



### Introduction

AICVD Cardiac Risk Score is a novel artificial intelligence-based risk score system that provides information about the individual's risk of having coronary artery disease-related events in the next 10 years. Apollo Hospitals developed the risk Score with further validation from National and International institutions. The methodology helps stratify the patient's risk and provides an individualized protocol using a Clinical Decision Support System on the next best actions with an accuracy above 90%.

### Why is AICVD different?

1. Machine Learning Model developed with Indian Data having Higher Accuracy than conventional risk score
  - a. Cox Proportional Hazard Model + Deep Learning Classification Model
  - b. Model Built and Validated with Over 400K Patient data since 2008
  - c. Accuracy - AUC – 0.86 (Development) and 0.92 (Validation) Cohort
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

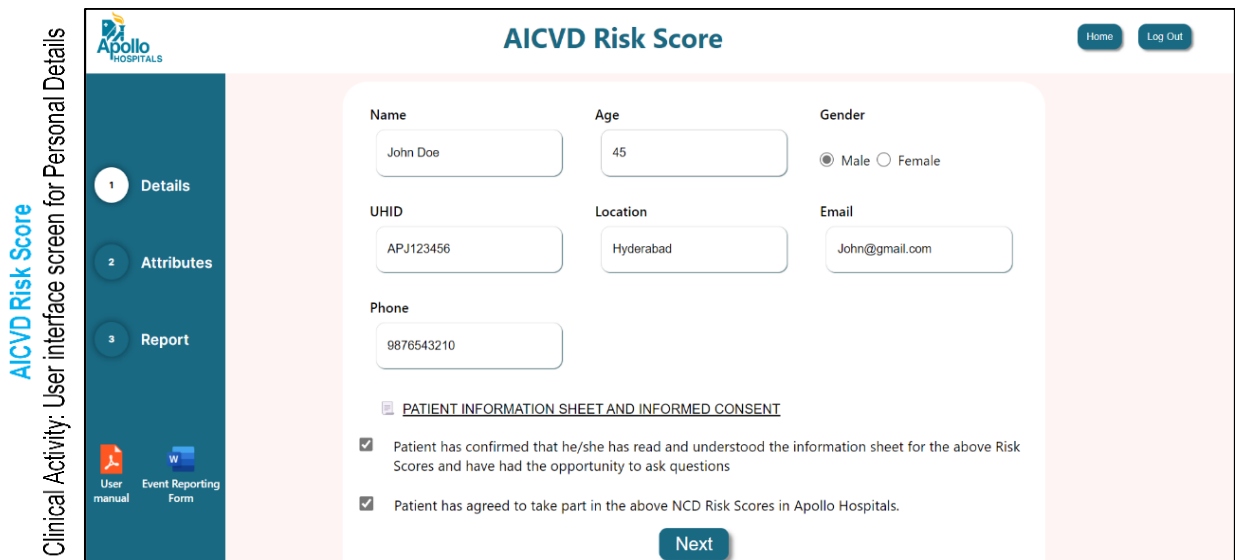
1. AI Algorithm + Clinicians - This Risk Assessment tool has been built as an adjunct tool for the physicians to identify the global/holistic risk for the patient.
2. Risk Identification and Prevention—This Risk Assessment Tool is not to be used to diagnose Coronary Artery Disease. Its limitations include already-diagnosed Cardiovascular Diseases and those currently under treatment.
3. Where to use - This Risk Assessment tool has been prepared for use at Preventive Cardiology Screening programs at the Outpatient Clinics and for Health Check Clinics

### 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 - Diet | Alcohol | Smoking | Tobacco Use | Physical Activity
    - c. History - Family History | Previous CAD | Dyslipidemia\* | Diabetes mellitus\* | Hypertension\* (\*Diagnosis or Medication)
    - d. Heart Related Attributes - Heart Rate | Systolic BP | Diastolic BP | Cardiac Symptoms | Rhythm | Respiratory Rate New! – Psychological Stress
  3. Output
    - a. Risk Categorization
    - b. Cardiac Risk Score and Optimum Risk Score for Individual Age / Gender
    - c. Top Modifiable Risk Attributes
    - d. Clinical Decision Support System (What Next to Do)
      - i. Lab, Imaging and Investigations
      - ii. Cardiology Referral
      - iii. Treatment Goals
      - iv. Education
      - v. Revisit Guidelines

Workflow of AICVD Risk Score



The screenshot shows the 'AICVD Risk Score' application interface. On the left, a vertical sidebar contains the text 'AICVD Risk Score' and 'Clinical Activity: User interface screen for Personal Details'. Below this are three numbered steps: 1. Details, 2. Attributes, and 3. Report. At the bottom of the sidebar are icons for 'User manual' and 'Event Reporting Form'. The main content area is titled 'AICVD Risk Score' and includes a 'Home' and 'Log Out' button in the top right. The form contains the following fields:
 

- Name:** John Doe
- Age:** 45
- Gender:** Male (selected), Female
- UHID:** APJ123456
- Location:** Hyderabad
- Email:** John@gmail.com
- Phone:** 9876543210

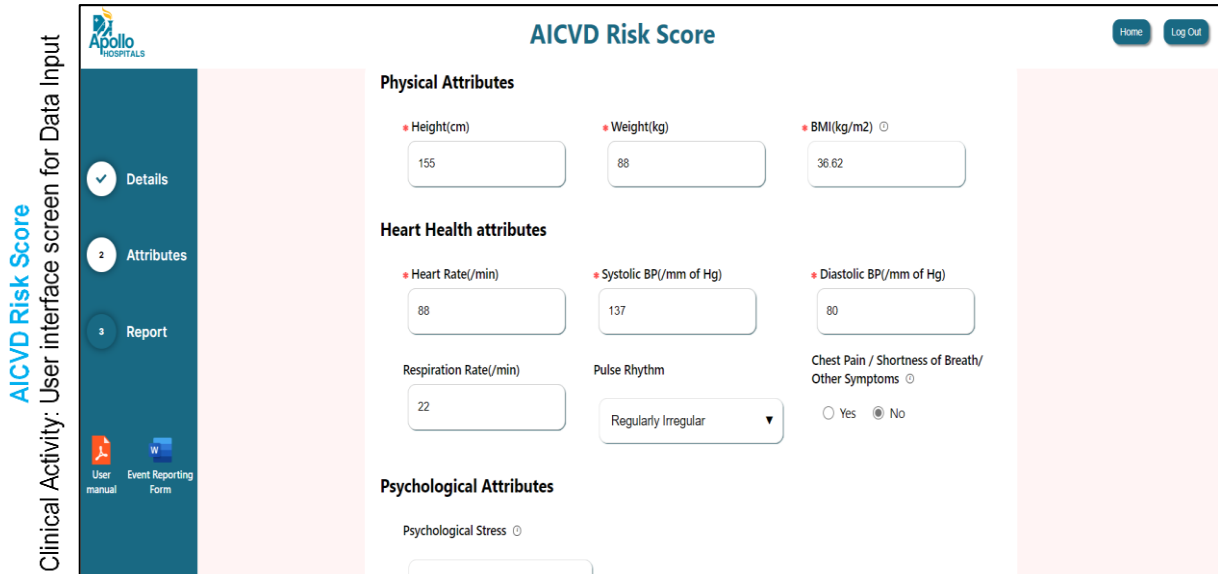
 Below the form fields is a section titled 'PATIENT INFORMATION SHEET AND INFORMED CONSENT' with two checked checkboxes:
 

- Patient has confirmed that he/she has read and understood the information sheet for the above Risk Scores and have had the opportunity to ask questions
- Patient has agreed to take part in the above NCD Risk Scores in Apollo Hospitals.

 A 'Next' button is located at the bottom center of the form area.

Figure 1: Entry of Personal Details

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



**AICVD Risk Score**

Home Log Out

**Physical Attributes**

- Height(cm): 155
- Weight(kg): 88
- BMI(kg/m2): 36.62

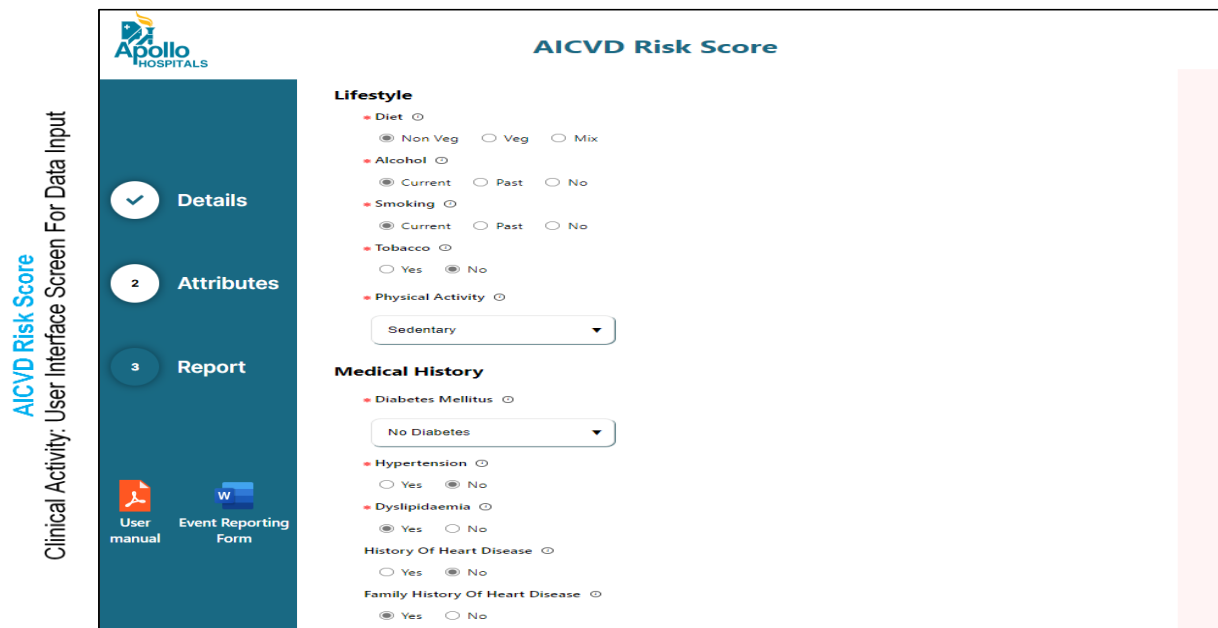
**Heart Health attributes**

- Heart Rate(/min): 88
- Systolic BP(/mm of Hg): 137
- Diastolic BP(/mm of Hg): 80
- Respiration Rate(/min): 22
- Pulse Rhythm: Regularly Irregular
- Chest Pain / Shortness of Breath/ Other Symptoms:  Yes  No

**Psychological Attributes**

- Psychological Stress

Figure 2: Entry of Patient Attributes



**AICVD Risk Score**

Home Log Out

**Lifestyle**

- Diet:  Non Veg  Veg  Mix
- Alcohol:  Current  Past  No
- Smoking:  Current  Past  No
- Tobacco:  Yes  No
- Physical Activity: Sedentary

**Medical History**

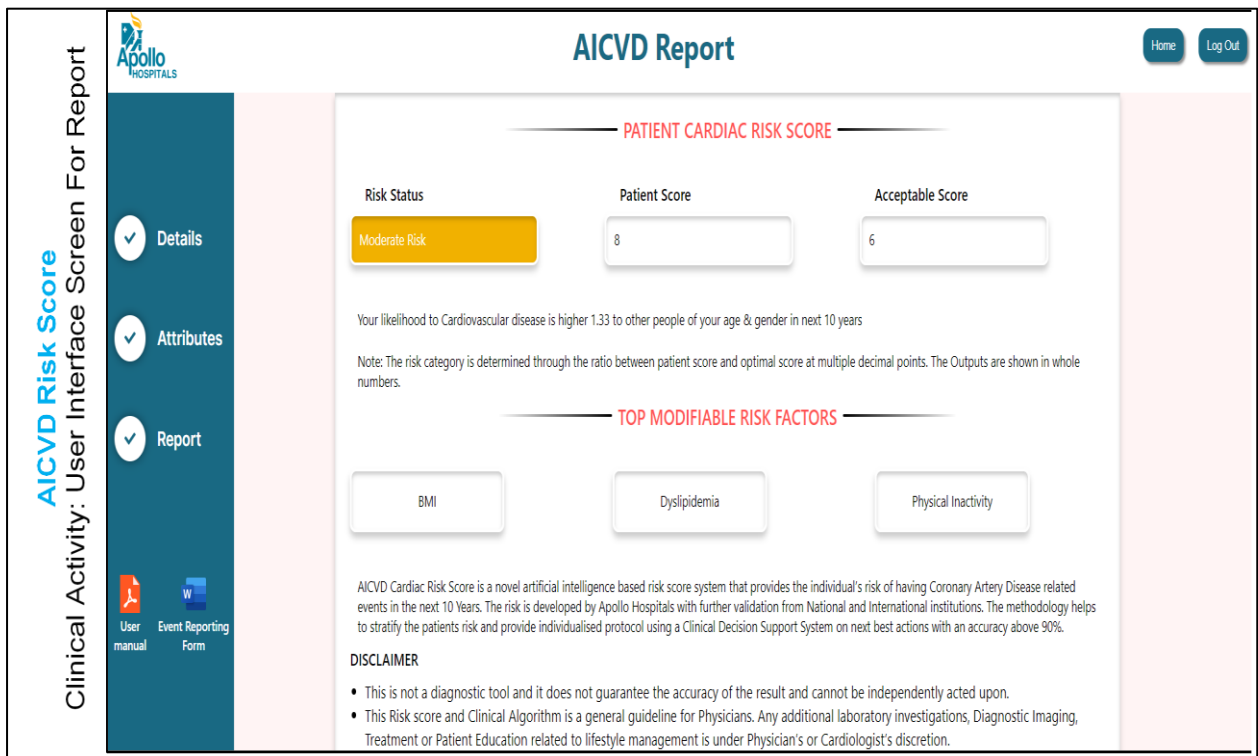
- Diabetes Mellitus: No Diabetes
- Hypertension:  Yes  No
- Dyslipidaemia:  Yes  No
- History Of Heart Disease:  Yes  No
- Family History Of Heart Disease:  Yes  No

Figure 3: Entry of Patient Attributes

Patient Attributes: The following categories are used to collect the patient attributes data:

- Physical Attributes
- Heart Health Attributes
- Psychological Attributes
- Lifestyle Attributes
- Medical History

These parameters are considered data inputs for the model.



The screenshot displays the 'AICVD Report' interface. On the left is a navigation sidebar with 'Clinical Activity: User Interface Screen For Report' and options for 'Details', 'Attributes', and 'Report'. The main content area shows the 'PATIENT CARDIAC RISK SCORE' section with a 'Risk Status' of 'Moderate Risk', a 'Patient Score' of 8, and an 'Acceptable Score' of 6. Below this, it states the patient's likelihood of cardiovascular disease is 1.33 times higher than others of their age and gender in the next 10 years. The 'TOP MODIFIABLE RISK FACTORS' section lists BMI, Dyslipidemia, and Physical Inactivity. A disclaimer at the bottom states that the tool is not diagnostic and should be used as a general guideline under a physician's discretion.

Figure 4: Risk Score Report Generation

Output:

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

- a. Risk Categorization
- b. Cardiac Risk Score and Optimum Risk Score for Individual Age / Gender
- c. Top Modifiable Risk Attributes
- d. Clinical Decision Support System (What Next to Do)
  - i. Lab, Imaging and Investigations
  - ii. Cardiology Referral
  - iii. Treatment Goals
  - iv. Education
  - v. Revisit Guidelines

Printed Report



## AICVD RISK SCORE REPORT

NAME: Sujoy	AGE: 46	LOCATION: Hyderabad
UHID: 123456	GENDER: Male	DATE OF REPORT: 14/9/2021

<b>Informed Consent</b>			
<b>Physical Attributes:</b> Height: 170 Weight: 85 Bmi: 29.41 <b>Psychological Stress:</b> Anxiety Syndromes	<b>Heart Health Attributes:</b> Heart Rate: 90 Systolic Bp: 120 Diastolic Bp: 80 Respiration Rate: 12 Pulse Rhythm: Regularly Regular Chest Pain / Shortness of Breath/ Other Symptoms: No	<b>Life Style:</b> Diet: Mix Alcohol: No Smoking: No Tobacco: No Physical Activity: Active	<b>Medical History:</b> Diabetes Mellitus: Controlled with medication Medication For Hypertension: Yes Dyslipidaemia: No History Of Heart Disease: No Family History Of Heart Disease: No

<b>Patient Cardiac Risk Score</b>		
RISK CATEGORY	PATIENT SCORE	OPTIMAL SCORE
<b>Moderate Risk</b>	<b>8</b>	<b>6</b>
<b>Top Risk Contributors</b>		
bmi	Physical Inactivity	Hypertension

<b>Recommended Protocol</b>
<b>LAB INVESTIGATION</b> Complete Blood Count, Fasting and Post Prandial Blood Sugar, Lipid Profile, Urea & Creatinine + Other Tests as deemed fit (e.g. HBA1C) Homocysteine Levels Lipoprotein a Neutrophil / Lymphocyte Ratio
<b>DIAGNOSTICS AND IMAGING</b> ECG, Chest X-ray, 2D Echocardiography, Dobutamine Stress Echo TMT
<b>REFERRAL</b> Cardiologist Referral (Routine)
<b>TREATMENT PROTOCOL</b> Weight control management It is recommended to consistently encourage weight control through an appropriate balance of physical activity, caloric intake, and formal behavioural programmes when indicated to achieve and maintain a healthy BMI (<25) Lipid management: To maintain a baseline. Annual control of lipids, glucose metabolism and creatinine are recommended. Diabetes: HbA1c < 7% (< 53 mmol/mol). Blood pressure control : < 140/90 mmHg Smoking / Tobacco Use cessation: No exposure to tobacco in any form or support in smoking cessation. Psychosocial management: Psychosocial risk factor screening should be considered

### 2. Disclaimer

- a. This is not a diagnostic tool and it does not guarantee the accuracy of the result and cannot be independently acted upon.
- b. 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 under the Physician's or Cardiologist's discretion.
- c. To ensure the information in the report is up to date, accurate, and correct, the Doctor shall be consulted for interpretation of the report.

- d. 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 AICVD Cardiac Risk Score without any intervention from their side.
- e. By usage of AICVD Cardiac 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.

## Research

Cardiovascular diseases (CVD) are one of the most prevalent diseases in India amounting to nearly 30% of total deaths. The dearth of research on CVD risk scores in the Indian population, limited performance of conventional risk scores, and inability to reproduce the initial accuracies in randomized clinical trials – have led to this study on large-scale patient data.

The objective is to develop an Artificial Intelligence-based Risk Score (AICVD) to predict CVD Events (e.g. Acute MI / ACS) in the next 10 years and compare the model with the Framingham Heart Risk Score (FHRS) and QRisk3. The study included 31,599 participants aged 18-91 years from 2010-2017 in six Apollo Hospitals in India. A multi-step risk factors selection process using the Spearman correlation coefficient and propensity score matching yielded 21 risk factors. Using a multi-layered neural network, the deep learning hazard Model was built on risk factors to predict event occurrence (classification) and time to event (hazard model). Further, the model was validated with independent retrospective cohorts of participants from India and the Netherlands and compared with FHRS and QRisk3.

The performance of the Deep Learning Hazard model was at AUC 0.853. Validation and comparative results showed AUCs between 0.84 to 0.92 with better Positive Likelihood Ratio (AICVD-6.16 to FHRS- 2.24 and QRisk3-1.16) and Accuracy (AICVD- 80.15% to FHRS 59.71% and QRisk3 51.57%). In the Netherlands cohort, The AUC of AICVD outperformed the Framingham Heart Risk Model (0.737 to 0.707).

The study concludes that the novel AI-based CVD risk score improves on accuracy and precision of prediction than conventional risk scores.

## Ethics Perspective

<b>Title</b>	Development and Validation of Multicenter Study on Novel Artificial Intelligence Based Cardiovascular Risk Score (AICVD)	<b>Centers</b>	India – Apollo Hospitals in Delhi, Kolkata, Hyderabad, Bangalore, Chennai and Mumbai King George Medical Univ. Lucknow Maastricht Univ. The Netherlands
<b>Principal Investigators</b>	Dr Shivkumar J (Apollo Hospitals), Prof Andre Dekker (Maastricht UMC), Prof Rishi Sethi (KGMU, Lucknow), Dr Sujoy Kar (Apollo Hospitals)	<b>Institutional Ethics Committee Approval</b>	All Centres between Sept 2018 to Nov 2019 and annually followed. CTRI Registration – done Microsoft Aether (Ethics) approved
<b>Data</b>	Retrospective – Prospective Jan 2008 to June 2018 September 2019 Onwards	<b>Safety</b>	Model advocates risk scores that are interpreted by clinicians through safe Machine (API) – Human (Clinician) Interaction
<b>Sample Size + Missing Data</b>	31599 + 3246 (Validation) + 1340 (KGMU) + 12588 (MUMC) No imputations	<b>Inclusiveness &amp; Fairness</b>	At admission data includes clinical comorbidities & conditions   No socioeconomic discrimination
<b>Personal Health information</b>	De-identified all PHI during analysis, model building, API hosting and Prospective Use	<b>Privacy &amp; Confidentiality</b>	Data secured at Apollo Azure Tenant with all relevant compliance + conforming to laws
<b>Addressing Bias (Geographical / Ethnic / Temporal / Gender etc.)</b>	Multiethnic – All Adult Population Group – Male to Female – 55 : 45 – Time Period – Jan 2008 to June 2018 Automation Bias addressed at API Clinical Use	<b>Accuracy + Efficacy</b>	Classification Metrics - sensitivity: 0.83   specificity: 0.9   Accuracy Score : 0.87
<b>Risk Groups</b>	Low – Moderate – High Risk of CVD	<b>Informed Consent</b>	Yes – Template & Protocol (Prototype Attached)
<b>Model Specification</b>	Cox Proportional Hazard + Deep Learning + Hazard Ratio + KM Plots	<b>API – Ease of Use + Interpretation</b>	Flows to Clinical Algorithm Standard Clinical Definitions + Lab Units Used
<b>Clinical Algorithm Update (Version)</b>	Version 3 – February 2021	<b>Validation + Peer Review</b>	American College of Cardiology Lancet Open Source BMJ Open – Under Review
<b>Intellectual Property Rights (IPR)</b>	Patent No 202241055803	<b>Certifications &amp; Compliance</b>	ISO 13485:2016 Certification   MD 763515 CDSCO Application No   Apollo-Hyderabad/M/MD/007509

## Frequently Asked Questions

### Introduction.

AICVD Cardiac Risk Score is a novel artificial intelligence-based risk score system that provides the individual's risk of having Coronary Artery Disease events in the next 10 Years. 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 with an accuracy above 90%

### Why is AICVD different or What is the advantage of this score?

1. Machine Learning Model developed with Indian Data having Higher Accuracy than conventional risk score
  - a. Cox Proportional Hazard Model + Deep Learning Classification Model
  - b. Model Built and Validated with Over 400K Patient data since 2008
  - c. Accuracy - AUC – 0.86 (Development) and 0.92 (Validation) Cohort
2. Feedback Loop from the prospective use in patients
3. Comprehensive & Holistic Risk Assessment
4. Validated at different National and international Institutions
  - a. King George Medical University, Lucknow (India)
  - b. Maastricht University Medical Centre (The Netherlands)
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 the physicians to identify the global/holistic risk for the patient.
2. Risk Identification and Prevention - This Risk Assessment Tool is not to be used for diagnosis of Coronary Artery Disease. Its limitations include already-diagnosed Cardiovascular Disease and currently under treatment.

### Where can the physicians use the AICVD tool –

This Risk Assessment tool has been prepared for use in Preventive Cardiology Screening programs at Outpatient Clinics and Health Check Clinics.

### What are the Risk Factors Included –

- a. Personal/VS – Age | Gender | Height | Weight | BMI
- b. Life Style Attributes - Diet | Alcohol | Smoking | Tobacco Use | Physical Activity
- c. History - Family History | Previous CAD | Dyslipidemia\* | Diabetes mellitus\* | Hypertension\* (\*Diagnosis or Medication)
- d. Heart Related Attributes - Heart Rate | Systolic BP | Diastolic BP | Cardiac Symptoms | Rhythm | Respiratory Rate New! – Psychological Stress

### What is the Output and Follow-Up For the Risk Score

- a. Risk Categorization – Low – Moderate – High Risk of Cardiovascular Disease in the next 10 years
- b. Cardiac Risk Score and Optimum Risk Score for Individual Age / Gender
- c. Top Modifiable Risk Attributes
- d. Clinical Decision Support System (What Next to Do)
  - i. Lab, Imaging and Investigations
  - ii. Cardiology Referral

- iii. Treatment Goals
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- 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 under the Physician's or Cardiologist's discretion.

How does one ensure the accuracy of the AICVD tool

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 be liable for any loss or damage as the said report is based on the AICVD Cardiac Risk Score without any intervention from their side.
- b. By usage of the AICVD Cardiac 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.

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 to maintain privacy and confidentiality.

Is this tool validated for research ethics committees

Yes. Institutional Ethics Committee Approval for All Centres between Sept 2018 to Nov 2019 and annually followed. ICMR CTRI Registration is also done for this research. Further, Microsoft AETHER (Ethics in AI) has also reviewed the tool.

How is Safety addressed?

The model advocates risk scores clinicians interpret through a 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/m<sup>2</sup>
- B. Normal,  $18.5 \leq \text{BMI} < 25$  kg/m<sup>2</sup>
- C. Overweight,  $25 \leq \text{BMI} < 30$  kg/m<sup>2</sup>



- D. Obesity
  - a. Obesity I,  $30 \leq \text{BMI} < 35$
  - b. Obesity II,  $35 \leq \text{BMI} < 40 \text{ kg/m}^2$
  - c. Obesity III,  $\geq 40 \text{ kg/m}^2$

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 ( $\geq 14$  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  $\geq 140$  (if at least two results  $\geq 14$  days apart), or
  - b. diastolic blood pressure average  $\geq 90$  (if at least two results  $\geq 14$  days apart)

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

#### Dyslipidemia or 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  $\geq 250 \text{ mg/dL}$
  - b) HDL  $< 40 \text{ mg/dL}$  for males and  $< 50 \text{ mg/dL}$  for females.
  - c) non-HDL value  $\geq 160 \text{ mg/dL}$

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

#### Family History of Heart Disease

- a) Arrhythmias
- b) Structural Heart Disease
- c) Cardiomyopathy
- d) Heart Failure
- e) CAD – Previously treated

#### History of Heart Disease

- a) Arrhythmias
- b) Structural Heart Disease
- c) Cardiomyopathy
- d) Heart Failure
- e) CAD – Previously treated

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

1. A fasting plasma glucose (FPG)  $\geq 126$  mg/dl. Fasting is defined as no caloric intake for at least 8 hr.
2. Symptoms of hyperglycemia and a casual (random) plasma glucose  $\geq 200$  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  $\geq 200$  mg/dl 2 hr after a 75 g (100 g for pregnant women) glucose load.
4. A haemoglobin A1c (HbA1c) value  $\geq 6.5\%$ .
  - a. Patient with no history of diabetes and previous record of normal FPG / OGTT /HbA1c – **Select NO**
  - b. Patient with a history of diabetes and a current record of HbA1c  $< 7.5\%$  - **Select Controlled**
  - c. Patient with a history of diabetes and a current record of HbA1c  $\geq 7.5\%$  - **Select Uncontrolled**

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

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

Symptoms include –

- a) Chest pain or chest discomfort
- b) Dyspnoea or shortness of breath

- c) Swelling of legs (Peripheral Edema)
- d) Palpitations and / or Syncope
- e) Others

History (As per NYHA)

- a. Underlying Etiology – Congenital, Hypertensive, Ischemic or Inflammatory
- b. Anatomic abnormalities – Heart Chambers; Hypertrophy or Dilated or both; Valvular disease – stenosis or regurgitation
- c. Physiological – Arrhythmia, Congestive Heart Failure, Coronary Artery Disease, etc
- d. Functional Disability – NYHA Class I – IV
- e. Family History of Sudden Cardiac Death

Source – Joseph Loscalzo M.D. Harrison’s Principles of Internal Medicine 20th Edition: The Criteria Committee of New York Heart Association

Psychological Stress

1. Negative Thought Patterns and Emotions
  - a. Depressive syndromes
    - i. Mild to moderate depressive symptoms
    - ii. Major depression
    - iii. Hopelessness
  - b. Anxiety syndromes
    - i. Generalized anxiety disorder
    - ii. Phobic anxiety
    - iii. Panic disorder
    - iv. Post-traumatic stress disorder
  - c. Hostility and anger
  - d. Worry and Pessimism
2. Chronic Stress
  - a. Work stress
  - b. Marital stress and dissatisfaction
  - c. Social isolation and lack of social support
  - d. Low socioeconomic status
  - e. Adverse childhood experience

Source: Alan Rozanski: Chapter 34 Psychological Risk Factors and Coronary Artery Disease etc. Preventive Cardiology: Companion to Braunwald's Heart Disease