Introduction

The Adult Early Warning System (Adult-EWS) is an innovative AI-based risk score system, utilizing a triphasic model developed by Apollo Hospitals to predict individual risks of Clinical deterioration and Mortality. In Phase 1, an XGB model achieved 83% accuracy with vital signs and demographics. Phase 2 incorporates a Neural Network, expanding inputs to vital signs, comorbidities, and symptoms, achieving 84% accuracy in predicting Mortality and Clinical deterioration. Phase 3 integrates an XGB model with comprehensive parameters, reaching 92% accuracy. Throughout all phases, the system provides numerical confidence levels and risk categorization, empowering caregivers with informed decision-making tools for patient care.

Why is EWS different?

1. Triphasic Machine Learning Model developed with Indian Data having Higher Accuracy than conventional scores such as National Early Warning Score - (NEWS) 2, Modified Early Warning Score (MEWS) for Clinical deterioration
   a. Phase 1 - vitals Algorithm - XGB model – Accuracy - 83%
   b. Phase 2 - Vitals + Comorbidities Algorithm - Neural Network– Accuracy - 84%
   c. Phase 3 - Vitals + Comorbidities + lab parameters Algorithm - XGB model– Accuracy -92%

2. Feedback Loop from the prospective use in patients, particularly high-frequency data from wearables and other devices
3. Comprehensive & Holistic Risk Assessment comprising Vitals + Clinical State + Lab parameters
4. Validated at different National & International Institutions (Ongoing)

What is the Interpretation & Adoption Message?

1. AI Algorithm + Clinicians - This Early Warning System - Risk Assessment tool has been developed as an adjunct tool for the physicians to identify the global/holistic risk for the patient's Clinical deterioration/mortality in the next 1 hour/7 days respectively.

2. Risk Identification and Prevention - This Risk Assessment tool provides a mortality risk prediction using clinical and laboratory parameters at Wards and Remote Health. This model is specially tailored to ensure that it can be used in low-cost settings to improve triage and resource allocation.

3. Where to use - This Risk Assessment tool is intended for use in Inpatient settings and Remote care settings to trigger a Rapid Response Team (RRT) or Medical Emergency team.

4. Limitations for Use –

    a. The model is based on a comprehensive coverage of the adult Indian population and It is not recommended for Pediatric Population

    b. Further research is needed to calibrate the model to other population zones like the US, Europe, Middle East, and South East Asia.

    c. This model should not be used in Emergency Room settings for determining immediate Triage categories. It doesn't replace or work as a triage algorithm

    d. The model results may vary in patients who are already under Non-Invasive or Invasive Ventilator Settings, and receiving IV inotropic support for maintaining blood pressure/circulation in Critical Care Settings

    e. Model is not built on data from Pregnant Women in Labour, Acute Psychiatric Conditions, and Individuals with substance abuse, and hence results may vary.

    f. The model doesn't recommend any changes in the protocol of Critical Care – in terms of diagnostic or prognostic investigations, therapy, and care.

    g. The model doesn't support End of Life Care protocols in clinical settings.

<u>How to Use (For Clinicians Only) –</u>

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

2. Risk Factors Included –
    a. Personal/VS – Age | Gender | Height | Weight | BMI
    b. Vital Signs - Heart rate | Systolic blood pressure | Diastolic blood pressure| Rate of respiration |Temperature | Oxygen Saturation| RBS
    c. Past surgery - Surgery Type| Surgery Name| ICD 10 PCS coding| Date of surgery
    d. Current diagnosis - ICD -10 Coding
    e. History/Comorbidities - History of Diabetes Mellitus| Hypertension | coronary artery disease | Heart Failure |Arrhythmia| lung disease | Central Nervous System Disorders | Immunocompromised state | chronic kidney disease
    f. Clinical symptoms – Allergies |Recent onset Fever| Cough| Weakness| Respiratory Distress| Cardiovascular Symptoms |Trauma | Unconsciousness |Abdominal signs and symptoms
    g. Laboratory parameters-
        i. Complete Blood Count - Hemoglobin| RBS| Platelet Count| WBC| Lymphocyte| RDW| Eosin

ii. Basic Biochemistry - Creatinine| AST| ALT| Sodium; Potassium| Alkaline Phosphatase| HBA1c| Urea|
iii. Coagulation Profile - INR| Prothrombin Time | D dimer| Activated Prothomboplastin Time|
iv. Inflammatory Markers - CRP| LDH| Ferritin| Interleukin-6| Procalcitonin.

3. Output –
   a. Algorithm employs an XGB model to predict the likelihood of Mortality/ Clinical deterioration in terms of Death, Transfer to ICU or Critical Care unit, Clinical Alert that requires a physician intervention or Rapid Response Team call in hospitalized patients.
   b. Risk Categorization – Low – Moderate – High Risk for Clinical deterioration in 24 hours and Risk of Mortality in the next 7 days.
   c. EWS Risk Score with Hourly Dial System
   d. Clinical Decision Support System (What Next to Do)

4. Useful References –

- Early Warning System Scores for Clinical deterioration in Hospitalized. https://www.atsjournals.org/doi/pdf/10.1513/AnnalsATS.201403-102OC.
- Impact of early warning systems on patient outcomes - University of York. https://www.york.ac.uk/crd/publications/effectiveness-matters/early-warning-systems/ .
- Early warning scores and critical care transfer - Springer. https://link.springer.com/article/10.1007/s11845-021-02558-7.
- The use of early warning system scores in prehospital and ... PLOS. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0265559.

Workflow for EWS App

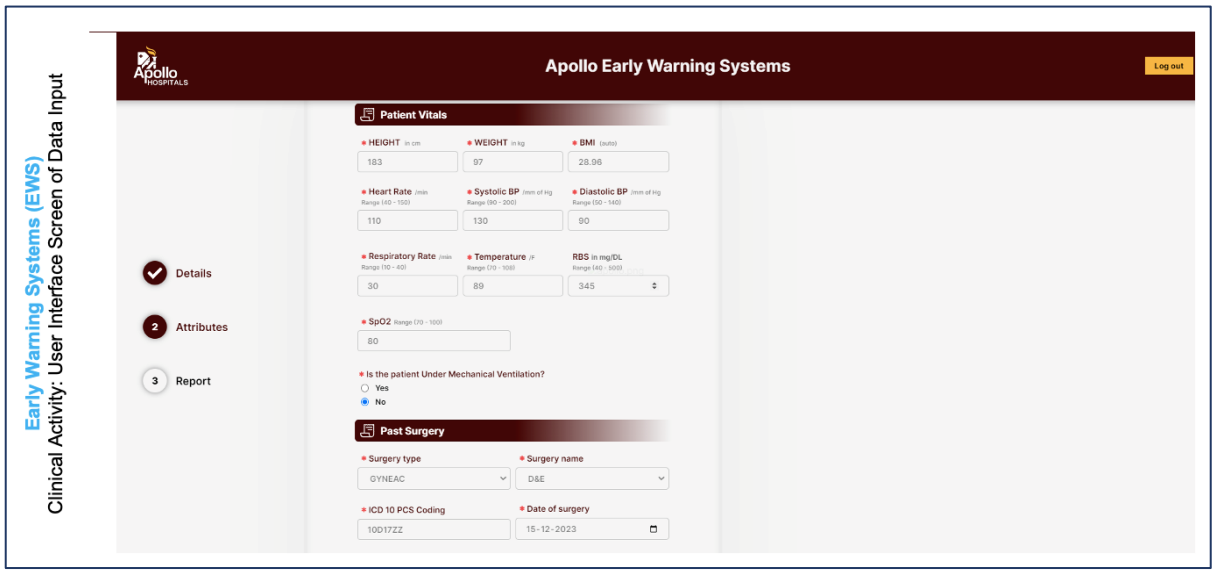


Figure 1 – Entry of Patient Vitals and Clinical Parameters (At admission & hourly)

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

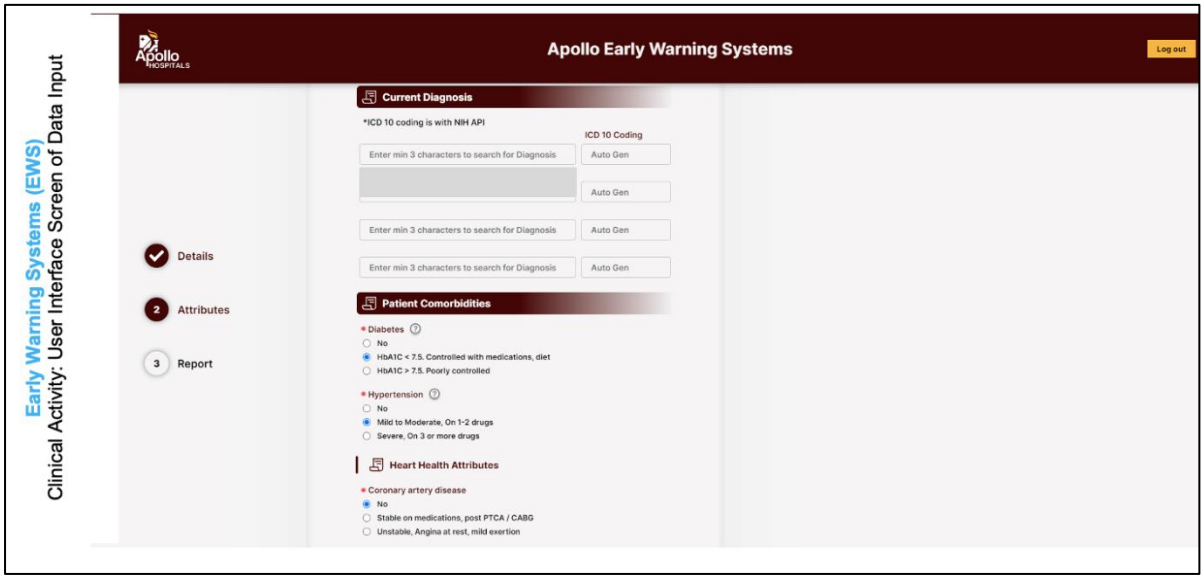


Figure 2 – Entry of Clinical Parameters (Once and when changed)

Patient Attributes: The following categories are used to collect the patient attributes data: Patient Vitals, Past Surgery with Procedure Coding, Current Diagnosis with ICD 10 Coding; Patient Comorbidities, Lung/Respiratory Health Attributes, Other Systems, Symptoms/History of Present Illness.

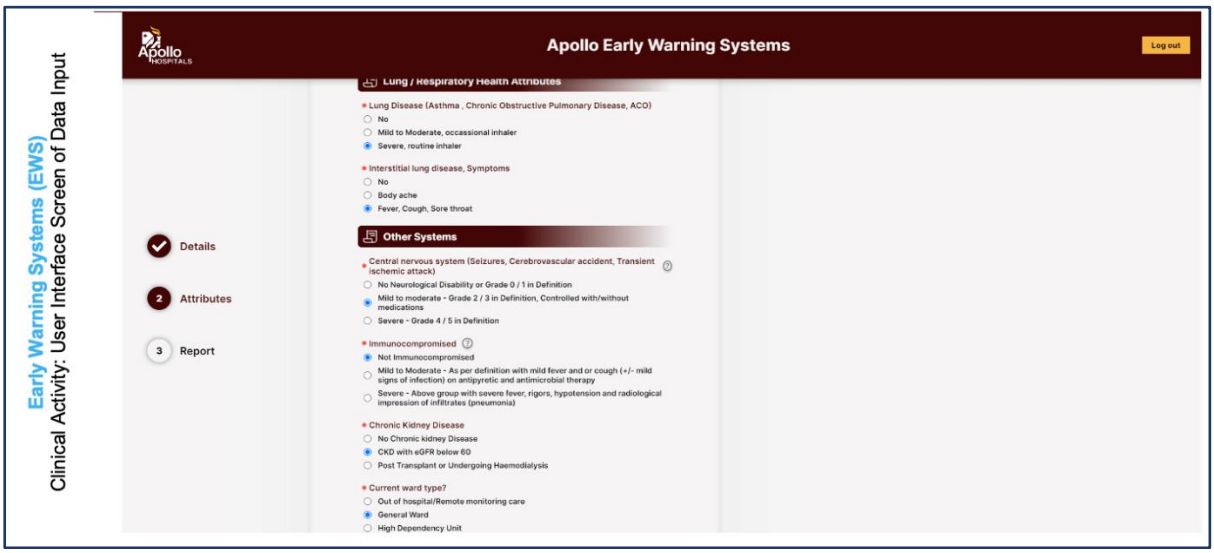


Figure 3 – Comprehensive Patient Clinical State Entry (Once and when changed)

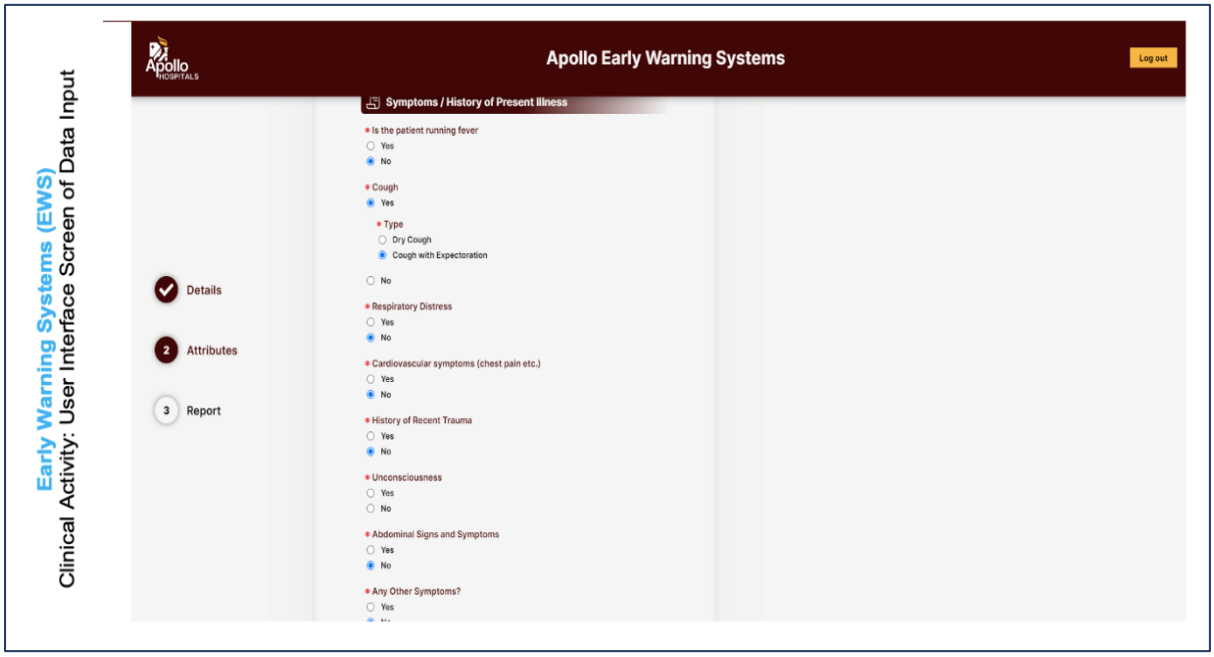


Figure 4 – Entry of patient symptoms in ease – binary ways (changes in the past 24 hours can also be reported)

Next is the entry of Laboratory parameters are categorized into –

a. Complete Blood Count (Mandatory)
b. Basic biochemistry including Kidney and Liver Profile Tests, (Mandatory)
c. Coagulation Profile including Prothrombin Time, International Randomized Ratio (INR), Activated Pro-thromboplastin Time (APTT) and D-dimer (Optional),
d. Inflammatory markers like C-reactive protein (CRP), Lactic Acid Dehydrogenase (LDH), Ferritin, Interleukin-6 (Optional), and Procalcitonin.

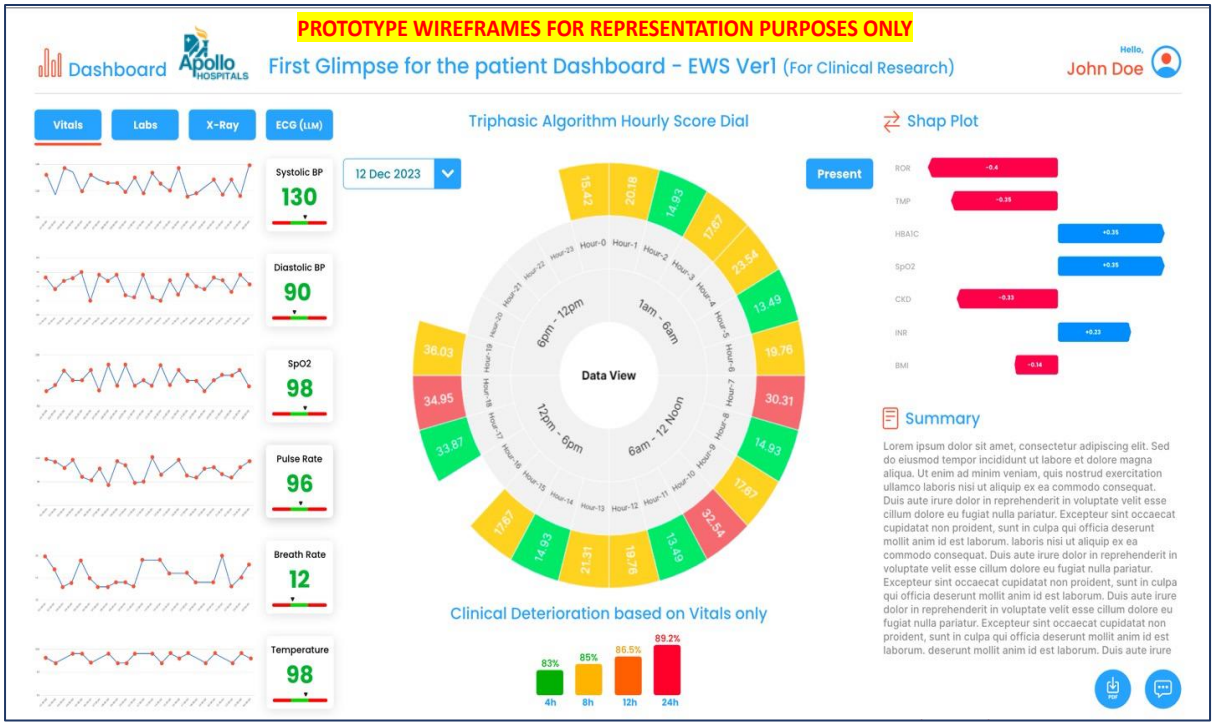


Figure 5 – EWS Dashboard Showing the Vital Sign

Figure 5: Shows the Output screen with Vitals on the Left side with the average of the last hour and trend chart; a 24-hour dial which represents each hour and patient score with color coding for the different zones (Default is <15 – Green (Low Risk); 15 – 30 – Yellow (Moderate Risk) and >30 – Red (High Risk); below the dial – it represents the probability of Clinical deterioration in next 4hrs – 8 hrs = 12 hrs – 24 hrs and SHAP & explainable values for the results on the right-hand side. Users can also view previous days' 24-hour dial, get a Generative AI report of the hour, and print of patient's current status.

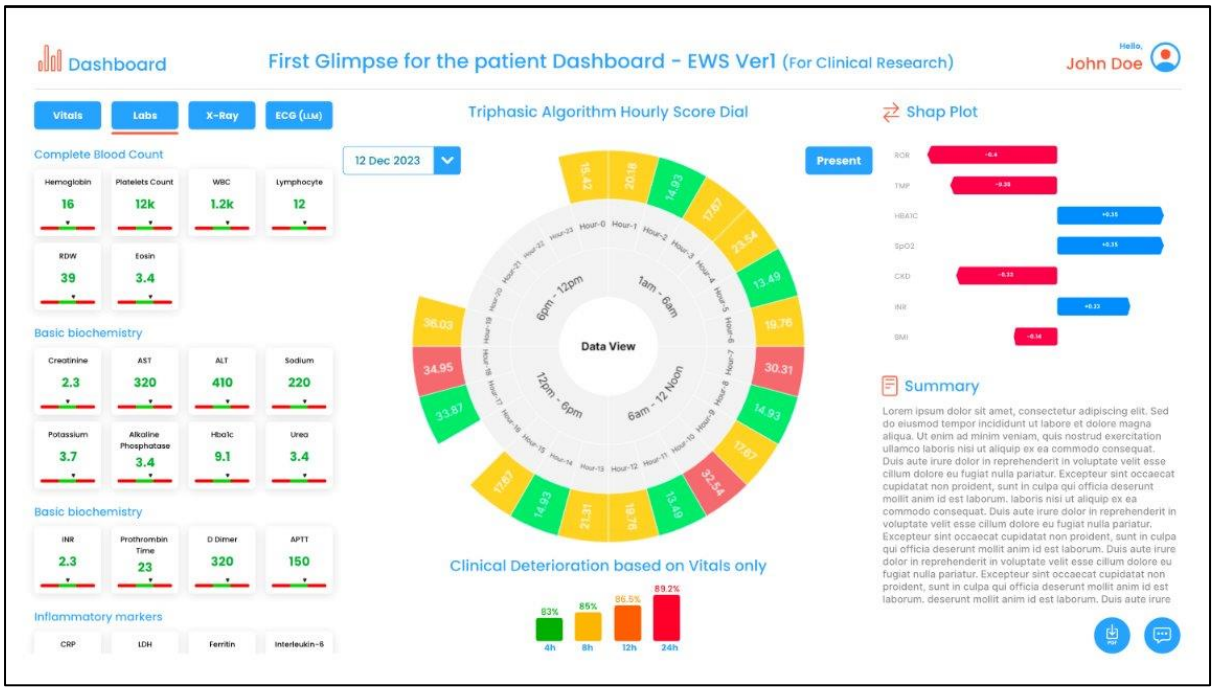


Figure 6 – As Figure 5, Showing the Lab Parameters

Printed Report

Apollo Early Warning Systems AI Report

UHID	: APJ10009873	Name	: JHON WICK	Age	: 41
Gender	: Male	location	: HYDERABAD	Mobile	: 9590438274

OBTAINED CONSENT

Patient Vitals

Height (in cm)	183	Weight (in kg)	97	BMI	28.96
Heart Rate (in min)	110	Systolic BP	130	Diastolic BP	90
Respiratory Rate	30	SpO2	80	Temperature	89
Random blood Sugar	345	Patient Ventilated	No	Ventilated Type	NA

Patient Comorbidities

Diabetes	Yes	Heart Failure	Yes
Hypertension	Yes	Arrhythmia	No
Coronary Artery Disease	No		

Lung / Respiratory Health Attributes

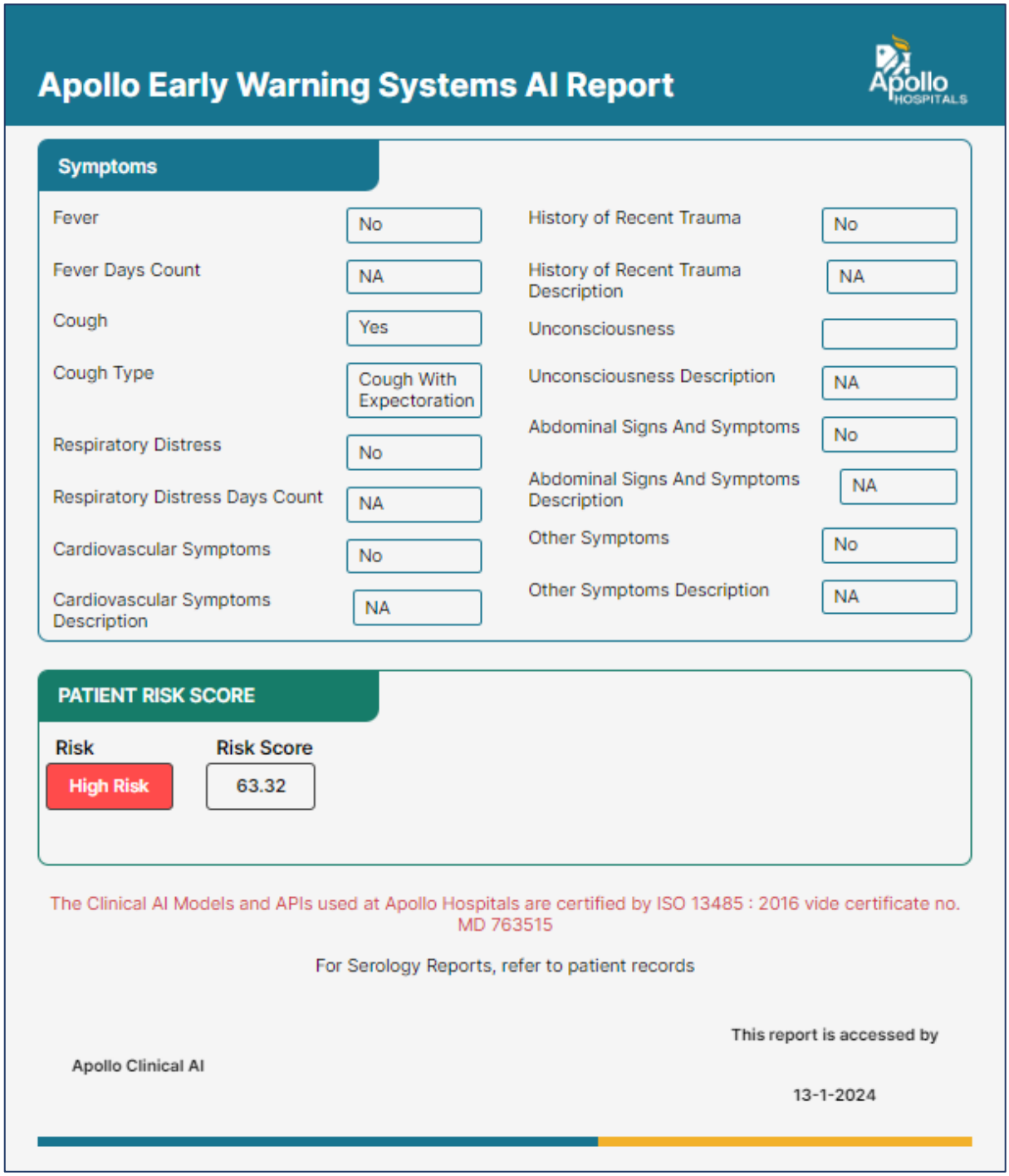
Lung Disease	Yes	Interstitial lung Disease	Yes

Other Systems

Central Nervous System	Yes	Ward Type	General Ward
Immunocompromised	No	Allergies	No Allergies
Chronic Kidney lung Disease	Yes		

This report is accessed by

Apollo Clinical AI



Apollo Early Warning Systems AI Report

Symptoms

Fever	No	History of Recent Trauma	No
Fever Days Count	NA	History of Recent Trauma Description	NA
Cough	Yes	Unconsciousness	
Cough Type	Cough With Expectoration	Unconsciousness Description	NA
Respiratory Distress	No	Abdominal Signs And Symptoms	No
Respiratory Distress Days Count	NA	Abdominal Signs And Symptoms Description	NA
Cardiovascular Symptoms	No	Other Symptoms	No
Cardiovascular Symptoms Description	NA	Other Symptoms Description	NA

PATIENT RISK SCORE

Risk	Risk Score
High Risk	63.32

The Clinical AI Models and APIs used at Apollo Hospitals are certified by ISO 13485 : 2016 vide certificate no. MD 763515

For Serology Reports, refer to patient records

This report is accessed by

Apollo Clinical AI

13-1-2024

5. 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 EWS without any intervention from their side
e. By usage of EWS, 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

An Early warning system (EWS) is a tool used in hospitals to help detect early signs of Clinical deterioration and trigger alerts that escalate the level of attention, which may include heightened nursing surveillance, notification of the care provider, or initiation of actions such as activating a Rapid Response Team (RRT) or Medical Emergency team.

At Apollo Hospitals, we've developed Early Warning System (EWS) Models using anonymized inpatient data of individuals aged 18 years and above. The Triphasic Model leverages advanced models for patient risk assessment.

The Event rate used in the Algorithm accounts for the Clinical deterioration and is considered 8.6 % from the test and validation data. The Event rate used in the Algorithm accounts for the Mortality and is considered as 2.8 % from the test and validation data. Further, we obtained propensity match scores to help address selection bias, unmeasured confounders, and heterogeneity of comorbidities, their intervention, and outcome features (Mortality/Clinical deterioration) which can vary in the subjects and cohorts over the studied period.

In Phase 1, an XGB model was developed using 32,000 patients and over 700 million vital data points training and testing datasets, incorporating vital signs and demographic information to forecast Clinical deterioration. It provides a risk score and categorizes risk levels, achieving an accuracy of 84%.

In Phase 2, a Neural Network has been developed using over 145,000 + Training and Testing datasets. The inputs have been expanded to include an array of vital signs, comorbidities, and symptoms. The model is designed to predict both Mortality and Clinical deterioration, achieving an accuracy rate of 84%.

Phase 3 involves the integration of an XGB model constructed using 145,000+ training and testing datasets. This model incorporates vital signs, comorbidities, and a comprehensive set of laboratory parameters to enable a holistic prediction of mortality or clinical deterioration, achieving an accuracy rate of 92%.

Across all phases, the system provides Numerical confidence levels and Risk categorization, aiding caregivers in making informed decisions.

Ethics Perspectives:

Title	Development and Validation of a Multivariable prediction model using Machine learning to predict the outcome of hospitalized and monitored patients at hospital	Centers	India – Chennai, Bangalore, Hyderabad, Delhi, Mumbai, Kolkata, Nashik, Bhubaneswar
Principal Investigators	Sujoy Kar. Sai Praveen Haranath, Bharath Potla, Sangita Reddy	Institutional Ethics Committee Approval	JAN 2023
Data	Retrospective – Phase 1 - JAN 2023 –OCT 2023 Phase 2&3 - JAN 2018- December 2022	Safety	Model advocates Risk Scores that are interpreted by clinicians through safe Machine (API) – Human (Clinician) Interaction
Sample Size + Missing Data	Phase 1 Model – 700 Million Data-2023 Phase 2 & 3 Model - 145k Data-2022	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 – Gender – All Phases - Male to Female - 58:42 Automation bias addressed at API clinical use	Accuracy + Efficacy	Classification Metrics - Phase 1- Accuracy-83%|Sensitivity-84%|Specificity -81% Phase 2- Accuracy-84%|Sensitivity72% |Specificity-86% Phase 3- Accuracy-92%|Sensitivity-74%|Specificity-96%
Risk Groups / Out put	Low – Moderate – High Risk of Clinical Deterioration/Mortality	Informed Consent	Yes – Template & Protocol (Prototype Attached)
Model Specification	Phase 1 - vitals Algorithm - XGB model Phase 2 - Vitals + Comorbidities Algorithm - Neural Network Phase 3 - Vitals + Comorbidities + lab parameters Algorithm - XGB model	API – Ease of Use + Interpretation	Flows to Clinical Algorithm Standard Clinical Definitions + Lab Units Used
Clinical Algorithm Update (Version)	Version 1 – May 2023	Validation + Peer Review	Lancet Digital Health (Under Peer Review)
Intellectual Property Rights (IPR)	Patent No|202441065935	Certifications & Compliance	ISO 13485:2016 Certification | MD 763515 CDSCO Application No for Medical Device| Apollo-Hyder-TE/M/MD/007509

Frequently Asked Questions

Is this a diagnostic tool?

This is not a diagnostic tool; 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 is the probability of clinical deterioration. Any additional laboratory investigations, Diagnostic Imaging, Treatment or Care escalation, or activating a Rapid Response Team (RRT) or Medical Emergency team is under the Physician's discretion.

How does one ensure the accuracy of the EWS 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 developed using Clinical Features such as Vitals, Comorbidities & Lab 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 EWS Risk Score without any intervention from their side.
b. By usage of the EWS 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 ensuring privacy.

Is this tool validated for research ethics committees?
Yes. Institutional Ethics Committee Approval for All Centers and annually followed.

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

1. Clinical Deterioration: Clinical deterioration is the process where a patient's health status declines, which could potentially lead to critical conditions or even death if not promptly addressed. In this study, we consider Clinical deterioration as –
    a. Transfer of patient to Critical Care Unit based on:
        i. Physiological Vital Sign Criteria (Classically used in traditional Early Warning Signs model)
        ii. Abnormal Laboratory values
        iii. Physical Findings like - Unequal pupils in an unconscious patient, Anuria, Airway obstruction, Coma, etc.
        iv. Specific Clinical Conditions requiring monitored care in different specialty

        Source: Gerry S, Bonnici T, Birks J, Kirtley S, Virdee P S, Watkinson P J, et al. Early warning scores for detecting deterioration in adult hospital patients: systematic review and critical appraisal of methodology BMJ 2020; 369 :m1501 doi:10.1136/bmj.m1501

    b. Rapid Response Team or Code Blue Calls: Situations when immediate responses are sought in hospital patients showing objective or subjective signs of clinical deterioration through detection of abnormal vital signs or significant clinical changes like difficulty respiration, bleeding, seizures, etc.

        Source: Jones, D., Rubulotta, F. & Welch, J. Rapid response teams improve outcomes: yes. Intensive Care Med 42, 593–595 (2016). https://doi.org/10.1007/s00134-016-4219-5

2. BMI: Body Mass Index (BMI) is a person's weight in kilograms (or pounds) divided by the square of height in meters (or feet).
    Source: Body Mass Index (BMI) | Healthy Weight, Nutrition, and Physical Activity | CDC

Vital Signs Definition

3. Hearth Rate: Heart rate, the number of times the ventricles of the heart contract and relax (that is, beat) per minute or other unit of time.
4. Systolic blood pressure (SBP): Systolic blood pressure, the top number, measures the force the heart exerts on the walls of the arteries each time it beats
5. Diastolic Blood pressure: Diastolic blood pressure, the bottom number, measures the force the heart exerts on the walls of the arteries in between beats.

6. Rate of Respiration/Respiratory rate (ROR): Respiratory rate is also known as your breathing rate. This is the number of breaths you take per minute.
7. Temperature: Body temperature is measured by a clinical thermometer and represents a balance between the heat produced by the body and the heat it loses.
8. SPo2: SpO2 stands for Saturation of Peripheral Oxygen, a measure of how much oxygen is bound to Hemoglobin in the blood. In this study, majority of the Oxygen Saturation (>92%) is determined by pulse oximetry – which is a non-invasive method that uses a sensor attached to the finger or earlobe to measure the oxygen saturation indirectly.

   Sources:
   - Heart rate | Description, Monitoring, & Facts | Britannica
   - Blood pressure chart: What your reading means - Mayo Clinic
   - How to measure your respiratory rate - Mayo Clinic
   - Body temperature | definition of body temperature by medical dictionary (thefreedictionary.com)
   - What is SpO2? | Pulse Oximetry | What is The Normal SpO2 Level? (somatechnology.com)

9. Identified Thresholds Based on Event rate of 8% (ICU Transfer + RRT Calls during Hospitalization) and XG Boost Machine Learning Algorithm, Current API provides the Hourly Output (time to event – 1 hour) in 24-hour dial format with –
   a. Low Risk (Green Zone) – less than 20/100 Score – 20% or less probability of Clinical deterioration
   b. Moderate Risk (Yellow Zone) – between 20- 50/100 Score – 50% or less probability of Clinical deterioration
   c. High Risk (Red Zone) – more than 50/100 Score = More than 50% probability of Clinical deterioration

   Under Research – Based on vital signs from medical devices – prediction of deterioration time to event in 4 / 8 / 12 / 24 hours ongoing. In Phase 2 & Phase 3 Algorithm, model predicts deterioration in 4 / 8 / 12 / 24 hours

10. Recommendations to Weigh Patients and Document Metric Weights to Ensure Accurate Medication Dosing (adopted October 25, 2018)

11. Forward Fill Imputation Technique: When dealing with time series data or datasets containing missing values, forward fill involves replacing those missing data points with the most recent known value. This approach assumes that the value remains constant until a new observation becomes available. The type of forward filling used in this model is – Last Observation Carried Forward while we continue to test other methods like Time Dependent Iterative Imputation

    Source: Jakobsen, J.C., Gluud, C., Wetterslev, J. et al. When and how should multiple imputation be used for handling missing data in randomised clinical trials – a practical guide with flowcharts. BMC Med Res Methodol 17, 162 (2017). https://doi.org/10.1186/s12874-017-0442-1

Omer Noy, Ron Shamir et al. Time-dependent Iterative Imputation for Multivariate Longitudinal Clinical Data
https://doi.org/10.48550/arXiv.2304.07821

Definition 12 Diabetes mellitus

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

a. A fasting plasma glucose (FPG) ≥126 mg/dl. Fasting is defined as no caloric intake for at least 8 hr.
b. Symptoms of hyperglycaemia and a casual (random) plasma glucose ≥200 mg/dl. Classic symptoms of hyperglycaemia include polyuria, polydipsia, and unexplained weight loss. (At the time of diagnosis as a diabetic, B cell function is at 25% to 30%.)
c. 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.
d. A haemoglobin A1c (HbA1c) value ≥6.5%.

In context of the study, data collection method and overall clarity, please follow –

a. Patient with no history of diabetes and previous record of normal FPG / OGTT / HbA1c – Select NO
b. Patient with history of diabetes and a current record of HbA1c <7.5% - Select Controlled (this is irrespective of the patient under / not under medication/treatment)
c. Patient with history of diabetes and a current record of HbA1c ≥7.5% - Select Uncontrolled (this is irrespective of the patient under / not under medication/treatment)

Source: ACP Guideline 2018 - American Diabetes Association. Standards of Medical Care in Diabetes-2018 Abridged for Primary Care Providers. Clin Diabetes. 2018 Jan;36(1):14-37. Doi: 10.2337/cd17-0119. PMID: 29382975; PMCID: PMC5775000.

Definition 13 Hypertension

Normal blood pressure (BP) in adults can be defined as systolic BP <120 mm Hg and diastolic BP <80 mm Hg.
Prehypertension is defined as systolic BP between 120 and 139 mm Hg or diastolic between 80 and 89 mm Hg.
Hypertension can be divided into
Stage 1: systolic BP from 140 to 159 mm Hg or diastolic BP from 90 to 99 mm Hg and
Stage 2: systolic BP ≥160 mm Hg or diastolic BP ≥100 mm Hg.

Source - Giles TD, Materson BJ, Cohn JN, Kostis JB. Definition and classification of hypertension: an update. J Clin Hypertens (Greenwich). 2009 Nov;11(11):611-4. doi: 10.1111/j.1751-7176.2009.00179.x. Erratum in: J Clin Hypertens (Greenwich). 2010 Jan;12(1):13. PMID: 19878368; PMCID: PMC8673286.

Definition 14 Coronary Artery Disease

Coronary artery disease (CAD) is a common type of heart disease that affects the blood flow to the heart muscle. It is caused by the buildup of plaque, a fatty substance, in the walls of the coronary arteries, which supply oxygen and nutrients to the heart. This plaque can narrow or block the arteries, reducing the blood supply to the heart and causing chest pain, shortness of breath, fatigue, or heart attack.
Source: https://www.cdc.gov/heartdisease/coronary_ad.htm

Definition 15 Heart Failure

According to the Universal Definition and Classification of Heart Failure, heart failure (HF) is a clinical syndrome with symptoms and/or signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion.

The classification of HF includes four stages:

i. At risk for HF (Stage A): Patients with risk factors for developing HF, such as hypertension, diabetes, obesity, or coronary artery disease, but without structural heart disease or symptoms of HF.
ii. Pre-HF (Stage B): Patients with structural heart disease, such as left ventricular hypertrophy, left ventricular dysfunction, or valvular heart disease, but without symptoms of HF.
iii. Symptomatic HF (Stage C): Patients with structural heart disease and current or prior symptoms of HF, such as dyspnea, fatigue, or edema.
iv. Advanced HF (Stage D): Patients with refractory HF require specialized interventions, such as mechanical circulatory support, continuous inotropic infusion, or palliative care.

The classification of HF also includes subgroups based on left ventricular ejection fraction (LVEF):

- HF with reduced ejection fraction (HFrEF): Symptomatic HF with LVEF ≤40%.
- HF with mid-range ejection fraction (HFmrEF): Symptomatic HF with LVEF 41-49%.
- HF with preserved ejection fraction (HFpEF): Symptomatic HF with LVEF ≥50%.
- HF with improved ejection fraction (HFimpEF): Symptomatic HF with a baseline LVEF ≤40%, a ≥10-point increase from baseline LVEF, and a second measurement of LVEF >40%.

Source:
Gregory Gibson, MD; Vanessa Blumer, MD; Robert John Mentz, MD, FACC; Anuradha (Anu) Lala, MD, FACC, Universal Definition and Classification of Heart Failure: A Step in the Right Direction from Failure to Function; Jul 13, 2021 https://www.acc.org/latest-in-cardiology/articles/2021/07/12/12/31/universal-definition-and-classification-of-heart-failure.
Classes and Stages of Heart Failure | American Heart Association. https://www.heart.org/en/health-topics/heart-failure/what-is-heart-failure/classes-of-heart-failure.

Definition 16: Arrhythmia

An arrhythmia is a problem with the rate or rhythm of the heartbeat. It can be too fast, too slow, or irregular. Arrhythmias can affect the blood flow to the heart and other organs and may cause complications such as stroke or heart failure.

Arrhythmias are often categorized into four groups:

i. Extra beats: These are additional beats that occur in the upper or lower chambers of the heart. They may cause palpitations or skipped beats.

Examples are premature atrial contractions, premature ventricular contractions, and premature junctional contractions.

ii. Supraventricular tachycardias: These are fast heart rhythms that originate in the upper chambers of the heart. They may cause symptoms such as chest pain, shortness of breath, or fainting. Examples are atrial fibrillation, atrial flutter, and paroxysmal supraventricular tachycardia.

iii. Ventricular arrhythmias: These are fast or chaotic heart rhythms that originate in the lower chambers of the heart. They are usually life-threatening and require immediate medical attention. Examples are ventricular fibrillation and ventricular tachycardia.

iv. Bradyarrhythmia: These are slow heart rhythms that may result from problems with the natural pacemaker of the heart or the electrical conduction system. They may cause symptoms such as fatigue, dizziness, or low blood pressure. Examples are sinus node dysfunction and atrioventricular block.

Source:
American Heart Association. https://www.heart.org/en/health-topics/arrhythmia/about-arrhythmia .
Categories of Arrhythmias | The Texas Heart Institute. https://www.texasheart.org/heart-health/heart-information-center/topics/categories-of-arrhythmias/.

Definition 17: Lung Disease

Definition and classification of COPD and asthma:

i. Chronic Obstructive Pulmonary Disease (COPD) is a group of diseases that cause airflow limitation and inflammation of the airways. It is usually caused by exposure to noxious particles or gases, such as cigarette smoke. COPD is diagnosed by a post-bronchodilator FEV1/FVC ratio of less than 70%. The severity of COPD is classified by the degree of airflow obstruction, measured by the percentage of predicted FEV1[1].

ii. Asthma is a chronic inflammatory disorder of the airways that causes variable and recurrent symptoms, such as wheezing, coughing, and shortness of breath. It is often triggered by allergens, irritants, or infections. Asthma is diagnosed by the presence of bronchial hyperresponsiveness, which can be assessed by a bronchodilator or a methacholine challenge test. The severity and control of asthma are determined by the frequency and intensity of symptoms, the use of rescue medication, and the level of lung function[2].

iii. Asthma-COPD overlap syndrome (ACOS) is a condition that has features of both asthma and COPD. It is characterized by persistent airflow limitation, eosinophilic inflammation, and increased reversibility of airway obstruction. ACOS is more common in older patients, smokers, and those with a history of asthma. The diagnosis of ACOS is based on clinical criteria, such as a history of asthma before the age of 40, a history of allergies, and a positive bronchodilator response of more than 12% and 200 mL[3][4].

Source:
COPD and Asthma | World Allergy Organization. https://www.worldallergy.org/education-and-programs/education/allergic-disease-resource-center/professionals/copd-and-asthma.

Asthma & COPD Overlap: Definitions, Measures | Journal of COPD Foundation. https://journal.copdfoundation.org/jcopdf/id/1142/Asthma-and-Chronic-Obstructive-Pulmonary-Disease-Overlap-The-Effect-of-Definitions-on-Measures-of-Burden.

Definition 18: Central Nervous System Disorder

Central nervous system (CNS) disorders are a group of neurological conditions that affect the brain and spinal cord, which together form the CNS. CNS disorders can be classified according to the primary location affected, the primary type of dysfunction involved, or the primary type of cause. Examples of CNS disorders are Traumatic brain injury (TBI), Spinal cord injury (SCI), Infectious diseases, Degenerative diseases, Structural defects, and Tumours.

CNS disorders can cause various degrees of disability, depending on the severity, location, and type of the condition. Disability can be measured by using different scales or criteria, such as the International Classification of Functioning, Disability and Health (ICF), the Glasgow Coma Scale (GCS), or the Disability Rating Scale (DRS). Disability can affect the quality of life, independence, and social participation of people with CNS disorders.

Definition 19: Immunocompromised state

An immunocompromised state is a condition where the immune system is weakened or impaired, making it less able to fight off infections and diseases. There are many causes and types of immunocompromised states, such as:

i. Primary immunodeficiencies: These are genetic or congenital disorders that affect the development or function of one or more components of the immune system, such as B cells, T cells, natural killer cells, or complement systems. Examples are common variable immunodeficiency, severe combined immunodeficiency, and DiGeorge syndrome[12].
ii. Secondary immunodeficiencies: These are acquired conditions that result from external factors that damage or suppress the immune system, such as infections, medications, treatments, or diseases. Examples are HIV/AIDS, chemotherapy, organ transplantation, diabetes, and malnutrition.
iii. Autoimmune diseases: These are disorders where the immune system mistakenly attacks the body's tissues, causing inflammation and damage. Examples are rheumatoid arthritis, lupus, and multiple sclerosis
iv. Allergic diseases: These are conditions where the immune system overreacts to harmless substances, such as pollen, dust, or food, causing symptoms such as sneezing, itching, or anaphylaxis. Examples are asthma, eczema, and food allergies

Immunocompromised states can be classified according to the severity, duration, and reversibility of the immune dysfunction. For example, some immunodeficiencies are mild and transient, while others are severe and permanent. Some immunosuppressive drugs or treatments can be stopped or reduced, while others are lifelong. Some autoimmune or allergic diseases can be controlled or cured, while others are chronic or progressive. Immunocompromised states can increase the risk of infections, cancers, and complications from vaccines or other medical procedures. Therefore, it is important to prevent, diagnose, and treat immunocompromised states, as well as to protect immunocompromised individuals from exposure to harmful agents.

Sources
https://www.yalemedicine.org/news/what-does-immunocompromised-mean.
https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-who-are-immunocompromised.html.

Definition 20: chronic kidney disease
CKD is defined as kidney damage or glomerular filtration rate (GFR) <60 mL/min/1.73 m2 for 3 months or more, irrespective of cause. Kidney damage can be detected by the presence of albuminuria, which is an excess amount of protein in the urine.
Classification: CKD is classified into five stages based on the level of GFR, from stage 1 (GFR >90 mL/min/1.73 m2) to stage 5 (GFR <15 mL/min/1.73 m2 or dialysis or transplantation). The cause, GFR, and albuminuria criteria (CGA classification) are used to further stratify CKD patients and assess their risk of progression and complications.

Source
https://kdigo.org/wp-content/uploads/2017/01/Position-Paper-Definition-and-Classification-of-Chronic-Kidney-Disease-in-Adults-Worldwide-2004.pdf.
https://www.kidney-international.org/article/S0085-2538%2815%2954924-7/pdf.

Definition 21: Allergies

"Allergy" is defined as "a hypersensitivity reaction initiated by proven or strongly suspected immunologic mechanisms".

Source

World Allergy.Org: https://www.worldallergy.org/education-and-programs/education/allergic-disease-resource-center/professionals/food-allergy

Definition 22: Fever
A fever is a temporary rise in body temperature. It's one part of an overall response from the body's immune system.

Source:
Mayoclinic.Org: Fever - Symptoms & causes - Mayo Clinic

Definition 23: Cough
A sudden, sharp-sounding expulsion of air from the lungs acts as a protective mechanism to clear the air passages or as a symptom of pulmonary disturbance.

Source:
Merriam-Webster Dictionary Cough Definition & Meaning - Merriam-Webster

Definition 24: Weakness

A state of debility caused by prolonged bed rest, muscle disease or wasting, severe infection, anemia, starvation or psychological disorder with loss of motivation.

Source:

weakness. (n.d.) *Collins Dictionary of Medicine*. (2004, 2005). Retrieved December 21 2023 from https://medical-dictionary.thefreedictionary.com/weakness

Definition 25: Respiratory Distress
Respiratory distress may be a result of disorders of the extrathoracic or intrathoracic airways (intrinsic or extrinsic compression-obstruction), alveoli, pulmonary vasculature, pleural spaces, or thorax.

Source: Nelson Pediatric Symptom-Based Diagnosis, 2018 https://www.sciencedirect.com/topics/medicine-and-dentistry/respiratory-distress

Definition 26: Cardiovascular Symptoms

Cardiovascular diseases (CVDs) affect your heart and blood vessels. Cardiovascular disease symptoms can vary depending on the cause
Chest pain (angina).
Chest pressure, heaviness or discomfort, sometimes described as a "belt around the chest" or a "weight on the chest."
Shortness of breath (dyspnea).
Dizziness or fainting.
Fatigue or exhaustion.

Source:
Cleveland Clinic Cardiovascular Disease https://my.clevelandclinic.org/health/diseases/21493-cardiovascular-disease

Definition 27: Trauma
Trauma is an emotional response to a terrible event like an accident, rape, or natural disaster.

Source: American Psychological Association https://www.apa.org/topics/trauma/

Definition 28: Unconsciousness
An abnormal state of lack of response to sensory stimuli, resulting from injury, illness, shock, or some other bodily disorder.

Source:
For Miller-Keane Encyclopedia:
unconsciousness. (n.d.) Miller-Keane Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health, Seventh Edition. (2003). Retrieved December 21 2023 from https://medical-dictionary.thefreedictionary.com/unconsciousness

Definition 29: Abdominal Signs & Symptoms

Abdominal signs and symptoms include abdominal pain and distension, as well as other signs assessed during the physical examination (e.g. palpation, percussion).

Source:Reintam Blaser A, Starkopf J, Malbrain ML. Abdominal signs and symptoms in intensive care patients. Anaesthesiol Intensive Ther. 2015;47(4):379-87. doi: 10.5603/AIT.a2015.0022. Epub 2015 May 14. PMID: 25973664.