Clinical Benefits of an Embedded Decision Support System in Anticoagulant Control

Tony Austin, Shanghua Sun, Nathan Lea, Steve Iliffe, Dipak Kalra, David Ingram, David Patterson

Abstract—Computer-based decision support (CDSS) systems can deliver real patient care and increase chances of long-term survival in areas of chronic disease management prone to poor control. One such CDSS, for the management of warfarin, is described in this paper and the outcomes shown. Data is derived from the running system and show a performance consistently around 20% better than the applicable guidelines.

Keywords—"Decision Support", "Anticoagulant Control"

I. INTRODUCTION

INFORMATION TECHNOLOGY (IT) has made a significant impact in the healthcare domain. Machines monitor human vital signs and, for example, provide images of a patient's anatomy showing locations of pathology. All of these devices provide information to the clinician so that he or she can make a more informed decision about how best to help the patient.

Computer-based Decision Support Systems (CDSS) can take this process one step further and provide candidate opinions based on available data that clinicians can use (or not) to shape their strategy for managing the condition. In their simplest form, CDSS operationalise guidelines and free the practitioner from having to memorise their details. In addition the computer system, with its large storage capacity and ability to check many probable outcomes very quickly, is able to deal with atypical cases and to audit the process and outcome of care when guidelines are applied.

If the computer system is available to patients, they can enter details of their own medical problems. This releases healthcare staff from labour-intensive repetitive tasks and means patients are equipped to make small treatment changes or to arrange an appointment with the doctor if necessary. Computer systems can clearly be used to assist not only with diagnosis and management of medical conditions but also for management and tracking of care providers and cost of services, appointment scheduling and so on.

In theory therefore, the use of a CDSS would offer patients the benefit of better management, whilst health service organisations could capture more accurate audit data. The possible additional cost of optimal management might be offset in some cases if patients or more junior staff were able to manage the less complex problems. Backed up by a decision support system they may well approach the competency of an experienced medical practitioner for specific diseases.

Nevertheless CDSS are not as widely deployed as computer-based approaches for the medical record. The solution to many problems depends on a sensitive personal interaction between the clinician and the patient, and clinicans object to a perceived mechanistic approach to their patients' care. In addition, the volume of information now collected about a patient both by multiple clinical staff members and by automated data collection tools [1], as well as the complexity of clinical decision making means that CDSS systems have not always had a large positive impact on clinical outcomes [2], although there is emerging evidence that changes can follow CDSS development in as complex a domain as dementia [3]. This paper describes one such CDSS, for monitoring anticoagulation, which has been tested and shown to improve patient care in a randomised controlled trial [4][5][6].

A. Anticoagulation

Anticoagulants reduce the clotting activity in the blood. There are two types of anticoagulant drug. The heparins are given intravenously or subcutaneously, and the coumarins are taken orally. Warfarin is the most commonly used coumarin in the UK and worldwide. Responses to coumarins can vary widely within a population and within the same patient over time, and the possible consequences of leaving the therapeutic range can be severe.

In the UK, anticoagulants are the one of the largest causes of drug-related adverse events in hospitalised patients. The average frequency of major haemorrhage with oral anticoagulant use is 1% to 3% per year of which 20% to 30% are fatal. Overall minor and major haemorrhage rates of around 10% per year have been reported [7]. The amount of International Normalised Ratio results (INRs) within a therapeutic range can vary from 50% to 78% for outpatients on maintenance treatment. The amount of time spent inside the therapeutic range varies from 50% to 60%. Trainee clinical staff may take decisions on treatment but audits have shown trainee doctors having poor knowledge of therapeutic range even when these were circulated as guidelines or printed on

T. Austin is with the Centre for Health Informatics and Multiprofessional Education (CHIME), UCL, UK (+44 207288 3372; e-mail: t.austin@chime.ucl.ac.uk). N. Lea, D. Kalra, D. Ingram are also affiliated with this department.

S. Sun is with Community Health Sciences, St George's, University of London, UK.

S. Iliffe is with the Department of Primary Care and Population Sciences (PCPS), UCL, UK.

D. Patterson is with the Department of Cardiovascular Medicine, Whittington Hospital, London, UK.

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pathology report forms.

Chin [8] found that decision support can improve adherence to clinical guidelines and further positive outcomes include rapid response to critical laboratory results and adverse drug reactions [9][10][11]. Subsequent analyses conducted by Chatellier [12][13] on the effectiveness of automated decision support also reached the conclusion that treatment can be more effectively controlled using this methodology.

B. Whittington Hospital

The Whittington is a community based teaching hospital in north London [14], serving a busy and cosmopolitan part of the capital city. It was once the largest in Europe. Through reciprocal links with University College Hospital it is able to offer a comprehensive and expanding range of patient care services. The hospital has a close relationship with University College London for medical student and postgraduate education, and with Middlesex University for the training of nurses and other health professionals. The consultants have close working relationships with local GPs and the hospital provides support for many GP educational activities.

The Department of Cardiovascular Medicine has three consultants and seven junior medical staff supported by several cardiac technicians and specialist cardiac nurses trained in anticoagulation and in resuscitation. The team provides care for around 1,800 emergency inpatient admissions, almost 7,000 outpatients and co-ordinates around 20,000 cardiac investigations per annum. The department's close working relationship with the Middlesex Hospital for tertiary referrals embraces cardiovascular medicine and cardiovascular surgery, and incorporates peripheral vascular as well as cerebrovascular disease.

The Department has been at the forefront of investigation into the provision of anticoagulant therapy, both through clinics within the department and increasingly by supervising activity in the community through secondary providers, for more than fifteen years.

II. METHOD

Control of warfarin may be poor because of its complex pharmacology, because of the failure of medical staff to follow guidelines, or because of the inexperience of trainee doctors who are responsible for the management of most patients on the drug. Poor control leads to increased morbidity and mortality, for example through abnormal bleeding problems and longer hospital stays. Computer based decision support can provide valuable assistance to the clinician and improve patient care.

A. Choices for DSS

The medical record underpins all activities in the healthcare domain. This is the link the patient has with all of the clinical personnel and systems participating in their care, potentially over their lifetime. A decision support system can derive data from, and contribute new data to, this central store. It is therefore physically connected to it as well as linked to it for information processing. A common way of regarding medical

evaluation is as three generic tasks (see fig. 1). An initial assessment of patient state, potentially utilising information in the record, provides a diagnosis. This feeds into a loop of treatment and therapy planning that continues indefinitely or until the patient is cured. Each of these tasks requires some sequence of reasoning steps that will then be written back into the record.
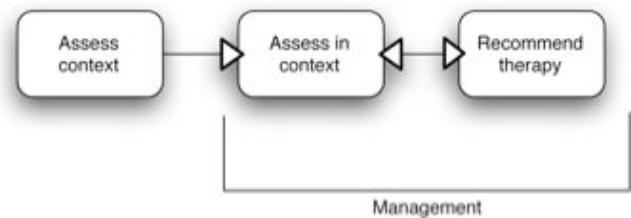

Fig. 1: The "Generic Tasks Model"

Each of these tasks utilises a model of reasoning that tends towards a solution or set of solutions. Just one example of such a model [15], was developed during the AIM GAMES-II project [16] (see fig. 2). This model is called the Select-and-Test (ST) model because of the order in which it calls reasoning functions. Data about which reasoning is to be performed enters the model at the point marked "Data". An abstraction phase is then performed which extracts useful information from the data. Abduction makes logically unsound predictions about what may have been the case in order to produce the effects noted. This results in a number of hypotheses that may be ranked and then tested by a deduction step. If a hypothesis was correct, a number of other findings may also be expected. The presence or absence of these may serve to confirm or dismiss the hypothesis.

There are several reasoning methodologies that can be used within the ST model. Some of the most widely used of these are described below. Each has advantages in certain situations.

1) Computational abstractions

Mathematics can provide a quick, repeatable reasoning mechanism ideally suited to computations of personal data such as "what is the rate of divergence of the current International Normalised Ratio (INR) reading from the preferred reading for this patient?" These calculations are often invaluable to the clinician and can be plotted as a graph for a visual cue.

2) Rules

The most widely used and easiest to understand reasoning mechanism is rule firing. At their lowest level rules are of the form {IF <conditional> THEN <do something>} or {IF <conditional> THEN <do something> ELSE <do something else>}. However, conditionals can be arbitrarily complex logical expressions and executed actions can include further rules which give considerable practical flexibility.

3) Bayesian belief networks

These are also known as "causal probabilistic networks" and can be thought of as chains of probability. If the probability of B occurring given A occurred is 1.0 then it is absolutely certain that if you observe A, B will follow. However if the chance that C occurs if B occurs is 0.1 then the likelihood of C given A is also 0.1 (1.0 $\xrightarrow[AB]{}$ × 0.1 $\xrightarrow[BC]{}$). In this way,

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likely outcomes from known truths can be plotted and used. This system gives a precise mathematical definition of cause and effect.
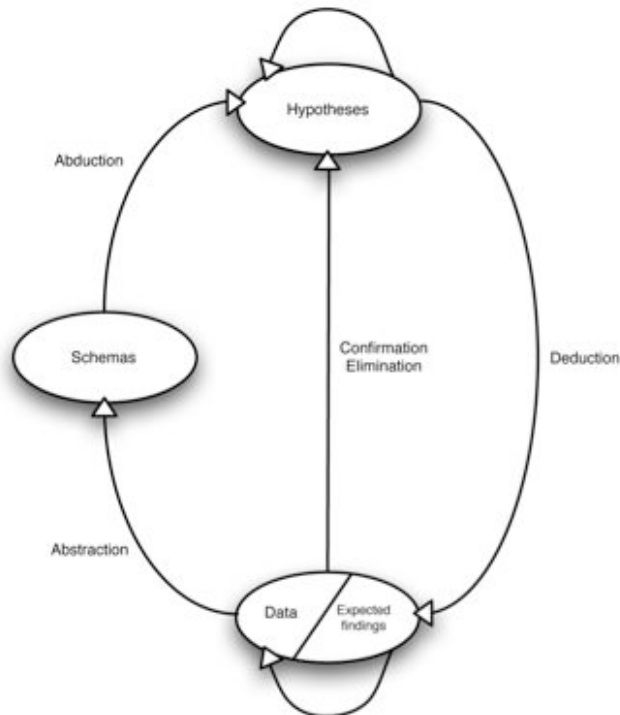

Fig. 2: The "Select and Test (ST) Model"

4) Machine learning algorithms

Machine learning groups together all algorithms that enable a computer to independently improve its own performance. There are several types of machine learning algorithm. One example is the genetic algorithm, where a machine makes two attempts at a solution and merges the most successful parts of each to obtain a closer solution.

Machine learning algorithms also include neural networks. These are models of the brain itself. In the most widely used version, called "back error propagation," (BEP), there is an input neuron layer and an output neuron layer, together with a definable number of hidden, internal layers. The machine makes a guess as to the required output given its inputs and if this is wrong, the difference between the desired output and the actual output is propagated back through the network giving an improved performance next time around.

B. Creating a CDSS

The creation of a Computer-based Decision Support System requires considerable effort:

1) The derivation of actual knowledge as understood by the clinician(s) (this necessitates either a panel of experts or some sort of systematic review of evidence);
2) The representation of the knowledge in the computer;
3) The creation of methods for manipulating the knowledge for a particular case;
4) The presentation of the resulting information to the user;
5) The evolution of the knowledge as further evidence is obtained, either from the domain or from the decision support system itself.

Any decision support system must utilise the services of a panel of highly experienced practitioners in the field of study. The panel first decides on the most relevant items of data. They then reach a consensus on management using any available established guidelines. This enables them to formulate abstractions and rules for the CDSS.

In order to validate the knowledge base, records of patients presenting with the disease suggested by the system are collected from practices or hospitals. These include the actual management decisions made by the responsible clinician. The cases are put through the decision support system and members of the panel give their opinion on the appropriate management. The knowledge base is then altered until it achieves the greatest possible agreement with the expert panel, taking into account actual management decisions made. Finally a prospective trial is often arranged where the decision support advice on a set of patients is compared to advice by a class of practitioner (e.g. nurse, or trainee doctor) on a different set [17].

All possible inputs in a computerised DSS must be analysed and a response given for each one. As new possible inputs become understood and the expert panel provides responses, they can be encoded onto the computer. Using this feedback loop the knowledge base can be brought not only into alignment with guidelines published after the development of the CDSS, but updated for changes in operational service. Obviously this approach, if audited appropriately, can also provide feedback to guidelines development. Consistent trends may show up and be documented and eventually become accepted practice.

C. Building an Anticoagulant CDSS

Vadher [7] showed that warfarin control is an area of cardiovascular medicine that can be automated both in terms of the recommendation of an appropriate dosage and in the regulation of clinic attendance. He developed an algorithm for warfarin dosing which was evaluated in a randomised controlled trial [6]. It was found that using the decision support tool the median time to achieve a stable dose was significantly lower and both inpatients and outpatients spent longer within the therapeutic range than did patients dosed by unassisted trainee doctors exclusively. These benefits can be realised by nurse practitioners with appropriate training [4].

The reasoning process Vadher developed for anticoagulation control is simple technically and after evaluating the options presented, best realised using a table look-up methodology. These are logically similar to rules but would appear to be a very large set of statements identical in all but key values, if realised in classic IF/THEN terms. The key values in this application consist of numeric evaluations based on historically recorded data in the record of the patient being managed. There are four significant table sets that have been found useful in anticoagulant control depending on whether the objective is an intensive 3-day initiation period, a slightly less intensive daily dose control, a weekly control, or a long-term maintenance control. By pre-computing these values for each controller it is possible to perform the look-ups with

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maximum efficiency. An extract from the maintenance controller is given in Table I. Other controllers are more complex and involve differential evaluations over time.

TABLE I
EXTRACT FROM THE ANTICOAGULANT MAINTENANCE TABLE LOOKUP

Target	Error Lower Bound	Error Upper Bound	Last Dose	Next Dose
2.5	0.71	0.51	10	11
2.5	0.71	0.51	10.5	11
2.5	0.71	0.51	11	12
2.5	0.71	0.51	12	13
2.5	0.71	0.51	13	14
2.5	0.71	0.51	14	15
2.5	0.71	0.51	15	16
2.5	0.71	0.51	16	17
2.5	0.71	0.51	17	18
2.5	0.71	0.51	18	19
2.5	0.71	0.51	19	20
2.5	0.71	0.51	20	21

In table 1, the controller is trying to maintain a patient at a Target INR of 2.5. This is typically associated with a Target INR Range of 2.0 - 3.0. The difference between this Target INR and the actual recorded INR at a given consultation is derived and then the table is searched for the upper and lower bounds that include that difference. The previous Last Dose is finally examined and from these factors, the Next Dose is established.

A minimal user interface has been created that enables these tables to be accessed without the need for an entire patient record application (see fig. 3). This has proved valuable in confirming the operation of the tables and is not intended for use by clinicians.
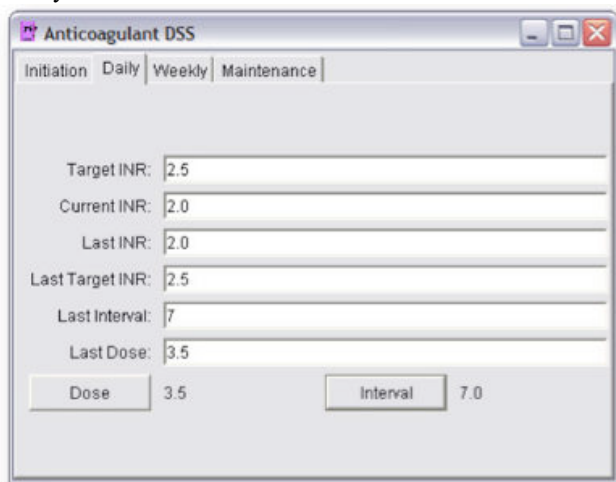

Fig. 3: An interface to the decision support system

D. Three Generations of Application

When the CDSS first came into use, the tables were embedded in a Microsoft® Access™ 2.0 database [18]. The user application was then implemented directly in the dialect of BASIC supplied with that product. However, because the variant of BASIC used by early versions of Access was not compatible with versions that came later, a significant rewrite

became inevitable. To ensure that such an inconvenience was not encountered again, the decision was taken to base the new version on Java™ instead. As the application itself is inherently of a tabular and form-filling nature, a decision was additionally made to make the client a Web style application.

The second application was actually realised as a set of Java Servlets which make calls to a database. Although in its original version the database existed on the same server as the running application, this was retrofitted to include the Jini™ grid technology, enabling the database to actually reside on any node in the local workgroup.

As well as the Java Development Kit version 1.4, and Jini 1.1, the departmental infrastructure therefore included a Apache Tomcat™ Servlet container running on a Windows™ 2000 Server provided by Dell®. The selected database was Oracle® 9i, taking advantage of the hospital site license for that product.

Novell® NDS™ was used to contain login information for clinicians and appropriately trained patients, and further stored patient identification information and information on all 30,000+ general practitioners in the UK, so that these could be searched by clinical staff for a presenting patient.
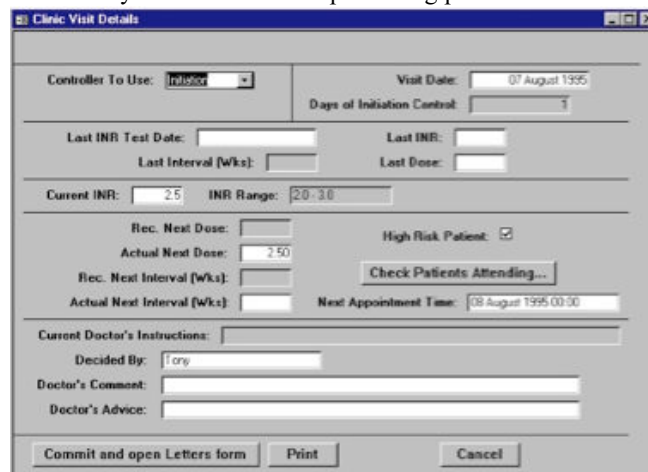

Fig. 4: The "Clinic Visit Details" screen in Access

Together these products comprised the technical infrastructure for the decision support system, which was then simply presented to end users on a regular Web browser. An example of the screens provided by the first and second systems is given in fig. 4 and fig. 5. Both demonstrate the Clinic screen, the main screen used by clinic staff when dosing patients on warfarin. In the second application, a detailed breakdown of the most recent INR test result is given at the top, with summary results of the previous five readings (where these are available) given in a table at the bottom. In the earlier version of the application the summary was separately presented (not shown). Decision Support (abbreviated "DS") is provided to recommend a next dose and next visit date for those patients within a therapeutic range.

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Fig. 5: The "Anticoagulant Application Clinic Contact" screen

In the most up-to-date version, HeartBeat, shown in fig. 6, the same decision support engine is used but now accessed via the Web using an "Asynchronous Javascript and XML" (AJAX) technique. As the user fills out the clinic contact pane, they can call for decision support based on values that have already been entered.
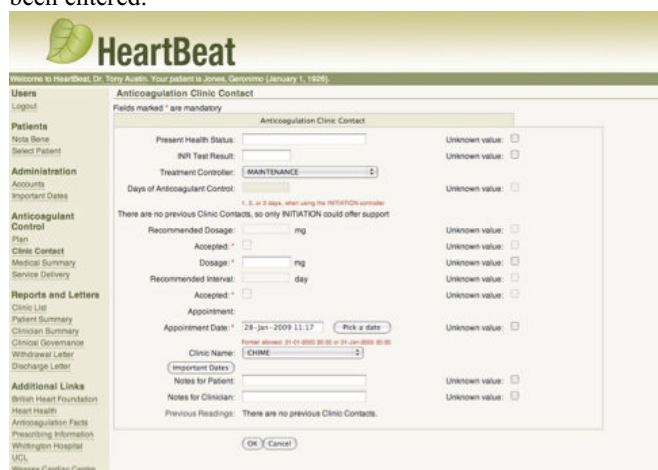

Fig. 6: The latest HeartBeat "Clinic Contact" screen

III. RESULTS

The three versions of the application have been running in the department for approaching 15 years. Although the decision support system has been written with more than one engineering approach in its lifetime, the underlying tabular methodology has been identical in all cases. Fig. 7 shows how the number of INRs taken per month has increased over the period of usage.

The results included in this section were derived from the audit data for the running system. Clinic contacts only were used, ignoring plans and other data captured by the system. Over the period studied, the total number of visits this represents is more than 142,000, from more than 4,700 individual patient IDs.

The decision support system differentiates between a target INR, which is the goal of the system to attain and maintain, and the therapeutic range, which is the goal of dosing generally. The British Committee for Standards in Haematology (BCSH) guidelines [19] suggest that outside of the therapeutic range, it is not ideal but nevertheless acceptable for a patient to INR within +/- 0.5 of it. Beyond that +/- 0.75 is less ideal still. A failure of dosing is assumed for responses further beyond that. In addition it is considered dangerous failure for an INR to be returned with an absolute value lower than 1.2 or above 8.0.

The BCSH standard also includes audit aspirations that it be routine for 50% of INRs to occur within 0.5 INR units, and 80% within 0.75 INR units. Fig. 8 shows how INRs returned over the period of usage fits within the range or diverges from it, and it can be seen that approximately 70.0% are within 0.5 INR unit and between 80% and 90% are within 0.75.

Over the entire period of usage only one month returned more than 5% outside the absolute range of INRs from 1.2 to 8.0. On average, the amount outside the absolute range was 1.90% with the lowest month at 0.24%.

If the decision support system is functioning as expected, then the quality of the advice should be independent of the amount of INRs being taken. Fig. 8 also shows that over the lifetime of usage, the quality of advice has stayed very consistent.

The results here are derived exclusively from hospital use of the system where the ability of most users is also relatively uniform. However so successful has the system been at the Whittington clinic that significant roll-out into the community is now being undertaken, with general practices and pharmacists being permitted to use the system after an accreditation process has been completed.

IV. DISCUSSION

At present, there is movement within the British National Health Service (NHS) towards greater and more comprehensive measurement of performance. Clinical audit requires cost-effectiveness measurement and mining of outcomes to determine if an organisation or professional is delivering an acceptable service. By analysing the results from the decision support system here, it would also be possible to determine the percentage of presenting patients outside the therapeutic range according to user, including those staff members most likely to override the decision support system to the detriment or otherwise of patients. It is possible to override the advice from the system but some application users do not record that it was overridden and early versions of the application did not require it to be recorded.

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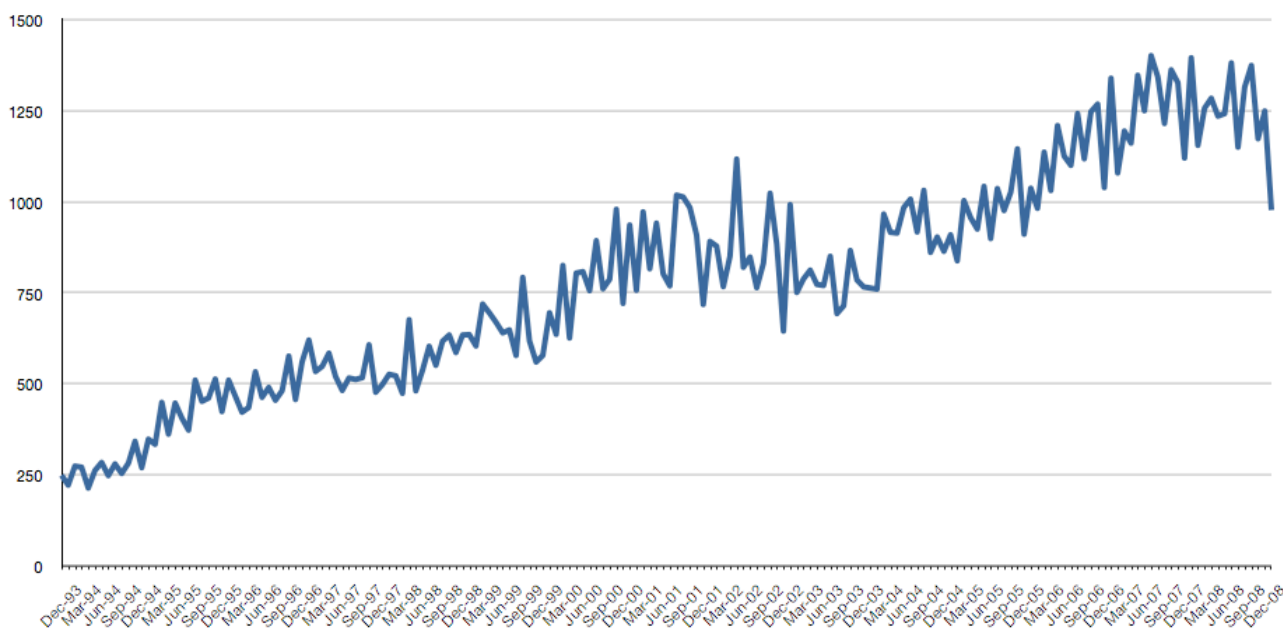International Journal of Computer and Information Engineering
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Fig. 7: The total INRs per month over the lifetime of the system
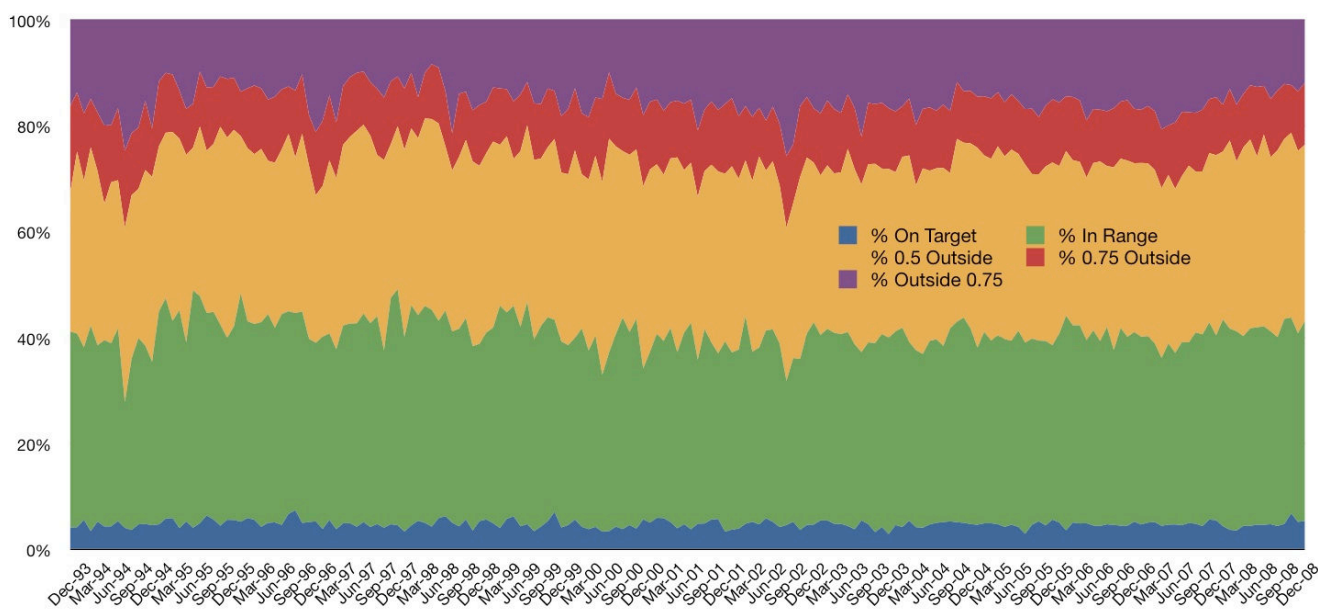

Fig. 8: The closeness of INR results to the therapeutic target

There are negative spikes in the charts, at around the middle of 1994, middle of 1996, and the middle of 2002. This could correspond to the arrival of new staff members who might need a period of training to become maximally efficient with the system. It could correspond to the introduction of new versions of the system itself, if users turned to manual dosing as they built up confidence. Alternatively it could correspond to periods of outage in the wider infrastructure environment. For example on one occasion a (computer) virus outbreak in the hospital caused many systems to be offline. In such a situation the department proceeds with a paper-based backup. This is possible because at the end of every contact a summary page is printed and a copy given to the patient. Because there is no decision support when the computer is not available,

users dose as best they can and then the data is transcribed when the system becomes available again.

A questionnaire survey was conducted in 2003 to solicit feedback from users as to whether patients were better informed since the introduction of the Web versions. A medium like the World Wide Web benefits from an immediate intuitiveness thanks to the accessibility of the browser used to view it. At the very least, patient help leaflets could be distributed in this way as well as actual decision support, possibly from a bookmark on the browser in use in the clinic office. Although the number of respondents from the busy clinic was too low for a statistical analysis, some written comments were telling. For example, one was particularly aware of patients responding to the graphical representation of

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the results. A graph on the page that displays the INR in relation to the therapeutic range can be of great value when explaining to patients about their treatment and concordance with medication.

Although standards will tend to reduce the price of individual hardware or software items through competition it may be necessary to recommend the purchase of more items or more robust items [20]. Typically server expenditure of this type would be undertaken by the hospital itself rather than by a department. An assumption is that a computer with enough power to run a simple browser is not an unduly significant requirement. However it is to be noted that while virtually all pharmacies have computers (at least for prescription labelling and stock control) they might well need a new machine in order to access the Web applications, and possibly a new network connection as well.

The Web is inherently able to integrate many types of media and sources of information. It is possible (although not exploited here) to offer staff partially anonymised records by simply changing the contents of the directory database for another with identical person identifiers and different actual details. Such modified records could enable medical students to become familiarised with the use of computer systems in medicine generally and to provide them specific domain experience. A scenario-based approach might involve an expert offering a set of clinical cases along with ideal responses and then grading the student on how close their actions were to those of the expert. It is also possible to use this record methodology with healthcare professionals to improve their own knowledge of, for example anticoagulant control, by drawing seamlessly on contemporary data. Ultimately this leads to a virtuous feedback loop, where data from anticoagulant control decisions leads to better understanding of the clinical practice itself. Note that the simple exchange of demographic identifiers is not a total solution in the case where identifiable data has been inserted into the record itself (like the real name of an information provider).

V. Conclusion

The decision support system described in this paper has been successfully validated in a randomised controlled trial and shown to be more effective than trainee doctors at dispensing warfarin and recommending a next appointment date [6]. With appropriate training it has been shown that nurse practitioners can also deliver an improved standard of care by following the CDSS recommendations [4]. The results here reinforce that the medical systems into which the CDSS has been built have delivered real benefits to the community, with better therapeutic range maintenance than the national average.

Because of the choice of Web application as the vehicle for delivering the decision support to the point of care, it is relatively easy to enable this to be widened into other hospitals or into the community. In the U.K. pharmacists are now being trained to use the system and this looks set to deliver convenient provision for patients without costly trips to hospital, whilst saving money in the health service by reducing the need for community practitioners to actually visit patients at home.

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