

---

*Use of Declarative Statements in  
Creating and Maintaining Computer-  
Interpretable Knowledge Bases for  
Guideline-Based Care*

---

Samson W. Tu, MS, Karen M. Hrabak, MSN, RNC, James R. Campbell, MD, Julie Glasgow, MD, Mark A Nyman, MD, Robert McClure, MD, James McClay, MD, Robert Abarbanel, MD, PhD, James G. Mansfield, PhD, Susana M. Martins, MD, MSc, Mary K Goldstein, MD, MS, Mark A. Musen, MD, PhD

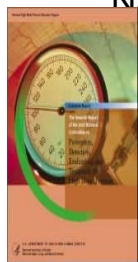
---

# Declarative statements in guideline knowledge base

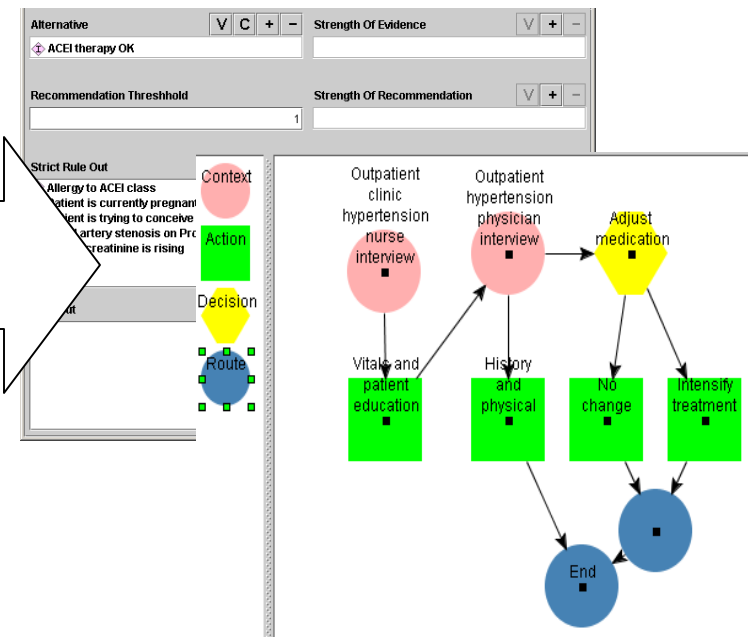
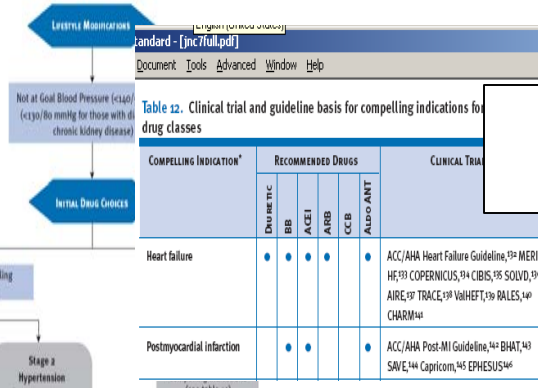
- Motivation
  - Representation
  - Uses and benefits
  - Related work
  - Discussion
-

# It is hard to create computer-interpretable knowledge bases for CDSS

- The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure



treatment of hypertension



# Representation format of one system is generally not re-usable by another system

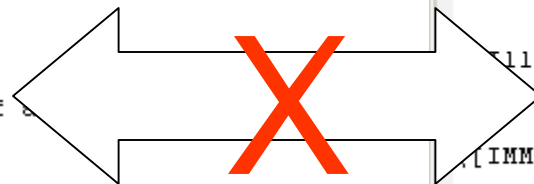
## Arden Syntax

```
email_destB := destination
  {'email', 'name' = "banfiel@cpmail-ar
    laywand@cudept.c
email_destC := destination
  {'email', 'name' = "sidelir@cucis.cis
    /* banfiel@cpmail-
queue_dest := destination
  {'queue', 'name'="UOFX"};

::
evoke: 60 minutes after time of
logic:
  /* use last to get rid of parens */
  if count display_service = 1 then
    display_service := last display_s
  endif;
```

## SAGE

```
File SAGE ers Tools Help
{[Illness+%28finding%29+%5BSNOMED+CT%5D] of
$Value
  (code "39104002")
  (codeSystem [30])
  (codeSystemName "SNOMED CT")
  (displayName "Illness (finding)")
  (label "39104002"))
[Illness+CEM] of CEMMetaClass
[IMMS2004_00003] of Guideline
  (description "SAGE Cycle 5 Immunize
$Sideline. All patients eligible for vaccinat
$ardless of age and clinical condition\n\nTH
$WING DEMONSTRATION MEDICAL GUIDELINE IS OFI
$R DEMONSTRATION PURPOSES ONLY AND SHOULD NO
$RE FOR RESEARCH PURPOSES OR SUBSTITUTED")
```



---

# Efforts to standardized representation format of guidelines have been stymied

- InterMed (1999 – 2002)
    - GLIF3
    - No wide-spread uptake
  - HL7 Clinical Decision Support TC
    - GELLO expression language
    - No implementation yet
  - HL7 Clinical Guideline SIG
    - No consensus
-

---

## What if we have a representation that...

- State relatively simple relationships between patient conditions and possible interventions
  - Has no flow-of-control or behavioral assumptions
  - Are reusable for different applications in different systems
  - Can be authored and maintained by clinician informaticians with minimal training in the modeling tool
-

---

# Declarative statement

- DeclarativeStatement ::= (Context) PatientCondition Relationship Intervention (RelationshipQualifier)\*
  - Example
    - Context: management of hypertension
    - PatientCondition: Presence of heart failure
    - Relationship: is a compelling indication for
    - Intervention: the user of ACE Inhibitor
    - Qualifier: According to JNC 7 (*Seventh Report of the Joint National Committee on Prevention, Diagnosis and Management of Hypertension*)
    - Qualifier: with evidence grade “based on randomized controlled trials”
-

---

# This representation was used in EON/ATHENA & SAGE projects

- EON
    - NLM-funded project to develop decision support architecture for guideline-based care
  - ATHENA
    - VA-funded projects to develop and evaluate CDSS
    - Uses EON model and software
    - Initial clinical domain was management of hypertension, being extended to others
  - SAGE
    - NIST-funded consortium to develop infrastructure for guideline-based CDS in enterprise clinical information systems
    - Led by GE Healthcare, includes Apelon, Inc., University of Nebraska Medical Center, Mayo Clinic, InterMountain Health, and Stanford University,
-



# EON/ATHENA Drug\_Usage

**ACE Inhibitor (Drug\_Usage)**

**Drug Class Name**     
 ACE\_Inhibitors

**Compelling Indications**     
 Heart\_Failure  
 Cerebral\_Vascular\_Diseases  
 Diabetes\_Mellitus  
 CKD by eGFR or ICD9 codes

**Relative Indications**     
 Proteinuria equals 1+ or higher <sup>M</sup>

**Absolute Contraindications**  
 Pregnancy  
 ACE I adverse reaction  
 K<sub>></sub>5.5 and on ACE  
 Presence of angioedem:

**Relative Contraindications**  
 Renovascular\_Disease

---

# SAGE Evidence Statements

- *With* statement subject management of hypertension,
  - *The* condition heart failure *has a*
  - compelling indication relationship *to*
  - *the* intervention ACE inhibitor,
  - *with strength of evidence* RA (*based on randomized controlled trial*)
  - *according to the* reference JNC 7
-

# SAGE Evidence Statement as viewed in Protégé

The screenshot shows a window titled "Heart failure is a Compelling Indication of ACE Inhibitor ...". The window is divided into four main sections, each with a search icon and a set of four diamond-shaped icons (one with a plus sign, one with a minus sign, and two without).

- Statement Subject:** Contains the text "Hypertensive disorder, systemic ...".
- Condition:** Contains the text "Heart failure".
- Relationship Type:** Contains the text "Compelling Indication".
- Intervention:** Contains the text "ACE Inhibitor Oral Preparation for...".

On the right side of the window, there are two additional sections:

- References:** Contains the text "JNC 7".
- Strength Of Evidence:** Contains the text "RA".

A text box at the bottom right of the window provides a definition for "RA": "RA Randomized controlled trials; also known as experimental studies".

---

# Uses and benefits of declarative statements

- Multiple uses of encoded knowledge
    - Write generalized decision-support criteria
    - Present nuanced explanations
    - Present patient-specific annotations
  - Ease of encoding and maintenance
-














---

## EON/ATHENA: Write generalized decision support criteria

- *If blood pressure is within targets, and there exists a prescribed antihypertensive agent that has **no specific indication**, and there exists a drug class that is **compellingly indicated** and not already prescribed or **contraindicated**, then consider substitution*
  - *Instead of numerous rules of the form*
    - *if patient is prescribed calcium channel blocker and ... and patient has heart failure and ... then consider substituting the prescribed calcium channel blocker with ACE inhibitor*
-

# Provide nuanced explanation

- ATHENA provides range of choices and explanation to help clinicians make decisions

 Compelling Indication  Relative Indication  Strong Contraindication  Relative Contraindication		
Consider one of the following therapeutic possibilities	Click here for important ...	Reasons
<b>Add ACE Inhibitors(lisinopril)</b>	<a href="#">Info</a>	 <b>Heart Failure</b>  <b>Renal Insufficiency</b>  <b>Hyperkalemia</b>
<b>Add DHP Calcium Channel Blocker (felodipine, nifedipine)</b>	<a href="#">Info</a>	 <b>Angina</b>
<b>Add Thiazide Diuretic (HCTZ)</b>	<a href="#">Info</a>	 <b>Heart Failure</b>  <b>Hypertension</b>  <b>Gout</b>
<b>Add (non-DHP) Calcium Channel Blocker (diltiazem)</b>	<a href="#">Info</a>	 <b>Angina</b>  <b>Heart Failure</b>

---

# Present patient-specific annotations

- SAGE DSS adds annotations to order sets
  - Community-acquired pneumonia guideline
    - Recommend admission for inpatient care through order sets
    - Pre-select recommended interventions
    - Annotate interventions with patient-specific comments
-

# SAGE Order Set annotations

## ▼ Medication

Choose among these:

- Administer first dose of antibiotics within 4 hours of admission

- ▼ No recent antibiotic therapy

There was no evidence of recent Abx therapy, please confirm.

Choose ONE of these:

- ▼ Macrolid plus Beta-lactam

Both of these are required:

- Ampicillin and sulbactam (Unasyn) 3 g IV Piggyback q6 hr
- Azithromycin 500 mg IV Piggyback q day (Infuse over 1 hr)

Pt is on Warfarin, monitor levels if using Azithromycin

- Moxifloxacin 400 mg IV Piggyback q day

Patient has an allergy to fluroquinolones. Patient has a relative contraindication to a fluroquinolone drug.

- Recent antibiotic therapy excluding fluoroquinolones



# SAGE Query for Evidence Statements

- Select Evidence Statement where
  - Condition evaluates to true and
  - Intervention is subsumed by ...
  - ...

The image shows two windows from the SAGE interface. The left window, titled "Relative contraindication to Fluroquinolone (instance o...", contains a "Query" box and several fields: "Label" (relative contraindication to Fluroquinolone), "Statement Subject" (Community acquired pneumonia (...)), "Relationship Type" (Relative\_contraindication), "Intervention" (Fluroquinolone Preparation), and "Relationship Class" (Evidence\_Statement). The "Presence" checkbox is checked. The right window, titled "Potential matching evidence statement", shows a "Statement Subject" (Community acquired pneumonia (...)), "Condition" (Epilepsy), "Relationship Type" (Relative\_contraindication), and "Intervention" (Moxifloxacin Preparation for CAP...). The "References" field lists "Micromedex, Epocrates".

subclass of

---

# Ease of encoding and maintenance

- ATHENA project update from JNC 6 to JNC 7
    - No change in generalized decision criteria
    - Minimal modifications to the clinical algorithm
    - 34 changes in the declarative statements about relationships between drugs and patient conditions (21 additions, 10 deletions, and 3 modifications)
  - SAGE project
    - 395 instances of Evidence Statements encoded in one day
-

---

## Related work: MachineProse

- Assertion ::= Entity Relationship Entity [AssertionQualifier]\*
- Summarize research findings, annotate biomedical publications, support sophisticated search
- 62% of 200 articles in PubMed can be summarized as assertions

Dinakarbandian D, Lee Y, et al. MachineProse: An ontological framework for scientific assertions. *J Am Med Inform Assoc* 2006;13(2):220-32.

---

---

# Discussion

- Declarative statements as a method to combine information
    - From guideline and non-guideline sources
    - From multiple guidelines
  - Declarative statements as alternative item for standardization
    - Represent simple relationships
    - Usable by different modeling formalisms
    - Easier to achieve consensus
-

---

# Acknowledgement

- The SAGE project was supported in part by grant 70NANB1H3049 of the NIST Advanced Technology Program.
  - The EON project was supported by NLM LM05708.
  - The ATHENA project was supported in part by VA HSR&D CPG-97-006, CPI-275, and RCD-96301.
  - Views expressed are those of the authors and not those of the Dept of VA and other funding agencies.
-

---

Thank you

- Questions?

---

# Decision criterion to check existence of compelling indications for current medications

- (defrange ?current\_med :FRAME Medication)
  - . . .
  - (exists ?current\_med
  - (exists ?med\_class
  - (and (subclass-of
  - (drug\_name ?current\_med) ?med\_class)
  - (exists ?indication
  - (and (Compelling\_indications
  - ?med\_class ?indication)
  - (exists ?finding
  - (subclass-of
  - (domain\_term ?finding)
  - ?indication)))))))))
-