RECONCILING PAIRS OF CONCURRENTLY USED CLINICAL PRACTICE GUIDELINES USING CONSTRAINT LOGIC PROGRAMMING

Szymon Wilk\textsuperscript{1,2}, Martin Michalowski\textsuperscript{3}, Wojtek Michalowski\textsuperscript{2}, Marisela Mainegra Hing\textsuperscript{2}, Ken Farion\textsuperscript{4}

\textbf{MET Research Group, University of Ottawa}

in collaboration with

\textsuperscript{1} Poznan University of Technology
\textsuperscript{2} Telfer School of Management
\textsuperscript{3} Adventium Labs
\textsuperscript{4} Children’s Hospital of Eastern Ontario
Motivation for the Research

• 50% of people 65 years old or older have at least one comorbid condition [Institute of Medicine, 2001]
• Physician treating a comorbid patient needs to manually reconcile multiple clinical practice guidelines (CPGs)
• Reconciliation involves verifying if multiple CPGs can be applied together and introducing necessary revisions

- A patient who is treated for a duodenal ulcer (DU) and experiences a transient ischemic attack (TIA)
- Physician needs to ensure aspirin on its own is not given to the patient as part of treatment plan

• We propose a method to automate the reconciliation process
Research Question

1. How to represent multiple CPGs associated with comorbid conditions as a single computable model?
2. How to process this model (verify, revise) to ensure a treatment plan for comorbid conditions exists?

- Our approach to be used as an “early alerting system” combined with a CPG execution engine
- Assumptions and simplifications
  - Pairs of interoperable CPGs considered at a time
  - CPGs applied during a single encounter (no temporal aspects)
  - Knowledge base (KB) with external (secondary) knowledge available during model’s processing stage
Methodology (1)

- A constraint logic programming (CLP) approach
- Major components of a CLP model
  - A set of variables $V$ and their respective domains $D$
  - A set of constraints $CL$ that restrict the possible combinations of values assigned to variables

$$V = \{V_1, V_2, \ldots, V_n\}$$
$$D = \{D_1, D_2, \ldots, D_n\}$$
$$CL = \{CL_1, CL_2, \ldots, CL_m\}$$

- Constraints implemented as clauses (rules) in a logic program
- Variables correspond to choices and tasks from a CPG
- Constraints represent restrictions on variables’ values derived from a CPG
Methodology

- Solving a CLP model: assigning values to all variables from $V$ such that no constraint from $CL$ is violated
  - Fills in missing values for patient data
  - Deduces patient’s state from limited available information
  - Helps verify if suggested therapeutic plans are feasible
- If solution does not exist
  - Source of infeasibility (point of contention, POC) can be identified
  - POC is a subset of variables that violate one or more constraints
  - A CLP model need to be revised to address the encountered POC (POC needs to be mitigated)
Reconciliation Process

1. Represent each CPG as activity graph
2. Transform each activity graph to a CLP-CPG model by enumerating all paths through graph
3. Combine individual CLP-CPG models and solve the single combined model
4. If solution exists, report *success*
5. If no solution exists, identify POC and attempt to mitigate it
   1. If solution exists after mitigation, report *success* with explanation of mitigation actions taken
   2. If reconciliation fails, report *failure* with identified POC

Technical details and pseudo-code available in paper
Activity Graphs

Concurrent application of CPGs for a patient who is treated for a duodenal ulcer (DU) and experiences a transient ischemic attack (TIA)
### Patient diagnosed with DU

---

**Decision node**: H. pylori test?
- **Action node**: Ulcer healed on endoscopy?

#### H. pylori test?
- **True**: Start eradication therapy [ET]
- **False**: Start PPI [PPI]

#### Ulcer healed on endoscopy?
- **True**: Stop aspirin if used [SA]
- **False**: Self care [SC]
- **False**: Refer to specialist [RS]

---

### Enhance Path Table (EPT) for DU

<table>
<thead>
<tr>
<th>Choice variables</th>
<th>Task variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>HP</td>
<td>HPN</td>
</tr>
<tr>
<td>P</td>
<td></td>
</tr>
<tr>
<td>true</td>
<td>true</td>
</tr>
<tr>
<td>true</td>
<td></td>
</tr>
<tr>
<td>true</td>
<td>true</td>
</tr>
<tr>
<td>true</td>
<td>true</td>
</tr>
</tbody>
</table>
Combining CLP-CPG Model

- Created from single CLP-CPG models

\[ V_{DU} = \{HPP, HPN, UH, UNH, SA, ET, PPI, SC, RS\} \]

\[ CL_{DU} = \{(HPP \land UH \land SA \land ET \land SC) \lor (HPP \land UNH \land SA \land ET \land RS) \lor (HPN \land UH \land SA \land PPI \land SC) \lor (HPN \land UNH \land SA \land PPI \land RS), HPP \oplus HPN, UH \oplus UNH\} \]

- Augmented with constraints from KB representing external knowledge about adverse and contradictory tasks
  - Treatment-treatment or treatment-disease interactions
  - ‘Do x’ and ‘do not do x’ contradictions (i.e. ‘start aspirin’ and ‘stop aspirin if used’)
Combined CLP-CPG Model

$\mathbf{V}_{DU,TIA} = \{ \text{HPP, HPN, UH, UNH, SA, ET, PPI, SC, RS, HA, HP, FN, FP, NSR, NSNR, RSN, RSE, EC, A, TS, PCS, D, NC} \}$

$\mathbf{CL}_{DU,TIA} = \{ \}$

$(\text{HPP} \land \text{UH} \land \text{SA} \land \text{ET} \land \text{SC}) \lor$
$(\text{HPP} \land \text{UNH} \land \text{SA} \land \text{ET} \land \text{RS}) \lor$
$(\text{HPN} \land \text{UH} \land \text{SA} \land \text{PPI} \land \text{SC}) \lor$
$(\text{HPN} \land \text{UNH} \land \text{SA} \land \text{PPI} \land \text{RS}),$
$\text{HPP} \oplus \text{HPN}, \text{UH} \oplus \text{UNH},$
$(\text{HA} \land \text{FN} \land \text{PCS}) \lor$
$(\text{HA} \land \text{FP} \land \text{NSR} \land \text{RSN} \land \text{A} \land \text{PCS}) \lor$
$(\text{HA} \land \text{FP} \land \text{NSR} \land \text{RSE} \land \text{A} \land \text{D} \land \text{NC}) \lor$
$(\text{HA} \land \text{FP} \land \text{NSNR} \land \text{TS} \land \text{NC}) \lor$
$(\text{HP} \land \text{EC}),$
$\text{HA} \oplus \text{HP}, \text{FN} \oplus \text{FP}, \text{NSR} \oplus \text{NSNR}, \text{RSN} \oplus \text{RSE},$
$\neg(\text{A} \land \text{SA}) \}$
Solving a Combined CLP-CPG Model

- Partial available patient information:
  - No signs of hypoglycemia ($HA = true$)
  - Passed FAST ($FP = true$)
  - Resolved neurological symptoms ($NSR = true$)
- CPG for TIA implies starting aspirin ($A = true$), while CPG for DU suggests stopping it ($SA = true$)
- Combined CLP-CPG model has no solutions due to violated constraint $\neg (A \land SA)$
- Identified POC points at $A$ and $SA$ as source of adverse interaction ($POC_{DU,TIA} = \{A, SA\}$)
- Combined CLP-CPG model needs to revised by mitigating adverse tasks from identified $POC_{DU,TIA}$
Mitigating a POC (1)

- Mitigation involves modifying paths in CPGs to remove conflicts identified by a POC
- Realized thorough mitigation operators (MOs) that operate on EPTs and are part of KB
- In order to mitigate $POC_{DU,TIA} = \{A, SA\}$ we use the MO that introduces the following changes
  - Aspirin ($A$) used together with dipyridamole ($D$) is augmented with PPI in the EPT for TIA
  - ‘Stop aspirin’ ($SA$) task is removed from the EPT for DU
Mitigating a POC (2)

Revised EPTs after applying the MO

Revised EPT for TIA

<table>
<thead>
<tr>
<th>Choice variables</th>
<th>Task variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>HA</td>
<td>HP</td>
</tr>
<tr>
<td>true</td>
<td>true</td>
</tr>
<tr>
<td>true</td>
<td>true</td>
</tr>
<tr>
<td>true</td>
<td>true</td>
</tr>
<tr>
<td>true</td>
<td>true</td>
</tr>
</tbody>
</table>

Revised EPT for DU

<table>
<thead>
<tr>
<th>Choice variables</th>
<th>Task variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>HP</td>
<td>HPN</td>
</tr>
<tr>
<td>true</td>
<td>true</td>
</tr>
<tr>
<td>true</td>
<td>true</td>
</tr>
<tr>
<td>true</td>
<td>true</td>
</tr>
<tr>
<td>true</td>
<td>true</td>
</tr>
</tbody>
</table>
Revised Combined CLP-CPG Model

Revised combined CLP-CPG model for DU and TIA after applying a mitigation operator:

\[
\begin{align*}
V_{DU,TIA} &= \{ HPP, HPN, UH, UNH, ET, PPI, SC, RS, \\
&\quad HA, HP, FN, FP, NSR, NSNR, RSN, RSE, EC, A, TS, PCS, D, NC \} \\
CL_{DU,TIA} &= \{ \\
&\quad (HPP \land UH \land ET \land SC) \lor \\
&\quad (HPP \land UNH \land ET \land RS) \lor \\
&\quad (HPN \land UH \land PPI \land SC) \lor \\
&\quad (HPN \land UNH \land PPI \land RS), \\
&\quad HPP \oplus HPN, UH \oplus UNH, \\
&\quad (HA \land FN \land PCS) \lor \\
&\quad (HA \land FP \land NSR \land RSN \land A \land PCS) \lor \\
&\quad (HA \land FP \land NSR \land RSE \land A \land D \land NC \land PPI) \lor \\
&\quad (HA \land FP \land NSNR \land TS \land NC) \lor \\
&\quad (HP \land EC), \\
&\quad HA \oplus HP, FN \oplus FP, NSR \oplus NSNR, RSN \oplus RSE \} 
\end{align*}
\]

- Revised CLP-CPG model can be solved given available patient information \((HA = true, FP = true \text{ and } NSR = true)\)
- Both CPGs for DU and TIA can be applied simultaneously
Constructing Revised CPGs

Revised Activity Graph for DU

- **Patient diagnosed with DU**
  - **H. pylori test?**
    - **H. pylori test positive [HPP]**
      - **Start eradication therapy [ET]**
    - **H. pylori test negative [HPM]**
      - **Start PPI [PP]**
  - **Ulcer healed on endoscopy?**
    - **Ulcer healed [UH]**
      - **Self care [SC]**
    - **Ulcer not healed [UNH]**
      - **Refer to specialist [RS]**

Revised Activity Graph for TIA

- **Patient diagnosed with TIA**
  - **Hypoglycaemia?**
    - **Hypoglycaemia present [HP]**
      - **Out-patient endocrinology consult [EC]**
    - **Hypoglycaemia absent [HA]**
  - **FAST?**
    - **FAST positive [FP]**
      - **Start aspirin [A]**
    - **FAST negative [FN]**
      - **Risk of stroke?**
        - **Risk elevated [RSE]**
          - **Start dipyridamole [D]**
          - **Out-patient neurological consult [NC]**
        - **Risk negligible [RSN]**
          - **Treat for stroke [TS]**
          - **Refer to primary care specialist [PCS]**
  - **Neurological symptoms resolved?**
    - **Symptoms resolved [NSR]**
    - **Symptoms not resolved [NSNR]**

- **Added ‘start PPI’ task**
- **Removed ‘stop aspirin if used’ task**

- Revised CPGs represented as revised activity graphs
- Physician presented with an encountered POC, applied MO and revised CPGs
Discussion

- Method for automatically reconciling multiple CPGs for treatment of a comorbid patient
  - Support of partial patient information
  - Identification of a POC with adverse and contradictory tasks
- Conflicting CPGs revised according to external knowledge given in form of MOs
- Assisting, not replacing the physician – the treatment decision ultimately rests with the MD
- Customizing CPGs to comorbid conditions of a specific patient – personalized medicine
Future Work

• Supporting the concurrent application of more than two CPGs and CPGs with sub-guidelines
• Formalizing and expanding knowledge base
  • Provide uniform definitions of constraint and mitigation operators
  • Incorporate and operationalize external sources
• Reformulating constraints to better identify POCs
• Study additional CPG feature dimensions
  • Temporal aspects
  • Dosages
  • Task priorities
  • Special treatment of missing values
  • …
Thank you!

Please visit us at http://www.mobiledss.uottawa.ca