Introduction

Prediabetes AI Risk Assessment is a novel artificial intelligence-based risk assessment system that provides the individual's risk of having undiagnosed prediabetes and Type 2 diabetes mellitus in the next 3 years. The risk score is developed by Apollo Hospitals leveraging a machine learning model (eXtreme Gradient Boosting - XGB) on more than 20K adult patient data. The methodology helps to stratify the patient's risk and provide individualized protocol using a Clinical Decision Support System on the next best actions with an AUC of 0.86.

Why is Apollo Prediabetes AI different?

1. Machine Learning Model developed with Indian Data having Higher Accuracy than conventional risk score
    a. XGB Model
    b. Model Built and Validated with Over 20K Patient data since 2013
    c. Accuracy - AUC – 0.86 (Development)
2. Feedback Loop from the prospective use in patients
3. Comprehensive & Holistic Risk Assessment
4. Validated at different National & International Institutions
5. Integrated Clinical Decision Support Tool (What Next to do)

Interpretation & Adoption Message

1. AI Algorithm + Clinicians - This risk assessment tool has been built as an adjunct tool for physicians to identify global/holistic risks for patients developing prediabetes.
2. Risk Identification and Prevention—This Risk Assessment Tool is not Intended for the diagnosis of Prediabetes or diabetes mellitus. Its limitations include already-diagnosed Diabetes undergoing treatment.
3. Where to use—This Risk Assessment tool has been designed for use in Preventive Health Screening programs at Outpatient Clinics and Health Check Clinics.
4. Limitations

a. Prediabetes is more difficult to predict than diabetes using any of the parameters across all of the models, which is expected.
b. This cohort is selected from the annual Health Check data which may not be representative of the community-based prevalence/incidence.
c. Data of HBA1c is taken for building the model. HBA1c may fluctuate for individuals (with similar risk factors) over the immediate past months
d. Models are built on 4-7% and 4-7.5% HBA1c outcome data, and HBA1c >7.5% is excluded as **Undiagnosed Uncontrolled Diabetes is beyond the scope of this Algorithm.**
e. Note on Uncontrolled / Gestational Diabetes and PCOD - The current model doesn't account for (Exclusion Criteria) –
    i. Uncontrolled and Undiagnosed Diabetes
    ii. Gestational Diabetes
    iii. Polycystic Ovarian Disease (PCOD)

Disclaimer (In Print Out)

- This is not a diagnostic tool and it does not guarantee the accuracy of the result and cannot be independently acted upon.
- This Risk score and Clinical Algorithm is a general guideline for Physicians. Any additional laboratory investigations, Diagnostic Imaging, Treatment, or Patient Education related to lifestyle management is at the Physician's or Endocrinologist's discretion.
- To ensure the information in the report is up to date, accurate, and correct, the Doctor shall be consulted for interpretation of the report.
- Apollo Hospitals and its Staff do not offer any assurance on the information made available or be liable for any loss or damage as the said report is based on the Prediabetes Risk Score without any intervention from their side.
- By usage of Prediabetes Risk Score, it is deemed that the beneficiary of this service has agreed to get the same done at his own risk and further agrees with this disclaimer without any limitation or any clauses or sub-clauses.
- Note on Uncontrolled / Gestational Diabetes and PCOD - The current model doesn't account for (Exclusion Criteria) –
    i. Uncontrolled and Undiagnosed Diabetes
    ii. Gestational Diabetes
    iii. Polycystic Ovarian Disease (PCOD)
    iv. Previously diagnosed and under treatment for Diabetes mellitus

How to Use (For Clinicians Only)-

1. Provide Appropriate –
    a. Demographic Details
    b. Obtain Patient Consent

2. Risk Factors Included –
    a. Personal/VS – Age | Gender | Height| Weight | BMI
    b. Life Style Attributes – Alcohol | Diet | Physical Activity
    c. History – Family History | Hypertension | Dyslipidemia | Past Medical History | Symptoms of Diabetes Mellitus
    d. Additional – Waist Circumference & change in body weight in the past 6 months

Workflow of Prediabetes App

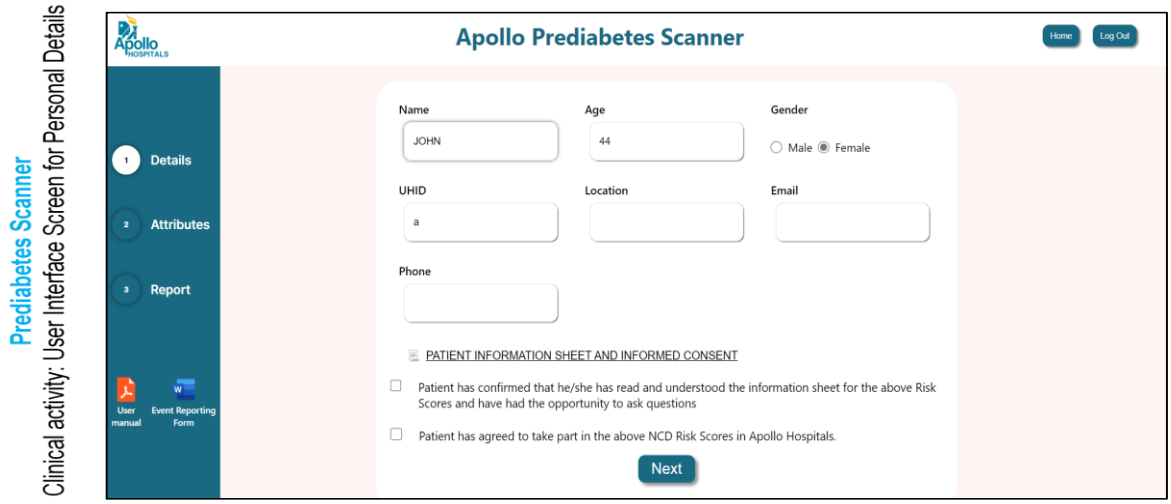


Figure 1 – Entry of Personal Details

Patient details Dashboard: The first step to using the Prediabetes AI App is to log into the Doctor Dashboard using your unique credentials. After login, fill in the Patient Details and accept consent.

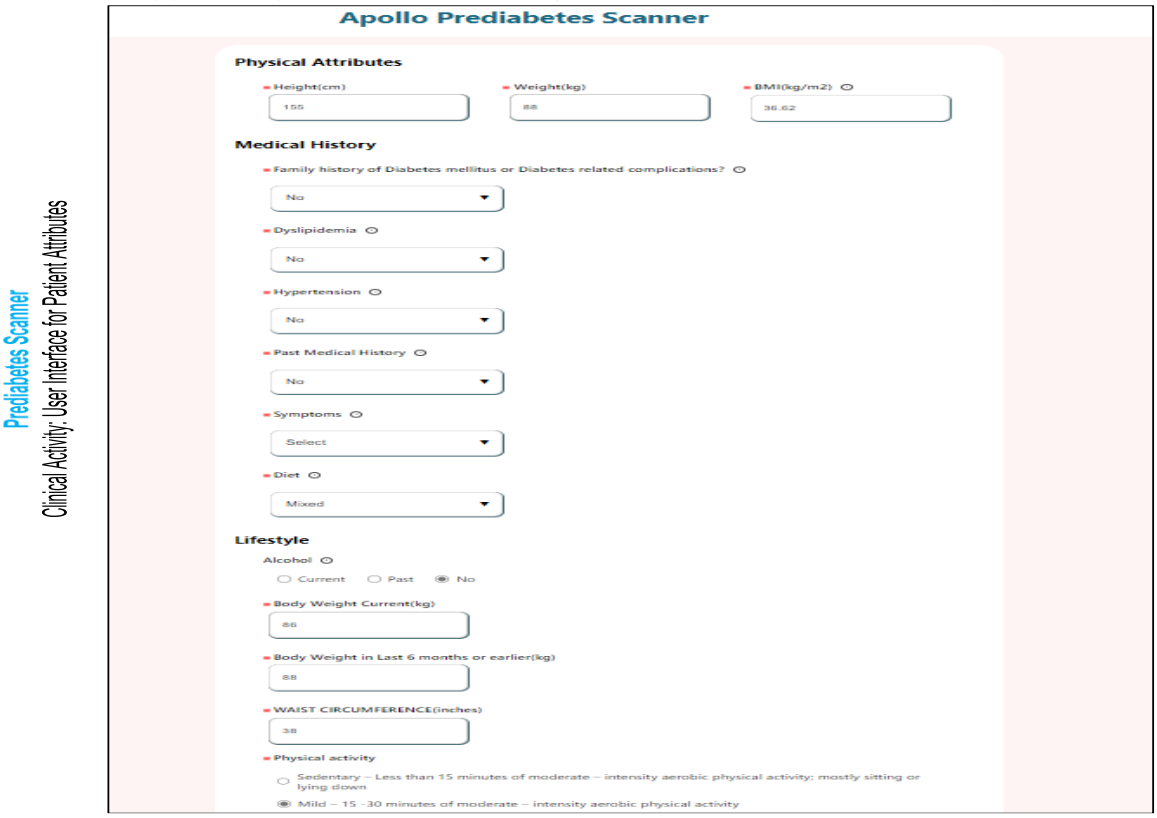


Figure 2 – Entry of Patient Attributes

Patient Attributes: The following categories are used to collect the Physical Attributes, Medical History & Lifestyle Attributes.

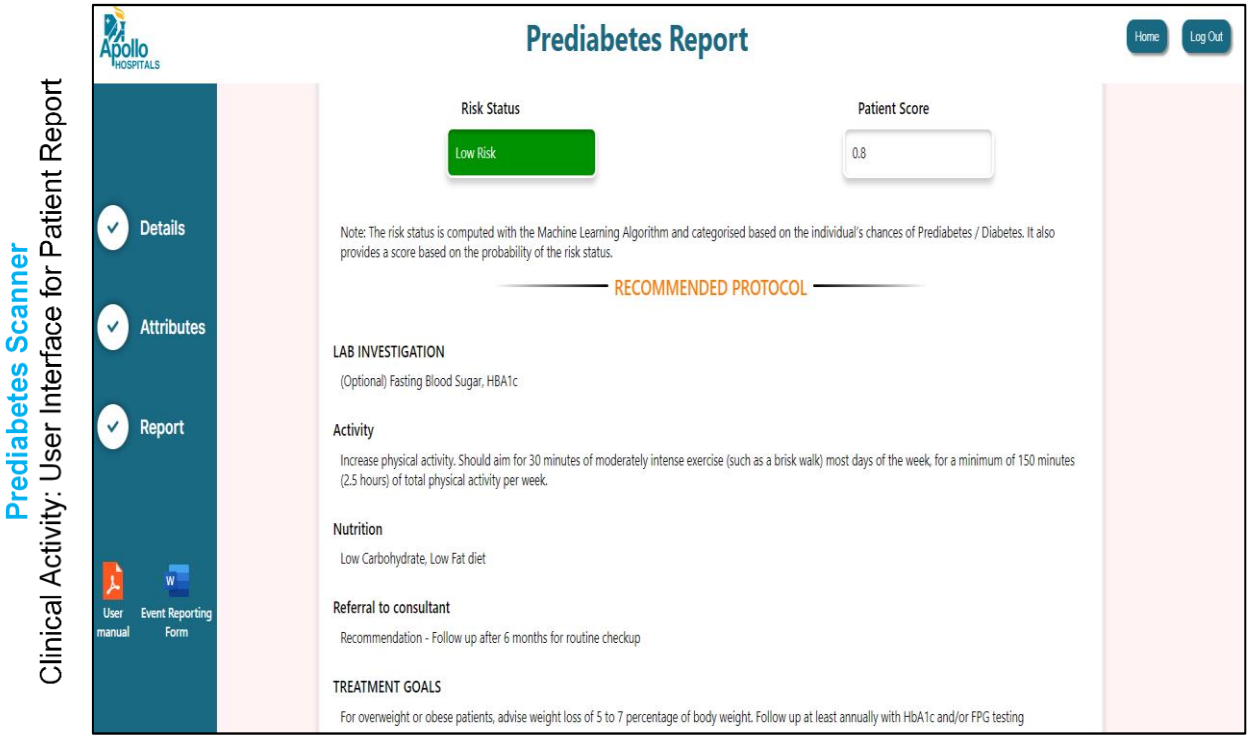


Figure 3 – Report

Output:

Considering the input parameters given, the model gives an output of

a. Risk Categorization – Low – Moderate – High Risk of Prediabetes
b. Prediabetes Risk Score
c. Top Modifiable Risk Attributes
d. Clinical Decision Support System (What Next to Do)
    i. Lab, Imaging, and Investigations
    ii. Endocrinology Referral
    iii. Treatment Goals
    iv. Education
    v. Revisit Guidelines

Report Format

PREDIABETES RISK SCORE

NAME: SAIRAM	AGE: 22	LOCATION: PALAKOL
UHID: 123456789	GENDER: MALE	DATE OF REPORT: 10-11-2021

PATIENT RISK SCORE

Risk	Score
Low Risk	80

INFORMED CONSENT: YES

Height	147	Weight	58
BMI	26.84	Diet	Non-Veg
Alcohol	No	Waist Circumference	34
Change In Body Weight	Same	Physical Activity	Mild
Family History of Diabetes	Yes	Dyslipidemia	No
Hypertension	Yes	Symptoms	No
Past Medical History	No		

RECOMMENDED PROTOCOL

Activity

Increase physical activity. Should aim or 30 minutes of moderately intense exercise (such as a brisk walk) most days of the week, for a minimum of 150 minutes (2.5 hours) of total physical activity per week.

Nutrition

Low Carbohydrate, Low Fat diet

Referral to consultant

Not Required

Tests follow up

REPEAT TESTING every year for: – All adults age ≥40 OR – Adults of any age if Dyslipidemia, Obesity or Hypertension persists or newly diagnosed as risk factors

Treatment goals

For overweight or obese patients, advise weight loss of 5–7% of body weight. Follow up at least annually with HbA1c and/or FPG testing

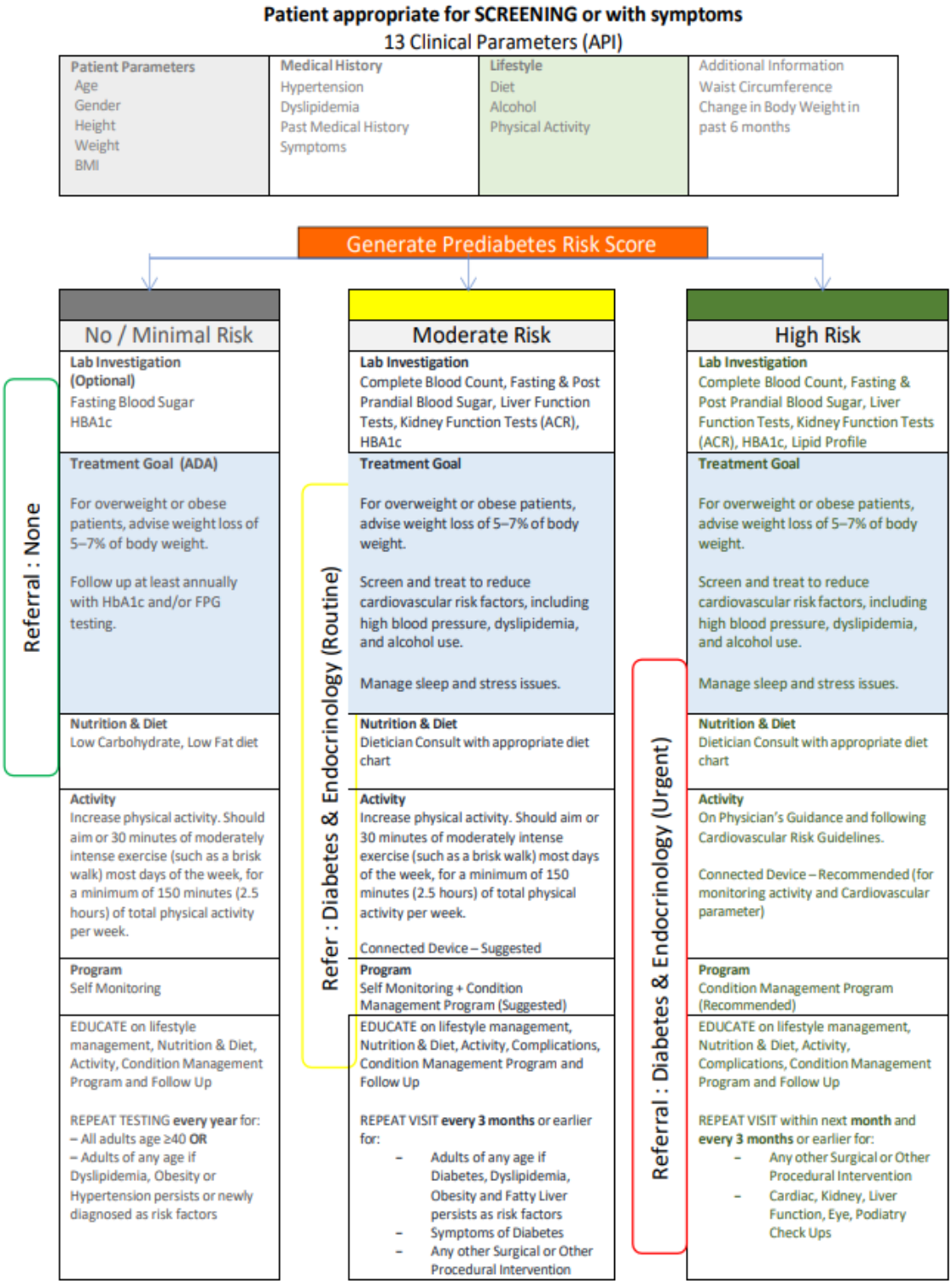
Lab investigation

(Optional) Fasting Blood Sugar, HBA1c

This report is accessed by Dr

Date: 10-11-2021
Time: 11:59:05 AM | Page 1

Clinical Algorithm



Research

Introduction - Prediabetes is a chronic metabolic condition where blood glucose levels are above the upper threshold considered normal but below the threshold for a diagnosis of diabetes. (Tabak AG, Herder C, Rathmann W, Brunner EJ, Kivimaki M. Prediabetes: a high-risk state for diabetes development. Lancet. 2012;379:2279–2290). Up to one-third of people with prediabetes will progress to diabetes in three to five years (CDC). This will increase their risk of cardiovascular disease, stroke, high blood pressure, blindness, kidney disease, nerve disease, and amputation (ADA). In addition, prediabetes itself is associated with early onset of neuropathy, retinopathy, microalbuminuria, and greater cardiovascular risk, suggesting that many patients with prediabetes may be already suffering adverse effects of abnormal glucose regulation (TAB)

Our Approach

1. The objectives of this Risk Assessment Tool include –
2. Identify individuals at risk for developing prediabetes and diabetes using a simplistic assessment tool like HRA.
3. Use the tool as a community-based risk tool for early diagnosis before estimation of blood levels of glucose or HBA1c
4. Provide appropriate preventive and therapeutic guidance to individuals for appropriate follow-up and management

Methodology

This Risk Assessment is built with a Machine Learning Model (eXtreme Gradient Boosting - XGB) on more than 20,000 adult patient data from Apollo Health Checks. The tool Identifies whether an individual has a Low / Mid / High Risk for Undiagnosed Prediabetes & T2DM using the XGB Model and the corresponding Probabilities displayed for Low / Mid / High. The current performance of the tool is around 0.86 AUC. Over 12 Consultants Endocrinologists, Data Scientists, and Engineers from Apollo Hospitals have contributed to building this tool.

Ethics Perspective

Title	Development and Validation of a Multivariable Prediction Model to determine the risk of Undiagnosed Prediabetes and Type 2 Diabetes Mellitus	Centers	India – Apollo Hospitals
Principal Investigators	12 Leading Endocrinology Consultants	Institutional Ethics Committee Approval	Applied for
Data	Retrospective – Prospective Jan 2013 to June 2020 September 2021 Onwards	Safety	Model advocates risk scores that are interpreted by clinicians through safe Machine (API) – Human (Clinician) Interaction
Sample Size + Missing Data	13366 [22560-dropped 9194 Patients-data due to missing data] | No Imputations	Inclusiveness & Fairness	At admission data includes clinical comorbidities & conditions | No socioeconomic discrimination
Personal Health information	De-identified all PHI during analysis, model building, API hosting and Prospective Use	Privacy & Confidentiality	Data secured at Apollo Azure Tenant with all relevant compliance + conforming to laws
Addressing Bias (Geographical / Ethnic / Temporal / Gender etc.)	Multiethnic – All Adult Population Group 25 to 65– Male to Female – 57 : 43 – Automation Bias addressed at API Clinical Use	Accuracy + Efficacy	Classification Metrics -sensitivity: 0.70 | specificity: 0.79 | AUC Score : 0.83
Risk Groups	Low – Moderate – High Risk of Prediabetes	Informed Consent	Yes – Template & Protocol (Prototype Attached)
Model Specification	XGB Classification + XGB Regression Hazard Ratio + KM Plots	API – Ease of Use + Interpretation	Flows to Clinical Algorithm Standard Clinical Definitions + Lab Units Used
Clinical Algorithm Update (Version)	Version 2 August 2021	Validation + Peer Review	In Process
Intellectual Property Rights (IPR)	Patent No|202441065930	Certifications & Compliance	ISO 13485:2016 Certification | MD 763515 CDSCO Application No | Apollo-Hyder-TE/M/MD/007509

Frequently Asked Questions

Introduction.

Prediabetes Scanner is a novel Artificial Intelligence-based Risk Score that provides the individual's risk of having Prediabetes / Diabetes in previously undiagnosed individuals. The risk is developed by Apollo Hospitals with further validation from National and International institutions. The methodology helps to stratify the patient's risk and provide individualized protocol using a Clinical Decision Support System on the next best actions, achieving an AUC exceeding 0.86.

Why is Prediabetes Scanner different or What is the advantage of this score?

1. Machine Learning Model developed with Indian Data achieving Higher Accuracy than conventional Risk score.
    a. XGB Model
    b. Model Built and Validated with Over 20K Patient data since 2013
    c. Accuracy - AUC – 0.86 (Development)
2. Feedback Loop from the prospective use in patients
3. Comprehensive & Holistic Risk Assessment
4. Validated at different National & International Institutions
5. Integrated Clinical Decision Support Tool (What Next to do)

What is the Interpretation & Adoption Message?

1. AI Algorithm + Clinicians - This risk assessment tool has been built as an adjunct tool for physicians to identify global/holistic risks for patients developing prediabetes.
2. Risk Identification and Prevention - This Risk Assessment Tool is not to be used for diagnosis of Type 2 Diabetes Mellitus. Its limitations include already diagnosed Type 2 Diabetes Mellitus and currently undergoing Treatment.

What are the Limitations of the Prediabetes Scanner?

a. Prediabetes is more difficult to predict than diabetes using any of the parameters across models, which is expected.
b. This cohort is selected from the annual Health Check data which may not be considered representational of the community-based prevalence/incidence.
c. Data of HBA1c is taken for building the model. HBA1c may fluctuate for individuals (with similar risk factors) over the immediate past months
d. Models are built on 4-7% and 4-7.5% HBA1c outcome data, and HBA1c >7.5% is excluded as Undiagnosed Uncontrolled Diabetes is beyond the scope of this Algorithm.
e. Note on Uncontrolled / Gestational Diabetes and PCOD - The current model doesn't account for (Exclusion Criteria -
    i. Uncontrolled and Undiagnosed Diabetes
    ii. Gestational Diabetes
    iii. Polycystic Ovarian Disease (PCOD)

Where can the physicians use the Prediabetes Scanner –

This Risk Assessment tool is Intended for use in Preventive Screening programs at Outpatient Clinics and Health Check Clinics.

What are the Risk Factors Included –

Age | Gender | BMI | Alcohol | Family History | Diet | Physical activity| Hypertension | Dyslipidemia | Past Medical History | Symptoms Additional – Waist Circumference & change in body weight in past 6 months.

What are the Output and Follow-Up For the Risk Score?

a. Risk Categorization – Low – Moderate – High Risk of Prediabetes / Diabetes
b. Prediabetes Risk Score
c. Clinical Decision Support System (What Next to Do)
    I. Lab, Imaging, and Investigations
    II. Endocrinology Referral
    III. Treatment Goals
    IV. Education
    V. Revisit Guidelines

Is this a diagnostic tool?

This is not a diagnostic tool and it does not guarantee the accuracy of the result and cannot be independently acted upon.

Does this contradict the Physician's view?

This Risk score and Clinical Algorithm is a general guideline for Physicians. Any additional laboratory investigations, Diagnostic Imaging, Treatment, or Patient Education related to lifestyle management is at the Physician's or Endocrinologist's discretion.

How does one ensure the accuracy of the Prediabetes Scanner?

To ensure the information in the report is up to date, accurate, and correct, the Doctor shall be consulted for interpretation of the report. Additionally, the input data should be accurate and as per the conventional metrics used.

Is this a substitute for any diagnostic test or clinician's advice

Absolutely No. This is an adjunct tool made with Clinical Features and History of the Patient. It doesn't substitute for any tests or advice.

What are the disclaimers for the use of this tool?

a. Apollo Hospitals and its Staff do not offer any assurance on the information made available or shall not be liable for any loss or damage as the said report is based on the Prediabetes Scanners without any intervention from their side.
b. By usage of Prediabetes Scanner, it is deemed that the beneficiary of this service has agreed to get the same done at his own risk and further agrees with this disclaimer without any limitation or any clauses or sub-clauses.

Can the report be shared with other clinicians?

Yes, each patient shall get a printed report or PDF copy which can be kept by the patient maintaining privacy and confidentiality.

How is Safety addressed?

The model advocates risk scores that are interpreted by clinicians through safe Machine (API) – Human (Clinician) Interaction. Informed consent from each individual is obtained before the Risk Score generation.

Definitions

BMI

A. Underweight, <18.5 kg/m2
B. Normal, 18.5 ≤ BMI < 25 kg/m2
C. Overweight, 25 ≤ BMI < 30 kg/m2
D. Obesity
    a. Obesity I, 30 ≤ BMI < 35
    b. Obesity II, 35 ≤ BMI < 40 kg/m2
    c. Obesity III, ≥ 40 kg/m2

Source: Centers for Disease Control and Prevention: Overweight and obesity. Available at: http://www.cdc.gov/nccdphp/dnpa/obesity/.

Hypertension/High Blood Pressure

A. Two hypertension diagnoses (≥14 days apart)
B. A hypertension diagnosis and a hypertension medication prescription
    a. angiotensin-converting enzyme inhibitors (ACE),
    b. angiotensin II receptor blockers (ARB),
    c. beta blockers,
    d. calcium channel blocks, and/or
    e. diuretics
C. A hypertension diagnosis and
    a. systolic blood pressure average ≥ 140 (if at least two results ≥ 14 days apart), or
    b. diastolic blood pressure average ≥ 90 (if at least two results ≥ 14 days apart)

Source: Tania B. Babar M.D.: Ferri's Clinical Advisor 2019, 729-735.e5

Prediabetes

1) Previous prediabetes diagnosis
2) Lab results
    a. hemoglobin A1c lab result ≥5.7% and <6.4% or
    b. fasting plasma glucose ≥100 mg/dL and <126 mg/dL

Elevated Lipids

1. An elevated lipids diagnosis
2. A prescription for elevated lipids medication
    a) statins or statin combinations
    b) fibrates
    c) niacin
    d) bile acid sequestrates, and/or
    e) other lipid-modifying agents
3. Lab results
    a) triglyceride level ≥250 mg/dL
    b) HDL <40 mg/dL for males and <50 mg/dL for females.
    c) non-HDL value ≥ 160 mg/dL

Source: National Cholesterol Education Program (NCEP) Expert Panel on Cholesterol Levels Preventive Cardiology: Companion to Braunwald's Heart Disease

Family History of Diabetes

1. A diagnosis of a family history of diabetes, or

2. A record in the Medical Record denoting family history of diabetes

Diabetes Mellitus - The American Diabetes Association (ADA) defines Diabetes Mellitus as follows:

1. A fasting plasma glucose (FPG) ≥126 mg/dl. Fasting is defined as no caloric intake for at least 8 hr.
2. Symptoms of hyperglycemia and a casual (random) plasma glucose ≥200 mg/dl. Classic symptoms of hyperglycemia include polyuria, polydipsia, and unexplained weight loss. (At the time of diagnosis as a diabetic, B cell function is at 25% to 30%.)
3. An oral glucose tolerance test (OGTT) with a plasma glucose ≥200 mg/dl 2 hr after a 75 g (100 g for pregnant women) glucose load.
4. A haemoglobin A1c (HbA1c) value ≥6.5%.

Source - David Domenichini M.D. : Ferri's Clinical Advisor 2019, 424-433.e2

Diet:

1. Vegetarian – Diet which is plant-based with adequate servings of fruits and vegetables
2. Non Vegetarian – Diet which includes predominantly Meat, Poultry, Fish, and Eggs for more than 4 servings per week.
3. Mixed - Diet which includes Meat, Poultry, Fish, and Eggs for 4 or fewer servings per week and includes fruits and vegetables.

Source – Adapted from Cleveland Clinic

Alcohol: If a person is currently drinking Alcohol or in the past or does not drink

Physical Activity: Purposeful movement that the individual performs in addition to the normal daily routine, on most days:

1. Sedentary – Less than 15 minutes of moderate-intensity aerobic physical activity; mostly sitting or lying down
2. Mild – 15 -30 minutes of moderate-intensity aerobic physical activity
3. Moderate – 30 to 60 minutes of moderate-intensity aerobic physical activity
4. Activity - More than 60 minutes of moderate-intensity aerobic physical activity or at least 20 minutes of vigorous-intensity aerobic physical activity

Source – WHO [https://www.who.int/news-room/fact-sheets/detail/physical-activity] November 26, 2020

Past Medical History includes

a. Chronic Illness like Cardiovascular / Renal / Liver / Thyroid Disease / Stroke or Transient Ischemic Attack
b. Hypertension
c. Frequent Infections

Symptoms include –

1. Weight gain or loss
2. Polyuria/ polydipsia /polyphagia
3. Weakness/Fatigue
4. Blurred vision
5. Recent skin or other infection
6. Vulvovaginitis/balanitis
7. Abdominal pain

Source – Mayo Clinic

Snapshot of Information

Prediabetes & Diabetes Preventive – Clinical Aspects

Development and Validation of a Multivariable Prediction Model to determine the risk of Undiagnosed Prediabetes and Type 2 Diabetes Mellitus

Incidence

a. The age-standardized global prevalence of diabetes mellitus among adult population has nearly doubled since year 1980, rising from 4.7 to 8.5% WHO Global Report 2016
b. The greatest increase in the prevalence of diabetes mellitus is reported from low and middle-income countries. Indian J Endocrinol Metab 2014
c. India has more than 77 million people with T2DM – no accounted figures for Prediabetes. IDF 2020
d. In US, fewer than 13 % of those with prediabetes were aware of their condition, regardless of education level, income, insurance coverage, or healthcare use. CDC

Progression

a. Up to one third of people with prediabetes will progress to diabetes in three to five years. CDC
b. This will increase their risk of cardiovascular disease, stroke, high blood pressure, blindness, kidney disease, nerve disease, and amputation. ADA
c. In addition, prediabetes itself is associated with early onset of neuropathy, retinopathy, microalbuminuria, and greater cardiovascular risk, suggesting that many patients with prediabetes may be already suffering adverse effects of abnormal glucose regulation. TAB

Benefits of Prevention Program

1. In an U.S. Diabetes Prevention Program (DPP) study, patients in the intensive lifestyle intervention arm of the trial had a 58 % reduction in the rate of conversion to type 2 diabetes over three years, and a 34 % reduction at 10 years.
2. Risk of reduction was even more pronounced among individuals age 60 and older (71 % for a three-year reduction). ADA, KNO
3. The 10-year follow-up study of the DPP concluded that investment in lifestyle and metformin interventions for diabetes prevention in high-risk adults is very cost effective. HER

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