Behind the screens: Clinical Decision Support Methodologies - a Review.

Abstract

Clinical decision support systems (CDSSs) are interactive software systems designed to assist clinicians with decision making tasks, such as determining diagnosis of patient data. CDSSs are a widely researched topic in the Computer Science community but their workings are less well understood by clinicians. The purpose of this review is to introduce clinicians and policy makers to the most commonly computer-based methodologies employed to construct decision models to compute clinical decisions in a non-technical manner. We hope that a better understanding of CDSSs will open up discussion about the future of CDSSs as a part of healthcare delivery as well as engage clinicians and policy makers in the development and deployment of CDSSs that can meaningfully help with decision making tasks.

1 Introduction

Information technology (IT) is now commonplace in nearly every branch of healthcare. Electronic patient records, e-prescribing and digital medical image storage and retrieval are now well known to clinicians and have been implemented with varying degrees of success[1–3]. While the main task of healthcare IT is usually data storage and management, there are further tasks that are embedded in the main systems to support the central role. One often overlooked set of tools are CDSSs, which have been defined as tools for “providing clinicians with computer-generated clinical knowledge and patient-related information, intelligently filtered or presented at appropriate times"[4]. Frequently CDSSs operate in the background of the main application and provide the clinician with information about patient states including alerts, warnings or predictions about future states.

Generally, a CDSS is composed of four operational characteristics[5,6]:

1. *Triggers:* events that provoke decision support rules to be invoked (e.g. drug prescription);
2. *Input data:* information used by decision support functionality to make inference(s) about a patient (e.g. patient demographics or laboratory results);
3. *Interventions:* possible actions computed by the decision support function (e.g sending a reminder message to a physician or presenting a clinical practice guideline);
4. *Offered choices:* possible choices available to a clinician after invoking the CDSS functionality (e.g. choosing among different proposed therapies or medications).

The operational characteristics described above can be implemented to develop three main types of CDSSs:

1. *Passive systems*: This is the most common form of CDSS. In this mode, the user must explicitly make a request to the system for support.
2. *Semi-Active systems*: These systems trigger automatically and deliver information, generally accepted knowledge and procedural rules. They play the role of watchdog, alerting a clinician to a particular clinical situation.
3. *Active systems*: These are also triggered automatically and can make decisions without the intervention of the clinician. For example, orders for additional examinations based on health protocols, therapeutic examinations

(e.g., automatic control of a transfusion by a closed-loop system), or supervision systems (e.g., intelligent control of the parameters of a ventilator).

CDSSs have been shown to improve the quality of patient care and health outcomes[7], however they are still not widely accepted within clinical practice[4]. In fact, CDSSs are not often discussed in medical journals, and, when considered, they are usually described as part of:

1. Randomized Controlled Trials where results arising from the testing phase of a specific CDSS are reported without any technical details about the system[8–12];
2. Systematic Reviews, which summarize previously published Randomized Controlled Trials and assess the impact and potential of CDSSs in clinical practice[7,13,14];
3. Editorials which comment on the impact of technology in healthcare with CDSSs often presented as an important element of future medicine[15–17].

Generally, such publications tend to emphasize clinical impacts of CDSSs rather than provide technical details which would facilitate a proper understanding of how systems compute decisions. Consequently, clinician's knowledge of how CDSSs work in practice remains rather limited and this could have an influence on acceptance of such systems. Conversely, CDSSs are widely considered in Computer Science and Health Informatics journals. These publications often present good performances of a wide range of technical methodologies which could be effectively used to support delivery of care and generate positive clinical impacts for patients[7]. Since clinicians involvement in any phase of CDSS's design and development is essential to favour successful adoption, in the following sections we present a non-technical overview of some of the computing methodologies commonly used by CDSSs to compute decisions. The aim of the paper is to provide clinicians with a better understanding about CDSSs in order to allow them to be involved and have an active role in any phase of CDSS's design and development. It has to be noted that the focus of this paper is on the CDSS's methodologies and not on clinical outcomes which are outside the scope of our review.

2 Methods of Literature Search

Relevant articles were identified by a Scopus search using search terms "Clinical, Decision, Support, Systems, Medical, and Decision-Making". Since the objective was to identify the most used CDSS's methodologies, the search was limited to the main relevant Health Informatics journals (International Journal of Medical Informatics, Journal of the American Medical Informatics Association, Journal of Biomedical Informatics, Artificial Intelligence in Medicine, Computer Methods and Programs in Biomedicine, BMC Medical Informatics and Decision Making, Studies in Health Technology and Informatics, Methods of Information in Medicine, Medical Decision Making) from the period January 2005-January2014. The review process was composed of two steps: 1) articles were screened via title and abstract and papers about CDSSs were included; 2) after full text analysis, we reported only the articles that were judged as relevant examples by three clinicians.

3 Review of CDSS's Methodologies

The Scopus search retrieved 1684 papers. After screening via title and abstract, 92 papers were included. After full text analysis 18 articles describing CDSSs were judged as the most interesting and will be presented in this review.

From the subset of 92 retrieved papers, the main methodologies used by CDSSs have been grouped into umbrella categories shown in Figure 1. More than one method could be used to develop a CDSS and also one method could belong to more than one category, consequently the sum of the percentages is not 100. In the following paragraphs we outline and explain the main relevant methods from these umbrella categories and provide examples of how these methods have been implemented to develop specific CDSSs. It should be noted that the methodologies used to develop CDSSs are independent of CDSS types described in the Introduction and that each of the methodologies we describe could be used to develop any type of CDSS (passive, semi active, active). The precise implementation and usage is dependent on the characteristics of the clinical task that has to be accomplished.

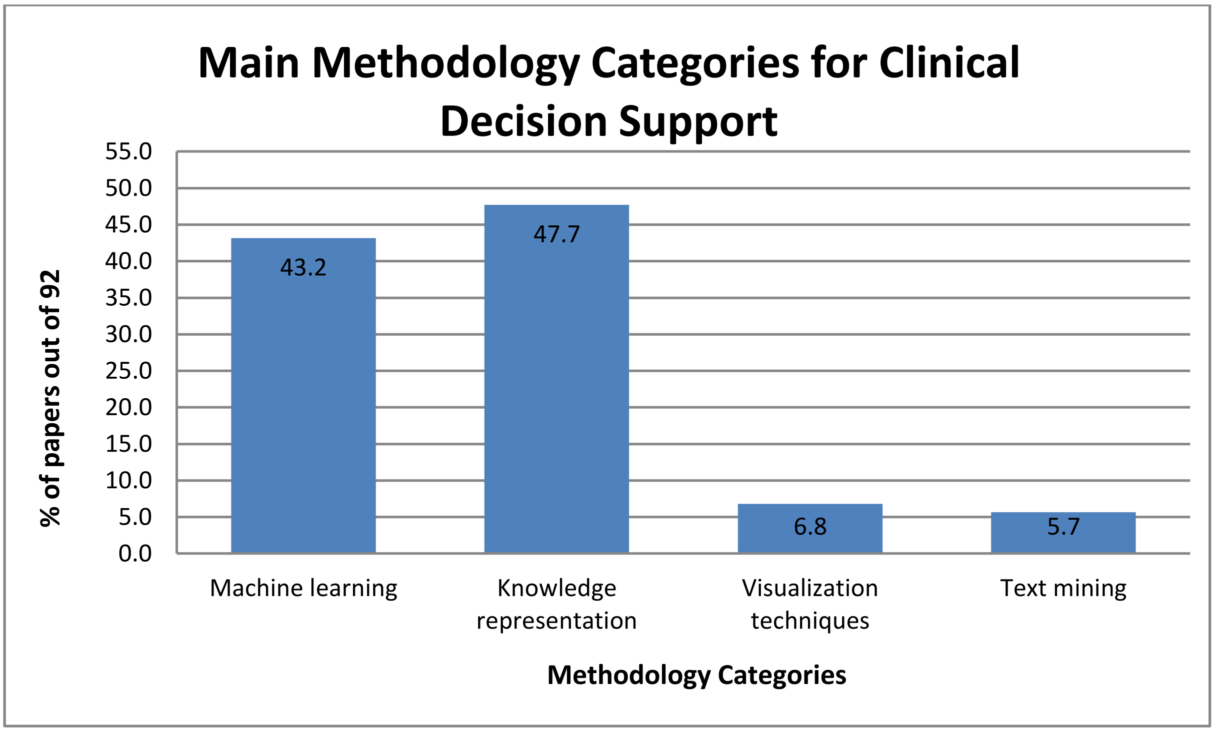

Figure 1: **Main Methodology Categories for Clinical Decision Support Systems identified during literature analysis.**

3.1 Machine Learning

Machine learning is focused on the development of systems which can learn from data[19]. They involve an initial training phase where the system learns how to complete the specific task, (e.g. prediction or classification), on a dataset composed of representative patient data (e.g. symptoms or laboratory results and information about the presence or the absence of the disease). After the training phase, the system can analyse new data composed of the same group of parameters, and attempts to make a prediction (e.g. about the patient state or whether the disease is present or not). It should be noted that there is no "perfect fit" machine learning method. For a given clinical problem, a certain method may achieve very high diagnostic accuracy while for another the same method may fail entirely. However the problem at which one method fails may be solved by other methods quite easily. This should always be considered, when implementing any machine learning-based CDSSs. In the next subsections we outline common machine learning methods used in the development of CDSSs.

3.1.1 Artificial Neural Networks (ANNs)

An ANN is a mathematical model which simulates the learning process of the human brain using a network of interconnected layers of artificial neurons to classify and find patterns in data[20]. As shown in Figure 2, a neural network usually takes some inputs and produces one or more outputs by employing an incremental learning algorithm to compute and modify the strength of the connections between the input, output and hidden layers of the network, where the hidden layers learn the patterns in the data.

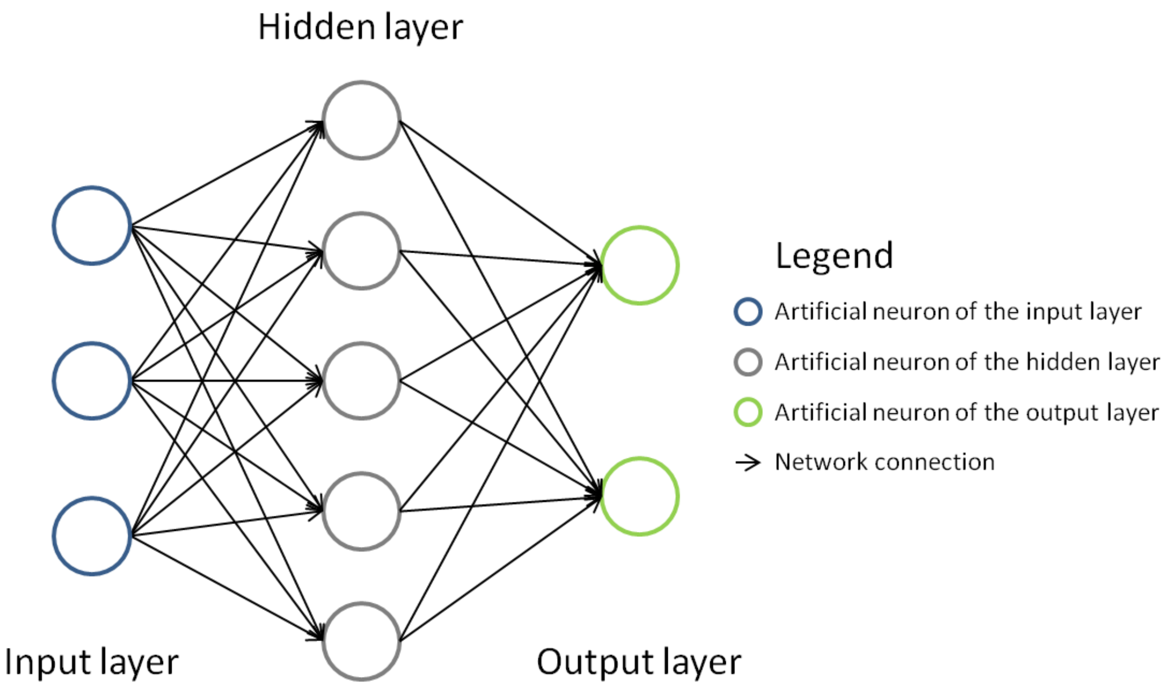

Figure 2: **Artificial Neural Network Example.**

Lin et al.[21] used ANNs to create an inference model to predict outcomes of kidney transplantation. The CDSS analysed relevant input variables for the recipient (e.g. demographics, physics, diabetes, cardiovascular diseases or history of hypertension), the donor (living/cadaveric, demographics and physic) and the transplantation (number of matched HLA antigens; cold storage time; and procedure type). The output of the network was a prediction of the survival time of the graft and recipient.

ANNs have also been widely implemented in diagnostic CDSSs. For example, Amaral et al.[22] carried out a comparison of several machine learning methods for automatically identifying chronic obstructive pulmonary disease using forced oscillation measurements as input parameters. ANNs were one of the techniques with the highest diagnostic accuracy.[22]

Neural networks offer a number of advantages – they quite simple to implement requiring less formal statistical training, they have the ability to implicitly detect complex nonlinear relationships between dependent and independent variables, as well as the ability to detect all possible interactions between predictor variables. Disadvantages include their "black box" nature meaning that how they compute a decision via the hidden layer is not transparent to the end user, and their proneness to overfitting (when the model describes random error or noise instead of the underlying relationship in the data).[23]

3.1.2 Support Vector Machines (SVMs)

Conceptually, SVMs are similar to ANNs; however they are more complex and powerful instruments which are particularly suitable when the classification task is difficult[24]. An SVM model represents examples from the dataset as points in space, so that the examples of the separate categories (e.g. disease present and absent) are divided by a clear gap that is as wide as possible. New examples are mapped into that same space and predicted to belong to a category based on which side of the gap they fall on.

Figure 3 shows two different examples of a classification task (black and white points belong to different categories). 3(a) represents a simple classification task where a linear classifier (e.g. ANN) can work well. 3(b) shows a complex classification task where a linear classifier cannot correctly classify all instances and thus a non-linear classifier is needed. 3(c) shows how a SVM can project the instances of 3(b) using the so-called “kernel trick” to non-linearly map the input data to a high-dimensional space where the classification task become easier.

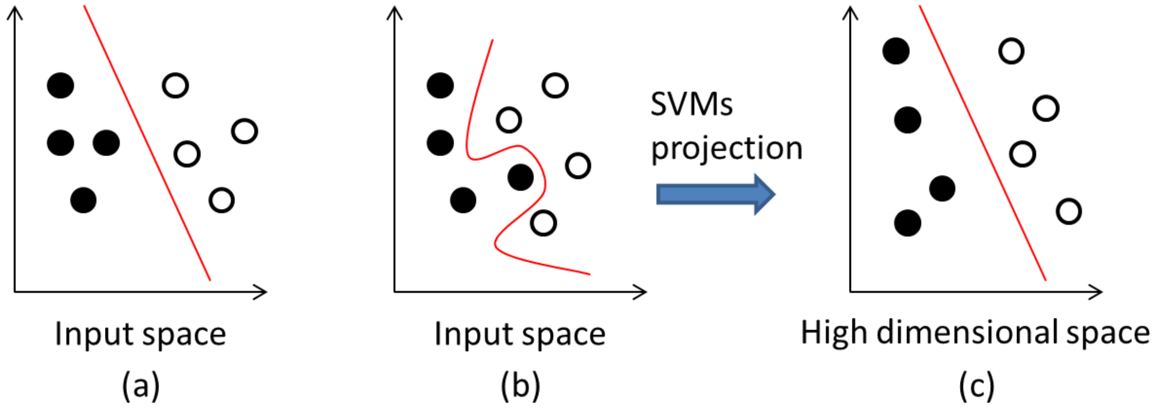

Figure 3**: Linear (e.g. ANN) vs non-linear (e.g. SVM) classifiers.**

Chi et al.[25] used a SVM to create a CDSS that computed hospital selection decisions. The system assessed the probability that a hospital could maximize a treatment's effectiveness for an individual patient. A physician recommended a treatment for a patient and the CDSS combined this with the patient's health conditions and other variables (e.g. distance of a hospital, available facilities and specializations, admission type, patient's age and sex, and their beliefs about the trade-offs among desired hospital features), to evaluate the hospitals with the biggest probability of treatment effectiveness for that patient.

Cho et al.[26] used a SVM to predict the onset of diabetic nephropathy. Using a dataset of 184 features, an SVM classifier was trained to predict the onset of diabetic nephropathy about 2-3 months before the actual diagnosis with high prediction performance from an irregular and unbalanced dataset which statistical methods such as logistic regression could not achieve.

3.1.3 Logistic regression

Logistic regression[27] aims to determine the influence of several independent variables in predicting the outcome of a categorical dependent variable (a dependent variable that can take on a limited number of values). It is particularly useful for identifying the most discriminative variables in a dataset when there are many variables to consider and the output variables can have only predefined values (e.g. positive or negative; or disease X, Y or Z). Logistic regression techniques can be used to develop CDSSs for identifying the most pertinent variables for a clinical condition and are often used in combination with other machine learning techniques. Logistic regression models tend to be less robust than more sophisticated models such as ANNs or SVMs particularly when using complex datasets, but as they use simpler linear models to compute decisions it is easier to interpret the outputs and how a decision is computed.

Logistic regression was adopted by Ji et al.[28] to develop a predictive CDSS for traumatic injury. Trauma experts must consider many aspects in a short period of time. In the first phase logistic regression was used to simplify the training dataset by identifying the most predictive variables (e.g. age, Abbreviated Injury Scale head and thorax, presence of Coagulopathy), while in the second phase the "simplified" dataset was used to train a predictive CDSS using other machine learning techniques.

3.2 Knowledge Representation

Knowledge representation and reasoning is focused on representing knowledge and facts from a clinical domain in order to create a knowledge description language (vocabulary) that is comprehensible and exploitable by computer systems[29]. The vocabulary which can be combined with an automatic reasoning system and therefore can make inferences. For example patient data (vocabulary) can be automatically reasoned over (e.g. using computerized rules from a clinical practice guideline) to make an inference about the patient health state and/or optimal treatment(s).

3.2.1 Ontology-based Systems

In Computer Science, an Ontology is the formal representation of the knowledge within a domain in a format which is comprehensible to and thus executable by computer systems. An Ontology describes a set of concepts (e.g. patients, diseases, therapies) and the relationships between these concepts. Once knowledge is represented in such a format, computer systems can analyse these concepts and their relationships.

Riano et al.[30] developed an ontology-based CDSS for chronic illness. In the first phase the authors formally translated the main concepts and relationships from chronic care into an ontology. An initial set of rules selected the contents of the ontology relevant for a patient with a given chronic illness. A second process used this sub-ontology to automatically transform intervention plans describing general treatments into an intervention plan for the specific patient. For co-morbid patients, this process concluded with the semi-automatic integration of several individual plans into a single personalized plan.

Another example of an ontology-based CDSS was provided by Farion et al.[31]. Different ontologies were used to represent essential components of a CDSS - patient data, machine learning models for solving clinical decision problems and models of computing platforms (desktop and mobile) upon which to execute CDSS's algorithms and to present recommendations. Relevant components from the ontology were combined when the system was invoked by the physician to compute a recommendation for a specific patient using the appropriate machine learning model and computing device being used by the physician.

3.2.2 Guideline-based

Knowledge representation and reasoning methods are particularly suitable for developing automated Clinical Practice Guidelines (CPGs). The representation of concepts, relations and decisions from CPGs allows for their translation into a computable format which improves the CDSS's ability to guide and support clinicians in their decisions. Following this approach it is possible to develop systems which, starting from patient data, can suggest the next step of a treatment, or alert the clinician about drug-drug interactions or incorrect medical decisions.

Choi et al.[32] developed a guideline-based CDSS to support nurses in screening and managing depression. The main concepts in depression screening and management were translated into a computable format which allowed for the development of computable CPGs that could be executed on patient data.

A guideline-based approach was followed by Martinez-Garcia et al.[33] to improve management of patients affected by multiple pathologies by providing relevant information from clinical practice guidelines using a web-platform which allowed all healthcare professionals involved in the care of a multimorbid patient to communicate and discuss treatments and strategies. The system directly integrated with the Electronic Health Record accessed patients information to perform safety checks according to clinical practice guidelines.

3.2.3 Fuzzy Logic

Fuzzy Logic is a probabilistic method that tries to emulate human reasoning in real world applications where reasoning is approximate (for example due to imprecise or missing information) rather than fixed[34]. The primary difference from binary logic methods (e.g. ANNs or SVM in machine learning) where output variables have “true” or “false” values is that fuzzy variables can have different “degrees of truth”, with a weight which indicates the strength of the connection. Fuzzy Logic is particularly suitable for analysis of digital images to find particular shapes or abnormalities and to identify clusters of related data in clinical datasets.

Esposito et al[35] used Fuzzy Logic to assess the health status of people affected by Multiple Sclerosis. The system analysed magnetic resonance brain images with clinically definite Multiple Sclerosis to identify normal brain tissues or clusters of potentially abnormal white matter lesions with different shapes. The authors identified several characteristics of the images with different possible values (e.g. volume: small, medium, large; tissue contrast: little, great) and developed IF-THEN rules to assess the normality/abnormality of brain tissues (figure 4).

***1) IF** [Sphericity is (Moderate **OR** High)] **AND** [Compactness is Strong]**AND** [Volume is Small] **AND** [TissueContrast is Great] **AND** [SurroundingWhiteMatter is Completely] **THEN** [TissueStructure is Abnormal]*

***2) IF** [Sphericity is Moderate] **AND** [Compactness is Strong]**AND** [Volume is Medium] **AND** [TissueContrast is Great] **AND** [SurroundingWhiteMatter is (AlmostCompletely **OR**Completely)] **THEN** [TissueStructure is Abnormal]*

***3) IF** [Compactness is Strong]**AND** [Volume is Large] **AND** [TissueContrast is Great] **AND** [SurroundingWhiteMatter is (Partially **OR** AlmostCompletely **OR** Completely)] **THEN** [TissueStructure is Abnormal]*

***4) ELSE** [TissueStructure is Normal]*

Figure 4[36]:**Rules to identify lesions.**

Fuzzy logic can be also used for depicting human perception of a given system. Mago et al.[36] adopted a particular type of Fuzzy Logic (Fuzzy Cognitive Mapping) to support meningitis diagnosis. Domain experts represented knowledge from the meningitis domain using a graphical model composed of nodes (variables, states, inputs, outputs) and fuzzy relationships between concepts. The graphical model was used to analyse patient data and indicate the presence/absence of the disease using different degree of truth.

3.3 Information Visualization (IV)

IV is a set of technologies that use visual computing to deal with abstract information[37]. Applications of IV allow for the analysis of data via exploration and interaction so users can develop an understanding of complex systems or datasets by observing the consequences of their interaction with the visualization.

Mane et al[38] developed a visual system to evaluate the effectiveness and risks of different therapeutic options in psychiatry using data from patients with similar conditions in an EHR. Figure 5 shows an overview of the system: label 1 shows demographics for the current patient while label 2 and 3 highlight treatments and comorbidities for the selected patient as well as for other patients from the EHR computed as being clinically similar to the current patient. Through the utilization of this information physicians could have a clear understanding of the possible therapeutic options and their outcome in previous comparable situations.

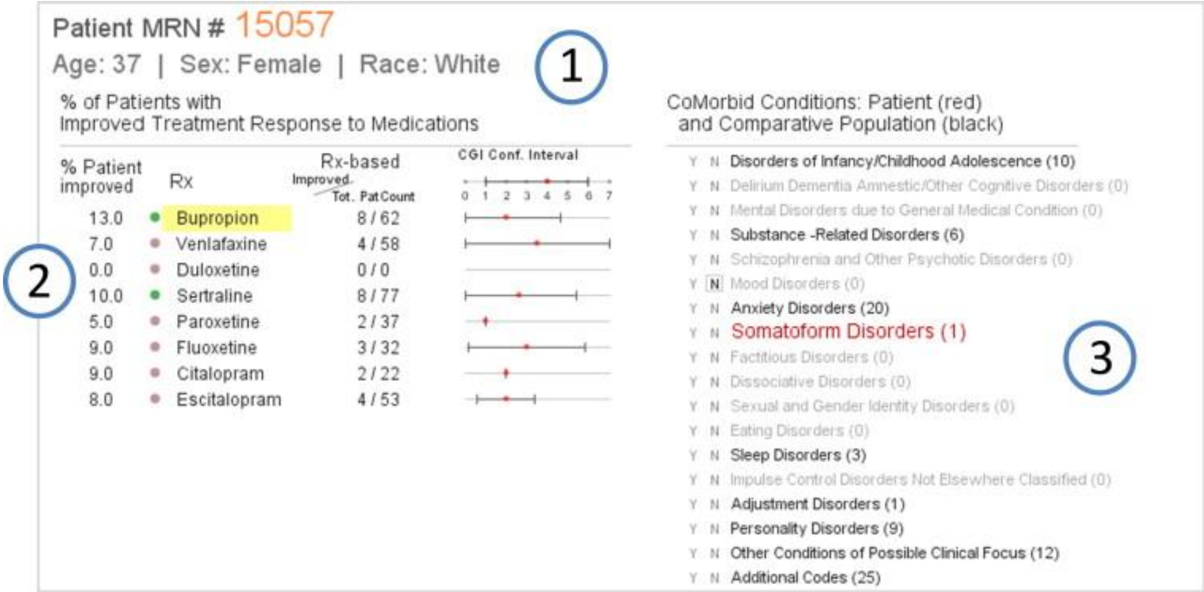

Figure 5[38]:**Label 1**: **data view for patient demographics. Label 2: summarized medication response of patients' in the Electronic Health Record. Label 3: Comorbidities.**

3.4 Text mining

Text mining adopts statistical, machine learning and linguistic techniques to extract high quality information from unstructured text (e.g. medical Internet repositories)[39] . Systems to retrieve and analyse textual information are needed to effectively exploit the increasing amounts of digital medical textual data which may be used to support clinicians during the decision making process.

3.4.1 Information retrieval (IR)

IR is a process through which relevant information (e.g. a document) is obtained and delivered to the user according to their specific information need[40]. In IR, documents are represented as an unordered collection of words, disregarding grammar and even word order. IR requires a preliminary indexing phase in which words within text resources are processed and represented. Subsequently search algorithms can retrieve information from the pre-processed resources using statistical methods (e.g. the frequency of words within documents).

O'Sullivan et al.[41] developed a system to support physicians in retrieving case-specific information directly at point of care in the paediatric asthma domain. Firstly, they applied index terms to systematic reviews from The Cochrane Library[42] where these index terms emphasized patient rather than population-oriented terms. These documents were subsequently retrieved and ordered by a search algorithm which presented relevant reviews to physicians during encounters.

3.4.2 Natural language processing (NLP)

NLP goes beyond IR by aiming to derive meaning from human or natural language input[43] rather than simply representing documents as a collection of words. NLP techniques can be used to automatically extract, summarize or categorize textual information and is especially relevant in a field as medicine where there are large numbers of free text documents (e.g. reports, letters, and clinical notes).

Matheny et al.[44] adopted NLP to identify symptoms of infections from clinical narratives in order to perform automated surveillance of possible unidentified infections. The authors created detection rules which were based on concepts and relationships in the main biomedical ontologies (e.g. Systemized Nomenclature of Medicine Clinical Terms®[45]) and then processed the text through such rules to identify symptoms for tuberculosis, acute hepatitis, and influenza by which they could infer previously unidentified infections.

3.5 Multi-purpose

Multi-purpose methodologies combine attributes and characteristics from the previous main categories and as such can be used for multiple purposes in CDSSs.

3.5.1 Decision trees (DTs)

DTs can be used in Machine Learning as well as in Knowledge Representation and Reasoning systems[46].

In Machine Learning, DTs are used for prediction or classification. Starting with a training dataset, DTs construct a model which is composed of many nodes, called “leaves” of the DT, where the input variables are analysed and according to their values, the decisional process flows through the different branches of the DT to carry out the assigned prediction or classification task. They are useful in medicine as they produce human-readable rules of classification. However they lose robustness when the number of input variables becomes large and are sometimes converted to Random Forests (RFs) which combine the results of several independently trained DTs.

In Knowledge Representation, a DT can be used to produce a graph which represents possible decisions and associated potential consequences. They are mainly utilized to develop action plans to achieve a specific objective (e.g. they are often used to represent Clinical Practice Guidelines).

Ji et al.[28] utilized a combination of DTs to support decision-making for traumatic injuries. The authors achieved good prediction results, using the most important patient variables (e.g. age, Emergency Department Revised Trauma Score and Injury Severity Score) as input variables, obtained by applying the Logistic Regression (section 4.1.3). Furthermore, they explained that the use of DTs allowed for the creation of transparent decision rules which were comprehensible by physicians who could follow the reasoning through the nodes of the DTs.

DTs were used for knowledge representation and reasoning by Bergman et al.[47] who compared a widely used paper and pencil diagnostic instrument, based on the “Diagnostic and Statistical Manual of Mental Disorders 4th Edition” (DSM-IV)[48], to a computerized system based on a DT. The system guided the users through the various branches of the DT based on "yes", "no" or "unclear" answers about each criterion. Finally, if the number of fulfilled criteria reached a certain level (according to DSM-IV) the program automatically suggested the corresponding DSM-IV diagnosis. The comparison showed that there were no significant differences between the paper and pencil method and the computerized one.

3.5.2 Bayesian Logic

Bayesian logic is an inference method based on Bayes’ law which is a statistical theorem with the ability of updating the estimated probability of an event with knowledge of new evidence[49]. Bayesian networks are probabilistic graphical models which consider a set of random variables and their conditional dependencies. For example, Bayesian networks could represent the probabilistic dependences between symptoms and diseases and given a list of symptoms they could calculate the probability of presence of the various diseases. From a machine learning perspective Bayesian networks are useful “white box” classifiers meaning that all parameters have a clear interpretation and the certainty associated to probabilistic predictions is intuitively understandable. However it is often difficult to get experts (clinicians) to agree on the structure of the model and the nodes that are important to be included as well as to express their knowledge in the form of probability distributions.

Elkin et al.[50] introduced a system called DX plain into the workflow of a teaching hospital where the system supported residents with regard to diagnostically challenging diseases. Starting with patients' symptoms, Bayesian logic was applied to provide residents with a set of differential diagnoses and their probabilities.

Bayesian Networks were used by Sadeghi et al.[51] to develop a CDSS to support nurses during the triage process at the emergency department. Firstly, several subdomains (e.g. abdominal pain) were accurately described and, relevant information and symptoms of diseases were identified. Secondly, the authors adopted the Bayesian Network approach to develop a graphical model which represented all possible interactions and links among previous data and provided a list of possible diagnosis starting from the results of a triage questionnaire.

4 Discussion and Conclusions

Decision Support Systems have been widely implemented and adopted in commercial fields[52]; however their acceptance within the medical domain remains limited[53,54, 55,56]. This review aimed to provide clinicians and policy makers with a better understanding of the methodologies CDSSs employ as the development and deployment of systems that can meaningful support clinicians in practice requires their collaboration.[18] For example, during CDSSs' design stage clinicians and policy makers are required to identify the real clinical needs a CDSS should satisfy; in the implementation phase clinicians could provide guidance on which of the methodologies described above would be best suited to a clinical problem, dataset or domain, in the validation phase informed participation of clinicians could sensibly improve the understanding of CDSSs' effectiveness from a clinical perspective and finally top level support from policy makers is required in the deployment stage to ensure adoption and acceptance of CDSSs as part of routine clinical practice. As described by Greenes[57]; the implementation of CDSSs decision support is a balancing act between clinical need and organizational management. The engagement of clinicians and policy makers in the development of CDSSs has the potential to change the drivers for widespread deployment of complex CDSSs by forcing vendors of Clinical Information Systems (CIS) to recognise the benefits of such systems and to focus their attention on the decision support needs of clinicians in addition to the operational tasks CIS's currently support.

Acknowledgements

Funding: None

Competing interests: None declared

Ethical approval: Not required

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