

Improving Patient Safety Using ATHENA-Decision Support System Technology: The Opioid Therapy for Chronic Pain Experience

Martha Michel, PhD; Jodie Trafton, PhD; Susana Martins, MD, MSc; Dan Wang, PhD; Samson Tu, MS; Naquell Johnson, MPA; Mary K. Goldstein, MD, MS

Abstract

The purpose of this paper is to describe potential improvements in patient safety resulting from design decisions in the development of a computerized decision support system (DSS) for managing opioid therapy for chronic noncancer pain. ATHENA-DSS is an automated decision support system developed in a collaboration between Stanford University and the U.S. Department of Veterans Affairs (VA) to increase guideline-adherent prescribing and to change physician behavior. Based on data in patients' computerized medical record and knowledge of the clinical domain encoded in a knowledge base, the system gives patient-specific recommendations to primary care providers at the point of care. ATHENA-Opioid Therapy is based on a previous system, ATHENA-Hypertension, and is designed to follow the VA/Department of Defense clinical practice guideline for the management of opioid therapy for chronic noncancer pain. We describe the rationale for development of decision support system elements and a graphical user interface to increase patient safety during primary care treatment for chronic pain. The ATHENA-Opioid Therapy system focuses on reducing patient risk in four main ways by: (1) identifying patients with comorbidities or concurrent prescriptions that raise risk for overdose and recommending more conservative dosing; (2) identifying patients with mental health problems that increase risk of medication abuse and recommending referral to psychiatric care and close monitoring; (3) assisting doctors with complex pharmacologic calculations to reduce the risk of mistakes when initiating, titrating, or switching medications; and (4) presenting relevant information to clinicians in an easy-to-use format. We describe a system evaluation plan that we believe is essential to ensure that deployment of ATHENA-Opioid Therapy leads to improvements in patient safety and increases in guideline-concordant prescribing, and we discuss the limitations of this system for patient safety efforts.

Introduction

As stated in the Institute of Medicine (IOM) report *Crossing the Quality Chasm*, information technology is widely recognized as an important means to improve patient safety in the health care setting.^{1, 2} Computerized clinical decision support systems are one method of addressing patient safety in the outpatient setting. These systems can highlight absolute and relative contraindications to drug therapy; alert about the presence of comorbidities or laboratory results that warrant consideration; make patient-specific, evidence-based recommendations; summarize patient data in easy-to-review graphical displays;³ and provide relevant information that is

integrated into the clinician's workflow. The clinician receives and reviews the information while making clinical decisions, such as during the clinic visit.

Introducing information technology can, however, create unforeseen errors.⁴ For example, a study by Cheng and colleagues⁵ examined the effects of computerized prescription order entry on workflow in an intensive care unit (ICU). Deployment of this order entry system increased workload on the health care team and raised the likelihood of new errors, such as those resulting from using a new graphical user interface and entering data incorrectly. In order to improve patient safety with a decision support system and prevent errors resulting from the technology, thoughtful development and careful testing of the system must occur before deployment, as well as monitoring after deployment.

ATHENA-DSS is a computerized decision support system (DSS) that can improve patient care and has been extensively tested for errors.^{3, 4, 5, 6, 7, 8, 9} It was initially deployed to improve management of hypertension (ATHENA-Hypertension) by providing patient-specific, evidence-based recommendations to primary care clinicians during the outpatient encounter. ATHENA-Hypertension is currently being deployed and studied in a large multisite randomized controlled trial.⁶

The ATHENA-DSS system integrates seamlessly into VistA—the electronic medical record (EMR) used at the U.S. Department of Veterans Affairs (VA)—and its user interface, the Computerized Patient Record System (CPRS). When an appropriate provider selects a patient in CPRS for whom ATHENA-DSS has a recommendation, the ATHENA-DSS displays a pop-up window in front of the CPRS cover sheet. This display is easily minimized or closed when the physician wants to view CPRS.

ATHENA-DSS consists of a knowledge base that allows knowledge engineers to codify and translate portions of a clinical practice guideline into a computable format and a reasoning engine; this, in turn, generates patient-specific recommendations by processing the patient data with the guideline knowledge in the knowledge base.¹⁰ Using patient data from VistA, ATHENA-DSS is able to reason about a patient's condition and issue guideline-based recommendations to improve care.

In 2004, the VA funded an additional ATHENA-DSS project to improve management of chronic noncancer pain using opioid therapy. Chronic pain is an important public health problem. It is estimated that half of VA patients are diagnosed with at least one type of chronic pain, and approximately one-third of these are prescribed at least one opioid pain medication.¹¹ The management of opioid therapy for chronic pain by primary care physicians presents a significant clinical problem. First, these providers tend to be undertrained in opioid therapy, and second, there is a high prevalence of substance use disorders and other psychiatric comorbidities that complicate opioid therapy in some patient populations.^{12, 13} Physician “best practice” must balance the need for pain relief against the risks of adverse effects and opioid misuse.

The VA/Department of Defense (DoD) Clinical Practice Guideline (CPG) for the Management of Opioid Therapy for Chronic Pain¹⁴ provides much needed guidance to physicians, but it is being underused. With the help of expert clinicians and authors of the guideline, we codified and translated the guideline into the ATHENA-Opioid Therapy knowledge base. ATHENA-Opioid

Therapy delivers patient-specific, guideline-based recommendations to primary care providers at the point of care and will be studied in a pilot implementation at the VA Palo Alto Health Care System.

In this paper, we examine the potential improvements to patient safety that can result from having primary care providers use ATHENA-Opioid Therapy. We also examine methods for identifying and addressing new potential errors when introducing a computerized clinical decision support system into the clinical workflow.

Elements of Athena-Opioid Therapy Designed to Increase Patient Safety

ATHENA-Opioid Therapy has been constructed specifically to address issues related to patient safety (Figure 1). ATHENA-Opioid Therapy focuses on reducing patient risk in three main ways: (1) identifying patients with physical conditions that raise risk for overdose and recommending more conservative dosing, (2) identifying patients with mental health problems or other risk factors that increase the likelihood of medication abuse and recommending close monitoring and referral to psychiatric care, and (3) assisting doctors with complex pharmacological calculations to reduce risk of mistakes when initiating, titrating, or switching medications. Furthermore, we designed the graphical user interface of ATHENA-Opioid Therapy to prioritize the display of information and to enhance patient safety features.

Reducing Risk of Overdose or Medication Abuse

Opioid overdose may be fatal due to respiratory depression. Several populations of patients are at risk for overdose, including: (1) patients with substance addiction or abuse problems who may overconsume medication; (2) patients with dementia or psychosis who may lack the mental capacity to take their medication as prescribed; (3) patients with lung, liver, or kidney problems who may have a greater sensitivity to opioid medication; and (4) patients on other medications that may amplify the effects of opioid medication.

ATHENA-Opioid Therapy identifies these patients based on three sources of data:

- Patients at risk because of diagnosed conditions (e.g., substance dependence, dementia, COPD) are identified based on diagnosis codes, ICD-9, in their medical records.
- Patients receiving prescriptions for medications that may increase their risk of overdose in combination with opioids (e.g., benzodiazepines, barbiturates) are identified using pharmacy records.
- Patients with suggestive laboratory results (e.g., positive drug screens for cocaine or opioids) are identified based on laboratory records.

For patients at risk due to mental health or substance use disorders, ATHENA-Opioid Therapy makes recommendations to the primary care provider to ensure that opioid use is closely monitored through urine drug screening, more frequent followup, use of patient contracts, and education of caregivers. The DSS also makes recommendations for appropriate referrals,

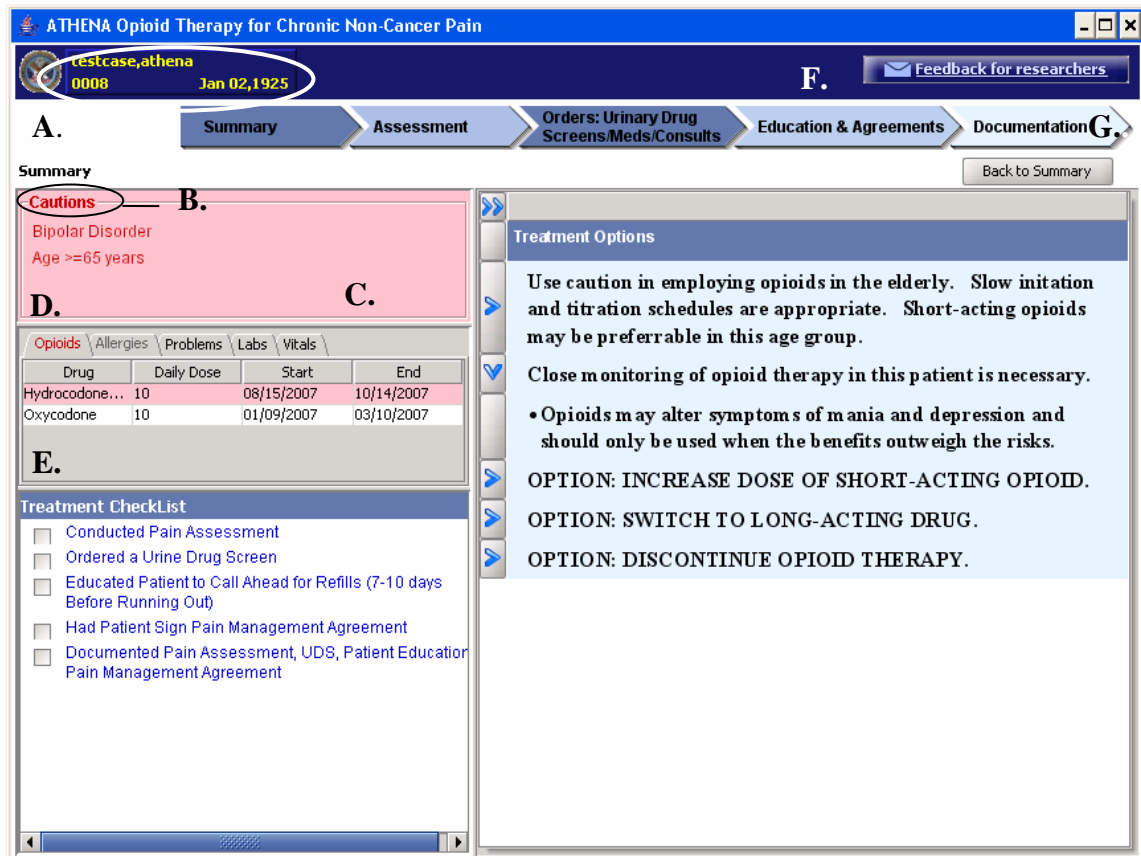


Figure 1. ATHENA-Opioid Therapy for chronic noncancer pain pop-up. Highlights of patient safety features in ATHENA-Opioid Therapy.

A. Patient identifiers: The graphical user interface (GUI) shows two identifiers: name and social security number, to help ensure information on the correct patient is presented.

B. Cautions: Important patient characteristics that are relevant to opioid prescribing are highlighted in red with a pink background to draw the provider’s attention to the area.

C. Treatment options: Patient-specific recommendations are issued. These provide information and recommendations relevant to patient characteristics highlighted in the cautions table, as well as detailed instructions for possible general treatment options the provider may be considering.

D. Data tables: Potentially relevant information on history of opioid prescriptions, allergies, diagnoses, labs, and vital signs are presented in tabular form. Information of clear relevance to opioid prescribing is highlighted in pink (e.g., a current active prescription for an opioid medication).

E: Treatment checklist: Recommended chronic pain care practices that should be carried out at all visits are listed for the provider to check when completed.

F. Feedback for researchers: This button provides a text box where comments to the research team can be added.

G. Drop-down tools: These drop down menus include tools to assist the primary care physician with chronic pain management. Tools include a structured pain assessment, instructions for conducting urine drug screens and making patient referrals to specialty care, a conversion calculator, patient education materials, a template for an opioid contract, and information about useful community resources.

assessment of prescriptions from providers outside the system, alternative or adjunctive therapy, and proper documentation of treatment.

For patients at risk because of medical conditions or concurrent prescriptions, the system recommends a modified opioid dosing schedule, including slower medication titration, lower initial starting doses, and more conservative conversions when switching medication, based on the patients' risk factors.

Reducing Risk of Prescription Errors

To reduce risk for prescription errors, two tools have been provided: (1) specific doses and schedules for titration and discontinuation and (2) a calculator for opioid conversion. Based on available information in VistA, the system issues specific medication dosing schedules for initiation, titration, and discontinuation. For example, if a patient has respiratory, kidney, or liver disease or is over age 65, the system recommends smaller and slower dose changes when escalating or reducing opioid levels.

Patients may also be harmed by errors in dosing calculations when physicians attempt to switch a patient's medication. To address this issue, ATHENA-Opioid Therapy has a conversion calculator that is easily accessible and usable (Figure 2). This calculator provides equianalgesic doses and instructions for medication titration during conversion from one opioid medication to another. The conversions have been reviewed by two experts in opioid therapy. Our preliminary studies on usability of the conversion calculator suggest that it is usable and will help avoid conversion errors.

The screenshot shows a web-based application window titled "ATHENA Opioid Therapy for Chronic Non-Cancer Pain". The interface includes a navigation bar with buttons for "Summary", "Assessment", "Orders: Urinary Drug Screens/Meds/Consults", "Education & Agreements", and "Documentation". A "Feedback for researchers" link is also present. The main content area is titled "Opioid Conversion Calculator" and contains the following elements:

- Instructions: "Please select the presently used opioid, the new opioid to switch to, enter the present dose and cross tolerance reduction percentage, then press calculate to obtain the equivalent dose for the new opioid."
- Form fields: "Converting From:" (Morphine), "To:" (Methadone), "Present Daily Dose (mg/day OR mcg/h Fentanyl only):" (120), and "Reduction for incomplete cross tolerance (%):" (0).
- Buttons: "Calculate" and "Back to Summary".
- Result: "Equivalent Daily Dose: 12.0 mg of Methadone (for 120 mg of Morphine at 0 % reduction)".
- Warning: "WARNING: When switching to methadone, the VA guideline recommends a dose no greater than 5 mg q 8 hrs (15 mg/day), and suggest consulting a specialist. Disregard the calculated equivalent dose if this limit is exceeded."

Figure 2. ATHENA-Opioid Therapy conversion calculator.

Graphical User Interface Elements to Improve Patient Safety

Just providing information to the clinician in his or her busy workflow will not necessarily influence clinical management of opioid therapy. It is necessary to provide information in a way that can capture the clinician's attention. The information has to be selective and organized in order to facilitate readability. The ATHENA-Opioid Therapy team made choices of what information was essential at the first layer, how to group such information, and the format for display. We relied on a "Less is more" paradigm, focusing first on highlighting risks to prevent medication error/abuse and second on providing general information to improve assessment, education and documentation of chronic pain management. Features of our graphical user interface (GUI) to improve patient safety are depicted in Figure 1 and include:

Cautions box. ATHENA-Opioid Therapy presents a cautions box which identifies patient-specific characteristics that may impact a doctor's prescribing decisions regarding opiate therapy for chronic pain (Figure 1). This box displays conditions that increase the risk of opioid prescription but might not be obvious to the primary care provider from reading the patient's health record. For example, clinicians are alerted if a patient has a diagnosis of a substance use disorder, a positive urine drug screen, or an elevated creatinine value.

Patient-specific recommendations. The system issues patient-specific recommendations that are tailored to the patient's conditions and current treatments. The recommendations are meant to encourage guideline adherence and address patient safety. For example, if a patient has a substance use disorder, the system will alert the physician that it is necessary to closely monitor the patient and provide information on referrals.

Detailed prescribing recommendations for general treatment options. Once the clinician has decided on a general treatment plan—such as initiating a short-acting opioid, switching from a short-acting to a long-acting medication, or discontinuing opioid medication—the system provides detailed recommendations for the choice of opiate and dosing schedule. Following these recommended dosing schedules should reduce risk of overdose, side effects, and withdrawal symptoms. The system would also alert the provider if a patient has an allergy to an opiate and he or she should not recommend that drug.

Data tables. Using a data table format, the system presents and highlights prescriptions, labs, allergies, vital signs, and medical conditions that are potentially relevant to opioid prescribing decisions. The system highlights relevant information that contributes to patient-specific recommendations in red, thus bringing important data about patient characteristics and treatment history to the provider's attention.

Pain management tools. Numerous tools that facilitate guideline-adherent opioid prescribing practices are included in drop-down menus on the user interface. These include the above mentioned conversion calculator, templates for opioid contracts, patient education materials, and instructions for addressing medication side effects. These tools are designed to assist and encourage primary care clinicians to communicate with their patients about their opioid therapy plan, set goals and boundaries for prescribing, and ensure that side effects are minimized.

We have also developed templated assessment tools and checklists to help clinicians thoroughly and correctly assess and document the pain condition being treated and treatments tried

previously. Clinicians are given the option of having these assessments written back into the patient's medical record as a structured note. By encouraging good documentation practices, we hope ATHENA-Opioid Therapy will improve care coordination among members of the treatment team.

Two patient identifiers. To clearly identify the patient for whom the recommendations are being generated, the patient's name and social security number appear in yellow with a dark blue background at the top level of the window. This was an institutional requirement.

Text feedback box. We realize that timely interaction with clinicians using the system is needed to ensure patient safety in ATHENA-Opioid Therapy. For example, if a clinician identifies an unexpected problem with the accuracy of the recommendations, it is important that this information be quickly reported to the development team so that it can be promptly corrected. For this purpose, we created a feedback button that allows clinicians to send us text feedback about any issues they encounter using the system. This feedback is reviewed frequently, and responses are sent to clinicians. The importance of early detection of unexpected problems cannot be overstated to ensure the generation of correct recommendations.¹⁵

Redundant information. Patient information that is relevant to opioid prescribing is repeated many times in the GUI. For example a history of substance abuse will appear in red in the "Cautions" area, be highlighted in the patient data table, and be used in patient-specific recommendations, such as "Patient has a history of cocaine abuse. Consider referral to addiction specialist to manage pain." This helps to emphasize relevant clinical information for opioid management for busy clinicians.

Testing of the Athena-Opioid Therapy System

Before ATHENA-Opioid Therapy is deployed into general use it will have undergone extensive testing. Our testing will consist of three main phases:

Phase 1: System Testing. In addition to standard tests of the interoperability, functionality, VA integration, and performance of the ATHENA-Opioid Therapy system, specialized testing of the clinical information provided by the system is crucial to ensuring patient safety. Towards that end, we developed several methods for this testing.

To test the clinical algorithm, all elements of the algorithm encoded in the knowledge base were written into a "rules document." This rules document was iteratively reviewed by three members of the expert consensus panel that wrote the VA/DoD clinical practice guideline for the management of opioid therapy for chronic pain. It was revised based on their clarifications and corrections until consensus was reached. The knowledge base was then updated to match the consensus rules. As a further check of the accuracy of the ATHENA-Opioid Therapy recommendations, system recommendations for real patient cases are being reviewed by clinicians with expertise in the treatment of chronic pain, substance use disorder, and mental health problems, and identified errors are being corrected in the knowledge base.

Phase 2: Usability Testing. Clinical recommendations are only useful if they are viewed and followed by primary care physicians. To ensure that ATHENA-Opioid Therapy is designed so that primary care physicians can easily and reliably use the system without extensive training, we

are conducting usability testing with sample patient cases viewed in a laboratory setting. Volunteer providers are briefly trained on the elements of the system, and they then provide feedback on their understanding of these elements, their usability in clinical practice, the likelihood that they would use them with their patients, and their suggestions for system improvement. Providers then walk through an assessment of several patient cases using the system with a study team member to demonstrate how they would use the system during patient care. Based on usability testing, we have redesigned our GUI and altered the level of detail offered in initial recommendations. We will continue usability testing on the redesigned system with additional providers.

Phase 3: In-clinic testing. Once the system has passed initial system and usability testing, ATHENA-Opioid Therapy will be deployed into real-time practice with volunteer primary care physicians at the VA Palo Alto Health Care System. These clinicians will use ATHENA-Opioid Therapy with real patients and provide feedback on the accuracy, usability, and helpfulness of the system in four ways:

- Clinicians are encouraged to use the feedback button on the GUI, where they can enter comments about a specific patient case or the system in general as they interact with ATHENA-Opioid Therapy. These comments will be evaluated by the study team every 2 days.
- We will telephone volunteer clinicians monthly for a brief interview about their recent experience with the system, problems encountered, and recommendations for improvement.
- We will shadow volunteer primary care providers in the clinic to observe their use of the system during visits.
- Volunteer physicians will complete standardized assessments of software usability and user satisfaction, so that ATHENA-Opioid Therapy can be compared to similar decision support systems. We expect this in-clinic testing to improve patient safety by ensuring that the system provides accurate recommendations and information during real clinical use, does not interfere with the patient visit or distract from other patient care and safety issues, and fits with clinical workflow such that it is used regularly by primary care providers.

Discussion

The ATHENA-Opioid Therapy system has the potential to increase guideline-concordant prescribing, improve documentation of patient management, reduce misuse or abuse of opioids, and improve patient outcomes. Because of the inherent risks related to opioid prescription, we have designed a system that can help maximize patient safety and improve management of chronic noncancer pain.

Our ability to design patient safety features in ATHENA-Opioid Therapy has been limited by several factors. A substantial limitation is a lack of reliable, easily extractable, patient health information in VistA. In order to make appropriate decisions about whether to increase, decrease, maintain, or discontinue opioid therapy in a patient, a provider must monitor changes in chronic pain and social, emotional, and physical functioning over time and during trials of medication. While providers are supposed to enter this information in CPRS, we found that chronic pain

management plans are poorly documented in the medical record. When documented, this information is often written in free-text notes, making automated data extraction difficult.

Additionally, VistA contains data only on patient care received in the VA. Some patients receive care from non-VA providers who also may prescribe opioids or develop chronic pain management plans. While we have not been able to completely overcome this substantial limitation, we have made several design decisions to reduce the impact of this problem:

- We included structured chronic pain assessment templates among the system tools, and providers are encouraged to use them. These assessment tools will be written back to VistA in a structured format that will allow for later data extraction to inform clinical recommendations. Thus, we hope the system will not only improve documentation of pain management plans, but also ensure that information is available in a computer-accessible format.
- We provide recommendations and instructions to clinicians to ask patients about care and prescriptions received outside the VA.
- We acknowledge that the limitations of the patient data do not allow us to reliably make decisions about whether it is best to increase, decrease, maintain, or discontinue opioid therapy in a particular patient. Instead of presenting a “best guess,” the system presents physicians with detailed instructions on how to proceed once a treatment option has been chosen. Thus, we try to make optimal use of the ability of ATHENA-Opioid Therapy to make dosage and medication recommendations, while encouraging the provider to communicate with the patient to make decisions about the course of treatment.

The system is also limited by lack of specificity in the clinical practice guidelines. Although opioid therapy for pain is by no means a new treatment, there have been surprisingly few well-designed clinical trials on which to base clinical practice recommendations. Therefore, the current guidelines are based primarily on expert opinion, and we have had little empirical information to use when operationalizing the guideline recommendations. To address this limitation, we developed a protocol that included iterative review by clinical experts and guideline authors to ensure that the clinical algorithm encoded in the ATHENA-Opioid Therapy system accurately represented the expert consensus. We expect that recommended practices will change over time and that this will require updates to the knowledge base. Positively, the ATHENA-Opioid Therapy knowledge base is relatively easy to modify as knowledge evolves. The system is flexible enough to grow with the base of clinical evidence.

Clinician time constraints also limit the impact of the decision support system on patient care and patient safety. Primary care visits are short, and VA primary care patients typically have multiple disorders that require attention. Thus, primary care clinicians often have only minutes to devote to chronic pain management. In order to be helpful within this time frame, recommendations and tools must provide quick, concise information to guide decisionmaking. To balance the need to present detailed information to ensure patient safety with the reality of primary care practice, we display short objective recommendations to clinicians, supported by drop-down boxes with detailed information and clinical instructions, should the clinician require more information. Nevertheless, given the time constraints and competing interests found in the real-life clinical setting, we await empirical evaluation to assess whether ATHENA-Opioid Therapy can effectively modify clinician practice.

We met a specific patient safety challenge when trying to develop recommendations for the use of methadone for treatment of chronic pain in primary care. Methadone is an excellent, long-acting analgesic. It is substantially cheaper than other comparable opioid medications, costing up to 100 times less than other long-acting options for an equianalgesic dose. Thus, our local health care system encourages use of methadone and has recommended its use for treatment of chronic noncancer pain.

However, methadone can be difficult and dangerous to initiate and titrate up, as medication levels build up over the course of days and may not reach steady state for up to a week. A dose that is optimally analgesic on day one could build up to blood levels that could induce accidental overdose and death in subsequent days. Indeed, as use of methadone for chronic pain has increased in the recent past, rates of accidental overdose have increased. For example, a study in Utah from 1997 to 2004 found that, in conjunction with a 727-percent increase in number of methadone prescriptions, accidental methadone-related deaths increased 1,770 percent.¹⁶

An analysis of adverse events in Medicaid administrative claims data suggests that, compared to prescription of other opioid medications, methadone prescription is associated with greater risk of overdose symptoms.¹⁷ To address the conflicting goals of providing cost-effective pain management and minimizing serious adverse events related to opioid prescriptions, we have worked closely with our expert team and the head of primary care at our medical center to balance the benefits of the low cost and effectiveness of methadone with its patient safety risk. Thus, ATHENA-Opioid Therapy recommends conservative dosing practices for initiation, titration, and conversion to methadone, and it provides additional warnings about overdose risk when methadone is prescribed or recommended.

In addition to the more direct benefits of highlighting at-risk patients and preventing prescribing errors, we hope that ATHENA-Opioid Therapy will positively contribute to patient-provider communication. Pain and substance addiction can produce strong emotional reactions, leading both patients and providers to feel threatened, uncomfortable, and/or mistrustful during discussions about opioid prescribing. ATHENA-Opioid Therapy has the potential to encourage these discussions by initiating interactions about uncomfortable subject matter, depersonalizing concerns about substance use problems or mental health status, ensuring that the provider is aware of previous treatment plans, and outlining the proper practices of pain management for the clinician.

Conclusion

ATHENA-Opioid Therapy provides a model for the development of decision support systems to improve patient care by improving clinical guideline adherence with a focus on patient safety. Through a combination of careful design, multilevel iterative testing, and consideration of the realities of the clinical practice setting and the current medical record system, we developed a decision support system with a potential for reducing patient risk associated with opioid prescribing. Evaluation of the effectiveness of this system for improving clinical practice and reducing opioid overdose, side effects, and adverse events will determine the extent to which ATHENA-Opioid Therapy achieves this potential.

Acknowledgments

The ATHENA Opioid Therapy project was supported by VA Health Services Research and Development Service grant TRX 04-402. The EON project was supported by National Library of Medicine grant LM 05708. Dr. Michel is supported by a VA Postdoctoral Fellowship in Medical Informatics. Views expressed are those of the authors and not necessarily those of the Department of Veterans Affairs or other affiliated institutions.

Author Affiliations

VA Palo Alto Health Care System, Center for Health Care Evaluation (Dr. Michel, Dr. Trafton, Dr. Martins, Dr. Wang, Ms. Johnson); Stanford University Medical School (Dr. Michel, Dr. Trafton, Dr. Martins, Mr. Tu); Geriatrics Research Education and Clinical Center, VA Palo Alto Health Care System, and Center for Primary Care and Outcomes, Stanford University Medical School (Dr. Martins, Dr. Goldstein).

Address correspondence to: Martha Michel, PhD, VA Center for Health Care Evaluation, 3801 Miranda Avenue, Palo Alto, CA 94304-1290; e-mail martha.michel@va.gov.

References

1. Kohn LT, Corrigan JM, Donaldson MS, eds. To err is human: Building a safer health system. Institute of Medicine. Washington, DC: National Academies Press: 2000.
2. Corrigan JM, Donaldson MS, Kohn LT. Crossing the quality chasm: A new health system for the 21st century. A report of the Committee on Quality of Health Care in America, Institute of Medicine. Washington DC: National Academies Press; 2001.
3. Goldstein MK, Hoffman BB. Hypertension recordkeeping and electronic management systems. In: Izzo J, Black HR, eds. Hypertension primer: The essentials of high blood pressure. Philadelphia: Lippincott Williams & Wilkins; 2003. p. 393-396.
4. Goldstein MK, Hoffman, BB, Coleman RW, et al. Patient safety in guideline-based decision support for hypertension management: ATHENA DSS. J Am Med Inform Assoc 2002; 9 (6 Suppl): p. S11-16.
5. Cheng CH, Goldstein MK, Geller E, et al. The effects of CPOE on ICU workflow: An observational study. AMIA Annu Symp Proc 2003: 150-154.
6. Chan AS, Coleman RW, Martins SB, et al. Evaluating provider adherence in a trial of a guideline-based decision support system for hypertension. Medinfo 2004; 11: 125-129.
7. Chan AS, Shankar RD, Coleman RW, et al. Leveraging point-of-care clinician feedback to study barriers to guideline adherence. AMIA Annu Symp Proc 2005: 915.
8. Goldstein MK, Coleman RW, Tu SW, et al. Translating research into practice: Organizational issues in implementing automated decision support for hypertension in three medical centers. J Am Med Inform Assoc 2004; 11: 368-376.
9. Goldstein MK, Hoffman BB, Coleman RW, et al. Implementing clinical practice guidelines while taking account of changing evidence: ATHENA DSS, an easily modifiable decision-support system for managing hypertension in primary care. Proc AMIA Symp 2000: 300-304.
10. Shankar RD, Martins SB, Tu SW, et al. Building an explanation function for a hypertension decision-support system. Medinfo 2001; 10: 538-542.
11. Clark JD. Chronic pain prevalence and analgesic prescribing in a general medical population. J Pain Symptom Manage 2002; 23: 131-137.
12. Kandel D, Huang F, Davies M. Comorbidity between patterns of substance use dependence and psychiatric syndromes. Drug Alcohol Depend 2001; 64: 233-241.
13. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. JAMA 1990; 264: 2511-2518.

14. VA/DoD Opioid Therapy for Chronic Pain Working Group. The management of opioid therapy for chronic pain. Washington DC: Office of Quality and Performance, VA and Quality Management Directorate, US Army MEDCOM; 2003.
15. Chan AS, Martins SB, Coleman R, et al. Post-fielding surveillance of a guideline-based decision support system. In: Advances in patient safety: From research to implementation. Vol 1, Research findings. AHRQ Pub. 05-0021-1. Rockville, MD: Agency for Healthcare Research and Quality; 2005. Available at: www.ahrq.gov/downloads/pub/advances/vol1/Chan.pdf. Accessed April 30, 2008.
16. Sims SA, Snow LA, Porucznik CA. Surveillance of methadone-related adverse drug events using multiple public health data sources. *J Biomed Inform* 2007; 40: 382-389.
17. Hartung DM, Middleton L, Haxby DG, et al. Rates of adverse events of long-acting opioids in a state Medicaid program. *Ann Pharmacother* 2007; 41: 921-928.