A hybrid knowledge-based approach to supporting the medical prescription for general practitioners: Real case in a Hong Kong medical center

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Abstract

Objective

With the increased complexity and uncertainty in drug information, issuing medical prescriptions has become a vexing issue. As many as 240,000 medicines are available on the market, so this paper proposes a novel approach to the issuing of medical prescriptions. The proposed process will provide general practitioners (GPs) with medication advice and suggest a range of medicines for specific medical conditions by taking into consideration the collective pattern as well as the individual preferences of physicians' prescription decisions.

Methods and Material

A hybrid approach is described that uses a combination of case-based reasoning (CBR) and Bayesian reasoning. In the CBR process, all the previous knowledge retrieved via similarity measures is made available for the reference of physicians as to what medicines have been prescribed (to a particular patient) in the past. After obtaining the results from CBR, Bayesian reasoning is then applied to model the prescription experience of all physicians within the organization. By comparing the two sets of results, more refined recommendations on a range of medicines are suggested along with the ranking for each recommendation.

Results

To validate the proposed approach, a Hong Kong medical center was selected as a testing site. Through application of the hybrid approach in the medical center for a period of one month, the results demonstrated that the approach produced satisfactory performance in terms of user satisfaction, ease of use, flexibility and effectiveness. In addition, the proposed approach yields better results and a faster learning rate than

when either CBR or Bayesian reasoning are applied alone.

Conclusion

Even with the help of a decision support system, the current approach to anticipating what drugs are to be prescribed is not flexible enough to cater for individual preferences of GPs, and provides little support for managing complex and dynamic changes in drug information. Therefore, with the increase in the amount of information about drugs, it is extremely difficult for physicians to write a good prescription. By integrating CBR and Bayesian reasoning, the general practitioners' prescription practices can be retrieved and compared with the collective prescription experience as modeled by probabilistic reasoning. As a result, physicians can select the drugs which are supported by informed evidential decisions. That is, they can take into consideration the pattern of decisions made by other physicians in similar cases.

Keywords: Bayesian reasoning; Case-based reasoning; Decision support system; General practitioners; Medical prescription

1. Introduction

Medical prescription is facing the challenge of increased complexity and uncertainty from the very great increase in information on new drugs. Nowadays numerous new drugs are being developed and launched to treat new diseases. With the growing amounts of information, medical prescriptions made by physicians have become a contentious issue. This is particularly true from the general practitioners' (GPs) perspective. The explosive growth of data requires them to learn and remember many details so they can prescribe the right medication, in the right amount, for the right patient. The possible approaches to dealing with this problem are by means of electronic medical records (EMR) [1-5] and clinical decision support systems (CDSS) [6-10]. Through knowledge discovery from these disciplines of medical informatics, the medical prescription process can be facilitated and hence the quality of prescription decisions can be improved [46].

However, decision support for medical prescription provided by the existing medical informatics disciplines lacks flexibility in selecting and delivering relevant drug choices to physicians. The existing medical prescription support system can only assist medical experts in providing a better understanding of the problem in-hand by pooling the diagnostic experience of many physicians [2,11,12]. In this way, these approaches are limited to suggesting drugs based on diagnosis classification. The advice is far too vague to meet the real needs of therapeutic situations. To improve this situation, capturing specific knowledge from past medical cases can generate substantial and relevant knowledge in support of the prescription process of GPs.

In each diagnostic process, previous knowledge stored in medical records is important to physicians for making prescription decisions [39]. Case-based reasoning (CBR), a well-known problem solving technique that is capable for retrieving the most relevant cases that are most similar to the problems being diagnosed [45], is used to represent the prescription knowledge accumulated from specific situations. It is noted that drug recommendations extracted from the most relevant cases may not be appropriate for the problem at hand, Bayesian reasoning that discovers the general prescription patterns of physicians is thus employed to fine tune the medical prescription options, based on what medication is probably the most suitable, given a certain diagnosis and certain symptoms. These are distinct techniques, each with its own strengths and limitations. To the authors' knowledge, they are also seldom integrated together, particularly in the prescription domain. In other words, a "micro-view" of specific knowledge (modeled by CBR) and a "macro-view" of general knowledge (represented by Bayesian reasoning) are formulated and are leveraged using each other's strengths.

This paper proposes a hybrid knowledge-based approach to support medical prescription (HKSMP), as a complement to the existing statistical approach proposed in [2]. HKSMP incorporates CBR and Bayesian reasoning approaches in helping physicians to perform flexible prescription, in providing medication advice, and anticipating a range of medicine for the physicians. Furthermore, HKSMP is the first model that has attempted to handle the prescription solution by considering both specific knowledge and general knowledge. A case study in a Hong Kong medical centre is presented to illustrate the implementation of the proposed system and to validate the practicability in a real world application.

The remainder of the paper is organized as follows. Section 2 briefly reviews the relevant literature on common practices for medical prescription, and the application of CBR and Bayesian reasoning in the domain of interest. Section 3 illustrates the hybrid knowledge-based approach. A case study in applying this approach is elaborated in Section 4. Results are presented and discussed in Section 5. Finally, Section 6 concludes with a discussion and proposals for future research directions.

2. Research Background

2.1 Electronic medical record systems and decision support systems in medical prescription

A medical prescription is a medication order form written by a qualified medical professional [3]. It serves as a medium of communication between the physician and the pharmacist/nurses to ensure that the right medication is delivered to the patient. Fig. 1 depicts the medical prescription practices among physicians, nurses, pharmacists and patients. However, with voluminous drug information (i.e. more than 240,000 prescription drugs on the market) [34], it is not easy for medical experts to be knowledgeable and familiar with the use of different drugs and with dosage instructions. Even with the same diagnosis, the medical prescription may differ from one patient to another as the patient's age and physical condition must also be taken into consideration in the prescription. This is especially the case for GPs as they are primarily responsible for providing comprehensive health care to individuals seeking medical care, and for making arrangements for other health care personnel to provide specialist services when necessary [13]. Thus, learning about new drug information, and remembering the appropriateness and possible contradictions of a large number of drugs remain open challenges for GPs [14,15].

Many researchers have suggested that applying technology in medical practices can help GPs to stay informed about the latest development of drugs and thus can help to reduce medical errors and improve patient safety. To support the decision making process of the medical experts, Electronic Medical Records (EMR) have been introduced to transform the traditional handwritten medical records into digital ones. Rector et al. [4] present a model for an electronic medical record system which provides a permanent, complete record of patient care and the medical decisions made. Kohane et al. [5] applied client-server technology of the World Wide Web to design national electronic medical record systems (EMRSs). Hammond et al.'s study [16] has demonstrated that using EMR not only can improve the quality of patient care and decrease medical errors, but also can result in a positive financial return on investment. With such a sound financial achievement of EMR, many researchers are focusing on how to integrate medical records with decision making tasks. Shiffman et al. [17] and Linnarsson [18] claimed that integration of EMR with a decision support system (DSS) can enhance effectiveness in ensuring patient safety. The benefits of current DSSs used in general practice include assisting doctors in performing diagnosis, disease prevention, enhancing decision making quality in the primary care consultation and in selecting appropriate dosage [19]. All these are in line with Wang et al.'s results of a 5-year study [20].

DSS always have long been used by different industries to solve different problems that range from prediction, forecasting and data classification. For example, Panda et al. [40] and Chang and Liao [41] applied soft computing techniques to predict flank wear in drills and flow time in semiconductor manufacturing factories, respectively. The application of DSS in the medical domain has been mostly developed to provide physicians with advice on either diagnosis or treatment by means of artificial intelligence (AI) and Bayesian reasoning [21]. Because of the complexity of drug information, DSS demonstrates great potential in the area of medical prescription, however, only a few publications have addressed this issue. One of the publications, proposed by Warren et al. [11], describes how drug choices can be reduced after specifying the diagnosis; but it lacks consideration of physicians' prescription patterns and the patients' clinical background information. In this case, it can satisfy the 'five rights' (i.e. the right drug, the right dose, the right time, the right route and the right patient) of medication administration [35], which is a crucial standard of health care. Therefore, a more comprehensive medical prescription support approach is required to ensure the right medication of the right amount are administered to the right patient.

2.2 Knowledge discovery in medical prescription by Bayesian reasoning

Knowledge discovery is another popular research topic in medical informatics. It is a process that uses data mining algorithms to extract and identify what can be considered as knowledge from a large volume of data [22,23]. With the aid of computerization of medical records, all the individual diagnosis transactions are collected and stored, thus forming a data warehouse that stores the collective behaviors of the medical practices within the organization. Lian et al. [12] has pointed out that the prescription is specified by a preference function based on the user's preference in prior clinical experience. Thus, they propose a dose optimization framework based on probability theory. Susan and Warren [2] demonstrated that the conditional probability model is superior in optimizing the drug lists to the multiple linear regression and discriminant analysis models. The strong relationship between diagnosis and medication allows one to determine a posterior probability (what medication is needed) based on a priori probability (what diagnosis has been made) [11].

Conditional probability is a popular statistical modeling technique in Bayesian reasoning that studies the probability that one event happens given that some other event has happened. In the medical domain, conditional probability is particularly useful in prescription decision support, because it can quickly determine the probability of a certain drug being required if a certain diagnosis has been made. Spenceley et al. [24] argued that their model, based on the conditional probability, can reduce prescription choices by more than a half when compared with the conventional model. Nevertheless, it relies heavily on diagnosis classification, and there could be some problems such as the failure to take physician’s prescription pattern and patient’s details (such as allergy to specific medicine) into consideration.

2.3 Case-based reasoning in medical prescription

In recent years, the concept of knowledge-based systems has gained acceptance in both medical diagnosis and medical prescription. An important task in a knowledge-based system is to support human decision making, learning and action by extending and querying the knowledge base. In the area of medical informatics, a knowledge base is typically useful in supporting the decision making involved in medical prescription [19]. Over the past two decades, numerous knowledge-based techniques have been successfully applied to prescription [7,27]. However, Schmidt et al. [29] argued that CBR is the one technique which is particularly suitable for medical knowledge based systems.

CBR is a plausible generic model of an intelligent and cognitive science-based method as it gives users much more information for situation assessment [30]. With its cognitive model, CBR can describe past experience and hence retrieve similar cases or solutions. In other words, it is an intelligent problem-solving model that relies on the reuse of past practices to tackle new problems. To achieve accurate results, CBR needs to undergo a revision process by modifying the cases and has to store revised cases in the database for solving future problems. The benefits of applying CBR applications to medical prescription include responsiveness to changes, being easy to set up, having the ability to capture domain knowledge, flexibility (i.e. supporting dynamic behavior), and providing intelligent decision support. Recently, CBR has attracted considerable research interest to support the selection and recommendation of treatment. Zhuang et al. [36] combined data mining and CBR methodologies to provide GPs with intelligent decision support for pathology tests ordering. They guarantee that the integrated system can enhance the testing ordering in terms of its evidence base, situational relevance, flexibility and interactivity. Huang et al. [37] proposed a model of a chronic diseases prognosis and diagnosis (CDPD) system by integrating data mining and CBR to support the treatment of chronic diseases. Khan and Hoffmann [38] presented an approach that allows GPs to automatically construct a menu which is strongly tailored to the individual requirements and food preferences of a client. Concerning medical prescription practices, Marling and Whitehouse [31] developed AUGUSTE to support treatment planning in Alzheimer's disease by using CBR to determine if a neuroleptic drug should be prescribed and then to select the approved drugs for a patient via a rule-based mechanism. Hartge et al. [32] proposed a similarity measurement algorithm for a CBR system to support drug-related events in minimizing inappropriate selection of drugs and inappropriate drug-drug interaction. In these applications, CBR provides a potential extension to support the medical prescription process.

With sound results in applying CBR for problem-solving in the medical domain, several researchers argued that the chance of reusing a case from CBR is not high in some areas, such as insurance claims prediction [42] and multiple medical disorder cases [43]. Such a statement is also true in the domain of prescription support. Since the solution of a prescription case typically involves multiple medicines, not all the medicines are effective in addressing the problem in a new case. Thus, further modification of CBR is required to improve the accuracy of selecting the appropriate set of medicines in prescription support. However, very few research studies and empirical investigations have been done for prescription related topics. Therefore, the HKSMP method proposed in this paper focuses on improving the solution extracted in CBR and providing relevant and objective evidence in prescription decision support. Furthermore, CBR and Bayesian reasoning are often applied separately. The HKSMP approach proposed is based on a parallel flow of CBR and Bayesian reasoning. The work differs from the above studies in that it combines the results of CBR and Bayesian reasoning by adopting rule sets. In contrast to the traditional methodologies which provide simplistic suggestions at a specific point in time, the proposed methodology is capable of providing suggestions (i.e. medicines to be prescribed) at any stage after clinical judgments have been made by physicians. The HKSMP proposes a novel measure that adopts an "ensemble learning method" [44] in combining the solutions of CBR and Bayesian reasoning by means of a rule base rather than choosing among them, thus getting solutions that outperforms those obtained from any single one of the models, so as to assist the physicians in identifying a medication list that is suitable for the patient.

3. Hybrid Knowledge-based Approach to Supporting Medical Prescription (HKSMP)

Given a set of historical medical prescription records stored in a knowledge base, the objective of HKSMP is to suggest a range of medicines from which physicians can choose. In general, Fig. 2 depicts the logical view of HKSMP. The approach starts when the physicians input the symptoms and diagnosis of the patient, and ends with the solution (i.e. suggested medicines) generation. All details in the approach are discussed in the next section.

3.1 Concept of 'Micro-view' and 'Macro-view'

In each diagnostic process, the physician may reuse previous solutions in relevant situations to address the new problem. Therefore, we apply the CBR approach proposed by [36] to specifically retrieve previously experienced cases with information on concrete problem situations and their solutions. As each retrieved case represents a particular patient's medical history on the basis of a physician's specific knowledge of the prescription practices, the solution obtained in the CBR process relates a specific patient to the physician (i.e. patient-centric). When a patient has consulted several physicians in the past, more knowledge in diagnostic and prescription decisions related to that particular patient will have been acquired. The associated network, that formulates a patient-physicians relationship, represents a 'micro-view' in the medical data (Fig. 3a).

On the other hand, when applying Bayesian reasoning, the prescription patterns of the diagnostic experiences within the organization can be captured and characterized through a probabilistic measure. Such statistical approximation expresses the knowledge that is accumulated from all the physicians, thus the solution obtained in Bayesian reasoning depicts a peer-based relationship among the physicians. The associated network, at this time, centers on the characteristics of the whole organization. The physician-physicians (within the organization) relationship, thereby forms a 'macro-view' in the medical data (Fig. 3b).

3.2 Algorithm of the Hybrid Model

As shown in Fig. 2 and Fig. 4, the universal set of drugs captured from the EMR will first pass to the HKSMP to serve as the drug bank for the preparation of the recommended medical prescription list for the GPs. Results of diagnoses made by a physician are entered into both the CBR and Bayesian reasoning processes within the model for extraction and discovery of the pattern of the drugs prescribed. The two drug sets generated from the model (i.e. one from CBR and another one from Bayesian reasoning) are combined via a set of 'IF-THEN' statements (i.e. rule-based results aggregator) to obtain the solutions. If a drug appears in the results of CBR as well as Bayesian reasoning, it is classified as a recommended drug to fit the new situation. In this regard, the results from CBR and those from Bayesian reasoning supplement each other to provide an intelligent way of optimizing the drug choices. Furthermore, HKSMP can explain whether the past prescription was effective or not.

3.2.1 Retrieving the micro-view of prescription behavior

The provision of the micro-view of prescription behavior is the main concern of the recommended prescription solution. Different GPs may have their own prescription practices and style (in the use of drugs), therefore CBR will help GPs to make informed drug choices with references to the old cases stored in the knowledge base. The proposed approach first retrieves a set of similar cases from the case base through the nearest-neighbor retrieval (NNR) technique, and hence evaluates the similarity between each case in the database. In HKSMP, a case contains the medical information of the patient such as the patient's demography, treatment and administrative data (including age, sex, treatment date, symptoms, diagnosis, payment, number and duration of sick leaves). We then use the numerical function of NNR to compute the similarity between stored cases and newly input cases using weights assigned to applicable features. As suggested by Kolodner [30], these weights are assigned by human experts, as these experts are expected to be knowledgeable and experienced in determining which dimensions make good predictors. In measuring the degree of similarity between cases, weighted Euclidean distance measurement is used. The degree of similarity between cases is formulated by Eq. (1).

$$similarity(Case^I, Case^R) = DIS_{f_i^I f_i^R} = [\sum_{i=1}^{n} w_i^{\,2} \times (f_{ik}^I - f_{jk}^R)^2]^{\frac{1}{2}} \quad (1)$$

where w_i = importance weighting of the i th feature

$similarity()$ = similarity function of features

f_i^I, f_i^R = values for feature i in the input and retrieved cases, respectively

The drug list which is presented shows the past cases which have the highest degree of similarity to the present case. The solution of CBR can be represented as follows:

$$CBRsolution = \{cbrdrug_i, cbrdrug_{ii}, cbrdrug_{iii}, ..., cbrdrug_n\} \quad (2)$$

where $cbrdrug_i$ to $cbrdrug_n$ are the medicines prescribed in the retrieved case

Before producing the solution to the user, the retrieved cases will be adjusted by the result from Bayesian reasoning in order to identify what drugs have been prescribed in similar situations by other medical experts, without losing the general prescription practices.

3.2.2 Retrieving a macro-view of prescription behavior

The objective of forming a macro-view is to model the existing knowledge of prescription behavior as peer-based evidence to facilitate prescription support and complement the results of the micro-view. To determine the macro-view of the prescription behavior, Bayesian reasoning is used to build a model of the conditional probability of drugs being prescribed, given the diagnosis selected [2].

In order to guarantee that the previous mistakes in the prescription of drugs are not repeated, a set of rules showing the relationship between diagnosis and drug properties are evaluated and approved by the physicians for ensuring the quality of the modeling. An example of the rules is for Mylanta that is used to treat acid indigestion, heartburn, and sour stomach. These rules are stored in the database and can be modified if necessary (for example, if a new side-effect of a particular drug is discovered). The pre-defined rules therefore filter the drug choices according to the diagnoses chosen by the physicians at each patient visit. The remaining appropriate drug will then be determined by the conditional probability of the drugs required. This is based on the co-occurrence of specific drugs with the selected diagnosis. Generally, a conditional probability in Bayesian reasoning demonstrated in Eq. (3), in which $P(drug_i \mid diagnosis)$ is a posterior probability of $drug_i$.

$$P(drug_i \mid diagnosis) = \frac{P(diagnosis \mid drug_i)P(drug_i)}{\sum_{j=1}^{n} P(drug_j)P(diagnosis \mid drug_j)} \tag{3}$$

For the situation where one patient has multiple diagnoses, we will first look up the data warehouse to find the exact cases that persisted previously. If a matching result can be found, it will follow the conditional probability defined in Eq. (3) to compute the ranking. However, if there is no matching result, we will apply an approximation mechanism from the fuzzy set theory illustrated in Eq. (4). All the candidates are ranked by the $\max$ operator. For example, if the patient has the diagnosis of "upper respiratory tract infection (URTI), gastroenteritis, and dermatitis", drugs are ordered according to the highest probability of occurrence among the three diagnoses.

$$\begin{aligned} &P((drug_i \mid diagnosis_1)\,\&\,(drug_i \mid diagnosis_2)\,\&\ldots\&\,(drug_i \mid diagnosis_n)) \\ &\equiv \max(P(drug_i \mid diagnosis_1), P(drug_i \mid diagnosis_2), \ldots, P(drug_i \mid diagnosis_n)) \end{aligned} \tag{4}$$

Thus, the solution of Bayesian reasoning can be represented as follows:

$$Bayesiansolution = \{baydrug_i, baydrug_{ii}, baydrug_{iii}, \ldots, baydrug_n\} \tag{5}$$

where $baydrug_i$ to $baydrug_n$ are the medicines prescribed in descending order, based on the probability result

3.2.3 Rule-based results aggregator

The objective of the rule-based results aggregator is to match the results between CBR and Bayesian reasoning. In the matching algorithm, the ranking of drugs is represented in the form of three different 'IF-THEN' statements as shown in Fig. 5.

The first statement classifies the drugs which appear in both CBR and Bayesian reasoning, into Rank A, which is the top ranking recommended list, for the physician's consideration. However, if the drugs do not match any instances (neither in CBR nor in Bayesian reasoning), they will be classified as Rank C. For the remaining prescribed instances (the drugs appear either in CBR or Bayesian reasoning), they will be grouped into Rank B. Since CBR considered more features related to the case, it is perceived that the result of CBR is more relevant to the new situation. Thus, the drugs recommended from CBR will be placed higher on the list in Rank B, whereas the drugs from Bayesian reasoning will be placed lower down on the list in Rank B. An example of such illustration can be found in Fig. 6. Furthermore, the prescribing pattern of the physician can even be visualized and compared with the pool of prescriptions of many physicians. The physician can learn from this comparison. The entire rule-based results aggregator is repeated until all the drugs are categorized into corresponding areas. Thus, the final solution in the combined medication list is represented as follow:

$$Finalsolution = \begin{cases} drug_{RankA} & if \quad (drug_{RankA} \in cbrsolution) \text{ and } (drug_{RankA} \in bayesiansolution) \\ drug_{RankB} & if \quad \text{otherwise} \\ drug_{RankC} & if \quad (drug_{RankA} \notin cbrsolution) \text{ and } (drug_{RankA} \notin bayesiansolution) \end{cases} \tag{6}$$

In HKSMP, the appropriate drug choice is optimized concurrently with the matching algorithm and illustrated as a ranking list to promote the flexibility and possibility of considering both individual behavior and collective behavior. Because of the complex nature of prescribing, the recommended medicine selection list serves only as a reference for physicians which they can use for quick identification of the relevant medicines from past experience. The physician can deviate from the recommendations at any time as they have complete autonomy; thus the final decision still rests with the individual physician.

3.2.4 Retaining the solution in the knowledge base

Once the physician selects the medicines to be prescribed, HKSMP has achieved its goals. The new problem situation and its corresponding solution are then be stored in the database automatically. Such a retaining process is considered as the actual learning process for facilitating the GPs future decision making on drug prescription.

4. Case Study

In order to demonstrate the hybrid approach described above, an EMR with an intelligent prescription system was designed on the basis of the HKSMP and then applied in a Hong Kong medical centre named Humphrey & Partners Medical Services Limited (HPMS). It was found during the study that by using the intelligent prescription system, the medical prescription process was more effective and more accurate than the method used previously (see Section 5). The case study is described below.

4.1 Case study background

HPMS is one of the largest multi-disciplinary medical services providers in Hong Kong. It was founded by a team of dedicated medical practitioners, and consists of 4 core clinics located in different parts of the city and about twenty medical experts working on a rotational basis to provide various, high quality medical services to its patients. The general practice in a treatment consists of several steps, including patient registration, GP diagnosing, medical prescription and delivery of drugs. At HPMS, GPs find the current medical information system is not user friendly as they find it difficult to identify and choose the drugs (from two hundred drugs available in the clinic) required for the treatment; which makes the prescription process more complicated. Thus, EMR in intelligent medical prescription support system can support GPs to easily and quickly retrieve the patient information for the whole treatment process. The hybrid model can thus help the GPs to look up and select the required drugs efficiently by ranking the drugs based on diagnosis and on the doctor's individual method of prescription.

4.2 An illustrated example – from EMR to intelligent medical prescription support

The hybrid approach has been tested in HPMS to validate the feasibility of this solution in an actual operational environment. Totally, seven phases are involved in building the EMR and HKSMP (Fig. 7). An EMR system with a knowledge-based medical prescription support approach is first introduced to the GPs in two different HPMS clinics within the period 1st March 2009 to 31st March 2009.

4.2.1 Phase 1: Diagnosis by medical expert

The system interface for the GPs to make treatment is shown in Fig. 8. After registering in EMR, the patient information, including patient name, sex, age, allergies, past medical history, are transferred to the GP's computer. In order to obtain a better result in the hybrid approach, the symptoms and diagnosis are pre-defined in the system, in which GPs just simply select and check the box under the symptoms/diagnosis column. On the other hand, for those symptoms and diagnosis that have not been encountered before, an input area is designed for GPs to type in specific information.

4.2.2 Phase 2: Pre-processing of cases

This phase focuses on turning the data warehouse into a data mart for easy access to frequently needed data. Before retrieving the cases to find similar solutions, a pre-processing method is used to index and extract the specific information from the data warehouse. Some irrelevant data is removed in the knowledge base. For example, "referral" does not have any effect on the decisions made in drug prescription and is thus removed.

4.2.3 Phase 3: Retrieving the solution from cases

After the GP decides the diagnosis and the pre-processing phase, all the relevant information is gathered to perform the CBR process. Table 1 summarizes the attributes for case featuring. It involves the patient information and past treatment details (such as last record, number and duration of sick leaves, payment, diagnosis, symptoms, additional services). Before storing in the case base, all these cases will be validated by the board of directors (BODs) in HPMS who are specialists in various medical disciplines. With their experience, all the stored cases are validated and the collection of these cases covers a wide range of illnesses treated by a large group of physicians. The main purpose of CBR is to retrieve similar cases of patients suffering from the same condition. If the diagnosis and patient information match perfectly with the existing case, the solution of the existing case will be used as the reference to the physician without any change. However, if no exact match is found, Eq. (1) is applied to retrieve and propose the most appropriate medical prescription list. All the weights of the features are given by the BODs in HPMS. On the basis of the data captured from EMR, the BODs discuss the weightings one by one and finally reach a solution. This helps in ranking all the cases in the knowledge base. A typical case in the knowledge base is shown in Fig. 9. It contains the problems (description of the treatments with patient information) and the medical prescription choice with the probability for further matching (See Section 4.2.4).

4.2.4 Phase 4: Computing the probability of drugs being prescribed given the diagnosis

By using Eq. (3) and Eq. (4) to generate the conditional probability, we can rank all the drugs prescribed in descending order of probability based on the input from phase 1. The probability is computed based on the frequency of drug selection captured from the past instances of prescription. Fig. 10 illustrates an example of the probability of drugs prescribed if the diagnosis is URTI and under the 'WP001' clinic.

4.2.5 Phase 5: Matching the two results

It is realized that the experience of GPs is directly proportional to the number of cases they have dealt with. Therefore, this phase aims at combining the results from the two different models by weighting with their experience in order to reduce the bias of the drug choice. Similar to phase 2, the weight is provided by the BODs with reference to the number of visits to the GP, past history and patient revisit rate. The weight is adjustable from low to high (on a scale from 0 to 100%). This is useful when there is a change in performance of a particular GP.

4.2.6 Phase 6: Generating an intelligent medical prescription list

After combining the results from phase 4, the GP can have the recommended medical prescription list regarding to the patient's problems. Thus, the most commonly prescribed drugs from two different models will be placed on the top, whereas the remaining drugs will be ranked in descending order of the probability of their being prescribed. Fig. 11 shows the final result of the recommended medical prescription list.

5. Performance evaluation and discussion

After implementing the hybrid knowledge-based medical prescription support approach to facilitate decision making in the drug selection process, the performance result is compared with those derived from the existing experience-based approach (i.e. based on the human experience and knowledge to make the prescription). Ten GPs work on rotation in two different clinics and they use the system in the course of their normal work. They were invited to provide user feedback about the usage of the system through interviews. The purpose of the interview was concerned with the following dimensions:

- User satisfaction – Is the system useful for them?
- Ease of use – Is it easy to learn and use?
- Flexibility – Is it easy to cope with developments in the future?
- Effectiveness – Can the system provide the appropriate prescription references to GPs? Can the system reduce errors in prescription?

The result of the user feedback is illustrated in Table 2. From the result, it is found that the physicians agree that the system can improve their work in the different dimensions mentioned above; and GPs are willing to use it in future.

Furthermore, as one of the objectives of HKSMP is to complement the existing statistical approach proposed by [2], real case data that collected from HPMS were randomly selected from the database for verifying the retrieval correctness between the hybrid approach and the separation of approaches (i.e. CBR and Bayesian reasoning). Each medical record contains a particular patient's medical information, in which all the attributes are shown as Table 1. Since the study scope focuses on GP prescription, only GP-related patient records were retrieved and used in this experiment. In total, 500 cases which ranged from 1st March 2009 to 31st March 2009 were used. One experiment was used to measure the retrieval correctness of the medicine(s) generated by the HKSMP, whereas another one was used to measure the hit rate in each rank of HKSMP.

5.1 Experiment 1: Evaluation of the retrieval correctness among the three approaches

According to the general practices in HPMS, physicians usually prescribe 5 to 7 medicines to a patient. Therefore, the focus of this experiment was to investigate the retrieval correctness of the top 5, 6, and 7 suggested medicines recommended by HKSMP. It was found that the three approaches may recommend more than 7 medicines, therefore only the top 5, 6, and 7 medicines suggested were used in this evaluation. The leave-one-out method was then used as the validation method for determining how accurately a learning algorithm will be able to predict data that it was not trained on. In this method, the learning algorithm was trained multiple times, using all but one of the training cases. This validation method is useful because it does not waste data. Correctness, in this paper, refers to the ratio of the number of correct medicine(s) produced by the approaches among the total number of medicines actually prescribed. An example of calculating the correctness is shown below:

Suggested medicines recommended by an approach: {Drug A, Drug B, Drug C}
Actual prescription result of physicians: {Drug A, Drug B, Drug D, Drug E}

Correctness = No. of correct medicines / Total no. of medicines actually prescribed
= {Drug A, Drug B} / {Drug A, Drug B, Drug D, Drug E}
= 2 / 4
= 0.5

To verify the scalability of the proposed approach, experiments were carried out with different numbers of training cases (i.e. 100-500 cases with increments of 100 cases). Also, equal feature weightings were used in the CBR and HKSMP analysis. Only the first most similar case was retrieved in the CBR analysis. Accuracy analysis as mentioned above was then applied for the performance measurement by comparing the suggested solutions of the three analysis method against the actual solution. The experimental setup is depicted in Fig. 12.

Table 3 shows the results of solution retrieval correctness among the three different approaches. On average, it was found that the proposed approach performs best and results in faster learning than either CBR or Bayesian reasoning alone, because the integration takes advantages of both individual and collective wisdom in the medicine prescription process. In addition, HKSMP has a higher retrieval correctness when the number of learning cases increases. The figure reveals that the combination of the two approaches (i.e. HKSMP) outperforms the current approach to medical prescription support proposed by Bayesian reasoning and CBR alone.

5.2 Experiment 2: Evaluation of the hit rate in the three ranks of HKSMP

As proposed, three different ranks (i.e. Rank A, B, and C) are introduced in Section 3.2.3. To verify the performance in each rank (i.e. the ratio of the number of correct medicine(s) produced in each rank among the total number of existing relevant medicine(s) in each rank), we measured the hit rate of GPs in each visit. After the clinical investigation performed by the physician, a range of drugs will be recommended and listed under Rank A, B or C. The hit rate refers to the number of matches between the HKSMP's recommendations and the drugs actually prescribed by the physicians. The experiment setup is depicted in Fig. 13.

The results of performance evaluation in different ranks are shown in Table 4. It is noted that the hit rate of solution retrieval of Rank B is higher than that of Rank A and Rank C because most of the medicines are obtained using either CBR or Bayesian reasoning. From the result, the suggested medicines allow the physician to decide on a prescription because on average at least one medicine has been prescribed in each rank. Furthermore, most of the medicines that will be prescribed can be found in either Rank A or Rank B, in which physicians can select around 2 to 3 medicines (out of the actual solution of 5 to 7 medicines being selected) in the recommended medication list in HKSMP. These results show that the proposed system allows physicians to identify the required drugs easily.

5.3 Impact of HKSMP: Ethical issues

As explained in previous discussions, the use and applications of HKSMP is proven to be beneficial and advantageous in the medical field. This is because the use of such a system focuses on the efficiency and efficacy of providing appropriate medication to different diseases encountered by GPs. It also assists healthcare professionals in supporting prescription decisions in terms of past medical knowledge applied by other physicians. Indeed, HKSMP poses several positive effects and advantages in the decision support in medical prescription. However, a number of negative impacts can be identified, which can be perceived as ethical issues related to the use of the system.

The decision making process of GPs is first considered as an ethical issue. It is noted that few physicians might have the perception that HKSMP was designed as an autonomous system that replaces their human judgment. In this way, the right of a patient to obtain the best form of medical treatment or service is assured. Given that HKSMP aims to enhance knowledge in the medical prescription process, a list of appropriate medicines (instead of several medicines) will be generated in the system. In this regard, physicians can make use of this information (or they may even ignore the information) and their own clinical judgment to provide the most suitable medication to a patient. In other words, it is important to let the physician understand that the proposed system is a kind of decision support tool on which they should not completely rely in making decisions.

Another ethical issue is related to privacy and confidentiality of the information provided by the patients and physicians. It is recognized that HKSMP makes use of the electronically stored health information to infer the medical prescription decision support. In this way, the privacy and confidentiality of the information provided by a patient is not entirely recorded in the EMR, but rather it is retrieved for use in the HKSMP. It is claimed that confidentiality and privacy might be threatened with the use of such a system. Thus, one of the solutions to counteract this issue is to get the consent of patients, making them understand that the information is used for enhancing the case base of the system and will not be used for other purposes such as education and commercial purposes. Another solution is to introduce carefully thought-out policies that outline the system use of permissions and restrictions to reduce any ethical lapses.

5.4 Limitations of the study

The limitations of both CBR and Bayesian reasoning have been mentioned earlier (i.e. it is impossible to rely solely on past experience to treat the current situation), and it was observed that our approach works excellently when the patient condition in each visit was similar. In this case study, we found that more than 75% of the visits were similar to each other (e.g. the patients got similar or the same diagnoses) in which the drug selection is nearly the same as the previous visit. This may be due to the reasons that GPs employ the same rules or standards to treat the patients for the same diseases each time. On the limitation of the case study and the experimental set-up, the size of the knowledge base (i.e. the company and GPs involved) and the number of drugs available in the database are too small. IT is aware that the relatively small data set does limit the findings of the study, however it is believed that the results obtained show that HKSMP could be applied to a larger store of records in making suggestions on a range of medicines that could be used in medical prescription. Normally, more information can provide better decision support in CBR and Bayesian reasoning. As the approach can be launched in other medical centers, the knowledge base and drug information have the potential to grow rapidly, and become more knowledgeable to support the current complex medical prescription problems. It is also interesting to note that even though making the prescription is a complex process involving numerous variables (up to a hundred) in making decision, the proposed hybrid approach can greatly assist the domain expert by reducing the prescription choices and by identifying appropriate medicine for the physician's consideration. There is considerable saving in time compared with the conventional statistical approach for retrieving the previous prescription of each patient.

6. Conclusion remarks and further research

A hybrid knowledge-based decision support approach capable of extracting comprehensible individual and collective prescription behavior with good accuracy in medical prescription is proposed in this paper. With the growth in the amount of information about drugs, it is difficult for physicians to make a good prescription without a flexible drugs list. Mistakes in prescription are not only harmful but in serious cases they can also be fatal. The hybrid knowledge-based approach presented makes use of CBR to retrieve the micro-view of the physician's practices and Bayesian reasoning to model the macro-view. Subsequently, a rule-based results aggregator is introduced to match the results and hence categorize them intelligently into a drug list. The physician can then select the drugs that he or she will prescribe by taking into consideration the decisions made by a number of other physicians who treated similar cases.

The proposed hybrid approach has been validated in a medical center. The satisfactory results demonstrate the potential for adoption of this method in various medical organizations. However, there is still room for further development. Further research will consider more factors to determine the recommended drug lists. For example, combining the drug supply chain concept can further improve the results of drug selection. In addition, mining the relationships between drugs can generate more precise drug lists. Thus, we will extend our hybrid approach for medical prescription to take more and different factors into consideration.

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List of Figures:

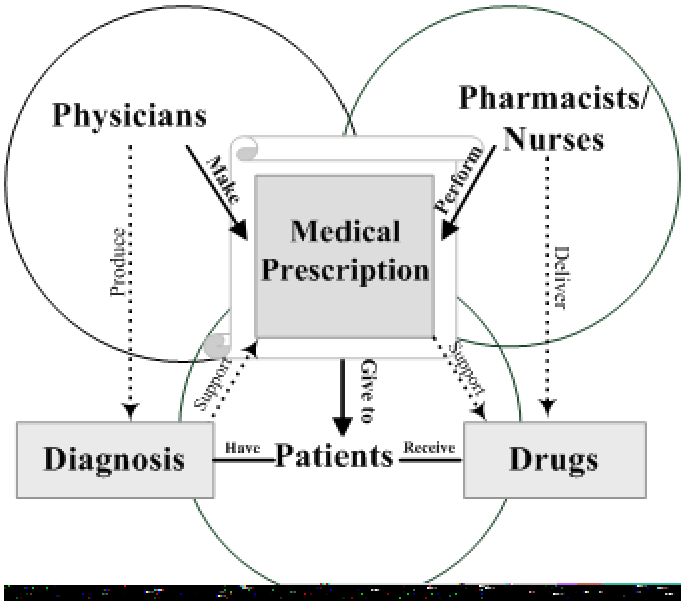


Fig. 1. Relationships between physicians, pharmacists and patients in general medical prescription practice

Fig. 2. Logical view of HKSMP

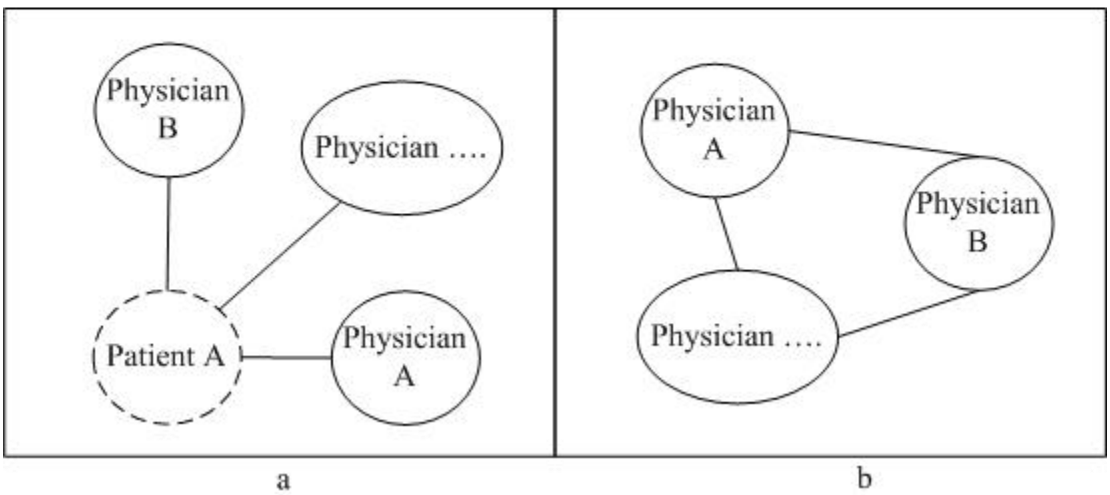


Fig. 3. Assuming that a Patient A has visited and diagnosed by various physicians, (a) shows the patient-physician relationship in 'Micro-view' and (b) shows the

physician-physician relationship in ‘Macro-view’

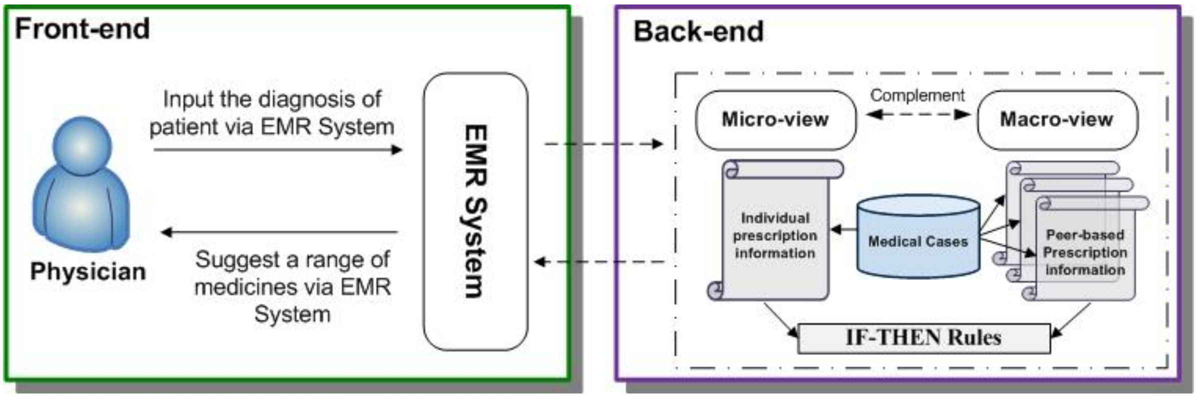


Fig. 4. Interaction between physician and HKSMP

Input: Results in CBR and Bayesian reasoning
Output: A set of medicines in three different ranking list

Rule-induction matching algorithm
FOR EACH (drug name)
    IF (the drug name in both CBR and Bayesian reasoning) **THEN**
        (put the drug name into Rank A List)
    ELSE IF (the drug name in either CBR or Bayesian reasoning) **THEN**
        (put the drug name into Rank B List)
    ELSE IF (the drug name in not in either CBR or Bayesian reasoning) **THEN**
        (put the drug name into Rank C List)
  END IF
END FOR

Report the results

Fig. 5. Algorithm of rule-based results aggregator

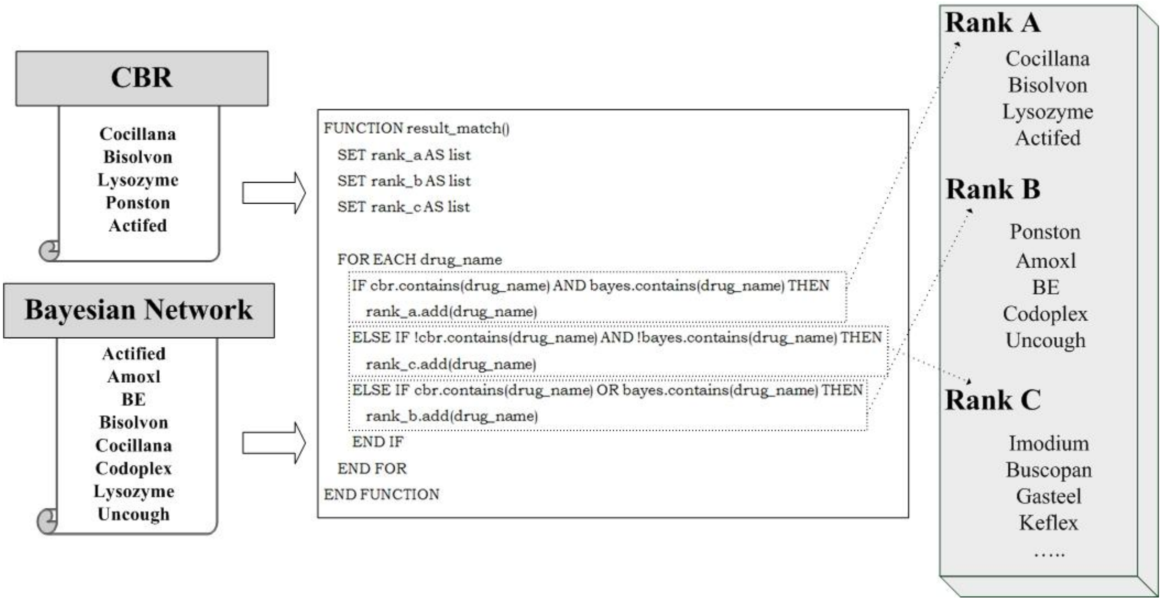


Fig. 6. Rule-based results aggregator

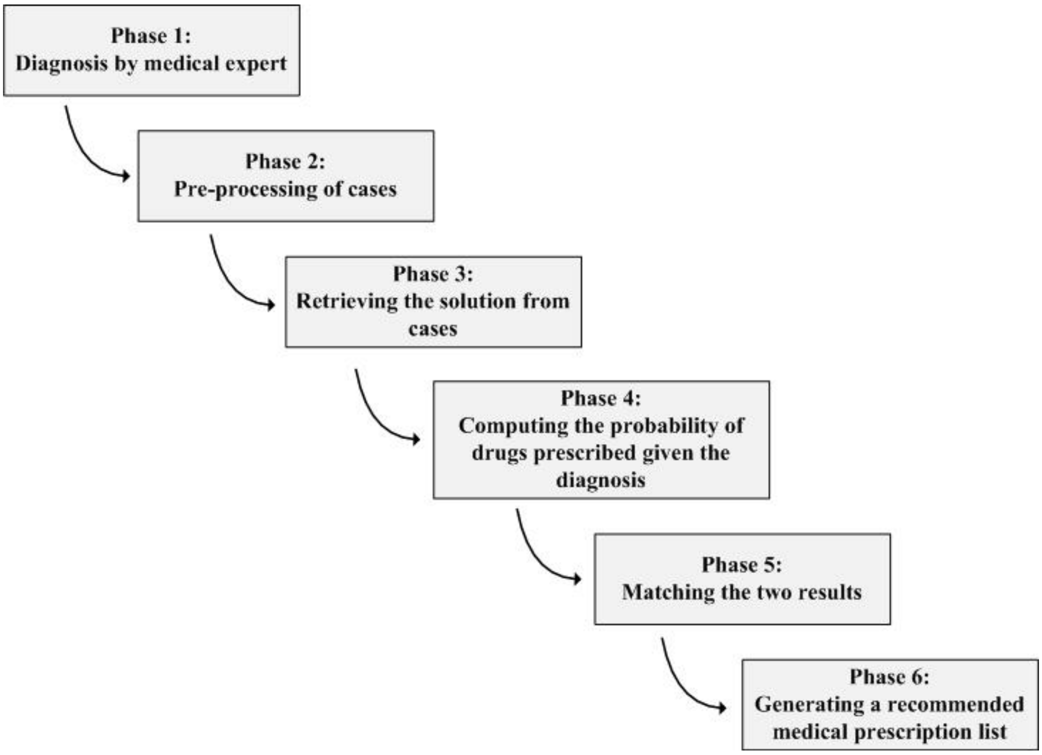


Fig. 7. Phases in an illustrated example

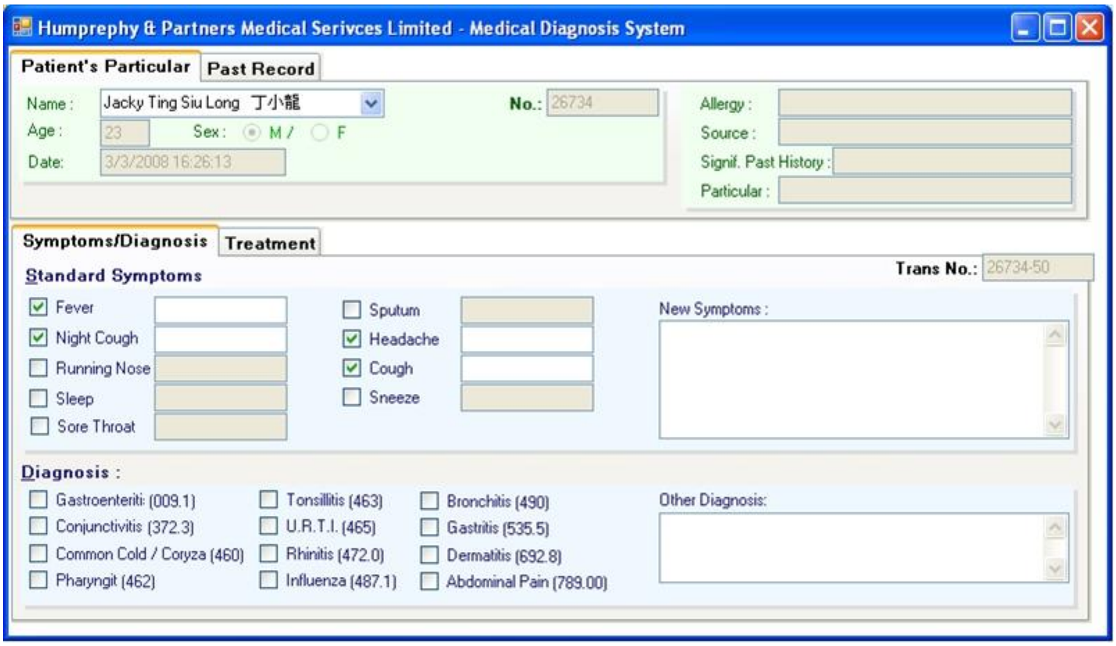
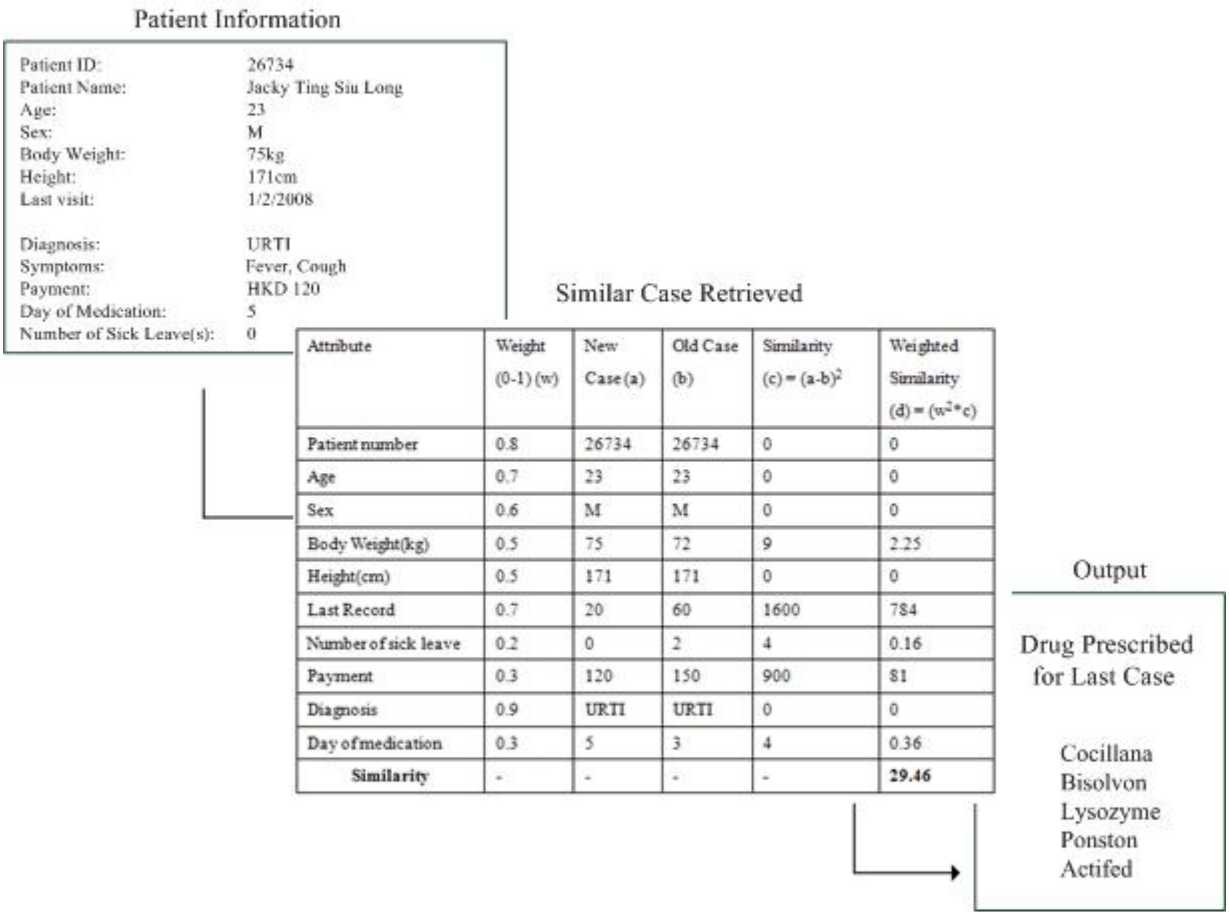


Fig. 8. Diagnosis of medical expert



Attribute	Weight (0-1) (w)	New Case (a)	Old Case (b)	Similarity (c) = $(a-b)^2$	Weighted Similarity (d) = $(w^2 * c)$
Patient number	0.8	26734	26734	0	0
Age	0.7	23	23	0	0
Sex	0.6	M	M	0	0
Body Weight(kg)	0.5	75	72	9	2.25
Height(cm)	0.5	171	171	0	0
Last Record	0.7	20	60	1600	784
Number of sick leave	0.2	0	2	4	0.16
Payment	0.3	120	150	900	81
Diagnosis	0.9	URTI	URTI	0	0
Day of medication	0.3	5	3	4	0.36
Similarity	-	-	-	-	**29.46**

Fig. 9. An example case and the proposed solution

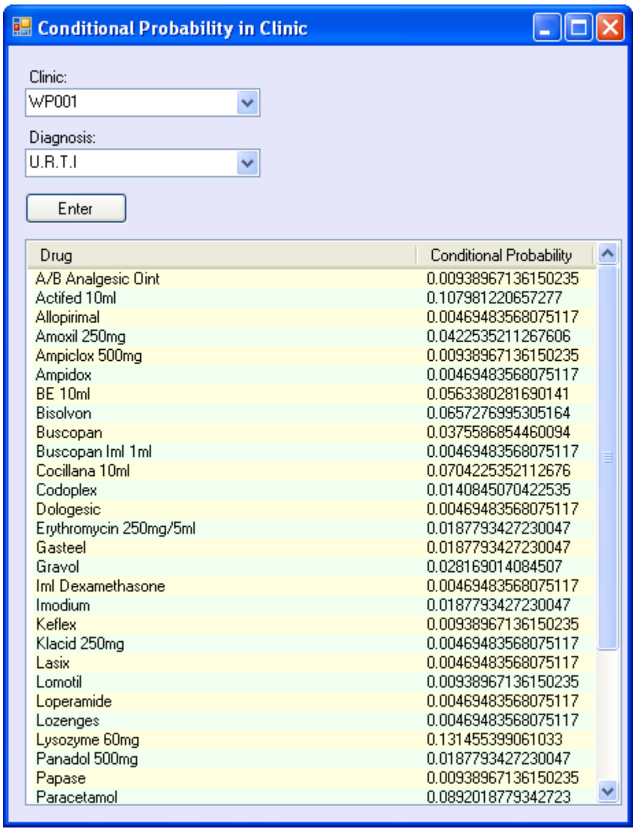


Fig. 10. An example conditional probability of drug prescribed

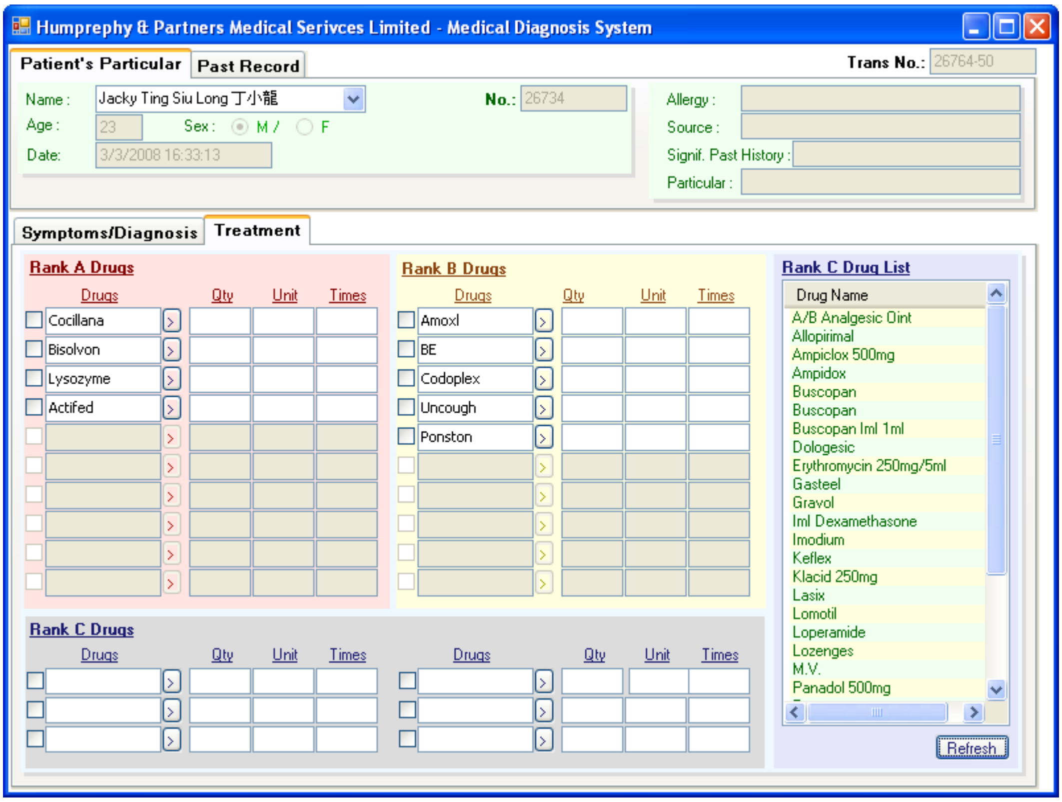


Fig. 11. The recommended medical prescription list produced in HKSMP

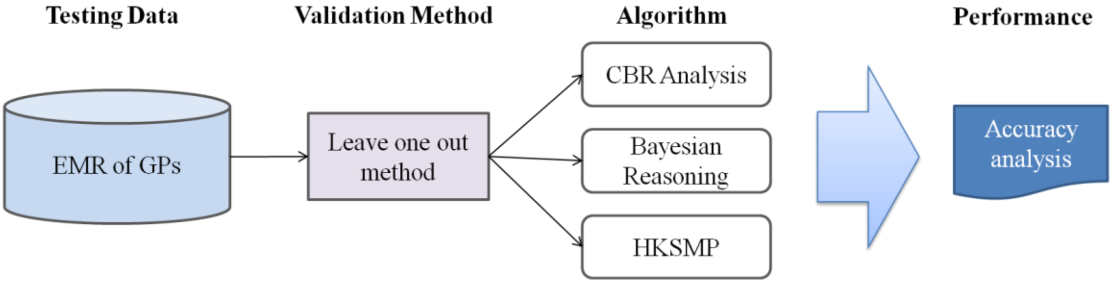


Fig. 12. The experiment setup for measuring the retrieval correctness of HKSMP

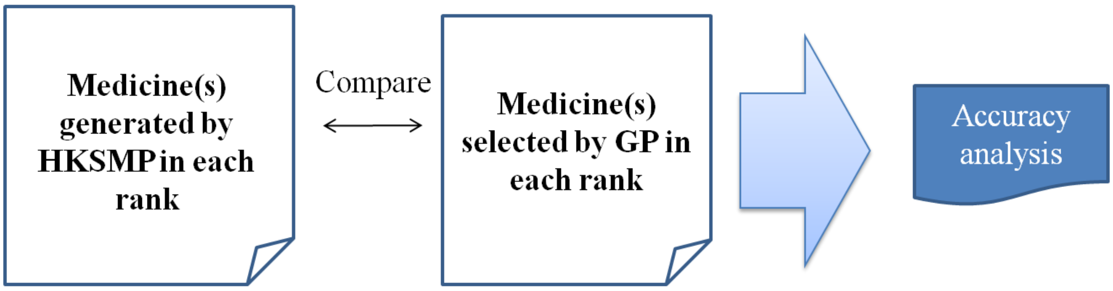


Fig. 13. The experiment setup for measuring the hit rate of HKSMP

List of Tables:

Table 1: Summary of the case attributes

Attribute	Possible values
Patient number	Unique ID (e.g. 34458, 32251, 1121)
Age	Positive Integer (1-100)
Sex	M, F
Body Weight(kg)	Positive Integer (1-100)
Height(cm)	Positive Integer (1-250)
Last Record	Positive Integer (today – last treatment date)
Number of days of sick leave	Positive Integer (0-30)
Payment	Positive Integer (20-1000)
Diagnosis	Multi-value ($\{URTI, Gastroenteritis, ..., Rhinitis\}$)
Symptoms	Multi-value ($\{Fever, Cough, ..., RunningNose\}$)
Days of medication	Positive Integer (0-5)

Table 2: User feedback for the HKSMP performance

	Very Dis-satisfied	Dissatisfied	Normal	Satisfied	Very Satisfied
Overall system performance					
Data input	0%	10%	20%	45%	25%
Information retrieval	0%	0%	25%	50%	25%
Decision support function	0%	15%	25%	40%	20%
Data input					
Efficiency (compared with the old process)	0%	5%	20%	50%	25%
Simplicity	0%	10%	45%	30%	15%
Design of user interface	0%	10%	30%	30%	30%
Information retrieval					
Correctness of content	0%	25%	30%	20%	25%
Sufficiency of content	0%	15%	25%	40%	20%
Ease to understanding	0%	0%	40%	50%	10%
Decision support function					
Efficiency (compared with the old process)	0%	0%	30%	45%	25%
Usefulness of prescription advice	0%	15%	40%	25%	20%

Table 3: A comparison of retrieval correctness of CBR, Bayesian reasoning and HKSMP among the 500 medical cases

Number of suggested medicines	CBR					Bayesian reasoning					HKSMP				
	No. of learning cases					No. of learning cases					No. of learning cases				
	100	200	300	400	500	100	200	300	400	500	100	200	300	400	500
5	0.20	0.24	0.27	0.30	0.37	0.27	0.27	0.28	0.29	0.30	0.49	0.50	0.53	0.54	0.56
6	0.29	0.32	0.35	0.38	0.41	0.50	0.51	0.53	0.53	0.54	0.59	0.60	0.62	0.62	0.64
7	0.52	0.54	0.55	0.57	0.58	0.69	0.71	0.72	0.72	0.73	0.80	0.80	0.83	0.85	0.86

Table 4: Evaluation of medicines selected in different ranks of HKSMP

	Rank A	Rank B	Rank C
Average hit rate	1.40	1.87	1.47
Standard Derivation	0.81	1.01	0.90
Minimum number of medicine retrieved	0	0	0
Maximum number of medicine retrieved	2	4	3