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

Szymon Wilk[1,2], Martin Michalowski[3], Wojtek Michalowski[2], Marisela Mainegra Hing[2], Ken Farion[4]

MET Research Group, University of Ottawa

in collaboration with

[1] Poznan University of Technology

[2] Telfer School of Management

[3] Adventium Labs

[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

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

  - 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 (2)

- 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

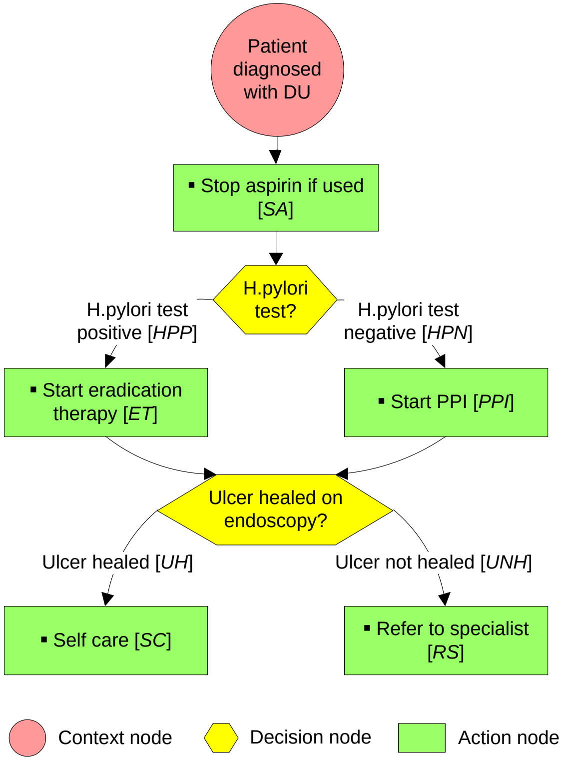
1. Represent each CPG as activity graph
2. Transform each activity graph to a CLP-CPG model by enumerating all paths through graph
3. Combine individual CLP-CPG models and solve the single combined model
4. If solution exists, report *success*
5. If no solution exists, identify POC and attempt to mitigate 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)

Activity graph for DU



Patient diagnosed with DU

- Stop aspirin if used [*SA*]

H.pylori test?

H.pylori test positive [*HPP*]

H.pylori test negative [*HPN*]

- Start eradication therapy [*ET*]

- Start PPI [*PPI*]

Ulcer healed on endoscopy?

Ulcer healed [*UH*]

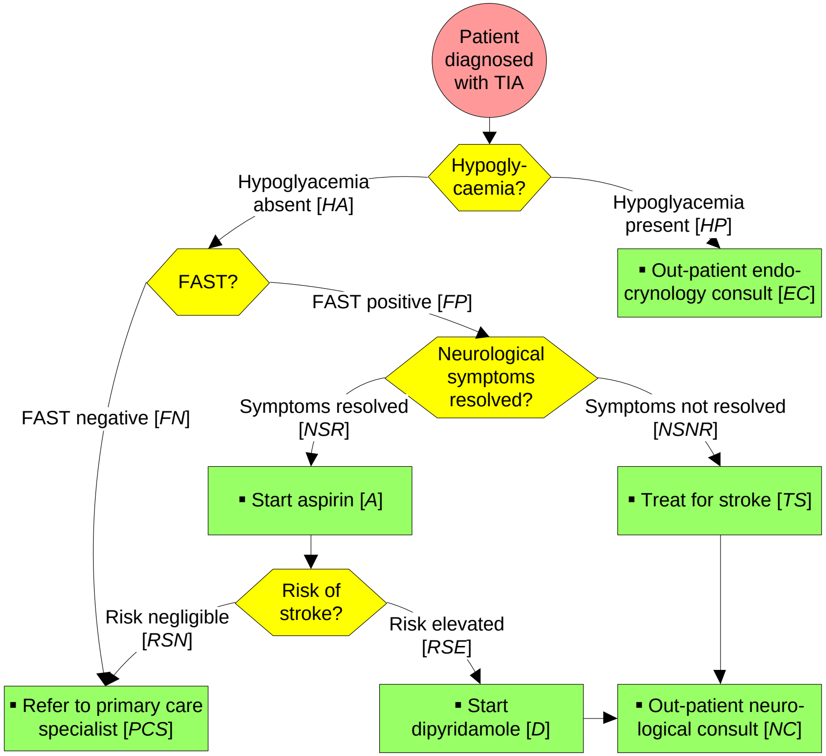
Ulcer not healed [*UNH*]

- Self care [*SC*]

- Refer to specialist [*RS*]

● Context node ⬢ Decision node 🟩 Action node

Activity graph for TIA



Patient diagnosed with TIA

Hypogly-caemia?

Hypoglyacemia absent [*HA*]

Hypoglyacemia present [*HP*]

- Out-patient endo-crynology consult [*EC*]

FAST?

FAST positive [*FP*]

FAST negative [*FN*]

Neurological symptoms resolved?

Symptoms resolved [*NSR*]

Symptoms not resolved [*NSNR*]

- Start aspirin [*A*]

- Treat for stroke [*TS*]

Risk of stroke?

Risk negligible [*RSN*]

Risk elevated [*RSE*]

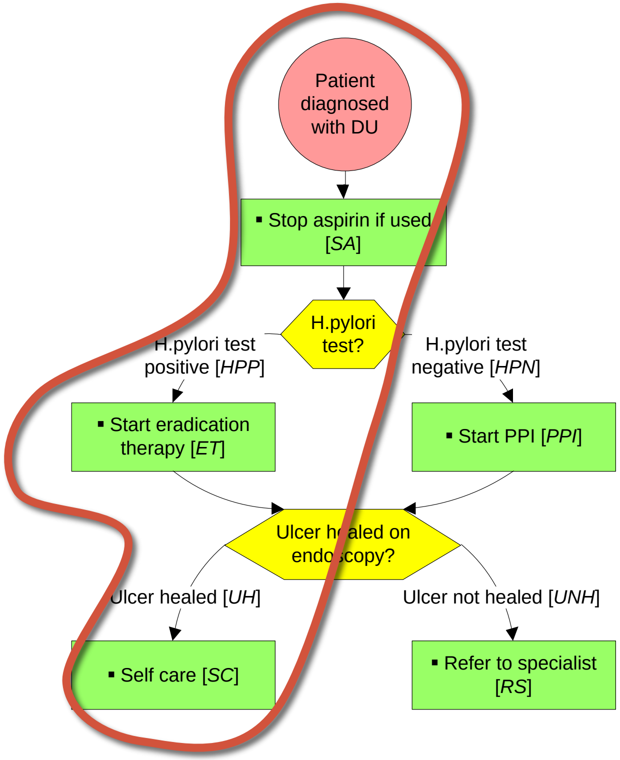
- Refer to primary care specialist [*PCS*]

- Start dipyridamole [*D*]

- Out-patient neuro-logical consult [*NC*]

Enumerating Paths

Activity Graph for DU



Enhanced Path Table (EPT) for DU

Choice variables				Task variables				
HPP	*HPN*	*UH*	*UNH*	*SA*	*ET*	*PPI*	*SC*	*RS*
true		true		true	true		true	
true			true	true	true			true
	true	true		true		true	true	
	true		true	true		true		true

Combining CLP-CPG Model

- Created from single CLP-CPG models

$$\boldsymbol{V}_{DU} = \{$$
$$HPP, HPN, UH, UNH, SA, ET, PPI, SC, RS\ \}$$
$$\boldsymbol{CL}_{DU} = \{$$
$$(HPP \wedge UH \wedge SA \wedge ET \wedge SC) \vee$$
$$(HPP \wedge UNH \wedge SA \wedge ET \wedge RS) \vee$$
$$(HPN \wedge UH \wedge SA \wedge PPI \wedge SC) \vee$$
$$(HPN \wedge UNH \wedge SA \wedge PPI \wedge RS),$$
$$HPP \oplus HPN, UH \oplus UNH\ \}$$

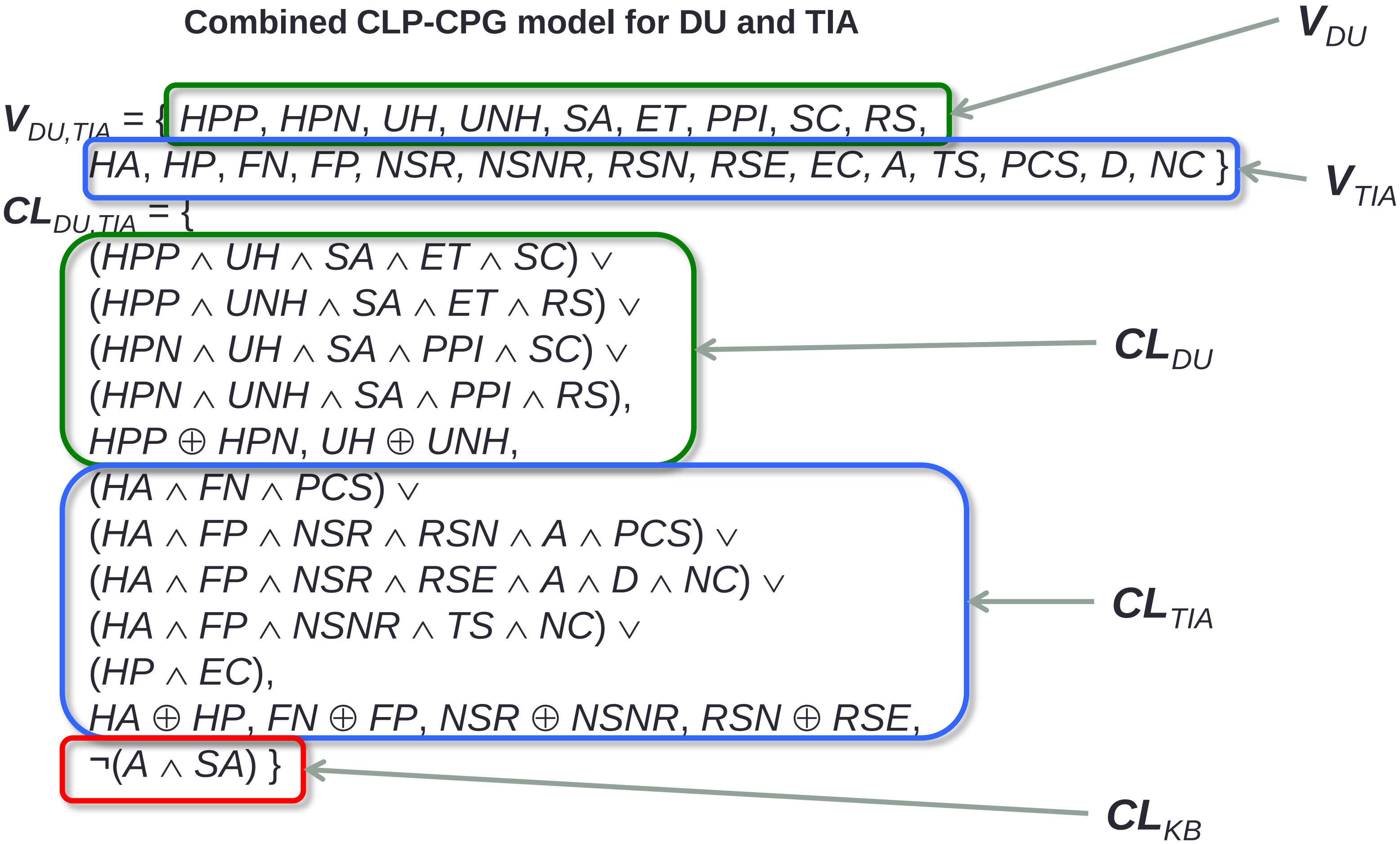
Constraints obtained from EPT

Constraints implied by types of decision nodes

- 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

Combined CLP-CPG model for DU and TIA



$$\begin{aligned}
V_{DU,TIA} = \{ & HPP, HPN, UH, UNH, SA, ET, PPI, SC, RS, \\
& HA, HP, FN, FP, NSR, NSNR, RSN, RSE, EC, A, TS, PCS, D, NC \}
\end{aligned}$$

$$\begin{aligned}
CL_{DU,TIA} = \{ & \\
& (HPP \wedge UH \wedge SA \wedge ET \wedge SC) \vee \\
& (HPP \wedge UNH \wedge SA \wedge ET \wedge RS) \vee \\
& (HPN \wedge UH \wedge SA \wedge PPI \wedge SC) \vee \\
& (HPN \wedge UNH \wedge SA \wedge PPI \wedge RS), \\
& HPP \oplus HPN, UH \oplus UNH, \\
& (HA \wedge FN \wedge PCS) \vee \\
& (HA \wedge FP \wedge NSR \wedge RSN \wedge A \wedge PCS) \vee \\
& (HA \wedge FP \wedge NSR \wedge RSE \wedge A \wedge D \wedge NC) \vee \\
& (HA \wedge FP \wedge NSNR \wedge TS \wedge NC) \vee \\
& (HP \wedge EC), \\
& HA \oplus HP, FN \oplus FP, NSR \oplus NSNR, RSN \oplus RSE, \\
& \neg(A \wedge SA) \}
\end{aligned}$$

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 $\neg(A \wedge SA)$
- 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

Choice variables								Task variables						
HA	*HP*	*FN*	*FP*	*NSR*	*NSNR*	*RSN*	*RSE*	*EC*	*A*	*TS*	*PCS*	*D*	*NC*	*PPI*
true		true									true			
true			true	true		true			true		true			
true			true	true			true		true			true	true	true
true			true		true					true			true	
	true							true						

Revised EPT for DU

Choice variables				Task variables				
HPP	*HPN*	*UH*	*UNH*	~~*SA*~~	*ET*	*PPI*	*SC*	*RS*
true		true		~~true~~	true		true	
true			true	~~true~~	true			true
	true	true		~~true~~		true	true	
	true		true	~~true~~		true		true

Revised Combined CLP-CPG Model

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

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

$\mathbf{CL}_{DU,TIA} = \{$
$(HPP \wedge UH \wedge ET \wedge SC) \vee$
$(HPP \wedge UNH \wedge ET \wedge RS) \vee$
$(HPN \wedge UH \wedge PPI \wedge SC) \vee$
$(HPN \wedge UNH \wedge PPI \wedge RS),$
$HPP \oplus HPN, UH \oplus UNH,$
$(HA \wedge FN \wedge PCS) \vee$
~~$(HA \wedge FP \wedge NSR \wedge RSN \wedge A \wedge PCS) \vee$~~
$(HA \wedge FP \wedge NSR \wedge RSE \wedge A \wedge D \wedge NC \wedge PPI) \vee$
~~$(HA \wedge FP \wedge NSNR \wedge TS \wedge NC) \vee$~~
$(HP \wedge EC),$
$HA \oplus HP, FN \oplus FP, NSR \oplus NSNR, RSN \oplus RSE \,\}$

SA removed

PPI added

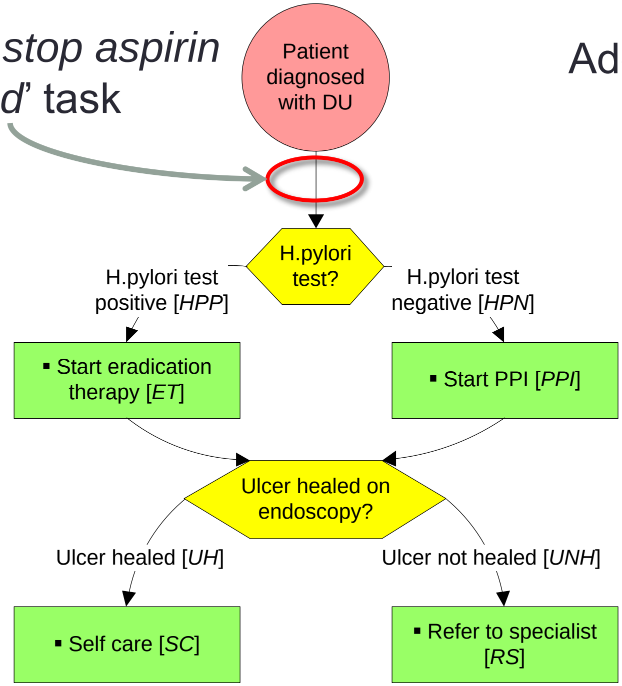
$\neg(A \wedge SA)$ removed

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

Constructing Revised CPGs

Revised Activity Graph for DU

Removed '*stop aspirin if used*' task



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Ulcer not healed [*UNH*]

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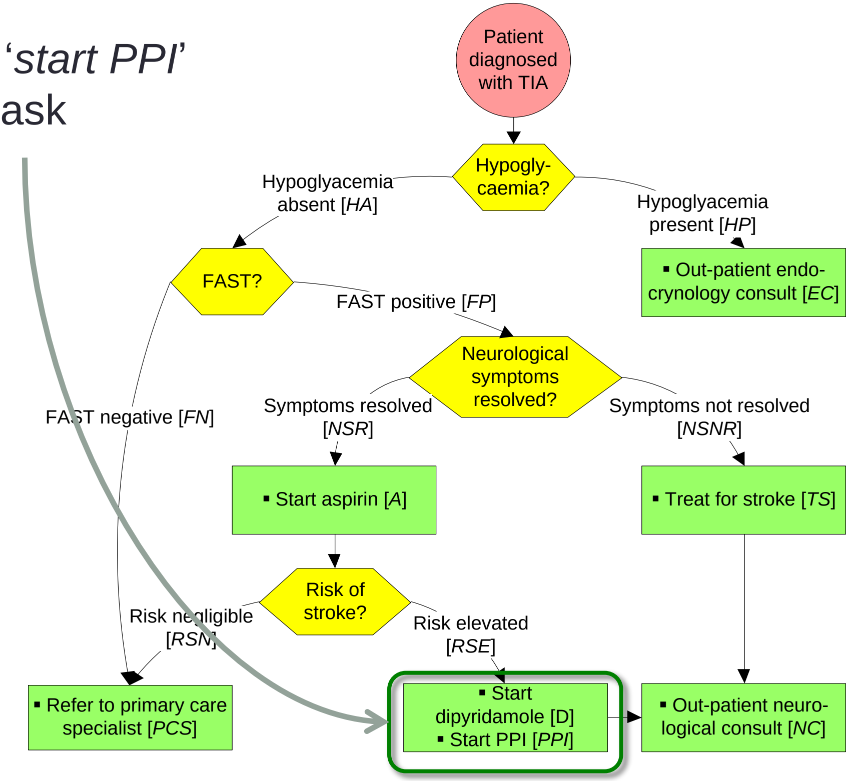
- Refer to specialist [*RS*]

Revised Activity Graph for TIA

Added '*start PPI*' task



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- Treat for stroke [*TS*]

Risk of stroke?

Risk negligible [*RSN*]

Risk elevated [*RSE*]

- Refer to primary care specialist [*PCS*]

- Start dipyridamole [D]
- Start PPI [*PPI*]

- Out-patient neuro-logical consult [*NC*]

- 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!

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