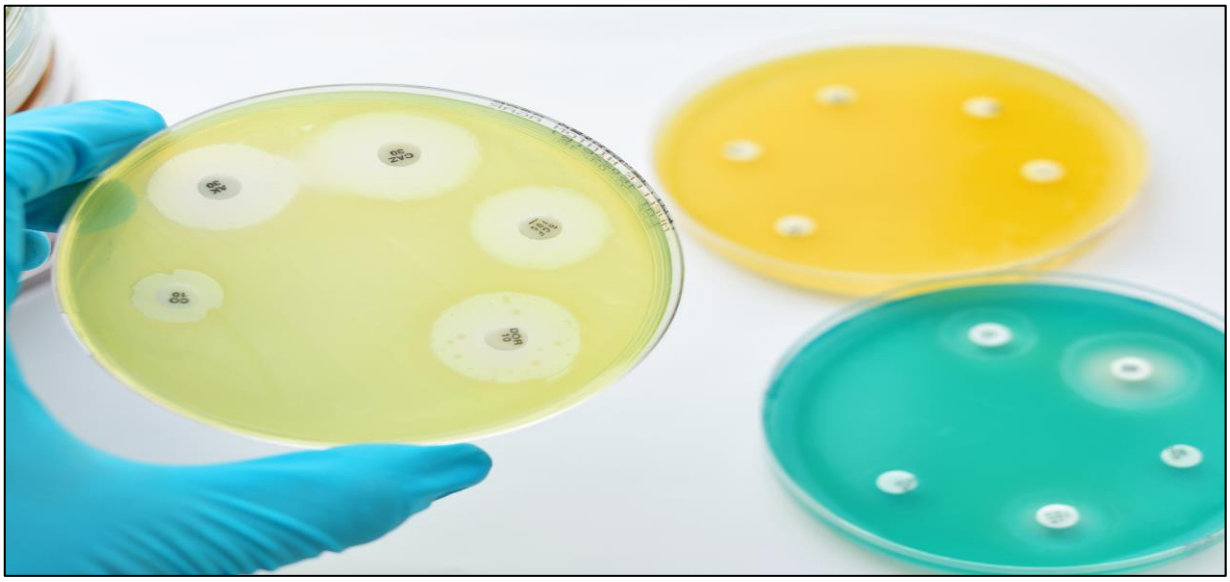

Introduction

At Apollo Hospitals, we have been able to analyze over 363k bacterial isolates pan India in the past 5+ years (2018 – 2023) and have been able to provide antibiotic-associated trends for age, gender, inpatient or outpatients, site of infection, and day from admission. This analysis and further use of Machine Learning Recommendation System (Content Based) include 33% Outpatient and 66% Inpatient Isolates. The current accuracy of the Model for prediction, of the top 3 probable organisms with their sensitivity pattern, is over 87% (which is comparative owing to multiclass classification). The model is updated every quarter with inputs from over 20 Apollo Hospitals which have been consistently reporting Antibiotic Sensitivity as part of WHONET and AWARE Classification (WHO).

Overall dimensions of the program include the following – Period - 2019 – 2023
Locations - 20+ Locations pan India Gender - All AGE Group (0 – 90+ years)
Quantum – 363K Isolates | 57 Specimen Types | 180 Organisms | 141 Antibiotics

Problem Statement

Objectives

a. Detect, Respond, and Contain Resistant Pathogens - Laboratory and Diagnostics: Gold- standard lab capacity | On-the-ground lab expertise and assistance

b. Prevent the Spread of Resistant Infections
   i. Surveillance and Science: More effective tracking and preventing community and healthcare-associated infections etc.
   ii. Improved Antibiotic Use: Improving antibiotic use to ensure antibiotics are available and work to protect people from life-threatening infections or sepsis by providing a Clinicians Guide on the Choice of Empirical Antibiotic Use

c. Encourage Innovation for New Strategies - Insights for Practice: Innovations and collaborations within Apollo Hospitals' Clinicians and use of Machine Learning – Recommendation to identify and implement new ways to prevent antibiotic-resistant infections and their spread through judicious use of Antibiotics

Workflow of AI-EARS App

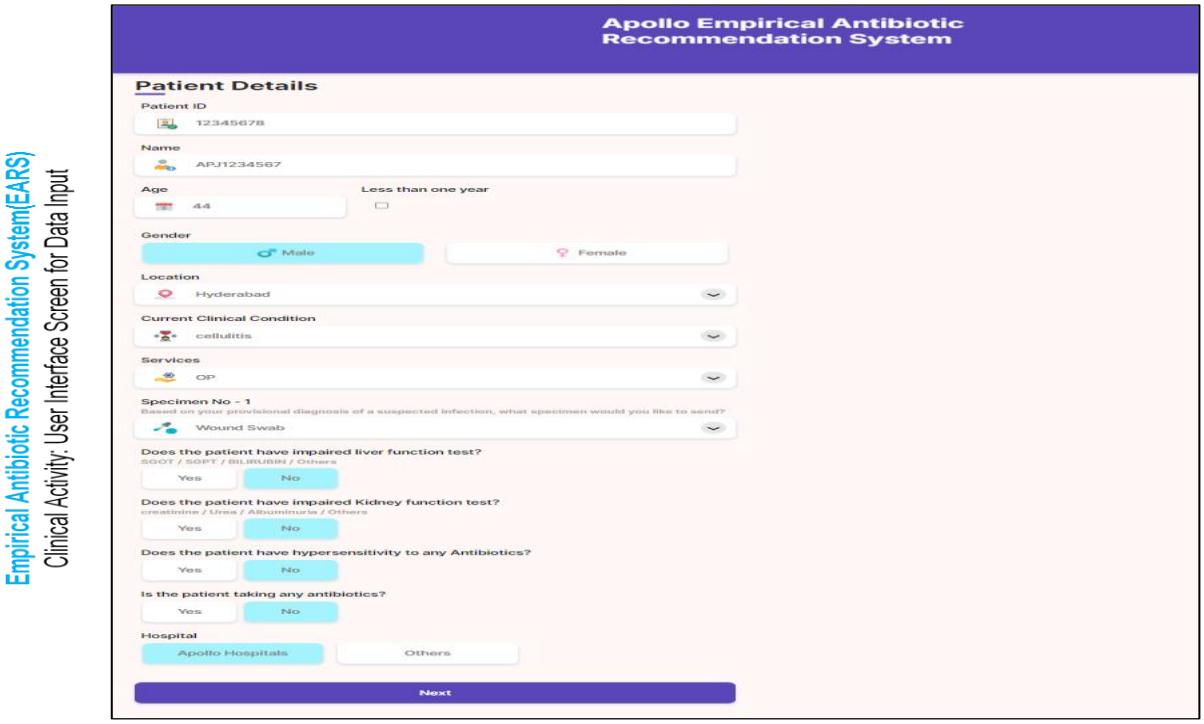

Figure 1 – Entry of Patient Vitals and Clinical Parameters

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

The patient attributes include Personal details such as Name, Age, gender, and pregnancy status, demographic Details, Current clinical condition, service type (such as outpatient, emergency room, or inpatient, including the number of days since admission if inpatient), specimen type, liver and kidney function, hypersensitivity to antibiotics, and antibiotic use history.

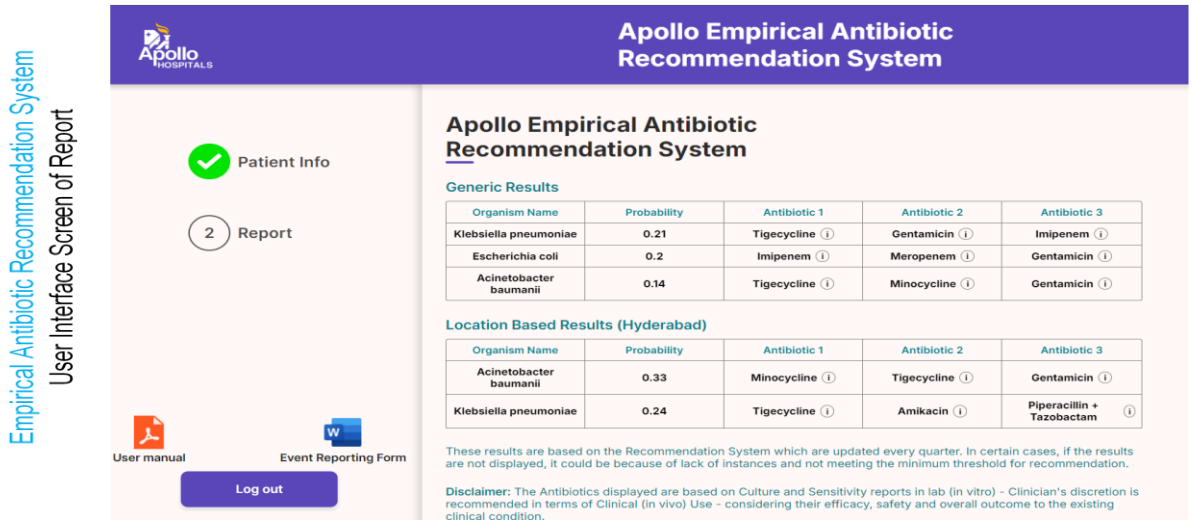

Figure 2 – Antibiotics Recommendation Report Generation

Output:

Considering the input parameters given, the model gives an output that is displayed in the User Interface Screen of Report

a. Generic Results of Top 3 Organisms & Sensitive Antibiotics
b. Location-Based Results of Top 3 Organisms & Sensitive Antibiotics
c. Standard Dosing Guidelines & Color-Coded Precautions

Printed Report

Apollo Empirical Antibiotic Recommendation System

NAME: JANE DOE	AGE: 44	LOCATION: HYDERABAD
UHID: APJ12345678	GENDER: MALE	DATE OF REPORT: 30-9-2024

Clinical Condition	CELLULITIS	Day For Admission	1
Ward Type	General Ward	Specimen	Wound Swab
Service	IP	Kidney Disease	Yes
Liver Disease	No	Hypersensitivity	No

Generic Results (Recommendation Organism, Probability & Sensitive Antibiotics.)

Organism Name	Probability	Antibiotic 1	Antibiotic 2	Antibiotic 3
Klebsiella pneumoniae	0.21	Tigecycline	Gentamicin	Imipenem
Escherichia coli	0.2	Imipenem	Meropenem	Gentamicin
Acinetobacter baumanii	0.14	Tigecycline	Minocycline	Gentamicin

Location Based Results (Recommendation Organism, Probability & Sensitive Antibiotics.)

Organism Name	Probability	Antibiotic 1	Antibiotic 2	Antibiotic 3
Acinetobacter baumanii	0.33	Minocycline	Tigecycline	Gentamicin
Klebsiella pneumoniae	0.24	Tigecycline	Amikacin	Piperacillin + Tazobactam

These results are based on the Recommendation System which are updated every quarter. In certain cases, if the results are not displayed, it could be because of lack of instances and not meeting the minimum threshold for recommendation.

Disclaimer: The Antibiotics displayed are based on Culture and Sensitivity reports in lab (in vitro) - Clinician's discretion is recommended in terms of Clinical (in vivo) Use - considering their efficacy, safety and overall outcome to the existing clinical condition.

This report is accessed by

Date: 30-9-2024
Time: 4:05:59 pm | Page 1

Apollo Empirical Antibiotic Recommendation System

NAME: JANE DOE	AGE: 44	LOCATION: HYDERABAD
UHID: APJ12345678	GENDER: MALE	DATE OF REPORT: 30-9-2024

Antibiotic	Standard Dose
Tigecycline	0.1 g loading dose followed by 50 mg x 2 iv
Gentamicin	6-7 mg/kg x 1 iv
Imipenem	0.5 g x 4 iv over 30 minutes
Meropenem	1 g x 3 iv over 30 minutes
Minocycline	0.1 g x 2 oral
Amikacin	25-30 mg/kg x 1 iv
Piperacillin + Tazobactam	(4 g piperacillin + 0.5 g tazobactam) x 4 iv 30-minute infusion or x 3 iv by extended 4-hour infusion

- The input parameters show that patient is currently receiving this antibiotic.
- Indicates that this antibiotic needs to be used with caution when there is existing liver disease and deranged liver enzymes.
- Indicates that this antibiotic needs to be used with caution with kidney diseases and increased levels of creatinine and urea.
- This denotes an existing hypersensitivity of the patient with this antibiotic or similar antibiotic of same group.
- Some antibiotics do not work on certain Organisms due to inherent resistance or their mechanism of action. The existing combination of Organism and antibiotic could fall in this category.
- Some antibiotics do not work on certain Organ systems. Therefore we recommend this particular site - antibiotic combination should be appropriately verified before use.
- This antibiotic needs appropriate caution for use in Pregnancy or Breast Feeding.

Apollo 24|7 Ask Apollo

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The Research

Methodology

Source of data - The retrospective data (for the development cohort) was collected from the anonymized clinical and laboratory records of Outpatient and Admitted Patients from the discharge summaries of the patients and a standardized template (WHONET) from 20+ Apollo Hospitals in India from January 2019 to December 2021.

What is WHONET –
WHONET is a free software developed by the WHO Collaborating Centre for Surveillance of Antimicrobial Resistance for laboratory-based surveillance of infectious diseases and antimicrobial resistance.
The principal goals of the software are:

- To enhance local use of laboratory data; and
- To promote national and international collaboration through the exchange of data.

WHONET analytical tools facilitate:

- The understanding of the local epidemiology of microbial populations;
- The selection of antimicrobial agents;
- The identification of hospital and community outbreaks; and
- The recognition of quality assurance problems in laboratory testing.

Objective and Outcome – The primary outcome of the Study was to develop comparable models with improved accuracy parameters, which would yield recommendations for probable organisms and their sensitive antibiotics at the Point of Care.

Predictors
The Clinical Variables included the patient's basic information, including Age and Gender, Comorbidities, Vitals, Previous Medication History including recent antibiotic history. Other data used in the recommendation include the specimen, organisms, and antibiotics for analysis, content-based filtering in the recommendation system, and then machine learning. The stepwise methodology is provided below in **Figures 1 to 4.**

Sample size
The initial study included a total population of 186,000 culture and sensitivity samples, including 33% in Outpatient Units from 20+ Centers in India – from 2019 through 2021 [Jan to Dec]. The subsequent prospective sample size through the year 2022 – 71223 [samples] and the year 2023 – 82286 [samples]. We also added a retrospective cohort of 23,518 samples from 2018 from July 2018 onwards for comparison.

Missing data
No imputations were used in the development or validation cohort.

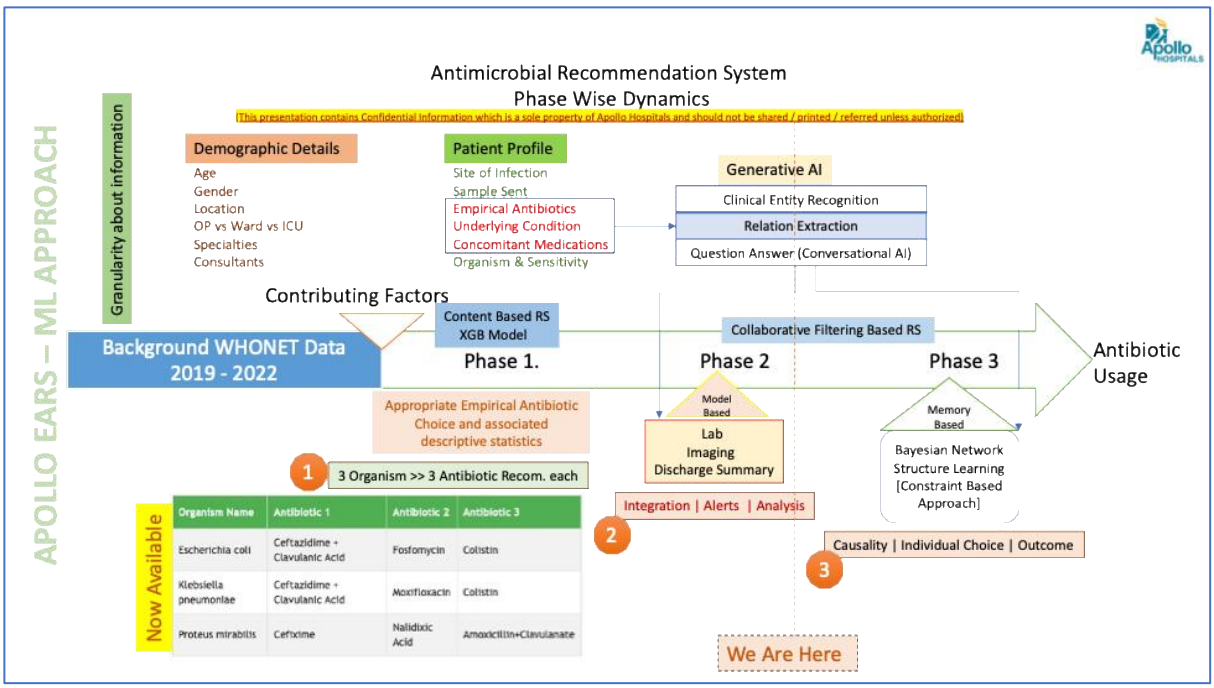


Figure 1 - Schema of the Phase Wise Antimicrobial Recommendation System – where we are using demographic and conventional culture and sensitivity data and data from the EMR to phase-wise build the recommendation engine. This includes the Content and Collaborative Filtering Based Recommendation System, NLP layers, Bayesian Network and Causality Analysis.

Statistical analysis and Modelling approach

The model is built in 3 layers.

1. Recommendation System using Content-based filtering which yields 3 Top Probable Organisms with their corresponding 3 Antibiotic Sensitivity (which are stacked) at the first output layer. (Illustration in Figure 2)
2. 2nd Layer determines the probabilities of each of these 3 organisms using a Bayesian Framework outputs a summation of the probabilities for the top 3 recommended organisms and creates secondary output data. Results of the Metrics – Cosine Similarity between Original Organism vs Top 3 Predicted Organism is provided below. (Illustration in Presentation)
3. 3rd Layer uses a Gradient Boosting Algorithm on secondary output data and estimates the accuracy of the model (and multiple sub-models - as illustrated) using a 70-30 Train-Test data divide. This provides us with the metrics for AUROC / AUPRC as illustrated in the chart. (Illustration in Presentation)

Python language is used to code the program. Python ML packages, namely Sklearn, numpy, and pandas library are used for this work. After the training model and successful testing, the model is pickled and saved. This pickled model is hosted and serves as the back end for requests from the front-end user. The user's values will act as input for the model, and the predicted response will be output.

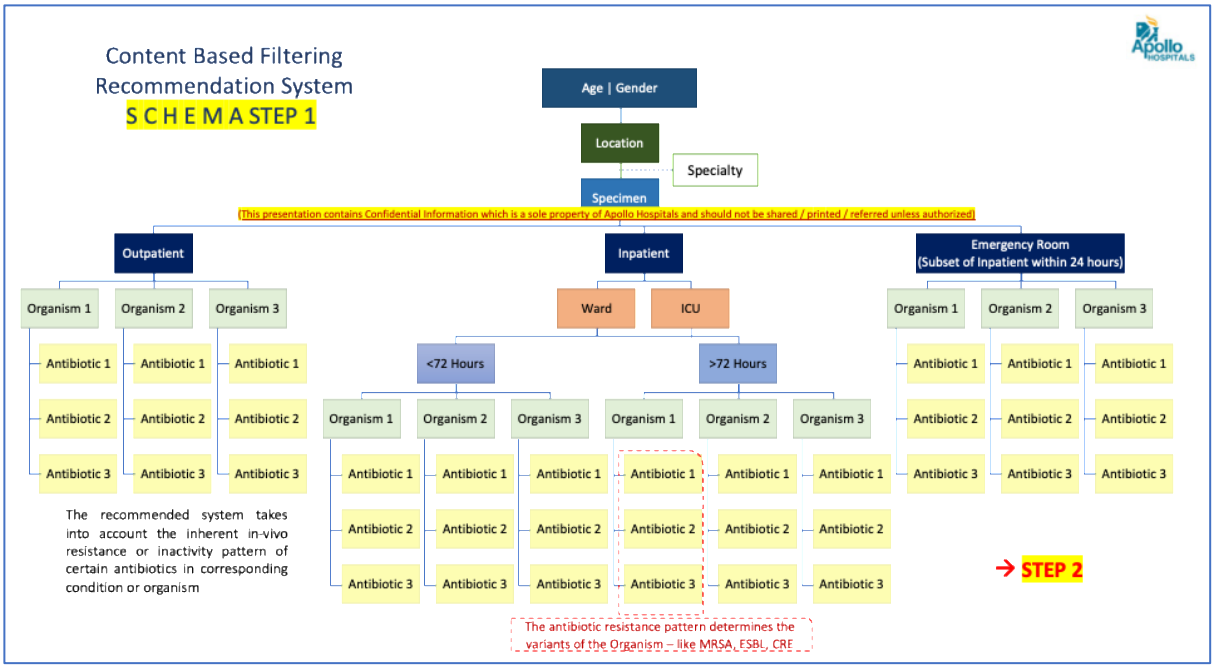


Figure 2 - Recommendation System using Content-based filtering which yields 3 Top Probable Organisms with their corresponding 3 Antibiotic Sensitivity (which are stacked) at the first output layer.

The advantage of Content-based filtering in antibiotic selection involves recommending appropriate antibiotics based on the specific characteristics of bacterial infections, such as bacterial strain type, infection site, and patient history, matching these features to known effective antibiotics, thereby personalizing treatment and improving outcomes by targeting the most relevant therapeutic options.

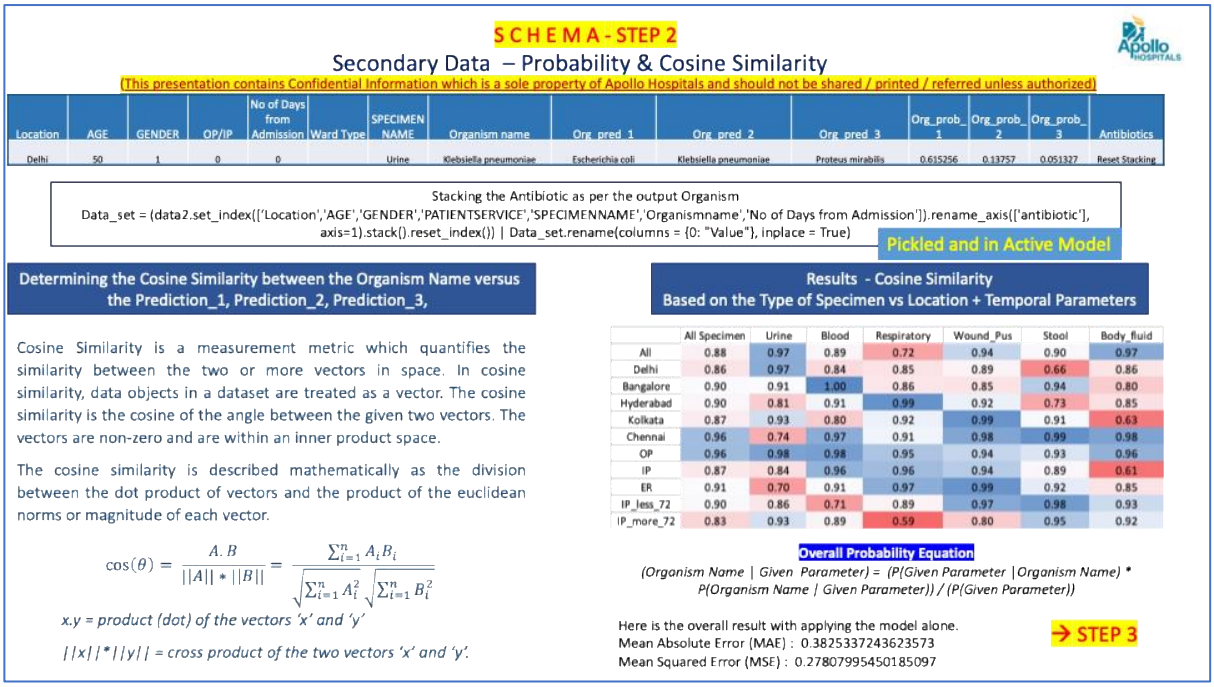


Figure 3 - 2nd Layer determines the probabilities of each of these 3 organisms using a Bayesian Framework and outputs a summation of the probabilities for the top 3 recommended organisms and creates secondary output data. Results of the Metrics – Cosine Similarity between Original Organism vs Top 3

Predicted Organism is provided above.

The methodology involves –

1. Data Set Structure: The data includes patient information such as location, age, gender, days of admission, and specimen name.
2. Cosine Similarity: This metric is used to quantify the similarity between organism names and predictions (Prediction_1, Prediction_2, and Prediction_3). It measures the cosine of the angle between two feature vectors.
3. Stacking Approach: The antibiotics are selected based on the output organism, using a combination of cosine similarity and temporal features (days from admission).

Cosine similarity is a suitable approach in the context of antibiotic selection for several reasons:

1. Handling High-Dimensional Data: In antibiotic selection, patient characteristics (e.g., age, location, and specimen type) and infection attributes (e.g., bacterial strain) form high-dimensional feature vectors. Cosine similarity efficiently handles these vectors, allowing comparisons without being affected by the vector's magnitude, focusing on the orientation of vectors

2. Similarity-Based Selection: Antibiotic recommendations depend on how similar a new case (patient's infection profile) is to previous cases. Cosine similarity provides an accurate measure of similarity between these cases, helping match a patient's infection profile with previously successful antibiotic treatments.

3. Interpretation in Sparse Data: Medical datasets, especially involving organisms and treatments, can often be sparse (e.g., many zeros in the vector for different organism strains). Cosine similarity is robust in such scenarios because it only considers the non-zero elements (i.e., features that exist), making it more reliable than other metrics like Euclidean distance.

4. Normalization: Since cosine similarity normalizes the feature vectors, it minimizes biases from large variations in individual features (e.g., length of hospital stay or dosage values) and ensures that the focus remains on the relative pattern of the features rather than their absolute values.

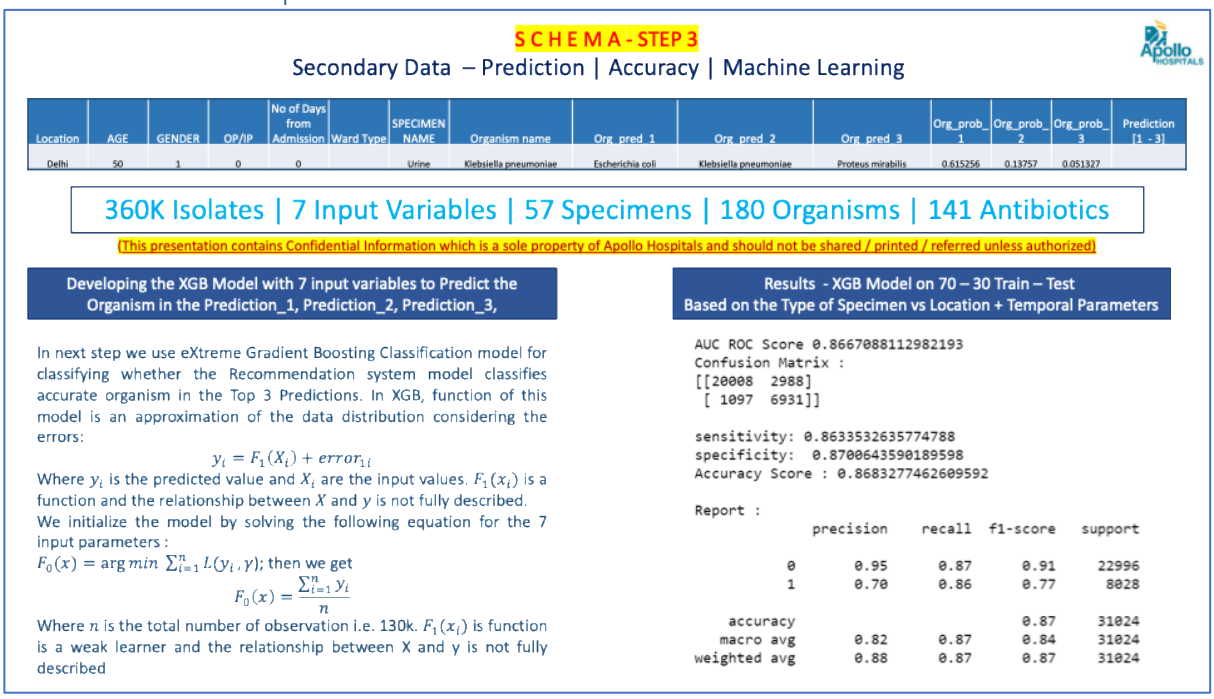


Figure 4 - 3rd Layer uses a Gradient Boosting Algorithm on secondary output data and estimates the

accuracy of the model (and multiple sub-models - as illustrated) using 70-30 Train - Test data divide. This provides us with the metrics for AUROC / AUPRC as illustrated in the chart.

Results

The results are provided in two approaches –

a) Initial key results considering the Cosine Similarity Model and XGB model with secondary data
b) Comparative Results for different years – 2022 & 2023

Initial Results

The results provided highlight the performance of two different models used for predicting the probable organism and supporting empirical antibiotic selection:

1. Cosine Similarity Model (All Samples and Locations)

a. **Overall Cosine Similarity**: The cosine similarity measure achieved a value of **0.86**, indicating a high degree of similarity between predicted organisms and the actual organisms. This demonstrates that the model effectively identifies similar cases based on the given parameters (patient profile and infection characteristics).
b. **Interpretation**: A cosine similarity score close to 1 suggests that the organism predictions are well-aligned with previous cases, supporting reliable antibiotic recommendations.

2. Regression Model Performance

a. **Mean Absolute Error (MAE)**: The MAE is **0.383**, meaning the average absolute difference between the predicted and actual values is approximately 0.383 units. This error metric provides insight into the accuracy of continuous predictions (e.g., prediction scores for each organism).
b. **Mean Squared Error (MSE)**: The MSE is **0.278**, showing a relatively low average squared difference between predicted and actual values. A lower MSE indicates that the model provides precise predictions, essential for recommending the correct antibiotic treatment.

3. Gradient Boosting Model Results (Classification)

a. **Sensitivity**: The model achieved a sensitivity (true positive rate) of **0.867**, meaning it correctly identifies approximately 86.7% of the actual organisms. This is important for ensuring that critical infections are correctly identified for appropriate antibiotic selection.
b. **Specificity**: A specificity of **0.87** indicates that 87% of true negatives (i.e., cases where the organism does not match the prediction) are correctly identified, minimizing the chances of recommending inappropriate antibiotics.
c. **AUC (Area Under Curve)**: The AUC is **0.867**, reflecting the model's overall ability to discriminate between different classes (organisms). A high AUC signifies good classification performance.
d. **Accuracy**: The model accuracy is **0.868**, indicating that around 86.8% of the predictions for the probable organism are correct, supporting effective empirical antibiotic selection.

These results collectively show that both the regression model (using cosine similarity) and the gradient-

boosting classification model perform well in predicting probable organisms and guiding antibiotic selection, achieving high accuracy, sensitivity, and specificity. This ensures that empirical antibiotic decisions are based on robust predictions tailored to individual patient profiles.

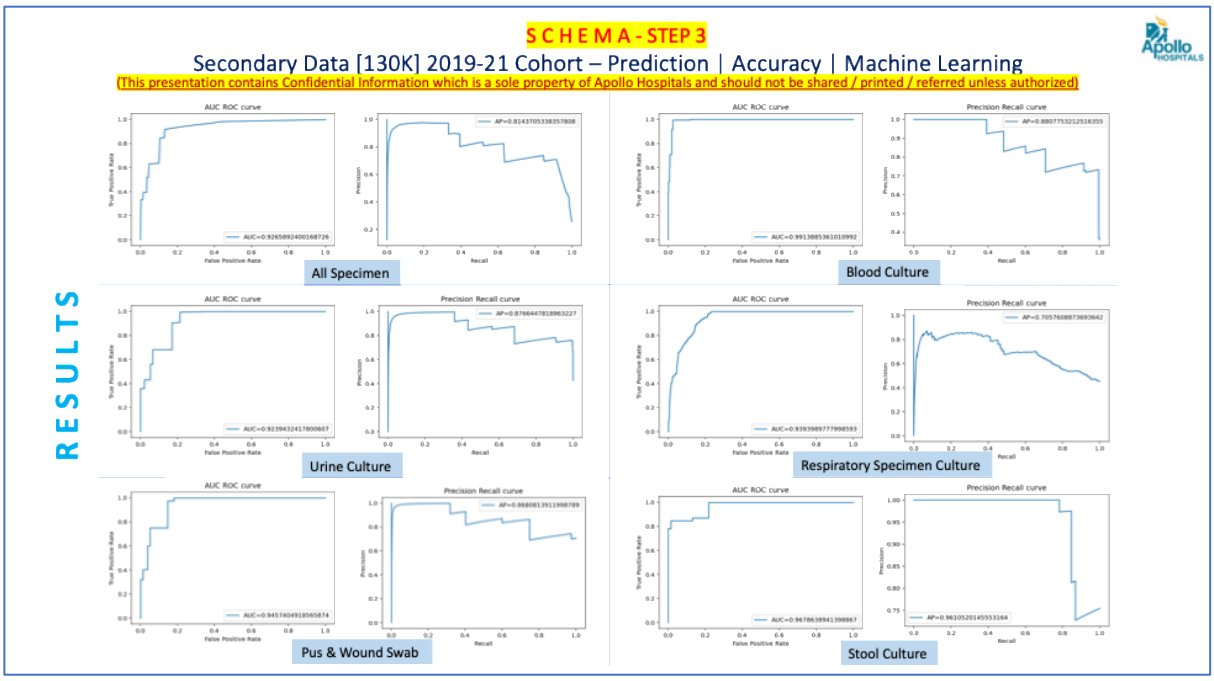


Figure 6 - XGB Model AUROC / AUPRC – Based on Major Samples in Best Performance Settings

The machine learning model's performance across different specimen types in predicting probable organisms using secondary data from a 2019-21 cohort (130K cases). The performance metrics shown include AUC (Area Under the Curve) ROC curves and Precision-Recall curves.

Key Points:

a. All Specimens: The AUC ROC curve shows strong performance with an AUC value of 0.92, and the precision-recall curve reflects high precision at 0.81.
b. Blood Culture: The AUC value for blood culture is 0.87, indicating reliable predictive accuracy, with precision decreasing slightly to 0.75 as recall increases.
c. Urine Culture: The model achieves a high AUC of 0.90, reflecting strong predictive performance for urine samples, with precision-recall values close to 0.87.
d. Respiratory Specimen Culture: The AUC is 0.86, showing the model's ability to predict organisms in respiratory infections accurately, with a precision of 0.71.
e. Pus & Wound Swab: The AUC value is 0.94, with precision-recall curves demonstrating good predictive performance at 0.87 precision.
f. Stool Culture: The stool culture has an AUC of 0.91, showing moderate predictive power, though the precision value drops to around 0.80, indicating room for improvement.

These results demonstrate the model's robustness and strong predictive power across various infection types and specimen sources.

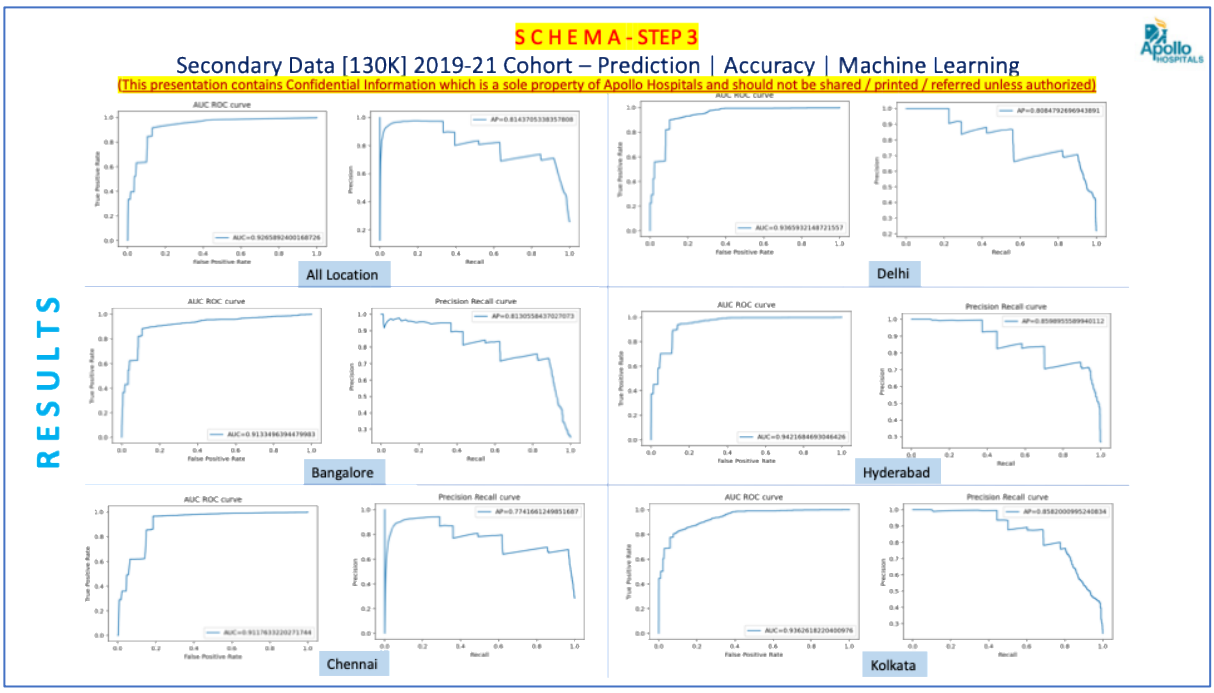


Figure 7 - XGB Model AUROC / AUPRC – Based on Major Locations

The performance of the XGB model with the secondary dataset, designed to predict probable organisms for guiding empirical antibiotic selection, across various geographic regions in India. The model's predictive accuracy was evaluated using area under the curve (AUC) ROC and precision-recall metrics for each region.

Results indicated robust performance across all locations, with accuracy values ranging from 0.84 in Kolkata to 0.91 in Bangalore. Precision values varied from 0.75 in Kolkata to 0.82 in Bangalore, while overall model performance for all locations achieved an AUC of 0.92, with precision-recall values near 0.80.

These findings demonstrate the model's strong ability to predict infectious organisms, supporting timely and appropriate empirical antibiotic therapy. The results underscore the potential of machine learning in improving clinical decision-making and enhancing personalized infection management across diverse patient populations and healthcare settings.

Comparative Results

The results of 2022 are as follows: -

	Year 2022 - Samples wise				
Specimen	Total No. of Samples	Precision Score	Recall score	AUC and ROC	Accuracy
All	71223	0.71	0.88	0.90	0.82
Blood	16878	0.98	0.81	0.98	0.90
Respiratory	6861	0.73	0.71	0.88	0.80
Urine	25101	0.99	0.97	0.99	0.97
Wound Pus	10104	0.93	0.69	0.95	0.88
Stool	382	0.94	0.98	0.98	0.96
Body Fluids	569	0.67	0.60	0.89	0.92

Table 1 – Analysis of the results – Sample Wise in Year 2022

	Year 2022 – Location wise				
Region	Total No. of cases	Precision Score	Recall score	AUC and ROC	Accuracy
All	71223	0.91	0.88	0.96	0.92
Delhi	8198	0.96	0.94	0.98	0.97
Bangalore	9806	0.87	0.96	0.97	0.93
Hyderabad	12506	0.89	0.95	0.96	0.94
Kolkata	6054	0.88	0.99	0.96	0.88
Chennai	27716	0.95	0.85	0.91	0.93
Mumbai	2607	0.81	0.93	0.93	0.85
Bhubaneswar	4336	0.97	0.93	0.99	0.95

Table 2 – Analysis of the results – Location Wise in Year 2022

Key Findings:

a) Sample-wise Performance (Table 1):
   a. Blood Culture: In 2022, the model achieved an accuracy of 0.90, showing improvement from 0.87 in the previous cohort (2019–2021). These highlight enhanced predictive performance in identifying organisms from blood cultures.
   b. Urine Culture: Accuracy increased to 0.97 in 2022, compared to 0.90 in the prior cohort, demonstrating improved predictions for urinary tract infections.
   c. Respiratory Specimens: Accuracy remained stable at 0.88, showing consistency across both periods.

b) Location-wise Performance (Table 2):
   a. Bangalore: The model's AUC improved to 0.97 in 2022 from 0.90 in the earlier cohort, reflecting better prediction accuracy in this region.
   b. Kolkata: Accuracy increased to 0.96 in 2022, up from 0.94 in the previous cohort, showing notable improvement in organism prediction.
   c. Chennai: Performance remained consistent at 0.91 in both timeframes.

These results indicate overall improvements in predictive accuracy for both samples and locations in 2022 compared to the 2019–2021 cohort.

The results of 2023 are as follows: -

	The year 2023 - Samples wise				
Specimen	Total No. of Samples	Precision Score	Recall score	AUC and ROC	Accuracy
All	82286	0.72	0.78	0.89	0.80
Blood	17892	0.99	0.63	0.98	0.90
Respiratory	11090	0.75	0.70	0.85	0.81
Urine	30179	0.92	0.95	0.97	0.91
Wound Pus	13400	0.76	0.60	0.88	0.83
Stool	429	0.91	0.69	0.89	0.83
Body Fluids	1515	0.71	0.73	0.88	0.91

Table 3 – Analysis of the results – Sample Wise in Year 2023

	Year 2023 – Location wise				
Region	Total No. of cases	Precision Score	Recall score	AUC and ROC	Accuracy
All	82286	0.98	0.74	0.96	0.90
Delhi	9760	0.98	0.85	0.97	0.95
Bangalore	11721	0.96	0.82	0.96	0.93
Hyderabad	15296	0.99	0.87	0.97	0.95
Kolkata	7839	0.95	0.94	0.98	0.95
Chennai	30257	0.98	0.86	0.96	0.94
Mumbai	2280	0.83	0.90	0.93	0.87
Bhubaneswar	5133	0.97	0.87	0.95	0.94

Table 4 – Analysis of the results – Location Wise in Year 2023

Sample-Wise Performance (2023 vs. Previous Years):

a) **Blood Culture**: In 2023, accuracy remained consistent **at 0.90**, unchanged from 2022. This suggests that the model's performance in predicting organisms from blood cultures has stabilized since its initial improvement from 0.87 in the 2019-2021 cohort.
b) **Urine Culture:** Accuracy improved slightly to **0.92** in 2023, up from 0.91 in 2022, continuing the upward trend from 0.90 in the 2019-2021 cohort, indicating progressive refinement in the model's predictions for urinary infections.
c) **Respiratory Specimens**: Accuracy dropped to **0.81 in 2023** from 0.83 in both prior periods, indicating a potential area for improvement in the model's respiratory infection predictions.

Location-Wise Performance (2023 vs. Previous Years):

a) **Bangalore:** AUC performance in 2023 reached **0.92**, improving from 0.91 in 2022 and 0.90 in the earlier cohort, reflecting continued enhancements in model performance.
b) **Kolkata:** Performance remained stable at **0.86,** matching the 2022 improvement from 0.84 in the 2019-2021 period.
c) **Chennai:** Accuracy increased to **0.87** in 2023, showing improvement from the stable 0.86 observed in previous years.

These results reflect ongoing refinements and improvements in model accuracy, particularly for urinary cultures and regional performance in Bangalore and Chennai, with some areas, like respiratory specimen predictions, needing further development.

Summary Results on Samples

Blood Culture:

Across all three cohorts (2019–2021, 2022, and 2023), the **predictive accuracy for blood culture samples demonstrated consistent performance**.

a) **2019-2021 Cohort**: Accuracy was **87%**, with steady predictive performance in identifying organisms and recommending antibiotics.
b) **2022 Cohort**: There was a marginal improvement, with accuracy rising to **88%**.
c) **2023 Cohort**: The accuracy remained stable at **90%**, reflecting a plateau in the model's ability to

predict organisms in blood culture samples.

d) **Relative Percentage**: Blood cultures comprised approximately **30-35%** of the overall samples across cohorts.

Respiratory Samples:

The model's performance for respiratory samples **experienced minor fluctuations**.

a) **2019-2021 Cohort**: Accuracy was **83%**, reflecting robust predictions.
b) **2022 Cohort**: Performance remained steady with an **83%** accuracy.
c) **2023 Cohort**: A slight decline to **81%** was observed, indicating potential areas for model refinement.
d) **Relative Percentage**: Respiratory samples represented about **20-25%** of the overall samples in each cohort.

Urine Samples:

Urine samples saw the **most improvement in predictive performance across all cohorts**.

a) **2019-2021 Cohort**: Accuracy was **90%**, already reflecting strong model performance.
b) **2022 Cohort**: There was a minor increase, with accuracy improving to **91%**.
c) **2023 Cohort**: The trend continued upward, with accuracy reaching **92%**.
d) **Relative Percentage**: Urine samples accounted for **35-40%** of the overall data, making it a significant category in model performance analysis.

The results in this analysis show a consistent and improving trend in the machine learning model's predictive performance, particularly in urine samples, while blood and respiratory cultures show stability or minor fluctuations. These findings align with other research in the predictive modeling of infectious diseases. For instance, a study by Schuetz et al. (2021) found that machine learning models could accurately predict bacterial infections in blood cultures with a performance range of **85-90%**, like the **88%** accuracy observed in this study. However, the slight decline in respiratory culture accuracy from **86%** to **85%** in the 2023 cohort may warrant further investigation. This drop might reflect the complexities of respiratory infections, which, as noted by Seymour et al. (2019), can be more difficult to predict due to the variability in pathogens and the influence of comorbidities in respiratory conditions.

The most notable improvement is observed in urine samples, where accuracy increased from **90%** to **92%** between the 2019–2021 and 2023 cohorts. This aligns with studies such as those by Gupta et al. (2022), which highlighted the effectiveness of machine learning in predicting urinary tract infections with a similar high accuracy. These trends indicate that continued refinement and specific focus on challenging areas, such as respiratory infections, could further enhance predictive capabilities.

Deployment

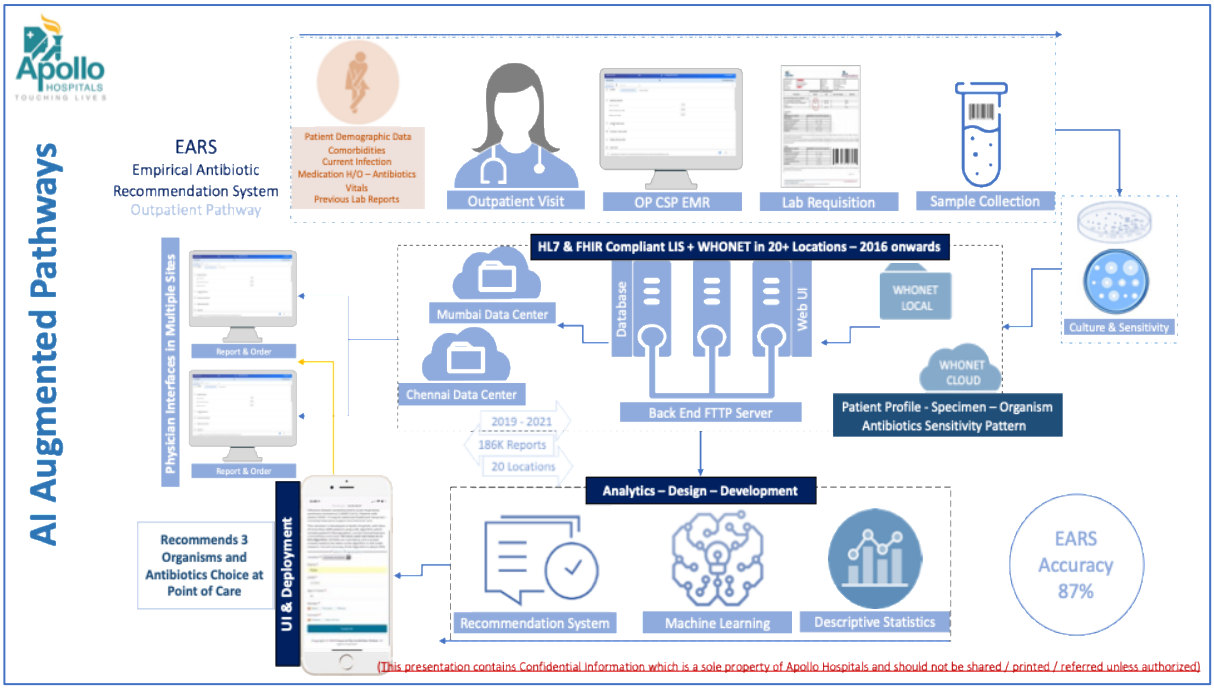


Figure 8 – Schematic Representation of the Outpatient Infectious Patient Visit and Design, Development, and Deployment of Apollo EARS Program based on WHONET Microbiology Results

Flow –

a) Data Flow is described above
b) The Antibiotics Reports are generated and stored with the following details
    a. Name & UHID
    b. Age and Gender
    c. Date & Time of Sample and Report Generation (+ Date & Time of Admission)
    d. Department – Specialty – Consultant
    e. Specimen – Organism – Growth Characteristics
    f. Antibiotics – Sensitive or Resistant Patterns
c) The Data Flows into the Web AI and Back FTTP server where it is stored in the Data centers (Primary and Secondary) in the same prescribed WHONET Format maintaining the HL7 and FHIR Compliance and Traceability
d) The Data is pulled every 3 months through SQL Query and analyzed, ingested into the Machine Learning – Recommendation System
e) The Output is Integrated into the UI API of the Apollo EARS and used in the Point of Care in Mobile Compatible App.
f) Provides data based on the entire antibiotic sensitivity pattern + local sensitivity pattern with 3 Organisms and 3 corresponding antibiotic recommendations.
g) User feedback is carried out to understand how useful it is

Ethics Perspective

Title	Development & validation of Empirical Antibiotic Recommendation System (AI-EARS)	Centers	India – Apollo Hospitals – Delhi, Bangalore, Hyderabad, Kolkata, Chennai, Bhubaneshwar
Principal Investigators	Sujoy Kar ,Bharath Potla, Jospin Dhivya	Institutional Ethics Committee Approval	Obtained
Data	Data Quantum | Locations - 20+ Locations pan India Gender - All AGE Group (0 – 90+ years) Quantum - 363K Isolates | 57 Specimen Types | 180 Organisms | 141 Antibiotics	Safety	Model advocates Antibiotic Recommendations that are interpreted by clinicians through safe Machine (API) – Human (Clinician) Interaction
Sample Size + Missing Data	Retrospective –Time Period 2019 – 2023	Inclusiveness & Fairness	At Inpatient and outpatient settings – Uses Demographic, clinical, and microbiological data| 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 All AGE Group (0 - 90+ years) Automation Bias addressed at API Clinical Use	Accuracy + Efficacy	Generic Results – AUC value of 0.92 | precision - 0.81
Risk Groups /outcome	Top 3 Probable Organisms & Sensitive Antibiotics & Location Specific Recommendations	Informed Consent	Yes – Template & Protocol (Prototype Attached)
Model Specification	Content based filtering Recommendation System Cosine Similarity & Bayesian Framework XGB Model	API – Ease of Use + Interpretation	Flows to Clinical Algorithm Standard User Manual
Clinical Algorithm Update (Version)	Version 1 - May 2022	Validation + Peer Review	Ongoing
Intellectual Property Rights (IPR)	Patent No|202441065932	Certifications & Compliance	ISO 13485:2016 Certification | MD 763515 CDSCO Application No| Apollo-Hyder-TE/M/MD/007509

Frequently Asked Questions

Why is AI-EARS different or What is the advantage of this?

1. *Detect, Respond, and Contain Resistant Pathogens - Laboratory and Diagnostics:*
   Gold-standard lab capacity | On-the-ground lab expertise and assistance
2. *Prevent Spread of Resistant Infections*
3. *Surveillance and Science:*
   More effective tracking and prevention of community and healthcare-associated infections etc
4. *Improved Antibiotic Use:*
   Improving antibiotic use to ensure antibiotics are available and work to protect people from life-threatening infections or sepsis by providing Clinicians Guide on Choice of Empirical Antibiotic Use
5. *Encourage Innovation for New Strategies - Insights for Practice:*
   Innovations and collaborations within Apollo Hospitals, Clinicians and use of Machine Learning – Recommendation to identify and implement new ways to prevent antibiotic-resistant infections and their spread through judicious use of Antibiotics.

What are the Interpretation & Adoption Messages?

1. AI Algorithm + Clinicians – This Recommendation System has been built as an adjunct tool for physicians to identify the global/holistic risk for the patient developing Antibiotic Resistance.
2. *Limitations:*

- The EARS doesn't account for Surgical Prophylaxis or Medical Prophylaxis for Any Procedures and Conditions. For Surgical Prophylaxis, consult your organization's Anti-Microbial Stewardship Program.
- The EARS currently doesn't recommend on –
    - Antiviral Therapy including HAART
    - Anti-Malarial or Parasitic Infections Therapy
    - Anti Mycotic or Anti-Fungal Therapy
    - Anti-TB Medications

- Specialty Specialty-specific recommendations are being worked on and are not deployed in the Model.

- For Specific Syndromic Approach, Refer to ICMR Guidelines – the EARS model doesn't recommend Empirical Antibiotics in this category yet.

Where can the physicians use the AI EARS tool?
Integrated into an Application Programming Interface, this multi-model approach provides an accurate Empirical Antibiotic Recommendation for the Physician at the point of care in Outpatient Clinics, Emergency Rooms, Wards, and Critical Care units depending on the patient profile.

What are the Risk Factors Included?
At present, there are no risk factors included in the model, except for teratogenic drugs.

What is the Output?
The AI EARS output yields recommendations of probable organisms and their sensitive antibiotics at the Point of Care.

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. **This is a Class 1 Device and Registered with CDSCO – TE/M/MD/007509**

Does this contradict the Physician's view?
This Recommendation System and Clinical Algorithm is a general guideline for Physicians. Any additional laboratory investigations, Diagnostic Imaging, Treatment or Patient Education related to disease management is under the Physician's discretion.

How does one ensure the accuracy of the AI EARS 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?
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 report is based on the EARS without any intervention from their side.

b. By usage of AI EARS, 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.

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

How is Safety addressed?
The model advocates drug recommendations that are interpreted by clinicians through safe Machine (API) – Human (Clinician) Interaction. Informed consent from each individual is obtained before the Recommendation generation.

Definitions & Clinical Terms are additionally used to safeguard patients with common comorbidities.

Liver Disease
Individuals with signs and symptoms of Liver Disease like skin and eyes that appear yellowish (Jaundice), abdominal pain and swelling, swelling in the legs and ankles, itchy skin, dark urine color, chronic fatigue, nausea and vomiting, loss of appetite and tendency to bruise easily. It also includes derangement of Liver function tests (described below) and/or findings of Fatty Liver or Fibrosis in Ultrasound or other imaging techniques of the upper abdomen or liver.
Ref: Mayo Clinic

Liver Details (from previous Ultrasound Reports) -
1. Liver Size – Normal or Enlarged
2. Fatty Liver – Yes/No

Liver Disease History – Any previous diagnosis of:
i. Alcoholic Hepatitis
ii. Infectious Hepatitis
iii. NASH
iv. Other Liver Diseases

Chronic Kidney Disease
Chronic Kidney Disease (CKD) is a long-term condition characterized by a gradual loss of kidney function over time. It is defined by the presence of kidney damage (e.g., albuminuria) or a reduction in kidney function, measured by a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2, for a period of at least three months, regardless of the cause. CKD is progressive and can eventually lead to end-stage renal disease (ESRD) if untreated, requiring dialysis or kidney transplantation. Common causes include diabetes, hypertension, and glomerulonephritis, though genetic and autoimmune factors can also contribute.
Key Sources:

- **National Kidney Foundation (NKF)**: Provides guidelines for the diagnosis and classification of CKD, emphasizing the importance of GFR and albuminuria in staging the disease.
- **KDIGO (Kidney Disease: Improving Global Outcomes)**: Offers global clinical practice

guidelines that define CKD and outline its management.

- **Centers for Disease Control and Prevention (CDC)**: Explains the prevalence, risk factors, and impact of CKD on public health.

References:

- National Kidney Foundation. "Chronic Kidney Disease (CKD) Basics."
- KDIGO. "2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease."
- Centers for Disease Control and Prevention. "Chronic Kidney Disease Initiative."

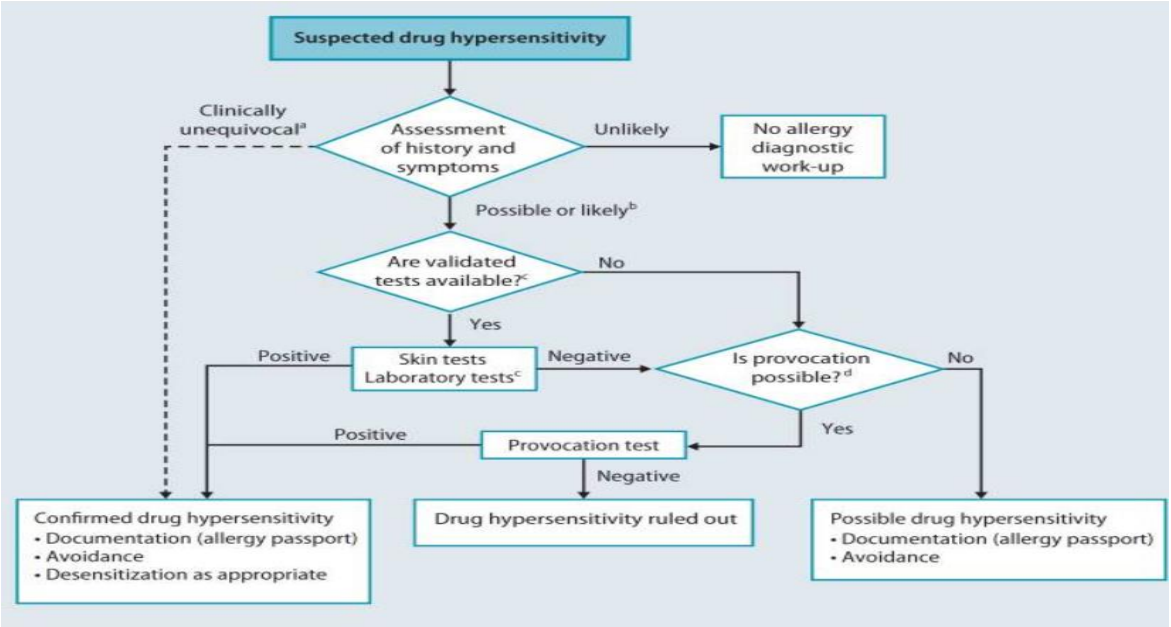
Hypersensitivity

Hypersensitivity reactions are exaggerated or inappropriate immunologic responses occurring in response to an antigen or allergen (or) It is an exaggerated response by the immune system to a drug or other substances. Ref: National Library of Medicine

Types of Hypersensitivity:
Coombs and Gell classified hypersensitivity reactions into four forms. Type I, type II, and type III hypersensitivity reactions are known as immediate hypersensitivity reactions (IHR) because they occur within 24 hours. The fourth type is considered a delayed hypersensitivity reaction because it usually occurs more than 12 hours after exposure to the allergen, with a maximal reaction time between 48 and 72 hours.

- Type I: reaction mediated by IgE antibodies
- Type II: cytotoxic reaction mediated by IgG or IgM antibodies
- Type III: reaction mediated by immune complexes
- Type IV: delayed reaction mediated by cellular response

Pathway for Suspected Drug Hypersensitivity:



(Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4479479/)

Clinical Manifestations of Hypersensitivity:

- Immediate-type symptoms – Examples: flushing, urticaria, angioedema, bronchospasm, anaphylaxis
- Delayed-type symptoms – Examples: maculopapular drug eruptions, acute generalised exanthematic pustulosis (AGEP), severe cutaneous adverse reactions: Stevens-Johnson-Synrom (SJS), toxische epidermale Nekrolyse (TEN), "drug reaction with eosinophilia and systemic symptoms" (DRESS)
- Specific symptoms – Examples: hepatitis, cytopenias, autoimmune diseases

Pregnancy & Lactation

A pregnancy is divided into three stages called trimesters: first trimester, second trimester, and third trimester. A trimester lasts between 12 and 14 weeks, while a full-term pregnancy lasts around 40 weeks from the first day of a woman's last period. In each trimester, the fetus will meet specific developmental milestones.

- The First Trimester (0 to 13 Weeks)
- The Second Trimester (14 to 26 Weeks)
- The Third Trimester (27 to 40 Weeks)

Lactation is the process of producing and releasing milk from the mammary glands in your breasts. Lactation begins in pregnancy when hormonal changes signal the mammary glands to make milk in preparation for the birth of your baby. It has three stages:

- Stage I lactogenesis: This begins around the 16th week of pregnancy and lasts until a few days after you give birth.
- Stage II lactogenesis: This stage starts about two or three days postpartum (after giving birth). It's when milk production intensifies.
- Stage III lactogenesis: This describes the rest of the time you lactate.

Ref: Cleveland Clinic

A few groups of drugs that are not safe during Pregnancy:

- Tetracyclines
- Fluoroquinolones
- Metronidazole
- Nitrofurantoin
- Sulfamethoxazole/trimethoprim

Please get in touch with a Clinical Pharmacologist before taking any medications to prevent any teratogenic effect on the fetus or infants.

Previous Antibiotics Use

Medication histories are important in preventing prescription errors and consequent risks to patients. Apart from preventing prescription errors, accurate medication histories are also useful in detecting drug-related pathology or changes in clinical signs that may be the result of drug therapy. A good medication history should encompass all currently and recently prescribed drugs, previous adverse drug reactions including hypersensitivity reactions, any over-the-counter medications, including herbal or alternative medicines, and adherence to therapy.

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2723207/