Implementing Clinical Practice Guidelines While Taking Account of Changing Evidence: ATHENA DSS, an Easily Modifiable Decision-Support System for Managing Hypertension in Primary Care

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This paper describes the ATHENA Decision Support System (DSS), which operationalizes guidelines for hypertension using the EON architecture. ATHENA DSS encourages blood pressure control and recommends guideline-concordant choice of drug therapy in relation to comorbid diseases. ATHENA DSS has an easily modifiable knowledge base that specifies eligibility criteria, risk stratification, blood pressure targets, relevant comorbid diseases, guideline-recommended drug classes for patients with comorbid disease, preferred drugs within each drug class, and clinical messages. Because evidence for best management of hypertension evolves continually, ATHENA DSS is designed to allow clinical experts to customize the knowledge base to incorporate new evidence or to reflect local interpretations of guideline ambiguities. Together with its database mediator Athenaeum, ATHENA DSS has physical and logical data independence from the legacy Computerized Patient Record System (CPRS) supplying the patient data, so it can be integrated into a variety of electronic medical record systems.

INTRODUCTION

Hypertension affects 50 million people in the United States and is the most prevalent chronic disease in most primary care practices. Hypertension is a major risk factor for coronary heart disease, congestive heart failure, and stroke; treating hypertension substantially decreases these risks. Yet, most patients' hypertension is inadequately controlled, and trends in drug prescribing for hypertension suggest that guidelines for drug therapy are not well followed. Computer reminders can improve physician concordance with clinical care rules.[1] However, reminders alone are not sufficient: Because management of hypertension can be complex, and because evidence about it evolves continually, a decision support system (DSS) must educate as well as remind, and it must be easily modifiable.

Barriers to Guideline Implementation. Clinical practice guidelines assist clinicians by summarizing current evidence and recommending best practices; however, they are not always effective in changing physician behavior. Guidelines for practice may predispose physicians to consider changing their behaviors, but specific strategies such as reminders and clinical opinion leaders are necessary to effect change in practice.[2, 3]

Operationalizing Guidelines. Electronic medical records (EMRs) and the increasing availability of computers in clinical settings have provided an opportunity to make guidelines available to clinicians for patient-specific use. Previous attempts to automate guidelines have shown that the published guidelines must be supplemented with additional information. For example, when Tierney et. al. automated the AHCPR heart failure guideline,[4] they found that it lacked explicit definitions for symptoms and adverse events, and did not account sufficiently for comorbid conditions. To operationalize it, they supplemented it with rules to implement such concepts as "optimum doses of ACE inhibitors." Based on their experience, they concluded that "translation" of guidelines is necessary for implementation.[4]

Many aspects of detection, evaluation, and treatment of high blood pressure have been extensively studied. The information from these studies has been assembled into one of the most thorough evidence-based guidelines available: The Sixth Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC6).[5] JNC6, however, does not provide detailed information on how to actually use the drugs it recommends, which requires a relatively sophisticated understanding of the clinical pharmacology of these drugs. Operationalizing the JNC6 rules in a DSS requires extensive translation.

Incorporating New Evidence. New data from large clinical trials often call for changes in medical practice. For example, recently, extensive evidence has appeared on the benefits of beta adrenergic

receptor antagonists in congestive heart failure, previously considered a contraindication to their use. Furthermore, JNC6 listed angiotensin converting enzyme (ACE) inhibitors as first line agents only for Type 1 diabetics with proteinuria; however, recent reports show that ACE inhibitors can improve cardiovascular outcomes in type 2 diabetics, beyond those expected from lowering blood pressure alone.[6] These important changes in the evidence underlying clinical guidelines require changes to the knowledge base (KB) rules. This paper describes the development of a DSS for management of hypertension. The DSS operationalizes the JNC6 rules in a KB that is easily browsable and modifiable by clinical domain experts.

DEVELOPMENT OF THE ATHENA* SYSTEM

ATHENA DSS is an automated DSS for guideline-based care. The DSS has been developed as part of the ATHENA (Assessment and Treatment of Hypertension: EvideNce-based Automation) project to evaluate the implementation of clinical practice guidelines for hypertension. ATHENA DSS has two components: a KB that models hypertension knowledge independently of its use, and a guideline interpreter that creates patient-specific treatment recommendations consistent with the knowledge in the KB. The KB was created with Protégé. Protégé is an application that a knowledge engineer, working with a physician expert in the clinical domain, uses to enter guideline knowledge into a KB. The knowledge is accessible through user-friendly customizable template frames.[7] Figure 1 shows the ATHENA DSS hypertension guideline KB's opening frame. Developers use drop-down menus to specify eligibility criteria, treatment goals, and risk groups. Similar frames allow entry of other information. We developed the KB with specifications for inclusion and exclusion criteria, and specifications for hypertension control with separate rules for diabetics and non-diabetics. The KB also contains drug therapy logic and recommendations based on the comorbidities and history of adverse effects. Because the knowledge is maintained separately from the guideline interpreter, physicians maintaining the ATHENA knowledge base can easily modify it as medical policies are changed or locally elaborated.

The guideline interpreter is a based on EON's general architecture for guideline-based decision support.[8] The EON system consists of (1) the guideline KB created with Protégé; (2) a guideline execution engine that interprets the KB; (3) a component to answer database queries for evaluating guideline criteria as they apply to a patient; and (4) a method that recognizes temporal patterns in patient data. An EON-based system determines (1) whether or not the guideline is applicable to the patient, (2) which portion of the guideline is applicable to the patient, and (3) whether the guideline's goal (e.g., target blood pressures) has been reached. Finally, EON (4) applies criteria for selecting one course of action over another and generates advisories about therapy. EON's model for the guideline reasoning is general enough that it can be used for any medical treatment guideline.

Figure 1. A Knowledge Base Screen.

Figure 2 (next page) shows a portion of the model for the hypertension guideline. The guideline consists of scenarios (rectangles), choice steps (diamonds), and action steps (ovals). When a scenario's criteria are satisfied, the program can take a choice step. Next, action steps specify the alternatives to the current therapy. Recommendations are displayed in the window of an EMR, or can be printed.

Clinical inputs. For each patient case, the program requires a diagnosis list, a medication list, blood pressures, and laboratory values (serum sodium, potassium, and creatinine, lipid profile, and urinary protein), and any allergy/adverse drug reactions. Diagnoses are converted from ICD-9 codes to hypertension-relevant disease categories. Drug doses are combined with information on the monthly number of dispensed pills to calculate a total daily dose. Integrating the software with the legacy system computerized patient medical record is key to a successful implementation at a clinical site.[9] Conflicts between the data models of legacy database systems and the data models assumed by a decision

* Athena in Greek mythology is a symbol of good counsel, prudent restraint, and practical insight.

support application occur frequently. ATHENA DSS addresses this problem by using a database mediator called *Athenaeum*,[9] which ensures that ATHENA DSS will be usable at institutions with varied EMRs. *Athenaeum* maps the legacy database onto the data model of the ATHENA DSS in two steps: (1) it makes a physical map that transforms a legacy database into a relational database, and (2) it makes a logical map that creates the temporal database and maps local terminology to the guideline terminology in the KB. *Athenaeum* uses a mapping model KB separate from the guideline KB.

Figure 2. Model of ATHENA guideline.

Clinical Decision Criteria. Many of the ATHENA clinical decision criteria are based on the following treatment principles: (1) Encourage appropriate health behavior changes to lower blood pressure. (2) Encourage use of beta adrenergic receptor antagonists and/or diuretics, which have established effectiveness in reducing long-term morbidity and mortality, except where another drug class is strongly indicated. (3) Select drug partners with favorable interactions, for example, diuretic and ACE inhibitor. (4) Avoid drug partners with potential adverse interactions, for example, ACE inhibitor and potassium-sparing diuretic (increases risk of hyperkalemia.) (5) Avoid drug partners that may not have added efficacy. (6) In patients with additional diseases, select drugs that are appropriate for dual effects, for example, alpha$_1$ adrenergic antagonist in men with benign prostatic hyperplasia. (7) Avoid drugs that may aggravate other health problems, for example, beta adrenergic receptor antagonists in patients with Type I diabetes who have recurrent hypoglycemia. (8) Alert clinicians to potential drug withdrawal syndromes, for example, from beta receptor antagonists or clonidine. The source of each rule is tracked in the program.

Translation from JNC6 to ATHENA. Table 2 of JNC6 (classification of blood pressure), and Tables 4 and 5 (risk stratification), map closely to ATHENA, as does Figure 8, Algorithm for Treatment of Hypertension. Table 9, which lists comorbidities to consider when individualizing therapy, is the basis for the drug-disease rules in ATHENA, with modifications as noted. Portions of JNC6, such as the discussion of public health challenges, serve as motivation for emphasizing in ATHENA the adequacy of control of blood pressure but are not explicitly included in the program. Future versions will incorporate recommendations to improve patient adherence to therapy (Table 13.) Note that some portions of JNC6 are omitted because they are irrelevant to ATHENA, which is designed for the vast majority of hypertensives, who are non-pregnant adult outpatients with Stages 1 and 2 primary hypertension.

ADVISORY FOR CLINICIANS

The output for display in the EMR includes *clinical assumptions* used in the reasoning, and *recommendations* for management. Clinical assumptions, including the most recent blood pressure measurements, can be modified, and the recommendations can be updated.

Clinical Assumptions. The patient's risk class as per JNC6 is calculated and displayed. Other data from the patient's record used in the reasoning process are available for viewing. The program also displays a patient's target blood pressure and a prominent message reporting whether or not his blood pressure is adequately controlled. The physician can enter additional blood pressure readings, and can designate a "typical" blood pressure on which the clinical management decision is to be based. The program recommends intensifying therapy if the blood pressure is inadequately controlled. If blood pressure data are unavailable, the program computes and presents the recommendations twice: once each for the assumptions of adequately and inadequately controlled blood pressure.

Recommendations. To encourage individualization of therapy, recommendations (Figure 3) are phrased in terms of options to consider. If the patient's BP is inadequately controlled and his current dose of antihypertensive drugs is less than the most efficacious dose for those drugs, the recommendation may involve increasing the dose of current drugs or

adding another specific drug from a list of recommended drugs. If the patient's BP is inadequately controlled and his currently prescribed drugs are at their most efficacious doses, the program recommends adding a drug from a list of recommended drugs. Dosing rules encourage good practices: For example, we have locally set the maximum dose of hydrochlorothiazide recommended by the DSS at 25 mg., because for most patients there is little or no additional antihypertensive effect at higher doses, but there is and increasing risk of hypokalemia.

The DSS makes recommendations to add, substitute, or delete drugs on the basis of comorbid diseases that represent "compelling" (per JNC6) indications (e.g., beta adrenergic receptor antagonists after myocardial infarction), possible indications (thiazides for patients with osteoporosis), possible clinical concerns (beta adrenergic receptor antagonists for patients with depression), and contraindications (beta adrenergic receptor antagonists for patients with asthma.) Each drug recommendation is presented with the rationale for its use.

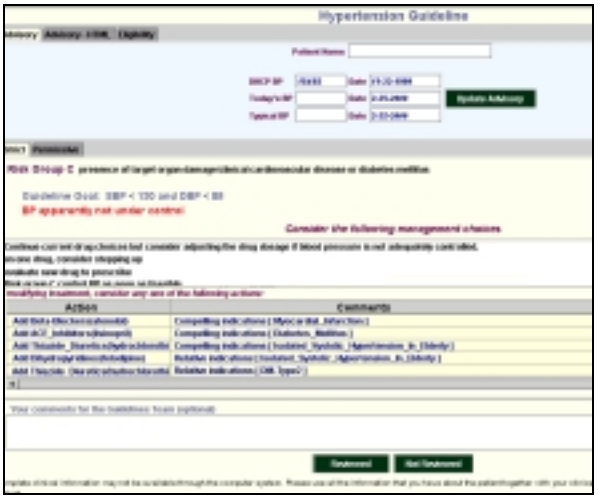

Figure 3. Portion of Recommendation Screen.

Various additional messages are triggered by specific sets of conditions. For example, a warning is issued about an increased potassium concentration if a patient has a prescription for an ACE inhibitor. Some of the messages address the complexity of management of hypertension in patients with multiple comorbid diseases. For example, if a patient has diabetes, myocardial infarction, and benign prostatic hyperplasia, he has compelling indications for ACE inhibitor and beta adrenergic receptor antagonist for renoprotective effects and secondary prevention of myocardial infarction, respectively. He also has an indication for alpha$_1$ adrenergic antagonist to alleviate symptoms of prostatic hyperplasia and to lower the risk of urinary retention. For this patient, the DSS generates a message to sequence addition of the drugs over time and to adjust the dose of each drug to avoid hypotension.

In preparation for deployment of ATHENA DSS as the source of recommendations in the primary care clinics at VA Palo Alto, we evaluated it in comparison to physician review of 100 randomly selected cases with actual patient data (manuscript in preparation).

LOCAL CUSTOMIZATION

Customization for local use is important for engaging clinical opinion leaders and overcoming barriers to guideline implementation. ATHENA can be customized in several ways. First, the KB can be modified to incorporate new evidence and to incorporate local interpretation of guideline ambiguities. The local formulary can be used to designate a preferred drug within each drug class, when the evidence points to a drug class rather than specific drug. The text of on-screen messages can be readily modified, and rules to trigger new on-screen messages can be added. Local managers can set the program to run under either of two modes: *strict* interpretation of the guidelines, in which changes to guideline-recommended drugs are suggested even if the blood pressure is adequately controlled, and *permissive* interpretation, in which recommended drugs are suggested, as additions, only if the blood pressure is not adequately controlled.

Example of KB Modification: JNC6, lists "diabetes mellitus (type 1) with proteinuria" as a compelling indication for ACE inhibitor. For Type 2 diabetes without proteinuria, JNC6 lists diuretics as the drug class that may have a favorable effect on the comorbid condition. This recommendation conflicts with some local guidelines, which regard ACE inhibitors as first line drugs for all diabetic patients with hypertension. The conflict occurs because ACE inhibitors may have value in preventing renal disease and cardiovascular disease in Type 2 diabetics, based in part on evidence that was published after JNC6 was released.[10] Additional controversy arises over the role of beta adrenergic receptor antagonists in diabetics.[11] We anticipate that the KB will be modified by the clinical leaders when major new evidence requires it.

MAXIMIZING THE IMPACT OF REMINDERS

The DSS is designed to maximize the impact of reminders. We designed the system to present

patient-specific recommendations during clinic visits because computer recommendations regarding clinical care achieve maximal impact when the reminders are linked to a particular patient and are provided at the time of patient contact, rather than later.[12,13] Concordance with recommendations also is greater when clinicians must respond to the computer-generated reminder, even if only to accept an option of "not applicable to this patient."[14] Our recommendation screen includes a button to click for "reviewed" or "not reviewed." Finally, the tradeoff as perceived by clinicians between the inconvenience of using the system and the gains in quality of care must be favorable. Accordingly, ATHENA DSS--by providing clinicians options to view the automatically triggered recommendations and move on immediately to other work or to interact with the system for more information--allows clinicians to determine the tradeoff for each case.

DISCUSSION

The ATHENA DSS presents guideline recommendations about clinical management to physicians at the time of clinic visits with hypertensive patients. ATHENA DSS serves as a reminder system, encouraging physicians to focus on achieving adequate control of blood pressure, and also includes the more sophisticated and complex reasoning necessary to operationalize JNC6 to arrive at therapeutic recommendations. ATHENA can also be used retrospectively to process multiple cases for quality review purposes. The KB is easily browsable and modifiable, so that clinical opinion leaders can customize the KB to their local environments, and can update it as new clinical trial data are published. Tracking the source of each knowledge frame facilitates KB maintenance. The database mediator specifies how data in the EMR are transformed for use by ATHENA DSS. Along with the guideline KB, this mapping KB will allow us to customize ATHENA DSS to different healthcare systems. Stanford's EON architecture provides us with broad technology that represents a generalizable approach to automation of guideline-directed therapy**.**

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