RECONCILIATION OF CONCURRENTLY APPLIED CLINICAL PRACTICE GUIDELINES USING CONSTRAINT LOGIC PROGRAMMING

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Outline

- Clinical Practice Guidelines (CPGs)
- Clinical Case Study
- Methodology
- Managing Multiple CPGs
- Discussion and Future Work
Clinical Practice Guideline (CPG)

CPG: systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances

Challenge: lack of de facto standards for representing CPG in a structured and executable format
Some Gaps in CPG Research

• Most of the attention has been paid to translating evidence into a guideline and representing an individual CPG
• 50% of people 65 years old or older have a co-morbid condition [Institute of Medicine, 2001]

• Usability issues include (among others):
  • Customization to local practice (site-specific)
  • Customization for a patient with comorbidity
  • Use with missing patient data?

Research question: *How to create executable CPG model that can be applied to a patient with comorbidity?*
Clinical Case Study

• Concurrent application of CPGs for a patient who is on treatment for a duodenal ulcer and experienced a transient ischemic attack (TIA)

• Four phase process:
  • Phase 1: represent each CPG (GLIF3) as a decision graph and enumerate all paths in the graph,
  • Phase 2: construct expanded path tables (EPTs) to represent the enumerated paths,
  • Phase 3: for each CPG generate constraint logic programming model (CLP-CPG model) from an EPT and merge these models into a combined CLP-CPG model,
  • Phase 4: solve the combined model given available patient data

• Decision tool to support a physician at the point of care
Methodology

• A constraint logic programming (CLP) approach
• CLP model is composed of:
  • A set of variables $V = \{V_1, V_2, ..., V_n\}$ and their respective value domains $D = \{D_1, D_2, ..., D_n\}$
  • A set of constraints $C = \{C_1, C_2, ..., C_n\}$ that restrict the possible combinations of values assigned to each variable
  • A set of clauses $CL = \{CL_1, CL_2, ..., CL_n\}$ that define the logic program, a disjunction of n-ary predicates (literals)
• Variables = decision and action steps
• Constraints = restrictions on variables’ values derived from a CPG
• Solving a CLP model provides:
  • Fills in missing values
  • Deduces a patient’s state from limited information
  • Helps to identify if therapy is consistent with a patient’s health status (in case of co-morbid condition)
Phase 1: Decision Graphs and Paths

- Decision graph provides
  - A concise representation of a CPG
- Transforming CPG from a formal representation like GLIF3 into a decision graph [Hing et al., 2010]
- Obtained directed graph has two types of nodes
  - Action nodes corresponding to action steps
  - Decision nodes corresponding to decision steps
Concurrent Application of the CPGs Phase 1 cont.

Decision graph for TIA

- **H** Hypoglycaemia observed
- **EC** Out-patient endocrinology consult
- **F** FAST (Face Arm Speech Test) positive
- **NSR** Neurological symptoms resolved
- **A** Give aspirin
- **TS** Treat for stroke
- **NC** Out-patient neurological consult
- **ERS** Elevated risk of stroke
- **AD** Give antiplatelet drugs
- **PCS** Refer to primary care specialist

Decision graph for ulcer

- **SA** Stop taking aspirin if used
- **HPP** H. pylori test positive
- **ET** Eradication therapy
- **PPI** Give PPI (proton pump inhibitor)
- **HE** Healed on endoscopy?
- **SC** Self-care
- **RS** Refer to specialist

All paths enumerated from root to leaves
Concurrent Application of the CPGs

Phase 2: Constructing EPTs

**EPT for TIA**

**Expanded Path Table (EPT)**

- Columns are variables
- Rows are paths
- Decision variables not in path = no value
- Action variables not in path = false
Concurrent Application of the CPGs

Phase 3: Building Individual and Combined CLP-CPG models

- A CLP-CPG model is created from the EPT assuming:
  - Boolean variables $V_i$
    - All columns from the EPT
  - Constraint $Cl_i$
    - A disjunction of conjunctions representing expanded paths from the EPT
    - Requires at least one expanded path to be evaluated as true

- Combined CLP-CPG model for diseases $i$ and $j$ has:
  - Variables: $V_i \cup V_j$
  - Knowledge about adverse and contradictory actions: $CL_{kb}$
    - Treatment-treatment or treatment-disease interactions
    - Do X and do not do X
  - Constraints: $CL_i \cup CL_j \cup CL_{kb}$
Concurrent Application of the CPGs  Phase 3  cont.

Combined CLP-CPG model for TIA and ulcer CPGs
Concurrent Application of the CPGs

Phase 4: Solving a Combined CLP-CPG

- Solving CLP-CPG model implies assigning a value to each variable such that no constraints are violated
- Open source constraint programming system ECLiPSe
- Combined CLP-CPG model:
  - Has no overlapping variables/constraints, then solution always exists
  - Has overlapping variables/constraints
    - If solution exists, then no adverse or contradictory actions
    - If solution doesn’t exist, then points of contention (POC) need to be identified
- POC
  - Represents adverse or contradictory actions resulting from concurrent use of multiple CPGs
  - Flags sources of the adversities and contradictions
Concurrent Application of the CPGs Phase 4: Example

• Combined CLP-CPG model has no solution:
  • Variable $A$ (aspirin) := $true$ instantiated in TIA model and variable $SA$ (stop using aspirin) := $true$ instantiated in ulcer model violates model constraint $\neg(A \land SA)$
  • $A$ and $SA$ are identified as sources of POC

• Mitigation
  • Manually performed by physician
  • Automatically via mitigation operators (MO)
    • Operators stored in an external knowledge base
Mitigation Operator for TIA and Ulcer

\[ m_1: <\text{TIA, ulcer, \{A, SA\}, } A \land \neg AD, \neg A \land CL, \{SA\}> \]

- **Mitigation operator**
  - 6-tuple: \(<bd, td, poc, lhs, rhs, ma>\)
    - \(bd\) and \(td\) are base and target disease labels
    - \(poc\) indicates the point of contention mitigated
    - \(lhs\) and \(rhs\) describe modifications introduced to the EPT for \(bd\)
    - \(ma\) indicates mitigated and discarded actions in the EPT for \(td\) (can be empty)

- \(m_2\) operator implies supplementing aspirin taken with antiplatelets \((lhs = A \land AD)\) with PPI \((rhs = A \land AD \land PPI)\) for TIA and removing \(SA\) from ulcer CPG
Mitigation Operator: cont.

<table>
<thead>
<tr>
<th>Decisions</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EC</td>
</tr>
<tr>
<td>true</td>
<td>true</td>
</tr>
<tr>
<td>false</td>
<td>false</td>
</tr>
<tr>
<td>false</td>
<td>false</td>
</tr>
<tr>
<td>false</td>
<td>false</td>
</tr>
</tbody>
</table>

Modified EPT for TIA after application of operator $m2$

- Selection of MOs is described in paper
  - Application of MOs uses domain-independent criterion that favors simpler modifications (smaller number of modified variables) over complex ones
Modified Combined CLP-CPG Model

\[ V = \{H, F, NSR, ERS, EC, A, TS, NC, AD, PCS, HPP, HE, ET, PPI, SC, RS\} \]

\[ CL = \{ \]

\[ (H \land EC \land \neg A \land \neg TS \land \neg NC \land \neg AD \land \neg PCS \land \neg PPI) \lor \]

\[ (\neg H \land F \land \neg NSR \land \neg EC \land \neg A \land TS \land NC \land \neg AD \land \neg PCS \land \neg PPI) \lor \]

\[ (\neg H \land F \land \neg NSR \land \neg ERS \land \neg EC \land A \land \neg TS \land \neg NC \land \neg AD \land PCS \land \neg PPI) \lor \]

\[ (\neg H \land F \land \neg EC \land \neg A \land \neg TS \land \neg NC \land \neg AD \land PCS \land \neg PPI), \]

\[ (HPP \land HE \land ET \land \neg PPI \land SC \land \neg RS) \lor \]

\[ (HPP \land \neg HE \land ET \land \neg PPI \land \neg SC \land RS) \lor \]

\[ (\neg HPP \land HE \land \neg ET \land PPI \land SC \land \neg RS) \lor \]

\[ (\neg HPP \land \neg HE \land \neg ET \land PPI \land \neg SC \land RS) \} \]
Solving Modified Combined CLP-CPG

• Search for solution using ECLiPSe produces
  • \{EC := false, A := true, TS := false, NC := true, AD := true, PCS := false, ET := true, PPI := true, SC := false, RS := true\} and m1 does not need to be applied

• Action variables communicated to physician
  • A (give aspirin), EC (out-patient endocrinology consult), AD (give antiplatelet drugs), ET (eradication therapy), etc.
  • Used to help with therapeutic plan
Discussion

• Method to build an executable CPG model
  • Constraint logic programming
  • Incorporating external knowledge (i.e. drug-disease interactions)

• Identify inconsistencies
  • No solution to a combined model

• Revise models as needed
  • Extended path tables (EPTs)
  • Mitigation operators (MOs)

• Customize CPGs to co-morbid condition of a patient
  • Personalized medicine
Future Work

• Supporting the concurrent application of more than two CPGs
• Expand external knowledge bases
  • Incorporate and operationalize additional information on resolving drug-drug and drug-disease interactions, i.e. Epocrates
• Reformulating constraints to better identify POCs
  • Reduce the need for physician revisions
• Study additional CPG feature dimensions
  • Temporal, priorities, utility of missing values, and others
Thank you!