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Bench to Bedside Clinical Decision Support:

The Role of Semantic Web Technologies in Clinical and Translational Medicine

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Current State of Translational Medicine

- 17 year innovation adoption curve from discovery into accepted standards of practice
- Lack of innovation adoption planning in the discovery process
- Even if an innovation is accepted as a standard of practice, patients have a 50:50 chance of receiving appropriate care, a 5-10% probability of incurring a preventable, anticipatable adverse event
- Adverse effect anticipation in discovery and surveillance in the trial/post-market process is inadequate
- The market is balking at healthcare inflation, new diagnostics and therapeutics will find increasing resistance for reimbursement

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The Volume and Velocity of Knowledge Processing Required for Care Delivery

- Medical literature doubling every 19 years
  - Doubles every 22 months for AIDS care
- 2 Million facts needed to practice
- Genomics, Personalized Medicine will increase the problem exponentially
- Typical drug order today with decision support accounts for, at best, Age, Weight, Height, Labs, Other Active Meds, Allergies, Diagnoses
- Today, there are 3000+ molecular diagnostic tests on the market, typical HIT systems cannot support complex, multi-hierarchical chaining clinical decision support

Covell DG, Uman GC, Manning PR.
Ann Intern Med. 1985 Oct;103(4):596-9

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Benefits to Healthcare and Lifesciences from Semantic Web Technologies…

- Reduce the cost, duration, risk of drug discovery
  - Data integration, Knowledge integration, Visualization
  - Knowledge representation → New Knowledge Discovery
- Reduce the cost/duration/risk of clinical trial management
  - Patient identification and referral
  - Trial design (ie to capture better safety surveillance)
  - Data quality and clinical outcomes measurement
  - Post-market surveillance
- Reduce the cost/duration/liability of knowledge acquisition and maintenance for clinical decision support and clinical performance measurement
  - Knowledge provenance and representation
  - Conversion of "discovery algorithms" into "clinical practice algorithms"
  - Event-driven change management and propagation of change

Intersection Points between the Practicing Clinician and the Translational Model

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Patient Encounter

Test ordering and documentation guidance

Clinical Trials Referral

Personalized Medicine Decision Support Services and Knowledge Repository

Structured Test Result Interpretations

Tissue-bank

Knowledge Acquisition, Discovery And Maintenance Services for Clinical Care

Therapeutic ordering and documentation guidance

Structured Research Annotations

Bench R&D

Clinical Trials 1- 4

Pharmacovigilance

Clinical Surveillance & Signal Detection

Integrated Genotypic and Phenotypic Research Clinical Data Repository

R&D Discovery Services

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Today's EMR
Knowledge Management Capabilities:

- Knowledge "hardwired" or structured in proprietary modes into applications, not easily updated or shared
- Little or no standardization of HIT vendors on SNOMED, no shared interface terminologies for observation capture, no standard order catalogues
- Most EMRs have a task-interfering approach to decision support, sub-optimal usability, limited surveillance support
- Knowledge-engineering tools typically edit into transaction, no support for provenance, versioning, life-cycle, propagation, discovery or maintenance
- Consequently, clinical systems implementations are under-resourced with adequate knowledge to meet research, safety and quality needs
- Labor of converting knowledge into Clinical Decision Support is vastly underestimated
- Doesn't bode well for personalized medicine

Clinical Decision Support: Execution and Knowledge Propagation Safety Surveillance and Innovation Adoption

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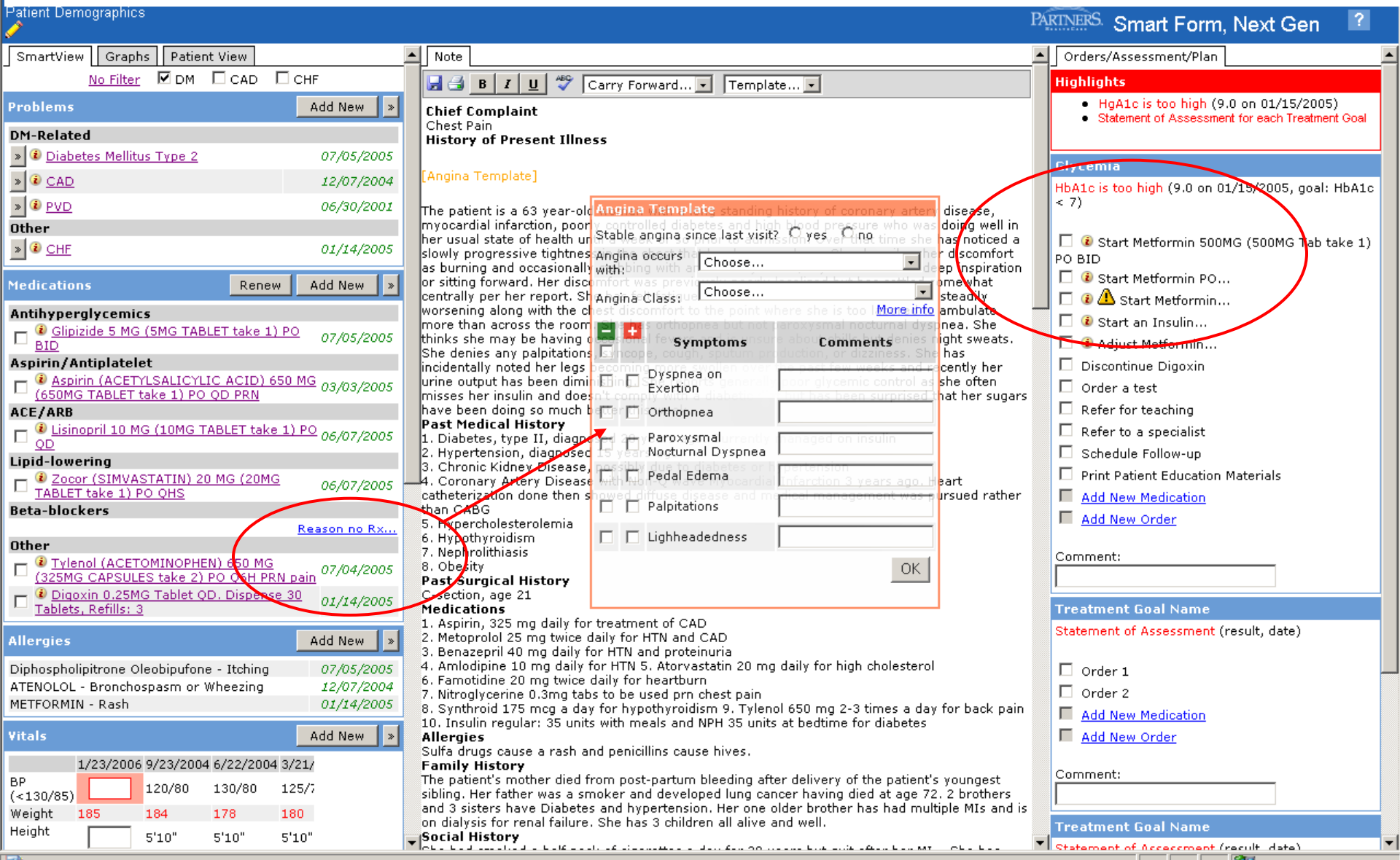
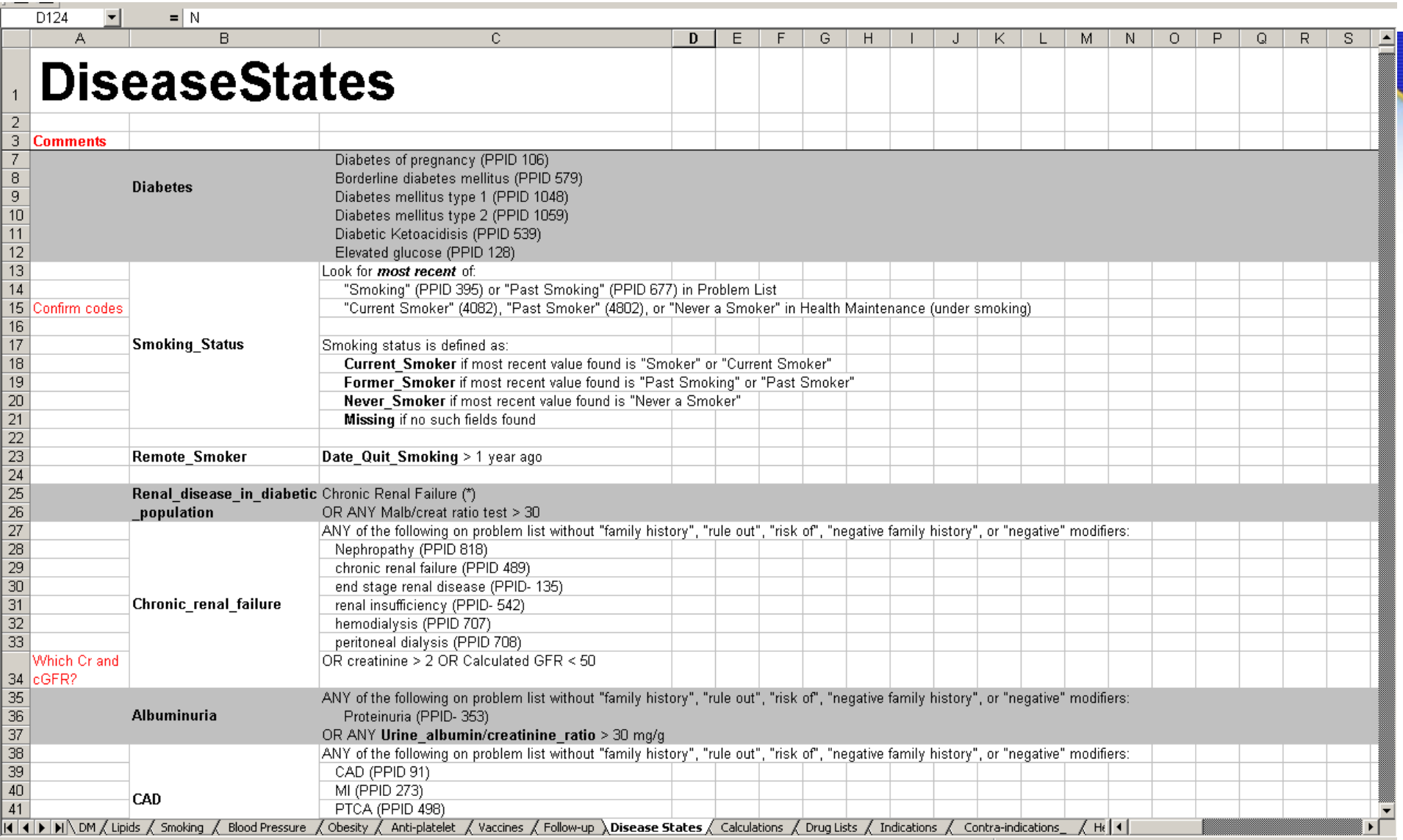
- Imagine a new therapeutic with the possible guideline:
  - All Patients with Obesity should be on a **New Appetite Suppressant Drug** unless there is a "contraindication"
  - All patients on this new obesity drug should be followed for liver function test abnormalities every 6 months
- Must define who has Obesity and Contraindication State
  - available data would include problems, documentation (ie BMI > 30), active medications (other appetite suppressants or diet orders), test results (basal metabolic rate, LFTs), and last resort, claims),
- Must maintain these state definitions in a common way (ontology management) instead of replicating these in rules, templates, reporting environments, etc.
- Must be able to adapt protocols rapidly in responses to discovery of new knowledge (knowledge event management)

Composite Decision Support Application: Diabetes Management

Guided Data Interpretation Guided Observation Capture Guided Ordering



Disease State Definitions, Typically Maintained in a Spreadsheet, Hard-coded into Rules, Forms and Reporting Tools Again and Again and Again



D124 = N

DiseaseStates

Comments		
	Diabetes	Diabetes of pregnancy (PPID 106) Borderline diabetes mellitus (PPID 579) Diabetes mellitus type 1 (PPID 1048) Diabetes mellitus type 2 (PPID 1059) Diabetic Ketoacidisis (PPID 539) Elevated glucose (PPID 128)
	Smoking_Status	Look for ***most recent*** of: "Smoking" (PPID 395) or "Past Smoking" (PPID 677) in Problem List
Confirm codes		"Current Smoker" (4082), "Past Smoker" (4802), or "Never a Smoker" in Health Maintenance (under smoking)
		Smoking status is defined as: **Current_Smoker** if most recent value found is "Smoker" or "Current Smoker" **Former_Smoker** if most recent value found is "Past Smoking" or "Past Smoker" **Never_Smoker** if most recent value found is "Never a Smoker" **Missing** if no such fields found
	Remote_Smoker	**Date_Quit_Smoking** > 1 year ago
	Renal_disease_in_diabetic_population	Chronic Renal Failure (*) OR ANY Malb/creat ratio test > 30
	Chronic_renal_failure	ANY of the following on problem list without "family history", "rule out", "risk of", "negative family history", or "negative" modifiers: Nephropathy (PPID 818) chronic renal failure (PPID 489) end stage renal disease (PPID- 135) renal insufficiency (PPID- 542) hemodialysis (PPID 707) peritoneal dialysis (PPID 708)
Which Cr and cGFR?		OR creatinine > 2 OR Calculated GFR < 50
	Albuminuria	ANY of the following on problem list without "family history", "rule out", "risk of", "negative family history", or "negative" modifiers: Proteinuria (PPID- 353) OR ANY **Urine_albumin/creatinine_ratio** > 30 mg/g
	CAD	ANY of the following on problem list without "family history", "rule out", "risk of", "negative family history", or "negative" modifiers: CAD (PPID 91) MI (PPID 273) PTCA (PPID 498)

DM | Lipids | Smoking | Blood Pressure | Obesity | Anti-platelet | Vaccines | Follow-up | **Disease States** | Calculations | Drug Lists | Indications | Contra-indications_ | He

Propagation and Inheritance

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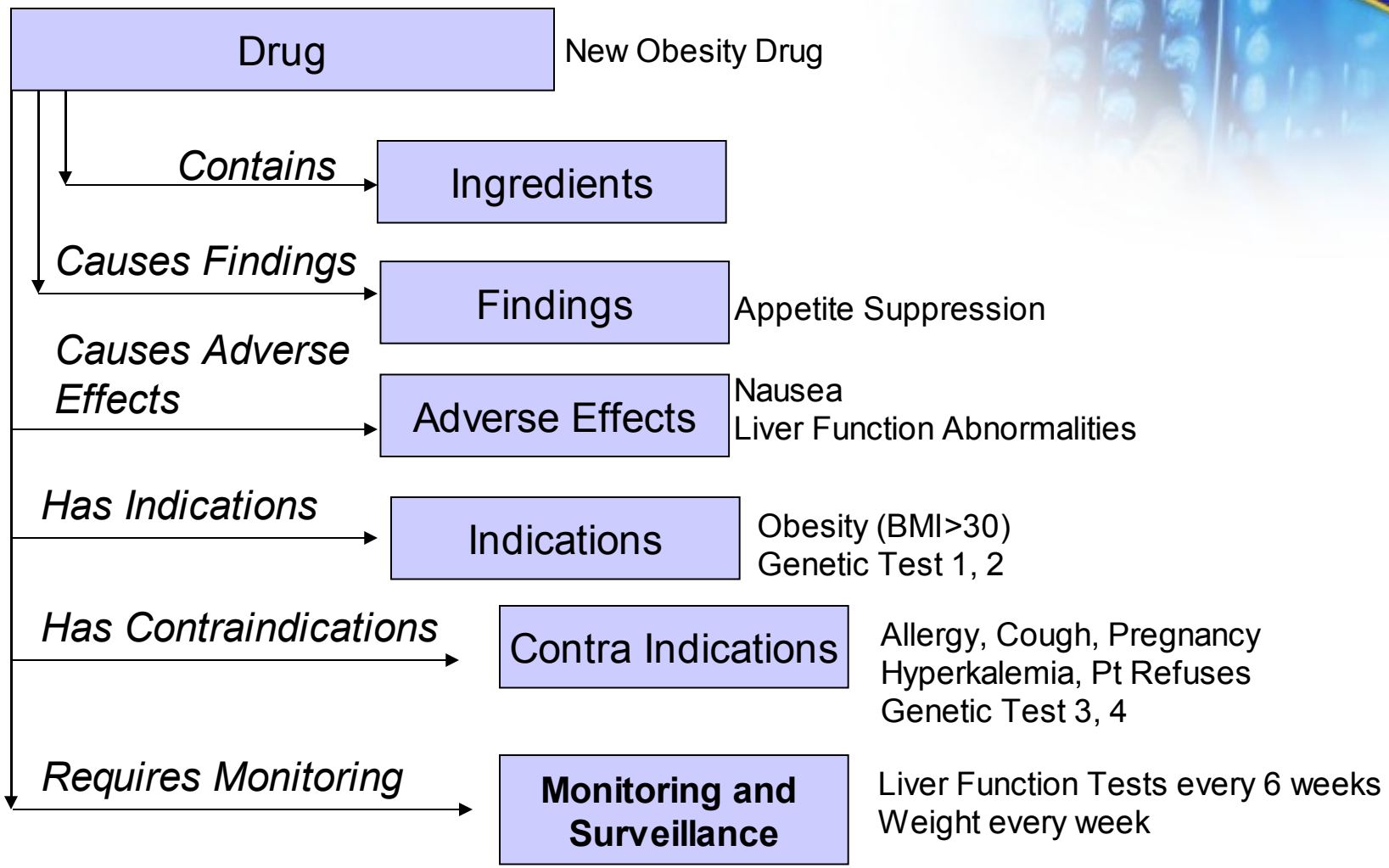
- Define "Contraindication to New Obesity Drug"
  - Allergy – from allergy list to related drug ingredients
  - Nausea symptoms on adverse reaction list
  - Hyperkalemia on problem list or high K test result
  - Pregnancy (100+ sub- definition components)
  - Elevated Liver Function Tests (AST > 100 or documented cirrhosis)
  - Patient refuses or failed the drug
  - This definition must be the same in any related rules, documentation templates to capture observation, and reporting and surveillance tools to track adverse effects and outcomes
  - Rate of change a drug indication or contraindication definition will grow exponentially with molecular diagnostics
- This "change management" problem is generalizable to all systems requiring structured observation capture for discovery and/or decision making

Drug Domain Ontology (Complex Definition)



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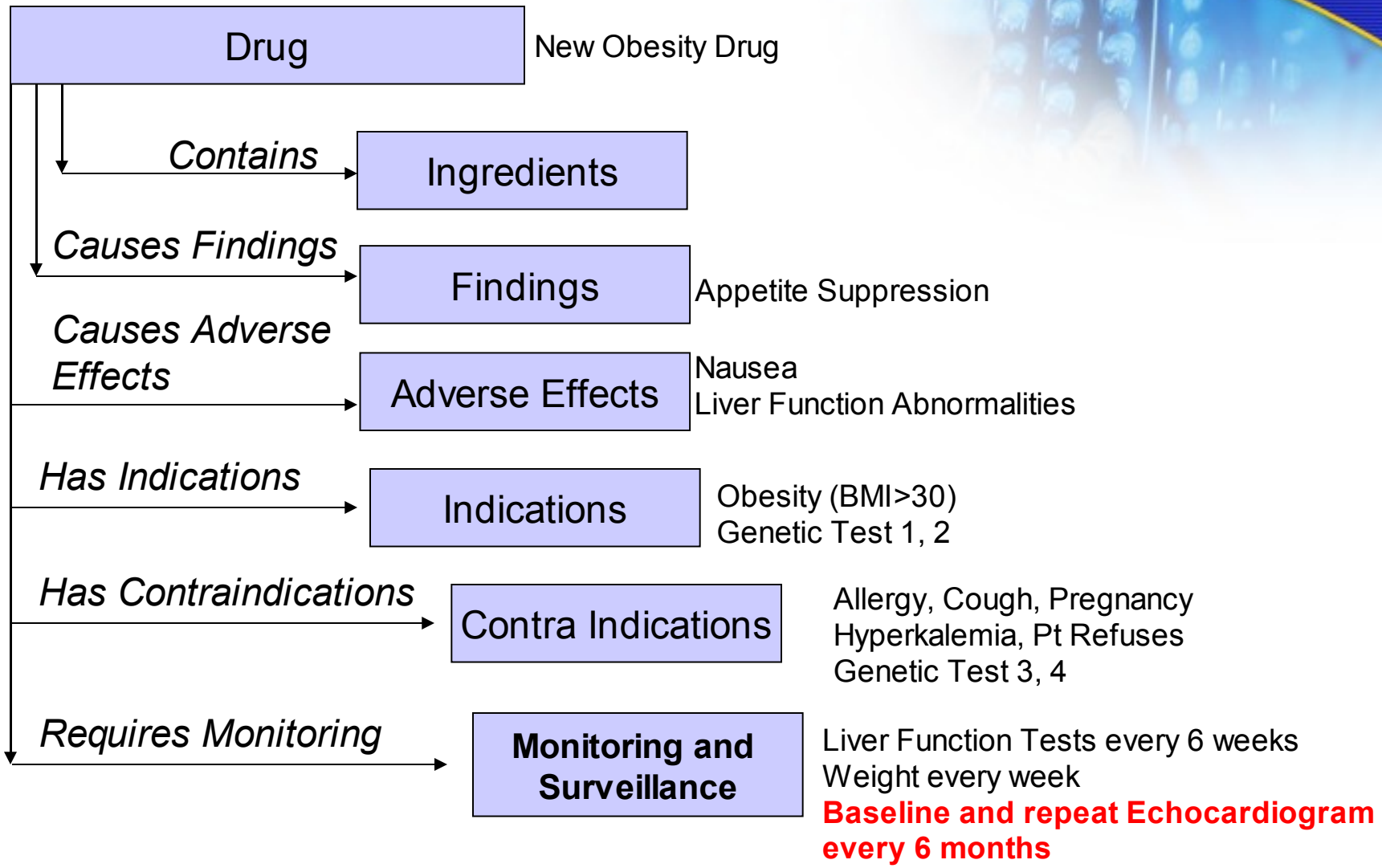
"Knowledge Event Management" Requires Robust Semantic Infrastructure

- What happens when signal detection services notice a spike in heart valve complications, how do we rapidly update the surveillance protocol to include routine echocardiogram monitoring?

- When a molecular diagnostic test result is currently of "unknown significance" and later, with new research, this result now indicates "non-responder" to an active medication, how do we quickly update the clinical decision support protocols?

Drug Domain Ontology Update and Propagation….



Bench to Bedside:
Knowledge Must Flow Bi-directionally

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