Helping Doctors Tackle Antibiotic Resistance:

Applying Machine Learning to the Development of an Intelligent Decision Support System for Antimicrobial Prescribing

Done by: Kan Yan Ting Jamie

Project Supervisor: Dr Pau Herrero Viñas, Dr Pantelis Georgiou

Background

Motivation

- Rising antimicrobial resistance is a major problem in UK and around the world.[1,2]
- Inappropriate prescriptions is one of the main causes of antimicrobial resistance.[2]
- Effective antimicrobial prescription is especially crucial for critically ill patients as antimicrobial therapy often must be administered before laboratory results is available.

Objectives

1. Understand the decision process of an expert when he prescribes antimicrobials and incorporate this into an Intelligent Decision Support System (IDSS)
2. Develop an IDSS that, when given a new case, is able to suggest suitable antimicrobial therapy options based on the thinking process of an expert.
3. Measure the performance of the system.

Methodology

Intelligent Decision Support System

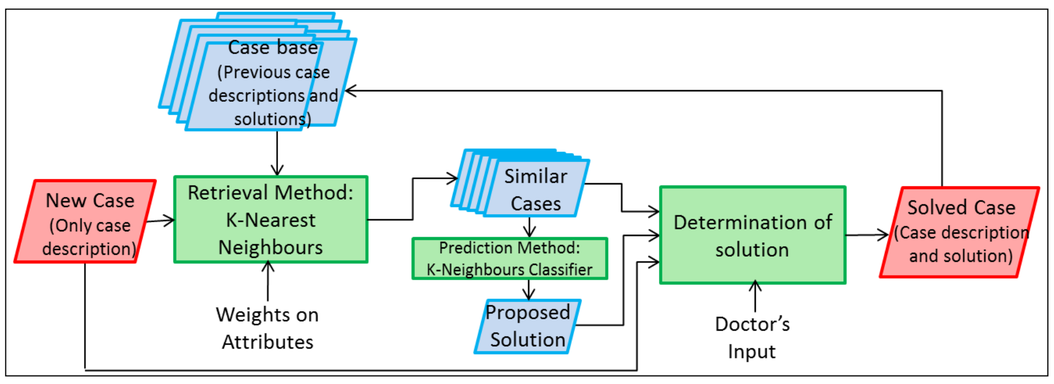

Fig 1: Flow chart showing concept of IDSS

The system uses the technique of Case Based Reasoning[3] (Fig. 1):

1. A new case is received containing attributes e.g. age, lactate levels. Similar cases are retrieved from the case base of previous cases using the *K*-Nearest Neighbours (KNN) algorithm.
2. The solutions of the *K* most similar cases (lowest overall distance), together with a proposed solution (if available), are presented as possible treatments to the doctor, who decides on final treatment.
3. The solved case (attributes and solution) is added into the case base.

Measuring Performance of IDSS

- Cross validation is used to measure system performance using the existing case base. The case base is split into a training set and a testing set using stratified K-folds.
- The proposed solution is compared to the actual solution of the test case and its accuracy is calculated

Calculating Accuracy of the Solution

The accuracy of the proposed solution is calculated using two measures:

1. {Hypothesis} is the set of drugs proposed using the IDSS.
   {Solution} is the set of drugs actually prescribed by the doctor.

$$Overall\ Accuracy = \frac{Size\ of\ \{Hypothesis\} \cap \{Solution\}}{Size\ of\ \{Hypothesis\} \cup \{Solution\}}$$

2. Given TP: True Positive , TN: True Negative,
   FP: False Positive, FN: False Negative

$$Sensitivity = True\ Positive\ Rate(TPR) = \frac{No.of\ TP}{No.of\ TP+FN}$$

$$Specificity = True\ Negative\ Rate(TNR) = \frac{No.of\ TN}{No.of\ TN+FP}$$

$$Positive\ Likelihood\ Ratio\ (LR+) = \frac{Sensitivity}{1-Specificity}$$

Results

Clustering using Principal Component Analysis (PCA)

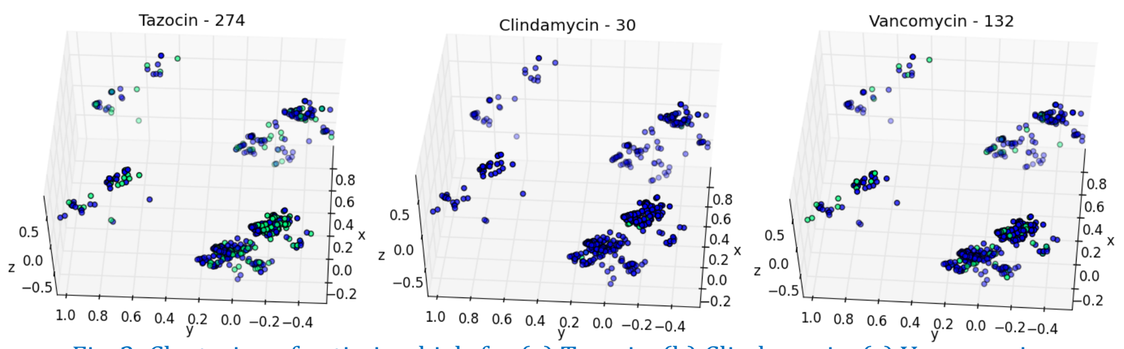

Fig. 2: Clustering of antimicrobials for (a) Tazocin, (b) Clindamycin, (c) Vancomycin

- Broad-spectrum antimicrobials (e.g. Tazocin) occur in all 4 main clusters.
- Narrow-spectrum antimicrobials (e.g. Clindamycin) are well clustered.
- Vancomycin is a special situation: narrow spectrum antimicrobial but frequently prescribed and occurs in all the clusters. Doctors have confirmed that it was overprescribed.

Novel Application – Using Weights to find Relative Importance of Attributes

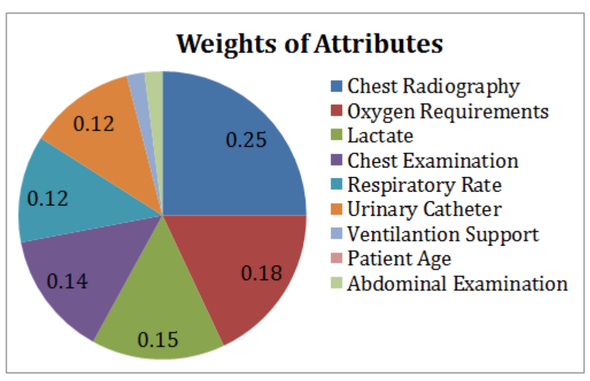

Fig. 3: Weights for highest overall accuracy

- By using IDSS with equal weights, overall accuracy of 56% per case.
  - ➢ Concept of KNN for IDSS suitable.
- Can improve the system further by optimally assigning weights (Fig. 3).
  - ➢ Overall accuracy per case increases to 66%.
- Attribute's weight indicates how important an expert perceived that attribute to be.
  - ➢ Chest radiography and chest examination forms almost 40% of weightage – could indicate heart and lung problems.[4]

Accuracy of Prediction

Drug Names	Basic		Best	
	TPR	TNR	TPR	TNR
Vancomycin	27.7%	86.3%	38.8%	89.1%
Ceftriaxone	22.7%	96.6%	39.2%	96.4%
Amikacin	6.3%	97.6%	11.6%	98.3%
Clindamycin	28.7%	95.9%	34.0%	98.5%

Table 1: Sensitivity(TPR) and Specificity(TNR) focussing on 4 antimicrobials as key examples out of 12 antimicrobials studied

- Basic: Equal weights given to all attributes.
- Best: Optimal set of weights for each drug.
- True Positive Rate (TPR) indicates **Sensitivity**: How likely a proposed drug is an accurate suggestion and actually prescribed by the expert.
- Best TPR > Basic TPR for all 12 antimicrobials.
  - ➢ Optimal weights improves accuracy.
- True Negative Rate indicates **Specificity**: If the IDSS suggests not to use a drug, how likely that it was also not used by the expert.
- Best TNR > 88% for all 12 antimicrobials.
  - ➢ IDSS very successful w.r.t. specificity.
- Broad-spectrum antimicrobials have a lower LR+. E.g. Amikacin's best LR+ = 6.8
  Narrow-spectrum antimicrobials have a higher LR+. E.g. Clindamycin's best LR+ = 22.7

Conclusion

1. The IDSS developed was successful in modelling the decision making process of the doctor especially with regards to specificity. By adjusting the weights of the attributes, there is also an improvement in sensitivity. The sensitivity of the IDSS should improve over time as more data is added into the case base.
2. Vancomycin-Resistant Enterococci (VRE) is a bacteria that is resistant to Vancomycin. From this project, it was identified that Vancomycin was overprescribed using clustering by PCA. As a narrow-spectrum antimicrobial, its low LR+ also indicate over-prescription. This system may be used to identify other antimicrobials that are overprescribed and prevent antimicrobial resistance to these drugs.
3. The next step is to perform clinical trials to measure the usefulness of the IDSS in a real-world application.

References:

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2. The NHS in England – NHS Choices (2014, September 24) *The Antibiotic Awareness Campaign* [online] Available: http://www.nhs.uk/NHSEngland/ARC/Pages/AboutARC.aspx [accessed 15 August 2015]
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4. National Heart, Lung, and Blood Institute (2010, August 1) *What Does a Chest X Ray Show?* [online] Available: http://www.nhlbi.nih.gov/health/health-topics/topics/cxray/show