GLARE

(GuideLine Acquisition Representation and Execution)

- Introduction
- Representation formalism
- Architecture: acquisition and execution modules
- Decision-making facilities: hypothetical reasoning
- Temporal reasoning facilities
- Context-adaptation facilities
- Summary

Introduction

Clinical guidelines are a means for specifying the “best” clinical procedures and for standardizing them

Adopting (computer-based) clinical guidelines is advantageous

Different roles:

- support
- critique
- evaluation
- education
- …...

Many different computer systems managing clinical guidelines (e.g., Asgaard, GEM, Gliff, Guide, PROforma,…)

GLARE
(GuideLine Acquisition Representation and Execution)

-Joint project with:

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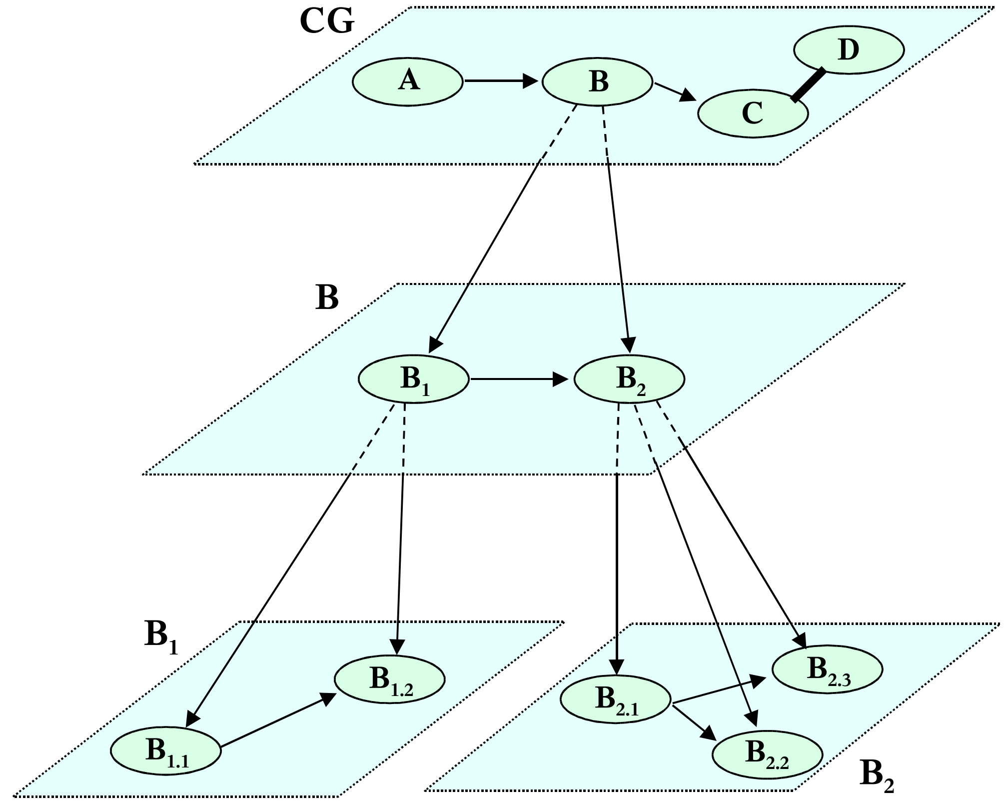
- Domain independent

  (e.g., bladder cancer, reflux esophagitis, heart failure)

- User-friendly (limited number of primitives)

GLARE (Guideline Acquisition, Representation and Execution)
Representation Formalism

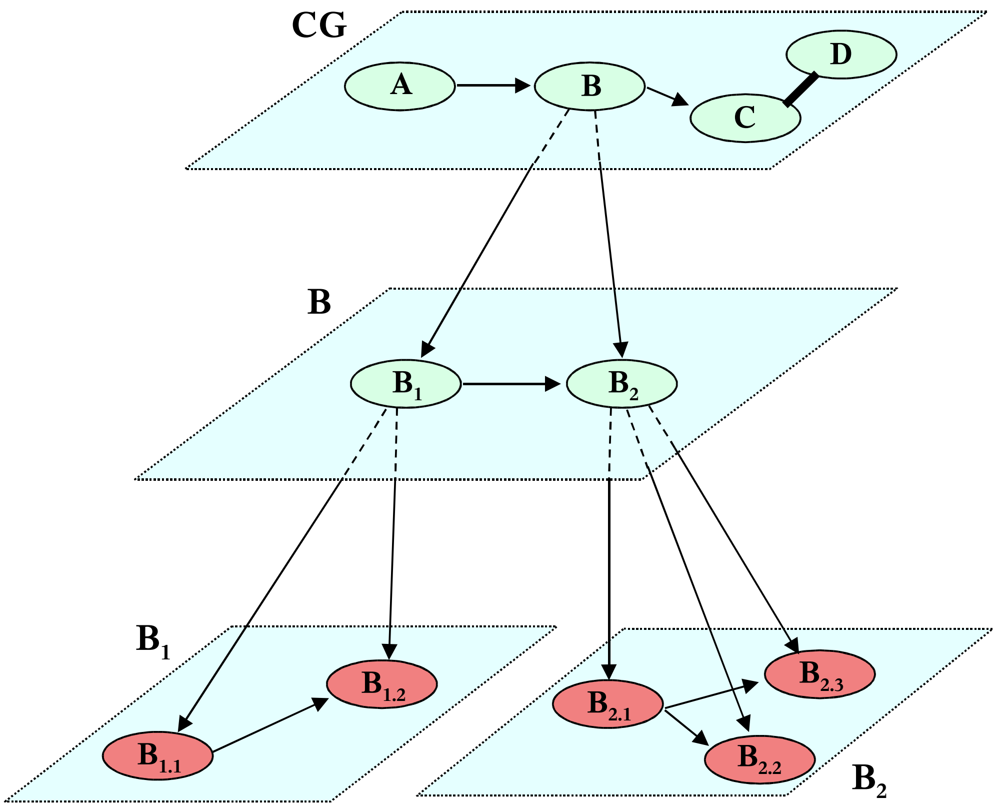
Tree of graphs



Representation Formalism

Tree of graphs

Atomic actions

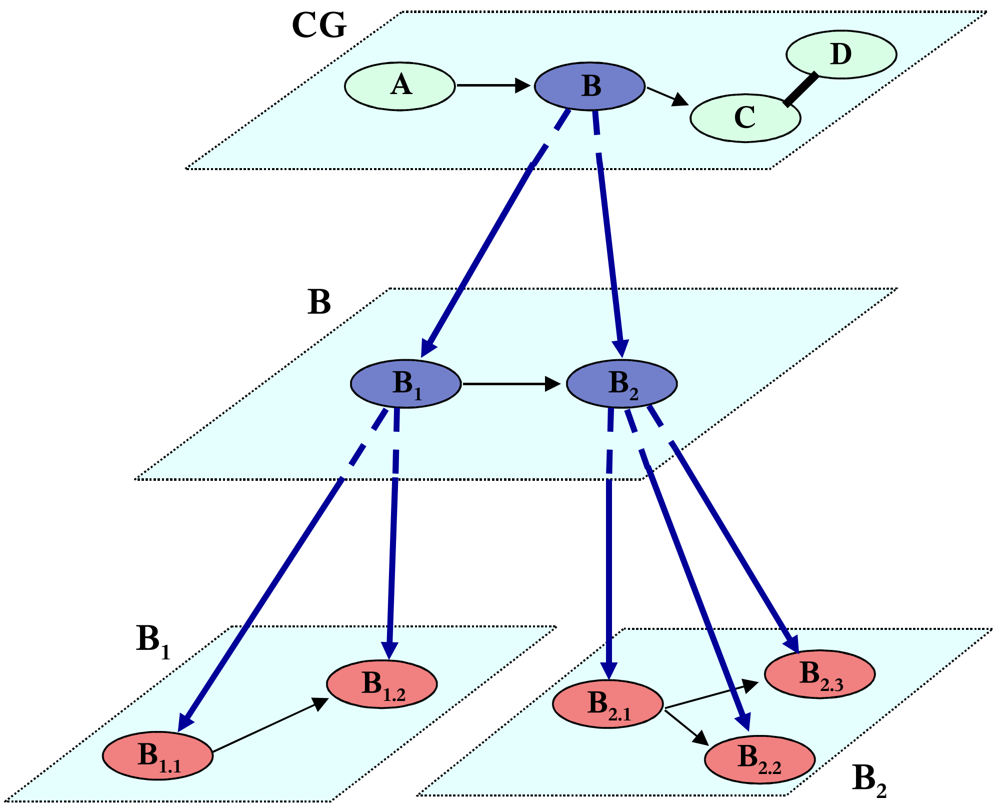


Representation Formalism

Tree of graphs

Atomic actions

Composite actions (plans)



Representation Formalism

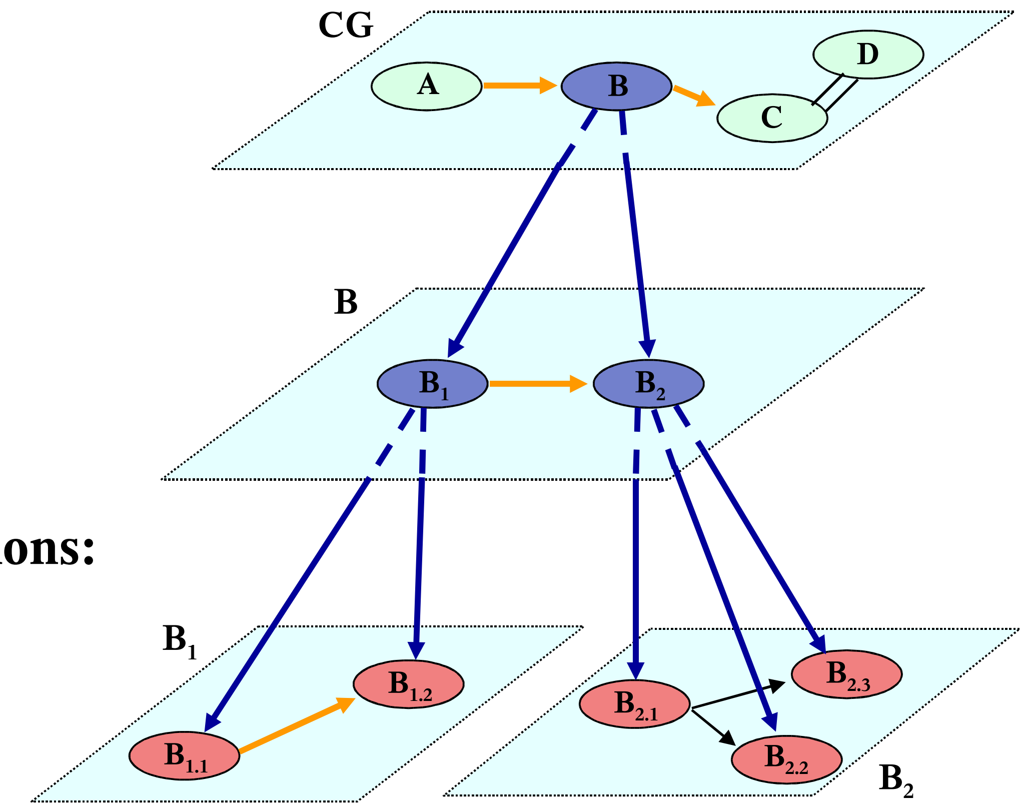
Tree of graphs

Atomic actions

Composite actions (plans)

Control relations between actions:

- sequence



Representation Formalism

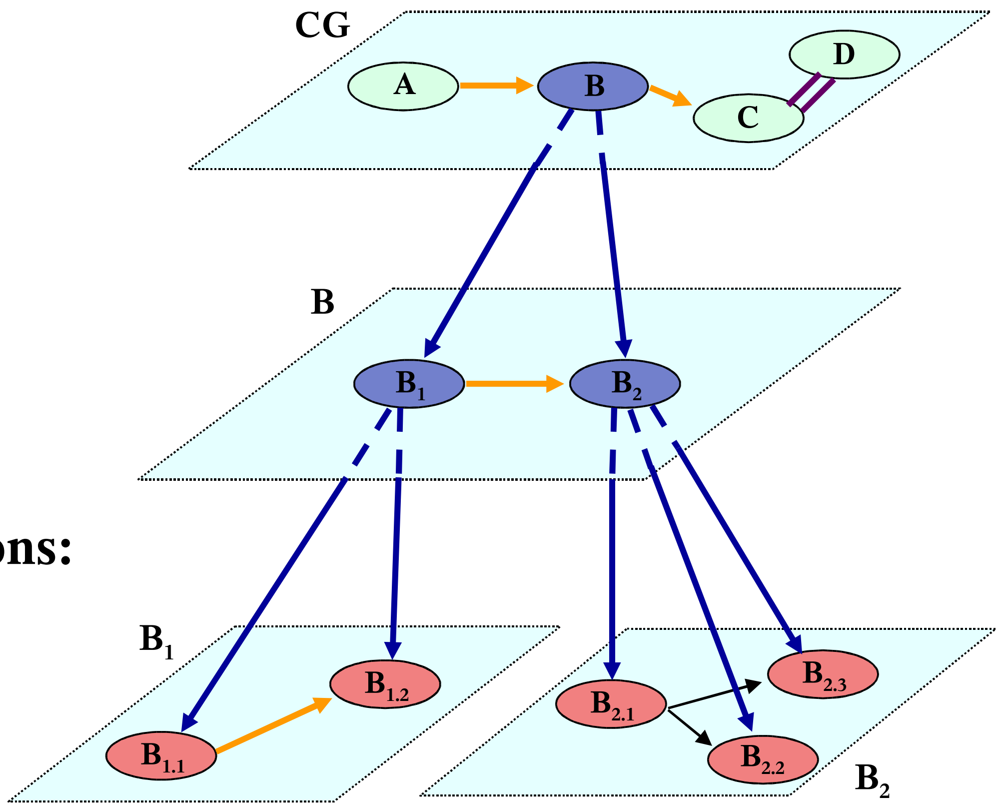
Tree of graphs

Atomic actions

Composite actions (plans)

Control relations between actions:

- sequence
- “controlled” (e.g., during)



Representation Formalism

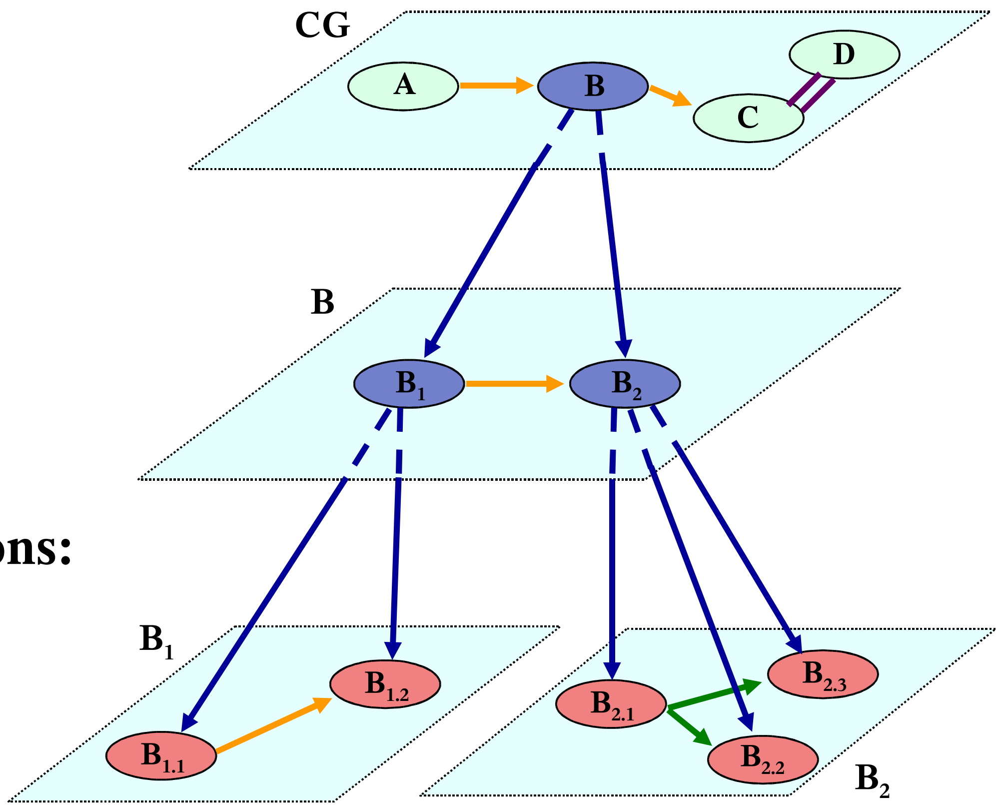
Tree of graphs

Atomic actions

Composite actions (plans)

Control relations between actions:

- sequence
- “controlled”
- alternative



Representation Formalism

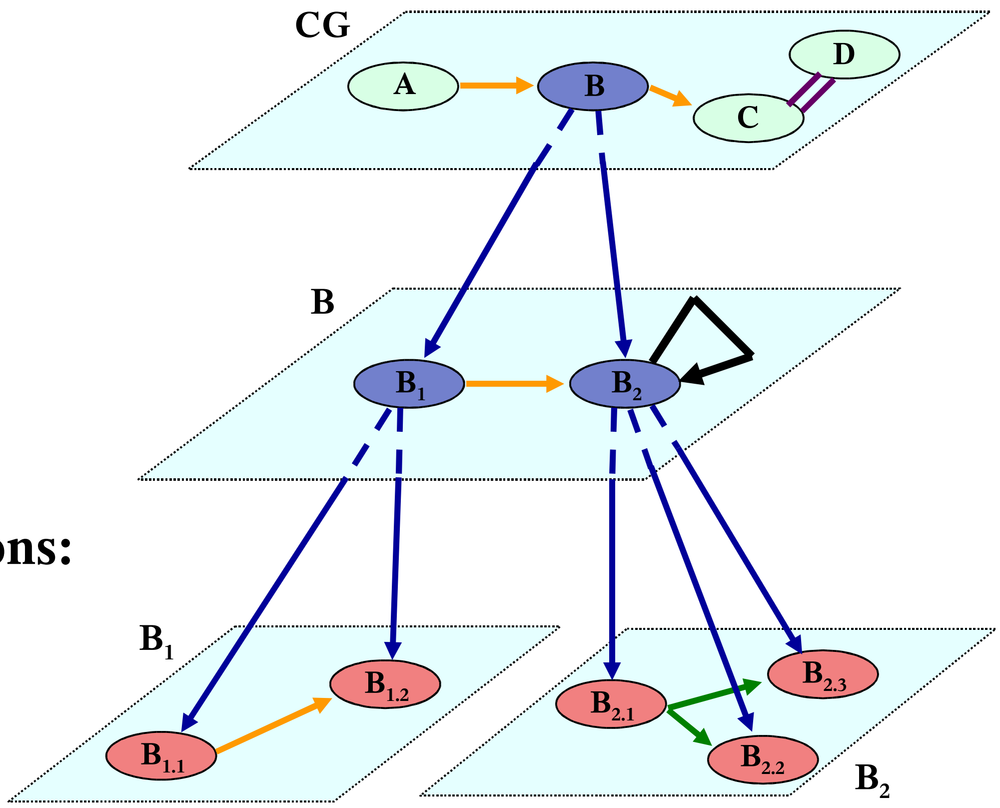
Tree of graphs

Atomic actions

Composite actions (plans)

Control relations between actions:

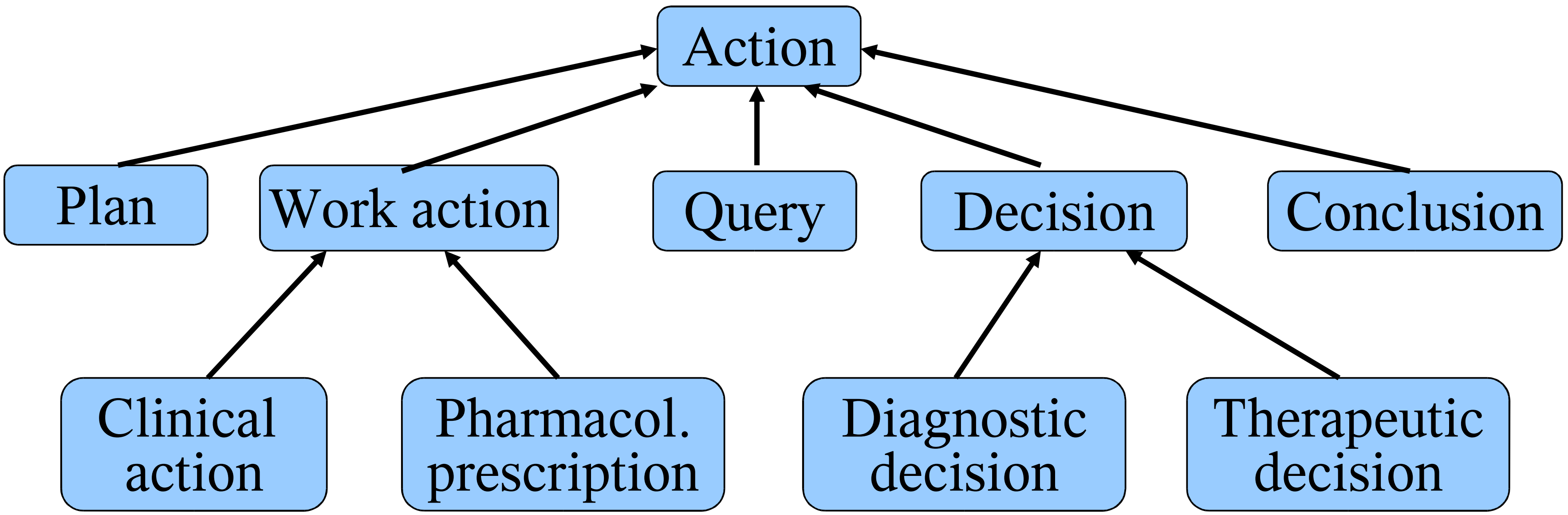
- sequence
- "controlled"
- alternative
- repetition (e.g. "3 times each 2 days for a month")



Representation Formalism

Temporal constraint associated with atomic actions and control relations (see below)

Representation Formalism
Hierarchy of Action Types



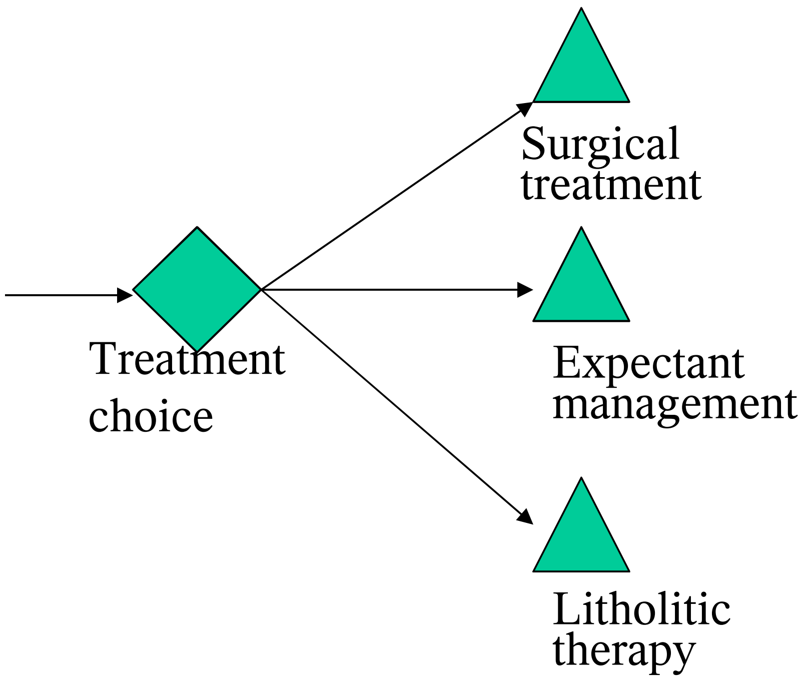
Representation Formalism
description of a clinical action

- basic description
  - name
  - description (text)
- preconditions
  - logical
    - must include
    - may include
    - must exclude
    - may exclude
    - conflicts
  - contextual
    - cost
    - time
    - resources
- goals (text)
- repetitions
  - frame time
  - action-time
  - delay time
  - T-time
  - execution time
  - frequency
  - exit_condition

Therapeutic decisions

Fixed set of parameters (effectiveness, cost, side-effects, compliance, duration)

Treatment choice for symptomless gallbladder stones



Local information associated with treatment choice (in the symptomless gallbladder stones guideline)

Strategy	Effectiveness	Cost	Duration	Compliance	Side effects
Expectant management	-	-	-	++++	-
Surgery	+++	++	+	-	++
Litholytic therapy	+	++	+++	++	+

Diagnostic Decisions

* Decision parameters
  <finding, attribute, value>

* Decision criteria
  score-based mechanism

  For each alternative

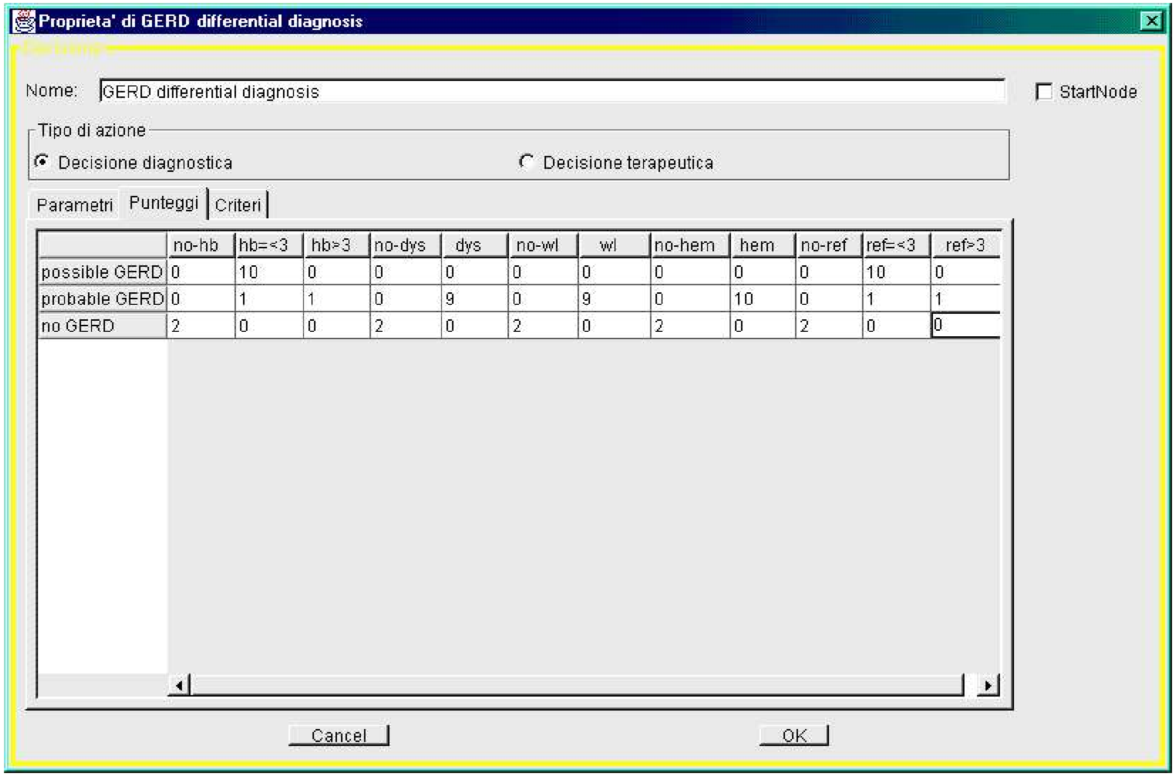
  For each parameter

  $\Rightarrow$ score

  $\Rightarrow$ (additive) threshold range

Diagnostic Decisions

(Gastro Esophageal Reflux Disease)



	no-hb	hb=<3	hb>3	no-dys	dys	no-wl	wl	no-hem	hem	no-ref	ref=<3	ref>3
possible GERD	0	10	0	0	0	0	0	0	0	0	10	0
probable GERD	0	1	1	0	9	0	9	0	10	0	1	1
no GERD	2	0	0	2	0	2	0	2	0	2	0	0

PARAMETERS: heartburn absent (“no-hb”), heartburn lasted not more than 3 months (“hb=<3”), heartburn r lasted more than 3 months (“hb>3m”); dysphagia absent (“no-dys”); dysphagia present (“dys”); occurrence of weight loss (“wl”) or non-occurrence (“no-wl”); hemathemesis absence (“no-hem”); hemathemesis presence (“hem”); postural reflux absent (“no-ref”), postural reflux lasted not more than 3 months (“ref=<3”); postural reflux lasted more than three months (“ref>3m”).
THRESHOLD: >9.
(One should conclude “no GERD” only if heartburn, dysphagia, weight loss, hematemesis and postural reflux are all absent.)

Acquisition

Strict interaction with DB's

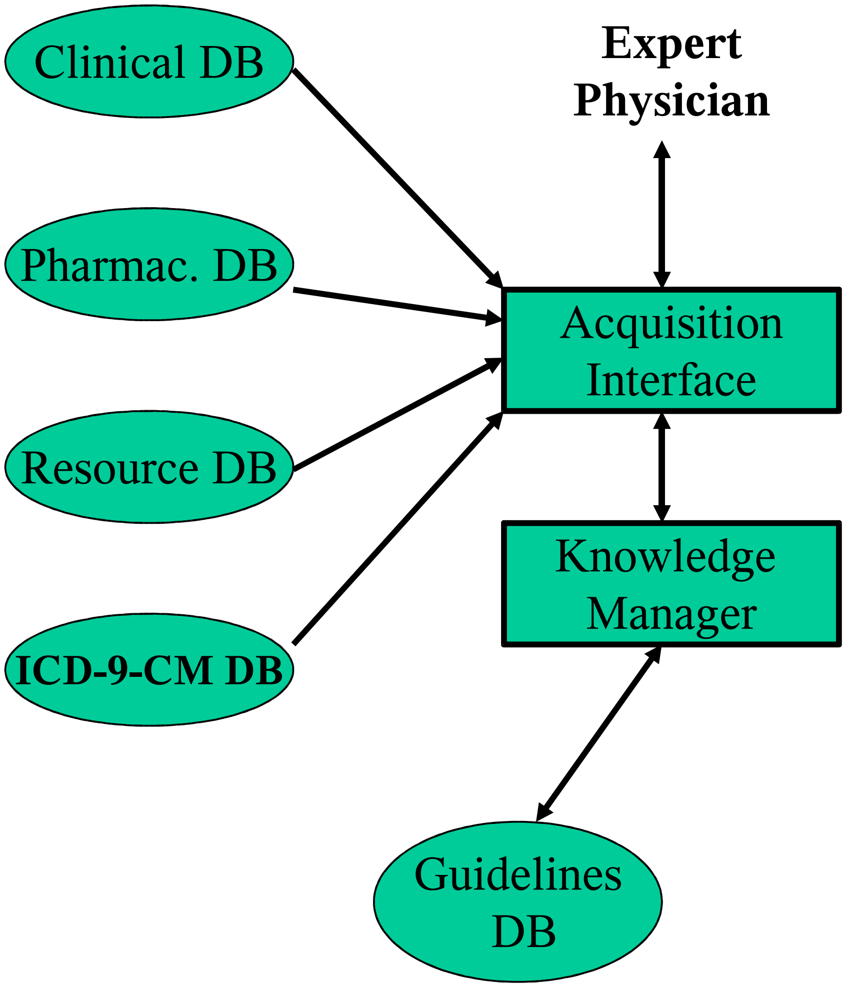
Clinical DB ≈ hierarchically organized vocabulary
→ Standardization
→ Data sharing
→ Support for semantic checks (e.g., legal attribute values)

NOTE: the organization (schema) of Patients DB is equal to the one of the Clinical DB
→ During acquisition, GLARE gets the information used at execution-time to retrieve automatically the patient's data (via automatically generated dynamic-SQL queries)

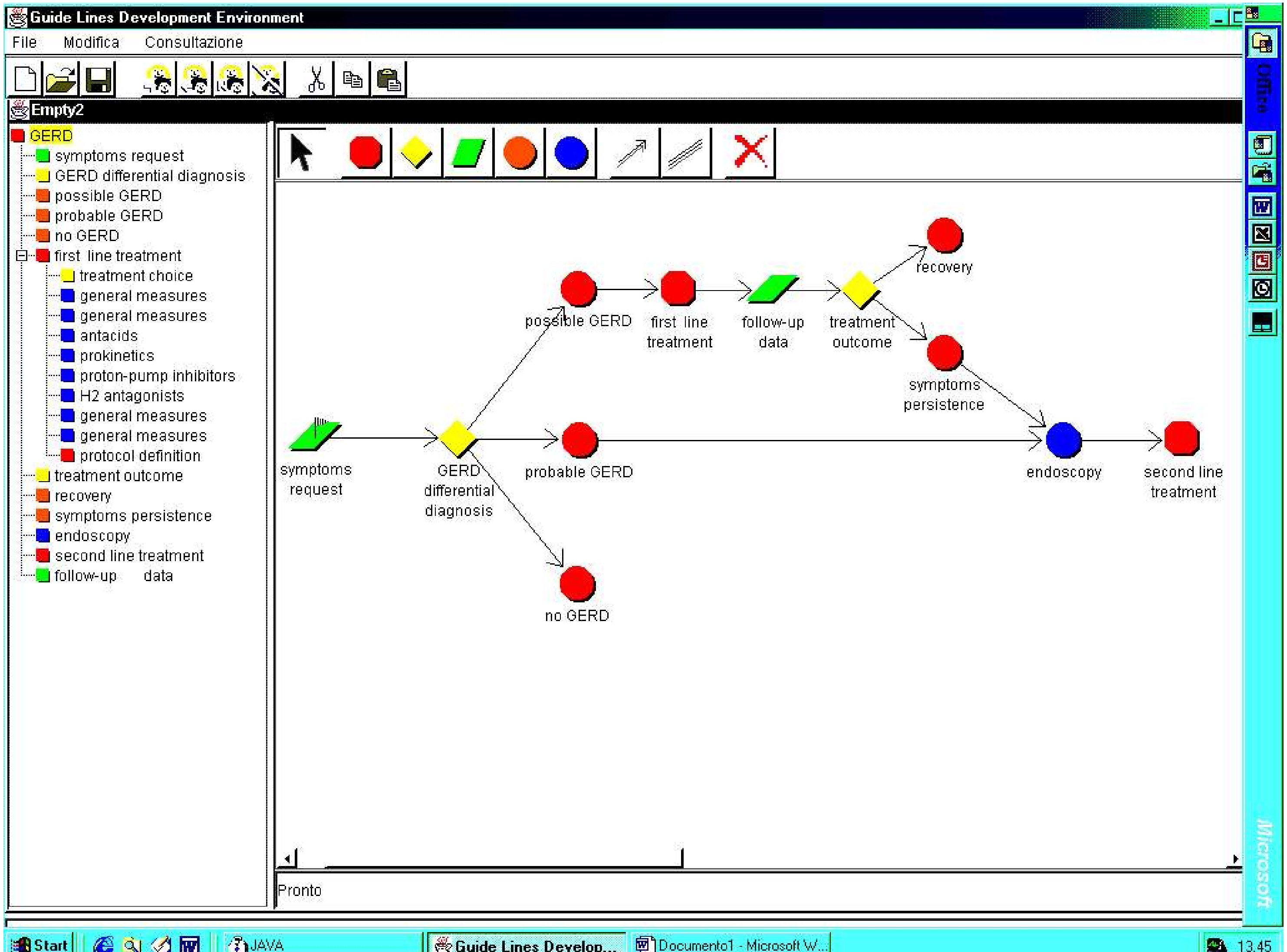
Acquisition
"Intelligent" helps (syntactic & semantic checks)

- "legal" names & "legal" values for attributes
- "logical" design criteria (no unstructured cycles, well-formed alternatives & decisions)
- "semantic" checks: consistency of temporal constraints

Architecture of the system
(Acquisition part)



Acquisition
Graphical Interface



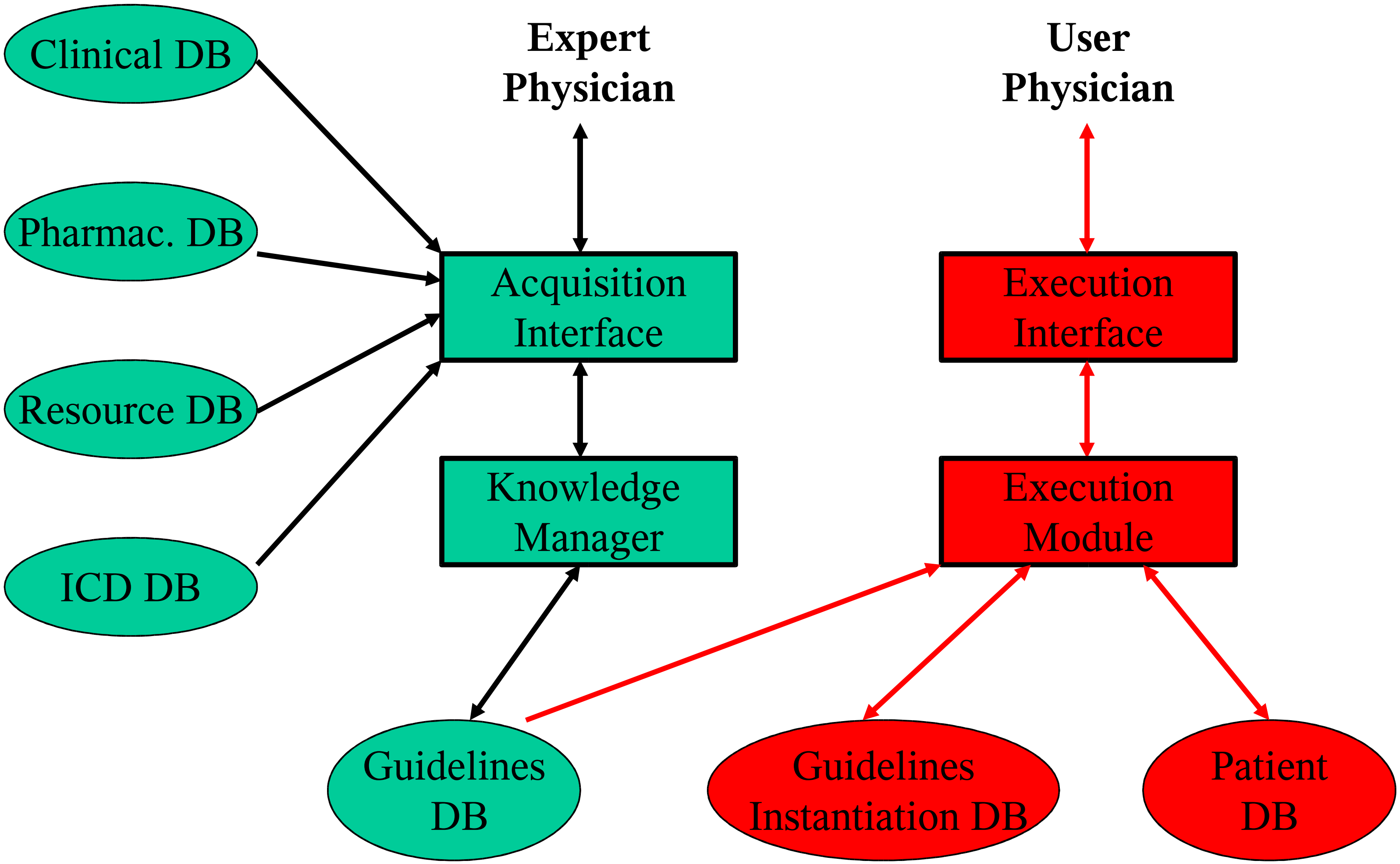
Clinical Guidelines Execution Module

"Instantiate" a general guideline on a specific patient

Basic Requirements

- Independent of the guideline
- Independent of the task (general purpose)
- Providing support to decisions

Architecture of the system



Agenda-based execution

In the agenda

- next actions to be executed
- execution time (earliest and latest e.t.)

- “On-line” execution: wait until the next e.t.
  (support physician in clinical activity)

- “Simulated” execution: jump to the next e.t.
  (education, critique, evaluation)

Executing atomic actions

Work actions:
- evaluate pre-conditions
- execute action within its range of time
- delete from the agenda

Query actions:
- retrieve data from patient's DB
- wait for data not already in the DB, or for the update of "expired" data

Conclusion actions:
- insert conclusion into the patient's DB

Decision actions: (see alternatives)

Executing composite actions

Sequence:

- evaluate next action e.t. (given current time and delay)
- execute it

Concurrent actions:

- execute actions according with the temporal constraints

Decision + alternative actions (e.g., diagnostic decision):

- evaluate parameter values for each alternative, using patient's DB
- determine the score for each alternative
- compare the score with the threshold
- show the alternatives to the user-physician (distinguishing between "suggested" and "not suggested" ones, and showing parameters and scores)
- execute the alternative chosen by the physician (warning available)

Executing Clinical Guidelines: other issues

- Repeated actions and user-defined periodicities
  - expressive language for user-defined periodicities [TIME'04]
  - computing next execution time

- Exits

- Failures
  return to previous decisions (chronological vs. guided backtracking)

- A user-friendly graphical interface

Implementation & Testing

Prototypical version (Java + Access) under revision

TESTS

(1) Using GLARE to build guidelines from scratch
take advantage of grafical and “intelligent checks” facilities
- bladder cancer algorithm

(2) Converting guidelines on paper to GLARE
inconsistencies/ambiguities detected!
- reflux esophagitis, heart failure, ischemic stroke

Supporting medical decision making hypothetical reasoning (“what if?”) facility

“local information”: considering just the decision criteria associated with the specific decision at hand

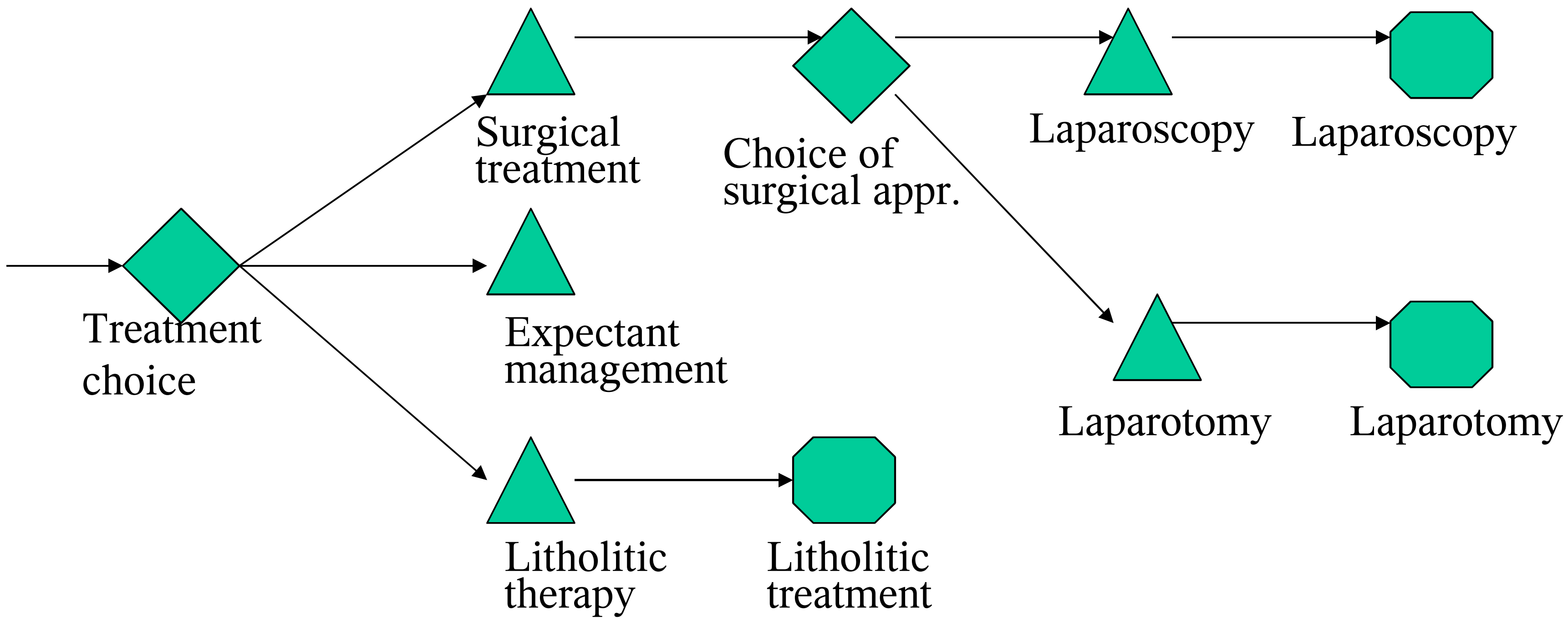
“global information”: information stemming from relevant alternative pathways in the guideline

“What if” facility

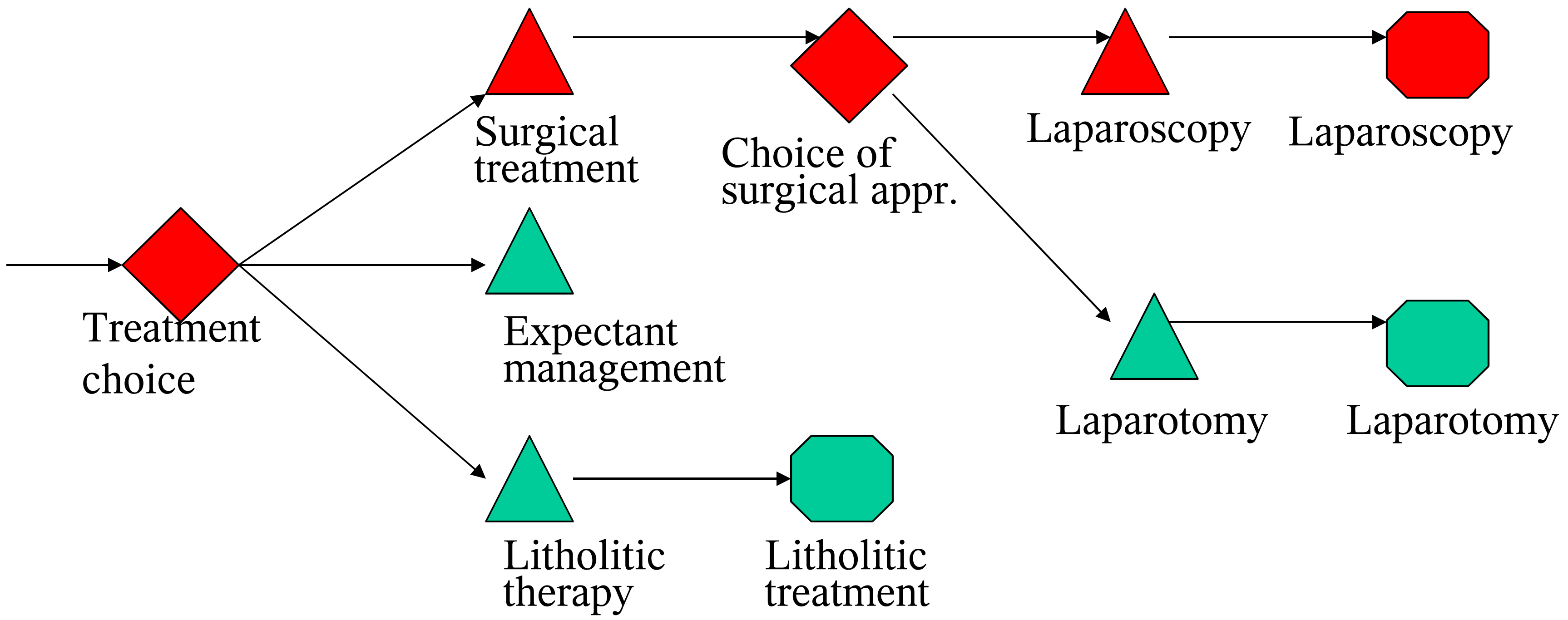
Facility for gathering the chosen parameter (e.g, resources, costs, times) from the “relevant” alternative paths on the guideline

It provides an idea of what could happen in the rest of the guideline if the physician selects a given alternative for the patient, and supports for comparisons of the alternatives

Syntomless gallbladder stones treatment choice: “global information”

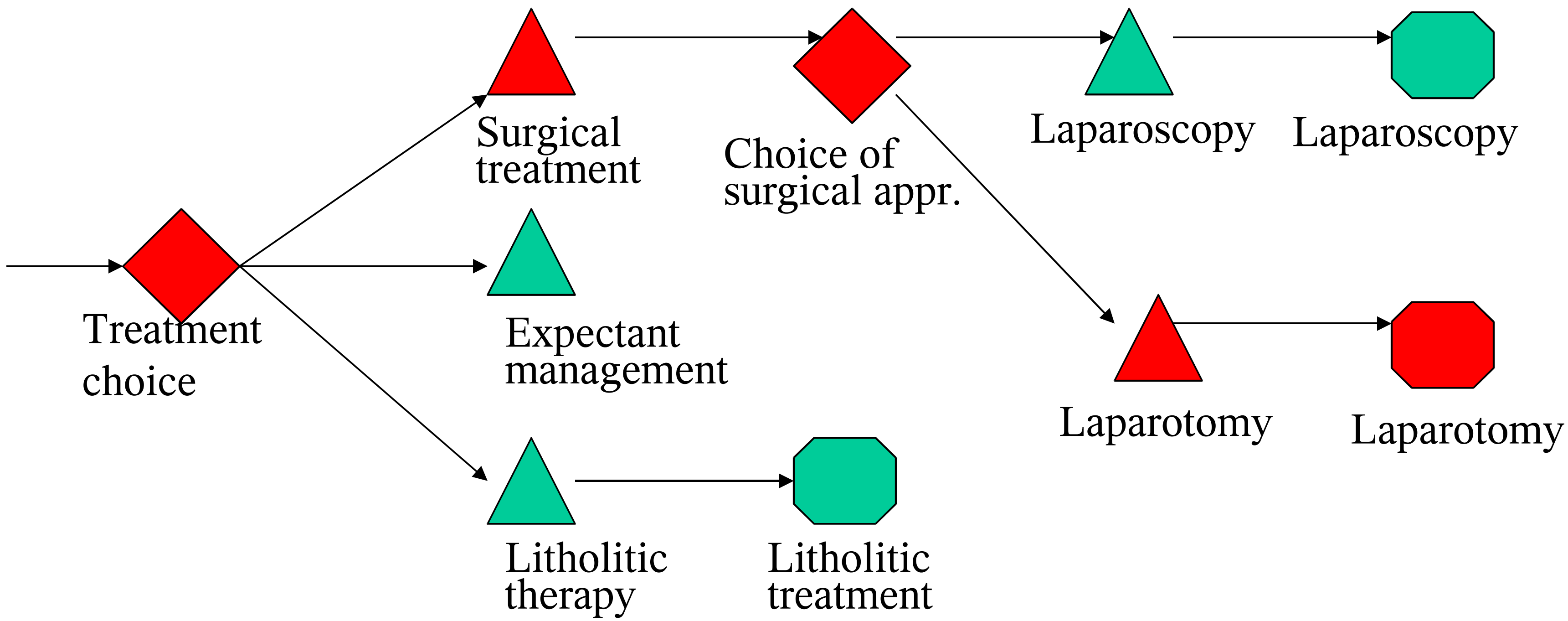


Syntomless gallbladder stones treatment choice: “global information”



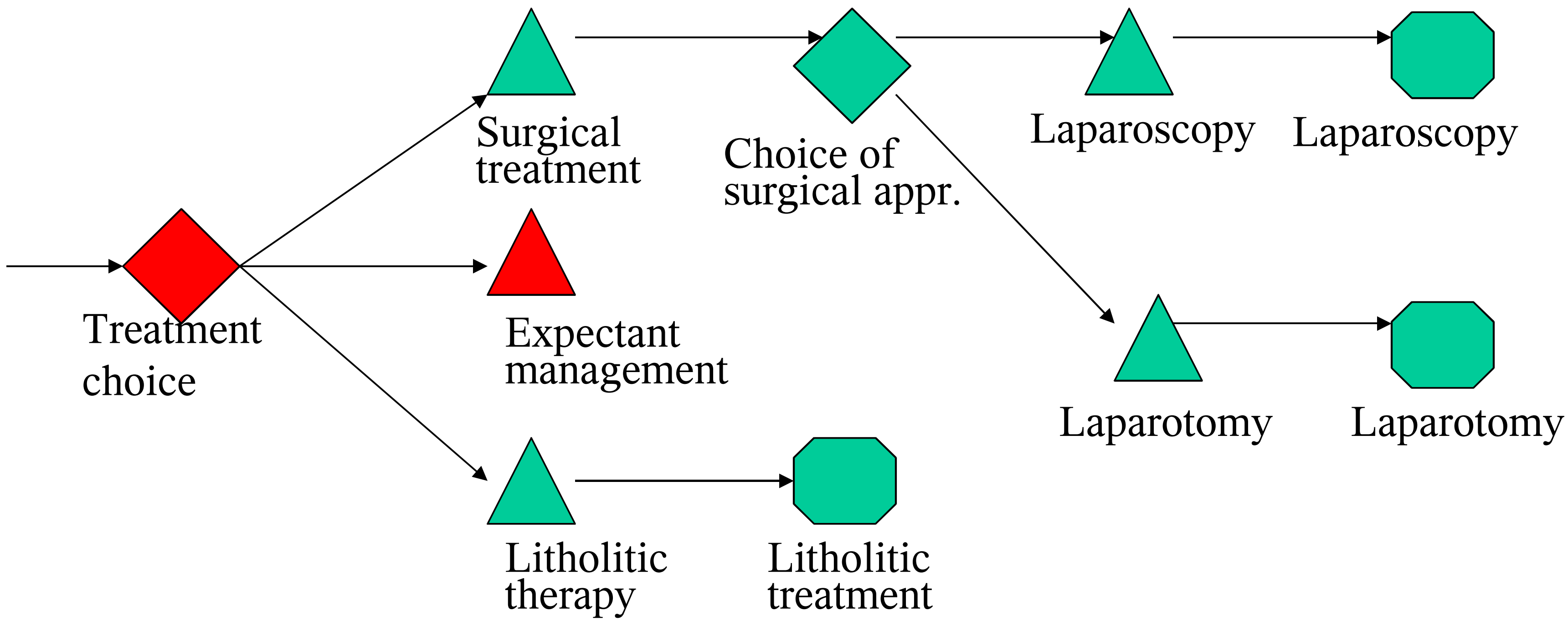
Duration min:2 days Max:3 days

Syntomless gallbladder stones treatment choice: “global information”



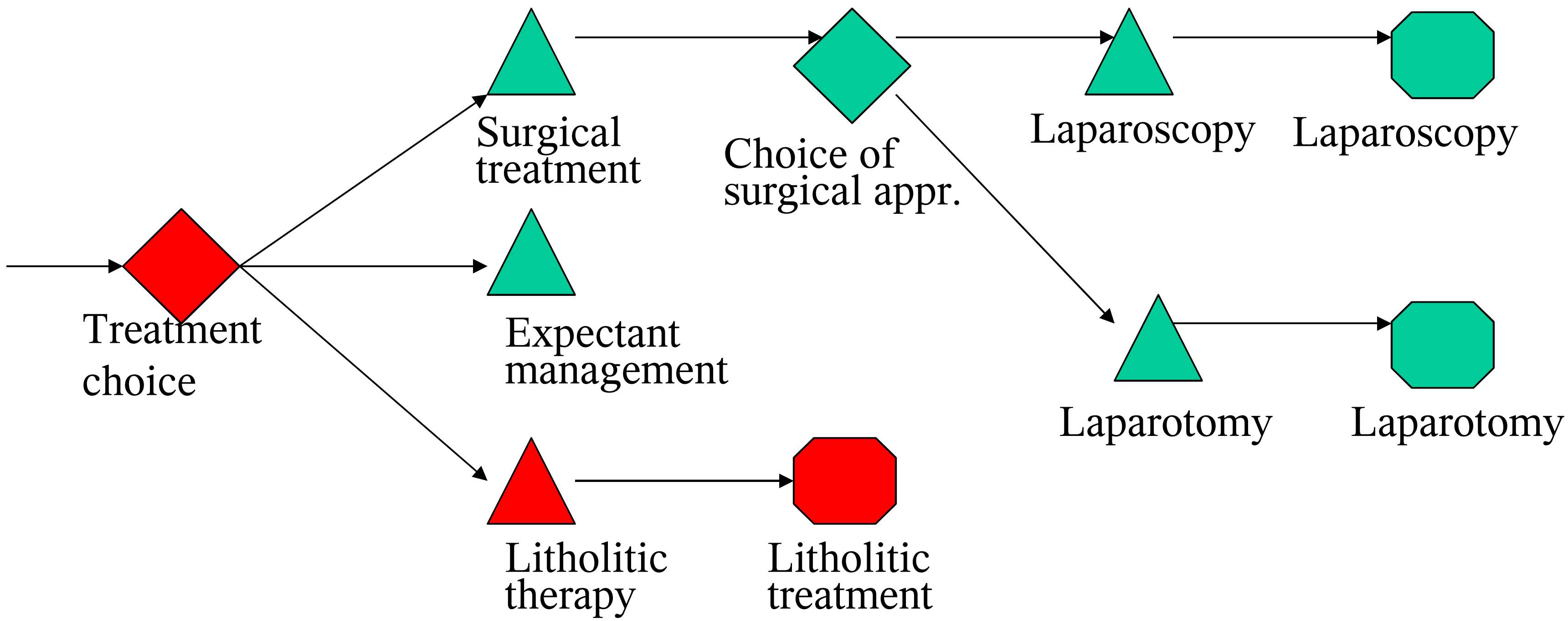
Duration min:6 days Max:8 days

Syntomless gallbladder stones treatment choice: “global information”



Duration min:1 day Max: all life long

Syntomless gallbladder stones treatment choice: "global information"



Duration min:2 months Max:1 year

Local information associated with treatment choice (in the symptomless gallbladder stones guideline)

Strategy	Effectiveness	Cost	Duration	Compliance	Side effects
Expectant management	-	-	-	++++	-
Surgery	+++	++	+	-	++
Litholytic therapy	+	++	+++	++	+

Digression

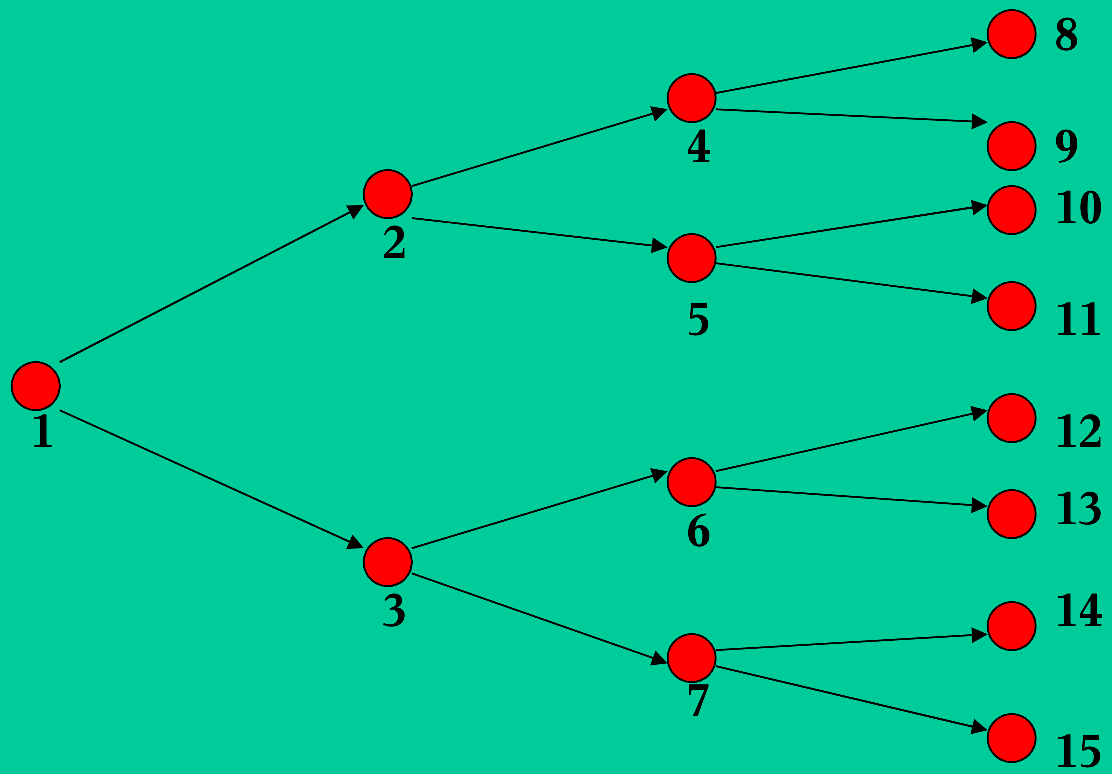
Why don't we put "global info (about paths)" locally in the decision actions?

Given "local info" in each node, collecting & storing might be automatic

HOWEVER:

- exponential space in each node
- data duplication (consistency after updates?)
- not user friendly (too many data!)
  - not all aternatives are "relevant"
  - data not always necessary

>> global data only at execution time, <u>on request</u>


1
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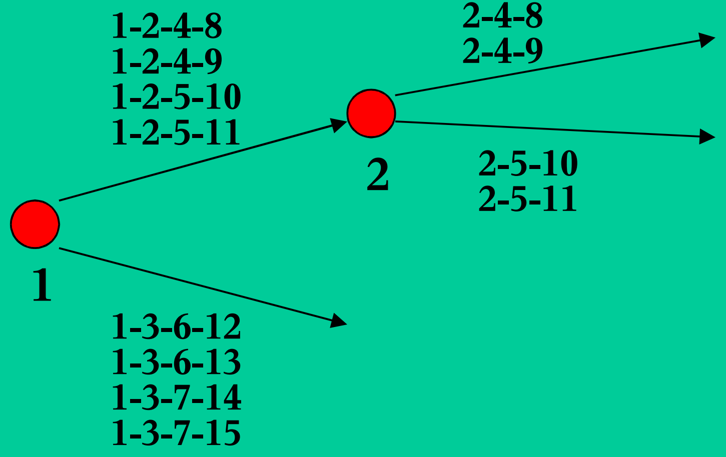

1-2-4-8
1-2-4-9
1-2-5-10
1-2-5-11
2-4-8
2-4-9
2
2-5-10
2-5-11
1
1-3-6-12
1-3-6-13
1-3-7-14
1-3-7-15

Extensions (current/future)

- exploiting decision theory within hypothetical reasoning (Stefania Montani, ECAI'04)
- improving the graphical interface in showing comparisons

Temporal Constraints Management in GLARE

- representing different types of temporal constraints

- correct, complete and tractable reasoning algorithms

Digression

Why tractability, correctness and completeness?

- tractability (i.e., polynomial time complexity) $\rightarrow$ “acceptable” response time
- correctness & completeness $\rightarrow$ reliable answers

PROBLEM: **trade-off** between:

- expressiveness of the (temporal) formalism
- correctness & completeness of tractable (temporal) reasoning

Temporal Constraints in Clinical Guidelines

ACTIONS: duration

CONTROL RELATIONS:

sequence, alternative: delay

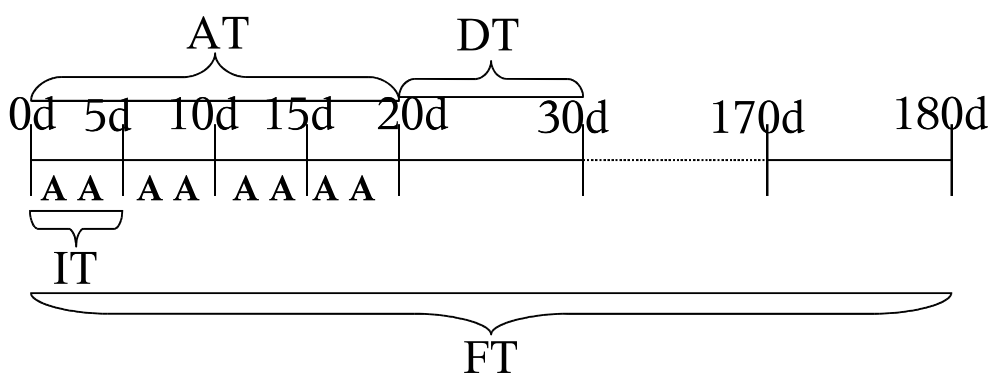
controlled: temporal distance between endpoints

repetition: frame time (exit condition), action time, delay time, I-time, frequency

PART-OF RELATIONS

Temporal Constraints in Clinical Guidelines repetitions

"For six months, perform action A twice each five days for twenty days, and then suspend for ten days (and so on)"



Possible components of a repetition:

frame time -FT- (exit condition) → ***"six months"***

action time -AT- → ***"twenty days"***

delay time -DT- → ***"ten days"***

I-time -IT- → ***"five days"***

frequency → "twice"

Temporal Constraint Treatment

Two related problems:

1) Representing Constraint

2) Reasoning with Constraints

Temporal Constraint Treatment

WHEN Temporal Reasoning is useful in Guidelines?

ACQUISITION

- to check consistency

EXECUTION

- to compare the duration of paths, in hypothetical reasoning (query answering facilities)

- to check that the time of execution of actions on patients is consistent with the constraints in the guideline

Digression

STP framework [Dechter et al., 91]

Conjunctions of b.o.d. constraints

$$\mathbf{c \leq X\text{-}Y \leq d}$$

Can be used to represent distances between points (starting/ending points of actions)

Floyd-Warshall all-to-all shortest paths algoritm is correct and complete for the STP framework, and operates in $O(N^3)$ (where N is the number of variables - time points)

It produces the ***minimal network*** of the constraints (i.e., the shortest path between each pair of nodes)

Representation of temporal constraints

Goal: exploiting the STP framework

ACTIONS: duration → OK

sequence, alternative: delay → OK

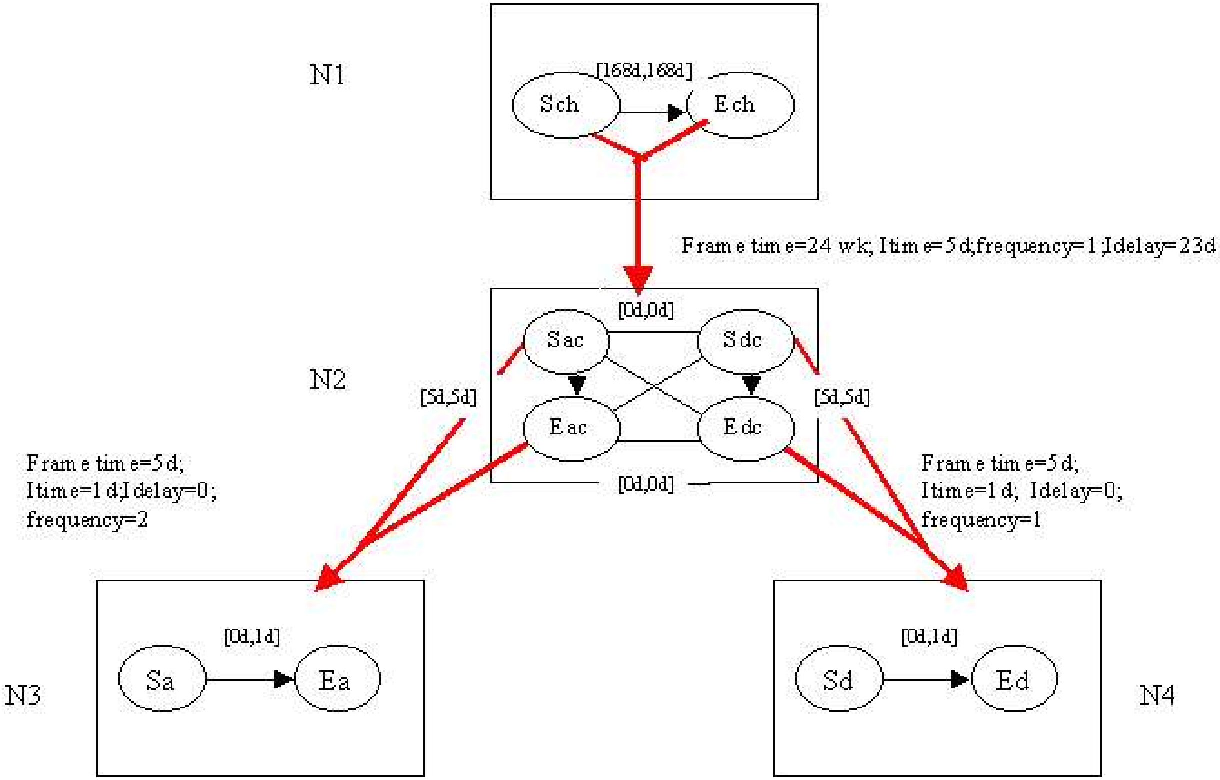
controlled: temporal distance between endpoints → OK

PART-OF RELATIONS → OK (?)

repetitions:

cannot be "expanded" (exit conditions) → NO

Labeled tree of STPs (STPs-tree)



Tree of STPs for the multiple mieloma chemotherapy guideline.
The overall therapy (node N1) s composed by 6 cycles of 5 days plus a delay of 23 days . In each cycle (node N2), two therapies are executed in parallel: Alkeran (node N3: Sa and Ea are the starting and ending nodes), to be repeated twice a day, and Deltacorten (node N4: Sd and Ed are the starting and ending nodes), to be repeated once a day. Arcs between any two nodes X and Y in a STP (say N2) of the STP-tree are labeled by a pair [n,m] representing the minimal and maximal distance between X and Y.

Consistency checking on STPs-trees

ALGO1: temporal consistency of guidelines

Top-down visit of the nodes in the STPs-tree

For each node in the STPs-tree:

1) the consistency of the constraints used to specify the repetition taken in isolation is checked;
2) the "extra" temporal constraints regarding the repetition are mapped onto bounds on difference constraints;
3) Floyd-Warshall's algorithm is applied to the constraints in the STP plus the "extra" bounds on difference constraints determined at step 2.

Property 1. ALGO1 is correct, complete, and tractable (it operates in $O(N^3)$, where N is the number of actions in the guideline).

Temporal reasoning algorithms on STPs-trees

STP_tree_consistency(X: STP; GL_X: guideline-action-description; freq: integer; Itime: duration; Idelay: duration; FT: duration; Ex_cond: boolean)

If (Not((Itime+Idelay) $\subseteq$ FT)) Then Return INCONSISTENT Else Begin

For each path P_i from the StartNode of GL_X to an ending-node of GL_X do impose (in X) that the maximum duration of P_i is the minimum between the current duration in X and Itime

If after the maximum duration of P_i becomes less than its minimum duration

Then Return INCONSISTENT Else Begin

Y <-- Floyd-Warshall(X);

If Y=INCONSISTENT Then Return INCONSISTENT Else Begin

. For each path P_i from the StartNode of GL_X to an ending-node of GL_X

do $Max_i \leftarrow$ minimum(Max_i , (Itime – (freq – 1) * min_i))

. Y <-- Floyd-Warshall(X);

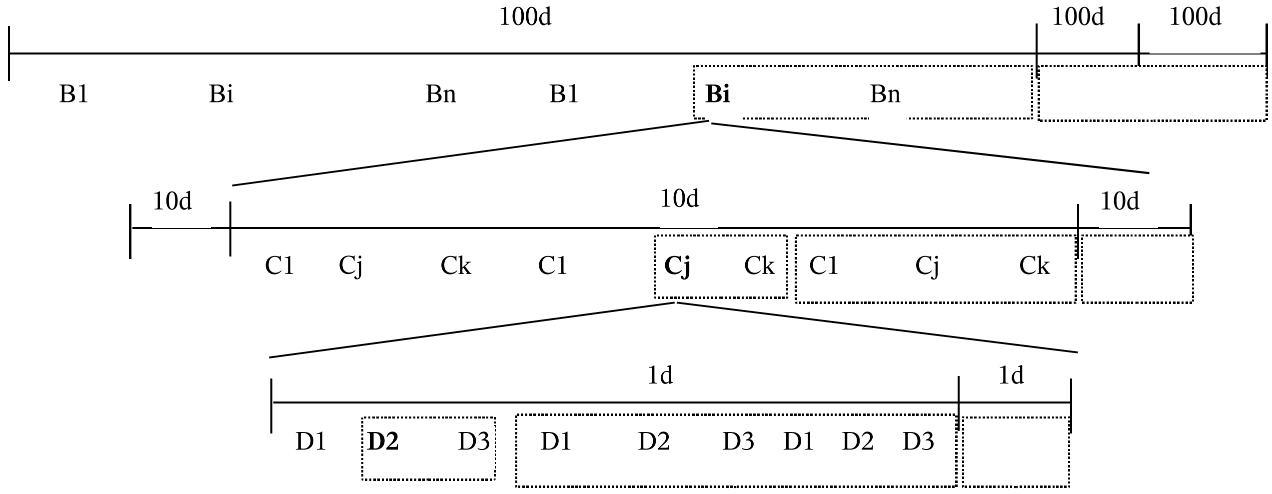
. If Y=INCONSISTENT Then Return Inconsistent Else Return X

(Temporal) Query Answering

- Cj is the sequence of D1 D2 D3, and must be repeated 3 times each day for 2 days ;
- Bi is the sequence of C1 … Cj …. Ck, and must be repeated 3 times each 10 days, for 30 days;
- A is the sequence of B1 … Bi … Bn, and must be repeated 2 times each 100 days for 300 days.

E.g., find the minimum distance between the action D2 occurring in the first repetition of Cj occurring in the fifth repetition of Bi in the second repetition of A and the end of A

Efficient "complete" algorithm which exploits the "local" minimal networks



Temporal reasoning on guidelines + instantiations

Idea:

- first, let instances inherit the correponding constraints from the guideline
- second, check the consistency of the constraints on instaces (base + inherited)

Temporal reasoning on guidelines + instantiations INHERITANCE

Unary constraints: duration

Binary constraints: delays, qualitative relations
* only correlated pairs of actions

N-ary constraints: repetition constraints
* periodicity, cardinality

Temporal reasoning on guidelines + instantiations
PREDICTION

If we can assume complete observability

if an action (on a given patient) has not been observed, it has not occured yet

→ an inconsistency may arise, in case the guideline constraint impose that it should have started before NOW!

A technical problem:

all temporal constraint propagation approach need an explicit representation of all actions

Our solution: hypothesizing actions

Temporal reasoning on guidelines + instantiations ALGORITHM (sketch)

ALGO2: temporal consistency on guidelines execution

(1) the existence of non-observed instances whose occurrence is predicted by the guideline is hypothesized;

(2) all the constraints in the general guidelines are inherited by the corresponding instances (consi dering both observed and hypothesized instances). This step also involves "non-standard" inheritance of constraints about periodicity;

(3) constraint propagation is performed on the resulting set of constraints on instances (via Floyd-Warshall's algorithm) , to check the consistency of the given and the inherited constraints;

(4) if constraints at step 3 are consistent, it is further checked that such constraints do not imply that any of the "hypothesized" instances should have started before NOW.

Temporal reasoning on guidelines + instantiations

Property 2. ALGO2 is correct, complete, and tractable.
It operates in $O((N+M)^3)$, where N is the number of actions in the guideline and M the number of instances of actions which have been executed (and observed).

Context Adaptation

The gap between guidelines generality and the contextual constraints is one of the biggest problem in the dissemination and use of clinical guidelines

Physical context (e.g., hospital)

→ resources (e.g., instruments for laboratory tests)

Software context

→ DBMS (and sw platform)

"Conceptual" context

→ Ontology/Vocabulary independent guidelines

(Gianluca Correndo, CGP'04)

Resource-based Adaptation

Idea:

pruning from general guidelines all those alternative paths that require unavailable resources

Realization:

pre-compilation phase

INPUT: general guideline GL + available resources

OUTPUT: context-based guideline $GL_{CONTEXT}$

$GL_{CONTEXT}$ only contains "legal" paths (i.e., paths for which all resources are available in the given context)

Software-based Adaptation

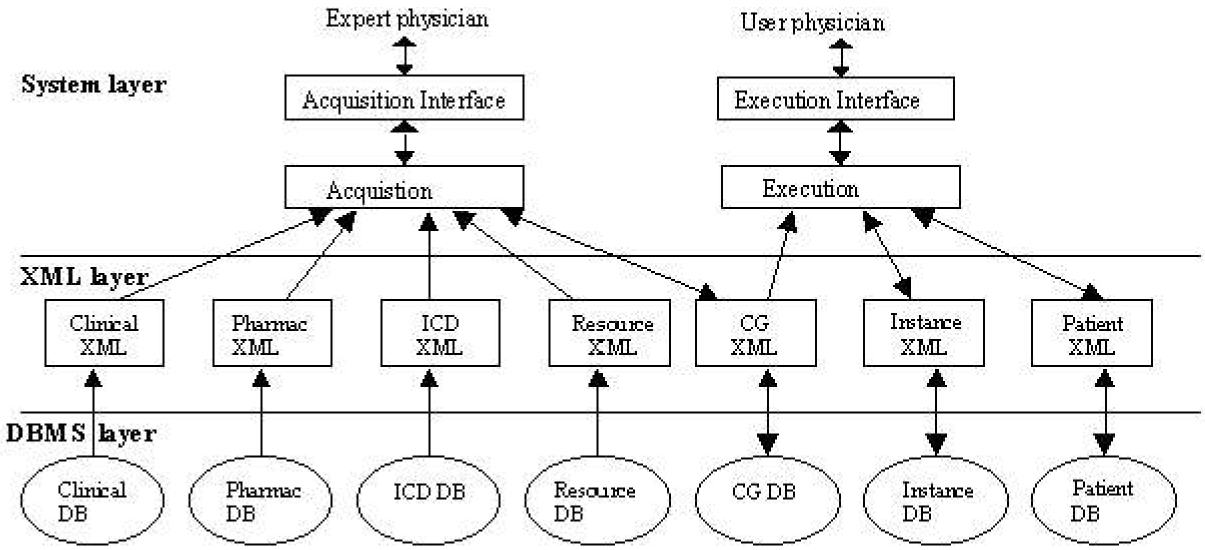
Idea:

making GLARE (mostly) independent of the DBMS

Realization:

layered architecture (XML-layer as an interlingua)

Software-based Adaptation



XML layer and DBMS layer manage the same data but offer different functionalities!

Merging the advantages of both approaches

Summary

- Introduction
- Representation formalism
- Architecture: acquisition and execution modules
- Decision-making facilities: hypothetical reasoning
- Temporal reasoning facilities
- Context-adaptation facilities