A1c (HbA1c), 5.7% to 6.4%; 38.8 mmol/mol to 46.4 mmol/mol
- Fasting plasma glucose (FPG), 100 mg/dL to 125 mg/dL; 5.6 mmol/L to 6.9 mmol/L
- Oral glucose tolerance test (OGTT; 2-hour plasma glucose after 75-g challenge), 140 mg/dL to 199 mg/dL; 7.8 mmol/L to 11.0 mmol/L

In the multistage model of diabetes development, the first abnormality in glucose regulation to occur is insulin resistance, which in turn leads to β -cell dysfunction. Both of these pathological conditions are present before the disease progresses to unstable early decompensation, when glycemic measures of prediabetes first become detectable.²

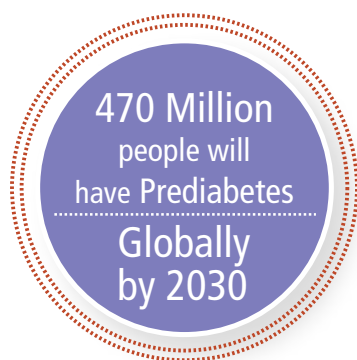
The objective laboratory parameters for prediabetes facilitate identification of individuals who are at increased risk of developing type 2 diabetes. It is estimated that 5%

to 10% of individuals who are prediabetic convert to diabetes each year, and up to 70% develop diabetes within their lifetime.²

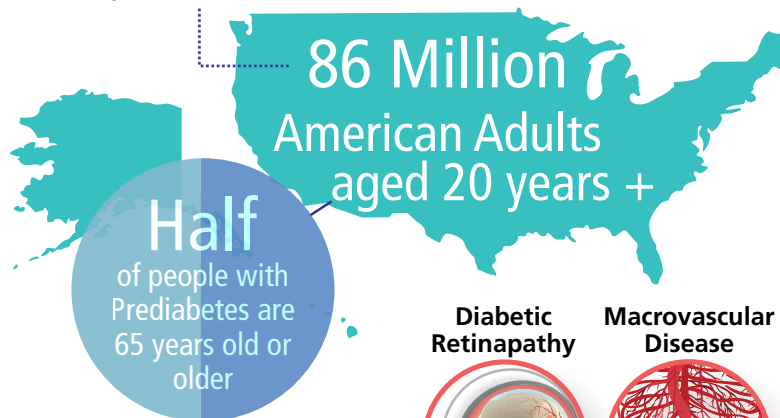
Individuals with prediabetes are also at risk of developing cardiovascular diseases, independent of vascular risk factors such as obesity, hypertension, and hyperlipidemia.² In addition, prediabetes has been associated with early forms of diabetic retinopathy, chronic kidney disease, nephropathy, and small fiber neuropathy.²

The prevalence of prediabetes in the US is significant. Based on the 2009-2012 National Health and Nutrition Examination Survey (NHANES) and the 2010-2012 National Health Interview Survey (NHIS), 37% of all adults aged 20 years or older have prediabetes.³ This translates to 86 million American adults with prediabetes.³ Prevalence is similar between races and ethnicities: 35% of non-Hispanic whites, 39% of non-Hispanic blacks, and 38% of Hispanics have prediabetes. Age prevalence rates are more disparate: 51% of American adults with prediabetes are aged 65 years or older.³

Prediabetes

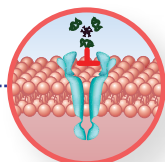


37% of the US has Prediabetes

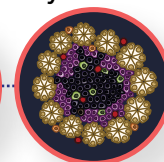


	HbA1C	Fasting Plasma Glucose (mg/dL)	Oral Glucose Tolerance Test (mg/dL)
Diabetes	≥ 6.5	≥ 126	≥ 200
Prediabetes	5.7-6.4	100-125	140-199
Normal	≤ 5.6	≤ 99	≤ 139

Insulin Resistance

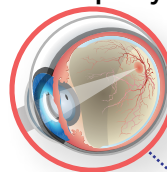


β -cell Dysfunction

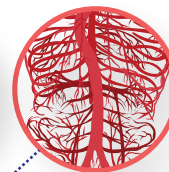


Both of these conditions are present BEFORE the disease becomes detectable by blood tests.

Diabetic Retinopathy



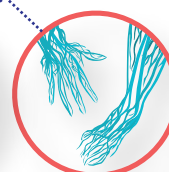
Macrovascular Disease



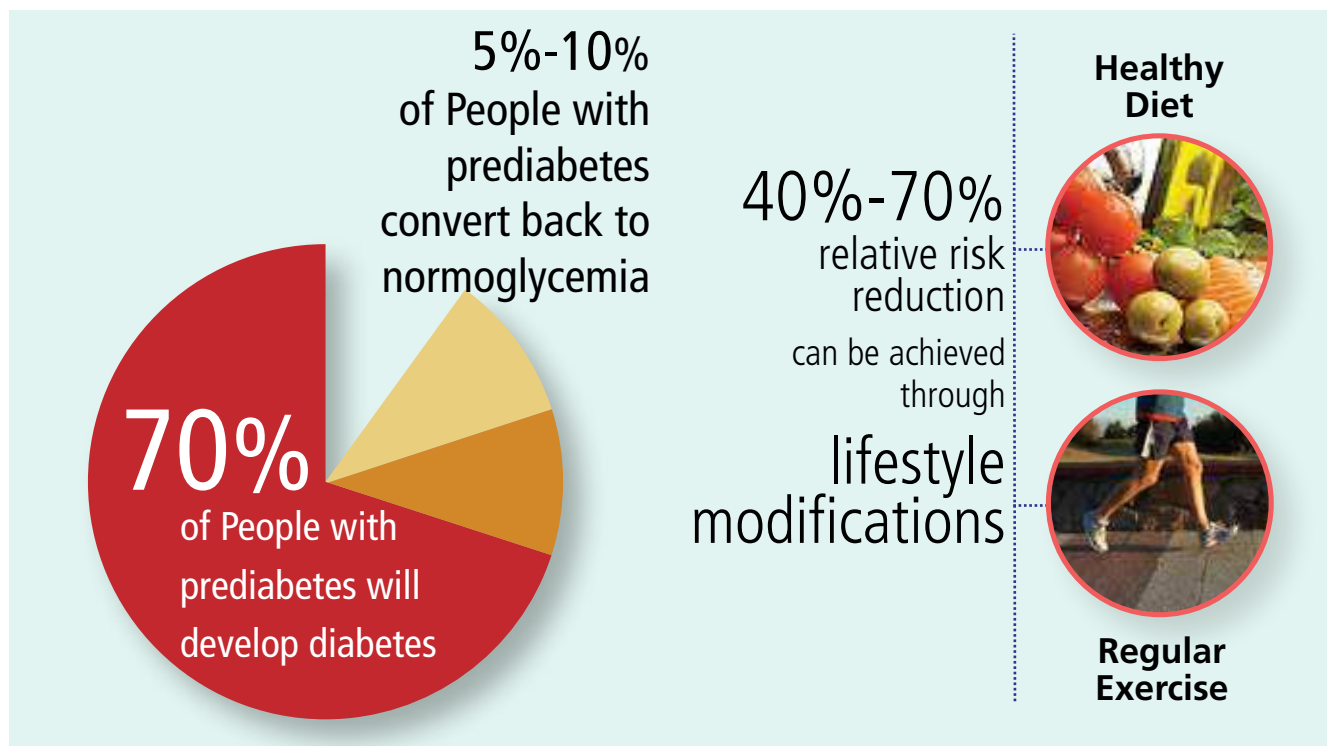
DISEASE ASSOCIATIONS



Nephropathy and Chronic Kidney Disease



Small Fiber Neuropathy



Mean fasting plasma glucose (FPG) levels are rapidly rising in all countries, driving an increase in the global prevalence of prediabetes. A 2008 survey of glycemic control in 2.7 million adults across 199 countries and territories found the mean FPG level worldwide to be 5.5 mmol/L for men and 5.4 mmol/L for women.⁴ This represents a rise in mean FPG of 0.1 mmol/L each decade since 1980.⁴ By 2030, prediabetes is projected to affect more than 470 million people worldwide.²

Approximately 5% to 10% of prediabetics convert back to normoglycemia annually.^{2,5} Normalization of glucose levels may be achieved through lifestyle modifications, or pharmacologic or surgical intervention. Lifestyle modifications can reverse the risk of diabetes for 40% to 70% of individuals with prediabetes and may even improve insulin sensitivity and β -cell function.²

Body weight and physical activity are the two most important modifiable risk factors.² The National Diabetes Prevention

Program addresses these two factors by setting goals for people with prediabetes:

- Reducing body weight by 5% to 7%
- Engaging in physical activity, such as a brisk walk, at least 150 minutes per week

While no pharmacologic intervention is currently approved in the US for the treatment of prediabetes, clinical trials have demonstrated that metformin (a biguanide) and acarbose (an alpha-glucosidase inhibitor) can reduce the risk of prediabetes progressing to diabetes.^{5,2,5} Relative to placebo, treatment with metformin reduced the progression to prediabetes by 25% to 45%,^{7,9} and treatment with acarbose reduced the progression to diabetes by 25% to 40%.¹⁰⁻¹²

References

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