Computational Thinking to Support Clinicians and Biomedical Scientists
June 21–22, 2011

Automated Reasoning for Application of Clinical Guidelines

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GLINDA: GuideLine INteraction Detection Architecture

- Computational methods for reasoning about evidence-based practice
- Mechanisms for dealing with the messiness of clinical situations
  - Application of multiple clinical-practice guidelines
  - Adjustments for patient co-morbidities
  - Adjustments for interactions among interventions

GLINDA Project Team

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Clinical Context of our Work

- Populations are aging worldwide
- Older adults tend to have multiple chronic conditions

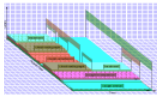
  75 million people in the US have two or more concurrent chronic conditions
- Management of multiple co-morbidities presents challenging problems
  - Competing therapeutic goals
  - Interventions that interact
  - Difficulty achieving parsimonious treatment plans

Role of Clinical Practice Guidelines

- Clinical practice guidelines define evidence-based best practices
- Lots of work on automating CPGs

  EON, InterMed (GLIF), SAGE,

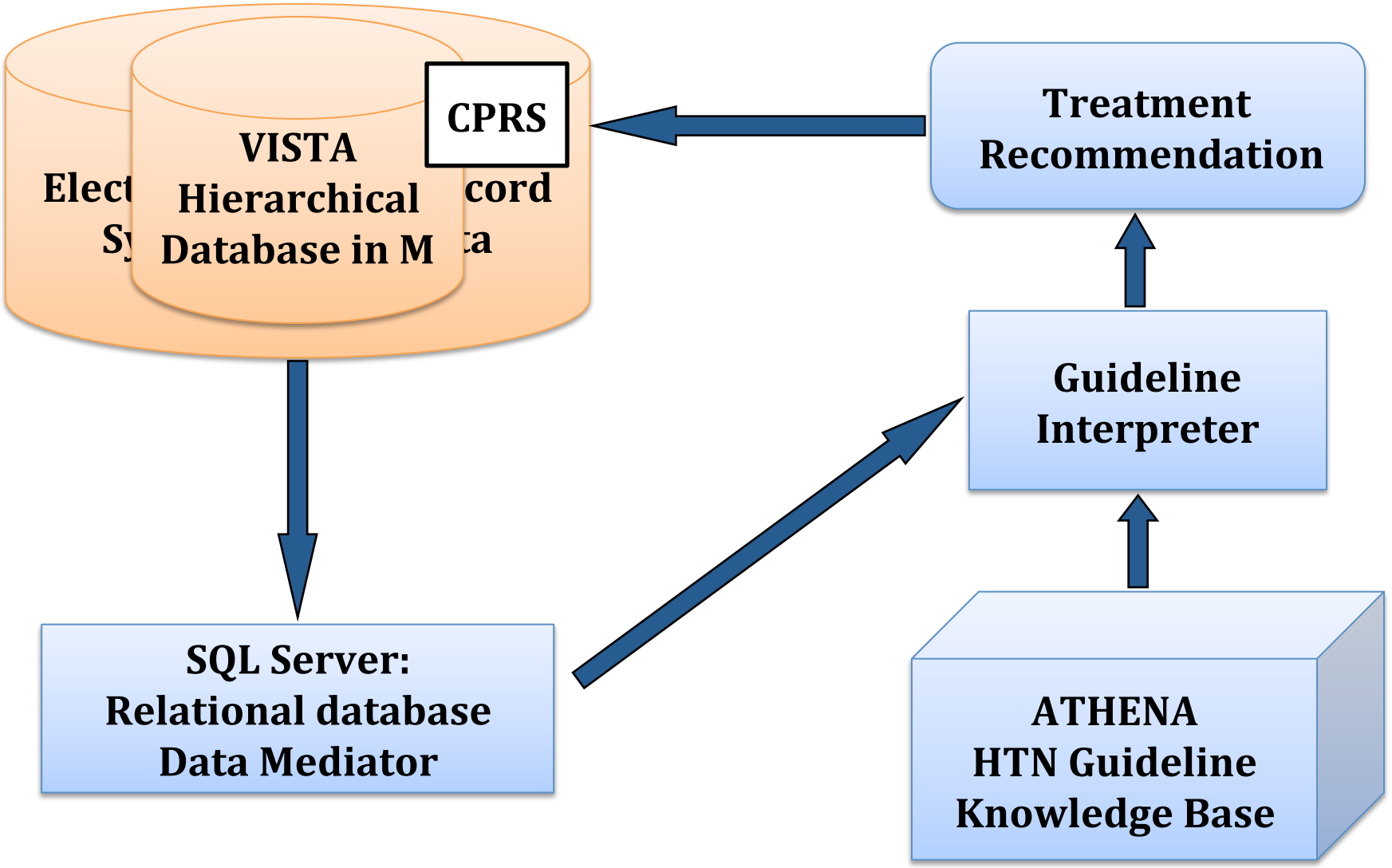
  PRO*forma*, Asbru, …

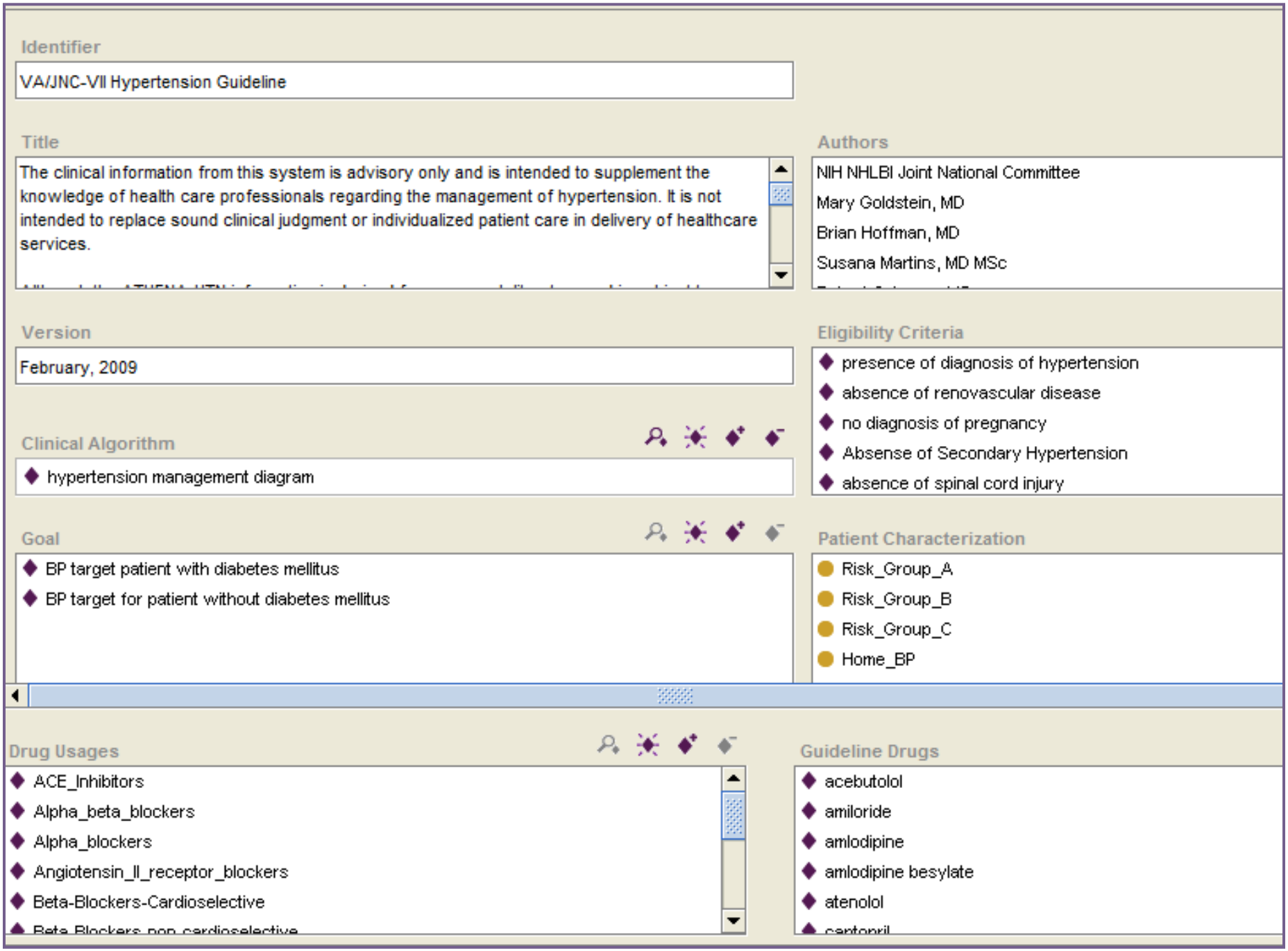


- Almost all CPGs—and all systems to automate treatment in accordance with CPGs—focus on single diseases

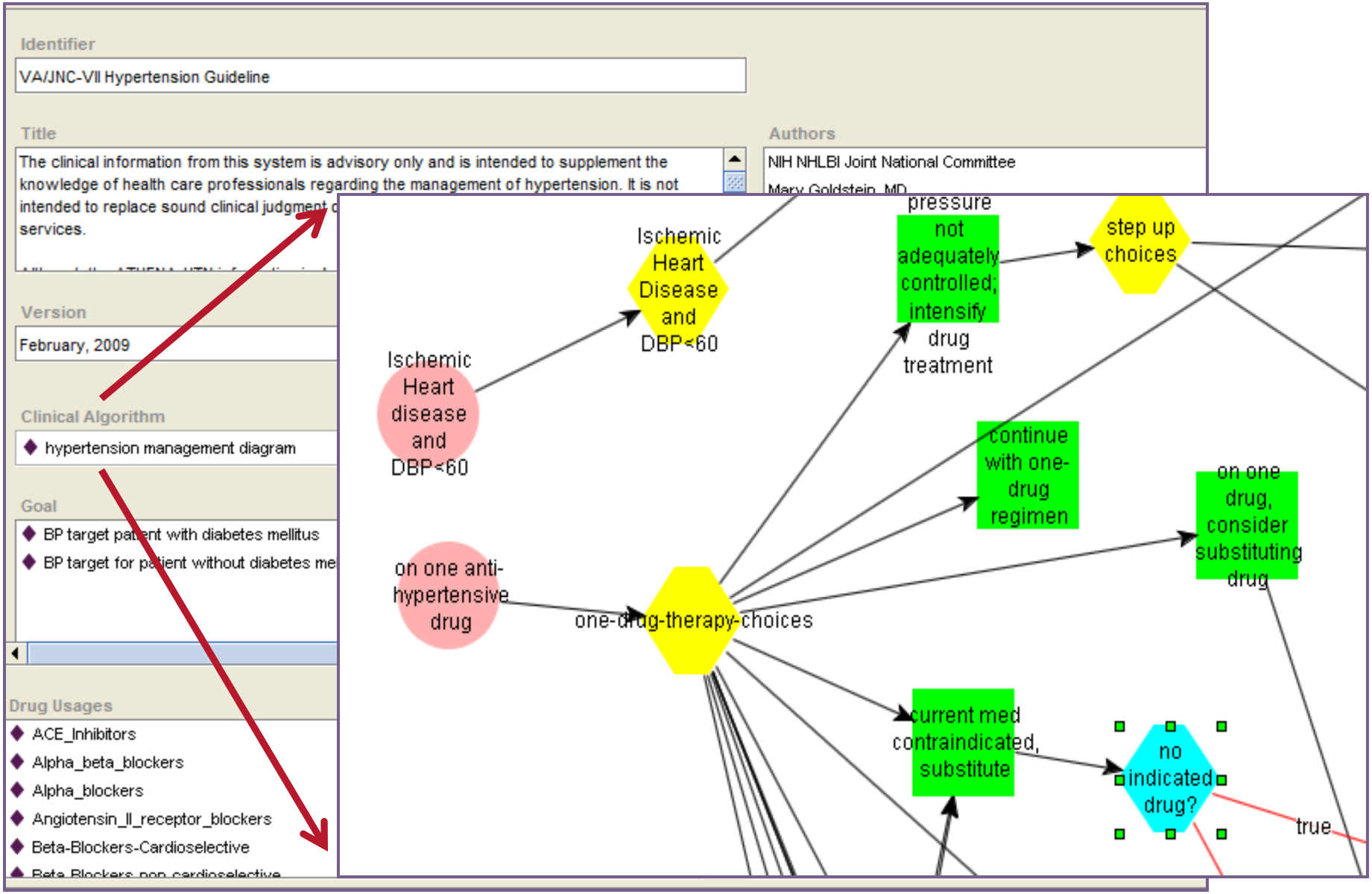
SYNTHETIC PATIENT DATA

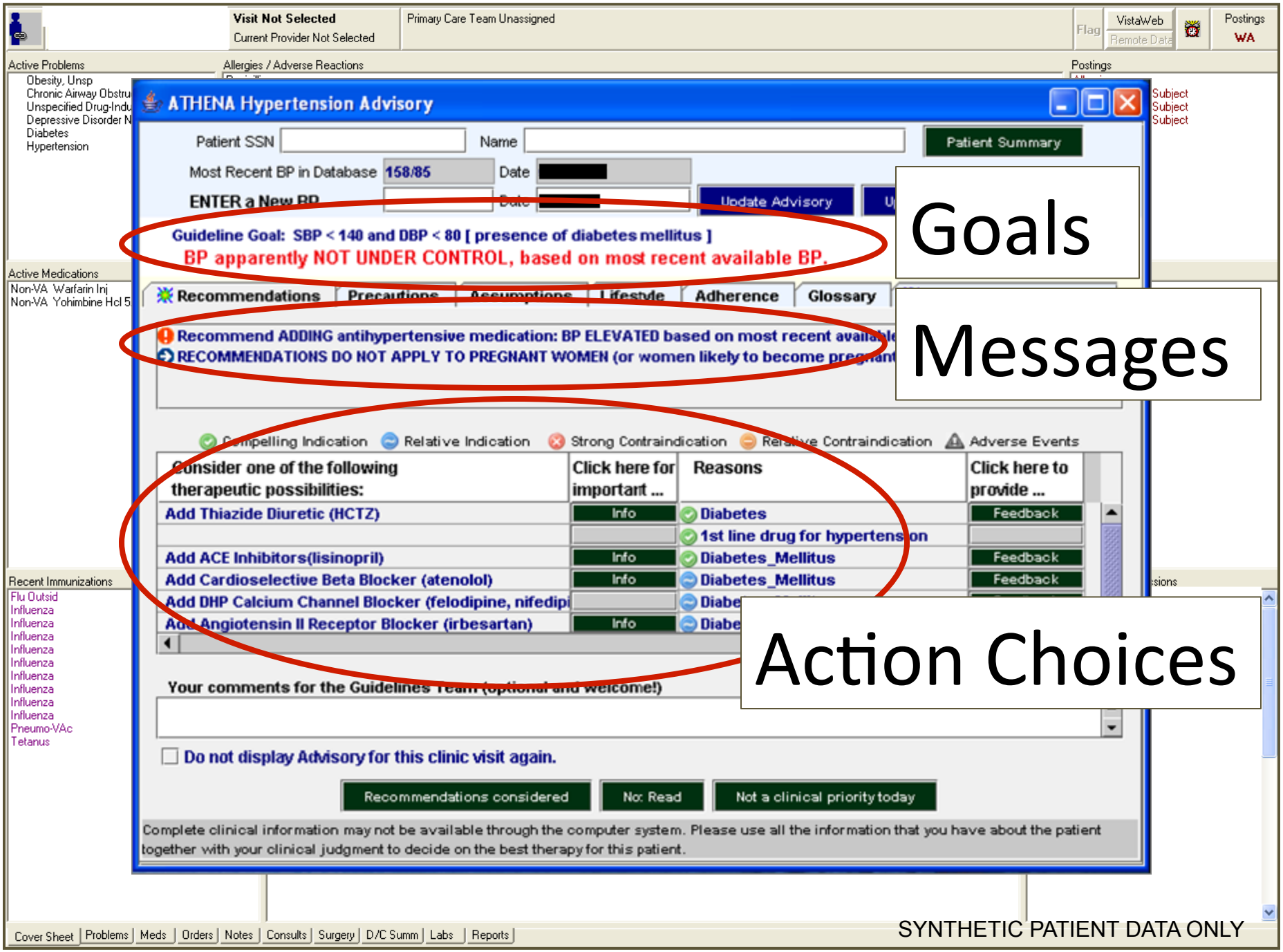
Simplified ATHENA Architecture



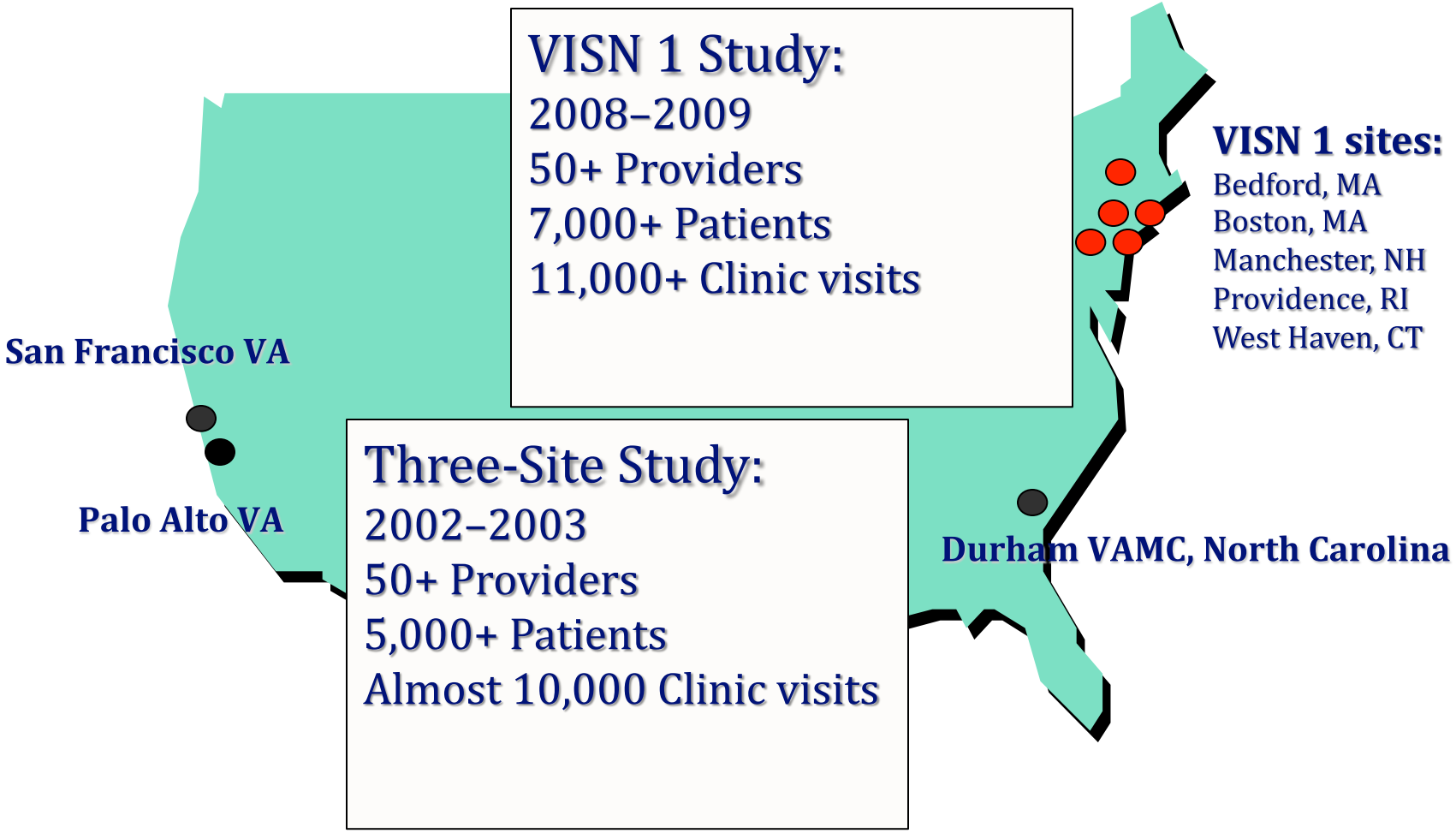

Identifier
VA/JNC-VII Hypertension Guideline
Title
The clinical information from this system is advisory only and is intended to supplement the knowledge of health care professionals regarding the management of hypertension. It is not intended to replace sound clinical judgment or individualized patient care in delivery of healthcare services.
Authors
NIH NHLBI Joint National Committee
Mary Goldstein, MD
Brian Hoffman, MD
Susana Martins, MD MSc
Version
February, 2009
Eligibility Criteria
presence of diagnosis of hypertension
absence of renovascular disease
no diagnosis of pregnancy
Absense of Secondary Hypertension
absence of spinal cord injury
Clinical Algorithm
hypertension management diagram
Goal
BP target patient with diabetes mellitus
BP target for patient without diabetes mellitus
Patient Characterization
Risk_Group_A
Risk_Group_B
Risk_Group_C
Home_BP
Drug Usages
ACE_Inhibitors
Alpha_beta_blockers
Alpha_blockers
Angiotensin_II_receptor_blockers
Beta-Blockers-Cardioselective
Guideline Drugs
acebutolol
amiloride
amlodipine
amlodipine besylate
atenolol

ATHENA HTN Knowledge Base



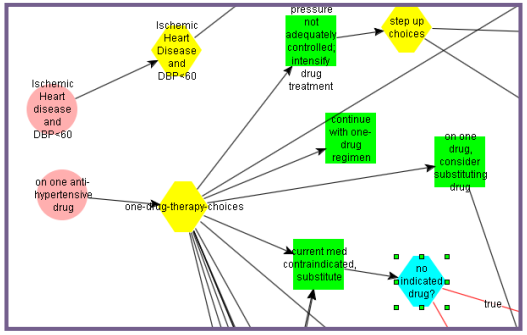

Visit Not Selected
Current Provider Not Selected
Primary Care Team Unassigned
Flag
VistaWeb
Remote Data
Postings
WA
Active Problems
Obesity, Unsp
Chronic Airway Obstru
Unspecified Drug-Indu
Depressive Disorder N
Diabetes
Hypertension
Allergies / Adverse Reactions
Postings
Subject
Subject
Subject
ATHENA Hypertension Advisory
Patient SSN
Name
Patient Summary
Most Recent BP in Database 158/85
Date
ENTER a New BP
Date
Update Advisory
Guideline Goal: SBP < 140 and DBP < 80 [presence of diabetes mellitus]
BP apparently NOT UNDER CONTROL, based on most recent available BP.
Goals
Recommendations
Precautions
Assumptions
Lifestyle
Adherence
Glossary
Recommend ADDING antihypertensive medication: BP ELEVATED based on most recent
RECOMMENDATIONS DO NOT APPLY TO PREGNANT WOMEN (or women likely to become
Messages
Compelling Indication
Relative Indication
Strong Contraindication
Relative Contraindication
Adverse Events
Consider one of the following therapeutic possibilities:
Click here for important ...
Reasons
Click here to provide ...
Add Thiazide Diuretic (HCTZ)
Info
Diabetes
Feedback
1st line drug for hypertension
Add ACE Inhibitors(lisinopril)
Info
Diabetes_Mellitus
Feedback
Add Cardioselective Beta Blocker (atenolol)
Info
Diabetes_Mellitus
Feedback
Add DHP Calcium Channel Blocker (felodipine, nifedipi
Diabe
Add Angiotensin II Receptor Blocker (irbesartan)
Info
Diabe
Action Choices
Your comments for the Guidelines Team (optional and welcome!)
Do not display Advisory for this clinic visit again.
Recommendations considered
Not Read
Not a clinical priority today
Complete clinical information may not be available through the computer system. Please use all the information that you have about the patient together with your clinical judgment to decide on the best therapy for this patient.
Active Medications
Non-VA Warfarin Inj
Non-VA Yohimbine Hcl 5
Recent Immunizations
Flu Outsid
Influenza
Influenza
Influenza
Influenza
Influenza
Influenza
Influenza
Influenza
Influenza
Pneumo-VAc
Tetanus
Cover Sheet
Problems
Meds
Orders
Notes
Consults
Surgery
D/C Summ
Labs
Reports
SYNTHETIC PATIENT DATA ONLY

ATHENA-HTN Evaluation Studies

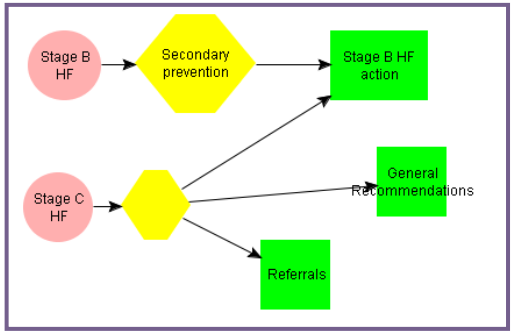


Encoded Guidelines

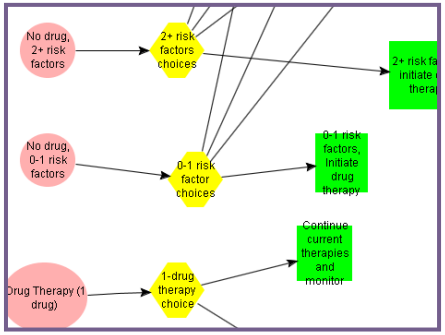
ATHENA Hypertension



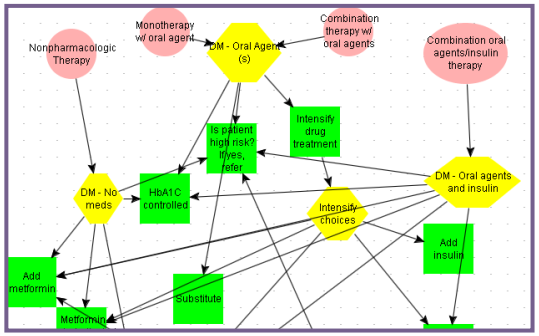
ATHENA Heart Failure



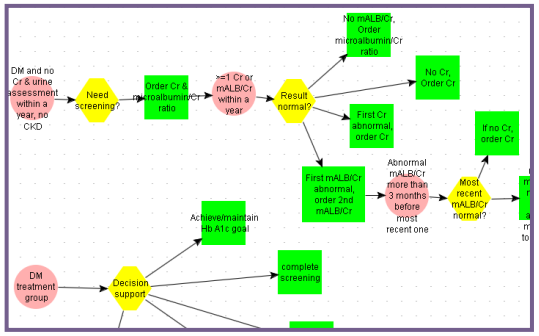
ATHENA Hyperlipidemia



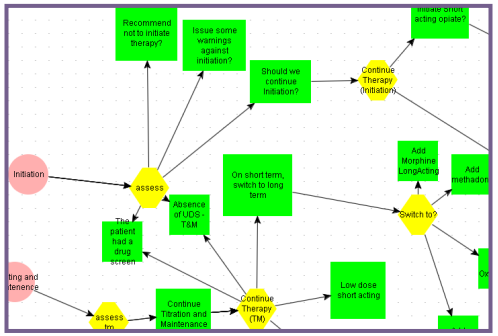
ATHENA Diabetes



ATHENA Kidney Disease



ATHENA Opioid Therapy



Limitations of Single-Disease Guidelines [Boyd et al. JAMA 2005]

- Simultaneous application of multiple guidelines leads to suboptimal care
  - Hypothetical 79-year-old woman with chronic obstructive pulmonary disease, Type 2 diabetes, osteoporosis, hypertension, and osteoarthritis
  - If the relevant CPGs were followed, the hypothetical patient would be prescribed 12 medications and a complicated, pharmacologically inappropriate regimen
- Application of CPGs needs to
  - Detect and repair conflicting interactions
  - Prioritize recommendations

Recommendations for Hypertension

Therapeutic Possibilities CLICK ON DRUGS FOR IMPORTANT	Indications	C
Add one or more of the following drugs		
DHP Calcium Channel Blocker (felodipine, nifedipine SA)	MI (BP not controlled), Diabetes Mellitus	
(non-DHP) Calcium Channel Blocker (diltiazem)	MI (BP not controlled)	

Recommendations for Hyperlipidemia

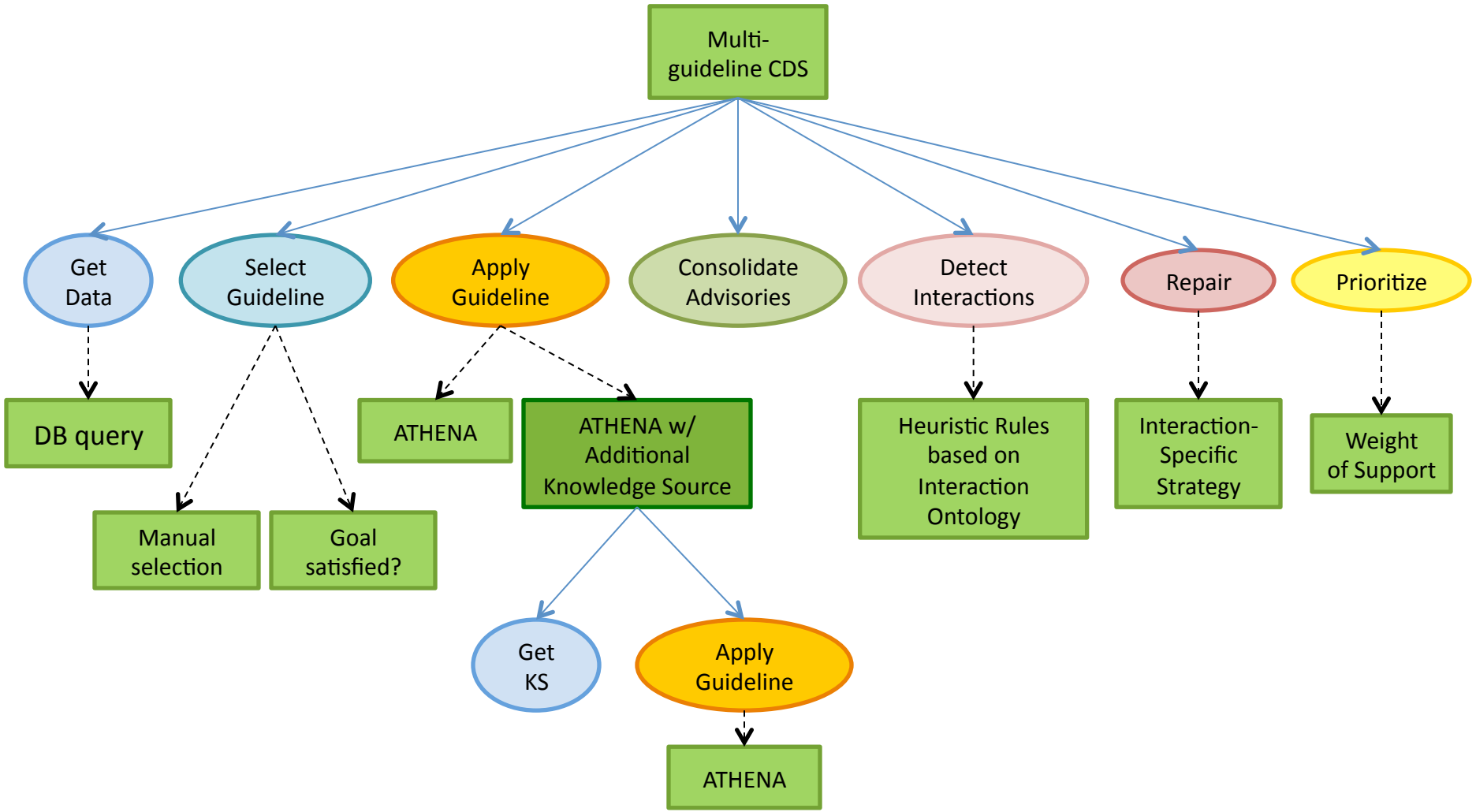
Therapeutic Possibilities CLICK ON DRUGS FOR IMPORTANT	Indications	Contraindications
Add one or more of the following drugs		
Statin	LDL not within guideline goal	
Bile Acid Sequestrant	LDL not within guideline goal	
Nicotinic Acid	LDL not within guideline goal	Diabetes Mellitus

Recommendations for Diabetes

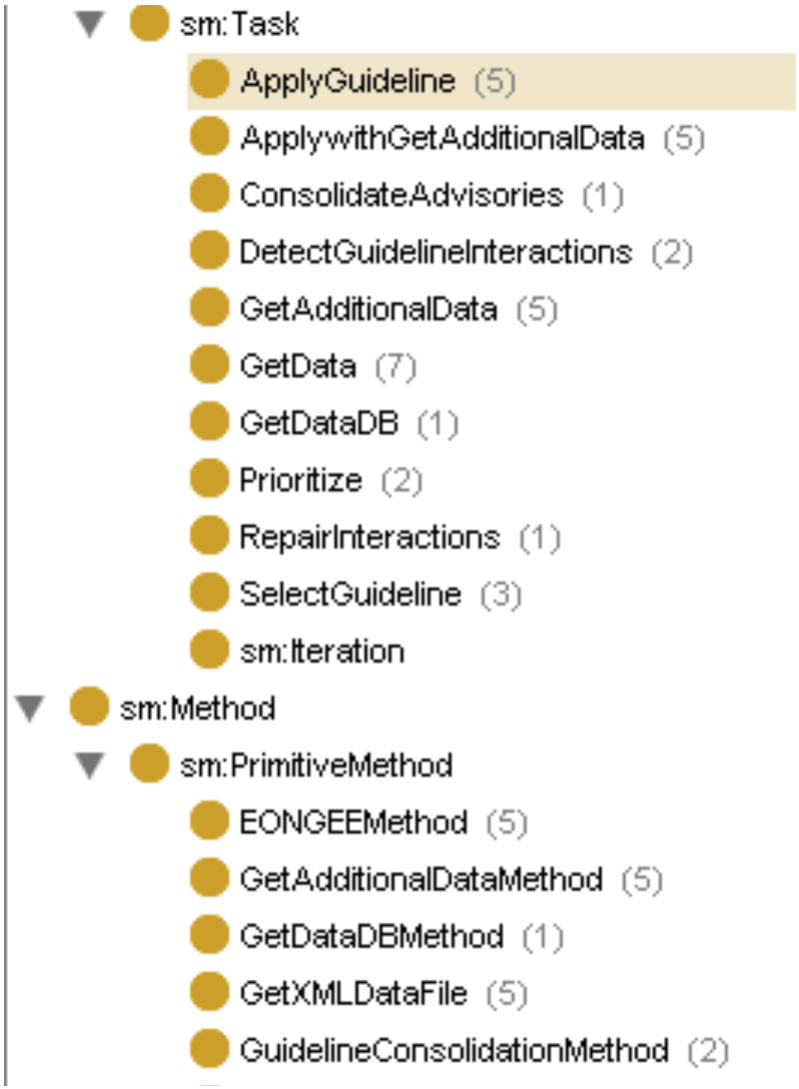
Overview of GLINDA Approach

- Incorporate our extensive experience with ATHENA CDS in an agent-oriented architecture
- Use task—method decomposition to create agent-oriented model of procedural elements
- Develop ontology of guideline interactions
- Develop agents for detecting conflicts, repairing conflicts, prioritizing and integrating treatment recommendations

GLINDA Task–Method Decomposition



Modeling tasks and methods in Protégé



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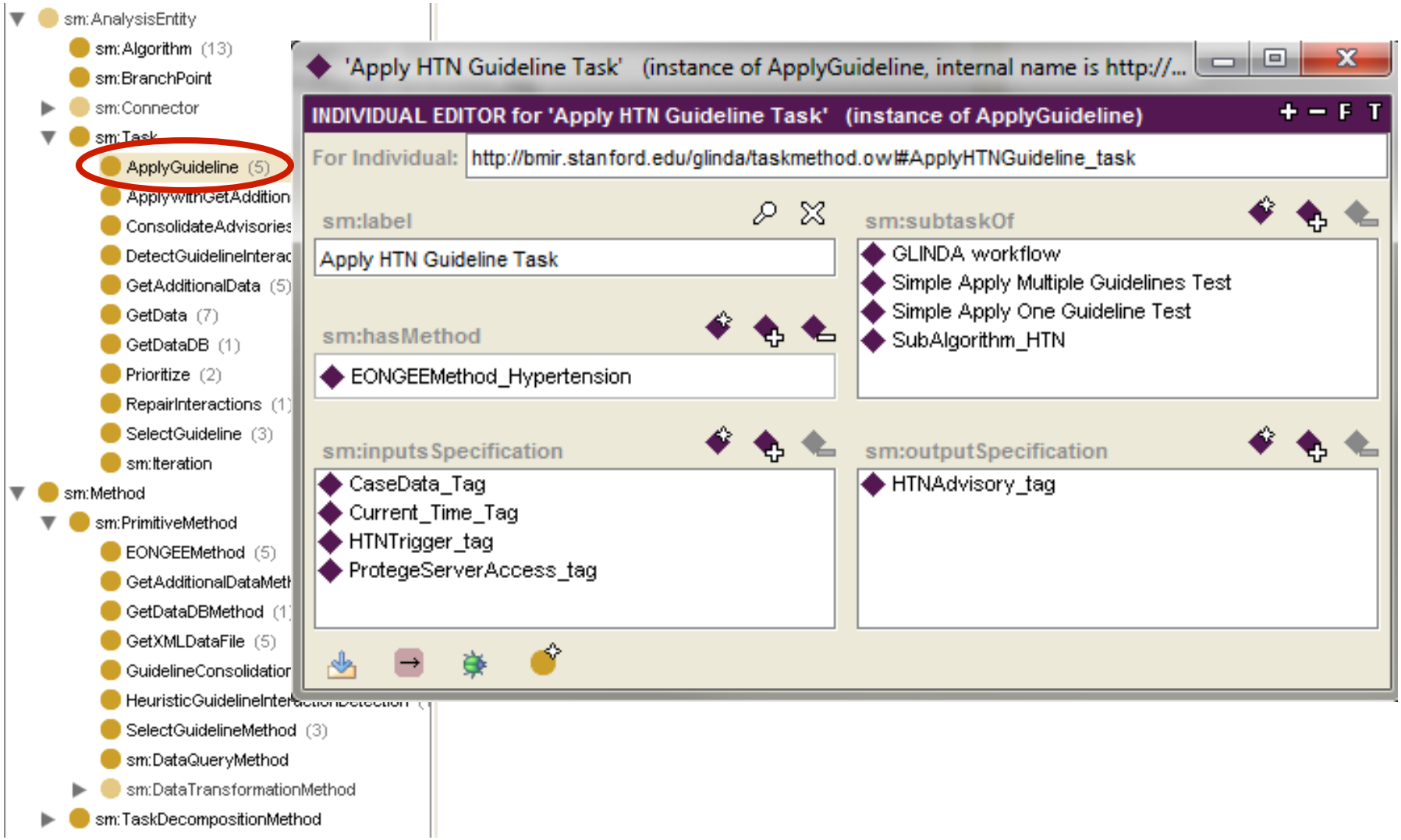
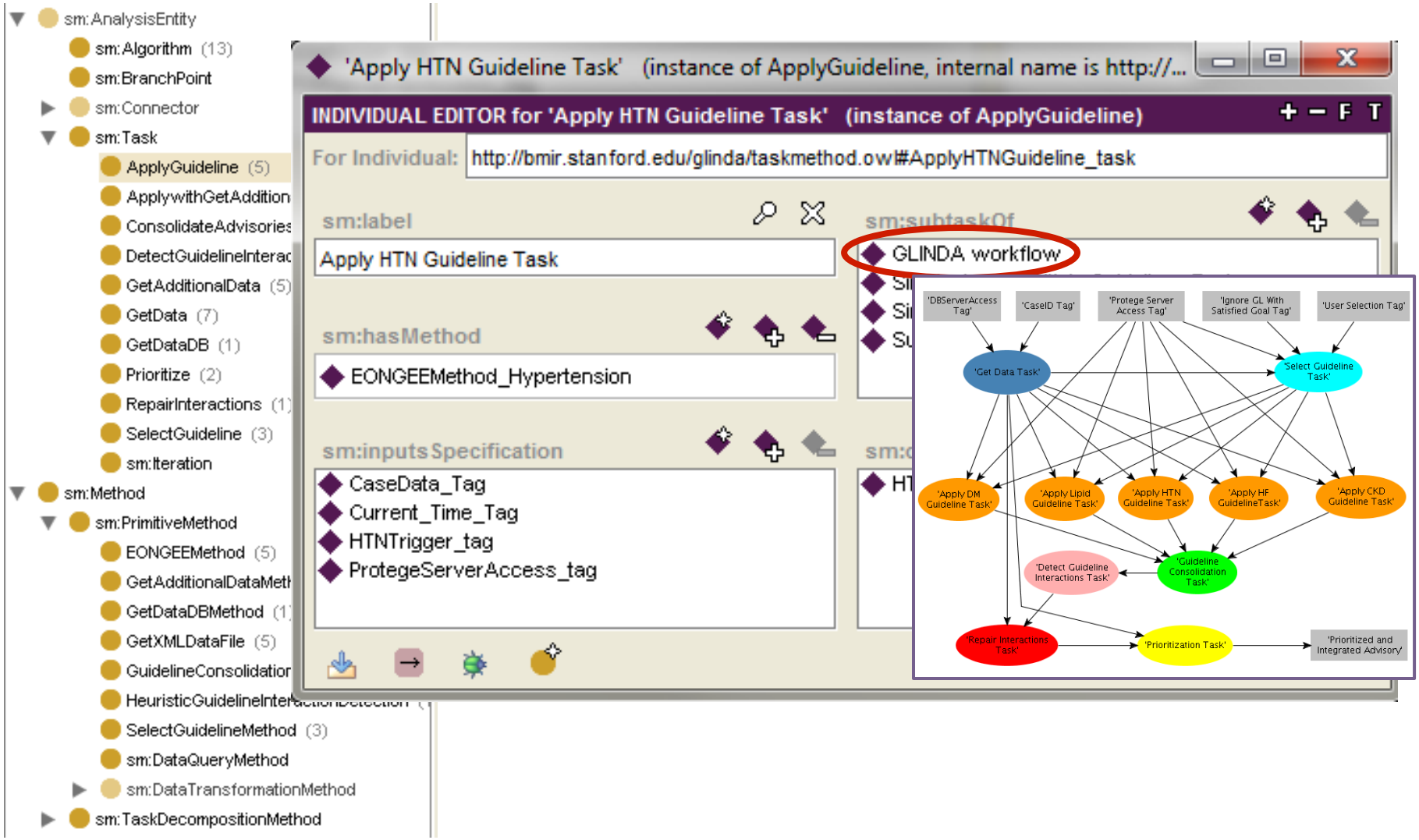
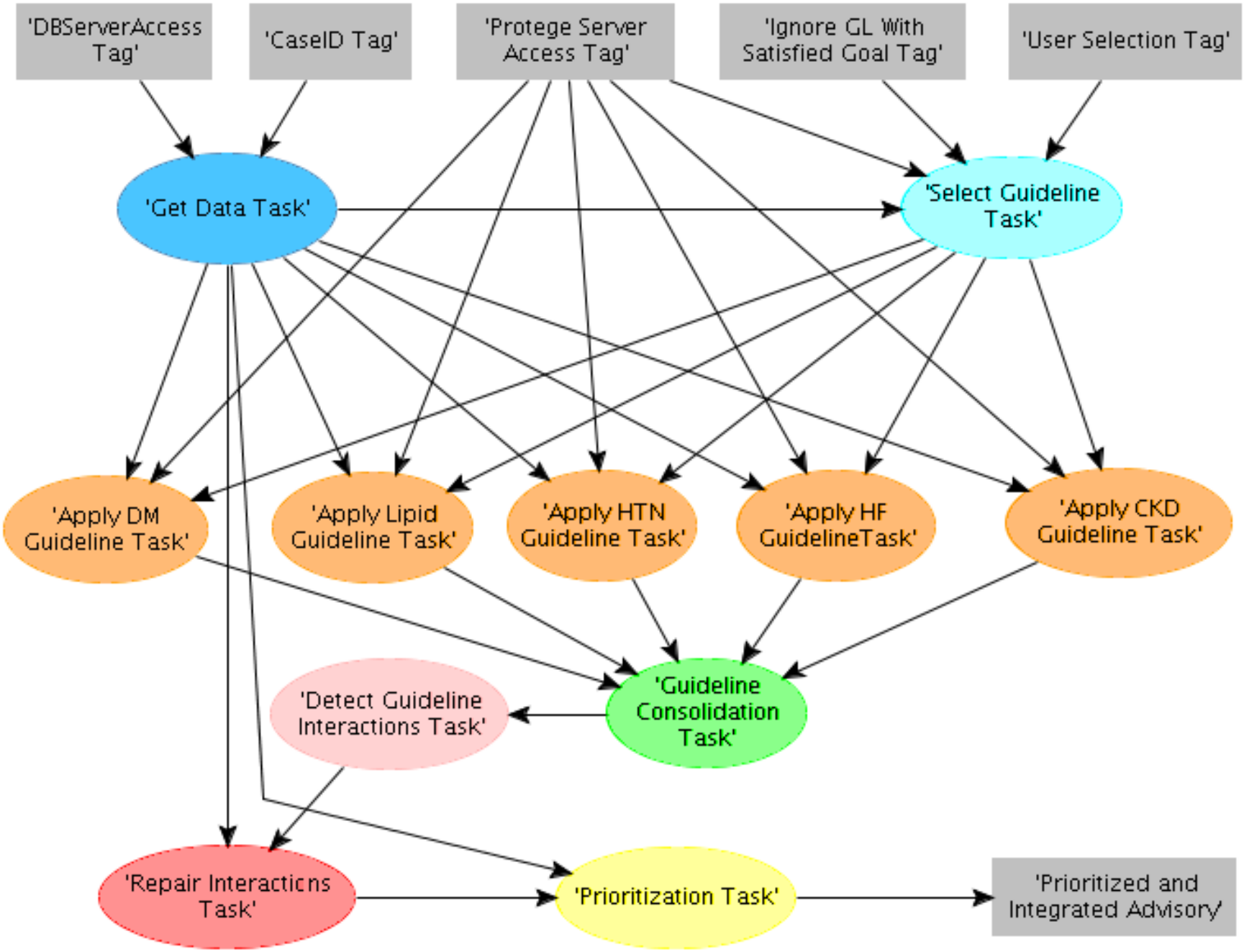


Modeling tasks and methods in Protégé

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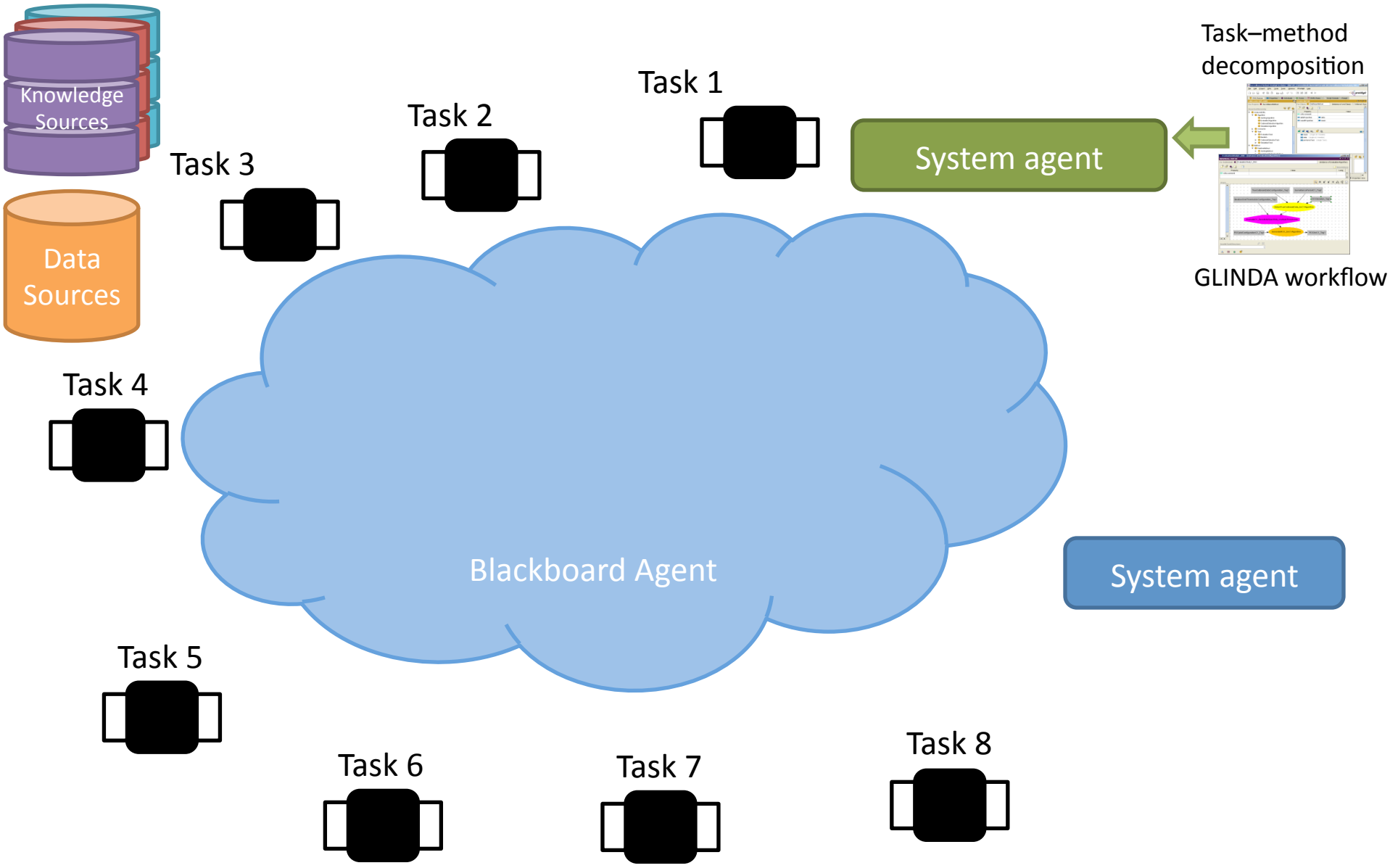
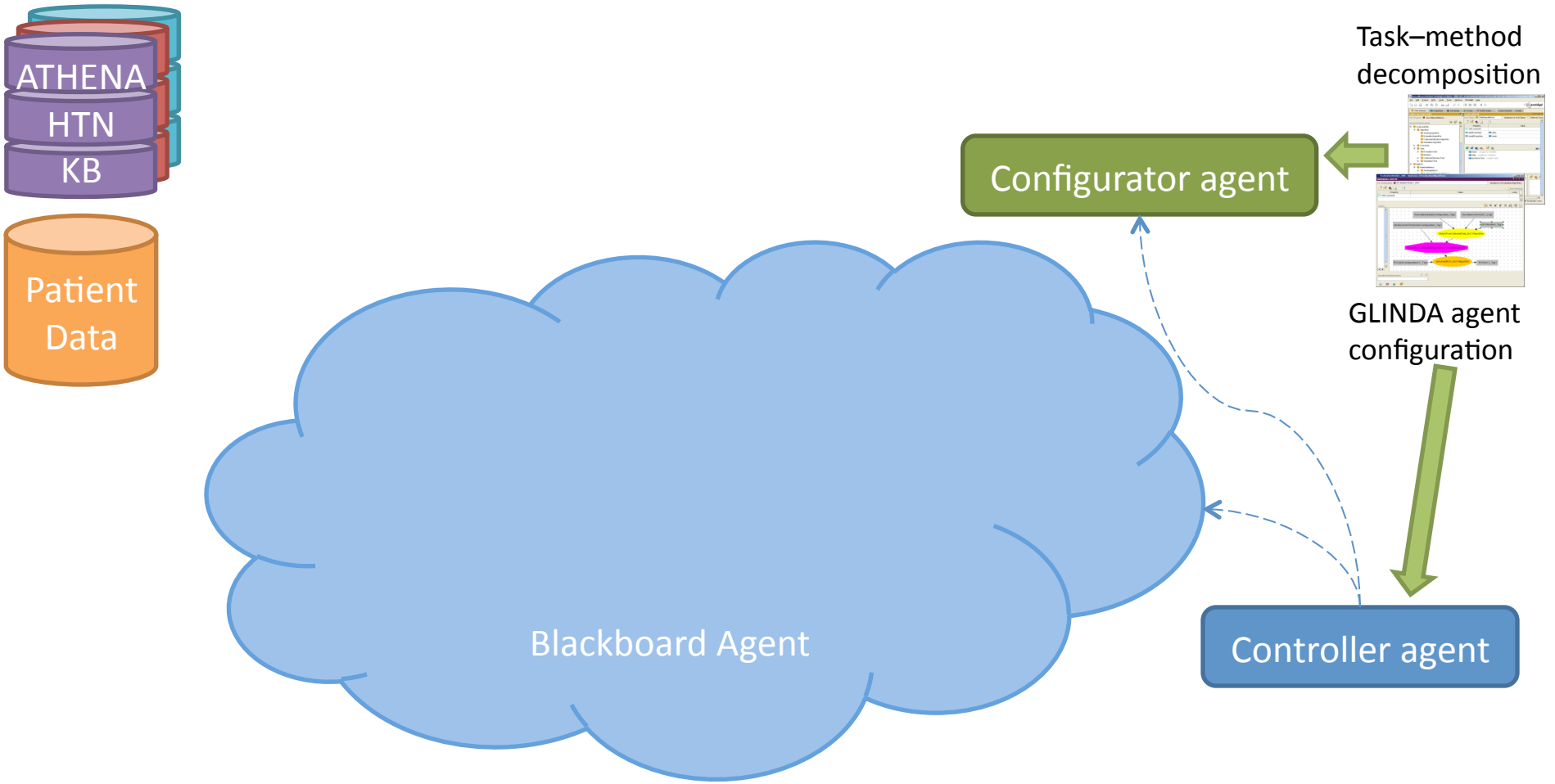
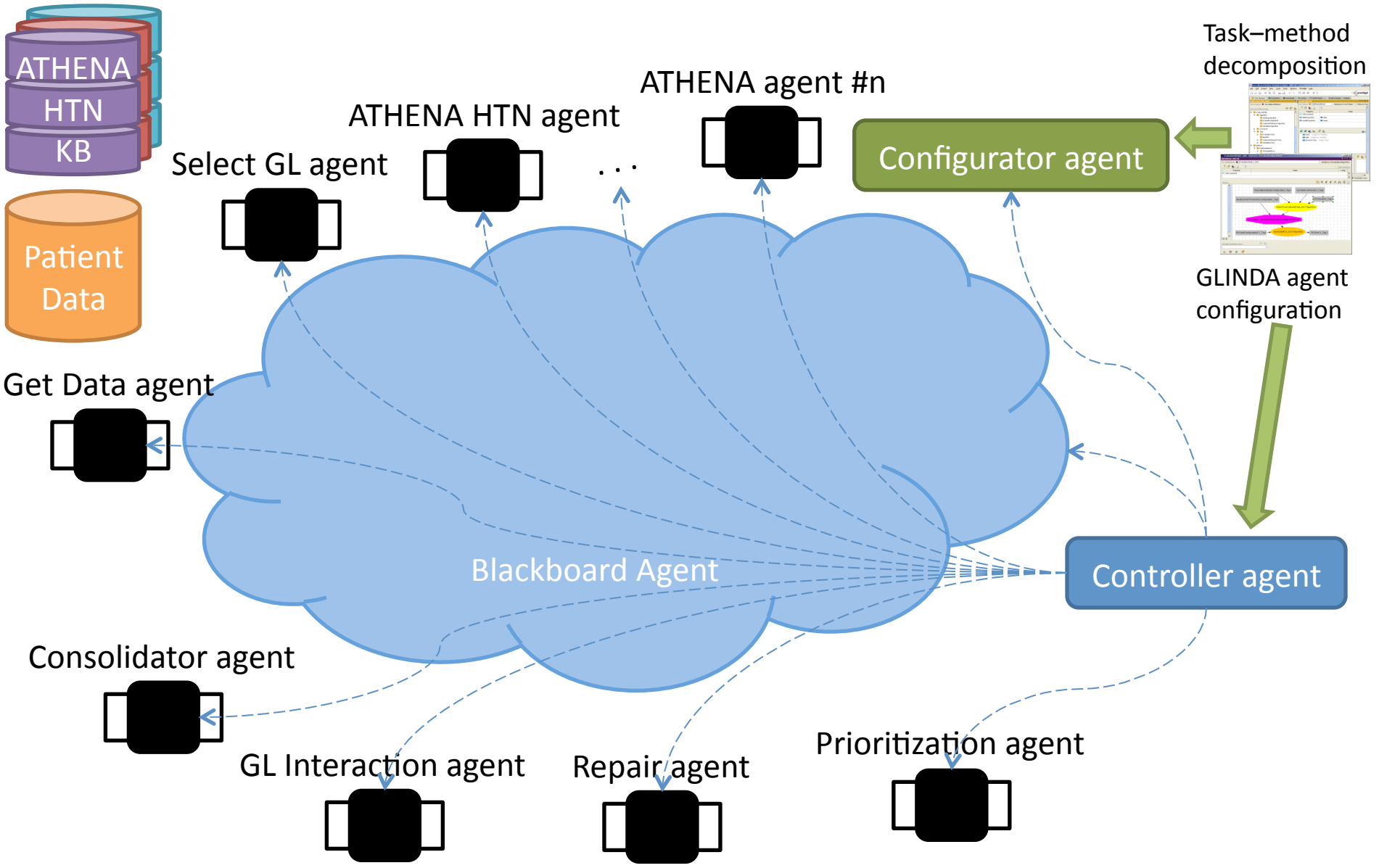
Implementation of Tasks and Methods in an Agent-Oriented Architecture



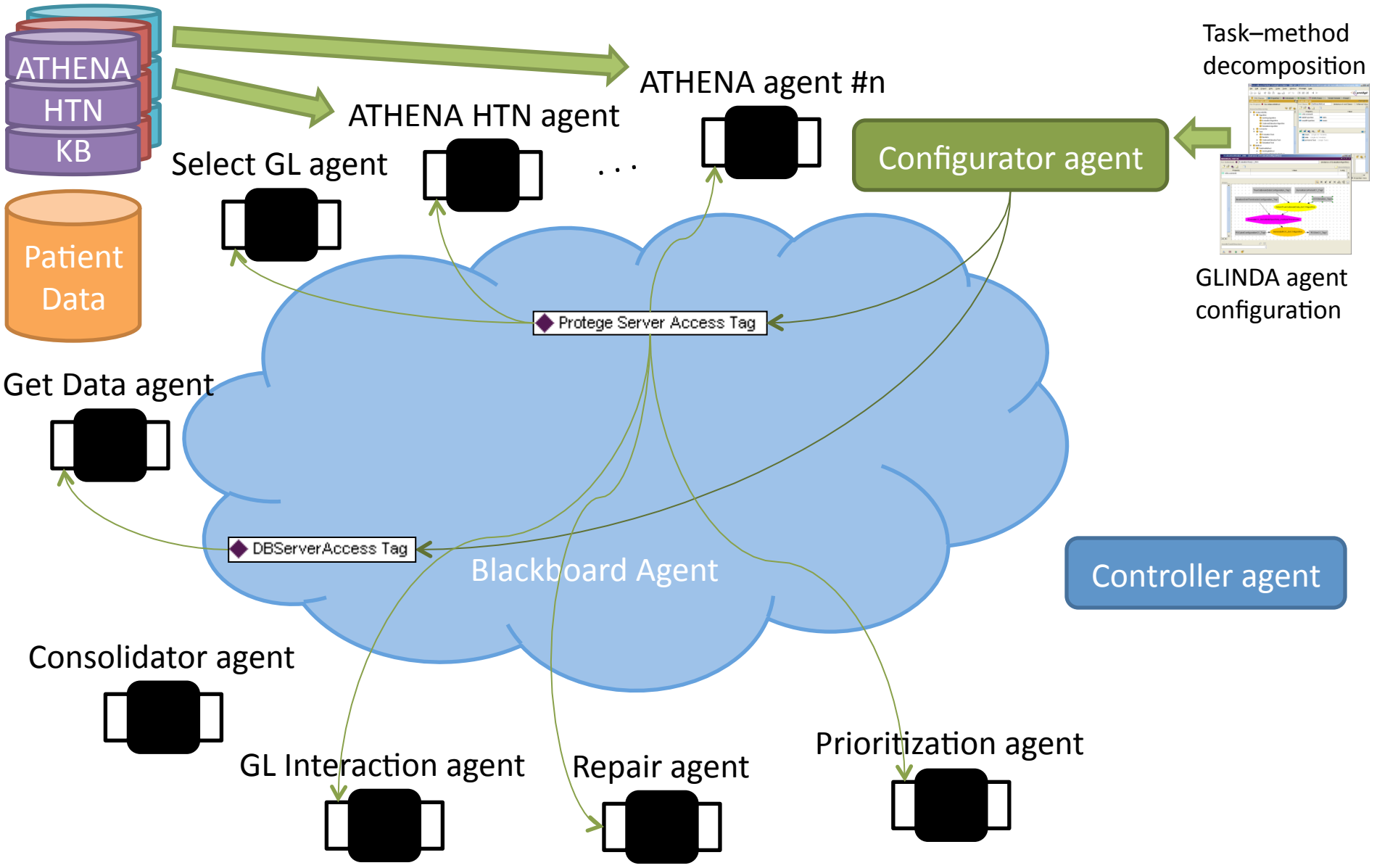
Running GLINDA – Initializing …



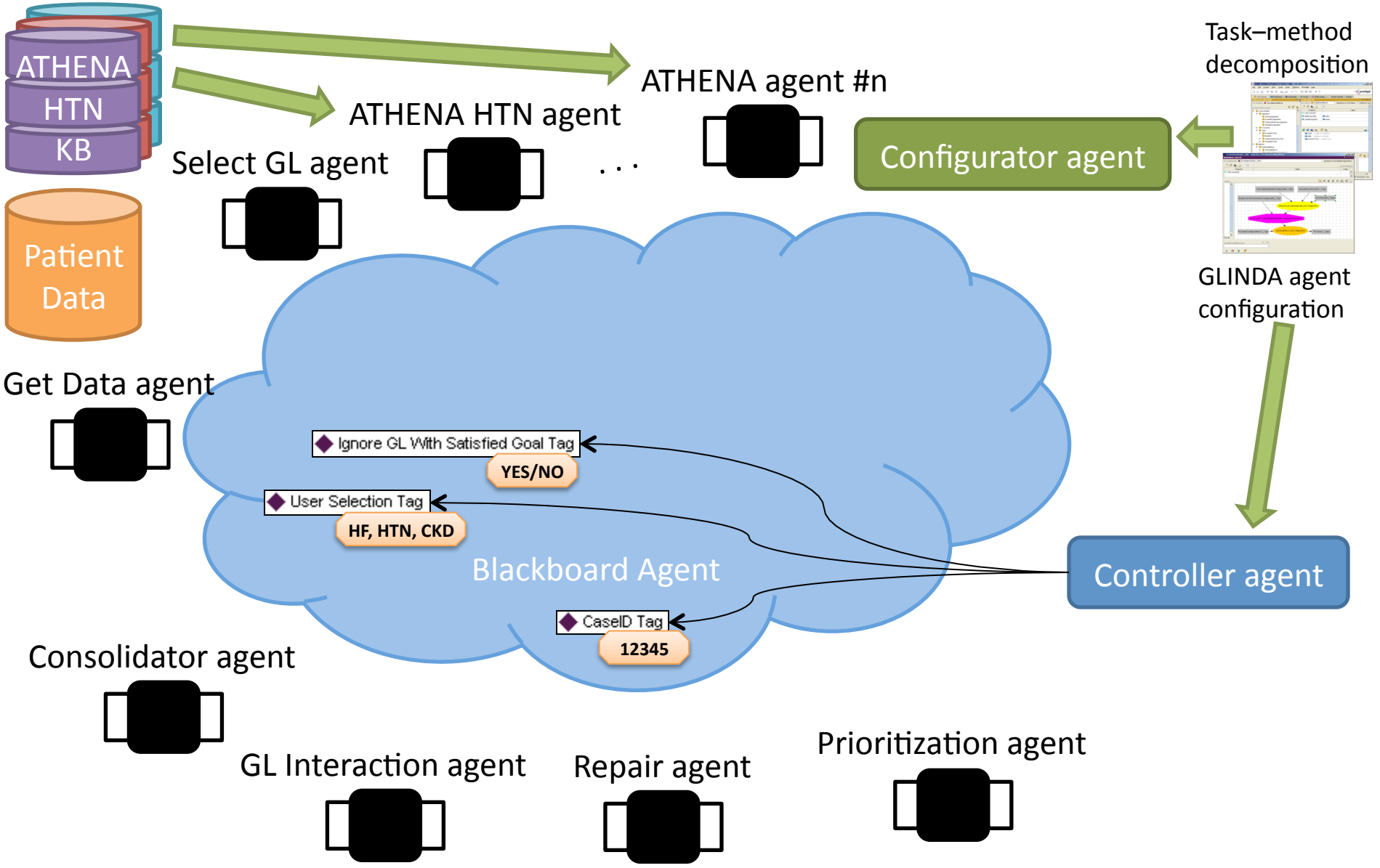
Running GLINDA – Creating Agents



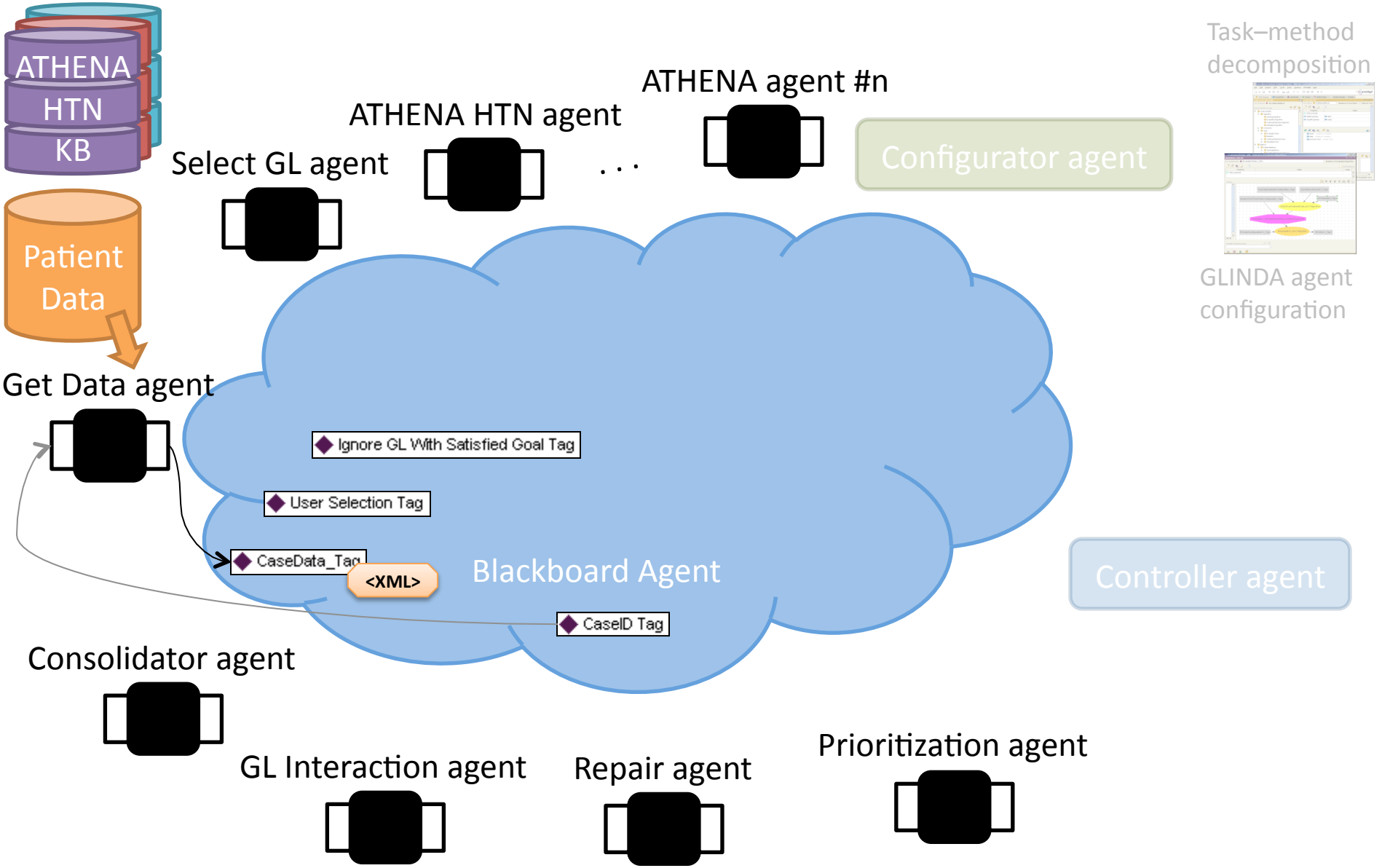
Running GLINDA – Configuring Agents



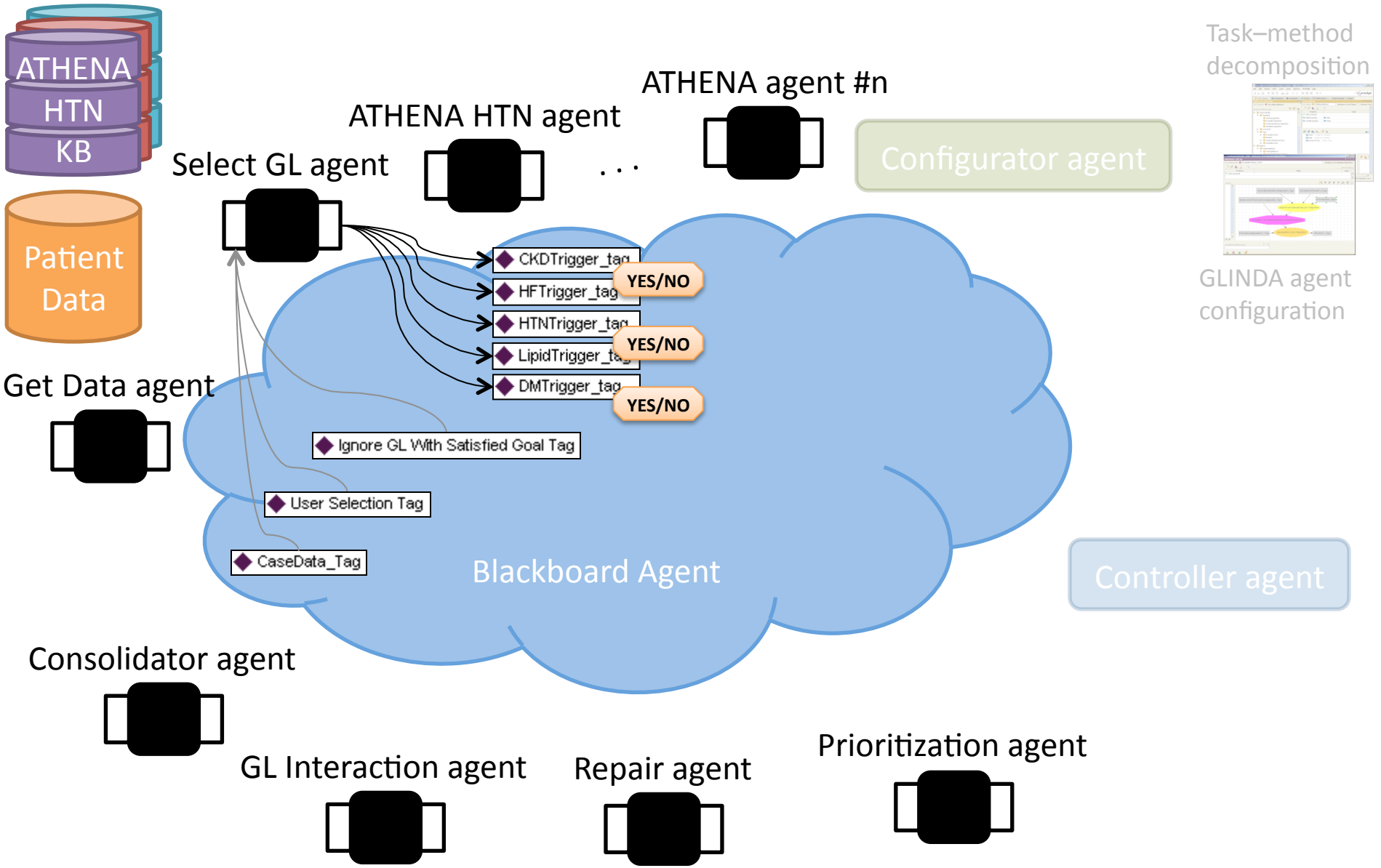
Running GLINDA – Activating Agents



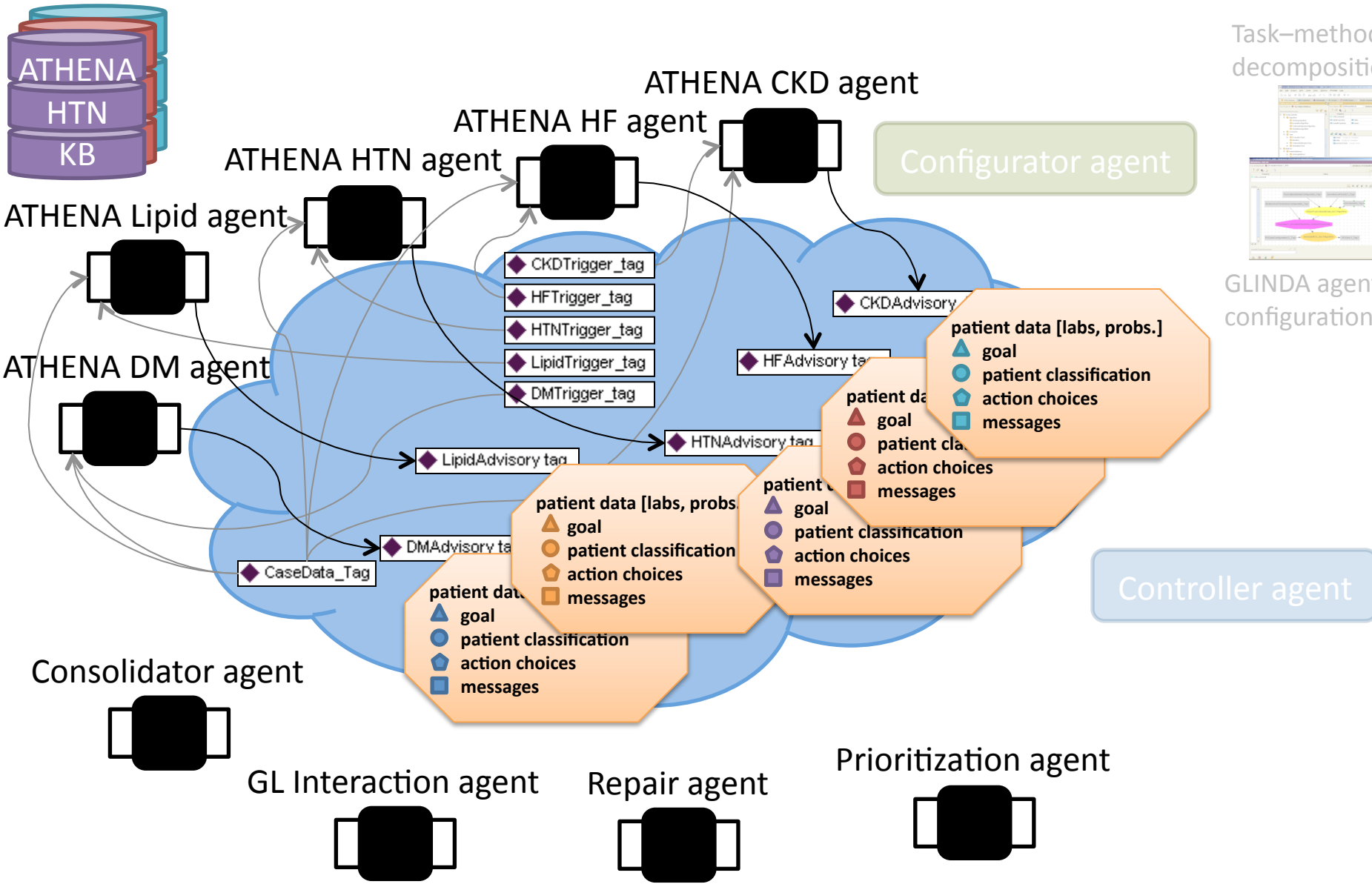
Running GLINDA – *Get Data*



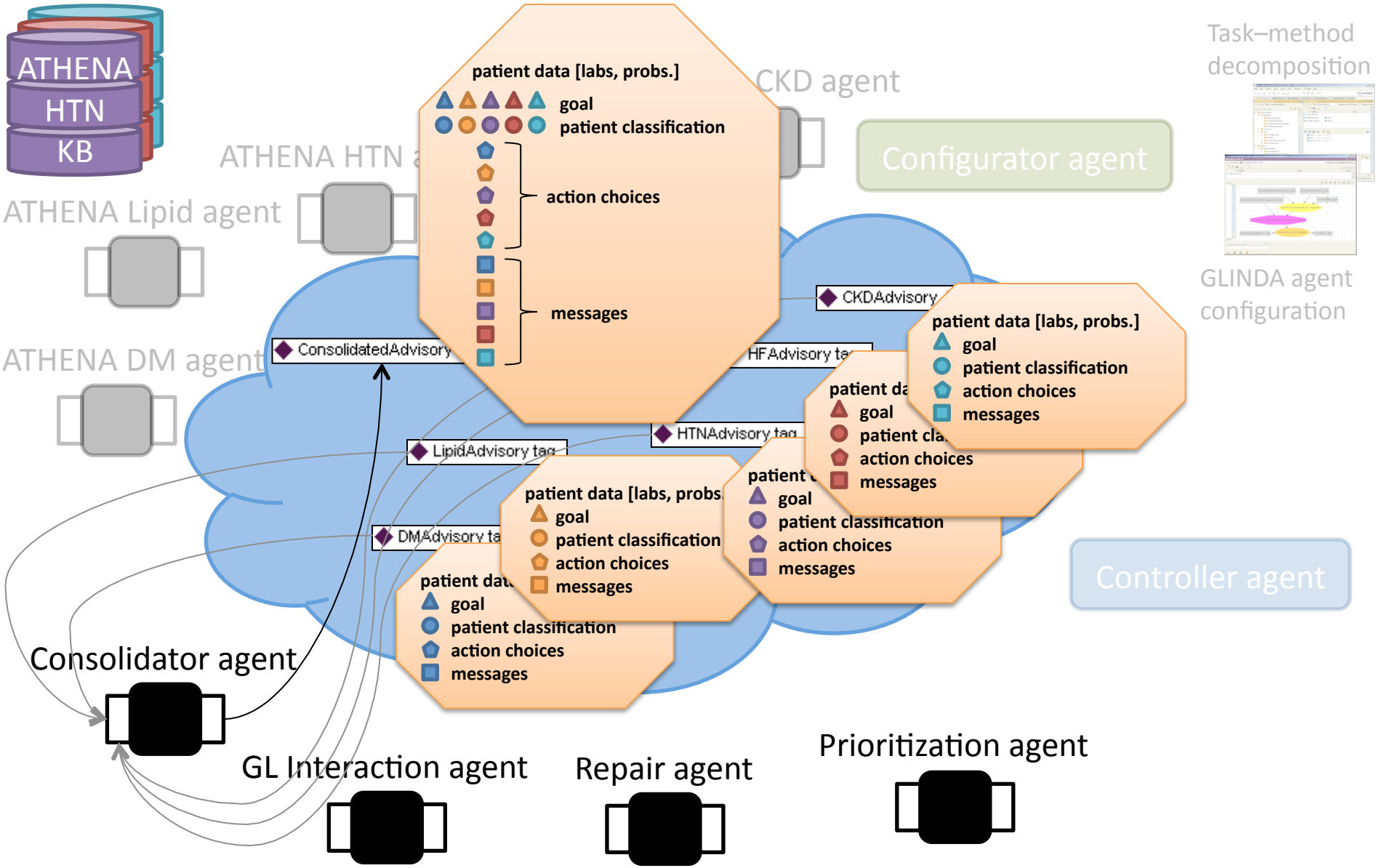
Running GLINDA – *Select Guideline*



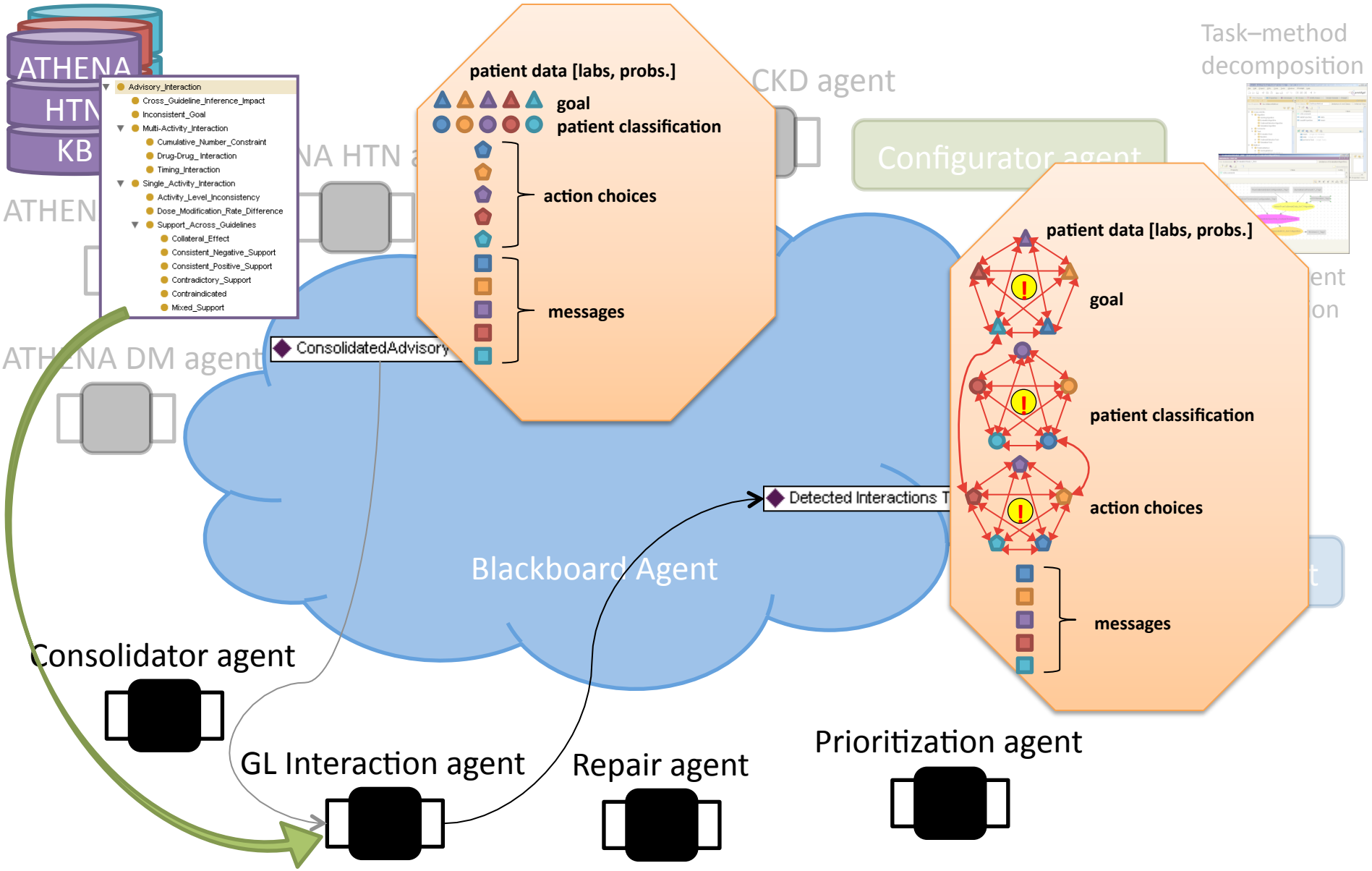
Running GLINDA – Run ATHENA Agents



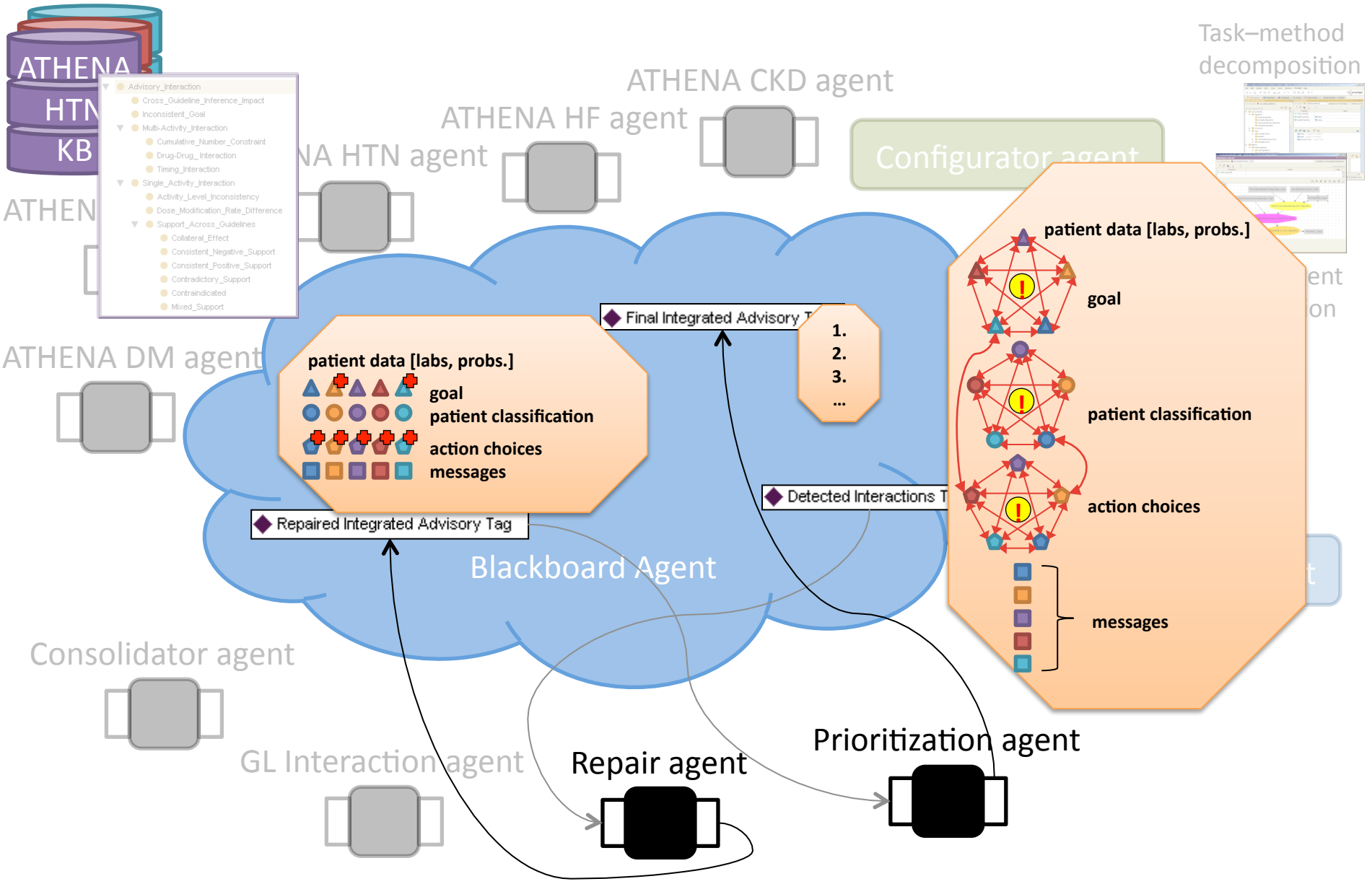
Running GLINDA – Consolidate Advisories



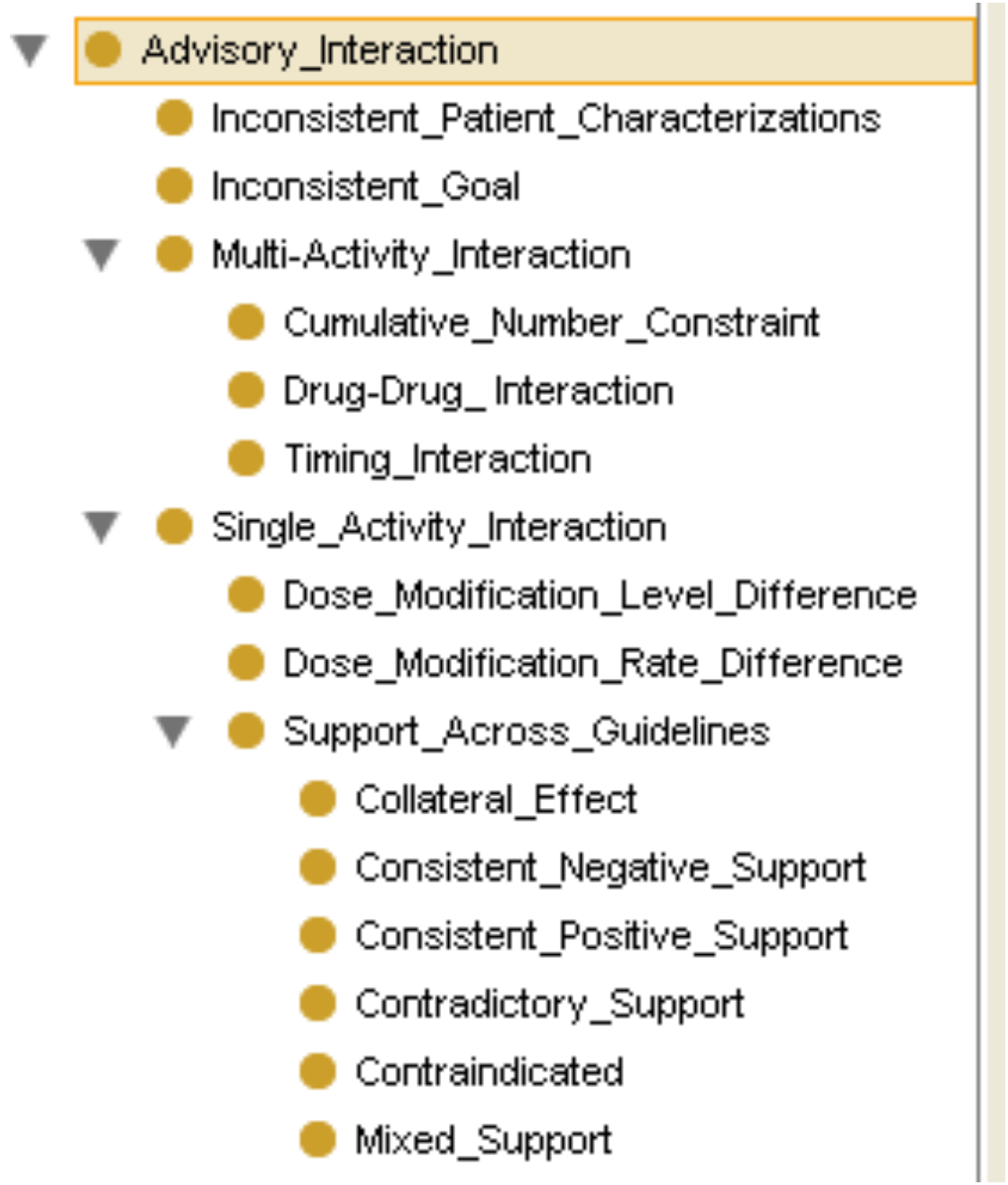
Running GLINDA – Calculate Interactions



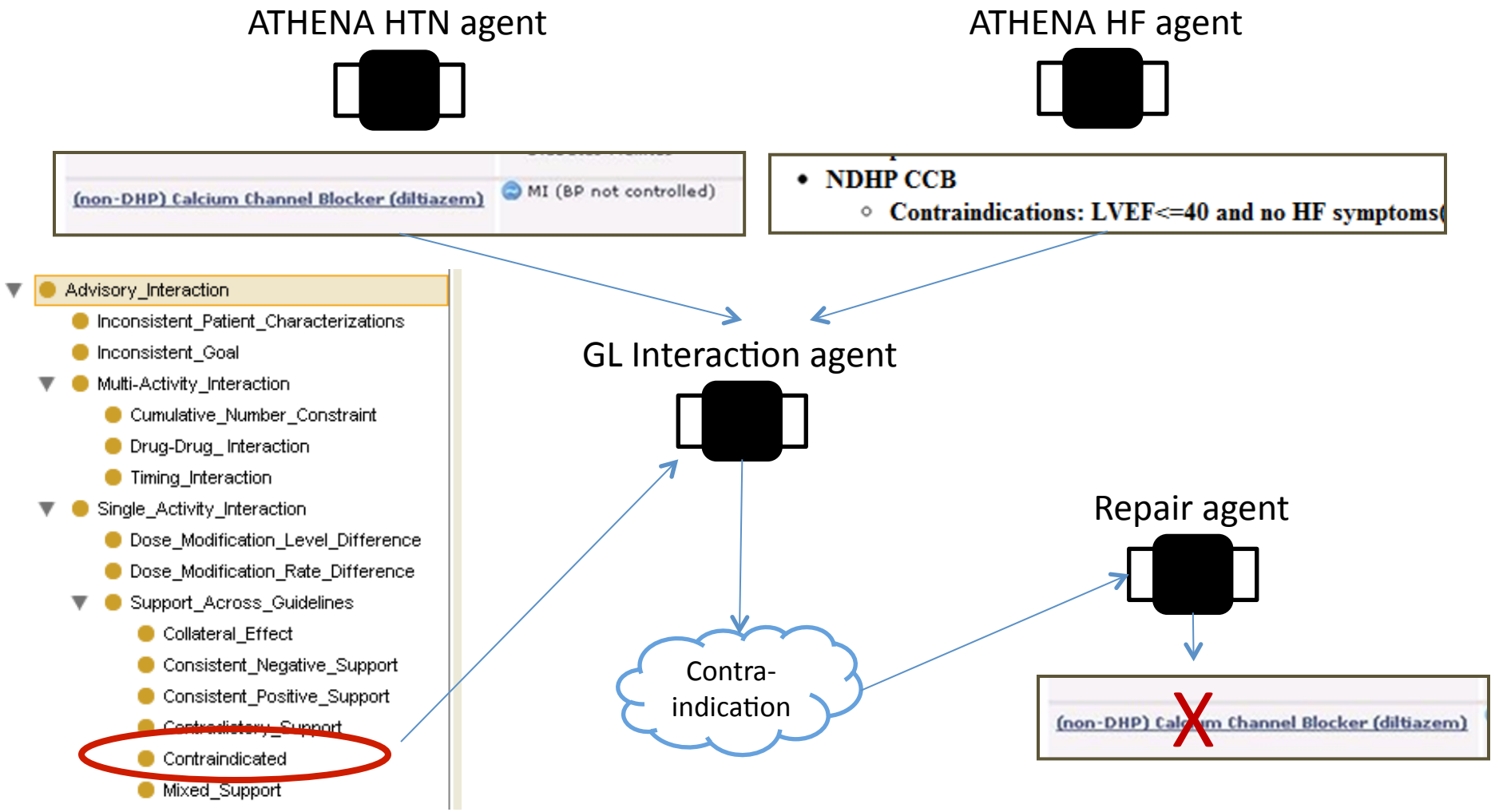
Running GLINDA – Repair and Prioritize



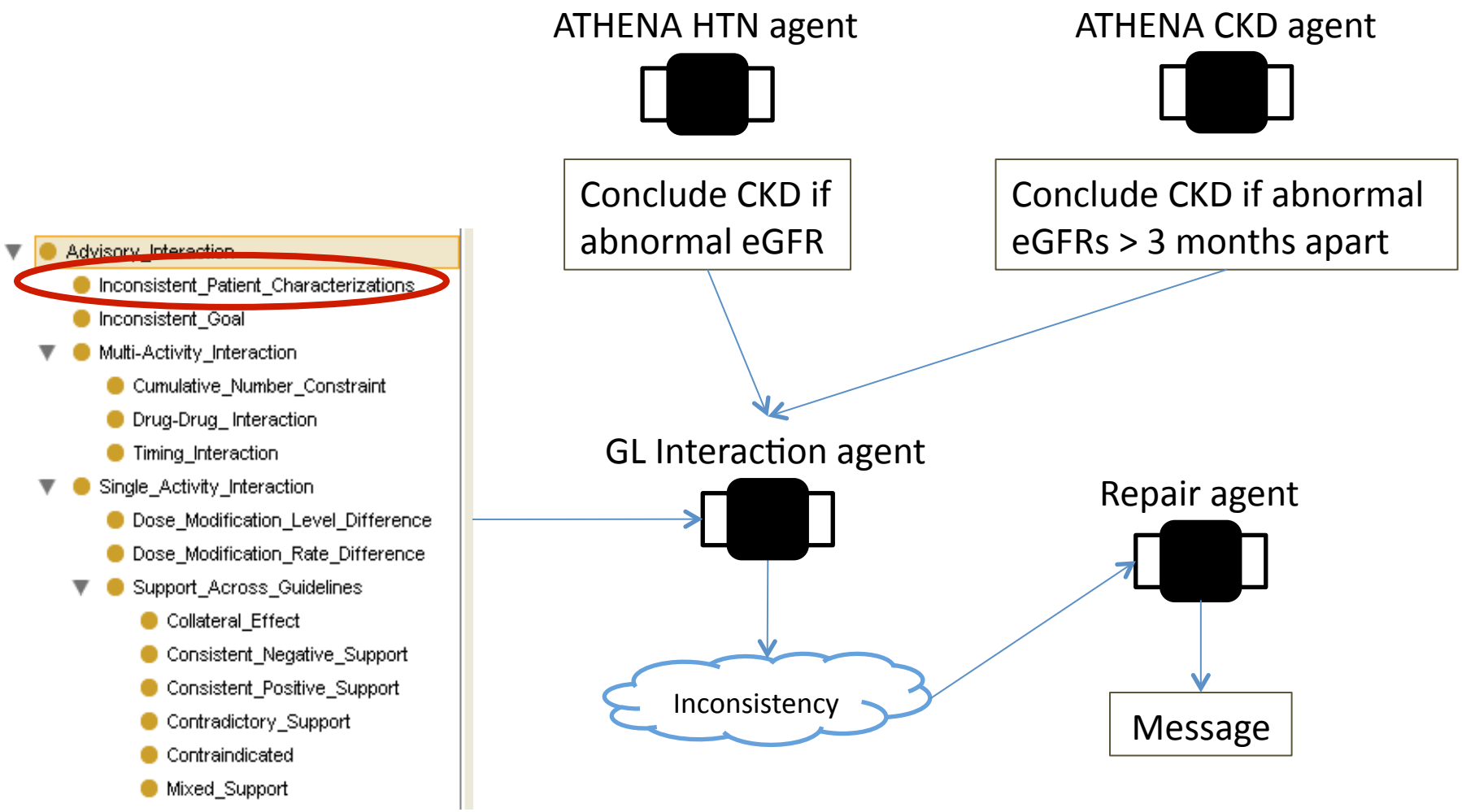
Ontology of Cross-Guideline Interactions Among Recommendations



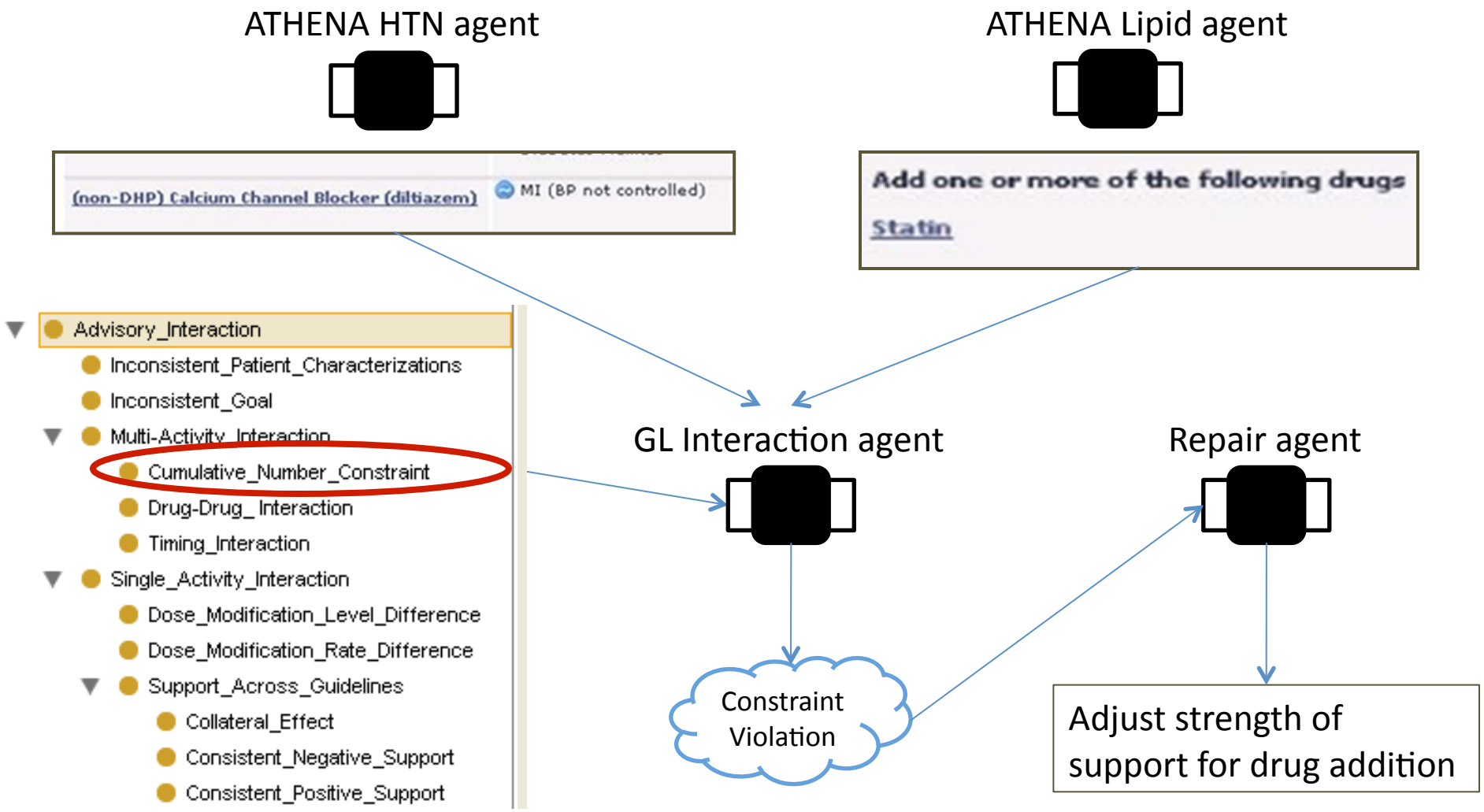
Example 1: Contradictory Recommendations

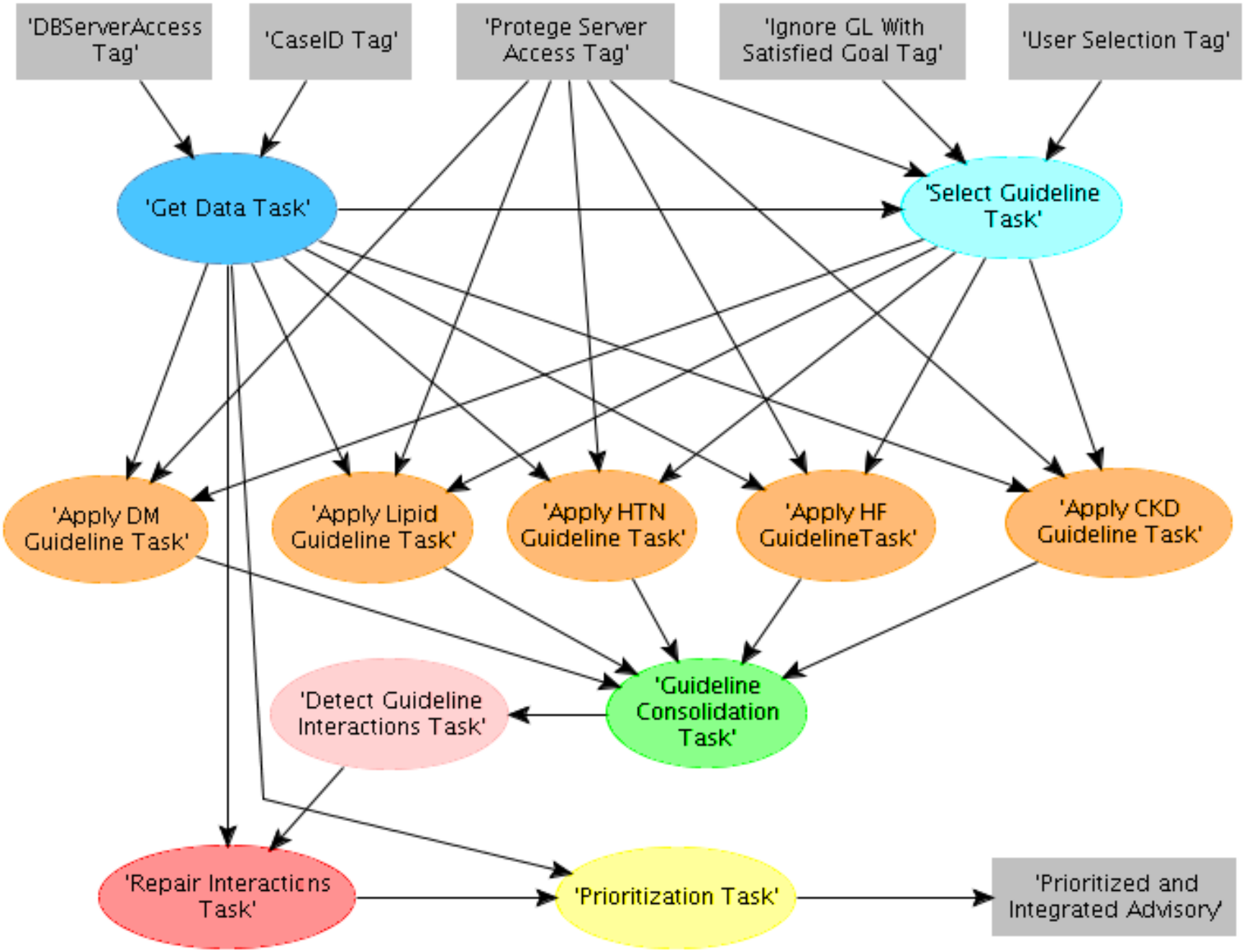


Example 2: Inconsistent Patient Characterizations



Example 3: Cumulative Number of Interventions

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Use of patient data to drive our work

- We extracted 2455 complex, deidentified patient cases from the Stanford Translational Research Integrated Database Environment (STRIDE)
- We are applying our method for interaction detection to 226 selected cases selected for their combination of diseases and number of drugs
- Formative evaluation of system performance drives knowledge-base evolution

https://clinicalinformatics.stanford.edu/research/stride.html

Conclusions

- Systems that assist with guideline-based care need to address the messiness of actual clinical situations
- An agent-oriented architecture allows for
  - Reasoning about comorbidities, application of multiple guidelines, and situation-specific interactions
  - Flexibility in experimenting with alternative computational workflows
- Creating GLINDA will drive development of formal models for computational thinking about
  - Guideline interactions
  - Repair mechanisms
  - Prioritization of interventions

This work has been supported by the National Library of Medicine

Any opinions expressed here are not necessarily those of the NLM or of the Department of Veterans Affairs