A Project Report

on

CLINICAL DECISION SUPPORT SYSTEM

Submitted in partial fulfillment of the requirement for the award of the degree of

Bachelor of Technology in Computer Science and Engineering



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SCHOOL OF COMPUTING SCIENCE AND ENGINEERING GALGOTIAS UNIVERSITY, GREATER NOIDA

CANDIDATE'S DECLARATION

I/We hereby certify that the work which is being presented in the project, entitled "CLINICAL DECISION SUPPORT SYSTEM" in partial fulfillment of the requirements for the award of the BACHELOR OF TECHNOLOGY IN COMPUTER SCIENCE AND ENGINEERING submitted in the School of Computing Science and Engineering of Galgotias University, Greater Noida, is an original work carried out during the period of JULY-2021 to DECEMBER-2021, under the supervision of Ms. INDRA KUMARI, ASSISTANT PROFESSOR, Department of Computer Science and Engineering of School of Computing Science and Engineering, Galgotias University, Greater Noida

The matter presented in the project has not been submitted by me/us for the award of any other degree of this or any other places.

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This is to certify that the above statement made by the candidates is correct to the best of my knowledge.

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CERTIFICATE

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Date: December, 2021

Place: Greater Noida

Abstract

CDSS are computer applications that are designed to help health-care professionals with making clinical decisions about individual patients (Shortliffe and Cimino 2006; Berner 2007). In other words, CDSS are active knowledge systems, which use two or more items of patient data to generate case-specific advice (Wyatt and Spiegelhalter 2011). A CDSS correlates data about patient traits with a trustworthy knowledge base to guide a clinician with patient-specific advice, assessments or recommendations.

Clinicians, health-care staff or patients can manually enter patient characteristics into the computer systems; alternatively, electronic medical records (EMR) can be queried for retrieval of patient characteristics. These kinds of decision-support systems allow the clinicians to spot and choose the most appropriate treatment. Provided decision-support is based on processes of sophisticated outcomes assessment and algorithms that use knowledge bases to inquire after the newest developments about best practice (Remmlinger 2012; Garg, Adhikari et al. 2011).

Computerized clinical decision support systems, or CDSS, represent a paradigm shift in healthcare today. There have been numerous published examples in the past decade(s) of CDSS success stories, but notable setbacks have also shown us that CDSS are not without risks. In this paper, we provide a state-of-the-art overview on the use of clinical decision support systems in medicine, including the different types, current use cases with proven efficacy, common pitfalls, and potential harms.

We conclude with evidence-based recommendations for minimizing risk in CDSS design, implementation, evaluation, and maintenance.

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Acronyms

CDSS	Clinical Decision Support System
ML	Machine Learning
DL	Deep Learning
MAPE	Mean Absolute Percentage Error
RMSE	Root Mean Square Error

CHAPTER-1

Introduction

A clinical decision support system (CDSS) is intended to improve healthcare delivery by enhancing medical decisions with targeted clinical knowledge, patient information, and other health information. In the chapter we are presenting the theoretical background, state of the art and modern research trends of Clinical decision support systems (CDSS). The challenges for success are derived and our experience is described with the presentation of a good practice example of employing CDSS in telemedicine.

CDSS systems are increasingly often integrated into telemedicine clinical practice.

In addition to using the same resources, namely digitally coded clinical data, CDSS systems are able to enhance the quality of telemedicine services in many cases. CDSS are computer applications that are designed to help health-care professionals with making clinical decisions about individual patients (Shortliffe and Cimino 2006; Berner 2007). In other words, CDSS are active knowledge systems, which use two or more items of patient data to generate case-specific advice (Wyatt and Spiegelhalter 1991).

These kinds of software use relevant knowledge, rules within a knowledge base and relevant patient and clinical data to improve clinical decision making on topics like preventive, acute and

chronic care, diagnostics, specific test ordering, prescribing practices (National Electronic Decision Support 2003; Pearson, Moxey et al. 2009).

A CDSS correlates data about patient traits with a trustworthy knowledge base to guide a clinician with patient-specific advice, assessments or recommendations. Clinicians, health-care staff or patients can manually enter patient characteristics into the computer systems; alternatively, electronic medical records (EMR) can be queried for retrieval of patient characteristics. These kinds of decision-support systems allow the clinicians to spot and choose the most appropriate treatment. Provided decision-support is based on processes of sophisticated outcomes assessment and algorithms that use knowledge bases to inquire after the newest developments about best practice (Remmlinger 2002; Garg, Adhikari et al. 2005).

Regardless of how we choose to define CDSS, we have to accept that the field of CDSS is rapidly advancing and unregulated. It has a potential for harm, if systems are poorly designed and inadequately evaluated, as well as a huge potential to benefit, especially in health care provider performance, quality of care and patient outcomes (Delaney, Fitzmaurice et al. 1999; Pearson, Moxey et al. 2009).

FORMULATION OF PROBLEM

Strategies to reduce medication errors commonly make use of CDSS. Errors involving drug-drug interactions (DDI) are cited as common and preventable, with up to 65% of inpatients being exposed to one or more potentially harmful combinations. CPOE systems are now designed with drug safety software that has safeguards for dosing, duplication of therapies, and DDI checking. The types of alerts generated by these systems are among the most disseminated kind of decision support.

However, studies have found a high level of variability between how alerts for DDIs are displayed (e.g., passive or active/disruptive), which are prioritized and in the algorithms used to identify DDIs. Systems often have varying degrees of irrelevant alerts presented, and there is no standard for how best to implement which alerts to providers. The US Office of the National Coordinator for Health Information Technology has developed a list of 'high-priority' list of DDIs for CDS, which has reached various levels of endorsement and deployment in CDSS' of other countries including the U.K., Belgium, and Korea.

TOOLS AND TECHNOLOGY USED

RAMP medical – Alerts & Reminders

Notifications and reminders are commonly associated with clinical decision support tools. They follow the clinician's actions, prescriptions and recommended procedures and notify the user via a pop-up alert. Warnings, reminders or notifications appear if the doctor prescribes medicines that cannot be taken together, if a patient has an allergy to some components.

Cohesic – Guided Clinical Workflows

This type of clinical decision support tool provides aid for clinical decision-making in multi-step care plans from a long-time care perspective. It provides evidence-based guidelines, recommendations, and pathways at the right time.

HERA-MI – Diagnostic Decision Support

Clinical decision support systems (DSS) aim at supporting and assisting with clinical decisionmaking tasks in diagnostics. They help clinicians consider a variety of diagnoses, ask patients more targeted questions, request some of the patient's data.

Tapa Healthcare – Condition-Specific Sets

Order sets represent another group of clinical decision support tools that work as a pre-defined template for clinical decisions making for a specific condition or medical procedure. This might be a grouping of orders that help clinicians effectively choose the appropriate items.

LITERATURE REVIEW/ PROJECT DESIGN

Patient data must be adequate to make a valid decision. The problem arises, when the clinician is met with an overwhelming amount of specific and unspecific data, which he/she cannot satisfactorily process. Therefore, it is important to assess when additional facts will confuse rather than clarify the patient's case. For example, usual setting for such a problem are intensive-care units, where practitioners must absorb large amounts of data from various monitors, be aware of the clinical status, patient history, accompanying chronic illnesses, patient's medication and adverse drug interactions, etc. - and on top of that make an appropriate decision about the course of action.

The quality of available data is of equal importance. Measuring instruments and monitors should be as accurate as technologically possible, since erroneous data could have serious adverse effect on patient-care decisions. Knowledge used in decision-making process must be accurate and current. It is of major importance that the deciding clinician has a broad spectrum of medical knowledge and access to information resources, where it is possible to constantly revise and validate that knowledge.

For a patient to receive appropriate care, the clinician must be aware of the latest evidence-based guidelines and developments in the area of the case in question. It is in clinician's hands to bring proven therapies from research papers to the bedside. CDSS analogously needs an extensive, well-structured and current source of knowledge to appropriately serve the clinician. Above all, good problem-solving skills are needed to utilize available data and knowledge.

Deciding clinicians must set appropriate goals for each task, know how to reason about each goal and take in to account the trade-offs between costs and benefits of therapy and diagnostics. In further reflection, we should not neglect, that skilled clinicians draw extensively from their personal experience.

Clinical Decision support systems should be possible by utilizing a various prediction model (Machine Learning Model, for example, support vector regression, artificial neural network, and that's only the tip of the iceberg. There are many advantages that cost free, property financial backers, and house developers can procure from the house-value model. This model will give a great deal of data and information seeking clinics, cure their disease and easily clinic center, like the valuation of disease cure in the current market, which will assist them with deciding house cost.

Functionality of Project

Random Forest

Random Forest is an ensemble model that aggregates the predictions of numerous decision trees to produce a more precise final prediction. Random Forest has been proven to be a powerful technique in prior studies. The random forest algorithm can be broken down into the steps below:

- Make an n-sample random bootstrap sample (randomly choose n samples from the training set with replacement).
- 2. From the bootstrap sample, create a decision tree with the following nodes:
- (a) Pick d features at random and leave them alone.
- (b) Split the node using the feature that delivers the best split in terms of the objective function, such as maximizing information gain.
- 3. Perform the steps a total of 1-2 thousand times. 4. By using a majority vote, assign the class label based on the predictions made by each tree.

We utilized the Random Forest Classifier class from sklearn in this paper. The n estimators argument in the Random Forest Classifier lets you to specify how many trees to build, which we set to 900. While increasing the number of trees in the random forest improves accuracy, it also increases the model's overall training time. The bootstrap parameter, which we set to True, is also included in the class.

However, only a limited collection of attributes will be used to introduce variation within the trees in random forest subsets. We improved the performance even further by iterating the model numerous times and adding a few parameters when we initialized the Random Forest Classifier:

- Set max depth = 20, limiting the depth of these trees to 20.
- Set min samples split = 10, which means that a node can only be split if it has at least ten rows.

The Random Forest classifier is built utilising an 80 percent split of the training dataset from the main dataset. After the decision tree model has been built, it is tested for accuracy by using it to categories the remaining 20% of the dataset, known as test data.

Gradient Boost

Gradient boosting is a machine learning technique that was developed in 1999 and is widely utilized due to its performance, consistency, and interpretability. Gradient boosting is cutting-edge in a number of machine learning tasks, including multistage classification, click prediction, and ranking. Gradient boosting has faced additional hurdles in recent years, particularly in terms of finding a compromise between accuracy and performance.

Gradient boosting has a limited set of parameters. The following procedures can be performed to ensure a dynamic balance between fit and regularity when selecting parameters: determining regularization parameters (lambda, alpha), lowering the learning rate, and determining thoseideal parameters once more.

Several approaches, including Mean Absolute Percentage Error (MAPE), Mean Absolute Error (MAE), and Root Mean Square Error (RMSE), were used to test the model proposed in this study (RMSE). The average percentage of the absolute error of each anticipated result is used to calculate MAPE. As a result, MAPE may be used to determine the amount of prediction error.

MAE calculate the average of absolute error for each predicted result. MAE is useful when measuring errors in certain units. MAE values can be calculated using.

RMSE is used to calculate predicted performance by considering the prediction error of each data.

RESULTS AND DISCUSSIONS

Success factors of CDSS

Despite the fact, that the computerized CDSSs were continuously in development since the 1970s, their impact on routine clinical practice has not been as strong as expected. The potential benefits of using electronic decision support systems in clinical practice fall into three broad categories (Coiera 2003):

- Improved patient safety (reduced medication errors and unwanted adverse events, refined ordering of medication and tests);
- 2. Improved quality of care (increasing clinicians' time allocated directly to patient care, increased application of clinical pathways and guidelines, accelerate and encourage the use of latest clinical findings, improved clinical documentation and patient satisfaction);
- Improved efficiency of health-care (reducing costs through faster order processing, reductions
 in test duplication, decreased adverse events, and changed patterns of drug prescribing, favoring
 cheaper but equally effective generic brands).

Developing CDSSs is a challenging process, which may lead to a failure despite our theoretical knowledge about the topic. Understanding the underlying causes, which lead either to success or either to failure, may help to improve the efficiency of CDSS development and deployment in day-to-day practice. Failures can originate from various developmental and implementation phases: failure to technically complete an appropriate system, failure to get the system accepted by the users and failure to integrate the system in the organizational or user environment (Brender, Ammenwerth et al. 2006).

There is an estimation that 45% of computerized medical information systems fail because of user resistance, even though these systems are technologically coherent. Some reasons for such a high percentage of failure may derive from insufficient computer ability, diminished professional autonomy, lack of awareness of long-term benefits of CDSS-use and lack of desire to change the daily workflow (Zheng, Padman et al. 2005).

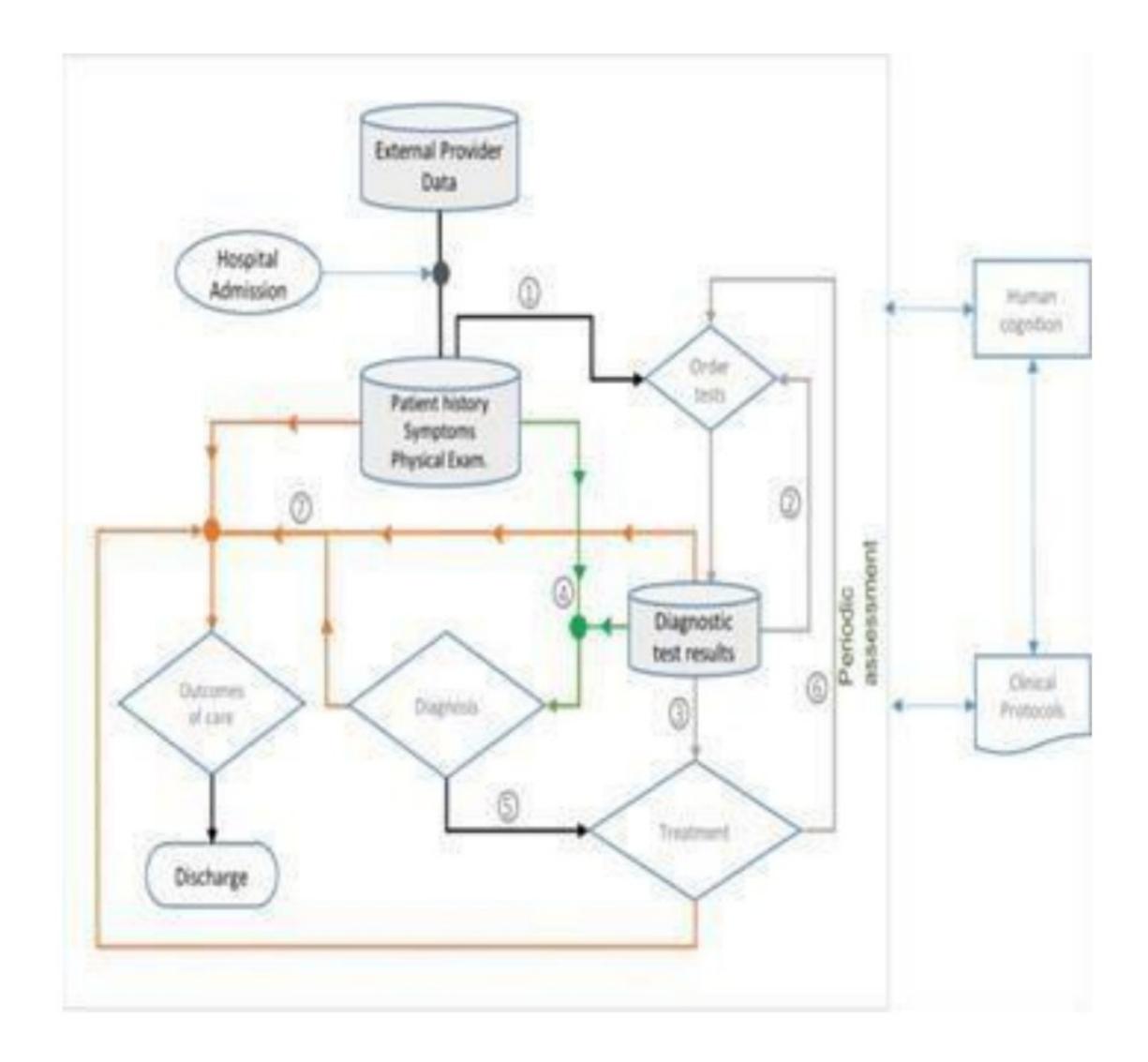
Despite the problems and failures that might accompany CDSSs, these systems have still been proven to improve drug selection and dosing suggestions, reduce serious medication errors by flagging potential drug reactions, drug allergies and identifying duplication of therapy, they enhance the delivery of preventive care services and improve adherence to recommended care standards. Recent studies suggest that there are some CDSS features crucial to success of these systems (Kawamoto, Houlihan et al. 2005; Shortliffe and Cimino 2006; Pearson, Moxey et al. 2009; Moxey, Robertson et al. 2010):

- CDSS should provide decision support automatically as part of clinicians' workflow, since systems where clinicians were required to seek out advice manually have not been proven as successful.
- Decision support should be delivered at the time and location of decision-making. If the clinician
 has to interrupt the normal pattern of patient care to move to a separate workstation or to follow
 complex, time-consuming startup procedures it is not likely that such system will be good
 accepted.
- Systems that were provided as an integrated component of charting or ordering systems were significantly more likely to succeed than alone standing systems. Generally speaking, the decisionsupport element should be incorporated into a larger computer system that is already part of the users' professional routine, thus making decision support a byproduct of practitioners' ordinary work practices.
- Computerized systems have been reported to be advantageous over paper-based systems.
- Systems should provide recommendation rather than just state a patient assessment. For instance, system recommends that the clinician prescribes diuretics for a patient rather just identifying patient being cardiologically decompensated.
- CDSS should request the clinician to record a reason for not following the systems' advice (the clinician is asked to justify the decision with a reason, e.g. "The patient refused").
- It should promote clinicians' action rather than inaction.

Kawamoto 2005 suggests that the effectiveness of CDSS remains mainly unchanged when system recommendations are stated more strongly and when the evidence supporting these prompts is expanded and includes institution-specific data. Similarly, the effectiveness and functionality

remains unaltered when recommendations are made more specific. Interestingly the CDSSs didn't achieve wanted results when local clinicians were recruited into the system development process nor when bibliographic citations were provided to support the system made recommendations (Kawamoto, Houlihan et al. 2005).

To sum up, when developing CDSSs, there are factors beyond software and content that must be taken into consideration. Fundamental issues include availability and accessibility of hardware, sufficient technical support and training in use of the system, the level of system integration into clinical workflow and the relevance and timeliness of the clinical messages provided.



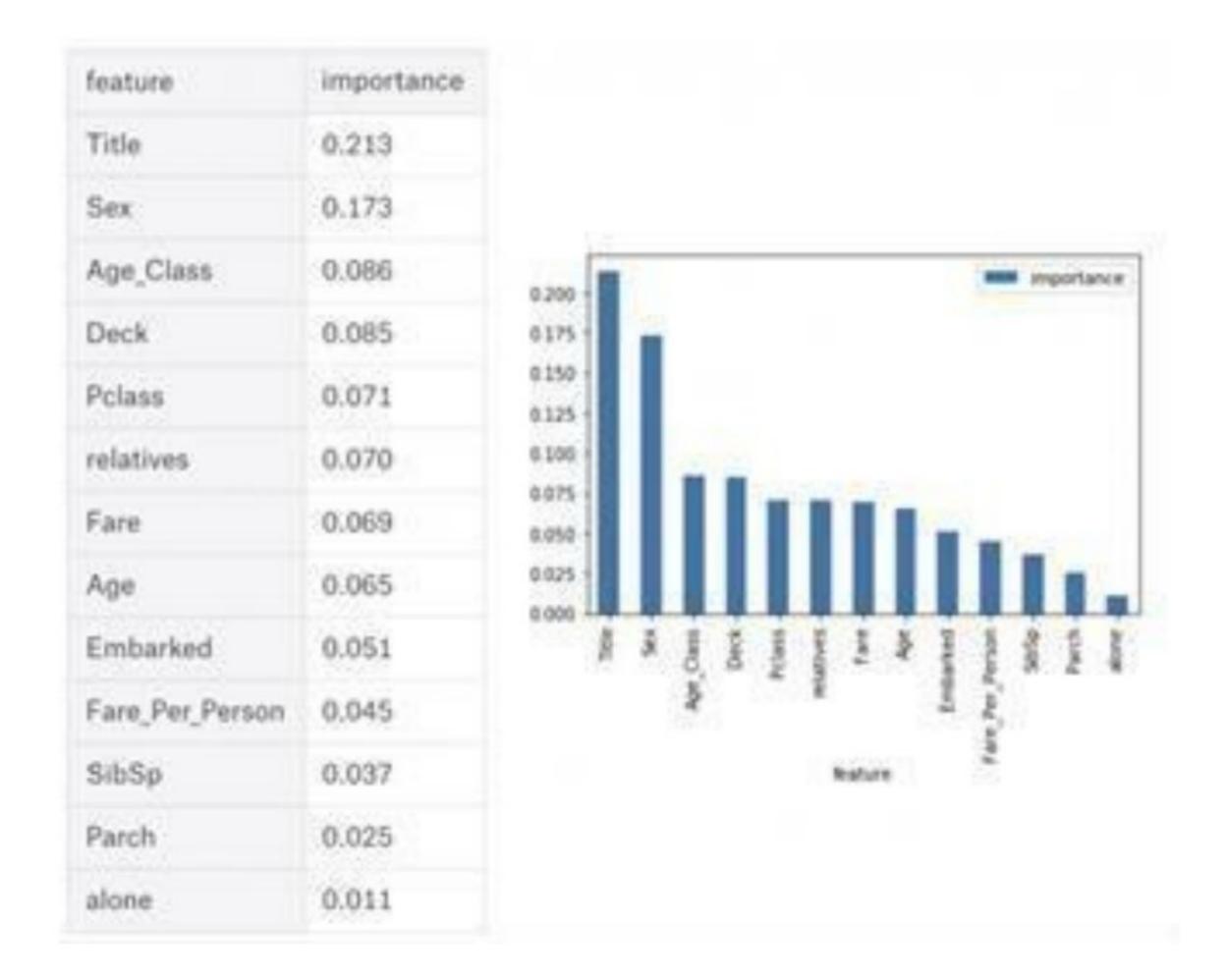
Like random forests, gradient boosting is a set of decision trees. The two main differences are:

- How trees are built: random forests builds each tree independently while gradient boosting builds one tree at a time. This additive model works in a forward stage-wise manner, introducing a weak learner to improve the shortcomings of existing weak learners.
- Combining results: random forests combine results at the end of the process while gradient boosting combines results along the way.

If you carefully tune parameters, gradient boosting can result in better performance than random forests. However, gradient boosting may not be a good choice if you have a lot of noise, as it can result in overfitting. They also tend to be harder to tune than random forests.

The results of our reasoning showed that two different practices are generally exercised in hospitals. One can be the manual way of prescribing the medicines by health professionals after analyzing the patient history and reports. The other can be by the use of Clinical Decision Support Systems. In Clinical Decision Support Systems, System Senses the disease or pain and based on the methodology used in its implementation, it suggests the prescription. On studying both practices on a relatively smaller scale, it is observed that the Clinical Decision Support Systems have several edges our manual systems. They are efficient, effective and low cost.

It provides an overview of the current practices regarding post operative pain and physiotherapy management of patients. The findings identify discrepancies in services provided to patients and highlight current research not always reflected in treatment provided. It highlights that the difference between the correct diagnosis by program and by physicians is 72% to 79%. In some cases such as diagnosis of CAD, the computer aided program being relatively simple and reliable makes it easy for physicians to estimate probability of CAD, Whether additional non-invasive diagnostic studies should be employed to improve probability of disease and to appropriate select patients to coronary angiography. On comparing the clinical decision support systems with non-clinical decision support systems it is observed that there is no way by which non clinical decision support systems can compete.



Random Forest algorithm is better to use than Gradient Boost. Random forests are bagged decision tree models that split on a subset of features on each split. This is a huge mouthful, so let's break this down by first looking at a single decision tree, then discussing bagged decision trees and finally introduce splitting on a random subset of features. Whether you have a regression or classification task, random forest is an applicable model for your needs.

It can handle binary features, categorical features, and numerical features. There is very little pre-processing that needs to be done. The data does not need to be rescaled or transformed.

CONCLUSION

It is clear that systems supporting clinical decision-making of doctors, nurses and other health-workers have an immense potential to benefit in their performance, provision of quality care and, what we strive for – better patient outcomes. In common sense, one can take better care of patients if one has superb knowledge about the clinical matters in question. For example, it could be said that with more information and knowledge a clinician has a better chance of solving a clinical problem in favor of the patient, the hospital and himself.

The problem is that nowadays global knowledge about a topic is often overwhelming for a clinician to process at the point of care or in urgent situations. CDSSs incorporate patient-specific data and an applicable, well-structured and current knowledge base or evidence-based guidelines, thus serving the clinician with enhancing his/her clinical decision-making process. Such support of basic cognitive processes involved in medical thinking to some extent relieves the clinician and provides him with new, better-formed and possibly superior methods to take best care of the ill.

Many characteristics of CDSSs are related to clinical effectiveness, functionality, error prevention, potential for acceptance in the clinical world, system portability, costeffectiveness etc., it is therefore important to fully understand the construction and different modalities of CDSS. The most successful CDSSs deal with therapy critiquing and consulting and/or drug dosing or prescribing. Latest CDSSs use EMR to provide data for analysis, and they provide the ability to the decision-maker to exert the recommended actions with ease, being completely integrated into the information system. Developers of CDSSs should thus be aware that there are factors beyond software and content that must be taken into consideration. Fundamental issues include the level of system integration into clinical workflow and the relevance and timeliness of the clinical messages provided, availability and accessibility of hardware and sufficient technical support and training in use of the system. Reasons for difficulties in implementing CDSS into everyday clinical practice come mainly from programmers' insufficient understanding of medical reasoning and decision analyses.

Such systems to some extent pose a threat to diminished clinicians' professional autonomy. Above all there is generally still a lack of awareness of long-term benefits of CDSS-use and lack of desire to change the daily workflow.

To encourage better health-processes, better individual patient care and better population health through CDSSs development, they need to be under constant improvement and their evolvement controlled from an appointed group of experts. To this end the American Medical Informatics Association developed a road map for action on CDSSs, regarding development, implementation and use. This road map comprises of three pillars, with their own subsets, which should bring sense into future evolvement and successful implementation of CDSSs (Lyman, Cohn et al. 2010).

- 1. Best knowledge available when needed;
- Represent clinical knowledge and CDSS interventions in standardized formats.
- There are multiple and most of the time very diverse types of formats used within CDSSs. The
 patient-specific data and thereafter computerized decision making is usually not exchangeable.
 This limits free interchange of patients between different institutions on national and
 international level. It thereby consequently limits the dispersion CDSSs and merits that global
 usage would bring.
- Collect, organize and distribute clinical knowledge and CDSS interventions in a way that users easily find suitable material and incorporate it in their own information systems.
 High adoption and effective use
- Address policy, legal and financial barriers
- The health care policy of e.g. European Union should support CDSSs implementation and development. One could expect that as EU directed the electronification of health care it should also direct further evolvement and implementation of CDSSs in everyday clinical practice. Review on research done in this field show multiple beneficial effects of using CDSS, resulting in better patient outcomes, enhanced health-care performance and consequently greater cost effectiveness of electronic health systems.
- With implementing CDSSs in everyday practice, we are obliged to consider the legal

wouldn't agree with CDSSs recommendations, which would in common medical sense, be wrong, but the clinicians' actions would anyway result in medical error or even death. How much weight would bear a decision of CDSS? How could we prove that the outcome would be different or better by following CDSS's decision-making? On the other hand CDSSs can impose a regulatory role in following the current medical guidelines. In a way CDSS can prevent a clinician in making medical errors by alerting about e.g. EU-accepted guidelines. CDSS can be viewed as a tool to track clinician's actions. Such information, if comprehensive and detailed, could be of great importance in a court of law.

- Improve the practice of deployment
- Improve the ease of usage 3. Continuous improvement of knowledge and CDSS methods
- Systematically capturing, organizing and examining existing CDSS deployments (e.g., http://www.openclinical.org)
- Advance care-guiding knowledge by using the data readily available in EMR, thus improving clinical knowledge and health management.
- Not only that EMR is time saving and basically essential for health information system (and thus a CDSS) to function successfully and be integrated into a workflow, it is also a source of data for forming new knowledge.

REFERENCES

- [1] D. Demmer-Fushman, J. Lin, "Answering Clinical Question with Knowledge-Based and Statistical Techniques." Association for Computational Linguistics, 2011, pages 63 103.
- [2] A. Soriano Paya, D. Fernandez, D. Gill Mendez, C. Hernandez. "Development of an artificial neural network for helping to diagnose diseases in urology." Bio-Inspired Model of Network, Information and Computing Systems, 2006, IEEE, pages 1 -4.
- [3] D. F. Pires, C. A. C. Teixeira, E. E. S. Ruiz, "A UMLS Interoperable Solution to Support Collaborative Diagnosis Decision Making over the Internet.", Proceedings of ACM symposium on Applied computing, 2008, pages 1400-1404.
- [4] D. J. Spiegelhalter, R. P. Knill-jones, "Statistical and Knowledge-based Approaches to Clinical Decision-support Systems, with an Application in Gastroenterology." J. R. Statist. Soc. 1984, pages 35-77.
- [5] M. P. Jenson, C. Chen, A. M. Brugger. "Interpretation of Visual Analog Scale Ratings and Change Score: A Reanalysis of two Clinical Trials of Postoperative Pain.", The Journal of Pain, 2013, pages 407-414.
- [6] S. Lin, A. H. B. Duffy, R. I. Whitfield, I. M. Boyle. "Integration of decision support systems to improve decision support performance." Knowledge & information Systems Springer-Verlag, 2011, pages 261 286.
- [7] M. Frize, C. M. Ennett, M. Stevenson, H. Trigg. "Clinical decision support system for intensive care units: using artificial neural networks." Medical Engineering & Physics, 2011, pages 217-225.
- [8] Autonomy, I. (2009). Autonomy Technology Overview. I. Autonomy. Bassingthwaighte, J. B. (2000). "Strategies for the physiome project." Ann Biomed Eng 28(8): 1043-1058. Berner, E. S. (2007).
- [9]Clinical decision support systems: theory and practice. New York, Springer. Brender, J., E. Ammenwerth, et al. (2009). "Factors influencing success and failure of health informatics systems--a pilot Delphi study." Methods Inf Med 45(1): 125-136.