RECONCILIATION OF CONCURRENTLY APPLIED CLINICAL PRACTICE GUIDELINES USING CONSTRAINT LOGIC PROGRAMMING

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

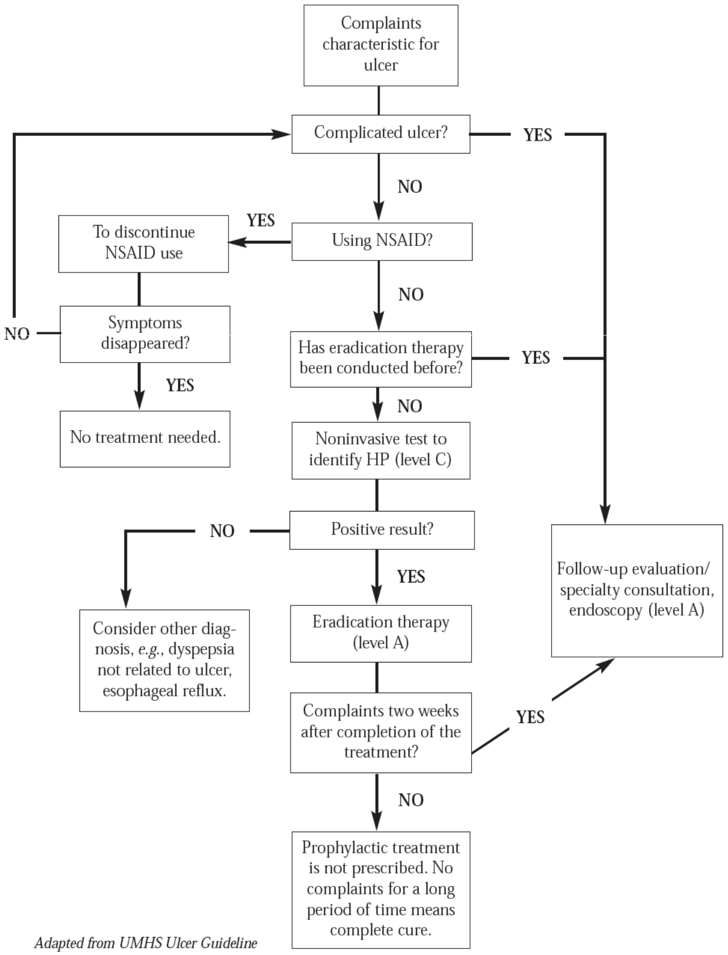
MET Research Group, University of Ottawa
in collaboration with
[1]Telfer School of Management
[2]Adventium Labs
[3]Poznan University of Technology
[4]Children's Hospital of Eastern Ontario

Outline

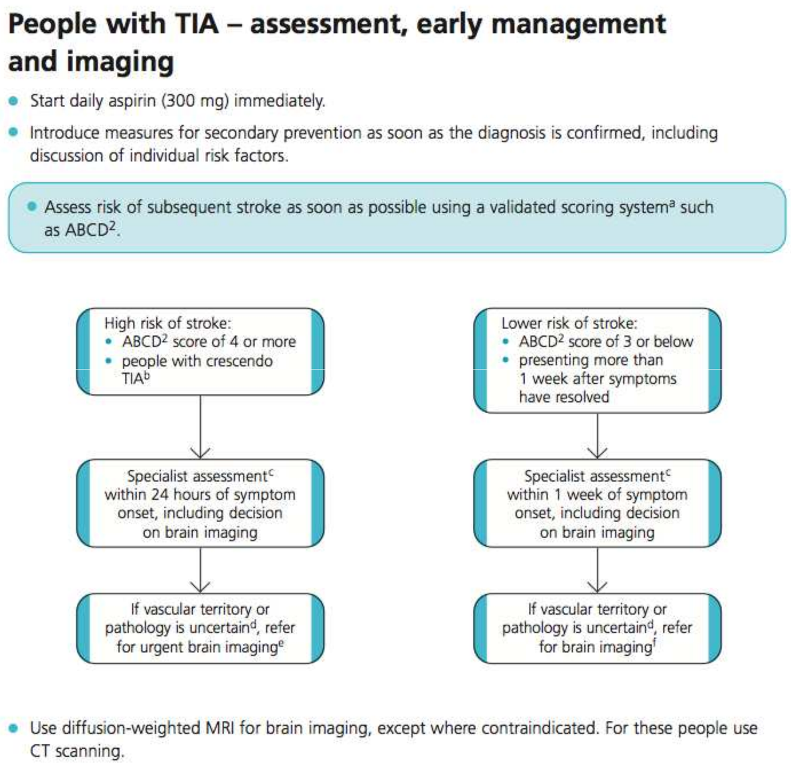
- Clinical Practice Guidelines (CPGs)
- Clinical Case Study
- Methodology
- Managing Multiple CPGs
- Discussion and Future Work

Clinical Practice Guideline (CPG)

DIAGNOSTIC ALGORITHM



Adapted from UMHS Ulcer Guideline



<u>CPG</u>: *systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances*

<u>Challenge</u>: *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?

<u>Research question: *How to create executable CPG model that can be applied to a patient with comorbidity?*</u>

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

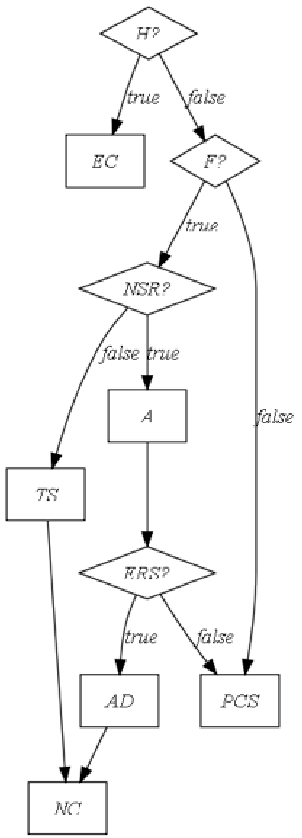
Methodology

- A constraint logic programming (CLP) approach
- CLP model is composed of:
  - A set of variables $V = \{V_1, V_2, \dots, V_n\}$ and their respective value domains $D = \{D_1, D_2, \dots, D_n\}$
  - A set of constraints C = $\{C_1, C_2, \dots, C_n\}$ that restrict the possible combinations of values assigned to each variable
  - A set of clauses CL = $\{CL_1, CL_2, \dots, CL_n\}$ 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

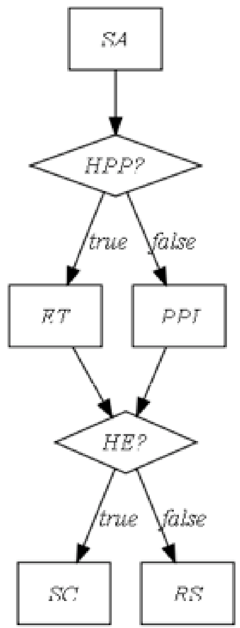
- Decision graph provides
  - A concise representation of a CPG
- Transforming CPG from a formal representation like GLIF3 into a decision graph [Hing et al., 2010]
- Obtained directed graph has two types of nodes
  - Action nodes corresponding to action steps
  - Decision nodes corresponding to decision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

Concurrent Application of the CPGs Phase 1 cont.



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 TIA

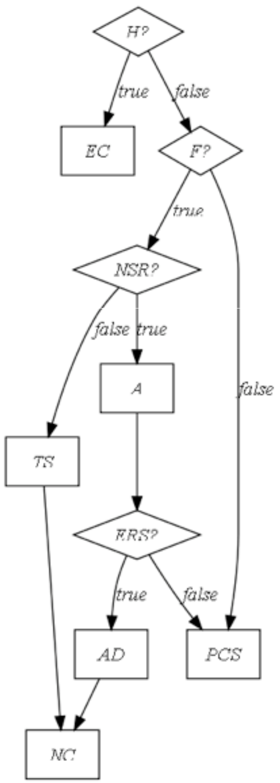


SA	Stop taking aspirin if used
HPP	H.pylori test positive
ET	Eradication therapy
PPI	Give PPI (proton pump inhibitor)
HE	Healed on endoscopy?
SC	Self-care
RS	Refer to specialist

Decision graph for ulcer

All paths enumerated from root to leaves

Phase 2: Constructing EPTs



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PCS Refer to primary care specialist

Decision graph for TIA

Decisions				Actions					
H	*F*	*NSR*	*ERS*	*EC*	*A*	*TS*	*NC*	*AD*	*PCS*
true				true	false	false	false	false	false
false	true	false		false	false	true	true	false	false
false	true	true	true	false	true	false	true	true	false
false	true	true	false	false	true	false	false	false	true
false	false			false	false	false	false	false	true

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*

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 U 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 U CL_j U CL_{kb}

Concurrent Application of the CPGs **Phase 3** cont.

$V = \{$ … $\}$

$CL = \{$

CL_{TIA}

CL_{ulcer}

$\neg(A \wedge SA) \leftarrow CL_{kb}$

$\}$

Combined CLP-CPG model for TIA and ulcer 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

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 $\neg(A \wedge SA)$
  - *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

$$m1\colon \langle TIA,\ ulcer,\ \{A, SA\},\ A \wedge \neg AD,\ \neg A \wedge CL,\ \{SA\} \rangle$$

- 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)
- *m2* operator implies supplementing aspirin taken with antiplatelets ($lhs = A \wedge AD$) with PPI ($rhs = A \wedge AD \wedge PPI$) for TIA and removing *SA* from ulcer CPG

Mitigation Operator: cont.

Decisions				Actions						
H	*F*	*NSR*	*ERS*	*EC*	*A*	*TS*	*NC*	*AD*	*PCS*	*PPI*
true				true	false	false	false	false	false	false
false	true	false		false	false	true	true	false	false	false
false	true	true	true	false	true	false	true	true	false	**true**
false	true	true	false	false	true	false	false	false	true	false
false	false			false	false	false	false	false	true	false

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

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

$\boldsymbol{CL} = \{$

$(H \wedge EC \wedge \neg A \wedge \neg TS \wedge \neg NC \wedge \neg AD \wedge \neg PCS \wedge \neg PPI) \vee$

$(\neg H \wedge F \wedge \neg NSR \wedge \neg EC \wedge \neg A \wedge TS \wedge NC \wedge \neg AD \wedge \neg PCS \wedge \neg PPI) \vee$

$\vee$

$(\neg H \wedge F \wedge NSR \wedge \neg ERS \wedge \neg EC \wedge A \wedge \neg TS \wedge \neg NC \wedge \neg AD \wedge PCS \wedge \neg PPI) \vee$

$(\neg H \wedge \neg F \wedge \neg EC \wedge \neg A \wedge \neg TS \wedge \neg NC \wedge \neg AD \wedge PCS \wedge \neg PPI),$

$(HPP \wedge HE \wedge ET \wedge \neg PPI \wedge SC \wedge \neg RS) \vee$

$(HPP \wedge \neg HE \wedge ET \wedge \neg PPI \wedge \neg SC \wedge RS) \vee$

$(\neg HPP \wedge HE \wedge \neg ET \wedge PPI \wedge SC \wedge \neg RS) \vee$

$(\neg HPP \wedge \neg HE \wedge \neg ET \wedge PPI \wedge \neg SC \wedge RS)$

$\}$

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!