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Review Article

Prediabetes Risk Factors and Management in Primary Health Care

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Abstract

Prediabetes is an intermediate metabolic state between normal plasma glucose and hyperglycemia that is below the diabetes mellitus (DM) threshold. While there are different proposed diagnostic criteria for prediabetes, this condition remains a state of high risk for progression to DM. For that, we performed an extensive literature search of the Medline, Cochrane, and EMBASE using the medical subject headings (MeSH) terms. Papers discussing prediabetes risk factors and management in primary health care; were screened for relevant information. There were no limits on date, language, age of participants or publication type. There are many risk factors to prediabetes reported in the literature. Risk assessment through the use of various risk scoring systems has been recently given more attention with more than one risk score system to detect those with prediabetes without laboratory need. These tools are easily-applicable, cost-effective, and highly effective. The management of prediabetes includes lifestyle modifications and pharmacological treatment. Lifestyle modifications are considered the first line of management in a case of prediabetes, showing a significant reduction in the risk of developing DM. However, there is no clear evidence regarding the efficacy of the pharmacological approach in preventing DM in adults with prediabetes. Metformin is a commonly used drug, while the use of other treatment options has been limited due to the associated adverse effects. Choosing the appropriate management approach should always follow a risk assessment process to determine which line of treatment will result in the best outcomes. Based on the controversies and variability regarding the definition, risk factors, risk assessment, and management, we aimed to conduct the current review to report all of the challenges associated with the various aspects of prediabetes as well as to report all the treatment options and the rationale for their use in the context of prediabetes.

Keywords: *Prediabetes; Risk Factors; Management; Primary Health Care*

Introduction

Prediabetes is commonly referred to as a metabolic condition, in which plasma glucose levels are higher than normal but lower than the diagnostic threshold of diabetes mellitus (DM). It includes impaired fasting plasma glucose (IFG), or impaired plasma glucose tolerance (IGT), or both. Based on the proposed diagnostic criteria of the American Diabetes Association (ADA), prediabetes was defined as

impaired fasting glucose, when fasting plasma glucose (FPG) value lies between 100 and 125 mg/dL and impaired glucose tolerance, when 2-hour plasma glucose value following an oral glucose tolerance test (OGTT) lies between 140 and 199 mg/dL [1]. Currently, there are 318 million individuals around the world diagnosed with prediabetes, while around 69.2% of the prediabetes population living in low- to middle-income countries [2].

A national urban diabetes survey study reported a prevalence rate of diabetes and impaired glucose tolerance of 12.1% and 14%, respectively [3]. Individuals with prediabetes, have a higher risk of development and progression to diabetes [4]. Till the current time, there is no clear understanding among primary healthcare practitioners and professional regarding this condition, and consequently, a lack of evaluation of this potentially-critical metabolic state [5]. Therefore, we conduct this investigation in order to review the available literature on the recent diagnosis criteria, risk factors, risk assessment scoring systems, and management of prediabetes.

Methods

We performed an extensive literature search of the Medline, Cochrane, and EMBASE databases on 13 December 2019 using the medical subject headings (MeSH) terms. Papers discussing prediabetes risk factors and management in primary health care; were screened for relevant information. There were no limits on date, language, age of participants or publication type.

Definition and diagnostic approach of prediabetes

Prediabetes often refers to an intermediate metabolic phase between normal glucose homeostasis and T2DM. In 2016, the American Diabetes Association (ADA) stated the three diagnostic criteria for prediabetes through the measurement of venous blood glucose levels: 1) impaired fasting plasma glucose (IFG) values between 100 and 125 mg/dL following at least 8 hours of fasting; 2) impaired plasma glucose tolerance (IGT) when blood glycemic values lie between 140 and 199 mg/dL two hours' following oral glucose tolerance test (OGTT) through the administration of oral glucose load of 75g; 3) glycosylated hemoglobin (HbA1c) level lies between 5.7% and 6.4% [6]. On the other hand, the diagnostic criteria proposed by the World Health Organization (WHO) is a little different. They defined prediabetes based on two specific parameters: 1) IFG, defined as fasting plasma glucose (FPG) of 110 to 125 mg/dL; 2) IGT, defined as 2-hour plasma glucose 140 - 200 mg/dL following the ingestion of 75g of oral glucose load or a combination of both based on a 2 hour-OGTT [7].

That being said, these cut-off points further lose their credibility due to poor reproducibility of such tests in the adult and pediatric populations [8,9]. Even though HbA1c is perceived as a representative of the average blood glucose level and should ideally represent hyperglycemia more accurately, this might not be entirely true. Various reports have noted that HbA1c is substantially determined by genetic factors that are independent of plasma glucose levels, and, thus, may be an imprecise tool to assess average plasma glucose level [10,11]. While there are valid concerns regarding the diagnostic approach of prediabetes, prediabetes remains to have a lower reproducibility of approximately 50% than DM (70%) [12]. Moreover, the use of the three proposed diagnostic criteria further complicates the diagnosis of prediabetes and makes it more error-prone compared to the diagnosis of diabetes. This is because the diagnosis of prediabetes relies on values lying between two cut-off points (rather than 1 for DM) fore measures that have substantial biological assay variability [13].

Based on the available evidence, it's noted that the prediabetic state is defined by various alternative diagnostic criteria, consisting of an overlapping group of individuals with one or more abnormalities in their glucose metabolism. It is possible that the presence of IFG and IGT helps in identifying individuals with different pathological abnormalities related to their impaired glucose metabolism, while the presence of both parameters signifies more advanced impairment related to the overall glucose hemostasis.

Lack of knowledge and sub-diagnosis of prediabetes

Even though prediabetes is globally recognized and accepted by major national and international Diabetes Mellitus-related guidelines, however, there is still no clear understanding and awareness among healthcare practitioners and professional regarding this conditions,

and consequently a lack of evaluation of this potentially-critical metabolic state [5]. Recently, a survey study was conducted among primary healthcare physicians in the United States of America (U.S.A), and it was noted that only 11% of the participants were able to clearly identify prediabetes risk factors [14]. A similar investigation was held in Colombia, where the same survey was applied to 429 primary care physicians who attended two internal medicine and diabetes academic events, and less than 10% of respondents were able to clearly identify the twelve risk factors proposed in the study survey [15].

Risk scoring systems for the detection of undiagnosed prediabetes

Identification of risk factors and the use of risk scoring scales, which are useful questionnaire-based tools, allows a more cost-effective approach for the screening and identification of various diseases, including prediabetes. More than ten different risk assessment tools/scoring systems have been proposed and available in the literature for the screening of DM, however, there are a very limited number of developed and validated risk score systems for prediabetes [16-19].

The most recent risk score system has been proposed by Rajput in 2018 in the Prediabetes Risk Evaluation Scoring System (PRESS) study [20]. The authors identified four significant variables associated with increased risk of prediabetes, including increasing age, family history of DM, increased diastolic blood pressure (DBP) above 90 mmHg, and raised waist-height ratio (WHtR) above 0.5, irrespective of gender, to incorporate into their risk score system. Moreover, it was found that raised WHtR above the value of 0.5 showed an independent association with the risk of prediabetes in both men and women. Various other reports in the literature found a similar correlation between these identified risk factors and the increased risk of prediabetes [21-23].

In this context, it was reported that a risk score of > 45 is suggestive of prediabetes with the need for laboratory-based confirmatory tests [20] using the previously mentioned diagnostic criteria of prediabetes [6,7]. The major advantage of this tool lies in the feasibility to be used by non-paramedical personnel in various field practice areas. This tool has a reasonably good sensitivity and specificity as well as negative and positive predictive values (NPV and PPV) at a cut-off point of 45. This offers a huge potential for its application and uses in resource-poor countries for the early identification of prediabetes. This risk assessment tool offers a very cost-effective option for the screening of prediabetes rather than testing the whole population. After confirmation, identified individuals can be advised to follow an appropriate lifestyle and dietary interventions.

Another risk scoring system has been proposed for identifying people at risk of prediabetes and T2DM, known as the Finnish Diabetes Risk Score (FINDRISC) [24]. It has been proven to be a simple, quick, cost-effective, non-invasive, and reliable tool and has also been evaluated worldwide in various countries of different income, which have shown different cut-off points correlation with risk, as well as variability in sensitivity and specificity [25,26].

FINDRISC, which does not require any laboratory tests as the previous risk score, is a questionnaire made up of 8 easy-to-answer questions to determine the presence of various risk factors associated with prediabetes, including age, Body mass index (BMI), physical activity, fruit and vegetable intake, treatment of hypertension, history of hyperglycemia, and family history of DM. The given answers generate a score for each risk factor, with the total sum of the scores helping in the classification of an individual's risk of developing T2DM within the next 10 years; there are 4 categories to the sum of the scores: low, moderate, high, and very high. The scoring system goes as follows: 1) Risk score of 0 - 14 points reflects a low or moderate risk of diabetes (1 - 17% chance of T2DM within the next 10 years); 2) Risk score of 15 - 20 points reflects a high risk of diabetes (33% chance of T2DM within the next 10 years); 3) Risk score of > 20 reflect a very high risk of diabetes (50% chance of T2DM within the next 10 years) [24].

In the same context, various studies were conducted to validate the applicability of this tool in different countries [25-27]. These investigations were conducted to evaluate the FINDRISC tool and to establish the scores associated with the raised risk of T2DM in their

populations. In Colombia, the FINDRISC tool was shown to be a useful screening tool in identifying people with unknown T2DM and to predict the incidence of T2DM among individuals with prediabetes, where the cut-off point for prediction in the prediabetic population was 13 and 16 in men and women, respectively [27].

On the other hand, Zhang., *et al*. [28] validated the FINDRISC tool among a U.S. undiagnosed prediabetic population. The total score for predicting prediabetes using the FINDRISC tool ranges from 0 to 2 [24]. The optimal cut-off point in the study of Zhang., *et al.* [28] was 9 in men with sensitivity and specificity of 60.94% and 62.43%, respectively, and a cut-off point of 10 in women with sensitivity and specificity of 68.72% and 60.89%, respectively.

There are some other risk tools reported in the literature; Poltavskiy., *et al.* [29] compared to different screening scoring systems from the American Diabetes Association and Centers for Disease Control and Prevention (CDC), which can be used to screen for prediabetes. It was concluded that the ADA score system performed slightly better than the CDC scoring system for prediabetes, with the Area Under Curve (AUC) of 0.72 - 0.74 and 0.70 - 0.71, respectively.

In conclusion, the FINDRISC and PRESS tools are effective, valid, and cost-effective tools in the screening of individuals with undiagnosed prediabetes. However, one can say that the PRESS scoring system is one of its kind for its ability to accurately exclude true negatives from healthy populations, with a negative predictive value of 94.48% [20].

Limitations in risk assessment of prediabetes and gap in the current literature

Despite the availability and applicability of the proposed risk scores in the literature, there is a major limitation to its usage, lying in its applicability to be used in both genders with the same cut-off points. This should be given more attention and should be investigated thoroughly. In 2015, a prospective cohort study in Primary Health Care on the Evolution of Patients with Prediabetes (PREDAPS-Study) was conducted in 1184 and 838 individuals with and without diabetes, respectively [30]. They found that abdominal obesity, low plasma levels of high-density lipoprotein (HDL)-cholesterol, and hypertension were independently correlated with the presence of prediabetes in both men and women. On the other hand, obesity, low HDL-cholesterol level, and hypertension were identified as modifiable risk factors independently correlated with the risk of developing prediabetes. However, it was noted that the magnitude of such associations was stronger for men than women. Alcohol consumption revealed an independent correlation with prediabetes in men, while general obesity revealed an independent correlation in women. The findings reported by Diaz., *et al.* [30] suggest that there are some variations between both genders, which should be taken into account when using risk assessment scores as well as implementing certain recommendations to prevent or delay the onset of DM in the adult population.

Till the current time, the available body of evidence is still limited and further investigation is needed to confirm these findings and propose possible explanations. The existence of variations between men and women highlights the need to analyze data separately by gender, in order to reach specific recommendations to primary prevention of DM and cardiovascular diseases in the adult population. Eventually, these findings may influence the primary care practice, where, for example, in men, alcohol consumption should be recognized as an additional risk factor of prediabetes.

Management of prediabetes in primary care facilities

The primary goal in the management of prediabetes is to normalize blood glucose levels as well as to prevent or delay the progression to DM along with the associated microvascular complications [31,32]. Management of various known prediabetes comorbidities such as obesity, hypertension, dyslipidemia, cardiovascular diseases, and chronic kidney diseases is also critical. Figure 1 and 2 show two protocols for the risk assessment of prediabetes and management approach.

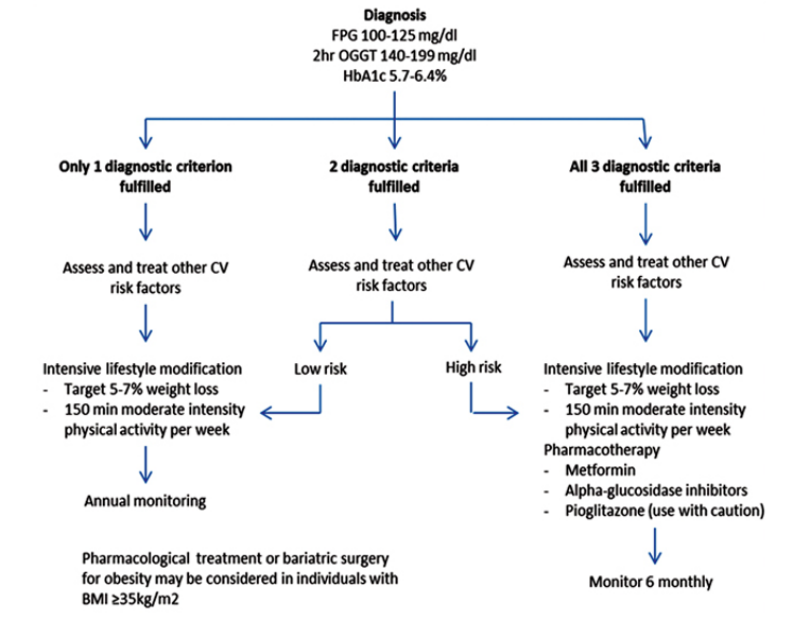

Figure 1: *Algorithm for the management of prediabetes [33].*

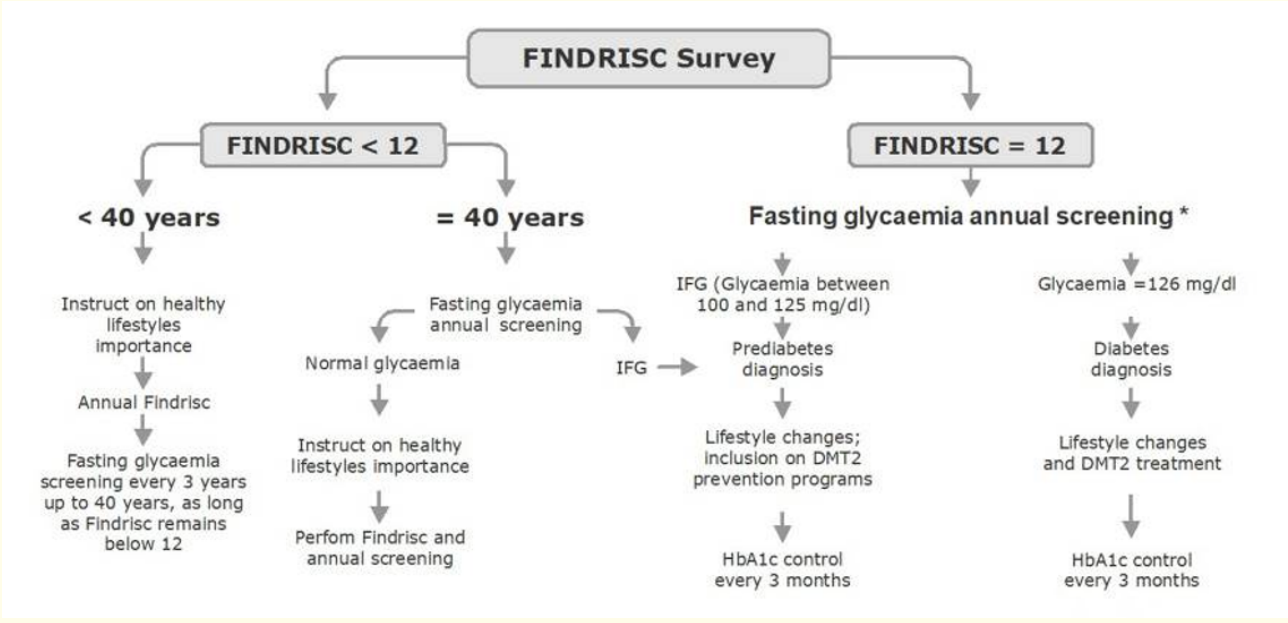

Figure 2: *Risk and Management algorithms of prediabetes [34].*

Therapeutic lifestyle modifications

Given its safety profile as well as the strong body of evidence supporting its effectiveness in improving glycemia and reducing the risk factors of cardiovascular diseases, intensive lifestyle management is considered the preferred approach for individuals with prediabetes [31,32]. This management approach should be discussed with all diagnosed patients during the time of diagnosis as well as throughout their lifetimes. This therapeutic approach includes medical nutrition therapy (MNT). MNT aims at lowering and modifying both caloric and saturated fat intake in order to achieve weight loss in subjects with increased body mass index (overweight or obese). This approach also includes following appropriately described physical activities, avoiding tobacco products, sleeping well both in quality and quantity, limiting alcohol consumption, and reducing stress [32].

Key recommendations in MNT include the following:

1. Consistency in day-to-day carbohydrate intake
2. Limitation of sucrose-containing or high-glycemic index foods
3. Adequate protein intake
4. Weight management.

That being said, compliance towards these lifestyle modifications might be hard to achieve, therefore, there are some proposed strategies that have been shown to increase the likelihood of patient success, which include patient self-monitoring, realistic and stepwise goal setting, stimulus control, cognitive strategies, social support, and appropriate reinforcement [31,32].

Primary care physicians (PCPs) regularly taken on the responsibility of encouraging patients with prediabetes to follow behavioral changes therapy. The Avoiding Diabetes Through Action Plan Targeting (ADAPT) trial conducted a system that combines known evidence-based interventions for behavioral changes with the pre-existing medical record technology to improve the ability of PCP to effectively counsel prediabetic patients on lifestyle behavioral changes. The ADAPT system is an easily-adaptable and scalable technology-based behavioral change tool for primary physicians [35,36].

The U.S. Diabetes Prevention Program (DPP) thoroughly assessed the efficacy of structured lifestyle management interventions, while comparing the resulting changes to metformin and placebo. Compared to placebo, lifestyle intervention was able to result in a more significant reduction in 3-year diabetes incidence (58%) than metformin (31%) [37]. These findings were confirmed in a 10-year follow-up study of the DPP, which revealed a 34% reduction in the incidence of T2DM compared to placebo [38].

Physical activity

Aerobic exercise has been reported to result in better outcomes related to CVD risk factors as well as in reducing the risk of falls and fractures and improving an individual's functional capacity and well-being. Physical activity should be recognized as a key element in both inducing and maintaining weight loss [31,32].

Key recommendations during counseling patients on physical activity:

1. Patients should be examined initially for contraindications and/or limitations to increased physical activity.
2. An exercise program should be adapted for each individual based on his or her goals and limitations.
3. Any new physical activity should be started slowly and built up gradually.

Weight loss

Weight loss is a fundamental aspect of the management of Prediabetes. All individuals must be advised on how to reach and maintain a healthy weight, corresponding to a BMI of 18.5 - 24.9 kg/m^2. Recommendations must be adapted based on patients' specific medical history, lifestyle, and behaviors [31,32].

Pharmacologic therapies to glucose management in prediabetes

The pharmacological approach should be considered in those who show failure and lack of improvement after 3 - 6 months of compliance to the lifestyle modifications protocol [32,39]. Meanwhile, there are no approved drugs by the US Food and Drug Administration (FDA) for the management of prediabetes. Therefore, any decision to include drugs during the management of prediabetes, especially in children, is off-label. This requires careful judgment and assessment of the risks and the benefits of each therapeutic drug for each individualized patient.

Noteworthy, risk scoring systems must be conducted prior to starting any drug regimens. Pharmacological drugs should be considered for the higher-risk group rather than the lower-risk group unless there is clear evidence regarding the progressive deterioration of plasma glucose levels despite lifestyle management. High-risk groups are defined according to the used risk scoring systems, as stated previously. These pharmacological drugs include:

- **Metformin:** It has been noted that metformin, when combined with lifestyle modifications, was found highly effecting in delaying or preventing T2DM in women with a history of gestational diabetes mellitus (GDM) and impaired plasma glucose [40]. In the DPP investigation, metformin alone was not as effective as the lifestyle intervention, however, it resulted in 31% reduction in T2DM incidence compared to placebo, with a 10-year reduction in the risk of T2DM by 18% [38].

- **Acarbose:** In the Stop Noninsulin-Dependent Diabetes Mellitus (STOP-NIDDM) trial, acarbose revealed significant improvement in CVD outcomes with a delay in the progression to DM in patients with impaired glucose tolerance, showing a 25% reduced risk of progression to DM compared to the placebo arm [31,41-43].

- **Thiazolidinediones:** Rosiglitazone and pioglitazone have been shown to prevent the progression to T2DM in 60% and 72% of high-risk patients, respectively [44,45]. That being said, their use in the management of prediabetes is still controversial due to the associated adverse events [32,39,46].

- **GLP-1 receptor agonists:** The glucagon-like peptide 1 (GLP-1) receptor agonist "exenatide" has been reported to result in weight reduction as well as improvement in glucose tolerance in obese patients and those with prediabetes [47]. Also, liraglutide 1.8 mg, the treatment dose of T2DM, resulted in a reduction of the risk of T2DM [48,49].

Conclusion

The diagnostic criteria proposed by ADA are different from those proposed by WHO. However, there are many applicable and highly effective and cost-effective risk assessment scoring systems that can be used to identify patients with undiagnosed prediabetes. Following a risk assessment, patients can then be categorized to undergo one of the prediabetes management protocols including lifestyle modifications and medical nutrition therapy, weight loss, physical activity, and pharmacological therapy. However, the efficacy and safety of drug therapy are questioned. Therefore, more studies are in need to assess the available observations and determine the efficacy and safety profiles of the various drug therapies used in prediabetes.

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None.

Conflicts of Interest

No conflicts related to this work.

Bibliography

1. Association American Diabetes. "Diagnosis and Classification of Diabetes Mellitus". *Diabetes Care* 27 (2004): S5.
2. Federation International Diabetes. "Idf Diabetic Atlas 7th Edition". (2017).
3. Ramachandran A., *et al*. "High Prevalence of Diabetes and Impaired Glucose Tolerance in India: National Urban Diabetes Survey". *Diabetologia* 44.9 (2001): 1094-1101.
4. Gerstein HC., *et al*. "Annual Incidence and Relative Risk of Diabetes in People with Various Categories of Dysglycemia: A Systematic Overview and Meta-Analysis of Prospective Studies". *Diabetes Research and Clinical Practice* 78.3 (2007): 305-312.
5. Lopez-Jaramillo P., *et al*. "Latin American Consensus on Hypertension in Patients with Diabetes Type 2 and Metabolic Syndrome". *American Journal of Hypertension* 31.2 (2013): 223-238.
6. Association, American Diabetes. "Standards of Medical Care in Diabetes-2014". *Diabetes Care* 37.1 (2014): S14-S80.
7. Organization, World Health. "Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycaemia: Report of a Who/Idf Consultation" (2006).
8. Balion CM., *et al*. "Reproducibility of Impaired Glucose Tolerance (Igt) and Impaired Fasting Glucose (Ifg) Classification: A Systematic Review". *Clinical Chemistry and Laboratory Medicine* 45.9 (2007): 1180-1185.
9. Libman IM., *et al*. "Reproducibility of the Oral Glucose Tolerance Test in Overweight Children". *The Journal of Clinical Endocrinology and Metabolism* 93.11 (2008): 4231-4237.
10. Bloomgarden ZT., *et al*. "The Proposed Terminology 'a(1c)-Derived Average Glucose' Is Inherently Imprecise and Should Not Be Adopted". *Diabetologia* 51.7 (2008): 1111-1114.
11. Cohen RM., *et al*. "Evidence for Independent Heritability of the Glycation Gap (Glycosylation Gap) Fraction of Hba1c in Nondiabetic Twins". *Diabetes Care* 29.8 (2006): 1739-1743.
12. Bansal Nidhi. "Prediabetes Diagnosis and Treatment: A Review". *World Journal of Diabetes* 6.2 (2015): 296-303.
13. Yudkin John S and Victor M Montori. "The Epidemic of Pre-Diabetes: The Medicine and the Politics". *BMJ* 349 (2014): g4485.
14. Tseng, E., *et al*. "Survey of Primary Care Providers' Knowledge of Screening for, Diagnosing and Managing Prediabetes". *Journal of General Internal Medicine* 32.11 (2017): 1172-1178.
15. Garay, Jennifer, *et al*. "Survey of Knowledge for Diagnosing and Managing Prediabetes in Latin-America: Cross-Sectional Study". *Diabetology and Metabolic Syndrome* 11.1 (2019): 102.
16. Bang H., *et al*. "Development and Validation of a Patient Self-Assessment Score for Diabetes Risk". *Annals of Internal Medicine* 151.11 (2009): 775-783.

17. Heikes KE., *et al*. "Diabetes Risk Calculator: A Simple Tool for Detecting Undiagnosed Diabetes and Pre-Diabetes". *Diabetes Care* 31.5 (2008): 1040-1045.

18. Hippisley-Cox Julia., *et al*. "Predicting Risk of Type 2 Diabetes in England and Wales: Prospective Derivation and Validation of Qdscore". *BMJ* 338 (2009): b880.

19. Kahn HS., *et al*. "Two Risk-Scoring Systems for Predicting Incident Diabetes Mellitus in U.S. Adults Age 45 to 64 Years". *Annals of Internal Medicine* 150.11 (2009): 741-751.

20. Rajput Rajesh Keshav Garg and Meena Rajput. "Prediabetes Risk Evaluation Scoring System [Press]: A Simplified Scoring System for Detecting Undiagnosed Prediabetes". *Primary Care Diabetes* 13.1 (2019): 11-15.

21. Muthunarayanan Logaraj Balaji Ramraj and John Kamala Russel. "Prevalence of Prediabetes and Its Associated Risk Factors among Rural Adults in Tamil Nadu". *Archives of Medicine and Health Sciences* 3.2 (2015): 178.

22. Ramachandran, A., *et al*. "Prevalence of Glucose Intolerance in Asian Indians. Urban-Rural Difference and Significance of Upper Body Adiposity". *Diabetes Care* 15.10 (1992): 1348-1355.

23. Viswanathan V., *et al*. "Risk of Future Diabetes Is as High with Abnormal Intermediate Post-Glucose Response as with Impaired Glucose Tolerance". *The Journal of the Association of Physicians of India* 55 (2007): 833-837.

24. Lindström Jaana and Jaakko Tuomilehto. "The Diabetes Risk Score: A Practical Tool to Predict Type 2 Diabetes Risk". *Diabetes Care* 26.3 (2003): 725-731.

25. Bergmann, A., *et al*. "A Simplified Finnish Diabetes Risk Score to Predict Type 2 Diabetes Risk and Disease Evolution in a German Population". *Hormone and Metabolic Research* 39.9 (2007): 677-682.

26. Schwarz PE., *et al*. "The Finnish Diabetes Risk Score Is Associated with Insulin Resistance and Progression Towards Type 2 Diabetes". *The Journal of Clinical Endocrinology and Metabolism* 94.3 (2009): 920-926.

27. Gomez-Arbelaez D., *et al*. "Evaluation of the Finnish Diabetes Risk Score to Predict Type 2 Diabetes Mellitus in a Colombian Population: A Longitudinal Observational Study". *World Journal of Diabetes* 6.17 (2015): 1337-1344.

28. Zhang, L., *et al*. "Evaluation of Finnish Diabetes Risk Score in Screening Undiagnosed Diabetes and Prediabetes among U.S. Adults by Gender and Race: Nhanes 1999-2010". *PLoS One* 9.5 (2014): e97865.

29. Poltavskiy E., *et al*. "Comparison of Screening Scores for Diabetes and Prediabetes". *Diabetes Research and Clinical Practice* 118 (2016): 146-153.

30. Díaz-Redondo Alicia., *et al*. "Modifiable Risk Factors Associated with Prediabetes in Men and Women: A Cross-Sectional Analysis of the Cohort Study in Primary Health Care on the Evolution of Patients with Prediabetes (Predaps-Study)". *BMC Family Practice* 16 (2015): 5-5.

31. Garber, A. J., *et al*. "Diagnosis and Management of Prediabetes in the Continuum of Hyperglycemia: When Do the Risks of Diabetes Begin? A Consensus Statement from the American College of Endocrinology and the American Association of Clinical Endocrinologists". *Endocrine Practice* 14.7 (2008): 933-946.

32. Handelsman Y., *et al*. "American Association of Clinical Endocrinologists and American College of Endocrinology - Clinical Practice Guidelines for Developing a Diabetes Mellitus Comprehensive Care Plan - 2015". *Endocrine Practice* 21.1 (2015): 1-87.

33. Priya Gagan. "Management of Prediabetes". *Primary Care Diabetes* 68.4 (2018).

34. Lopez-Jaramillo P., *et al*. "Prediabetes in Colombia: Expert Consensus". *Colombia Médica* 48.4 (2017): 191-203.

35. Devine EB., *et al*. "Usability Evaluation of Pharmacogenomics Clinical Decision Support Aids and Clinical Knowledge Resources in a Computerized Provider Order Entry System: A Mixed Methods Approach". *International Journal of Medical Informatics* 83.7 (2014): 473-483.

36. Mann DM and JJ Lin. "Increasing Efficacy of Primary Care-Based Counseling for Diabetes Prevention: Rationale and Design of the Adapt (Avoiding Diabetes Thru Action Plan Targeting) Trial". *Implementation Science* 7 (2012): 6.

37. Knowler William C, *et al*. "Reduction in the Incidence of Type 2 Diabetes with Lifestyle Intervention or Metformin". *The New England Journal of Medicine* 346.6 (2002): 393-403.

38. Knowler WC., *et al*. "10-Year Follow-up of Diabetes Incidence and Weight Loss in the Diabetes Prevention Program Outcomes Study". *Lancet* 374.9702 (2009): 1677-1686.

39. Garber AJ., *et al*. "Aace/Ace Comprehensive Diabetes Management Algorithm 2015". *Endocrine Practice* 21.4 (2015): 438-447.

40. Ratner RE., *et al*. "Prevention of Diabetes in Women with a History of Gestational Diabetes: Effects of Metformin and Lifestyle Interventions". *The Journal of Clinical Endocrinology and Metabolism* 93.12 (2008): 4774-4779.

41. Chiasson JL., *et al*. "Acarbose for Prevention of Type 2 Diabetes Mellitus: The Stop-Niddm Randomised Trial". *Lancet* 359.9323 (2002): 2072-2077.

42. Jean-Louis Chiasson MD., et al. "Acarbose Treatment and the Risk of Cardiovascular Disease and Hypertension in Patients with Impaired Glucose Tolerance: The Stop-Niddm Trial". *JAMA* 290.4 (2003): 486-494.

43. J-L Chiasson., et al. "Acarbose for the Prevention of Type 2 Diabetes, Hypertension and Cardiovascular Disease in Subjects with Impaired Glucose Tolerance: Facts and Interpretations Concerning the Critical Analysis of the Stop-Niddm Trial Data". *Diabetologia* 47.6 (2004): 969-975.

44. DeFronzo RA., *et al*. "Pioglitazone for Diabetes Prevention in Impaired Glucose Tolerance". *The New England Journal of Medicine* 364.12 (2011): 1104-1115.

45. Gerstein HC., *et al*. "Effect of Rosiglitazone on the Frequency of Diabetes in Patients with Impaired Glucose Tolerance or Impaired Fasting Glucose: A Randomised Controlled Trial". *Lancet* 368.9541 (2006): 1096-1105.

46. Garber, A. J., *et al*. "American Association of Clinical Endocrinologists' Comprehensive Diabetes Management Algorithm 2013 Consensus Statement--Executive Summary". *Endocrine Practice* 19.3 (2013): 536-557.

47. Rosenstock J., *et al*. "Effects of Exenatide and Lifestyle Modification on Body Weight and Glucose Tolerance in Obese Subjects with and without Pre-Diabetes". *Diabetes Care* 33.6 (2010): 1173-1175.

48. Astrup A., *et al*. "Effects of Liraglutide in the Treatment of Obesity: A Randomised, Double-Blind, Placebo-Controlled Study". *Lancet* 374.9701 (2009): 1606-1616.

49. Kim SH., *et al*. "Benefits of Liraglutide Treatment in Overweight and Obese Older Individuals with Prediabetes". *Diabetes Care* 36.10 (2013): 3276-3282.

Volume 16 Issue 2 February 2020