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Physicians raise two questions in every three patients they see and around 50% of those questions are not even pursued due to various reasons. These unanswered questions represent huge knowledge gap and could result in less than desirable treatment outcomes. The situation becomes even worse with the emergence of internet technologies which brought explosively increasing information and knowledge into everybody's lives. To make medical information more readily available and to facilitate physicians' decision making process, we designed and developed a medical knowledge summary system that automatically extract and synthesize relevant medical evidence from major resources including UpToDate and PubMed. We performed a pilot usability study to evaluate the effectiveness of the system and used the feedback from physicians to further the development effort. Physicians in general found our system intuitive to use and information delivered very valuable in filling in their knowledge gaps.

Headings:

Clinical Decision Support

User Evaluation

Data Visualization

User Interface Design

Information Retrieval

EVALUATION OF A PROTOTYPE OF COMPUTERIZED HEALTH KNOWLEDGE
SUMMARIES

by
Dongqiuye Pu

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Approved by

Javed Mostafa

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Introduction

Although physicians are familiar with approximately 400 diseases that are frequently encountered in practice, they don't, nor are they expected to, possess detailed knowledge regarding new diseases, rare diseases, comorbidity problems, or the latest technological developments. However, it's beneficial to both physician and patient populations if doctors keep up with clinical evidence and advancement. With updated knowledge repertoire, physicians are equipped to make better, more cost-effective diagnostic and treatment decisions. In the last century before most computerized technologies and solutions were introduced, physicians mainly turned to their colleagues for consultation and advice as the major information resource, followed by reading medical books and journals. These styles of information seeking behavior often led to prolonged decision process, suboptimal decision and lower quality of care. Time factor is critical in clinical settings, especially with acute and time-sensitive diseases. Delayed decision-making process may produce aggravated disease unsatisfactory outcome. Making the matter worse, the information needs are often unmet due to limited resources at the time of care, which ultimately leads to questionable clinical decisions.

Since the introduction of computerized technologies late last century, it has broadly penetrated the healthcare field with the promise of improving the ways that physicians access medical information. A large number of quality medical databases have been developed that provide comprehensive electronic resources for

healthcare professionals. Therefore, it's not an overstatement that physicians are fortunate to have access to enormous clinical evidence and knowledge. However, health professionals' information needs are still largely unmet and physicians often find themselves drowned in oceans of information and they are generally frustrated with the information seeking process. The reasons for this are many. However, it is mainly either due to overwhelmingly irrelevant information presented by electronic systems, or systems that are highly intrusive to the clinical workflow. Therefore, incorporating existing information databases into clinical workflow and mining and presenting the most relevant clinical evidence at the point of care remains an elusive challenge to overcome.

Literature Review

In this section, literature in relevant areas will be summarized that include physicians' information needs, physicians' information seeking behavior and current progress in clinical decision support systems.

Physicians' Information Needs

Investigation of physician's information needs has started about three decades ago when Covell et al. reported that physicians raise two questions for every three patients they see in office settings [1]. Only 30% of physicians' information needs were met during the patient visit, usually by another physician or other health professional. The key factors behind low use of print sources included the age of textbooks in the office, poor organization of journal articles, inadequate indexing of drug information sources, lack of

knowledge of an appropriate source, and the time required to find the desired information.

Since then numerous studies have been performed to investigate the information needs of a variety of healthcare professionals in the course of patient care, using diverse methods. Green et al was among the first to study the information needs of residents. The focus in residents as study group to analyze profiles of information needs was interesting because of their lack of clinical experience [2]. The study was performed in a university-based primary care internal medicine program where residents were interviewed after each patient encounter to determine whether they had any remaining clinical questions. The results showed that residents identified approximately 2 questions for every 3 patients, and the most frequent types of questions were related to therapy or diagnosis. Closer analysis of the questions raised by residents revealed that only 80% of these questions were pursued, most commonly by consulting textbooks, original articles, or attending physicians. More interestingly, by performing statistical analysis, the authors found that residents' belief that the patient expected the answer and their fear of malpractice exposure strongly influenced information pursuit. Lack of time and forgetting the question were the most frequent reasons for failing to pursue unanswered questions. These results greatly impacted the design of curricula to assist medical students to be more equipped to answer questions arising in the course of care.

Another interesting study conducted by Ely's group analyzed patterns of questions asked by physicians with the purpose of facilitating the development of knowledge bases for physicians and healthcare professionals [3]. The authors visited doctors office for two and half days and collected their questions. Results showed that questions about drug

prescribing, obstetrics and gynaecology and adult infectious disease were most common and comprised 36% of all questions asked. The taxonomy of generic questions included 69 categories; the three most common types, comprising 24% of all questions, were "What is the cause of symptom X?" "What is the dose of drug X?" and "How should I manage disease or finding X?" Answers to most questions (64%) were not immediately pursued, but, of those pursued, most (80%) were answered. Doctors spent an average of less than 2 minutes pursuing an answer, and they used readily available print and human resources. Clearly, those unanswered questions represent great knowledge gap and could lead to suboptimal clinical decisions. Although no statistical results were obtained by this study, these results were helpful in influencing developers to re-think the design of clinical decision support systems.

While realizing the information needs of physicians at point of care and the urgency of providing knowledge to unanswered questions, researchers also saw the inefficiency of information tools that are presented to clinicians [4]. Textbooks, journals and other paper based information tools were not adequate for answering the questions that arise: textbooks are usually out of date and the "signal to noise" ratio of journals is too low for them to be practically useful in daily practice. In fact, some researchers seen the need of new computer systems that would be able to extract and present clinical knowledge and evidence with unprecedented speed and relevance. Although vast progress has been made to integrate CDS systems into clinicians' daily workflow, we haven't seen dramatic increase of adoption rate of computer systems, due to a variety of reasons.

More recently, a systematic analysis of clinical questions revealed that more than two-thirds of physician questions fell into one of five competencies: cause of a clinical finding, test selection, prevention, treatment selection and prognosis [5]. In addition to benefiting educators in developing programs that directly address the information needs and questions of learners, it could greatly facilitate system developers in designing knowledge bases and corresponding interfaces.

In summary, by reviewing literature spanning two decades regarding physicians' information needs, it was obvious that information needs, measured by frequency of questions raised, has stayed the same in the past two decades or so. Granted, the increased medical complexity could be a contributing factor that masked the accomplishment that has been made in improving medical information systems. However, with current rate of unanswered clinical questions and the corresponding clinical knowledge gap, challenges still remain in satisfying the physicians' information needs and improving the clinical outcome.

Physicians' Information Seeking Behavior

Understanding the information seeking process of physicians is critical for designing CDS systems that have higher adoption rate. An array of studies have investigated the behaviour of physicians when confronted with unanswered questions. They mainly checked the frequency of information seeking, resources being utilized during the process and obstacles that prevent physicians from pursuing answers in clinical settings. By reviewing the literature, it has become clear that primary care physicians seek answers to only a limited number questions [6-8]. One of the major reasons for this behavioral

pattern is the time factor, as physicians are typically under enormous pressure when attending patients.

Regarding the motivation for information seeking in clinical settings, different studies have presented interesting findings and hypothesis. Herma et al reported that independent predictors of information-seeking behavior seemed to be 1) the urgency of a patient problem and 2) the expectation that a clear answer existed [7]. The authors identified two phases of information seeking: whether information is sought at all depends on the expected benefits, and the method of seeking is influenced by the expected costs of various search strategies. The obstacles and difficulties encountered by physicians while seeking information include a lot of irrelevant material, difficulty in finding correct search terms, inefficient indexes in books and journals, and badly organized volumes in their own practice. These difficulties were categorized according to five steps: acknowledge a gap in information, formulate a question, seek relevant information, formulate an answer, and apply the answer to patient care. These observations are also confirmed in several other research reports [8, 9, 10]

In another literature review, the authors reached interesting conclusions regarding the categories of questions encountered by doctors at point of care [8]. Specifically, 60% of the questions are simple (that is, only one concept) such as the dose of a drug. We observed that doctors should be comfortable answering questions such as these with a minimal amount of training on computers. For these cases, questions are easily formulated and a simple search would suffice in finding the answer. However, the remaining 40% are relatively complex questions and often require multiple steps in cognitive thinking, knowledge summarization, logical deduction and finally reaching

strategic plans and conclusions based on evidence found. Extensive literature searching and information gathering are required to arrive at sensible conclusions, which is probably the reason why most of those complicated questions remain unanswered in clinical settings.

Current Progress in Clinical Decision Support Systems

Based on findings of previous literature reviews, it is clear that physical books and journals are still the favorite resources when it comes to information seeking in clinical settings. However, with the explosion of medical knowledge and evidence over the past two decades, it is also clear that innovative approaches of seeking information have to be explored. With the introduction of personal computers late last century, and the smart handheld devices and the wide adoption and use of smart wearable more recently have changed our perceptions in how information could be collected, managed and sought after. Here, I will review several recent studies and reports regarding the progress made in clinical decision support systems as well as their influence in decision making at point of care.

A literature review published by Pluye et al summarized most of key research focusing on information retrieval of clinical information before 2005 and their impact on information seeking by physicians [11]. Impact was defined as an effect or influence of the use of clinical information-retrieval technology. They found out that over one-third of the information searched by information retrieval technologies had a positive impact on physicians. However, results from several studies did not support greater impact of information technology as compared to other sources of information, notably printed

educational material. The general conclusion was that modern information retrieval technology may affect physicians information seeking behavior as well as the outcome, but further research needs to be conducted to examine its impact in everyday practice.

Peter et al reported a study that associated the adoption of a clinical knowledge support system with improved patient safety, reduced complications and shorter length of stay in acute care hospitals in US [12]. The authors compared hospitals with online access to UpToDate resource with other acute care hospitals on a variety of performance dimensions such as quality and efficiency. Prespecified outcomes were risk-adjusted mortality, complications, the Agency of Healthcare Research and Quality Patient Safety Indicators and hospital length of stay among Medicare beneficiaries. Results of statistical analysis showed that hospitals with access to UpToDate were associated with significantly better performance than other hospitals in the Thomson database per each of the metrics mentioned before. This research complements the previously mentioned on in that it demonstrates the impact of technology on clinical outcomes. However, this study was retrospective and observational and could not fully account for additional feature at the included hospitals that may have contributed towards better health outcomes. Another similar study basically confirmed the conclusion in this study, stating that patients admitted to hospitals using UpToDate had shorter lengths of stay than patients admitted to non-UpToDate hospitals overall based on six prespecified conditions [13]. Further, patients admitted to UpToDate hospitals had lower risk-adjusted mortality rate for 3 of the 6 conditions.

In a separate study, Patel et al compared the speed, validity, and applicability of two different protocols for searching the primary medical literature [14]. The two

protocols investigated were MEDLINE first versus pre-appraised resources first. The findings indicated that searching MEDLINE was perceived by residents to take longer than pre-appraised resources, although residents needed both MEDLINE and pre-appraised resources to answer questions generated during clinical care of patients. The implication of this study is that though pre-appraised resources were useful in answering clinical questions, access to the primary literature was still required to answer the questions; this observation may serve as an essential component of training in information skills provided to clinicians.

UpToDate and MEDLINE are two of the most popular clinical knowledge resources used by physicians, and Arjen et al compared these two resources extensively in clinical settings [15]. A variety of outcomes, including the percentage of answers retrieved by these information resources, searching results with regard to different medical topics and time spent searching for an answer using these resources respectively, were evaluated. The study setting was internal medicine and they found that UpToDate answered more questions than PubMed on all major medical topics, but a significant difference was detected only when the question was related to etiology or therapy. Also, it typically took less time for physicians to answer a question using UpToDate than PubMed, although the result was not statistically significant. They concluded that specialists and residents in internal medicine generally use less than 5 minutes to answer patient-related questions in daily care and more questions are answered using UpToDate than PubMed on all major medical topics.

Aiming at providing easy-to-access tools for physicians at point of care, question-answering services were frequently developed and evaluated at clinical settings to

analyze effectiveness in satisfying information needs of physicians. Elizabeth et al described that physicians usually found it difficult to directly apply research in their practices [16]. The authors implemented a question-answering service trying to ease the way of applying research evidence to point-of-care settings. They found that focus group participants appreciated critically appraised summaries of evidence and stressed the time-saving benefit of the service. Clinicians without a medical training were least confident in applying evidence. Attitudes to research were positive, but concern was expressed about its potential misuse for political purposes. Therefore, education about the use of research may help clinicians to be more evidence based. Another study evaluated the question-answering service of the information center of the Emma Children's Hospital AMC to determine the role of a specialised information center in an academic children's hospital, identifying the appropriate resources for the service and potential positive effects [17]. They concluded that taking over the task of providing readily available, good quality information that healthcare professionals can use to inform their patients will lead to less time investment of these more expensive staff members. Additionally, a specialised information service can anticipate the information need of parents and persons involved with the pediatric patient. Such a service improves information by providing with relatively simple resources that has the potential to improve patient and parent satisfaction and coping and medical results. Therefore, a specialized information center is a valuable and affordable asset to an academic children's hospital.

Another very interesting study performed an analysis of whether online discussion forum help establish social network of practitioners and thus facilitate the communication and knowledge seeking during point of care [18]. The study was performed among

emergency practitioners as they have very little time in responding to unanswered questions during practice and have to seek answer to questions asynchronously with their working pace. Content analysis indicated that an online discussion forum could be useful for seeking various categories of knowledge across a range of content topics. It is possible that formal facilitation sessions at each site and longer exposure to the tool may assist in building trust in this online community of practice and may increase network density measures. The volume of sharing events linked with the seeking events suggests that this medium presents another alternative for practitioners looking for evidence-based information to support their practice. The authors also stated that a follow-up study is required to determine if practitioners would indeed transfer the knowledge gained in this environment to their practice setting.

Infobuttons are decision support tools that provide linked within electronic medical record systems to relevant content in online information resources [19]. They gained significant attractions within clinical communities as they aim to help clinicians promptly meet their information needs. Guilherme et al performed a study in 2008 evaluating whether infobuttons links that direct to specific content topics ("topic links") are more effective than links that point to general overview content ("nonspecific links"). They found out that subjects with access to topic links spent significantly less time seeking information than those only with access to nonspecific links. It is unclear whether the statistical difference demonstrated will result in a clinically significant impact. However, the overall results confirm previous evidence that infobuttons are effective at helping clinicians to answer questions at the point of care and demonstrate a modest incremental change in the efficiency of information delivery for routine users of this tool.

Finally, as smart handheld devices are becoming increasingly important for information seeking, a recent study evaluated the effectiveness of wireless handheld computers for online information retrieval in clinical settings and the role of MEDLINE in answering clinical questions raised at the point of care [20]. They used MD on Tap, an application for handheld computers, as a reference tool to evaluate the information seeking process. They concluded that handheld computers with internet access are useful tools for healthcare providers to access MEDLINE in real time and MEDLINE citations can answer specific clinical questions when several medical terms are used to form a query. The MD on Tap application is an effective interface to MEDLINE in clinical settings, allowing clinicians to quickly find relevant citations. This study outlined a potential of using mobile devices in clinical settings for information seeking.

Evaluation of A Clinical Knowledge Summary System

Project Background

As discussed in the introduction and literature review sessions, physicians raised approximately two questions for every three patients seen in both outpatient and inpatient settings. In over 70% of the cases, these questions were not answered, due to various reasons including lack of time, lack of belief that they would locate the information in relatively short time, lack of education on how to efficiently and effectively retrieve medical information especially with the new computer technology, and so on. To a large extent, information needs are related to gaps in medical knowledge that providers need to fill in order to make, confirm, or carryout patient care decisions. Ultimately, knowledge

gaps lead to suboptimal decisions, lowering the quality of care. In addition, unanswered clinical questions represent important missed opportunities for self-directed learning and possibly for changes in practice patterns. The increasingly rapid pace at which medical knowledge is produced is likely to aggravate this problem.

Numerous online health knowledge resources have become available, especially with the advent of the web. Although knowledge resources have the answers to most clinicians' information needs, major barriers hinder a more efficient and effective use of these resources. To overcome these barriers, tools are needed to help providers quickly identify relevant, high quality knowledge in the context of need.

"On demand" access to summarized evidence and best practices has been considered a sound strategy to satisfy clinicians' information needs and enhance decision-making. Effective and efficient use of online knowledge resources is limited by barriers, such as lack of time, doubt that an answer exists, and poor searching skills. As a result, clinicians seldom use these resources to fulfill their information needs. According to a systematic review, clinicians use knowledge resources from 0.3 to 9 times a month.

To that end, our team is motivated to provide easier and more organized approaches of accessing and searching information online. In this project, we designed and evaluated methods to improve clinician decision-making by generating clinician-tailored and patient-specific knowledge summaries (Figure 1). Knowledge summaries consists of semantic fragments (i.e., small units of text that provide meaningful information) that are relevant to a clinician's patient-specific information needs. Semantic fragments are extracted from online knowledge resources (e.g., PubMed, UpToDate) leveraging data in the patient's electronic health record (EHR); and tailored using cognitive and contextual

factors that contribute to clinicians' information needs and information-seeking behavior. We are pursuing this kind of decision support because clinicians often raise information needs in the course of patient care and these needs are largely unmet. Unmet information needs are missed opportunities for self-directed learning and improved patient care. We hypothesized that given sufficient convenience and relevance, this form of decision support will help providers meet their information needs and enhance decision-making. Answers to clinicians' questions can often be found in online health knowledge resources. But significant barriers limit the use of these resources for patient care, especially clinicians' lack of time. An increasingly popular approach to lowering these barriers is to provide context-sensitive "infobutton" links within EHR systems. Based on the clinical context, infobuttons anticipate clinicians' information needs and provide relevant links to knowledge resources. Infobuttons are simple to implement and are being increasingly adopted by knowledge resources and EHR systems. Infobuttons do a good job helping clinicians' meet simple information needs, especially drug reference information while prescribing or reviewing a patient's medications. Infobuttons are less optimal when (i) answers cannot be easily found without substantial cognitive effort scanning the information retrieved; and (ii) the information need is associated with data not displayed on the EHR screen.

Project Methodology

System Architecture

The clinical decision support system we designed consists of two major components: backend information extraction, retrieval and ranking component and frontend information representation component.

Backend algorithm development

The algorithm and service which generates relevant sentences and knowledge were developed and published in a previous study and thus will only be mentioned briefly here [21]. The backend system to generate knowledge summaries is built as a pipeline that combines the following natural language processing (NLP) tools and resources: Unified Medical Language System (UMLS) Metathesaurus for extracting concepts, SemRep for extracting semantic predications, and the TextRank algorithm for ranking the sentences that contain those semantic predications. The whole pipeline consists of four major steps: query processing, information retrieval, information extraction, and sentence ranking. One important note is that the algorithm breaks down the abstract of articles from PubMed into individual sentences and information extraction process is thus taking place at the sentence level. At the end, two case studies were used to evaluate the effectiveness of the system: depression and Alzheimer's disease. The strength of the sentence retrieved by the system was rated based on four attributes: relevant, conclusive, comparative and contextually-constrained. Overall, the system retrieved a high rate of relevant sentences (96% for depression and 88% for Alzheimer's disease). This is highly desirable, given that clinicians' lack of time is one of the main barriers to using knowledge resources at the point of care. Sentence rank was not significantly associated with relevancy. This finding is possibly due to the overall high relevancy found in the

study, which leaves little room for improvement. Nevertheless, relevancy could be further enhanced by improving the precision of SemRep. Importantly, only about one-third of the sentences retrieved included a conclusive statement. Retrieving conclusive sentences is challenging but could be approached through a combination of methods such as sentence position, comparative predications, and linguistic cues such as hedges. In that study, conclusive sentences were located much closer to the end of the abstract than non-conclusive sentences. In addition, structured abstracts include a Conclusion section that is typically composed of conclusive sentences. Although only a small number of Medline citations contain a structured abstract, the percentage of structured abstracts in Medline increased from 2.4% in 1992 to 20.3% in 2005. Finally, sentences with treatment and comparative predications may be more likely to be conclusive sentences. The knowledge and information revealed in the study were critical in designing the representation interface as well as in evaluating the testing the overall performance of the system.

Web interface design and implementation

The other major component of the system is the representation layer which we designed to be a web system. The overall design philosophy is to make the interface intuitive and simple to use. Information overloading is another barrier for physicians' information seeking as they can easily be drowned with overwhelmingly large amount of information being presented to them at point of care. We used a highly interactive website design tool Balsamiq (<http://balsamiq.com/>) to mockup our interface design and share with team members.

The web interface is a simple but highly interactive representation as user has many options of how they would like the information to be presented. An iterative design strategy was implemented in that design cycles were kept intentionally short and improvements were built up gradually based on evaluation results. On the technical side, the interface was implemented mainly in Javascript as well as its associated jquery library.

Case Vignettes Design

Eight case vignettes were carefully designed including rheumatoid arthritis, diabetes mellitus, vesicoureteral reflux, chronic obstructive pulmonary disease, urethritis, congestive heart failure, atrial fibrillation and depression. These vignettes intentionally mimic a clinical setting where the testing subject is trying to treat the patient referred in the case vignette. The vignette text was presented at the beginning of every evaluation session to bring the testing physician into clinical context. Note that the case vignettes used during the study were all from standard resources that have been proved to be effective and manageable by previous studies.

Post-Evaluation Questionnaire Design

At the end of each vignette session, physicians are asked to complete a questionnaire that summarized the evidence gathering experience. The questionnaire include the following categories of questions: 1) what is the physician's prior experience regarding the vignette; 2) are they successful in locating the evidence that is needed to answer the treatment question in the vignette and if so what are those; 3) how helpful is the evidence/knowledge from different sources. Most of the questions require nominal

answers which are normally classified into five different levels. At the very end of the study, physicians are asked to complete a final questionnaire for rating different features in the knowledge summary tool that we designed. Note that both questionnaires are attached in the appendix session of this paper.

Subject Recruitment

Physician subjects were recruited both at our collaboration site (University of Utah) and our home site (University of North Carolina at Chapel Hill) independent of their specialties. Our study protocol was approved by the Institutional Review Board (IRB) at both universities. The total targeting sample size was 20, with 13 from University of Utah and 7 from UNC-Chapel Hill. Recruitment strategies include direct contact, email recruiting and advertisement at medical conferences and meetings.

Study Design

Each study session lasted for approximately 40 minutes in length including a warm-up session and two formal testing sessions. A study script was designed to ensure the smoothness of the evaluation session. Hypercam 2 was used to capture the computer screen as well as audio during the study. At the start of the study, physician was presented with a relatively simple case vignette with the purpose of getting themselves familiar with the system. A series of straightforward questions were asked to assist the process of navigating through the tool (e.g., “what is the title of the article?”, “what would you do if you want to read more systematic review articles?”). The physician was asked to speak aloud as they proceed with the warm-up session. Two more case vignettes were successively presented with the main aim of answering the embedded treatment

questions within the vignette text. Two search methods (knowledge summary and manual search on PubMed and UpToDate) were compared in the study and each case vignette was randomly assigned with a search method before the test. The subjects were not required to voice their thoughts during the formal testing sessions but they were encouraged to highlight the information they were focusing on at the moment as they went through. Also, we asked the subjects to clearly signal the starting and the ending moment of each session so that we could accurately record the session time later on. At the end of each testing session, we presented the subject a questionnaire to record their final decisions regarding the vignette as well as their comprehensive impression of the whole searching experience. At the very end of the study, we further provided an additional questionnaire gathering their opinions regarding the different features we designed for the system. As part of iterative design process, our research team regrouped after every few sessions to discuss feedback and suggestions from subjects and possible improvement points and aspects. Therefore, to verify the possible improvement aspects of the system, we typically initiated a quick discussion session at the end to gather opinions and general comments.

Data Analysis and System Improvement

As mentioned previously, the whole study session was screen-captured and audio-recorded by using the software Hypercam 2. Each recorded video was studied extensively by all the team members to extract valuable feedbacks from the subject. Important searching behavior and pattern were typically revealed from the video and possible improvement points were extracted and implemented after each round of review session.

Knowledge Summary (back)

Filters

- ☐ Biological Response Modifier Therapy (40)
 - ☐ abatacept (32)
 - ☐ anakinra (6)
- ☐ Disease-modifying antirheumatic drugs (DMARDs) (292)
 - ☐ azathioprine (5)
 - ☐ hydroxychloroquine (10)
 - ☐ leflunomide (12)
 - ☐ methotrexate (142)
 - ☐ sulfasalazine (14)
 - ☐ tofacitinib (18)
- ☐ Glucocorticoids (15)
 - ☐ prednisone (10)
- ☐ Nonsteroidal antiinflammatory drugs (NSAIDs) (37)
 - ☐ celecoxib (3)
- ☐ Tumor necrosis factor (TNF) inhibitors (116)
 - ☐ adalimumab (26)
 - ☐ etanercept (26)
 - ☐ infliximab (22)
 - ☐ rituximab (23)

UpToDate (276 sentences)

Initial treatment of moderately to severely active rheumatoid arthritis in adults

INTRODUCTION "These observations regarding the course of disease and the efficacy of current therapeutic approaches, coupled with limits in the ability to accurately identify individuals with a poor prognosis, support our view that every patient with established active RA should be treated with DMARDs at the earliest stage of disease, ideally within three months of symptom onset."

DEFINITION OF MODERATELY TO SEVERELY ACTIVE RA "Evidence of inflammation on plain radiography of the hands, wrists, or feet, such as osteopenia and/or periarthritis swelling."

Pretreatment interventions "We take a number of important precautions before using DMARDs, including laboratory assessment (complete blood count, serum creatinine, aminotransferases, and other studies as indicated), evaluation of comorbidities, vaccinations, and screening for hepatitis C, hepatitis B, and latent tuberculosis infection."

MTX versus initial combination therapy "Combinations of MTX with either sulfasalazine (SSZ) or hydroxychloroquine (HCQ), with both SSZ and HCQ, or with a biologic DMARD also have proven efficacy for initial treatment of highly active RA in patients with poor prognostic features."

Systematic Reviews (37 citations)

[Effect of biotherapies on fatigue in rheumatoid arthritis: a systematic review of the literature and meta-analysis, *Rheumatology \(Oxford\)*, 2012.](#) Few studies reported the impact of biotherapies on fatigue. The effect of biotherapies on fatigue in RA is small.

[Safety of medium- to long-term glucocorticoid therapy in rheumatoid arthritis: a meta-analysis, *Rheumatology \(Oxford\)*, 2009.](#) Medium- to long-term glucocorticoid therapy in RA is associated with limited toxicity compared to placebo.

[Efficacy of resistance exercises in rheumatoid arthritis: meta-analysis of randomized controlled trials, *Rheumatology \(Oxford\)*, 2012.](#) Resistance exercise in RA is safe, and the improvement in most outcomes was statistically significant and possibly clinically relevant for RA disability.

[Trends in cardiovascular mortality in patients with rheumatoid arthritis over 50 years: a systematic review and meta-analysis of cohort studies, *Rheumatology \(Oxford\)*, 2009.](#) Our results show that RA is associated with a 60% increase in risk of CV death compared with general population. Despite changes in RA course over the past decades, SMR for CV death has not changed. This suggests that targeting a reduction in CV mortality should still be considered as a major issue in RA.

Clinical Trial (110 citations)

[Golimumab in patients with active rheumatoid arthritis after treatment with tumour necrosis factor alpha inhibitors \(GO-ALTER study\): a multicentre, randomised, double-blind, placebo-controlled phase III trial, *Lancet*, 2009.](#) (Industry funding) [n=461]. Golimumab reduced the signs and symptoms of rheumatoid arthritis in patients with active disease who had previously received one or more TNFalpha inhibitors.

[Effect of interleukin-6 receptor inhibition with tocilizumab in patients with rheumatoid arthritis \(OPTION study\): a double-blind, placebo-controlled, randomised trial, *Lancet*, 2008.](#) (Industry funding) [n=623]. Tocilizumab could be an effective therapeutic approach in patients with moderate to severe active rheumatoid arthritis.

[A pilot study of potassium supplementation in the treatment of hypokalemic patients with rheumatoid arthritis: a randomized, double-blind, placebo-controlled trial, *J Pain*, 2008.](#) (Industry funding) [n=717]. This article reports a trial evaluating the effect of potassium supplementation in the treatment of pain in hypokalemic patients with rheumatoid arthritis. The elevated serum cortisol and potassium values in the treatment group correlate negatively with patient's assessment of pain intensity, reflecting an anti-pain effect for potassium supplementation.

[Tofacitinib or adalimumab versus placebo in rheumatoid arthritis, *N. Engl. J. Med.*, 2012.](#) (Industry funding) [n=717]. In patients with rheumatoid arthritis receiving background methotrexate, tofacitinib was significantly superior to placebo and was numerically similar to adalimumab in efficacy. (Funded by Pfizer, ORAL Standard Clinical Trial no. number NCT00855881)

(A)

KNOWLEDGE SUMMARY (BACK TO VIGNETTES)

Filters

- ☐ Biological Response Modifier Therapy (40)
 - ☐ abatacept (32)
 - ☐ anakinra (6)
- ☐ Disease-modifying antirheumatic drugs (DMARDs) (290)
 - ☐ azathioprine (5)
 - ☐ hydroxychloroquine (10)
 - ☐ leflunomide (12)
 - ☐ methotrexate (144)
 - ☐ sulfasalazine (14)
 - ☐ tofacitinib (18)
- ☐ Glucocorticoids (15)
 - ☐ prednisone (10)
- ☐ Nonsteroidal antiinflammatory drugs (NSAIDs) (37)
 - ☐ celecoxib (3)
- ☐ Tumor necrosis factor (TNF) inhibitors (116)
 - ☐ adalimumab (26)
 - ☐ etanercept (26)
 - ☐ infliximab (22)
 - ☐ rituximab (23)

UpToDate Excerpts

☒ Initial treatment of moderately to severely active rheumatoid arthritis in adults (10 sentences)

☒ Treatment of rheumatoid arthritis resistant to initial DMARD therapy in adults (10 sentences)

Systematic Reviews (37 citations)

[Effect of biotherapies on fatigue in rheumatoid arthritis: a systematic review of the literature and meta-analysis, *Rheumatology \(Oxford\)*, 2012.](#) Few studies reported the impact of biotherapies on fatigue. The effect of biotherapies on fatigue in RA is small.

[Safety of medium- to long-term glucocorticoid therapy in rheumatoid arthritis: a meta-analysis, *Rheumatology \(Oxford\)*, 2009.](#) Medium- to long-term glucocorticoid therapy in RA is associated with limited toxicity compared to placebo.

[Efficacy of resistance exercises in rheumatoid arthritis: meta-analysis of randomized controlled trials, *Rheumatology \(Oxford\)*, 2012.](#) Resistance exercise in RA is safe, and the improvement in most outcomes was statistically significant and possibly clinically relevant for RA disability.

[Trends in cardiovascular mortality in patients with rheumatoid arthritis over 50 years: a systematic review and meta-analysis of cohort studies, *Rheumatology \(Oxford\)*, 2009.](#) Our results show that RA is associated with a 60% increase in risk of CV death compared with general population. Despite changes in RA course over the past decades, SMR for CV death has not changed. This suggests that targeting a reduction in CV mortality should still be considered as a major issue in RA.

[Impact of total shoulder arthroplasty on generic and shoulder-specific health-related quality-of-life measures: a systematic literature review and meta-analysis, *J Bone Joint Surg Am*, 2012.](#) Total shoulder arthroplasty leads to significant improvements in scores for function and pain. Shoulder-specific measures of function and quality of life were also improved.

Clinical Trial (110 citations)

[Golimumab in patients with active rheumatoid arthritis after treatment with tumour necrosis factor alpha inhibitors \(GO-ALTER study\): a multicentre, randomised, double-blind, placebo-controlled phase III trial, *Lancet*, 2009.](#) (Industry funding) [n=461]. Golimumab reduced the signs and symptoms of rheumatoid arthritis in patients with active disease who had previously received one or more TNFalpha inhibitors.

[Effect of interleukin-6 receptor inhibition with tocilizumab in patients with rheumatoid arthritis \(OPTION study\): a double-blind, placebo-controlled, randomised trial, *Lancet*, 2008.](#) (Industry funding) [n=623]. Tocilizumab could be an effective therapeutic approach in patients with moderate to severe active rheumatoid arthritis.

[A pilot study of potassium supplementation in the treatment of hypokalemic patients with rheumatoid arthritis: a randomized, double-blind, placebo-controlled trial, *J Pain*, 2008.](#) (Industry funding) [n=717]. This article reports a trial evaluating the effect of potassium supplementation in the treatment of pain in hypokalemic patients with rheumatoid arthritis. The elevated serum cortisol and potassium values in the treatment group correlate negatively with patient's assessment of pain intensity, reflecting an anti-pain effect for potassium supplementation.

[Tofacitinib or adalimumab versus placebo in rheumatoid arthritis, *N. Engl. J. Med.*, 2012.](#) (Industry funding) [n=717]. In patients with rheumatoid arthritis receiving background methotrexate, tofacitinib was significantly superior to placebo and was numerically similar to adalimumab in efficacy. (Funded by Pfizer, ORAL Standard Clinical Trial no. number NCT00855881)

(B)

Figure 1. The figures shown here reflect the original interface design (A) and the improved interface after the first round of testing session (B).

User Interface Description

Figure 1(A) shows the original interface design before iterative testing. Three content boxes were shown on the right, whereas the filtering medication box was shown on the

left. In the parenthesis after each medication shows the number of sentences and articles retrieved for that particular filter. This was designed to assist physicians estimate the amount of information available for each treatment alternative and thus the information consumption time. In the UpToDate content box, when hovering over each sentence, a callout box will be presented within which we show the proceeding and following sentence with regard to the selected sentence. It was designed to provide more contextual information to physicians. Similarly, when hovering over article titles in Systematic Review and Clinical Trial boxes would present callout boxes within which the results and conclusion part of the article were presented. In all cases, clicking on the sentence would lead user to corresponding articles or sentences. Figure 1(B) shows the improved interface design based on user feedback and discussions within research group. Changes mainly took place in UpToDate content box which was the most used information reference during testing sessions. The titles of UpToDate articles were presented first while hiding all sentences to accelerate the scanning process of physicians. Furthermore, callout boxes were replaced with “show more” button as callout boxes usually interfered with user’s reading process.

Project Results and Discussion

This study was not intended to test any hypothesis based on statistically significant numbers, but rather to observe the physician behavior as they interact with the system to improve the algorithm and system design. Recorded video was reviewed and studied to reflect on any comments, suggestions, frustration that testing subjects may have during the interview session. At the end, post-session questionnaires were also collected and

reviewed for further feedback physicians had on each of the case vignette. Findings were listed and discussed in much more detail below.

Simple and Intuitive Interface Makes the Knowledge Tool Easier to Adopt

In general, physicians were very quick in adjusting to the new interface and were able to navigate through the system with ease after the warm-up session. Several physicians explicitly expressed the impact of simple interface design on more efficient information seeking at the point of care, with constrained time limit. The three content boxes on the main interface were obvious enough to the physicians allowing them to jump right into the content resource that they were most interested in. Almost all the physicians found it helpful to have the full screen as well as the “more” button that would show more contents when clicked. However, two physicians also pointed out that other two content boxes are too much distraction when they were trying to focus on one box. They suggested that instead of showing all three boxes at the landing page, it would be beneficial to show only one of the boxes and hide the other two while providing a means to access to them. They implied that it would mean less clicking and more focused on the core content.

Despite the quick pick-up of the content boxes, physicians were not so keen on filtering the contents using the medication panel on the left. At the beginning of the pilot study, the title of the left panel was designed as “Medication” and physicians found it difficult to realize the connection between the medications and the right side contents. When asked about the possible consequences of clicking the medications, several physicians responded that they had no idea. As a result, we changed the title of the left panel to “Filters” to clarify this functionality. After they clicked on one of the filters, they

immediately realized the reduced number of contents displayed on the right. The filter highlighting feature was important and critical for physicians to visualize the effect of filtering and the fact that the contents are displayed based on their selection of filters. Despite this change of title, physicians were still reluctant to use the filtering mechanism which was evidenced by lack of exploration during the study session. Most physicians were not even aware of some of the features embedded within the filtering box, such as “only” button that limit the selection only to the clicked medication and exclude all others, as well as the “clear” button that uncheck all the medications in order for physicians to restart their seeking process. Some of physicians did not possess deep knowledge in the area related to the case vignette entails and thus did not start by filtering the content, but rather self-educate themselves with the contents shown on the right. After a while of self-education, they were usually able to locate and click the relevant piece of information which would lead them directly to the corresponding resources. After following these steps, they usually stayed in that resource and utilized the searching functions provided by the particular site until they were either satisfied with the evidence gathered or frustrated with the process and gave up. Even physicians with relatively high technical skills spent very little time exploring the filtering feature which prompted us to investigate the reason for this behavioral pattern. When asked about this matter, one physician mentioned that it would be really helpful to specify the medication information in more detail, such as which medications the patient is already on and what are the alternatives. This information would trigger physician’s desire of streamlining their information seeking process by first clicking on the medication the patient is already on and successively try combinations of medications.

Furthermore, the numbers between the parenthesis are confusing to the physicians as they interact with the system. One physician suggested that we could consider adding the units after the number, such as articles or sentences. On another note, the numbers after the title of each content box were confusing to physicians as well because they overwhelmingly exceeded the actual number of articles/sentences displayed on the screen.

Physicians Use UpToDate More Frequently Than PubMed

It's no secret that most physicians prefer UpToDate site much more than PubMed because the information found in UpToDate are generally more actionable whereas PubMed resource is more research-oriented and thus is less useful at the point of care when timing is critical. We observed the very same trend in that physicians only explore systematic review and clinical trial contents during the warm-up session. During the actual evaluation, they all jumped directly to UpToDate content box, enlarged the box and started gathering information from there. In realizing this matter during the design stage, UpToDate box was intentionally placed at the bottom of the screen below systematic review and clinical trial boxes. However, after two interviews, it was clear that this design has flaws and often distracts and frustrates the physicians during the information seeking process. And as mentioned in the above session, some physicians even suggested that we should only display UpToDate content box in the landing page while providing buttons to access other content resources.

UpToDate Contents Need to Be More Cohesive

UpToDate sentences were extracted with text mining algorithms and ranked purely based on their relevance to the selected medications. The algorithm is completely agnostic of the location of the sentences within the original article. Therefore, this leads to the discontinuous flow of sentences extracted and displayed on the screen. During most of the sessions, physicians were presented with case vignettes that were outside of their expertise areas. Thus, most of them started by trying to read general materials regarding the disease situation and medications. Algorithmically, first few sentences are usually extremely relevant and actionable. However, they were overly specific which made them look out of context. Physicians usually kept scrolling down until they found the summary and conclusion section so that they could learn the gist of the article before jumping into treatment details. This observation suggested that we should add rules into the extraction algorithm so that more weight is placed on sentences from conclusion sections. However, this change is debatable upon further consideration since the desired target use cases will be physicians answering questions they came across within their expertise, in which case they are already familiar with general background and want direct case-related information.

Most Physicians Spend Small Amount of Time in Searching For Information

It is well-known that time is a critical factor when it comes to pursuing answers to questions encountered in clinical settings. This was further confirmed by our observation that if physicians were informed of the testing environment, they will usually spend between 10 and 15 minutes before they stopped either because they have gathered sufficient evidence for decision-making or they are frustrated with the seeking process

and ready to give up. This critical timing factor calls for more efficient content delivery system. It's been found that our algorithm is able to deliver highly relevant and actionable items particularly to those with specialty related to case vignettes.

Physician Specialty Will Affect Their Perception of the System

We've consistently found that the seeking behavior is highly related to the physicians' specialty. Specifically, if physicians were not familiar with the disease situation described in the vignette text, they would start with summary section of the article, followed by more specific and actionable items. However on the other hand, physicians who were already familiar with the case would start from the first sentence. This observation suggests that we should collect more information regarding the physician's background, such as how long they have graduated from medical school, their years of experience, their own perception of technical level and so on. This information would help us normalize the quantitative results we measured such as session time, etc.

Summary

In summary, we have designed and developed a clinical knowledge summary system that intends to extract the relevant information and evidence from various medical resources (including UpToDate and PubMed) and present them to physicians at point of care. As mentioned in literature review session, it has been shown that physicians raised approximately two questions in every three patients they see. Around 50% of those questions were not even pursued due to various factors including limited time and lack of confidence that the answer could be found. These unanswered questions caused

knowledge gaps and lead to unsatisfactory clinical outcomes. The recent information explosion with the emergence of computer technology only makes it even more difficult to sift through the ocean of information and find the desired evidence, especially given the time constraint at the point of care. With that in mind, we started off with the goal of providing a simple, straightforward, easy-to-use and yet highly accurate knowledge summary tool that could automatically extract relevant information from medical resources given physician's searching criteria. Based on the feedback we received from physicians, we were successful in designing an intuitive interface which minimized the presentation of irrelevant information. However, the key features must be further refined to improve information access and facilitate decision making during patient diagnosis and treatment by physicians.

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APPENDIX A: POST_VIGNETTE QUESTIONAIRE

1. What is your perceived complexity of the vignette? (1=least complex; 5=most complex)

2. What is your experience managing patients like the one in the vignette? (1=least experience; 5=most experience)

3. What is your final decision for this patient?

4. Could you please summarize in 1-2 sentences the gist of the evidence that guided your decision?

5. What other types of information could have helped you understand the gist?

6. The information I found 1=strongly disagree 5=strongly agree

	1	2	3	4	5
Enhanced my decision-making					
Increased my knowledge					
Helped me recall something I had forgotten					

Increased my level of uncertainty					
Frustrated me with the information-seeking process					
Increased my confidence in making the right decision					
Improved my comfort in managing this patient					
Made me more likely to refer this patient to a specialist					
Surprised me					
Took significant effort scanning / skimming information					

7. Rate the following types of information found for this vignette (1=Not at all; 5=A great deal; NA = not applicable):

	Helped with my decision	Updated my knowledge	Required significant effort scanning / skimming
Randomized			

trials			
Systematic reviews			
UpToDate			

APPENDIX E: POST-EVALUATION QUESTIONAIRE

1. How useful do you find each type of information?

1=Not useful

5=Very useful

	1	2	3	4	5
1. Article titles					
2. Study sample size					
3. Study funding source					
4. Link to abstract on PubMed					
5. Treatment filters					
6. Zoom button					
7. Hovering over UpToDate sentence brings up surrounding sentences					
8. Clicking on UpToDate sentence takes to sentence within UpToDate					

The screenshot displays a knowledge summary interface with several panels and annotations:

- Medication** (show all): A list of medications with checkboxes. Annotations include:
 - Treatment filters**: Points to the 'Disease-modifying antirheumatic drugs (DMARDs) (151)' category.
 - UpToDate document title**: Points to the title 'Initial treatment of moderately to severely active rheumatoid arthritis in adults'.
- Systematic Reviews (14 citations)**: A list of reviews. Annotations include:
 - Article titles**: Points to the title 'Effect of biotherapies on fatigue in rheumatoid arthritis: a systematic review of the literature and meta-analysis'.
 - Funding source type**: Points to the text 'Funded by Pfizer; ORAL Standard ClinicalTrials.gov number, NCT00853385'.
- Clinical Trial (58 citations)**: A list of clinical trials. Annotations include:
 - Zoom button**: Points to a button icon.
 - Link to abstract on PubMed**: Points to a link.
 - Sample size**: Points to the text '[623 patients]'.
- UpToDate (144 sentences)**: A list of sentences. Annotations include:
 - Hovering over sentence brings up dialogue with surrounding sentences**: Points to a sentence about 'Approach to drug therapy'.
 - Clicking on sentence takes to sentence within UpToDate**: Points to a sentence about 'MTX versus other DMARDs'.

2. Do you have any other suggestions or comments regarding the knowledge summary [record the answer as opposed to writing]?