

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

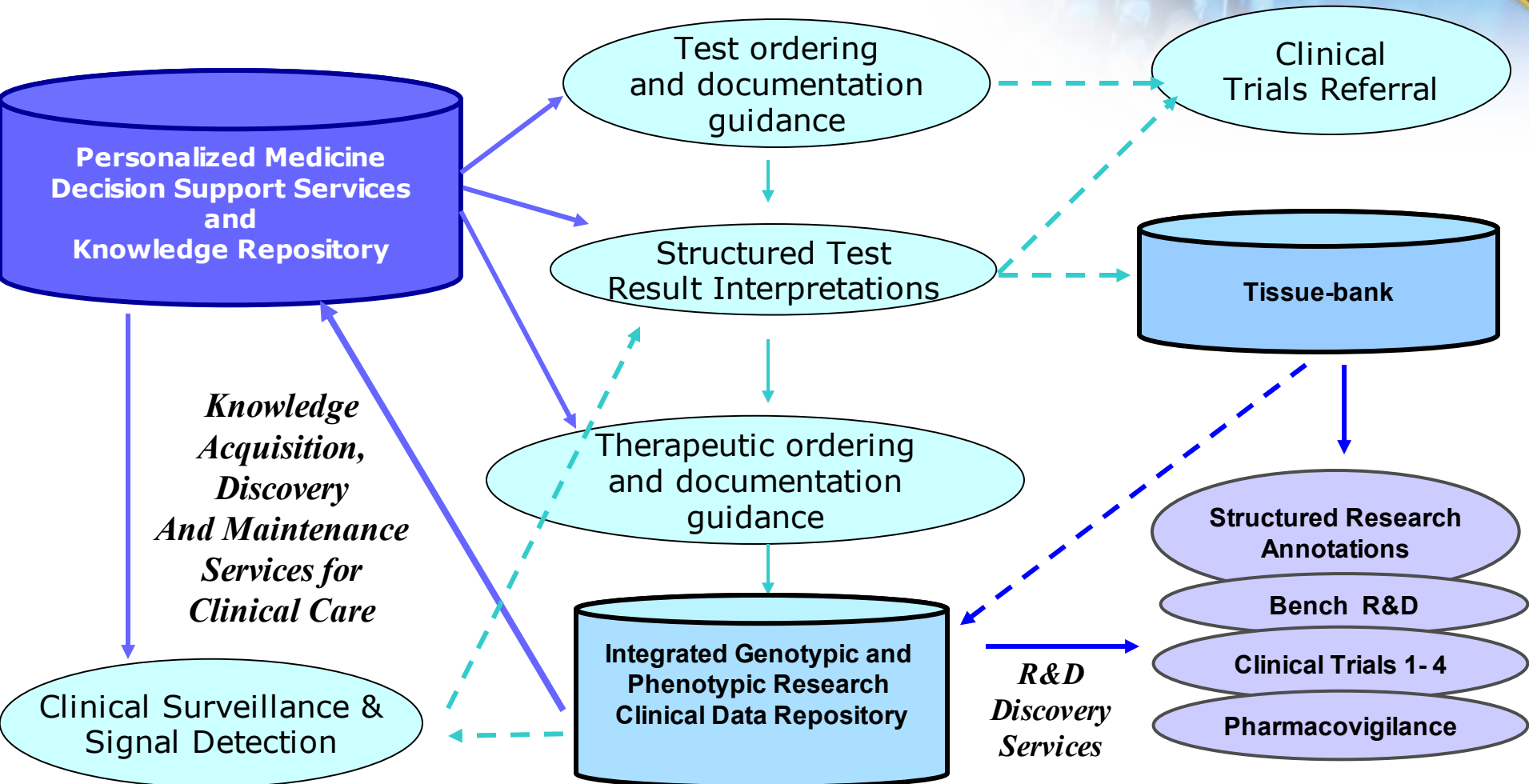
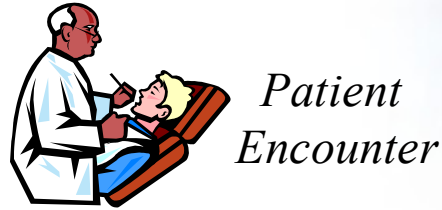
The Volume and Velocity of Knowledge Processing Required for Care Delivery

- 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

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



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

- 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

Patient Demographics PARTNERS Smart Form, Next Gen ?

SmartView | Graphs | Patient View

No Filter DM CAD CHF

Problems Add New >

DM-Related

- Diabetes Mellitus Type 2 07/05/2005
- CAD 12/07/2004
- PVD 06/30/2001

Other

- CHF 01/14/2005

Medications Renew Add New >

Antihyperglycemics

- Glipizide 5 MG (5MG TABLET take 1) PO BID 07/05/2005

Aspirin/Antiplatelet

- Aspirin (ACETYLSALICYLIC ACID) 650 MG (650MG TABLET take 1) PO QD PRN 03/03/2005

ACE/ARB

- Lisinopril 10 MG (10MG TABLET take 1) PO QD 06/07/2005

Lipid-lowering

- Zocor (SIMVASTATIN) 20 MG (20MG TABLET take 1) PO QHS 06/07/2005

Beta-blockers

[Reason no Rx...](#)

Other

- Tylenol (ACETAMINOPHEN) 650 MG (325MG CAPSULES take 2) PO Q6H PRN pain 07/04/2005
- Digoxin 0.25MG Tablet QD, Dispense 30 Tablets, Refills: 3 01/14/2005

Allergies Add New >

- Diphospholipitron Oleobipufone - Itching 07/05/2005
- ATENOLOL - Bronchospasm or Wheezing 12/07/2004
- METFORMIN - Rash 01/14/2005

Vitals Add New >

	1/23/2006	9/23/2004	6/22/2004	3/21/
BP (<130/85)		120/80	130/80	125/70
Weight	185	184	178	180
Height		5'10"	5'10"	5'10"

Note

Carry Forward... | Template...

Chief Complaint
Chest Pain

History of Present Illness

[Angina Template]

The patient is a 63 year-old male with a history of coronary artery disease, myocardial infarction, poorly controlled diabetes and high blood pressure who was doing well in her usual state of health until recently. She has noticed a slowly progressive tightness in her chest, which is worse with exertion or sitting forward. Her discomfort is described as burning and occasionally centrally per her report. She has noticed a steady increase in her chest pain, worsening along with the chest pain, more than across the room. She thinks she may be having a heart attack. She denies any palpitations or shortness of breath. She incidentally noted her legs becoming numb and tingling. Her urine output has been diminished. She misses her insulin and does not know how much to take. She has been doing so much better than CAGB.

Past Medical History

- Diabetes, type II, diagnosed 15 years ago, on insulin
- Hypertension, diagnosed 15 years ago, on metoprolol
- Chronic Kidney Disease, diagnosed 10 years ago, on lisinopril
- Coronary Artery Disease, diagnosed 10 years ago, had catheterization done then stents placed
- Hypercholesterolemia, diagnosed 10 years ago, on atorvastatin
- Hypothyroidism, diagnosed 10 years ago, on Synthroid
- Nephrolithiasis, diagnosed 10 years ago, on Tylenol
- Obesity

Past Surgical History

C-section, age 21

Medications

- Aspirin, 325 mg daily for treatment of CAD
- Metoprolol 25 mg twice daily for HTN and CAD
- Benazepril 40 mg daily for HTN and proteinuria
- Amlodipine 10 mg daily for HTN
- Atorvastatin 20 mg daily for high cholesterol
- Famotidine 20 mg twice daily for heartburn
- Nitroglycerine 0.3mg tabs to be used prn chest pain
- Synthroid 175 mcg a day for hypothyroidism
- Tylenol 650 mg 2-3 times a day for back pain
- Insulin regular: 35 units with meals and NPH 35 units at bedtime for diabetes

Allergies

Sulfa drugs cause a rash and penicillins cause hives.

Family History

The patient's mother died from post-partum bleeding after delivery of the patient's youngest sibling. Her father was a smoker and developed lung cancer having died at age 72. 2 brothers and 3 sisters have Diabetes and hypertension. Her one older brother has had multiple MIs and is on dialysis for renal failure. She has 3 children all alive and well.

Social History

She had smoked a half pack of cigarettes a day for 20 years but quit after her MIs. She has

Orders/Assessment/Plan

Highlights

- HgA1c is too high (9.0 on 01/15/2005)
- Statement of Assessment for each Treatment Goal

Glycemia

HbA1c is too high (9.0 on 01/15/2005, goal: HbA1c < 7)

- Start Metformin 500MG (500MG Tab take 1) PO BID
- Start Metformin PO...
- Start Metformin...
- Start an Insulin...
- Adjust Metformin...
- Discontinue Digoxin
- Order a test
- Refer for teaching
- Refer to a specialist
- Schedule Follow-up
- Print Patient Education Materials
- Add New Medication
- Add New Order

Comment:

Treatment Goal Name

Statement of Assessment (result, date)

- Order 1
- Order 2
- Add New Medication
- Add New Order

Comment:

Treatment Goal Name

Statement of Assessment (result, date)

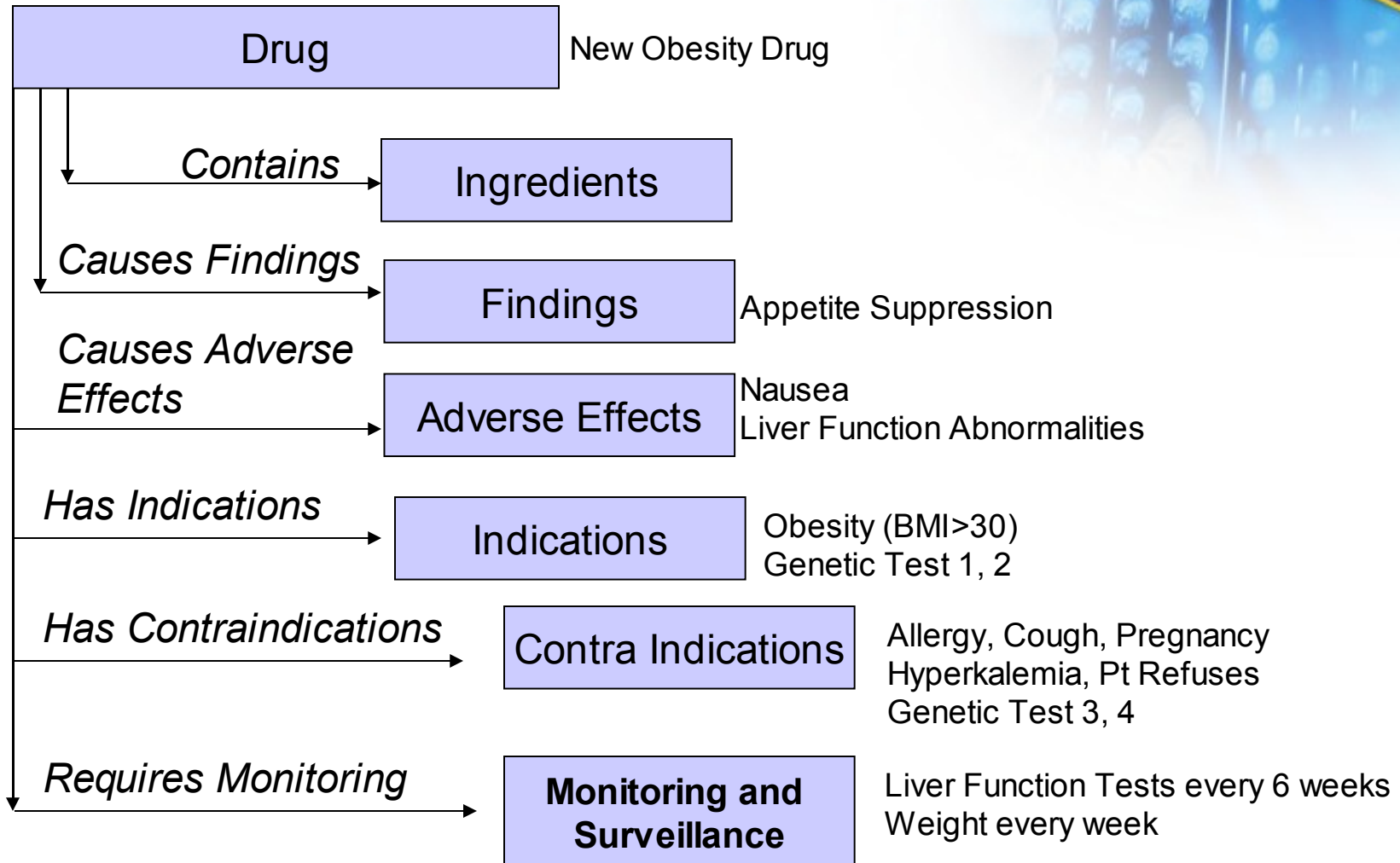
Disease State Definitions, Typically Maintained in a Spreadsheet, Hard-coded into Rules, Forms and Reporting Tools Again and Again and Again

D124		= N																	
A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	
1	DiseaseStates																		
2																			
3	Comments																		
7	Diabetes	Diabetes of pregnancy (PPID 106) Borderline diabetes mellitus (PPID 579) Diabetes mellitus type 1 (PPID 1048) Diabetes mellitus type 2 (PPID 1059) Diabetic Ketoacidosis (PPID 539) Elevated glucose (PPID 128)																	
13		Look for most recent of:																	
14		"Smoking" (PPID 395) or "Past Smoking" (PPID 677) in Problem List																	
15	Confirm codes	"Current Smoker" (4082), "Past Smoker" (4802), or "Never a Smoker" in Health Maintenance (under smoking)																	
16																			
17	Smoking_Status	Smoking status is defined as:																	
18		Current Smoker if most recent value found is "Smoker" or "Current Smoker"																	
19		Former Smoker if most recent value found is "Past Smoking" or "Past Smoker"																	
20		Never Smoker if most recent value found is "Never a Smoker"																	
21		Missing if no such fields found																	
22																			
23	Remote_Smoker	Date_Quit_Smoking > 1 year ago																	
24																			
25	Renal_disease_in_diabetic_population	Chronic Renal Failure (*) OR ANY Malb/creat ratio test > 30																	
26		ANY of the following on problem list without "family history", "rule out", "risk of", "negative family history", or "negative" modifiers:																	
27		Nephropathy (PPID 818)																	
28		chronic renal failure (PPID 489)																	
29		end stage renal disease (PPID- 135)																	
30		renal insufficiency (PPID- 542)																	
31	Chronic_renal_failure	hemodialysis (PPID 707)																	
32		peritoneal dialysis (PPID 708)																	
33		OR creatinine > 2 OR Calculated GFR < 50																	
34	Which Cr and cGFR?																		
35																			
36	Albuminuria	ANY of the following on problem list without "family history", "rule out", "risk of", "negative family history", or "negative" modifiers: Proteinuria (PPID- 353)																	
37		OR ANY Urine_albumin/creatinine_ratio > 30 mg/g																	
38		ANY of the following on problem list without "family history", "rule out", "risk of", "negative family history", or "negative" modifiers:																	
39		CAD (PPID 91)																	
40		MI (PPID 273)																	
41	CAD	PTCA (PPID 498)																	

Propagation and Inheritance

- 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

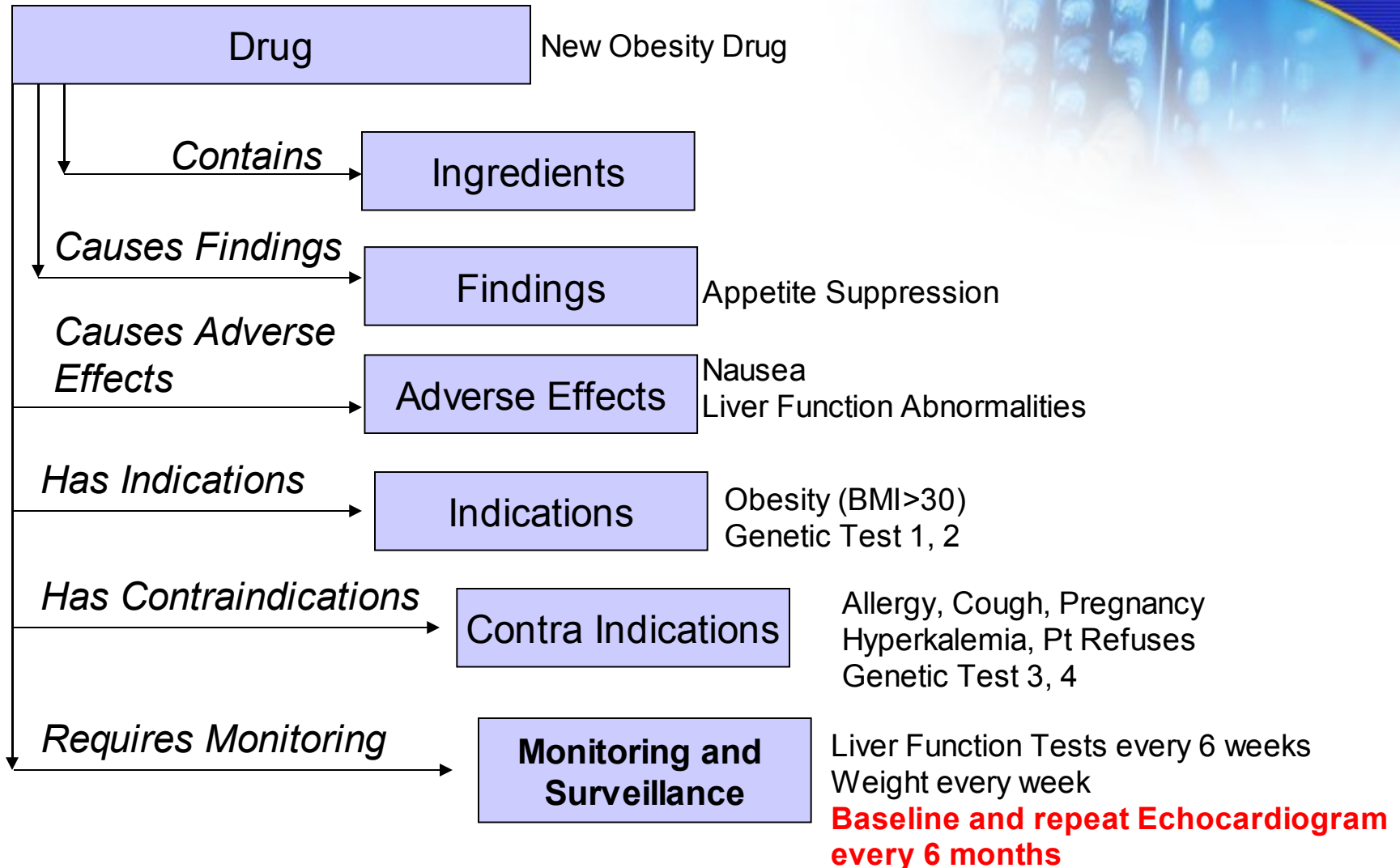
Drug Domain Ontology (Complex Definition)



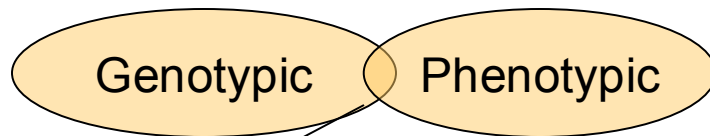
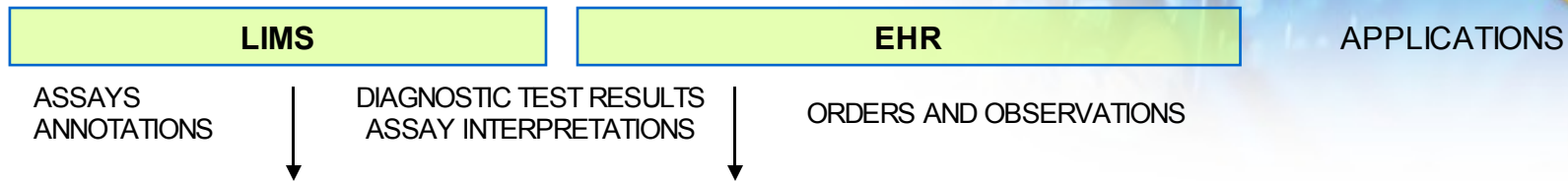
“Knowledge Event Management” Requires Robust Semantic Infrastructure

- 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



KNOWLEDGE and
WORKFLOW DELIVERY
SERVICES FOR ALL
PORTAL ROLES

DATA REPOSITORIES
AND SERVICES

KNOWLEDGE
ACQUISITION
AND DISCOVERY
SERVICES

