Prediabetes:
A wake-up call

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Abstract: Prediabetes continues to be a national and worldwide health concern, affecting 84 million adults in the US. Early identification and intervention have been successful in delaying and/or preventing the progression to type 2 diabetes mellitus (T2DM). To curb the increasing prevalence of T2DM, recognizing the importance of identifying and managing prediabetes is paramount.

Keywords: diabetes, diabetes prevention, impaired fasting glucose, impaired glucose tolerance, prediabetes, type 2 diabetes mellitus

PREDIABETES CONTINUES to be a national health concern, affecting one in three US adults. Of the estimated 84 million individuals who have prediabetes, only 11% have been officially diagnosed by a healthcare professional.[1-3] Individuals with prediabetes have a 4% to 19% annual risk of progression to type 2 diabetes mellitus (T2DM).[4] Early identification and intervention have been successful in delaying and/or preventing the progression to T2DM.[5] Lifestyle prevention programs are an integral part of prediabetes management, and the addition of pharmacotherapy is appropriate in high-risk patients.[6] In an attempt to curb the increasing prevalence of T2DM, recognizing the importance of identifying and managing prediabetes should remain in the national healthcare forefront.

Epidemiology

The data reporting on prediabetes and diabetes are staggering. Nearly 10% of the US population have diabetes, while 33% have prediabetes.[7] The US is not alone in this problem. The World Health Organization (WHO) reported that approximately 442 million adults around the world lived with diabetes in 2014.[8] Since 1980, the global prevalence of diabetes has almost doubled, which correlates with increasing rates of the most-prominent risks factors: overweight and obesity. Low-to-middle income countries are seeing a greater increase in diabetes prevalence than high-income countries.[8] Social determinants of health (economic, political, and social conditions) are

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directly linked to diabetes-related health inequities as well as the prevention of diabetes.[9]

The National Diabetes Statistics Report sheds light on prediabetes prevalence within the US population.[7] Age-adjusted data indicated that men are affected by prediabetes at a slightly higher rate than women.[7] Adults from racial and ethnic groups have a similar prevalence of prediabetes; however, Asians, non-Hispanic Blacks, and Hispanics have significantly higher rates of diagnosed diabetes compared with non-Hispanic Whites.[7,10] These data are also consistent among minority child and adolescent groups who have higher rates of T2DM than non-Hispanic White pediatric and adolescent groups.[7]

Between 2011 and 2012, over 5,000 children and adolescents ages 10 to 19 years were diagnosed with T2DM.[7] Within the adult population, lower education is linked with higher rates of diabetes.[7] Geographic patterns can also be noted in diabetes incidence and prevalence, with the highest areas being the Southern and Appalachian regions of the US.[7] Geographic data about prediabetes in 2014 illustrate that the disease is widespread (see *Prediabetes in adults across the US, 2014*).[11]

Pathophysiology
Multiple factors, including genetic and environmental, can lead to the development of diabetes. Autoantibodies have been linked with type 1 diabetes mellitus (T1DM). Causative factors of prediabetes and T2DM are less understood but linked to beta cell dysfunction. Pancreatic islet beta cells begin to fail as insufficient insulin secretion occurs, which is confounded as cells become insulin resistant.[12] Hyperglycemia is the clinical manifestation of beta cell dysfunction and demise.[9] Although the progression to T2DM is variable, patients are at risk for developing chronic complications when hyperglycemia begins to occur. Classification of prediabetes and diabetes is indicated related to the glucose state. For the purposes of this article, prediabetes will include the presence of impaired fasting glucose (IFG) or impaired glucose tolerance (IGT).

Prevention
Prediabetes is considered a preventable disease.[8] Unlike T1DM, prediabetes itself is known to be preventable, and progression to

Prediabetes in adults across the US, 2014

Percentage	
	3.8 - 4.9
	5 - 5.6
	5.7 - 6.4
	6.5 - 7.8
	7.9 - 14.1
	No Data

Source: Centers for Disease Control and Prevention. Prediabetes, age-adjusted percentage, adults aged 18+ years - U.S. states, 2014. iwww.cdc.gov/diabetes/data.
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T2DM can be delayed through modest weight loss and increasing physical activity.[6] Prevention is important at the individual level as well as in terms of population-based health.[8] Societal policies including agricultural trade, urban planning, health education, and even transportation can impact prevention.[8] Ultimately, prevention of prediabetes needs to encompass aims to reduce risk factors, including obesity, physical inactivity, and an unhealthy diet.[8]

Strong evidence has come from the Diabetes Prevention Program (DPP), which is sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases. The DPP resulted in a notable 58% reduction in T2DM at year 3 in the study for participants who were following an intensive lifestyle program.[13] Goals for participants were weight loss of 5% or greater, 30 minutes per day of brisk physical activity, reduction of daily fat intake to less than 30%, reduction of daily saturated fat intake to less than 10%, and a minimum daily fiber consumption of 15 g per 1,000 kcal.[14]

A trained group leader taught 16 sessions that included physical activity, reducing calorie intake, self-monitoring, social influences, and psychological challenges. Sustained benefits are evident from such programs; DPP lifestyle change participants had the most robust delay of diabetes development by 27% compared with a placebo group at the 15-year follow-up conducted by the DPP Outcomes Study.[5] Participants age 60 and older performed well, reducing the risk of developing T2DM by 71%.[6]

Collaboration between clinicians, nurses, and patients for decision-making is important in diabetes prevention. Shared decision-making is the process in which clinicians work with patients to select care plans rooted in clinical evidence that are considerate of patient preferences, abilities, and values.[15] This form of decision-making is invaluable when discussing diabetes-related care because treatment can impact multiple components of daily living.[15] A 2018 study tested the effectiveness of shared decision-making interventions with patients with prediabetes and their clinicians and had positive results.[16] Patients with prediabetes (A1C 5.7% to 6.4%) met in person with a pharmacist and, using shared decision-making, chose to either initiate a DPP lifestyle change course and/or take metformin or continue with usual care.

At 12 months, all patients in the shared decision-making intervention group had greater weight loss than the control group (−5.2 lb [2.35 kg] compared with −0.29 lb [0.13 kg]).[16] Forty-three percent of patients in the intervention group used the DPP and/or metformin compared with only 3% of matched control group.[16] The study provides evidence that shared decision-making not only increases patient engagement of evidence-based therapies for diabetes prevention but also promotes increased weight loss after 12 months.[16]

The National DPP is a partnership of public and private organizations aimed at preventing or delaying progression to T2DM.[17] These partnerships offer evidence-based, affordable lifestyle modification programs to help participants reduce their risk of developing T2DM. Federal agencies, health departments, community organizations, employers, public and private insurers, healthcare professionals, and businesses can partner with the National DPP.[17]

Population-based approaches reduce modifiable risk factors among the general population. Although no single policy can prevent diabetes,

Criteria for testing for diabetes or prediabetes in asymptomatic adults

1. Testing should be considered in overweight or obese (body mass index [BMI] ≥25 kg/m² or ≥23 kg/m² in Asian Americans) adults who have one or more of the following risk factors:
   - first-degree relative with diabetes
   - high-risk race/ethnicity (African American, Latino, Native American, Asian American, Pacific Islander)
   - history of cardiovascular disease
   - hypertension (≥140/90 mm Hg or on therapy for hypertension)
   - high-density lipoprotein cholesterol level <35mg/dL and/or a triglyceride level >250 mg/dL
   - women with polycystic ovary syndrome
   - physical inactivity
   - other clinical conditions associated with insulin resistance (severe obesity, acanthosis nigricans).
2. Patients with prediabetes (A1C ≥5.7% [39 mmol/mol], IGT or IFG) should be tested yearly.
3. Women who were diagnosed with gestational diabetes mellitus (GDM) should have lifelong testing at least every 3 years.
4. For all other patients, testing should begin at age 45.
5. 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 and risk status.

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legislation, environmental changes, and a heightened awareness of health impact can help promote healthier lifestyles.[8] Improving childhood nutrition and maternal health during pregnancy and breastfeeding can help create a healthy foundation for optimal growth during childhood and adolescence. Support for breastfeeding exclusively until age 6 months; introducing nutritious foods; avoiding foods that are high in fat, sugar, and sodium; and encouraging physical activity are early childhood interventions that have been shown to be beneficial in preventing prediabetes and diabetes.[3]

Physical environments play an important role in promoting physical activity. Urban planning strategies can promote safe and active transport accessibility. Physical environments that offer safe space for sports, recreation, and leisure activities promote active living for families.[8] Regulatory measures also play a role in promoting healthful diets. According to the WHO, initiating fiscal policies to increase the price of foods high in sugars and fats can decrease consumption.[8] Trade measures aimed to

reduce the availability of unhealthy foods can decrease access and are effective in helping change consump-

tion patterns.[8] Agricultural subsidies can also encourage increases in fruit and vegetable production. Emerging evidence supports fiscal and action policies to promote healthier foods.[8] Improving population health is multifactorial and an integral part of reducing prediabetes.

Nurses have evidence to follow when counseling patients on managing prediabetes. Weight loss is the most important component of treatment for patients with prediabetes.[12] A 7% weight loss can have significant positive impact.[13] At least 150 minutes of physical activity per week should be achieved.[11] Remind patients that brisk physical activities such as gardening, playing sports, or doing household chores can be beneficial in preventing disease and that these activities can be counted toward the recommended 150 minutes weekly of physical activity.[14]

Evidence supports that, in addition to reducing calories, the quality of fats is of greater benefit than dietary quantity. Diets high in monounsaturated fats, such as the Mediterranean diet, may reduce the risk of T2DM.[18] Diets high in nuts, berries, yogurt, coffee, and tea also reduce the risk of T2DM.[12] Along with dietary modifications and increasing physical activity, mobile applications for weight loss and diabetes prevention have been shown to be useful in improving A1C results in patients with prediabetes.[19]

Screening and diagnosis

Children, adolescents, and adults should be screened for prediabetes with informal assessment of risk factors or assessment tools. The American Diabetes Association (ADA) offers assessment risk tests to help clinicians determine if a diagnostic study is appropriate for early detection.[9] Prediabetes is often asymptomatic, increasing the importance of astute clinician

Weight loss is the most important component of treatment for patients with prediabetes.

Risk-based screening for T2DM or prediabetes in asymptomatic children and adolescents in a clinical setting*

Criteria

Overweight (BMI >85th percentile for age and sex, weight for height >85th percentile, or weight >120% of ideal for height) **A****

Plus one or more additional risk factors based on the strength of their association with diabetes as indicated by evidence grades:

- maternal history of diabetes or GDM during child's gestation **A**
- family history of T2DM in first- or second-degree relative **A**
- race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander) **A**
- signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, small-for-gestational-age birth weight). **B**

* Persons ages <18 years.
** ADA evidence-grading system: Level A = Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered; Level B = Supportive evidence from well-conducted cohort studies.

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screening. Physical assessment findings of the dermatologic condition acanthosis nigricans should increase suspicion of prediabetes or diabetes and requires additional workup.[20] The ADA offers clear criteria for prediabetes or diabetes testing in asymptomatic adults (see *Criteria for testing for diabetes or prediabetes in asymptomatic adults* and *Risk-based screening for T2DM or prediabetes in asymptomatic children and adolescents in a clinical setting*).

When the decision to screen for prediabetes has been made, there are three test options. Fasting plasma glucose (FPG) levels between 100 and 125 mg/dL identify IFG. An oral glucose tolerance test using a 75 g oral glucose load with 2-hour plasma glucose (PG) results between 140 mg/dL and 199 mg/dL identifies IGT. Finally, A1C results between 5.7% and 6.4% indicate prediabetes.[9] (See *Categories of increased risk for diabetes [prediabetes criteria]*.)

Although debate surrounds the use of A1C to diagnose children, the ADA continues to recommend its use, although recognizing its limits is important. Children with hemoglobinopathies, cystic fibrosis, or suspected T1DM should not be screened using the A1C method.[9] The American College of Endocrinology and the American Association of Clinical Endocrinologists include IGT, IFG, and metabolic syndrome for the diagnosis of prediabetes; any of the aforementioned diagnoses increase future T2DM risk fivefold.[21]

Treatment
The diagnosis and subsequent treatment of prediabetes should not be considered an isolated clinical disorder but should instead be viewed as an opportunity to reduce the future risk of diabetes and associated cardiovascular disease.[9] The root cause of prediabetes is most often over-

weight or obesity; subsequently, the main goal of prediabetes treatment is weight loss. As body weight decreases, decreases can also be noted in insulin resistance, lipid profile, and BP. Lifestyle therapy alone or combined with pharmacotherapy and/or bariatric surgery leading to weight loss can slow or halt the progression to T2DM.[12]

Currently, no pharmacologic agents are approved by the FDA for prediabetes management.[9] Positive results have been seen with the antihyperglycemic medications metformin and acarbose.[12,22] These medications are well tolerated, safe, and effective at reducing the risk of developing diabetes by up to 30% with a potential to reduce cardiovascular risk.[12] Metformin use in prediabetes is backed by strong evidence, demonstrating cost savings over a 10-year span compared with placebo.[23] Monitor patients for vitamin B12 deficiency with long-term metformin use.[9]

Thiazolidinediones were effective in preventing progression in up to 75% of patients with prediabetes; however, this class of medications can cause numerous adverse reactions, including weight gain, water retention, and worsening heart failure in patients with preexisting heart disease.[12] Glucagon-like peptide 1 receptor agonists have shown prom-

ising results in restoring normoglycemia in patients with prediabetes.[9] With the current lack of long-term safety data, these agents should be reserved for patients at the greatest risk of developing T2DM who are unsuccessful with other treatment modalities.

Patients affected by prediabetes are also at increased risk for atherosclerotic cardiovascular disease. As with patients with diabetes, patients with prediabetes should be counseled on lifestyle modifications and/or pharmacotherapy to achieve BP and lipid profile goals that reduce the risk of atherosclerotic cardiovascular disease.[12]

Emphasis on prevention
Prediabetes is a modifiable and largely preventable precursor to T2DM. Prediabetes and T2DM are global health concerns, affecting children, adolescents, and adults. Preventing prediabetes requires a comprehensive life course approach that includes healthy eating, physical activity, and policy approaches that support active living in safe environments and access to affordable healthy foods. Nonpharmacologic and pharmacologic interventions can have lasting impacts in treating prediabetes and preventing or delaying progression to T2DM. Multicomponent care of

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Categories of increased risk for diabetes (prediabetes criteria)*

FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG)

OR

2-h PG during 75-g oral glucose tolerance test 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT)

OR

A1C 5.7–6.4% (39–47 mmol/mol)

*For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at the higher end of the range.

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prediabetes can make a difference in reducing the incidence of diabetes and improving the lives of those affected. ■

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