



Automated medical literature retrieval

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RESEARCH

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Abstract

Background

The constantly growing publication rate of medical research articles puts increasing pressure on medical specialists who need to be aware of the recent developments in their field. The currently used literature retrieval systems allow researchers to find specific papers; however the search task is still repetitive and time-consuming.

Aims

In this paper we describe a system that retrieves medical publications by automatically generating queries based on data from an electronic patient record. This allows the doctor to focus on medical issues and provide an improved service to the patient, with higher confidence that it is underpinned by current research.

Method

Our research prototype automatically generates query terms based on the patient record and adds weight factors for each term. Currently the patient's age is taken into account with a fuzzy logic derived weight, and terms describing blood-related anomalies are derived from recent blood test results. Conditionally selected homonyms are used for query expansion.

The query retrieves matching records from a local index of PubMed publications and displays results in descending relevance for the given patient. Recent publications are clearly highlighted for instant recognition by the researcher.

Results

Nine medical specialists from the Royal Adelaide Hospital evaluated the system and submitted pre-trial and post-trial questionnaires. Throughout the study we received positive feedback as doctors felt the support provided by the prototype was useful, and which they would like to use in their daily routine.

Conclusion

By supporting the time-consuming task of query formulation and iterative modification as well as by presenting the search results in order of relevance for the specific patient, literature retrieval becomes part of the daily workflow of busy professionals.

Key Words

Literature retrieval

What this study adds:

1. Whilst many literature retrieval tools exist on the market, none provide an automated workflow to minimise the search effort.
 2. Our approach automatically finds relevant publications without much interaction by the doctor.
 3. Medical specialists are made aware of relevant literature even during patient consultation without taking attention away from the patient.
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Background

The publication rate of medical research articles is constantly increasing. This puts pressure on medical specialists who need to be aware of the outcome of recent studies in their field, recent discoveries and new technologies in order to provide the optimal diagnosis and treatment for their patients.^{1,2}

The search tools currently available to medical specialists allow them to instantly search all publications, however the retrieval process is time consuming and repetitious.³ The most widely used medical publication system PubMed⁴ provided by the United States National Library of Medicine is based on Boolean retrieval. It therefore only shows publications exactly matching the search terms entered into the system. Those search terms can be combined as



Boolean expressions using the logical operators AND, OR and NOT.

Specifying only a few search terms often results in hundreds of thousands of matching publications. However adding a few more search terms quickly leads to an empty result set. Doctors therefore tend to under-specify the query to avoid missing out on important articles. They also have to manually iterate through various combinations of related search terms and their homonyms to find all relevant articles. Whilst PubMed offers a range of features to assist the power user, including identification of related citations and automated query expansion, the search process is still an extremely time consuming and repetitive task. Medical practitioners working in a clinical setting need to be able to focus on the patient, rather than on retrieval technology.

The system we developed allows medical staff to retrieve the publications most relevant for an actual patient without the need to specify long queries describing the patient's current condition. Our main contribution is the automatic generation of a query including the use of term weights based on data in the patient record. We developed a prototype based on records of patients diagnosed with Cystic Fibrosis, a disease that is managed by a multidisciplinary team.

Cystic Fibrosis

Cystic fibrosis (CF) is the most common autosomal recessive disease resulting in premature death in Caucasian populations. In Australia the disease occurs 1 in every 2800 live births and the number of people with CF in Australia is approximately 3000.⁵ The disease is due to a mutation of the Cystic Fibrosis Transmembrane conductance Regulator (CFTR) which is responsible for controlling chloride (and therefore sodium and water) transport across cells.⁶

It is a multisystem disease with the respiratory tract being the most severely affected and respiratory failure being the common cause of death if lung transplantation is not available. The gastrointestinal tract including the pancreas and liver are commonly involved with resultant malabsorption. Ongoing pancreatic disease may also result in diabetes. Liver involvement may result in the development of liver damage with cirrhosis and portal hypertension. Abnormal function of the CFTR results in loss of sodium and chloride in the sweat and may lead to serum electrolyte abnormalities. In males with CF congenital absence of the vas deferens occurs in 95% of patients, rendering them infertile.

The important management strategies in the treatment of CF are:⁷

- management by a multidisciplinary team;
- treating respiratory tract infections;
- maintaining a high caloric, high fat diet;
- airway clearance i.e. ensuring the airways are free of mucous plugs and sputum.

The multisystem nature of the disease and the multidisciplinary treatment strategies means that any search engine must be able to cover many aspects of medicine from basic genetics to therapeutics, physiotherapy and dietetics. It is also important the results from literature searches be clinically relevant, current and in a format not requiring further searches through hundreds of pages. This was the challenge of this project. Blood electrolytes and glucose levels are often abnormal in patients with CF. We thought that searching on these biochemical indices would be an appropriate starting point to test the search engine logic.

Table 1. Age-related MeSH terms and their crisp definition compared to our fuzzy definition, for age ranges of patients in the database

Age-related MeSH term	Crisp definition:		Fuzzy definition:			
	Age from	Age to	a	b	c	d
Adolescent	13 yr	18 yr	10 yr	13 yr	18 yr	22 yr
Young Adult	19 yr	24 yr	14 yr	19 yr	24 yr	28 yr
Adult	19 yr	44 yr	15 yr	19 yr	200 yr	201 yr
Middle Aged	45 yr	64 yr	40 yr	45 yr	64 yr	70 yr
Aged	65 yr	79 yr	60 yr	65 yr	200 yr	201 yr

Materials and Methods

The following section describes the data used and the components of our system.

Corpus

The corpus of publications indexed is the subset of all CF-related publications accessible through PubMed. As the



system developed has been designed to be used by a multi-disciplinary team of medical researchers sharing care for CF patients, articles describing studies are of high relevance. For another audience in different applications it might be more suitable to limit the corpus to review papers or even clinical practice guidelines.

Search engine

Our tool is based on the probabilistic search engine PADRE⁸ which supports the use of weights for search terms. PADRE considers a query term with a term weight of 2 to be twice as important as a query term with the default weight of 1. Query terms and synonyms are therefore weighted in order to distinguish between more or less relevant search terms. Although some probabilistic search engines allow the manual weighting of query terms, they are only exploited for internal use such as relevance feedback since using them for manually entered queries would make the user interface too complex. We will show example query components in PADRE syntax with alternative terms being encapsulated in square brackets, e.g. `["search term"^weight "alternative term"^alt weight]`

The fundamental text-matching component of the PADRE ranking function is a slightly modified version of BM25.⁹ Page 4 of⁸ gives the precise formula. The BM25 score for a document, given a multi-term query, is the weighted sum of the scores due to each query term. Individual term scores are calculated using a *tf.idf* variant in which term frequencies are document-length normalised (parameterised) and subjected to a (parameterised) saturation function. Individual term scores are weighted (multiplied) by q_t , the weight calculated by our tool for term t .

Some studies show that certain domain experts are reluctant to move away from boolean retrieval systems.¹⁰

However, rather than just aiming for 100% recall, this tool has functions that simplify the retrieval process, which allow it to be embedded in a doctor's daily workflow.

Automatic query generation

The first step in taking a load off the doctor is to release him from the task of manually entering search terms describing the patient's situation.

This covers the first aspect of an Evidence-based medicine (EBM)¹¹ related search strategy described as the acronym PICO, where the doctor expresses clinical questions in four steps:

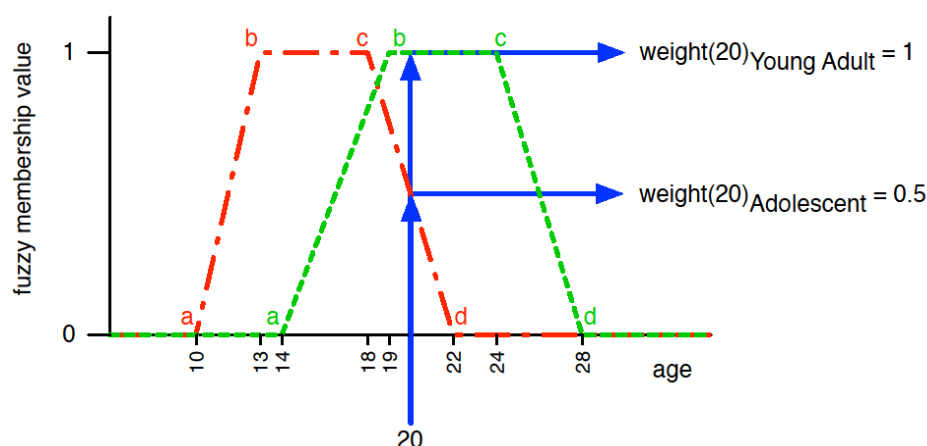
Patient	Who/what is the patient/problem being addressed?
Intervention	What is the intended intervention?
Comparison	What is the intervention compared to?
Outcome	What are the outcomes?

The query is automatically generated based on the electronic patient record. The automatic query generation is currently based on diagnoses, the age of the patient and results of recent blood test results.

Simple search terms: Diagnoses are already added manually into the patient record by one of the doctors in previous consultations. We extract those underlying diagnoses from the patient record and weight them with 1 as it would be as manually added search term.

Example query component: `"Cystic Fibrosis"^1`

Figure 1: Calculating term weights for age-related MeSH terms using fuzzy membership functions for a 20 year old patient. The fuzzy membership function for Adolescent is drawn in red (dash-dotted line), the one for Young Adult in green (dashed line).



Fuzzy mapped search terms: PubMed uses Medical Subject Headings (MeSH) terms to encode the age of the patients described within a publication. Those age-related MeSH terms are defined crisply and a PubMed search for a certain age group would not necessarily return publications mentioning patients that are only one year older. We compensate for this disadvantage of indexing using crisp MeSH terms. The age of the patient is mapped to age-specific search terms and weights are calculated based on fuzzy membership functions describing each of those terms. Table 1 lists the age-related MeSH terms and their crisp definition, as well as the fuzzy definition we expanded it to by adding the sides of the trapezoids. Notice that we only generated fuzzy membership functions for the age ranges of the patients currently in the database. Most importantly we extended the age range for the term *Adult*, which is defined within MeSH as 19 to 44 years. We do not believe that this is the common understanding of the term *Adult*. To reflect this, we de facto removed the upper boundaries for *Adult* and *Aged* by setting it to the artificially high age of 200 years to keep the algorithm simpler whilst still effectively removing one flank.

Formula 1: Weights based on fuzzy membership functions.

$$weight(age)_{term} = \begin{cases} 0 & \text{if } age < a_{term} \text{ or } age \geq d_{term} \\ \frac{age - a}{b - a} & \text{if } a_{term} \leq age \leq b_{term} \\ 1 & \text{if } b_{term} \leq age \leq c_{term} \\ \frac{d - age}{d - c} & \text{if } c_{term} \leq age \leq d_{term} \end{cases}$$

Figure 1 shows two overlapping trapezoidal membership functions for *Adolescent* and *Young Adult* and how search term weights are generated for a given age of 20 years. Using a crisp definition as in Table 1, only publications labeled with the MeSH term *Young Adult* would be returned. Our system however also retrieves publications indexed with the MeSH term *Adolescent*, but rank that search result lower, due to the reduced term weight.

The weight for an age-related search term is computed using Formula 1 for trapezoidal fuzzy membership functions, using the values a, b, c, d defined in Table 1.

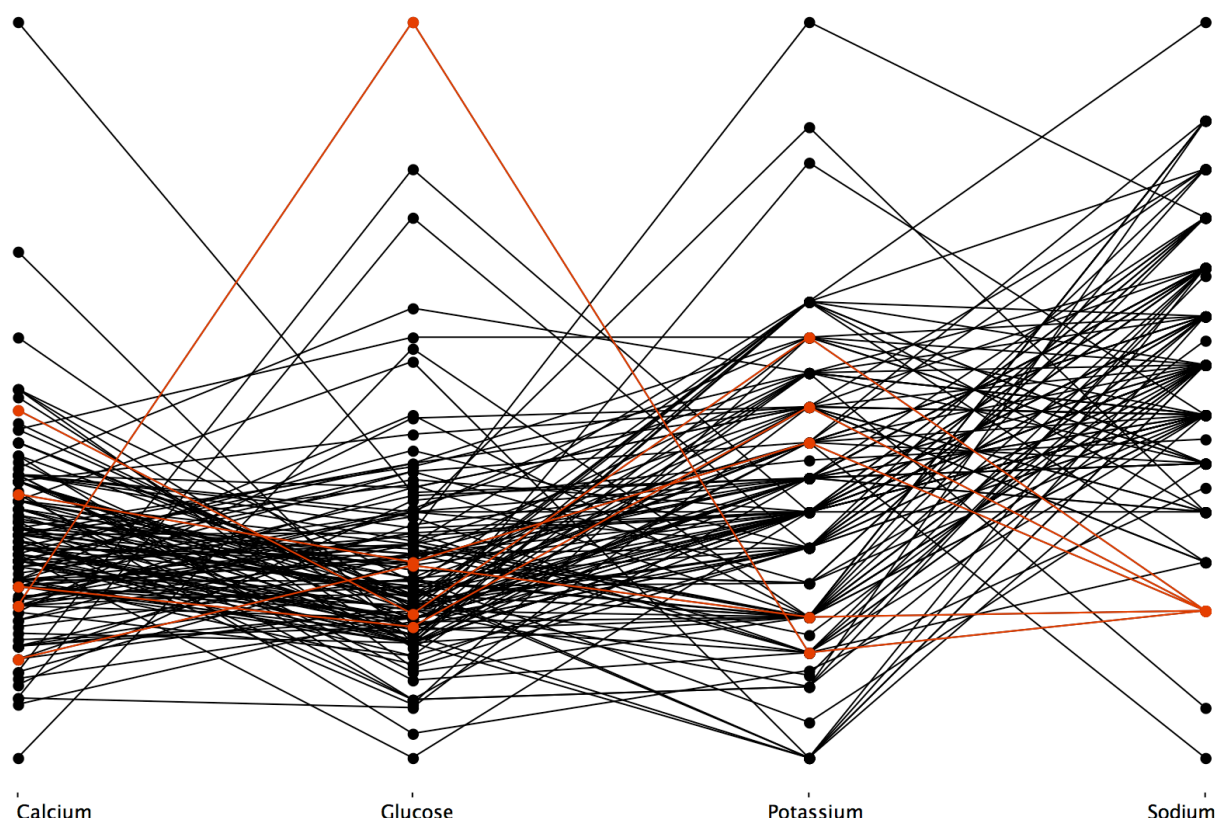
Example query component: ["*Young Adult*"^1 "*Adolescent*"^0.5]

Extremeness of blood test results: The results from recent blood tests are compared to minimal and maximum values

provided by the lab for each measurement. Using those ranges provided by the labs did not prove sufficient as for some blood tests such as glucose, where the mean value of the cohort of patients is already higher than the maximum defined by the lab. This phenomenon is caused by the fact that all patients in the database are CF patients and CF patients tend to develop CF-related diabetes.

Our tool also takes into account the cohort of patients in the database. The variability in the blood tests is shown in Figure 2; a Parallel Coordinates Plot.¹² Each line shows the most recent values of blood tests for each patient in the database. On the four vertical parallel axes labelled calcium, glucose, potassium and sodium, the data points are scaled to plot the lowest recorded value on the bottom and the highest recorded value on top of the axes. This visualisation was used to examine the variation in combinations of expressions across the patient cohort. The plot has been produced using the statistical environment R and a package called iPlots. The iPlot package allows the user to select a certain line or group of lines to see the combination of expressions. In the screenshot, a group of patients sharing a similarly low sodium level have been selected causing the lines to be drawn in red.

Figure 2: A Parallel Coordinates Plot showing the variety of combinations of blood test results in the cohort of patients.



This type of plot clearly shows that even though the five patients are low in sodium, the values of other blood test types are widely distributed. This variability in distribution shows that every patient's data is likely to generate a unique query even without taking the other query components into account.

Definition 1: Let $p(x)$ denote the percentage of observations of the metabolite that are lower than the observation x , for the patient of interest. Therefore x is the $p(x)$ percentile of the empirical distribution of the metabolite across all patients). We decided to increase the weight of search terms according to the following empirically defined exponential weighting Formula 2.

Formula 2: Percentile-based weights.

$$weight(x) = \begin{cases} 1.1^{100-p(x)} * 10^{-3} & \text{if } p(x) \leq 50 \\ 1.1^{p(x)} * 10^{-3} & \text{if } p(x) > 50 \end{cases}$$

According to Formula 2, a test result at the 50th percentile (the median) will receive a weighting of 0.1. This small weight will effectively result in the search term becoming insignificant.

Outlying values however will receive higher weights, for example a test result in the 5th (or 95th) percentiles will receive a weighting of 8.6 and therefore rank publications containing the search term much higher.

Introduction of homonyms and conditional homonyms

We manually compiled a list of homonyms to allow the specialist to fine-tune the system for their needs.

If the patient's test result is out of the range provided by the test lab, we also add the appropriate terms describing this condition. A high or low glucose level would therefore trigger the alternative search term *Hyperglycemia* or *Hypoglycemia* respectively to be added. The weight for this alternative search term is still determined by the percentile of the value.

Example query component:

`["Glucose"^0.2 "blood sugar"^0.2 "Hyperglycemia"^0.2]`

User interface design and result presentation

The design of the user interface was mainly guided by the following five design goals: easy to learn, simple to use, fast, comprehensible and visually appealing.



Figure 3: Screen shot of the medical literature retrieval tool developed.

HealthIR Publication Retrieval

Logged in as healthir. [Logout]

Cystic Fibrosis Project

PATIENT

Patient-ID	10237
Year of birth	1955
Gender	M

GENERATED QUERY

["Sodium"^0.4] ["Calcium"^3.3] ["Cystic Fibrosis"^1] ["Bronchiectasis"^1] ["Adult"^1] ["Glucose"^0.2 "blood sugar"^0.2 "Hyperglycemia"^0.2] ["Potassium"^2.5] ["Middle Aged"^1] ["Male"^1]

RELATED PUBLICATIONS

34

Recurrent acute pancreatitis in patients with **cystic fibrosis** with normal pancreatic enzymes.

35

Altered intestinal chloride transport in **cystic fibrosis**.

36

Should the **bronchiectasis** treatment given to **cystic fibrosis** patients be extrapolated to those with **bronchiectasis** from other causes?
Authors: Athanazio RA, Rached SZ, Rohde C, Pinto RC, Fernandes FL, Stelmach R.
Date: 2010
Publisher: Jornal brasileiro de pneumologia : publicação oficial da Sociedade Brasileira de Pneumologia e Tisiologia
Abstract: To profile the characteristics of **adult** patients with **bronchiectasis**, drawing comparisons between **cystic fibrosis** (CF) patients and those with **bronchiectasis** from other causes in order to determine whether it is rational to extrapolate the **bronchiectasis** treatment given to CF patients to those with **bronchiectasis** from other causes. A retrospective analysis of the medical charts of 87 patients diagnosed with **bronchiectasis** and under follow-up treatment at our outpatient clinic. Patients who had tuberculosis (current or previous) were excluded. We evaluated the clinical, functional, and treatment data of the patients. Of the 87 patients with **bronchiectasis**, 38 (43.7%) had been diagnosed with CF, through determination of sweat **sodium** and chloride concentrations or through genetic analysis, whereas the disease was due to another etiology in 49 (56.3%), of whom 34 (39.0%) had been diagnosed with idiopathic **bronchiectasis**. The mean age at diagnosis was lower in the patients with CF than in those without (14.2 vs. 24.2 years; $p < 0.05$). The prevalence of symptoms (cough, expectoration, hemoptysis, and wheezing) was similar between the groups. Colonization by *Pseudomonas aeruginosa* or *Staphylococcus aureus* was more common in the CF patients (82.4 vs. 29.7% and 64.7 vs. 5.4%, respectively). The causes and clinical manifestations of **bronchiectasis** are heterogeneous, and it is important to identify the differences. It is crucial that these differences be recognized so that new strategies for the management of patients with **bronchiectasis** can be developed.
MeshTerms: Adolescent!Adult!Bronchiectasis!Cystic Fibrosis!Female!Humans!Individualized Medicine!Male!Middle Aged!Retrospective Studies!Young Adult

37

Normal and **cystic fibrosis** airway surface liquid homeostasis. The effects of phasic shear stress and viral infections.

38

Could a defective epithelial **sodium** channel lead to **bronchiectasis**.

39

Determinants of chronic infection with *Staphylococcus aureus* in patients with **bronchiectasis**.

40

Newly diagnosed **cystic fibrosis** in middle and later life.

41

Sweat test in patients with **glucose**-6-phosphate-1-dehydrogenase deficiency.

42

Parotid gland function in children with **cystic fibrosis** and child control subjects.

43

Sodium, potassium, **calcium**, and magnesium in hair from neonates with **cystic fibrosis** and in amniotic fluid from mothers of such children.

44

Renal function in patients with **cystic fibrosis**.

QUERY

Patient

☒ Male

☒ Adult

☒ Middle Aged

Diagnoses

☒ Cystic Fibrosis

☒ Bronchiectasis

Blood test

☒ Calcium	2.4 mmol/L	▲	14.9
☒ Potassium	3.9 mmol/L	▼	18.1
☒ Sodium	139 mmol/L	▼	36.55
☒ Glucose	6.5 mmol/L	▲	42.42

Manual

Enter additional terms...

Execute query

HealthIR, a joint project by the CSIRO, the Australian National University and the University of Adelaide.

As shown in Figure 3, the user interface is divided into the following four sections:

Patient: A brief patient detail view allows the doctor to verify that he is investigating the correct patient. Notice that identifying details have been removed from the dataset due to requirements of the ethics committee for the study.

Query: The query section contains a form, which is constructed and pre-filled by the system according to the data in the patient record. The sex and matching age describing MeSH terms are displayed as well as the manually specified diagnoses.

Blood test results are shown for the four tests we decided to use in the prototype. Values that are out of the range specified by the lab are printed in red as they are in the system currently used by the doctors. The tests are ordered by their extremeness, which is printed and prefixed with a red up arrow or blue down arrow to indicate the value being too high or too low respectively.

The query only specifies the patient aspect of the PICO system. Other aspects can be entered using manual search terms.

Generated query: The generated query section is collapsed per default on purpose as it contains the complex PADRE



query used to retrieve the publications. This information is not needed in normal use, and only allows the doctor to examine the detailed effects of the selections in the query section described above.

Related Publications: The initial query is automatically generated and evaluated and the result is presented to the doctor as a list ordered by relevance. The number of search terms matched by each publication is indicated by a small pie chart icon. Articles published within the last three years are flagged in red, rose or grey respectively and allow a very quick indication if a publication is recent.

Doctors can scan the titles of the top results or quickly scroll through the list looking for publications flagged as *recently published* as new publications are more likely to be unknown to the doctor. Clicking on the title of a publications slide opens a detail view of the publication, containing metadata as well as the abstract. The selected publication in Figure 3 is well down the list, which is ordered by relevance. The small pie chart shows it does not satisfy all the search terms (e.g. potassium). The flag shows it is a recent publication. Matching keywords are highlighted in the abstract allowing the user to validate the relevance of the result. The reference to the publisher acts as a link back to PubMed where more information including a download link to the publication can be found.

In case the doctor is not satisfied with the results, the query can quickly be refined in the query section of the user interface.

The idea is to quickly grasp if relevant but unknown literature exists. The intended workflow is to open the tool with the patient-ID automatically passed in. The doctor can glance over the already displayed publications or quickly uncheck characteristics to be removed from the query.

Evaluation

System Behaviour

The first version of the prototype used PubMed directly as a backend and composed queries in PubMed syntax.

However this did not prove beneficial for various reasons:

- It took several seconds to retrieve the results through the PubMed API.
- PubMed does not allow the use of term weights.
- The results are not ordered by relevance, but e.g. by date of publication.
- A high number of query terms led to empty result sets.

We did not measure the exact query execution time for both systems for comparison, as the prohibitive problems of

the other three reasons listed above are of a qualitative nature.

User study

We approached medical staff providing ongoing medical treatment for CF patients at the Royal Adelaide Hospital to evaluate the system and asked them for feedback. Nine participants were recruited and contributed their feedback. Although this is a small number of participants and does not allow a quantitative analysis of the results, this is compensated for by our access to real patient data and that the participants are professionals actually treating CF patients and are therefore the potential future users of the system.

Pre-trial questionnaire: A pre-trial questionnaire handed out before introducing our system asked for a description their used literature retrieval procedure. Many participants indicated that they only have very limited time for literature searches and that it usually takes many iterations of modified queries to find what they need. Most of them indicated concerns about missing out on important results not retrieved by their current systems.

Post-trial questionnaire: After using the system to freely explore its behaviour searching for results for various patients, participants were asked to provide feedback via post-trial questionnaires. The questions were of an open nature and explicitly asked for elaborative answers. The feedback gathered was generally very positive. Most participants felt that they had to spend less time searching whilst being more confident that they had not missed important results. The most surprising comment added by several participants was that they wanted to use the system even without the case-based feature. This indicates that they found the system superior to their current literature retrieval tool and wanted to use it for general medical literature retrieval.

Discussion and Conclusions

The integration of this tool in the electronic patient record system will help medical practitioners to regularly review patients' cases with respect to any new literature available. Furthermore it will allow them to improve confidence in their diagnoses and decisions about the treatment, based on the knowledge that they are aware of the recent progress in the field. The doctor can simply focus on his patient rather than search engine peculiarities.

Future work might include a way for the researcher to specify the origin of publications as search preferences.



Additional resources such as clinical trials could be added to the searchable collection.

Furthermore, the homonyms could be resolved through a medical ontology or thesaurus; however this activity was beyond the scope of this prototype.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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ETHICS COMMITTEE APPROVAL

Australian National University Human Ethics Protocol Number 2009/438