Modeling Clinical Practice Guidelines using Predicate Logic for Reasoning with Incomplete Patient's Data

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Outline

- Clinical practice guidelines
- Executable guideline model
- Guideline as a decision and implication graph
- Reasoning from a guideline
- Discussion

Clinical Practice Guidelines (CPGs)

- Motivation for the CPG development and use: medical errors (IOM Study, 2001); need to practice evidence-based medicine; improve patient outcomes; control costs

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

- "Our" CPG: "set of decision steps of varying level of abstraction and detail for diagnosis and/or management of patients who have specific clinical condition"

CPG Research

- Some examples of CPG models/formalisms:

1. *Arden syntax*: Medical Logic Modules that include set of logical expressions implemented as production rules; has no execution standards
2. *GLIF*: a flowchart translated into object-oriented model; GLEE execution engine under development
3. *PROforma*: knowledge composition language for expert system-like use where CPG is modeled as a plan consisting of tasks; execution using Prolog-like interpreter
4. *Asbru*: time-oriented CPG representation as a set of skeletal plans; executed mostly as a visualization tool

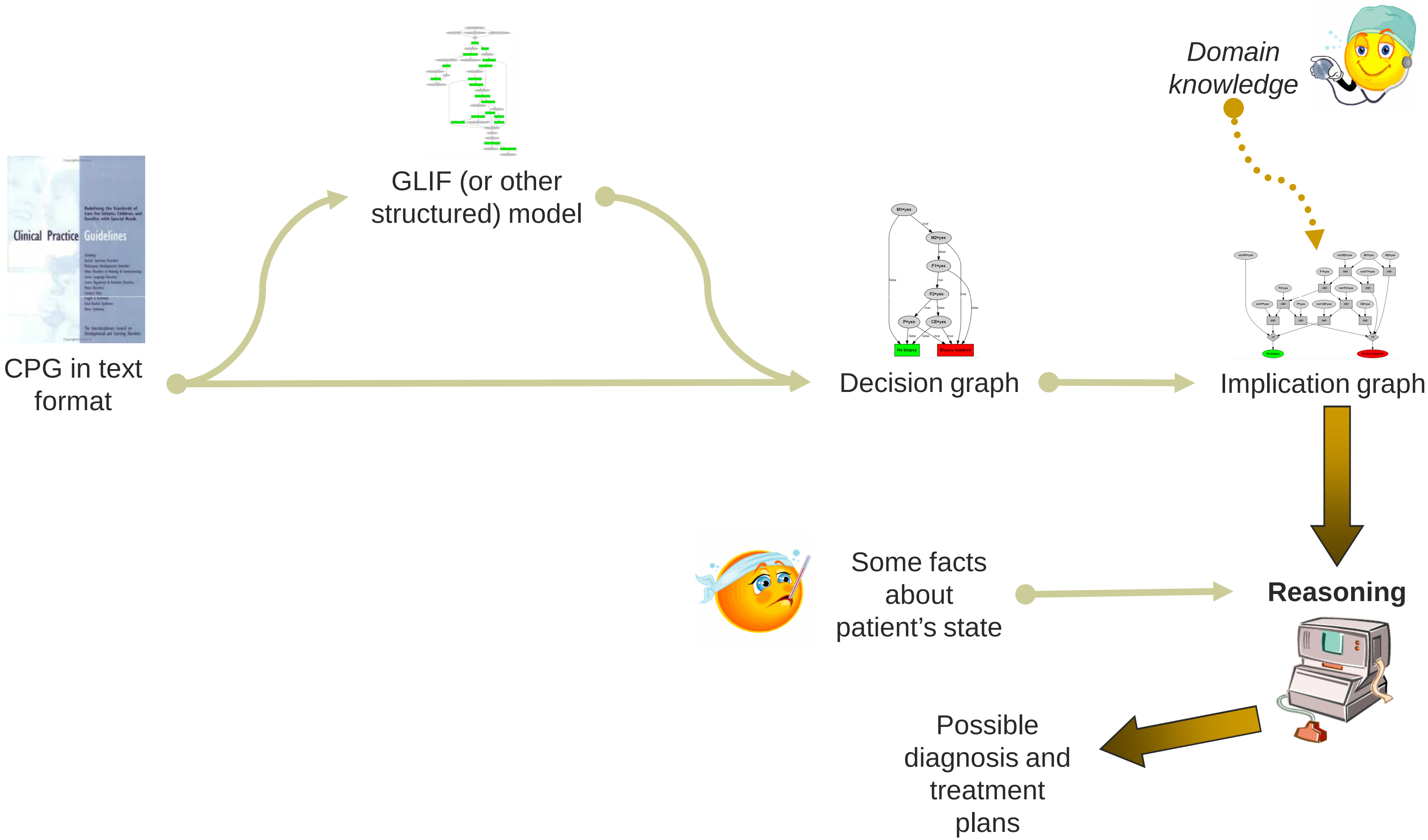
Gaps in Existing CPG Research

- Most of the attention has been paid to representing CPGs as models rather then implementing them clinically

- Implementation issues include:
  - How to customize CPG to local practice?
  - How to use CPG with missing or uncertain data?
  - How to integrate CPG with a decision support function?
  - How to adjust CPG to different levels of decision making expertise?

<u>Our research question: How to use CPG with missing data</u>

Proposed Approach: Enhance CPG Execution with Reasoning



Breast Mass (BM) CPG (1)

- Helps to decide whether a patient needs biopsy when breast mass was found (M. Borten. Breast Mass. In: Gynecological Decision Making, 1998)
- Possible outcomes:
  - biopsy required (to confirm or rule out malignant tumor)
  - no biopsy

BM CPG (2)

A. Breast self-examination is acknowledged to be of limited value principally because it is inconsistently reliable and few women are diligent and attentive. Despite this, the practice can be justified on the basis of the occasional breast cancer it detects. Teaching the needs for and the details of breast self-examination should be reinforced by encouraging the patient to practice it with regularity. The importance of early detection must be repeatedly stressed. Discovery of a mass in the breast will usually prompt a patient to visit her gynecologist, although some exhibit a regrettable reluctance to do so. Notwithstanding that the majority of breast masses are of a benign nature, it is essential to undertake a complete evaluation before one can reassure the patient. Elicit a background of risk factors for breast cancer in her personal and family history.

B. Inspection of the breasts is the first step in the examination. It should be carried out with the patient sitting, first with her arms at her sides and then overhead. Palpation of the breast is usually performed with the patient supine. Any abnormality noted on inspection or palpation should be further pursued by examination in the sitting and standing positions. Look for significant signs of asymmetry, nipple deviation, retraction, induration, edema, fixation, or tumor bulging. Breast cancer often initially presents as a nontender firm lump with ill-defined, in distinct margins. Identifying this dominant mass is the principal objective of the examination.

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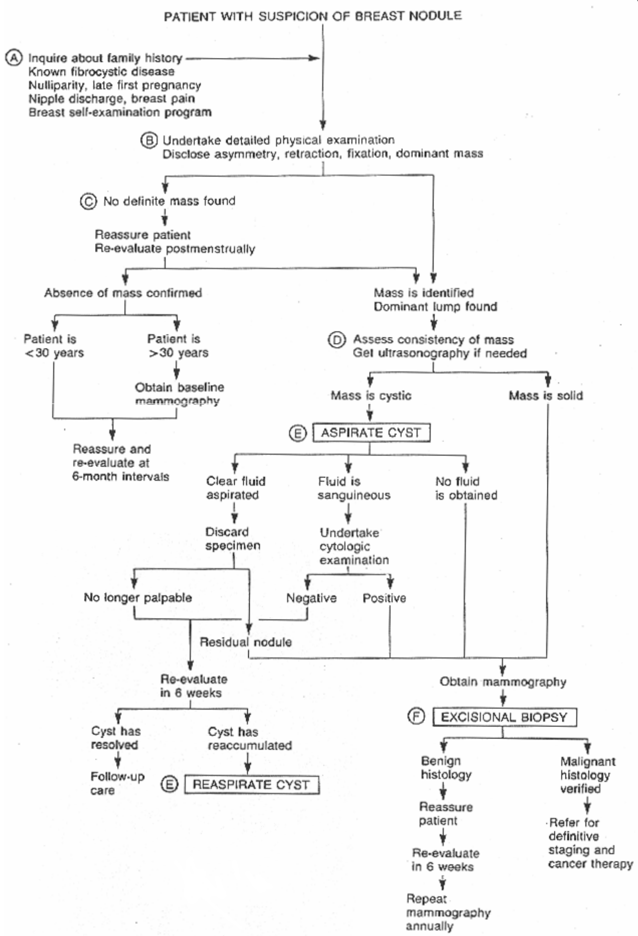
....
....



Source: http://www.smi.stanford.edu/projects/intermed-web/guidelines/breastmass.html

Representing BM CPG in GLIF

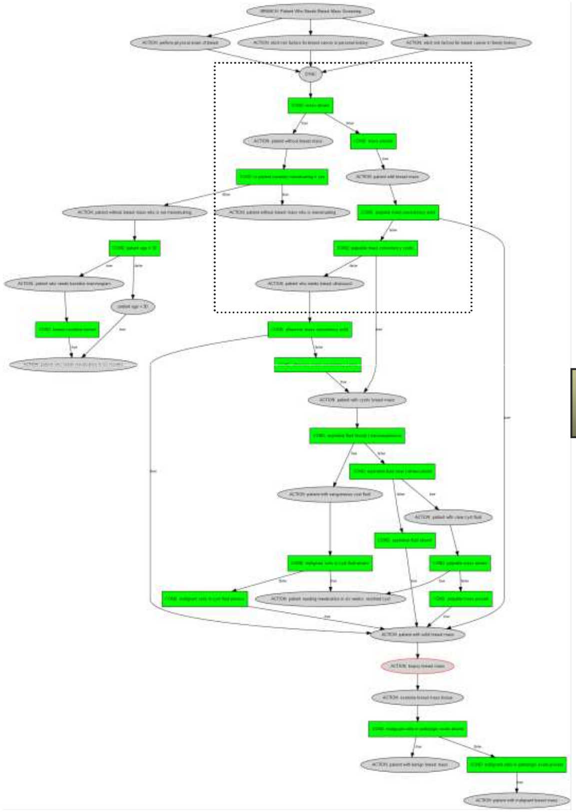
- Specification for structured representation of CPGs
  - Decision (conditional) step: palpable mass is cystic
  - Action step: aspirate cyst
  - Patient state step: patient requires biopsy
  - Branch and synchronization steps: sequencing
- Developed by the InterMed Collaboratory (Harvard, Stanford, Columbia, McGill) to facilitate sharing of CPGs
- Current specification – GLIF 3.5 (May 2004)

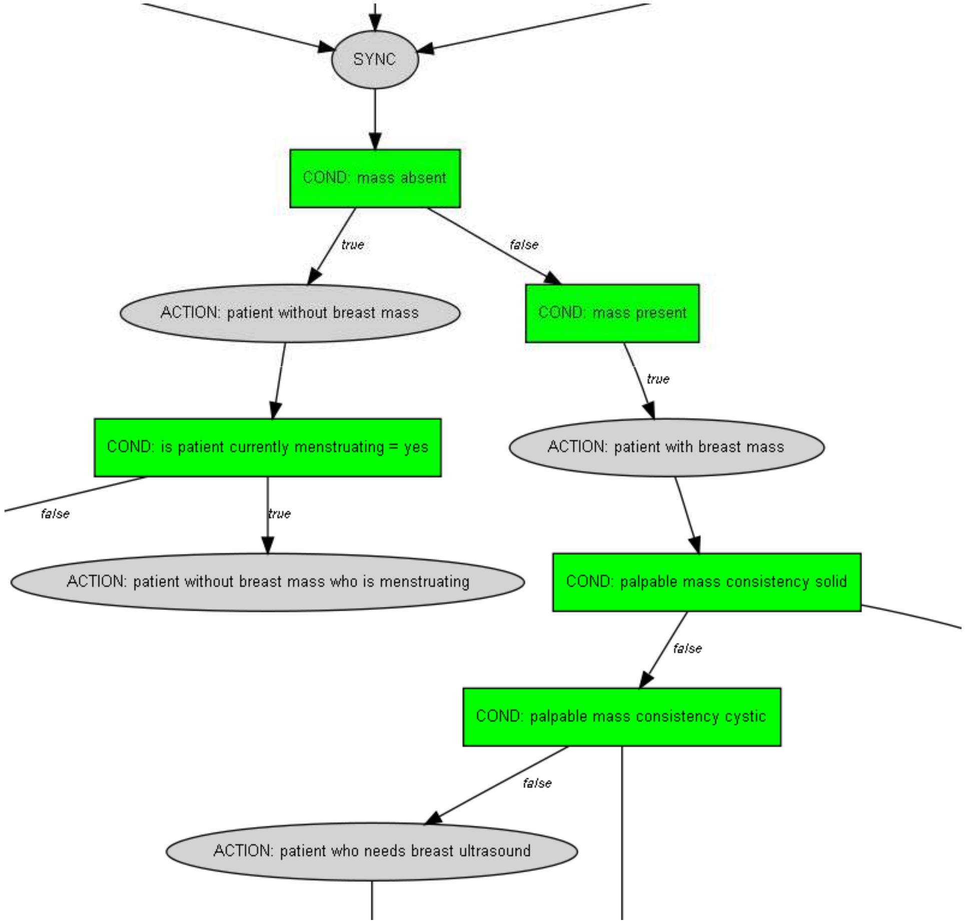
GLIF Model for BM CPG (1)

```
Guideline the_breast_mass_guideline
{
   name = "Breast Mass Guideline";
   authors = SEQUENCE 1 {"Max Borten, MD, JD";};
   eligibility_criteria = NULL;
   intention = "Evaluation of breast mass.";
   steps =
      SEQUENCE 40
      {
         (Branch_Step 1);
         (Action_Step 101);
         (Action_Step 102);
         (Action_Step 103);
         (Synchronization_Step 1031);
         (Conditional_Step 104);
         (Conditional_Step 105);
         (Action_Step 2);
         ...
};
   first_step = (Branch_Step 1);
   didactics =
      SEQUENCE 1
      {
         Supplemental_Material 0.1
         {
            label = "critique";
            MIME_type = "text/plain";
            material = "Published guideline does not contain
explicit eligibility criteria.";
         };
      };
}
```

```
...
Action_Step 5
{
   name = "PATIENT WHO NEEDS REEVALUATION IN SIX MONTHS";
   action =
      Action_Spec 5.1
      {
         name = "Schedule Appointment, current date + 6 months";
         patient_data = SEQUENCE 0 {};
         description =
            "Schedule Appointment * {date = (current date + 6 months)}";
         didactics = SEQUENCE 0 {};
   subguideline = NULL;
   next_step = NULL;
   didactics = SEQUENCE 0 {};
}
...
Conditional_Step 1001
{
   name = "";
   condition =
      Boolean_Criterion 10.1
      {
         type = k_three_valued;
         spec =
               "Breast_Palpation_Findings *
               {
                  subject = Mass;
                  presence = Absent;
               }";
         didactics = SEQUENCE 0 {};
      };
   destination = (Action_Step 11);
   otherwise = (Conditional_Step 1002);
   didactics = SEQUENCE 0 {};
}
```

GLIF Model for BM CPG (2)



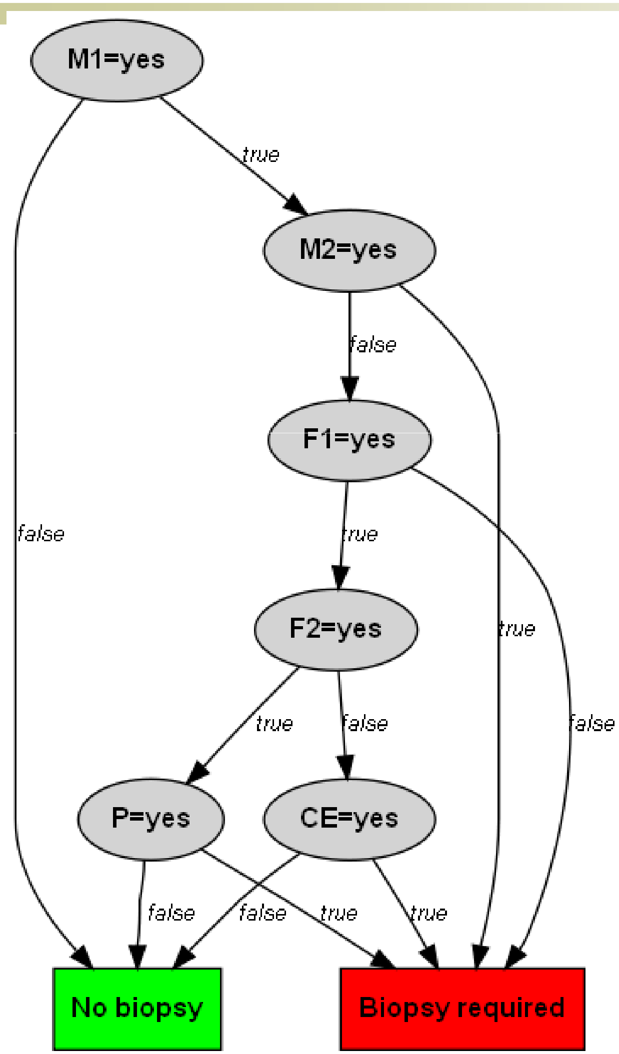


Decision Graph

- Created from the GLIF model (or other structured representation), but can be also developed from natural language CPG (expert knowledge required)

- Limited to decision and patient state steps (focus on clinical decision making)

Decision Graph for BM CPG



M1	Found breast mass
M2	Solid breast mass
F1	Fluid aspirated from cyst
F2	Clear aspirated fluid
P	Palpable breast mass
CE	Positive cytologic examination

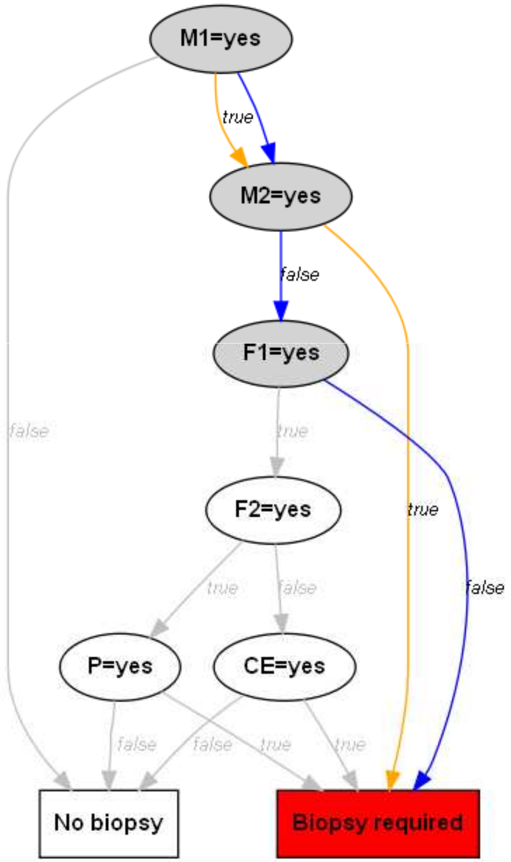
Implication Graph

- Inspired by implication trees used in legal reasoning (V. Walker, Visualizing the Dynamics around the Rule/Evidence Interface in Legal Reasoning*, Law, Probability and Risk* 6, 2007, 5-22)
- Based on the decision graph (→ inverted structure)
- Labeled arcs from the decision graph become nodes in the implication graph
- Additional nodes corresponding to conjunction and disjunction

From Decision to Implication Graph

- Step 1: Represent all paths in the decision graph as decision rules (*<u>if</u> conditions, <u>then</u> outcome*)
- Step 2: In the rules identify nodes of the implication graph
  - Fact and outcome nodes
  - Logical operator nodes (operator nodes in short)
- Step 3: In the rules identify arcs of the implication graph
  - Fact nodes connected to operator nodes
  - Operator nodes connected to other operator nodes and to outcome nodes

Step 1: Represent all paths as decision rules

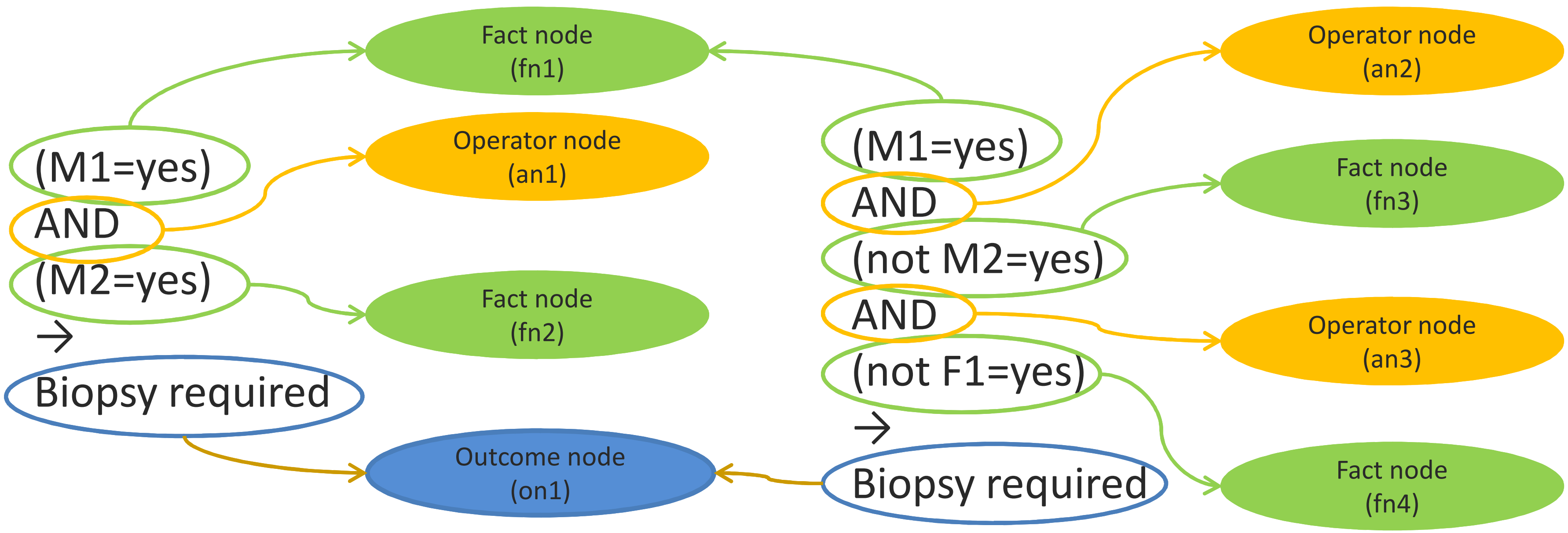


- Decison rules corresponding to two sample paths
  - ([M1=yes] = true)
    AND ([M2=yes] = true)
    → Biopsy required
  - ([M1=yes] = true)
    AND ([M2 = yes] = false)
    AND ([F1 = yes] = false)
    → Biopsy required

Simplified notation
([*A*=yes] = true) ➔ (*A*=yes)
([*A*=yes] = false) ➔ (not A=yes)

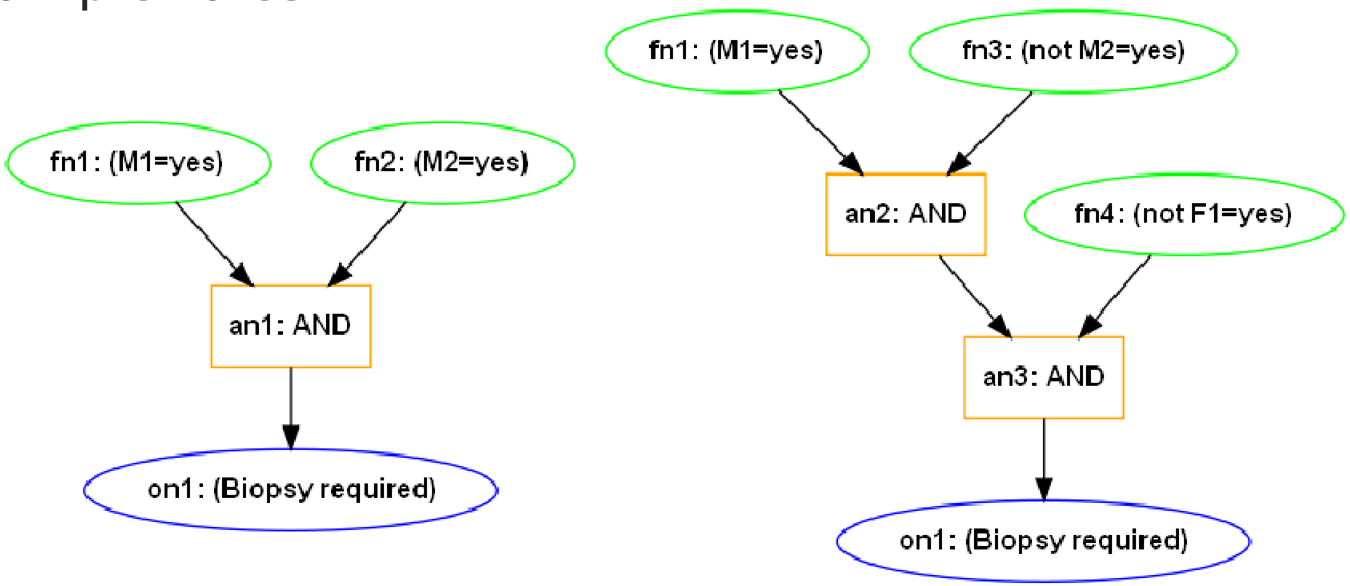
Step 2: Identify nodes in the implication graph

- Fact, outcome and logical operators nodes from the sample rules

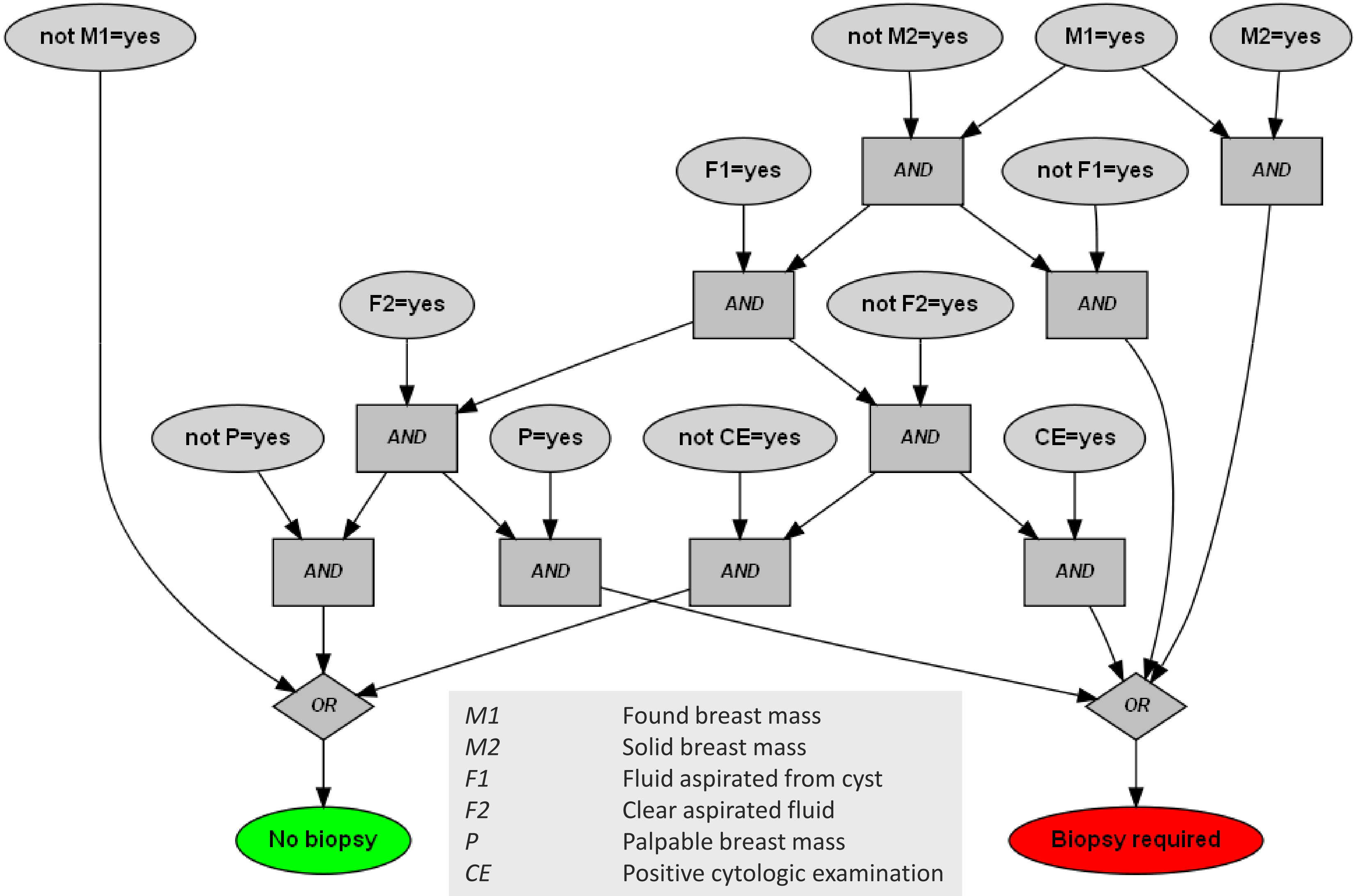


Step 3: Identify arcs in the implication graph

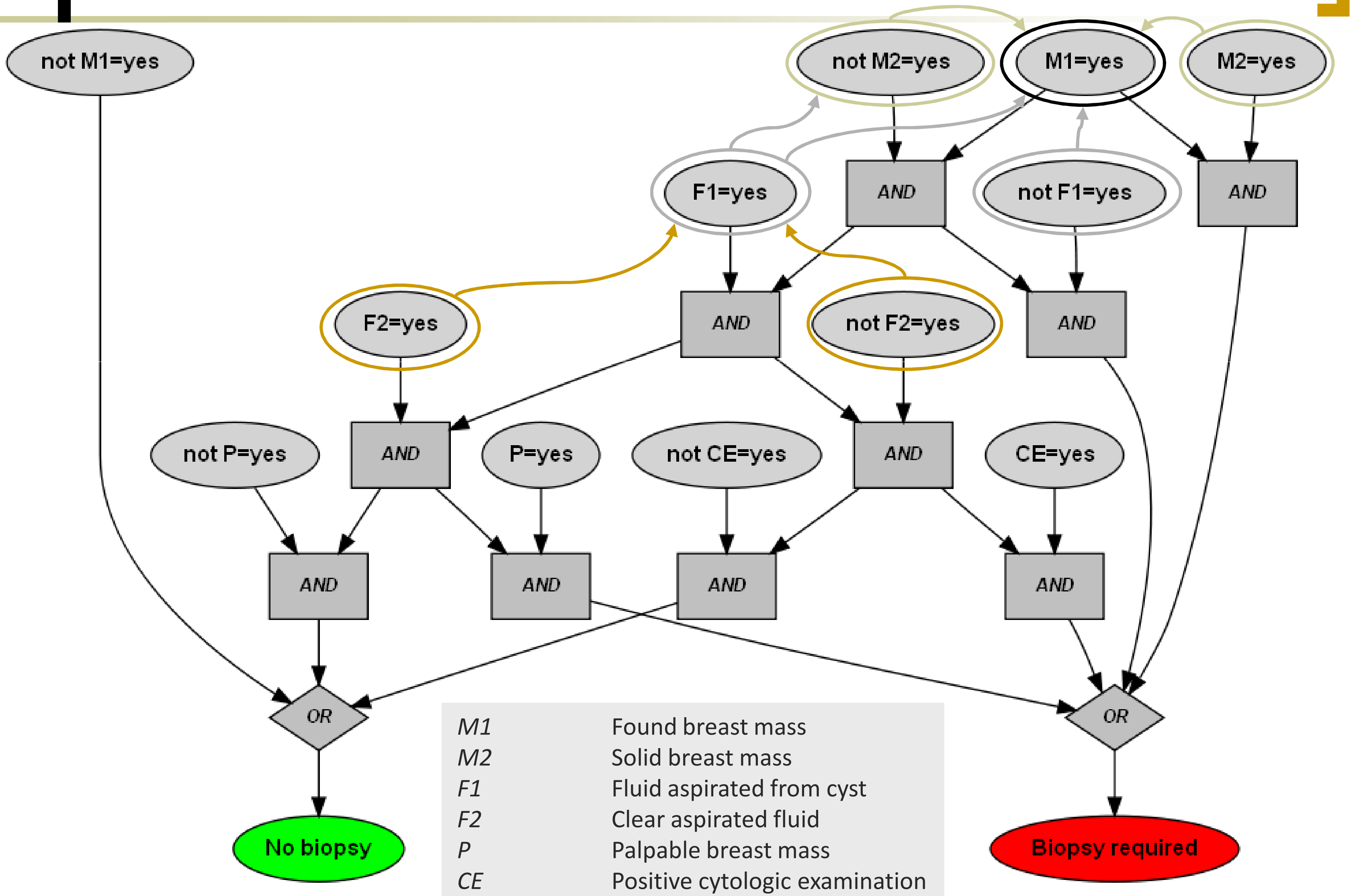
- Establishing arcs connecting the nodes from the sample rules



Implication Graph for BM CPG



Implication Graph for BM CPG



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Reasoning from the CPG: Terminology

- *Outcome*: one of N possible diagnoses (or recommendations) resulting from following a CPG (i.e. biopsy required).

- *Solution*: A set of clinical findings and the corresponding outcome. It is represented as a path in the implication graph (i.e. M1=yes, M2=yes, biopsy required).

Reasoning from the CPG: Input/Output

- Input data:
  - *Initial Clinical Results (ICR)*: Known clinical findings (facts) about the patient (clear fluid was aspirated)
  - *Background Knowledge (BK)*: A set of (meta) facts representing relationships between clinical findings (can aspirate fluid only from cystic breast mass)
  - *Query (Q)*: ICR linked with an outcome.
- Output:
  - A set of solutions for a given Q.

Reasoning process

- Load BK
- Load implication graph
- Input ICR
- Add clinical results (CR) through deduction using ICR and BK
  - CR<= deduce(ICR, BK)
- Input Q
- Generate the solutions. This is achieved by using Prolog’s goal-driven reasoning process

Internal Representation of Implication Graph

- Meta-facts – **`test_result(Test, Value, Source)`**

```
test_result(M1(yes), true, given).
test_result(not(M1(yes)), false, deduced).
test_result(not(M2(yes)), true, deduced).
test_result(CE(yes), unknown, unknown).
```

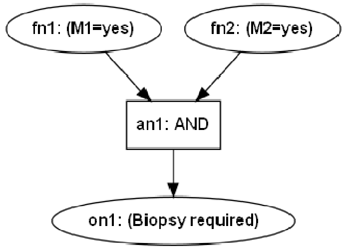
- Examining values of meta-facts

```
check_test(Test, Value) :-
    test_result(Test, Value, deduced).

check_test(Test, Value) :-
    test_result(Test, Value, given).

check_test(Test, Value) :-
    test_result(Test, unknown, _).
```

Internal Representation of Implication Graph

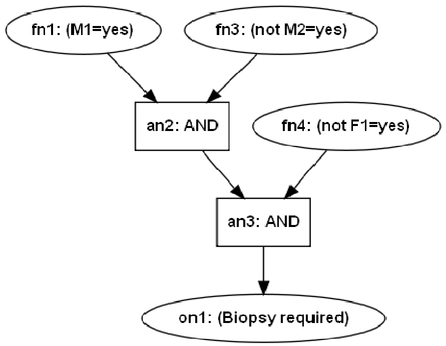
- Solution
  - (M1=yes) AND (M2=yes) → Biopsy required

```
outcome(on1) :-                          % on1/an1
        check_test(M1(yes), true),       % fn1
        check_test(M2(yes), true).       % fn2
```



  - (M1=yes) AND (not M2=yes) AND (not F1=yes) → Biopsy required

```
outcome(on1) :-                          % on1/an3
        check_test(not(F1(yes)), true)% fn4
        check_operator(an2).             % an2

check_operator(an2) :-                   % an2
        check_test(M1(yes), true),       % fn1
        check_test(not(M2(true)), true).% fn3
```



Background Knowledge

Knowing		Implies	
Test	Value	Test	Value
M2(yes)	true/false	M1(yes)	true
F1(yes)	true/false	M1(yes)	true
F2(yes)	true/false	F1(yes)	true
F1(yes)	true/false	M2(yes)	false

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Deduction

Facts	

Before	`test_result(M1(yes), unknown, unknown).`
	`test_result(M2(yes), unknown, unknown).`
	`test_result(F1(yes), true, given).`
	`test_result(F2(yes), unknown, unknown).`
	`test_result(P(yes), unknown, unknown).`
	`test_result(CE(yes), unknown, unknown).`

Deduction	`(F1(yes), true) => (M1(yes), true)` `(F1(yes), true) => (M2(yes), false)`

After	`test_result(M1(yes), true, deduced).`
	`test_result(M2(yes), false, deduced).`
	`test_result(F1(yes), true, given).`
	`test_result(F2(yes), unknown, unknown).`
	`test_result(P(yes), unknown, unknown).`
	`test_result(CE(yes), unknown, unknown).`

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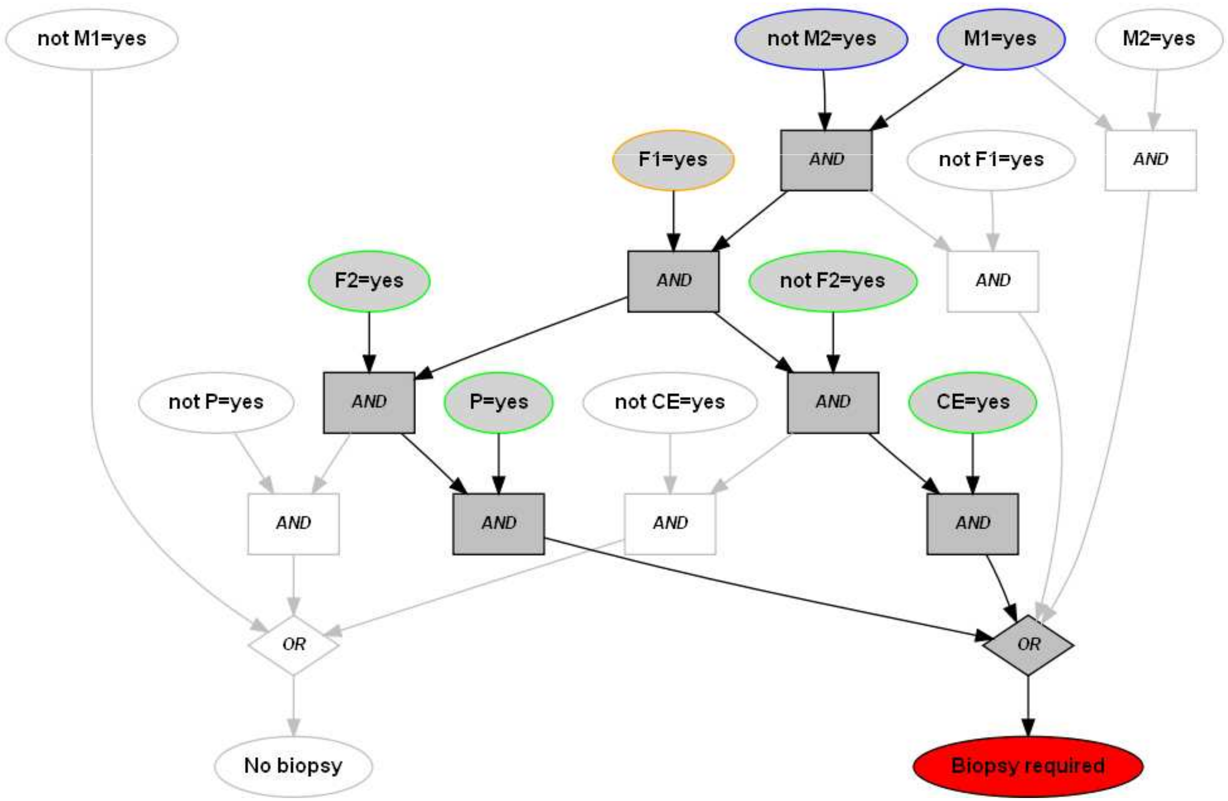
Sample Query Result

```
?- cpg_solutions(biopsy_required).
Adding new fact to KB  : knowing(F1(yes), true) => implies(M1(yes), true)
Adding new fact to KB  : knowing(F1(yes), true) => implies(M2(yes), false)

--- 1 ---
deduced(true(M1(yes)))
deduced(false(M2(yes)))
true(F1(yes))
assume(true(F2(yes)))
assume(true(P(yes)))

--- 2 ---
deduced(true(M1(yes)))
deduced(false(M2(yes)))
true(F1(yes))
assume(false(F2(yes)))
assume(true(CE(yes)))
```



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Discussion

- Use of CPG with incomplete data
- Identification of inconsistencies
- Explanation of the results
- Need to codify BK
- Need for expert advice with moving from textual CPG to decision graph
- Difficult to represent temporal processes

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