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

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

Arden Syntax

```plaintext
email_destB := destination
  {'email', 'name'= "banfield@cpmail-arlaywand@cudept.c
email_destC := destination
  {'email', 'name'= "sidelir@cucis.c"
  /* banfield@cpmail.
queue_dest := destination
  {'queue', 'name'="UOFX"};
```

SAGE

```plaintext
([Illness+%28finding%29+%5BSNOMED+CT%5D] o:
  @Value
    
    (code "39104002")
    (codeSystem [30])
    (codeSystemName "SNOMED CT")
    (displayName "Illness (finding)")
    (label "39104002")
```

```plaintext
Illness+CEM] of CIMMetaClass

([IMMS2004_00003] of Guideline
```

(description "SAGE Cycle 5 Immuniza
```
```
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,
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**
Heart failure is a Compelling Indication of ACE Inhibitor

Condition:
- Heart failure

References:
- JNC 7

Relationship Type:
- Compelling Indication

Intervention:
- ACE Inhibitor Oral Preparation for...

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

<table>
<thead>
<tr>
<th>Consider one of the following therapeutic possibilities</th>
<th>Click here for important ...</th>
<th>Reasons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Add ACE Inhibitors (lisinopril)</td>
<td>Info</td>
<td>Heart Failure, Renal Insufficiency, Hyperkalemia</td>
</tr>
<tr>
<td>Add DHP Calcium Channel Blocker (felodipine, nifedipine)</td>
<td>Info</td>
<td>Angina, Heart Failure</td>
</tr>
<tr>
<td>Add Thiazide Diuretic (HCTZ)</td>
<td>Info</td>
<td>Heart Failure, Hypertension, Gout</td>
</tr>
<tr>
<td>Add (non-DHP) Calcium Channel Blocker (diltiazem)</td>
<td>Info</td>
<td>Angina, Heart Failure</td>
</tr>
</tbody>
</table>
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**

<table>
<thead>
<tr>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choose among these:</td>
</tr>
<tr>
<td>- □ Administer first dose of antibiotics within 4 hours of admission</td>
</tr>
<tr>
<td>- ✔ ▼ No recent antibiotic therapy</td>
</tr>
<tr>
<td>There was no evidence of recent Abx therapy, please confirm.</td>
</tr>
<tr>
<td>Choose ONE of these:</td>
</tr>
<tr>
<td>1. ▼ □ Macrolid plus Beta-lactam</td>
</tr>
<tr>
<td>Both of these are required:</td>
</tr>
<tr>
<td>- Ampicillin and sulbactam (Unasyn) 3 g IV Piggyback q6 hr</td>
</tr>
<tr>
<td>- Azithromycin 500 mg IV Piggyback q day (Infuse over 1 hr) Pt is on Warfarin, monitor levels if using Azithromycin</td>
</tr>
<tr>
<td>2. □ Moxifloxacin 400 mg IV Piggyback q day</td>
</tr>
<tr>
<td>Patient has an allergy to fluoroquinolones. Patient has a relative contraindication to a fluoroquinolone drug.</td>
</tr>
<tr>
<td>- □ Recent antibiotic therapy excluding fluoroquinolones</td>
</tr>
</tbody>
</table>
Select Evidence Statement where
- Condition evaluates to true and
- Intervention is subsumed by ...
- ...

Potential matching evidence statement

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

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

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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))))))}