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A Call to Action on Prediabetes

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Abstract

Diabetes and prediabetes have become an American epidemic. The key to battling this public health challenge is to utilize an effective screening program and engage known evidence based interventions. Fortunately there are robust studies showing that intensive lifestyle interventions, medications and weight loss surgery all can reduce or delay new onset type 2 diabetes. This article will review the steps that physician assistants (PAs) can do to stay ahead of this disease.

Introduction

Prediabetes affects approximately 86 million American adults (1). According to the Centers for Disease Control and Prevention (CDC), nearly 90% of individuals with prediabetes do not know they have prediabetes (1). Up to 70% with prediabetes eventually go on to develop type 2 diabetes mellitus (T2DM) with progression taking as little as 5 years (2). Prediabetes is a substantial cardiac risk predictor with reversible aspects related to diet and lifestyle alterations. A recent metanalysis published in 2016 with over 1.6 million patients demonstrated an increased risk of cardiovascular disease including myocardial infarction and cerebrovascular disease (3). Other complications associated with T2DM including retinopathy can occur in prediabetes but the severity tends to be more mild (4).

The American Diabetes Association (ADA) and CDC both have screening tools which can help identify individuals at highest risk (5,6). Risk factors for prediabetes includes: age over 45 years, male, obesity, hypertension, dyslipidemia, family history of diabetes, history of gestational diabetes, and ethnicity (Hispanic, African American, Asian) (1). Modifiable risk factors such as poor dietary habits and inactivity further contribute to prediabetes and T2DM.

The cornerstone of treatment involves therapeutic lifestyles including a healthy diet, physical activity, and loss of excess weight. There is strong evidence that the progression from prediabetes to T2DM can be delayed or prevented. Evidence-based programs such as the National Diabetes Prevention Program (DPP) have been shown to reduce the risk of progression by 58% with lifestyle interventions (7). There is also evidence that some medications and weight loss surgeries can reduce this progression (7-11).

This paper will help PAs recognize the risk factors for prediabetes and develop screening mechanisms that will allow early intervention for this at risk population. The review will include lifestyle interventions, medications and surgical interventions to share best practices for the primary care PA.

Screening Tools for Prediabetes

Two widely used screening tests to identify people at risk for prediabetes and type 2 diabetes include the ADA and CDC screening tools (5,6). The CDC's website contains a validated prediabetes screening test (Table 1). Individuals with a score of 9 or more points should be receive biochemical screening for prediabetes/type 2 diabetes via one or more of the following: fasting blood glucose, hemoglobin A1c, or an oral glucose tolerance test.

The ADA has also has a validated prediabetes/diabetes screening test (5). This test was updated in the 2017 ADA's Standards of Medical Care in Diabetes. As depicted in Table 2, the "Diabetes Risk Test" bears a few notable differences from the CDC's "Prediabetes Screening Test", including differences in questions, and scoring. This test is also indicated to screen for asymptomatic patients with previously undiagnosed T2DM . When using the ADA's 2017 Diabetes Risk Test, individuals with a score of 5 or higher are recommended to complete blood testing for prediabetes. Blood tests include fasting blood glucose, oral glucose tolerance testing (OGTT), and A1C.

Screening recommendations

Risk factors for screening for prediabetes are similar as T2DM. Both the ADA and CDC screening tests include risk factors for developing prediabetes and T2DM. Tables 3 and 4 demonstrate the ADA recommendations for screening in asymptomatic adults and children/adolescents, and the associated risk factors for developing prediabetes and diabetes.

In contrast to the ADA, the USPSTF has a set of less specific recommendations for abnormal glucose and diabetes screening. The USPSTF recommends, "screening in adults aged 40-70 years who are overweight or obese" with a B grade recommendation (3). Table 5 depicts the USPSTF recommendation with the additional screening of individuals at higher risk. Thus, the USPSTF recommendation for clinicians is to consider other risk factors when considering screening among asymptomatic individuals outside of the 40-70 year age range and to "offer to refer patients with abnormal blood glucose to intensive behavioral counseling interventions to promote a healthful diet and physical activity." (13)

Diagnostic Tests

After initial screening tests are performed, the ADA, USPSTF, and CDC recommend further testing for individuals at high risk of developing prediabetes. Fasting blood glucose, hemoglobin A1C, and oral glucose tolerance test with a 75-mL glucose solution are all options as first line screening tests for diagnosis of diabetes and prediabetes. (12,13). Table 6 below depicts the accepted values for diabetes and prediabetes diagnosis established by the ADA. Many providers prefer A1c due to the convenience of the test since it does not require fasting.

In a large prospective study of over 18,000 patients, hemoglobin A1c based testing was the most specific for diagnosing prediabetes (15). From a standpoint of limiting long-term complications and mortality related to T2DM, using hemoglobin A1c may yield better risk discrimination for comorbidities such as chronic kidney disease, cardiovascular disease, peripheral artery disease, and all-cause mortality versus fasting glucose concentration-based definitions ($p < 0.05$). This increase in risk discrimination for clinical complications should be considered when performing diagnostic testing to screen individuals for prediabetes.

Lifestyle Interventions

Lifestyle modification is a fundamental aspect of prediabetes management, and includes healthy nutrition, increased activity, and if applicable, smoking cessation counseling. Weight management is important in those with prediabetes who are overweight or obese. Weight loss among individuals can delay the progression from prediabetes to type 2 diabetes (14,15). The ADA recommends a combination of activity and diet modification to attain moderate persistent weight loss in which reducing calorie intake is paramount. While the ADA does not endorse a “best diet,” the Mediterranean, DASH, and plant-based diets are all acceptable to achieve moderate weight loss among individuals with prediabetes. (12) Foods rich in sugar, including sugar sweetened beverages and candy should be avoided as they often replace healthy, more nutrient-dense food choices. (12) Rather, carbohydrates intake should consist of vegetables, whole grains, fruits, legumes and dairy products. Healthy food choices should be encouraged, and portion control is necessary in the nutritional aspect of lifestyle modification. New studies have found that diets rich in whole grains, nuts, berries, yogurt, coffee and tea are associated with reduced diabetes risk (12).

Physical activity is encouraged to maintain significant weight loss and prevent the progression from prediabetes to type 2 diabetes. The U.S. Department of Health and Human Services, American Diabetes Association, and the American College of Sports Medicine physical activity guidelines for Americans suggest that adults over the age of 18 years should engage in a minimum of 150 min/week of moderate-intensity, or 75 min/week of vigorous-intensity aerobic physical activity as a general health measure. Additionally, adults are encouraged to participate in muscle-strengthening activities involving major muscle groups 2 or more times per week. (17) For individuals over the age of 65, disabled, or who may be otherwise unable to perform strenuous activities, any physical activity that low impact physical activity is encouraged. Avoiding sedentary periods may also help to prevent the progression prediabetes to type 2 diabetes and improve glycemic control among individuals at risk (12). Individuals should be encouraged to break up sedentary periods with activity every 30 minutes consisting of standing, walking, stretching or other light physical activity (17). Based on these findings, the ADA recommends an intensive

behavioral style intervention program modeled on the National Diabetes Prevention Program (DPP) that encompasses many of the above characteristics effectively allowing patients to lose and maintain a 7% weight loss over the course of one year (12).

National Diabetes Prevention Program

The Diabetes Prevention Program (DPP) study aimed to determine the most effective method of preventing progression to type 2 diabetes: a lifestyle change intervention, metformin compared to routine care. The DPP lifestyle intervention focused on improving diet choices, reducing calories from fat, increasing physical activity to a minimum of 150 minutes per week, and an overall 7% weight loss goal for each participant. Results demonstrated the intensive lifestyle intervention group had a reduced incidence of type 2 diabetes by 58%, and metformin group by 31%, as compared to the placebo group with 17% after 2.8 years of data collection (7). A 10-year follow up study showed the original lifestyle intervention group had a continued decreased incidence of diabetes by 34%, and the metformin group had a decreased incidence by 18% (18). This showed that even participants discontinued healthy lifestyle modifications, lasting health benefits remained from the initial intervention.

The DPP is a well-validated community based program modeled after the DPP study but simplified for community implementation. The DPP program has a duration of 1 year consisting of at least 16 sessions over the first 6 months followed by at least monthly sessions in the second 6 months. The curriculum details sessions to take place weekly initially, transitioning to monthly at the midpoint of the program. The goals of DPP mirrors those of the DPP study and focuses on reducing caloric intake by reducing fat intake, and increasing physical activity to a goal of at least 150 minutes per week and striving for > 7% weight loss by the end of the program (19). By creating a constant, regular, and supportive group environment, DPP helps participants continuously healthy lifestyle choices and provides peer support on the journey to prevent diabetes. One of the DPPs main goals is for participants to apply the knowledge acquired from the DPP to successfully lead a healthier lifestyle.

To qualify for participation in the program, participants must have:

- BMI of at least 24 (or at least 22 if self-identified as Asian)
- *Plus* presence of 1 of 3 of the following blood glucose tests:
 - Hemoglobin A1c test with a value between 5.7 and 6.4%
 - Fasting plasma glucose of 100-125 mg/dL
 - 2-hour post glucose of 140-199 mg/dL (after 75gm glucose load)
- No previous diagnosis of type 1 or type 2 diabetes (note: gestational diabetes is okay)

- Exclusion criteria: Current diagnosis of diabetes or current insulin use or end stage renal disease

All fully recognized DPP programs are led by CDC certified lifestyle coaches and follow the CDC approved curriculum. In order to maintain full recognition, programs must meet the requirements put forth by the CDC, and undergo yearly evaluations early in the recognition process to ensure that programs meet all pertinent requirements.

The DPP is now covered under some insurance plans. However, in 2018 (estimated April 1, 2018) Medicare will provide the DPP as a mandated covered service. The payment for this will be based upon quality measures including weight loss goals are achieved, the patient may qualify for ongoing maintenance sessions of DPP based on their insurance. Many insurance companies, including Medicare, will cover the Diabetes Prevention Program, but individual copays and deductibles may still apply.

Medical Interventions for Prediabetes

Pharmacologic therapy has proven effective in the prevention or delay of type 2 diabetes as well. The ADA recommends (12) pharmacologic therapy to treat prediabetes for those with:

- BMI ≥ 35 kg/m²
- < 60 years old
- Past medical history of gestational diabetes
- Increasing A1C levels despite lifestyle intervention
- A1c > 6.0%

Metformin has shown the strongest evidence for the prevention of diabetes with the best long-term safety profile when compared with other agents (19). Despite its proven efficacy and safety profile, one study has shown metformin is rarely prescribed among working-age adults with prediabetes (20). It is not clear why metformin is not used more often, but we recommend PAs utilize metformin first-line in patients with prediabetes.

Aside from metformin, other anti-diabetes medications may be helpful in the treatment of diabetes. Acarbose, an alpha glucosidase enzyme inhibitor, has also proven effective in return of impaired glucose tolerance to normal glucose tolerance among individuals with prediabetes (21). However, this treatment can be poorly tolerated due to its gastrointestinal side effects. Both metformin and acarbose may also provide additional cardiovascular benefit for individuals with prediabetes and type 2 diabetes who are overweight or obese (22).

Studies have also shown orlistat (Xenical, Alli), a lipase inhibitor, was shown to decrease glucose levels among obese patients with impaired glucose tolerance (10).

Available over-the-counter under the brand name Alli, this medication has limited use due to its poorly tolerated gastrointestinal side effects experienced by some patients.

Other medications such as glucagon-like peptide 1 (GLP-1) receptor agonists (23) and thiazolidinediones may also be helpful in the treatment of prediabetes; however, their high cost may be a limiting factor in their use (9). Other weight loss medications including phentermine-topiramate have been shown to produce significant weight loss and reduce progression to type 2 diabetes in overweight/obese patients (24).

In an ethnically diverse study population, bariatric surgery resulted in significant long-term weight loss and fasting plasma glucose levels over a three year post-operative period (11). A recent study conducted in Sweden found that bariatric surgery greatly reduced the risk of microvascular complications among prediabetic patients at baseline (25). Though this study suggests efficacy of bariatric surgery in the risk reduction among prediabetic patients, the study does not endorse the use of bariatric surgery for the treatment of prediabetes; rather, it emphasizes the need for development of aggressive non-surgical treatments to aid in risk reduction among these at risk patients. While there is not an exact recommendation by the ADA for bariatric surgery in prediabetes, well-controlled individuals with T2DM and a BMI ≥ 40 kg/m² should be considered for this intervention (12). There is good evidence that bariatric surgery can prevent the progression of diabetes in patients with prediabetes (26).

It is important to remember that people with prediabetes have an increased Cardiovascular and complication risk. This is highlighted by the fact that 30% of people will already have a diabetes related complication at the initial diagnosis of type 2 diabetes. The ADA recommends vigilance in screening and treatment for cardiovascular disease among patients with prediabetes. Individuals in this at risk group often have hypertension and/or dyslipidemia and are at increased risk for cardiovascular disease, thus emphasizing the importance of early screening and treatment of CVD among these patients. (12).

Conclusion

PAs have an opportunity to address the public health epidemic of diabetes and prediabetes. PAs should identify options for lifestyle modification including NDPP in their area. If there are no NDPP cohorts locally, the authors recommend that the PA consider becoming a certified lifestyle coach through the CDC. In addition to lifestyle modification options, it is reasonable to initiate pharmacologic treatment. Metformin is the preferred medication for prediabetes, though other classes of medications may be tried, their side effects, cost and efficacy may vary (12). Bariatric surgery is another option for individuals and may provide the longest lasting effect, though it is much more invasive than pharmacologic treatments.

Screening for T2DM is key to preventing the associated comorbidities and complications associated with T2DM. PAs should consider following the American Medical

Association's campaign Prevent Diabetes STAT by (1) using the CDC's prediabetes screening test, (2) test glucose, and (4) refer to individuals with prediabetes to a diabetes prevention program (27).

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