

Clinical Decision Support

Jason Baron, MD

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Jason Baron, MD

Overview

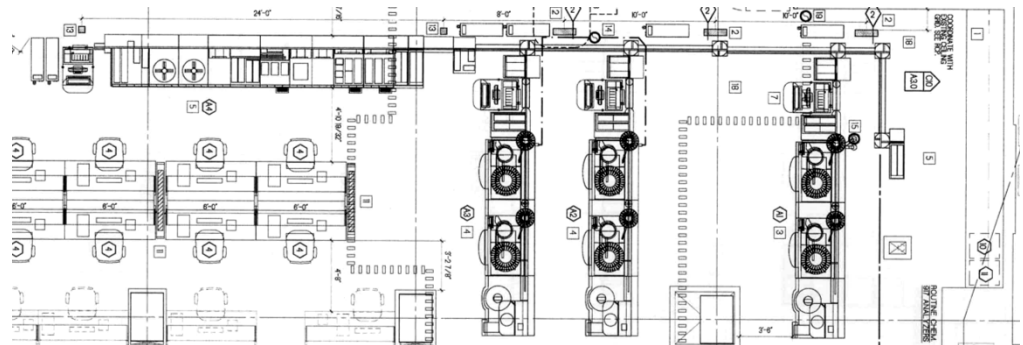
1. Why do we need decision support?
2. A high level view
3. Guidelines and quick refs
4. Just-in-time knowledge delivery
5. Human factors engineering
6. Computational knowledge derivation
7. Transforming expert knowledge into rule-based alerts
8. Computational Pathology—a 3 minute primer
9. Selected Challenges
 - a. Clinical data quality
 - b. Implementation—limits of current health IT infrastructure
 - c. Non-technical infrastructure

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The Need for Informatics

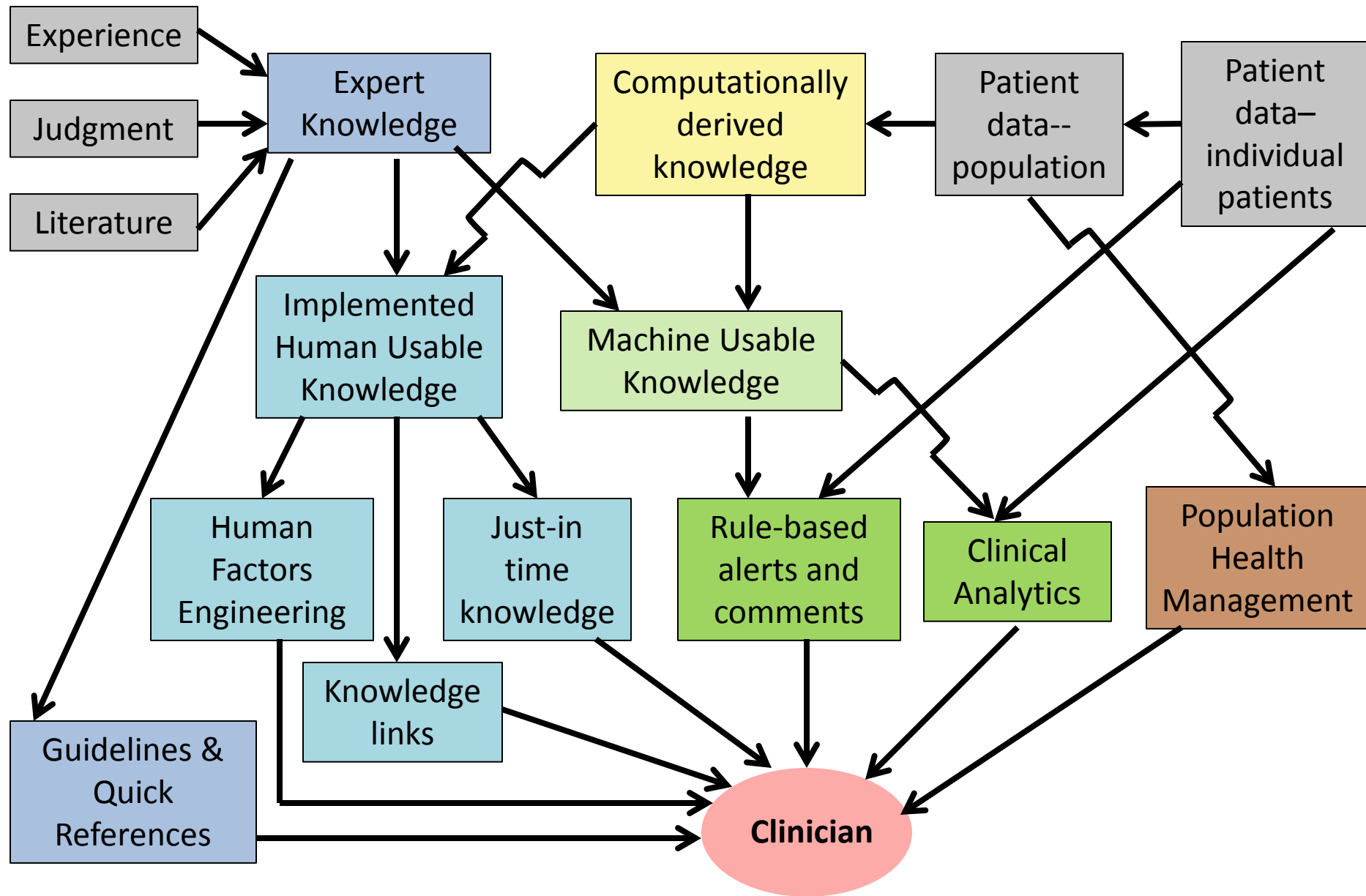
- Millions of results per year
- Rate of *data* production exceeds capacity of clinicians, pathologists and technologists to generate *information*
- The human brain is not well equipped to process high dimensional data



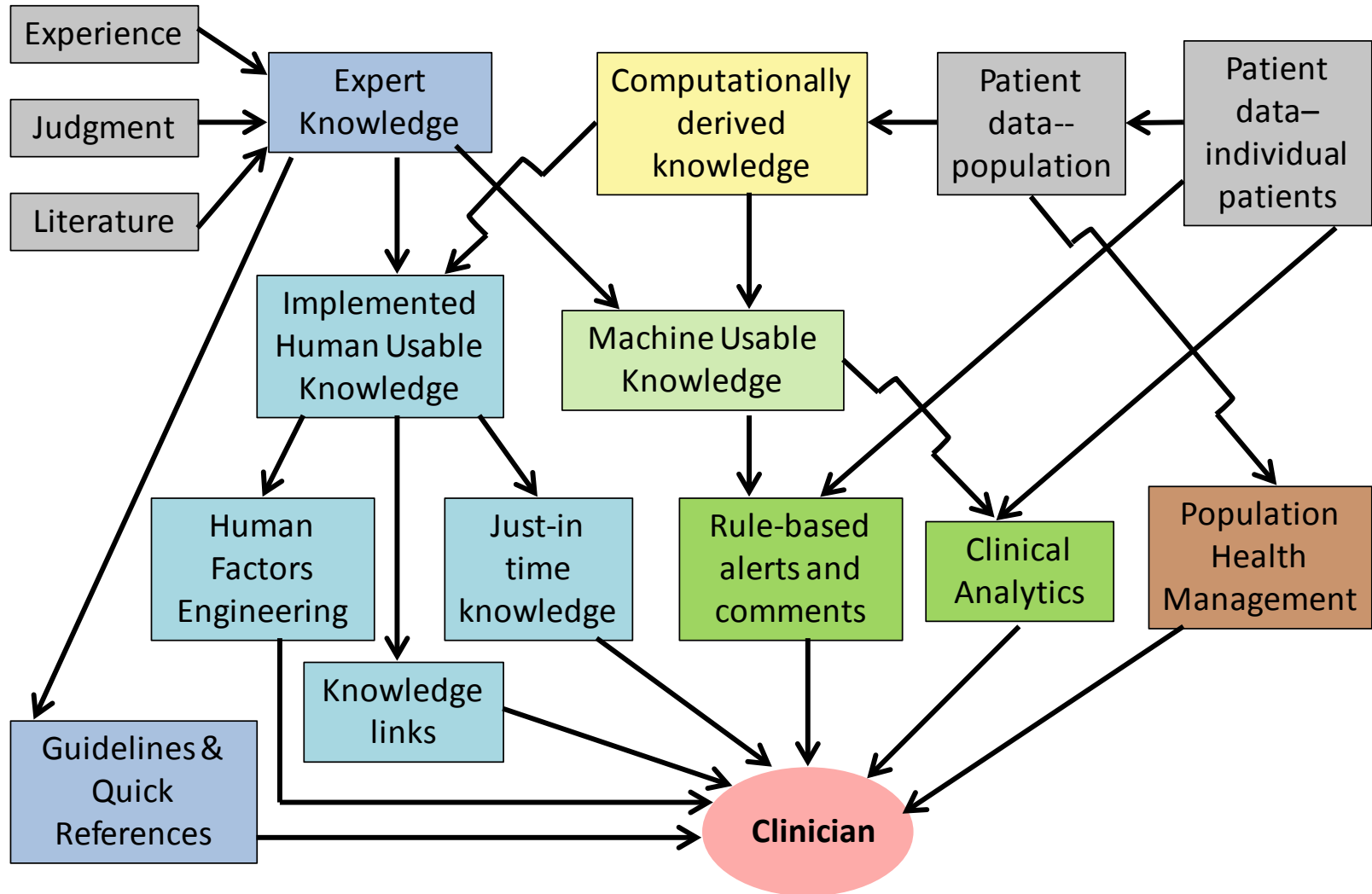
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A High Level View of Clinical Decision Support



Evolution of Decision Support

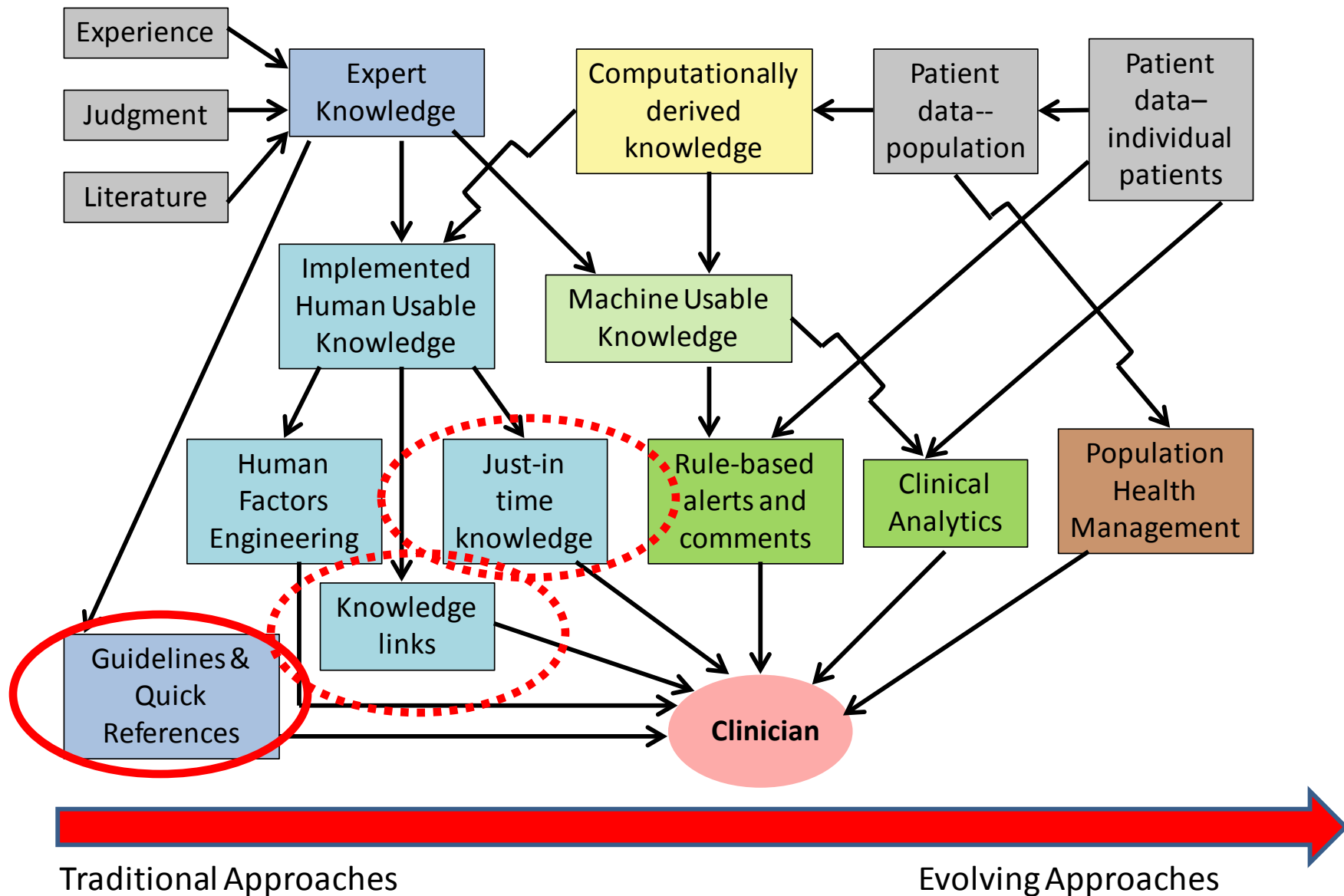


Traditional Approaches

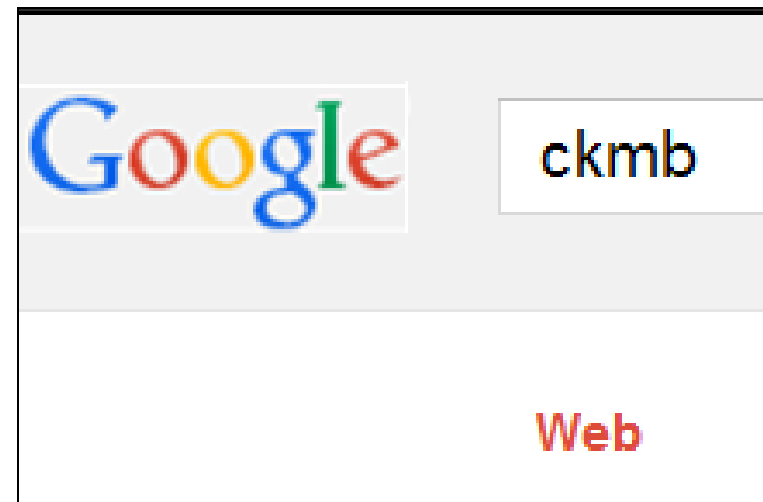
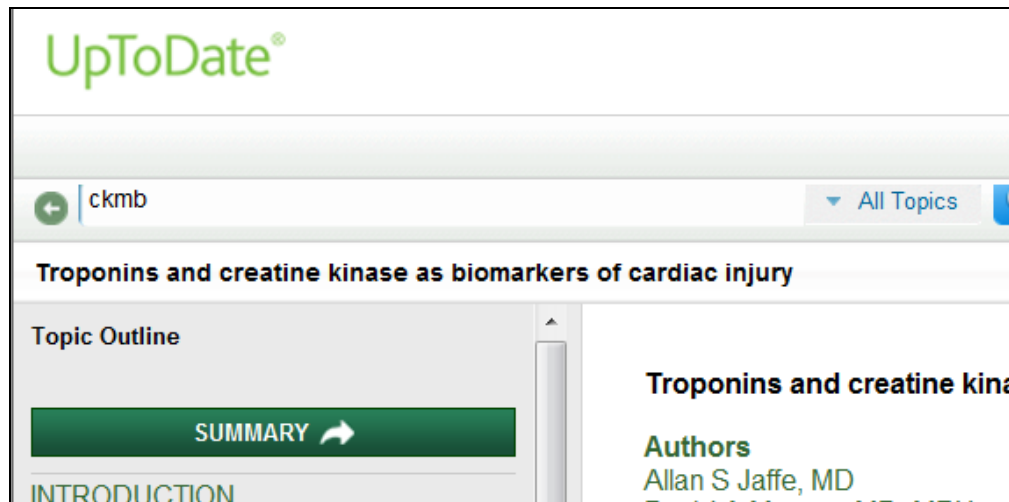
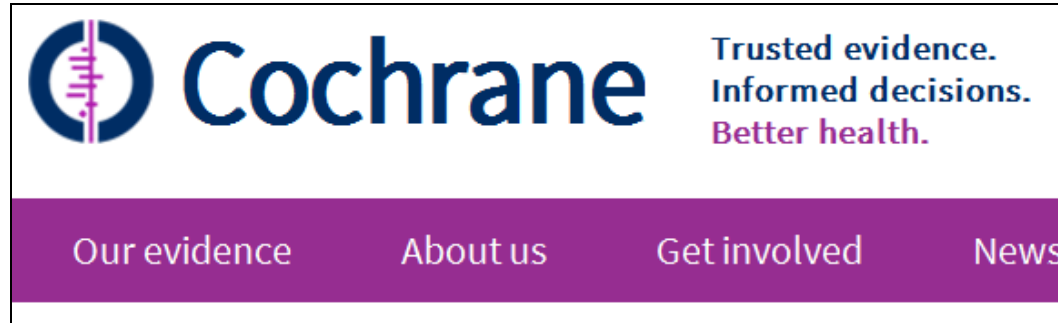
Evolving Approaches

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Guidelines & Quick References



Key Question: What Information Can be Trusted?

Guidelines & Quick References: Laboratory Handbooks

- Trusted Information
- Institution-specific
- Optimized Search
- Usage Analysis

The screenshot shows the homepage of the Massachusetts General Hospital Pathology Service Laboratory Handbook. The header includes the MGH logo, the text 'MASSACHUSETTS GENERAL HOSPITAL' and 'PATHOLOGY SERVICE LABORATORY HANDBOOK', and a navigation menu with links: Home, Lab Policies, Tubes and Reqs, Pneumatic Tube, Critical Values, Contact, and Help. A search bar with a 'Find' button is present. Below the search bar, there are links for 'Lab Questions? Call 617-724-LABS', 'Full List of Tests', and 'Advanced Search'. The main content area is titled 'Cytomegalovirus antigenemia assay'. It lists the following details: Lab: [Microbiology \(Virology\)](#); Inpatient Req: Microbiology (#11854); Outpatient Req: Clinical Labs (#83608); Specimen: Blood 10 ml Lavender; Result: 24-72 hours; Reference Interval: Negative. Below this, there are links for Related Tests: [CMV shell vial](#), [CMV culture](#), [CMV antibody \(IgG\)](#), and [CMV antibody \(IgM\)](#). An 'Important Information' section states: 'TEST OF CHOICE FOR BLOOD. Send specimen to laboratory at ROOM TEMPERATURE immediately after collection. Specimens are processed Monday - Friday and must be received before 3pm on Friday. The test is not performed on weekends or holidays. Positive results called back to requesting physician.' At the bottom, there is a link for 'Additional Resources: [Laboratory Evaluation of CMV Infection](#) PDF'.

MASSACHUSETTS GENERAL HOSPITAL PATHOLOGY SERVICE LABORATORY HANDBOOK

Home Lab Policies Tubes and Reqs Pneumatic Tube Critical Values Contact Help

Search Find

Lab Questions? Call 617-724-LABS • [Full List of Tests](#) • [Advanced Search](#)

Cytomegalovirus antigenemia assay

Lab: [Microbiology \(Virology\)](#)

Inpatient Req: Microbiology (#11854)

Outpatient Req: Clinical Labs (#83608)

Specimen: Blood 10 ml Lavender

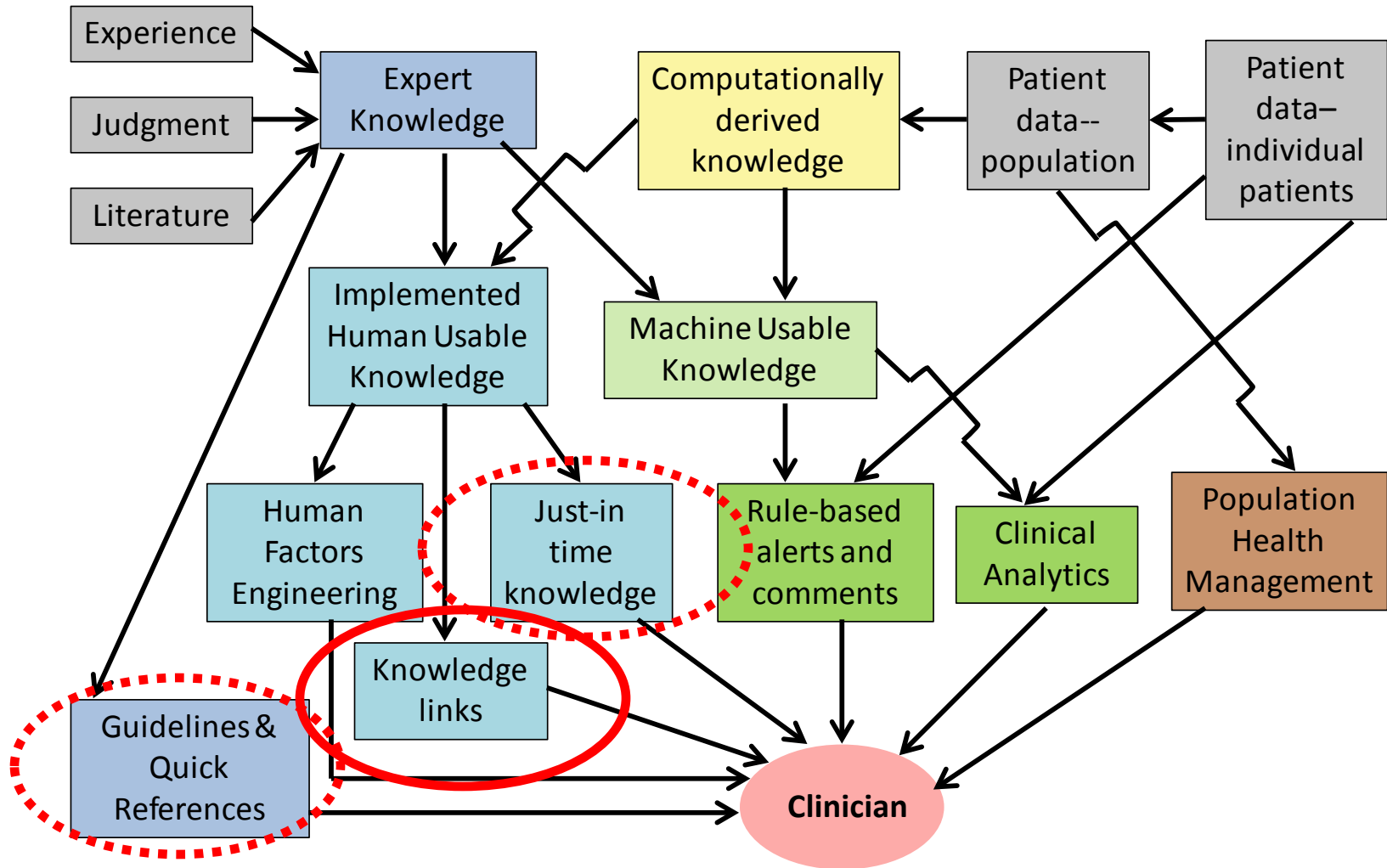
Result: 24-72 hours

Reference Interval: Negative

Related Tests: [CMV shell vial](#) • [CMV culture](#) • [CMV antibody \(IgG\)](#) • [CMV antibody \(IgM\)](#)

Important Information: TEST OF CHOICE FOR BLOOD. Send specimen to laboratory at ROOM TEMPERATURE immediately after collection. Specimens are processed Monday - Friday and must be received before 3pm on Friday. The test is not performed on weekends or holidays. Positive results called back to requesting physician.

Additional Resources: [Laboratory Evaluation of CMV Infection](#) PDF




Traditional Approaches

Evolving Approaches


Knowledge Links


Patient Name	MGHEMAPTEST, SIXTEEN	DOB	07/11/1965
Specimen Type:	ARTERIAL	Accession:	1017F53831
Ordering Provider:	DIGHE,ANAND S GRB 53	Reporting Lab:	MGH
Collected:	10/17/2014 12:41		
Received:	10/17/2014 12:41		
Logged In:	10/17/2014 12:41		

Test name	Result	Ref Range	Units	Completed
 Hemoglobin-POC	14.1	12.0-16.0	gm/dl	10/17/2014 12:57

Flag Key


L (Low or Critical)	H (High or Critical)	C (Corrected)
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 **KnowledgeLink**



Search Results for HGB (POC)

- [Micromedex LabAdvisor](#)
- [UpToDate](#)
- [MGH Lab Handbook](#)
- [Mayo Medical Laboratories](#)
- [Medscape](#)
- [Guidelines](#)
- [eTexts](#)
- [Patient Information](#)
- [EBM links](#)

 **Micromedex® 2.0**

Measurement of total hemoglobin concentration

Synonyms

Measurement of total haemoglobin concentration

Reference Range

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Just-in-time Knowledge Delivery: Non-Interruptive Alerts

Search for a Test

CK 2 tests found
[Double-click to select a test](#)

Name	Where	TAT	Cost
CK isoenzymes (CKMB+CPK) ...	In House	2 hours	\$
CPK (creatinine kinase)	In House	2 hours	\$

Ordering Message

UPDATED R/O MI protocol: Troponin T q8h x 3. Routine measurement of CK isoenzymes (CKMB+CPK) is no longer recommended. The use of CKMB should be restricted to the following exception: Post percutaneous coronary

Collection Instructions

Requires 3 ml Purple and 3 ml Green

To select a test: double-click on the test name OR single-click and then the Add button OR use the arrow keys and then Alt-A

Ordering Message

UPDATED R/O MI protocol: Troponin T q8h x 3. Routine measurement of CK isoenzymes (CKMB+CPK) is no longer recommended. The use of CKMB should be restricted to the following exception: Post percutaneous coronary

Just-in-time Knowledge Delivery: Interruptive Alerts



Test : CK isoenzymes (CKMB+CPK)

UPDATED R/O MI protocol: Troponin T q8h x 3. Routine measurement of CK isoenzymes (CKMB+CPK) is no longer should be restricted to the following exception: Post percutaneous coronary intervention.

Additional Information :

* Required fields

Indication

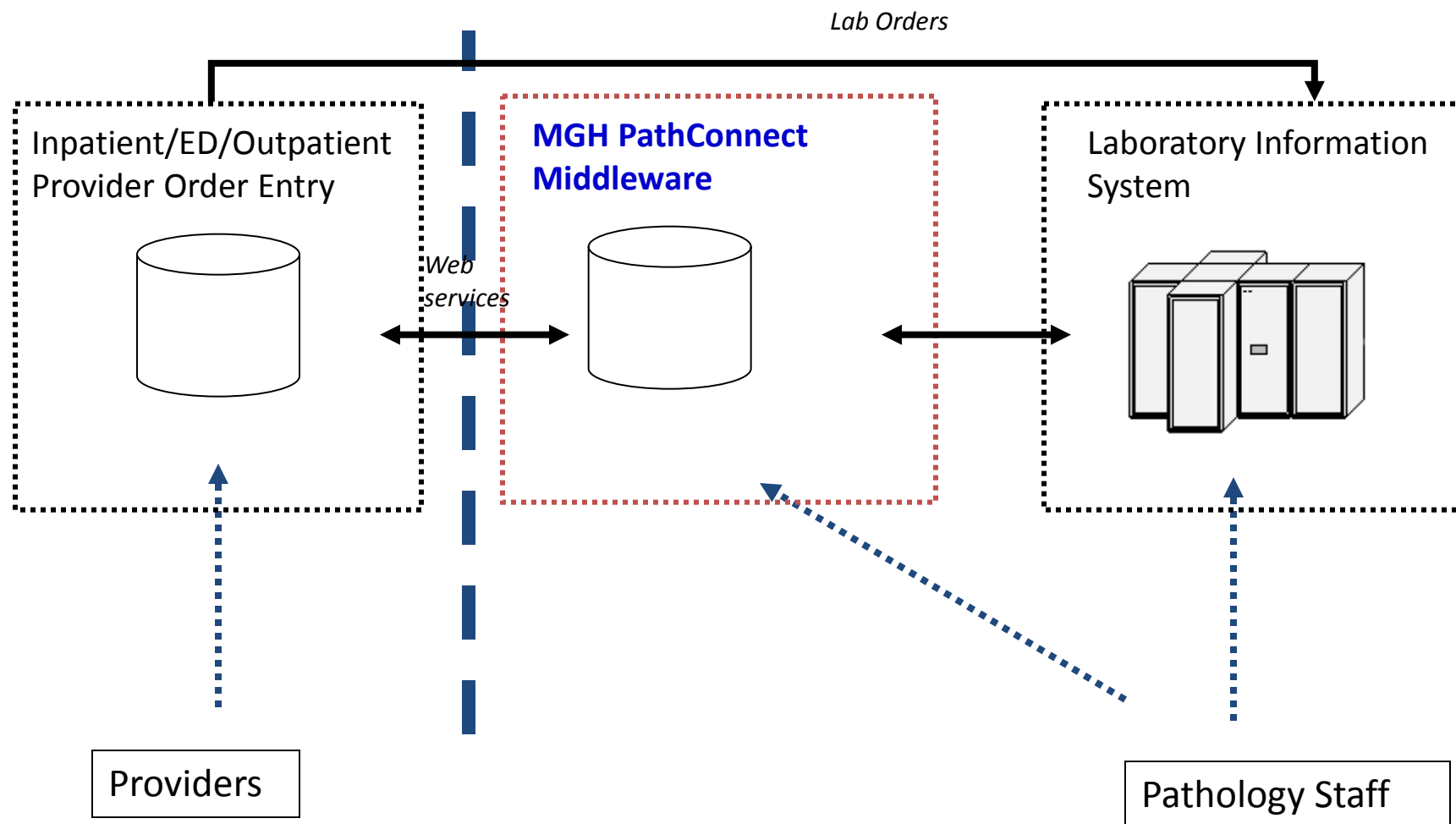
* Please review NOTE above and Cancel if not needed. Indication for CK-MB testing (REQUIRED):

Just-in-time Knowledge Delivery: Knowledge Management Systems, Pathology Portal

POE Test Name	CK isoenzymes (CKMB+CPK)
Test Active / Orderable	True
Test Orderable in POE	True
Test Orderable Environments	MGHED,MGHIN,MGHOP
Common Test	False,False,False
Test Population	Adult,Pedi,Neonate
Test Turn Around Time	2 hours
Test is Send Out	False
Cost	\$
Test Preferred Tube	GN3 + P3
Specimen Type	BLD
POE Test Ordering Message	UPDATED R/O MI protocol: Trop

Just-in-time Knowledge Delivery: Knowledge Management Systems

Permits Pathology to have control over Provider Order Entry screens



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Evolving Approaches

Human Factors Engineering

- Design systems to encourage a particular outcome
- Examples:
 - Design requisitions, templates or quick picks to include tests that are often appropriate and require specific searchers for uncommonly needed tests (that should usually be used by a specialty)
 - Use “smart” search to guide clinicians toward the correct test
- Guiding principle: Make it easy to do the right thing and hard to the wrong thing

Human Factors Engineering: Example Quick Picks


Laboratory Order Processing Active Pt: MGHEMAPTEST, SI

Select and/or Search for Tests
Double-click to select a test


- CBC
- CBC with Diff
- PT-INR
- PTT
- U/A (urinalysis)
- Electrolytes
- Glucose
- BUN/Creatinine
- Calcium
- Magnesium
- Phosphorus
- Albumin
- Alk Phos
- Bilirubin (direct and total)
- AST/ALT
- Amylase/Lipase (plasma)
- LFTs (hepatic panel)
- Troponin T
- Sed rate (ESR)
- Ionized calcium
- Arterial blood gas (MORE)
- Crit Care Blood Gas (MORE)
- Capillary blood gas (MORE)
- Blood culture/sensitivity (MORE)
- Urine culture/sensitivity (MORE)
- Respiratory culture/sensitivity (MORE)

Add >

< Remove



Tests Selected



Modify Additional Info.

Ordering message

Collection Instructions (file with order)

Requested Collection Time for all selected tests

☒ Routine ☐ Already collected ☐ Fasting

☐ STAT ☐ Draw If/When ☐ Special Billing/Research

Frequency

Total Collections

Start

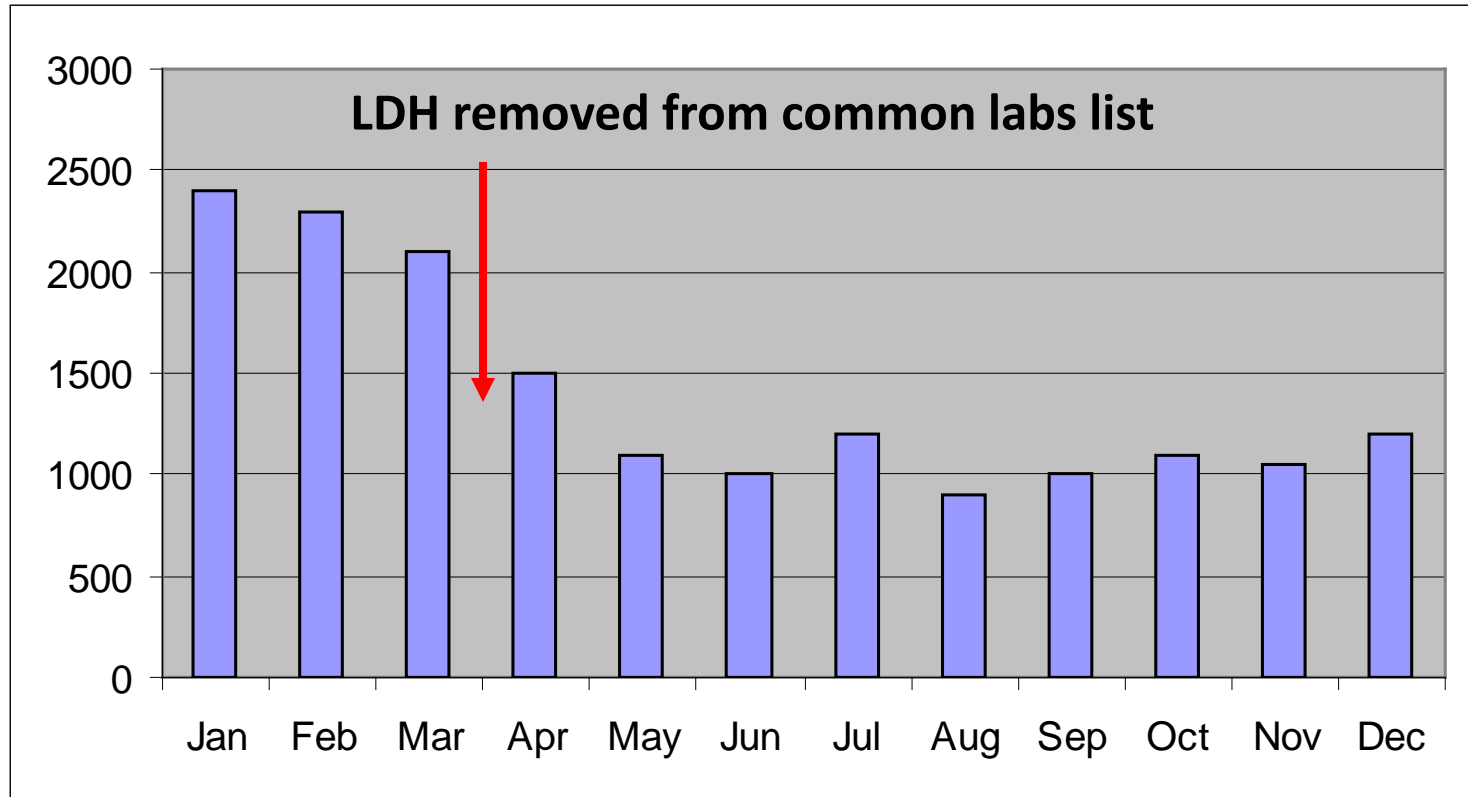
Search

Help

OK

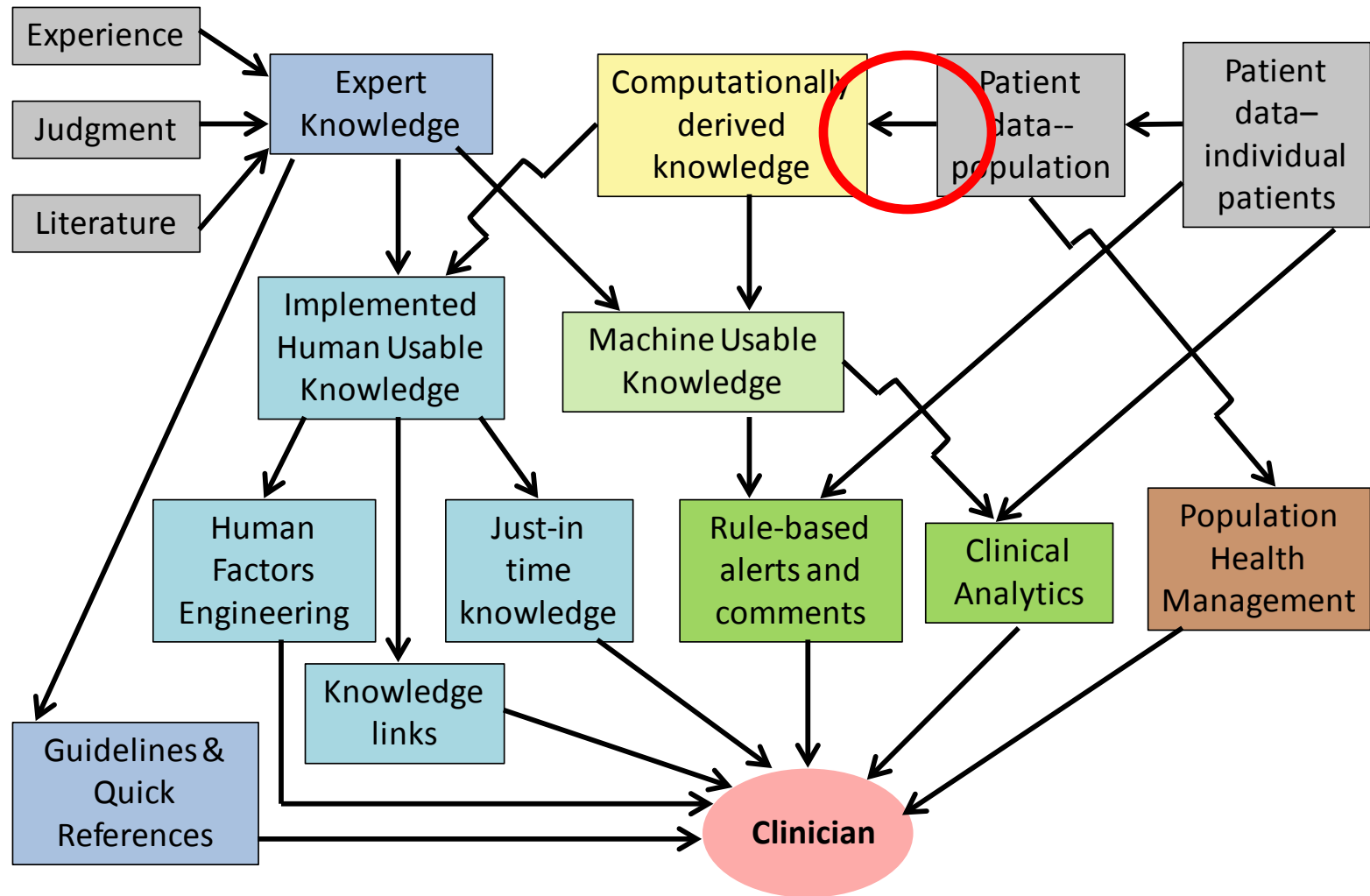
Cancel

Human Factors Engineering: Example LDH Quick Pick



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Traditional Approaches

Evolving Approaches

Traditional Vs. Computational Derivation of Knowledge

- Traditional Knowledge Sources

- Clinical and observational studies
- Clinician experience
- Expert Opinion
- Consensus guidelines

- Computational Knowledge Discovery

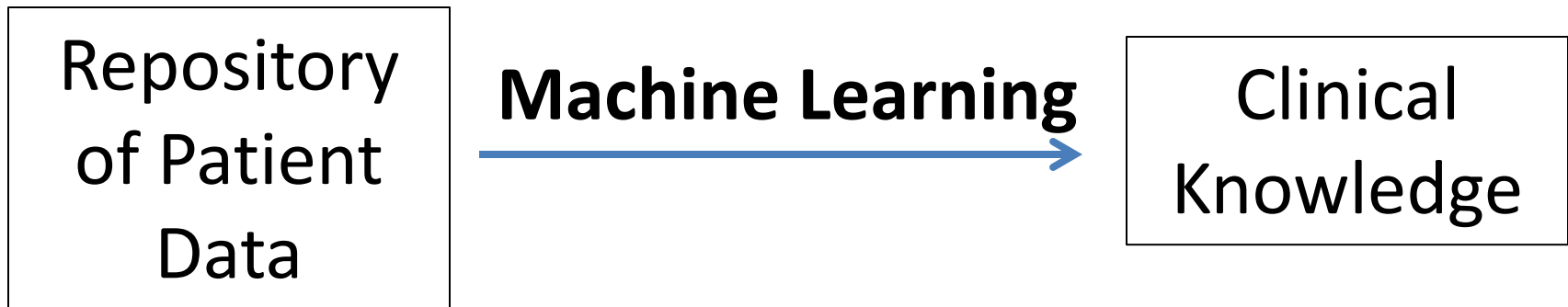
- Apply statistical and machine-learning approaches to existing clinical data to identify useful patterns

Advantages and Limitations of Traditional Vs. Computational Derivation of Knowledge

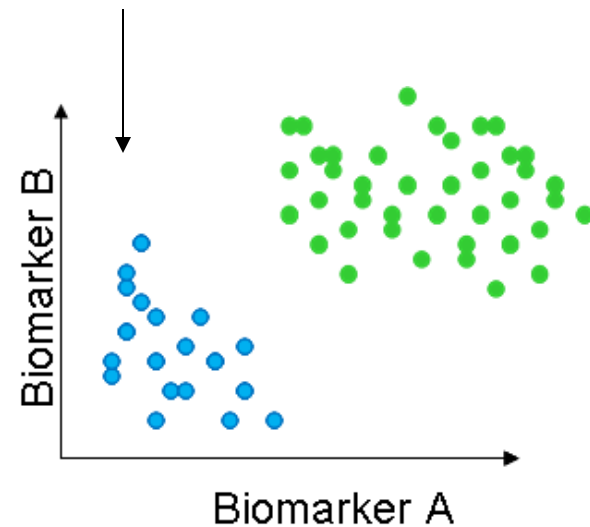
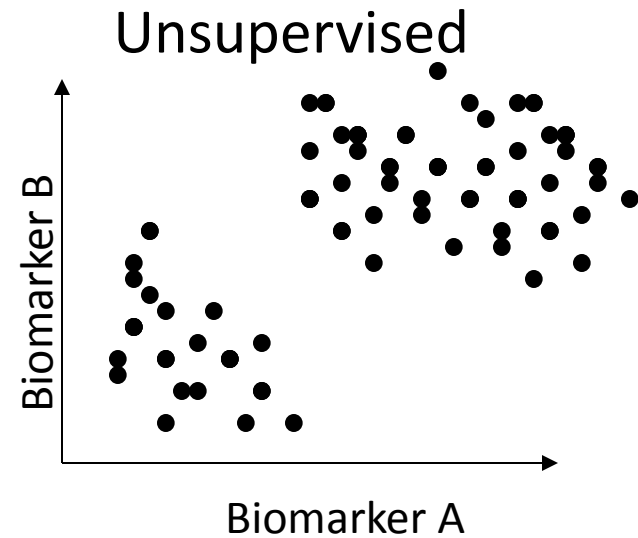
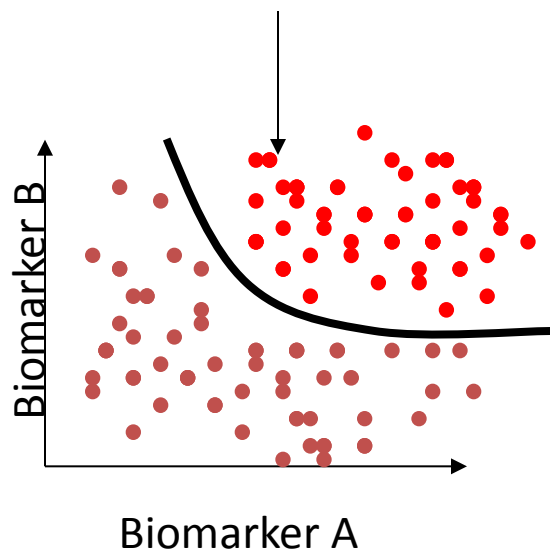
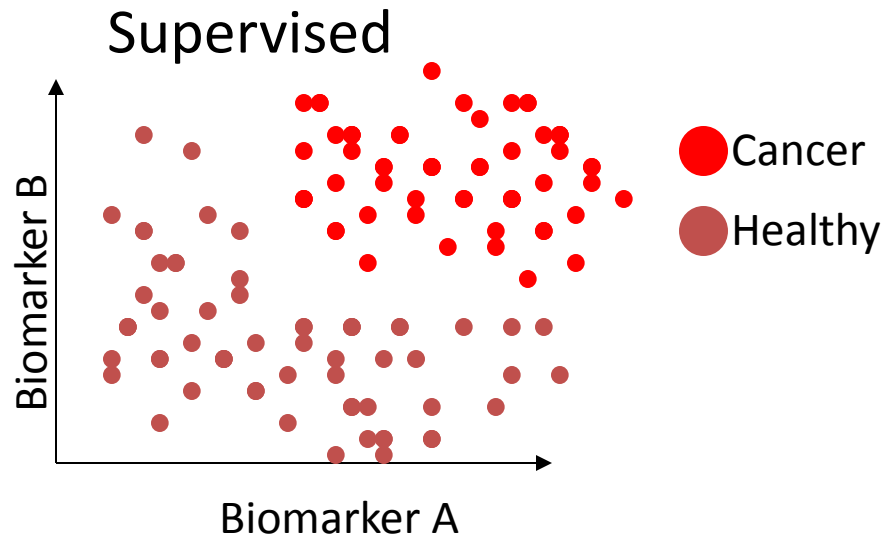
	Traditional Knowledge	Computational Knowledge
Advantages	<ul style="list-style-type: none">• Well established, easily understood• Incorporates clinical intuition• Often easily applied• In the case of well-defined studies, includes high quality evidence	<ul style="list-style-type: none">• Can learn from large datasets and potentially identify very subtle patterns• Often comparatively objective• Less expensive than RCTs• Provides opportunities for personalized medicine
Limitations	<ul style="list-style-type: none">• Can only incorporate high quality evidence for limited circumstances• Evidence/ guideline basis for individualizing care often limited• Can only “learn” from a limited dataset → insufficient for complex patterns	<ul style="list-style-type: none">• May be difficult to understand and apply• Limited by overfitting

Opinion: Need to Integrate both Types of Knowledge

Computational Knowledge Discovery: Machine Learning



Computational Derivation of Knowledge: Supervised Vs. Unsupervised Machine Learning



Overfitting: A Key Consideration

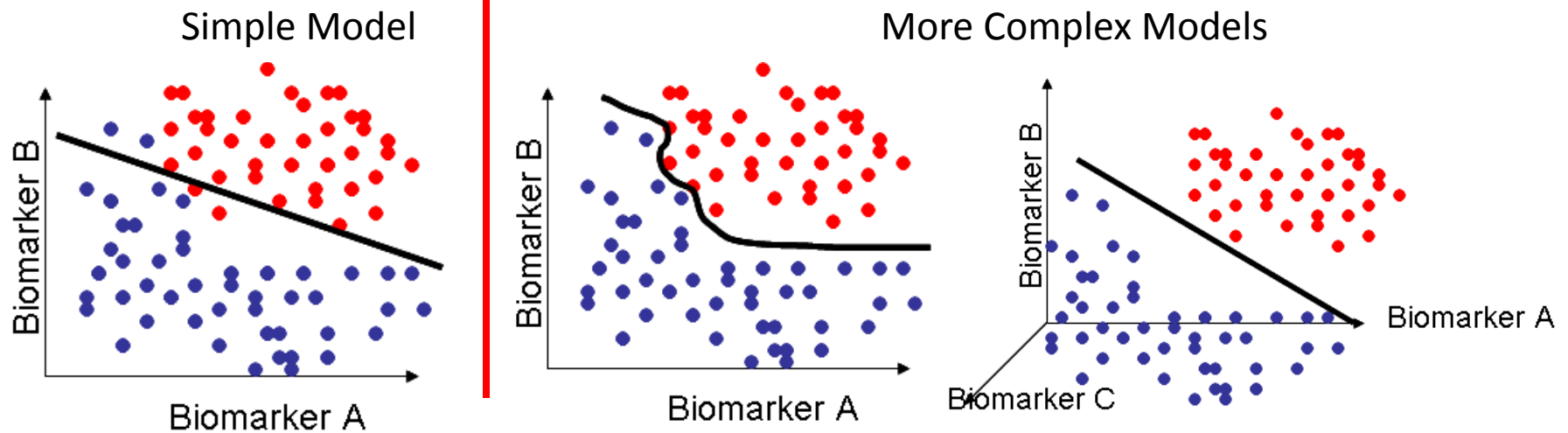
- Avoiding overfitting is a key challenge
- An **overfit** model:
 - Fits to random patterns in the training data that do not generalize
 - Mistakes “noise” for a real pattern
 - Performs better in classifying the training data than independent test data

Overfitting and the Red Sox

- Suppose I'm a superstitious Boston sports fan and want to know what "causes" the Red Sox to win
- I look at 20 games of which the Sox won 15
- I review my daily diary and find that on all 15 wins:
 - I had eggs for breakfast AND
 - Wore my lucky hat OR
 - Wore my lucky shirt (but not both)
- These conditions were not met on the for the losses
- I think I've found a pattern
- **Should I bet my savings?**

Computational Derivation of Knowledge: Overfitting, An Important Pitfall

- Overfitting tends to
 - Increase with model complexity AND
 - Decrease with the size of the training data set

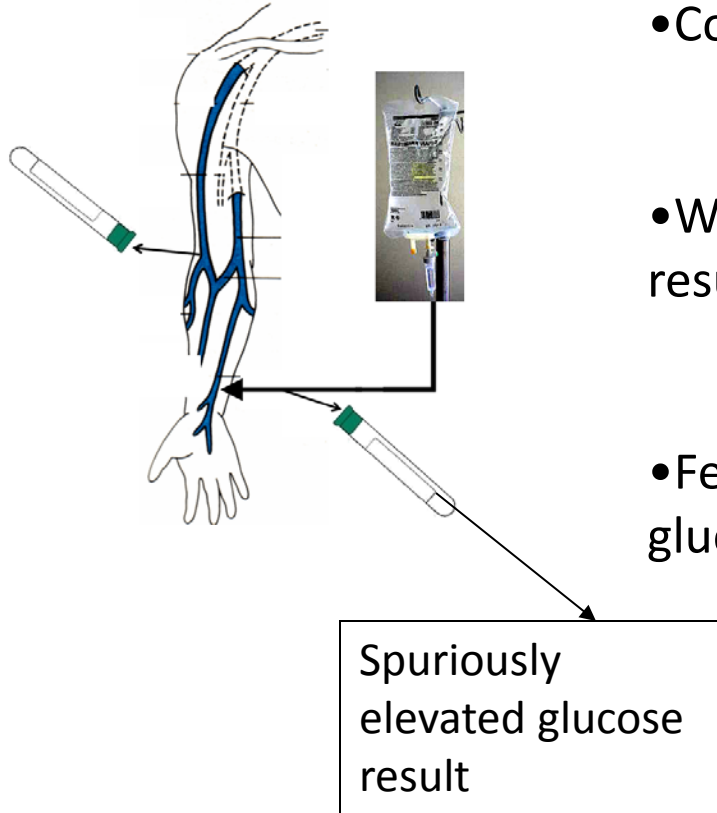


Computational Derivation of Knowledge:

Machine Learning, Sample Methods

- Linear methods
 - Ordinary least squares regression
 - Logistic regression
 - Perceptrons
- Decision trees
 - Recursive partitioning trees
 - Ensemble methods (random forest)
- Artificial neural networks
- Support vector machines
- K-means clustering

Computational Derivation of Knowledge: Example Spurious Glucose Identification



- Commonly problem at many hospitals
- We were seeing spurious critically elevated glucose results about once per day
- Fewer than 10% of these spuriously elevated glucoses were being identified

Goal: Develop an Algorithmic Protocol to Distinguish Spurious from Real Critically Elevated Glucose Values

Computational Derivation of Knowledge: Example Spurious Glucose Identification, Methods

Annotated Training Data (glucose >500 mg/dl)				
Patient	Glucose	Na	Additional Predictors (K, CO ₂ , AG, etc.)	Gold Standard Annotation
A	670	119	...	Spurious
B	710	141	...	Real
C	721	138	...	Real
...



Supervised
Machine Learning
(Recursive
partitioning
decision trees)



Test data or Un-annotated patient data	
Patient	Predictors (glucose, Na, K, AG, etc.)
X	...



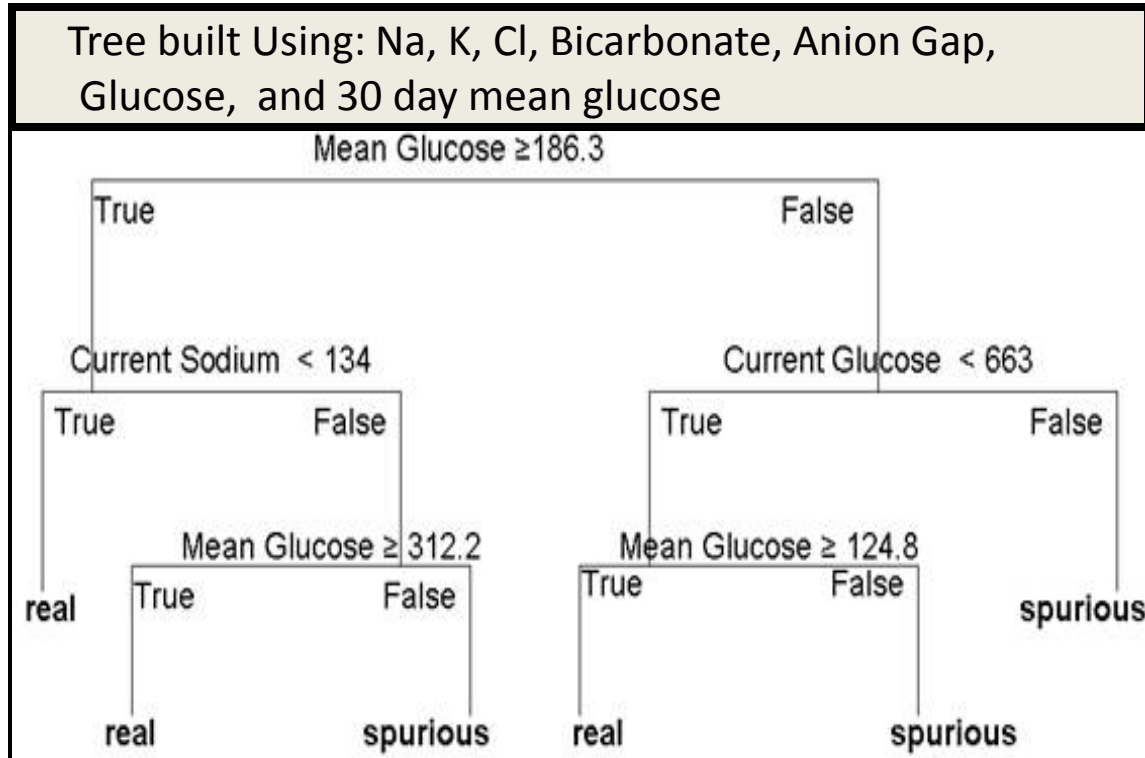
Decision Tree



Prediction as to whether
result is real or spurious

Computational Derivation of Knowledge: Example

Spurious Glucose Identification, Results



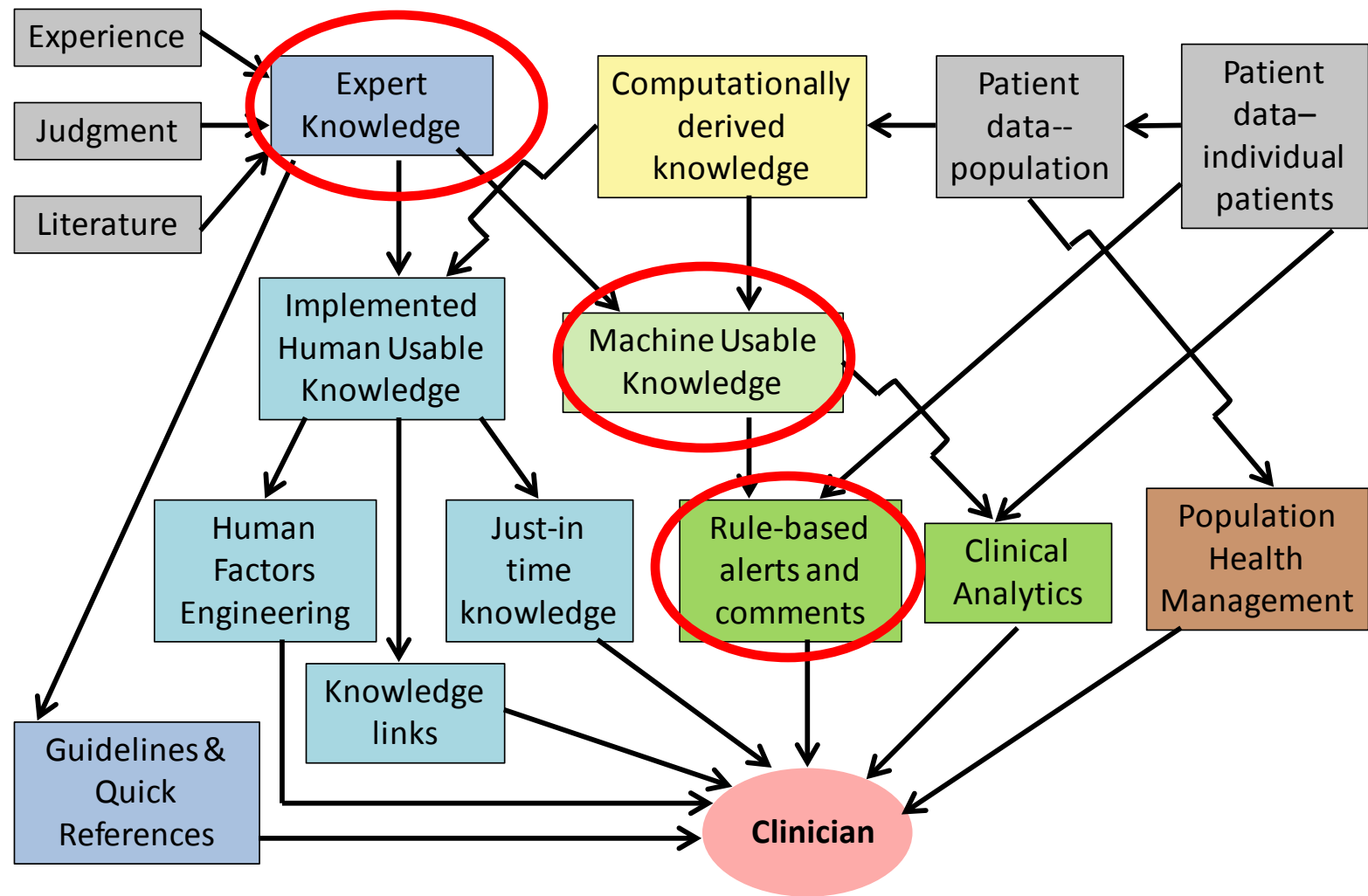
Implementation Discussed Later

	Training Data	Test Data
Spurious Correctly Classified	57	32
Total Spurious	61	37
Sensitivity (95% CI)	93% (84-98%)	86% (72-95%)
Real Correctly Classified	68	5
Total Real	77	6
Specificity (95% CI)	88% (79-9%)	83% (42-99%)

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Transforming Expert Knowledge into Rule-based Alerts and Comments



Traditional Approaches

Evolving Approaches

Transforming Expert Knowledge into Rule-based Alerts and Comments

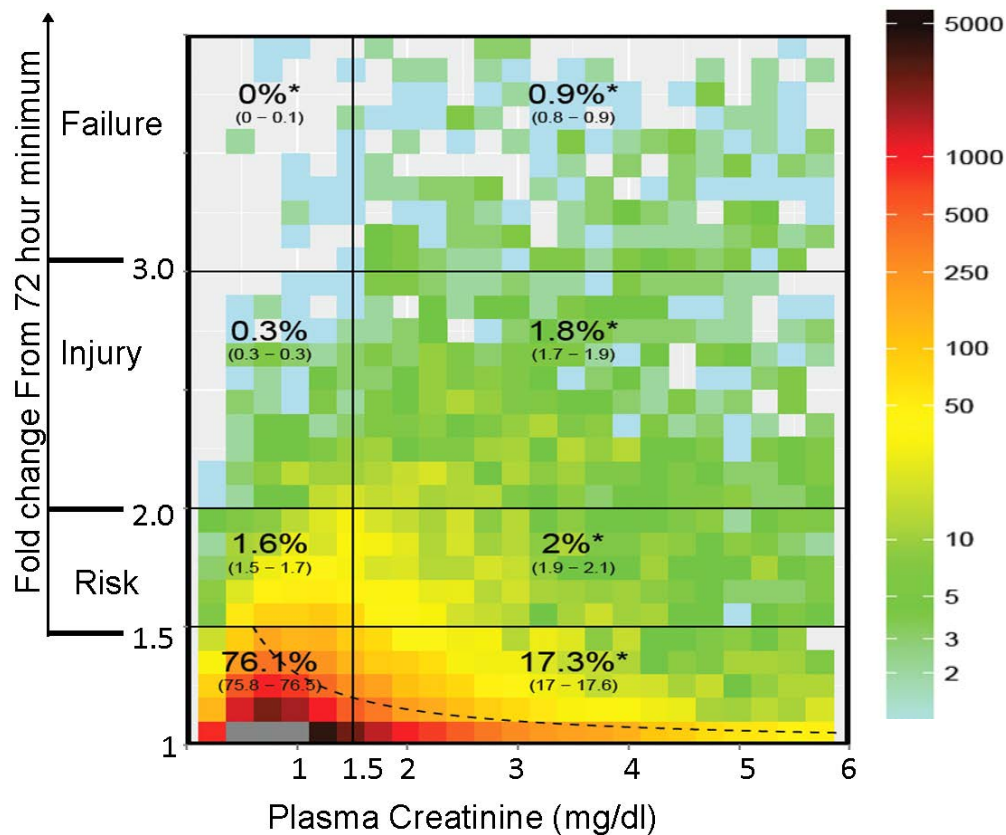
- Knowledge acquisition is only part of the battle
- Implementation of decision support can be a key challenge
- Many health information systems offer opportunities for rule-based alerts, but may still be limited in what rules can be implemented
- Building alerts can be resource intensive

Transforming Expert Knowledge into Rule-based Alerts

Example, Acute Kidney Injury Detection: Background

Acute Kidney Injury (AKI) and Creatinine Reporting Challenges

- AKI can be diagnosed based on trends in creatinine
- However, in standard reporting creatinine values are only flagged if outside of the reference range
- Values indicative of AKI often remain within the reference range
- Clinicians often quickly scan lab values for flagged result outside of reference range



AJCP (2015) 143:42:49

Transforming Expert Knowledge into Rule-based Alerts

Example, Acute Kidney Injury Detection: Approach

- Plan: Develop a flag within our LIS
- Challenge: LIS not well equipped for this type of problem
- Example, no function to calculate minimum creatinine over a time period
- Solution: Use “**tracked minimum**”, which can be calculated
- ?: What time period to use for baseline: 24hrs, 48hrs, 7 days
- **Final Decision: Flag creatinine values increased significantly from 72 hr tracked minimum**

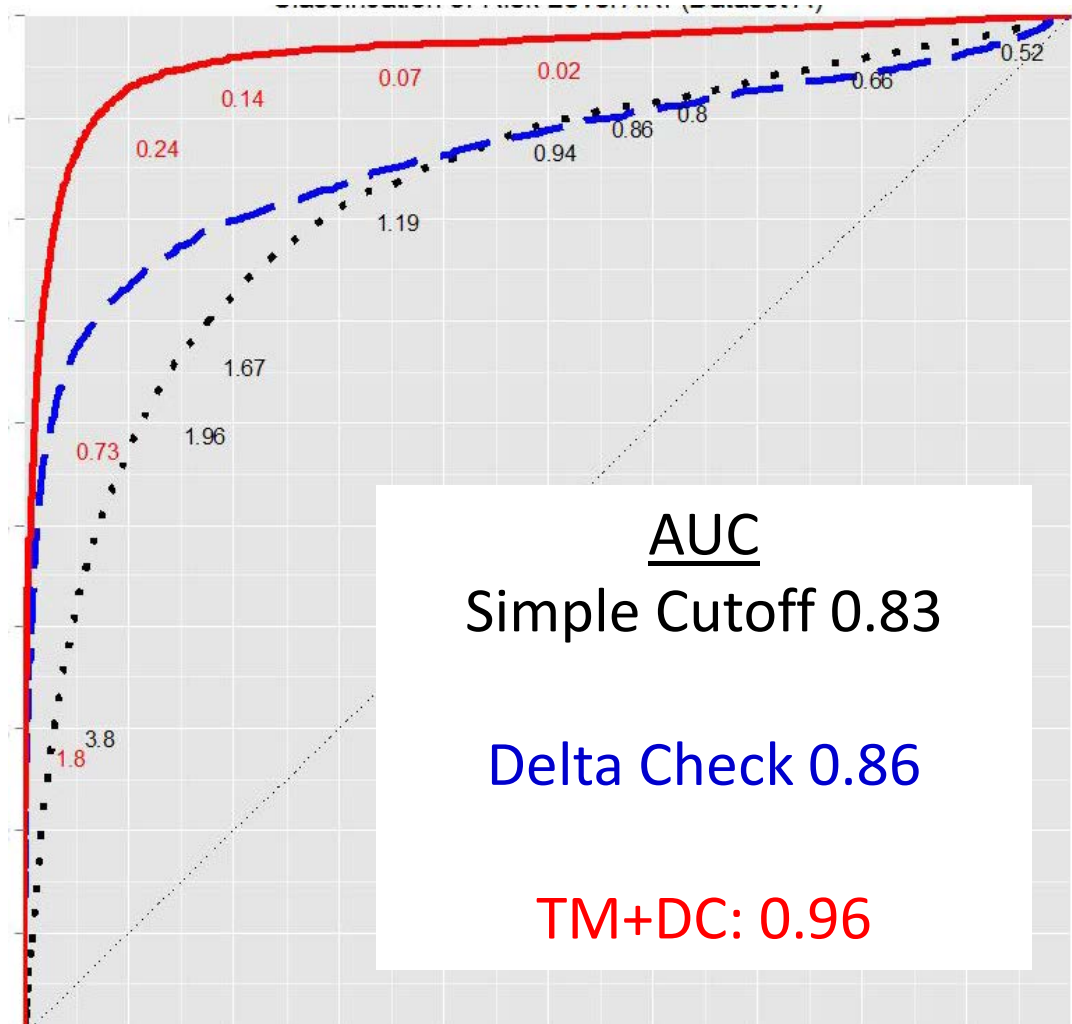
Transforming Expert Knowledge into Rule-based Alerts

Example, Acute Kidney Injury Detection: Tracked Minimums

The tracked minimum is updated to the current creatinine result when either

- i. The new creatinine result is less than or equal to the prior tracked minimum OR
- ii. When the prior tracked minimum “expires” (has not been updated in 72 hours)



Otherwise, each new tracked minimum is just the prior tracked minimum



Transforming Expert Knowledge into Rule-based Alerts

Example, Acute Kidney Injury Detection: Solution

	T=70	T=46 hrs	T=0
CRE	1.49(T)	1.35	1.11
EGFR	see detail	40(T)	50(T)

 Plasma Creatinine	1.49 INCREASED
 eGFR	<p>Patient creatinine values are increasing. The calculated GFR (shown below) may thus overestimate the true GFR and should not be used to guide medication dosing. Please also multiply the result shown below by 1.21 if the patient is African-American.</p> <p>Result = 35 mL/min/1.73m²</p>

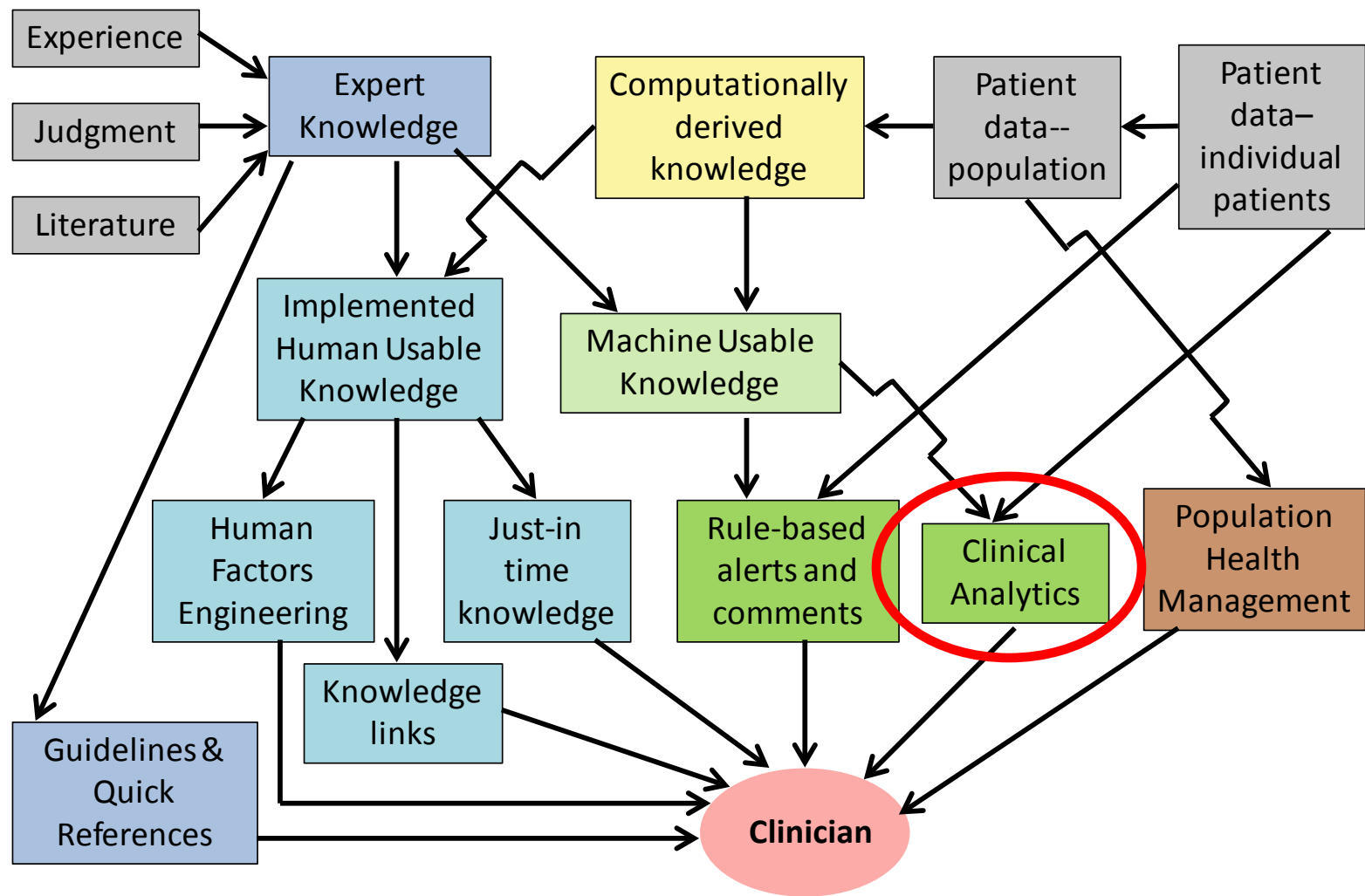
Transforming Expert Knowledge into Rule-based Alerts

A Call for a Better System

- The AKI flag required a large investment of resources in terms of MD and IT time
- We need a more streamlined approach

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Present

Computational
Pathology

Processed

Raw
Observations

Atomic
data

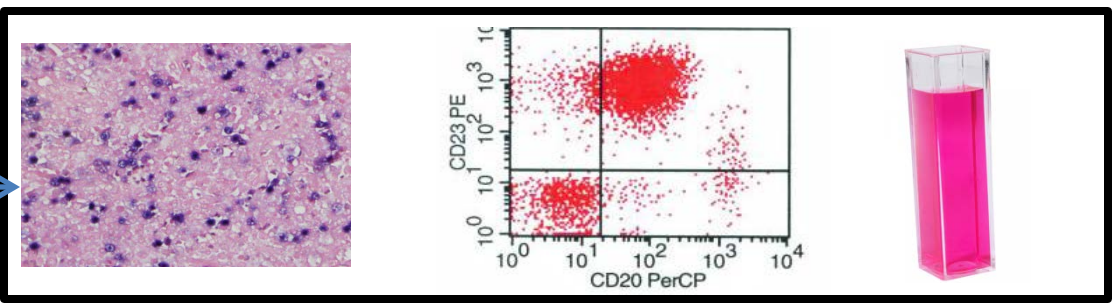
Interpretive
comments

Diagnoses

Integrative
Information

Predictive
Information

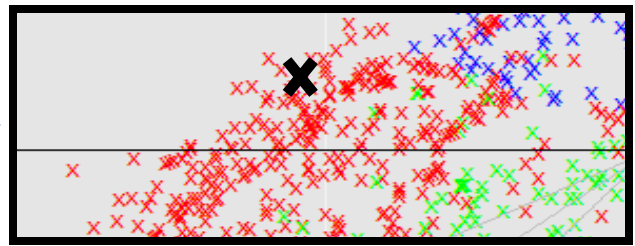
Raw



127	101	19	103
3.8	21	1.86	

“Patient creatinine values are increasing...”

“EBV-positive immunoblastic reaction,
consistent with infectious mononucleosis”

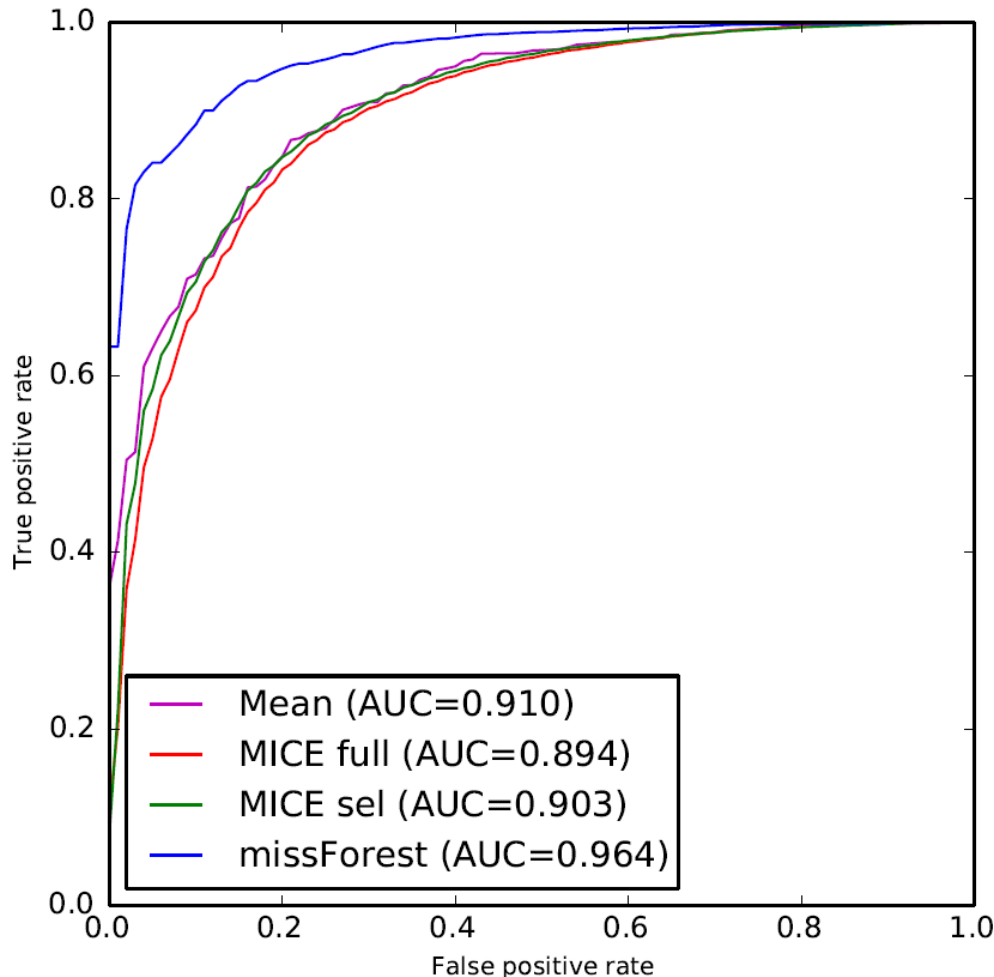


“Given this patient’s test results and clinical data,
administration of vancomycin will improve odds
of survival from 37% to 87%.”

Computational Pathology: Example, Ferritin Result Prediction

Can we predict ferritin results using patient demographics and other current laboratory test data?

Test Data



Findings

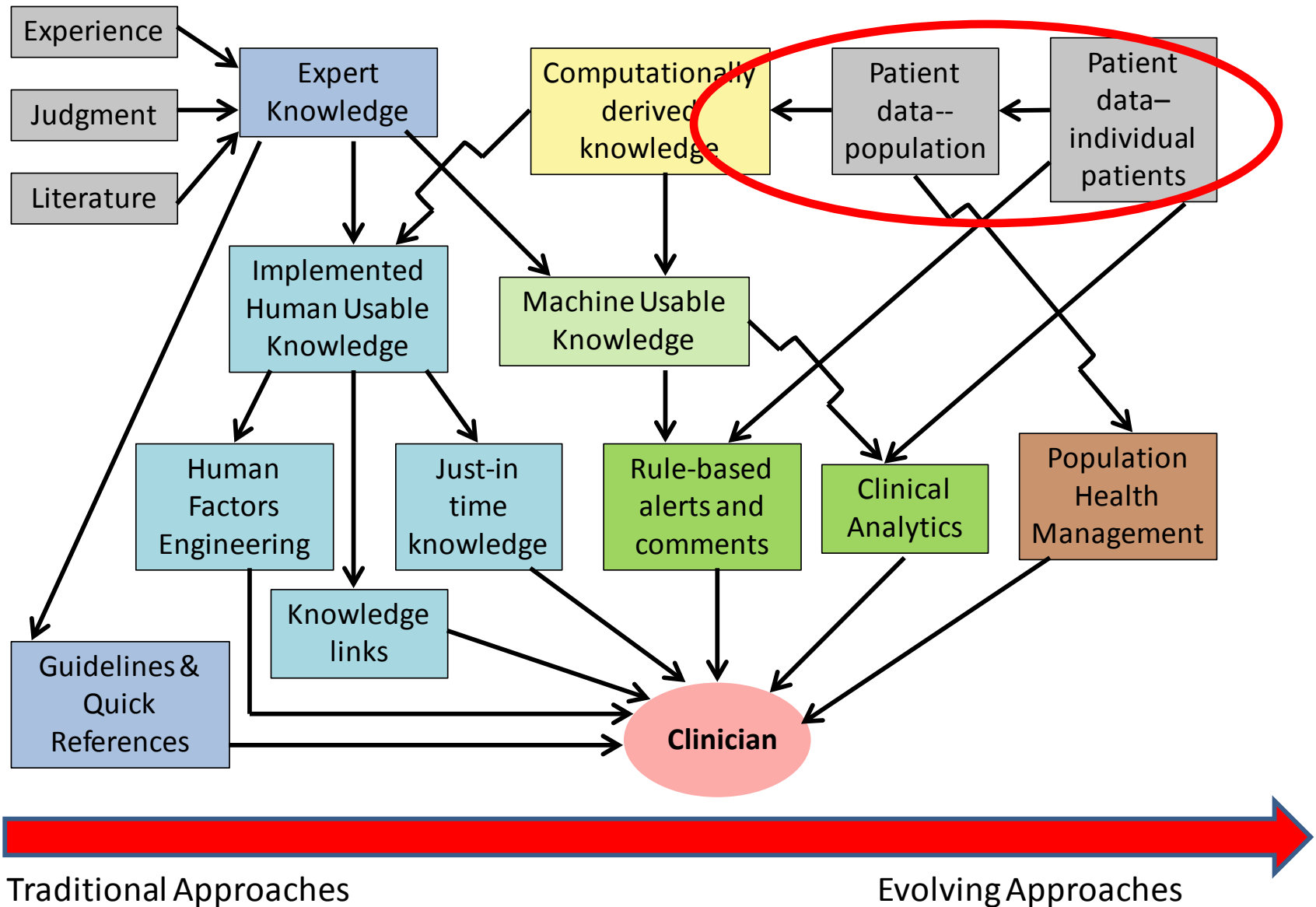
- Predicted ferritin classifications were highly accurate
- Predicted ferritin values were moderately accurate
- Predicted ferritin may have diagnostic value
- Suggests applications to decision support

Selected Challenges

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Challenge: Clinical Data Quality



Challenge: Clinical Data Quality

Patient	Family History
1	DM (mother); heart problems, unknown nature (father)
2	No endocrine problems, prostate CA—brother, colon cancer, mom
...	
100,000	noncontributory

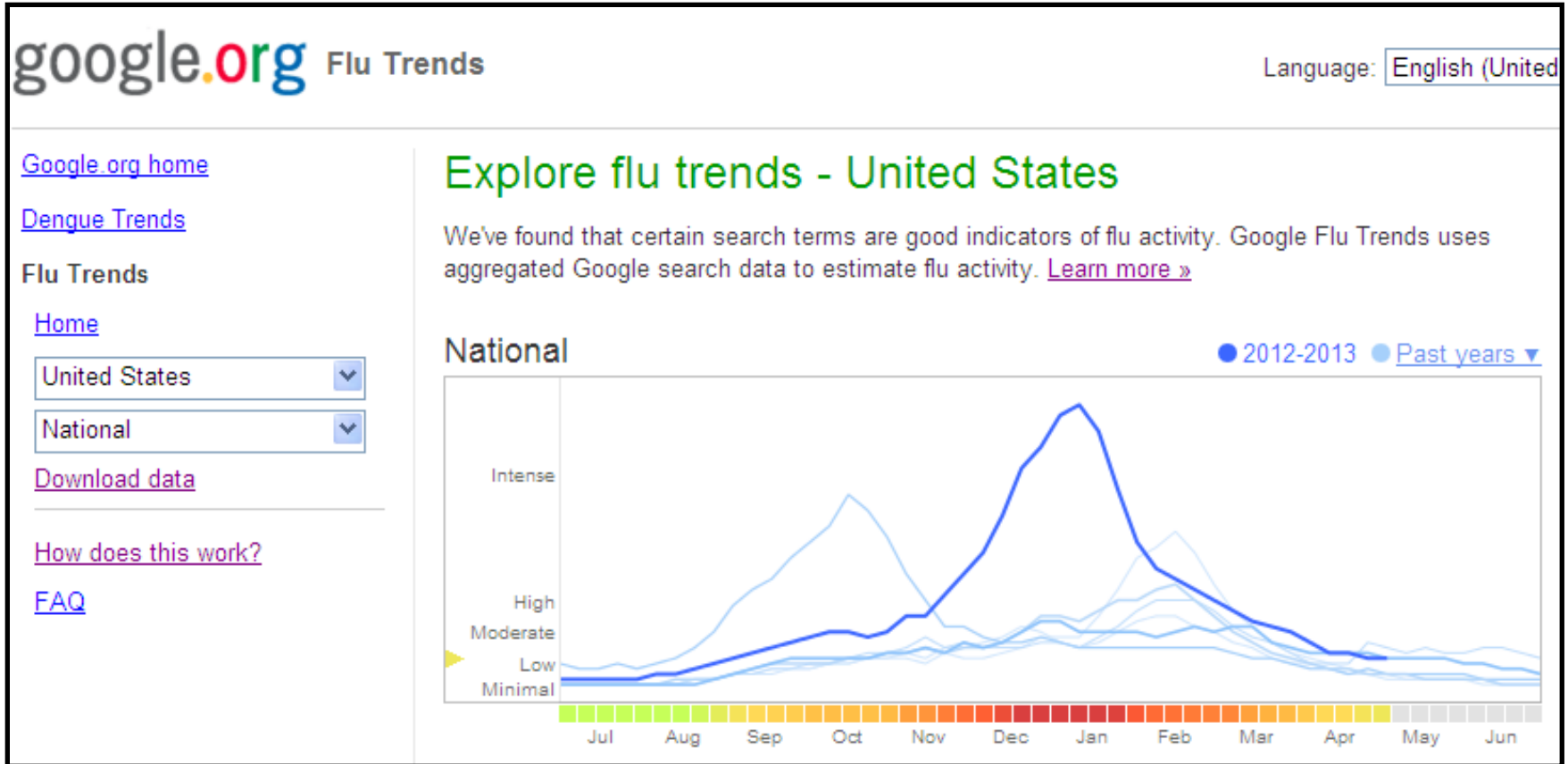
VS.

Patient	Family History of DCM
1	Yes
2	No
3	Yes
4	No

- Data quality may be limited by accuracy, completeness or structure
- Tradeoff between manual curation and data size
- Data structure may limit model complexity and reduce overfitting

Challenge: Clinical Data Quality: Is Big Data the Answer?

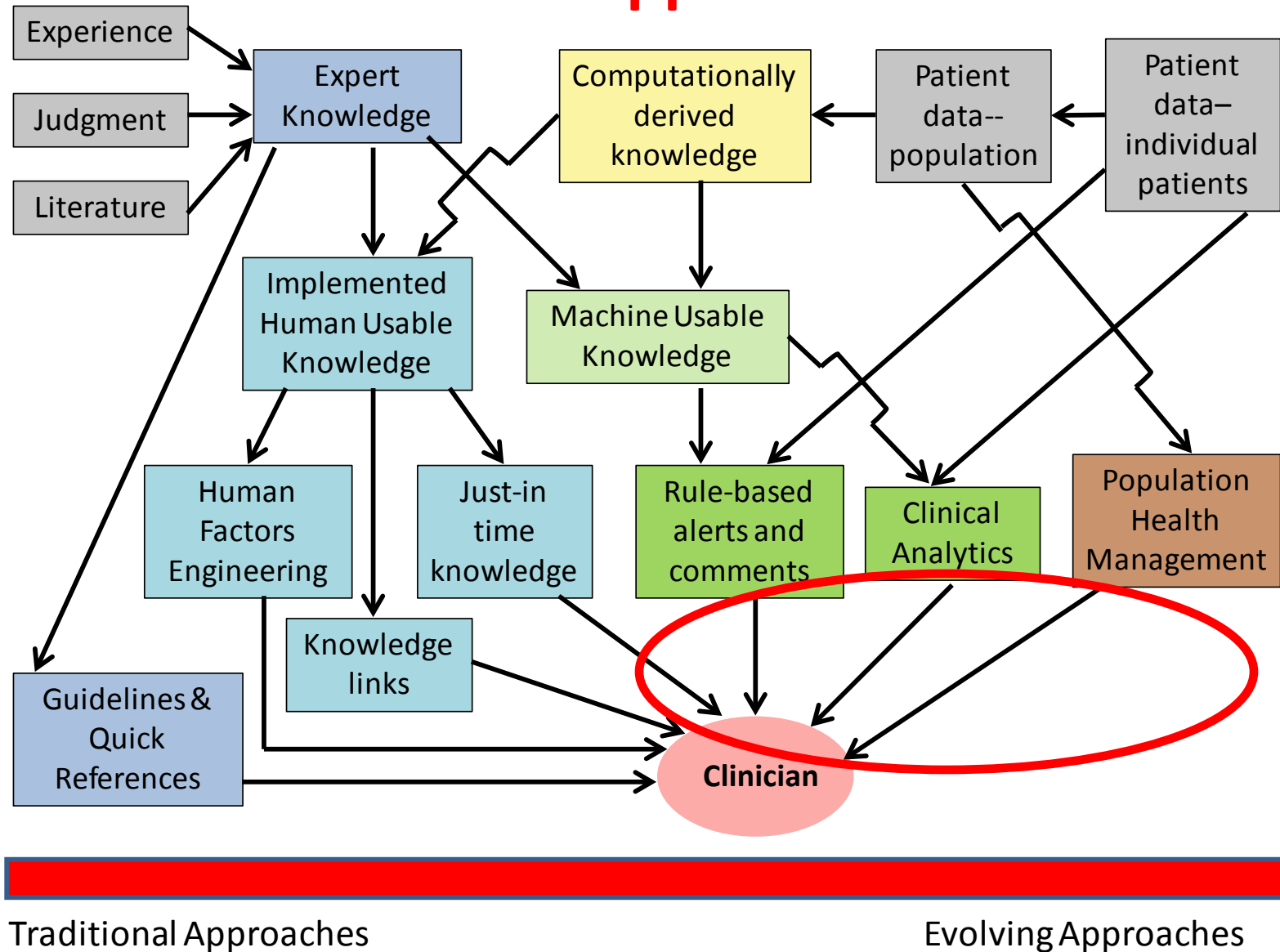
Can data quantify sometimes substitute for data quality?



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 - c. Non-technical infrastructure

Challenge: Implementation of Evolving Decision Support



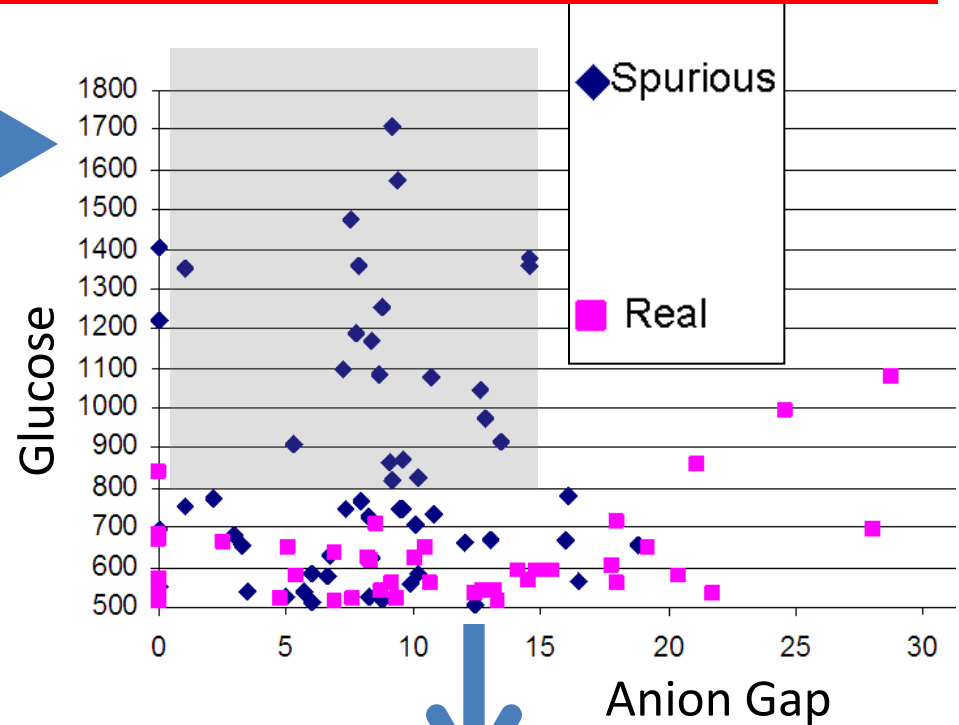
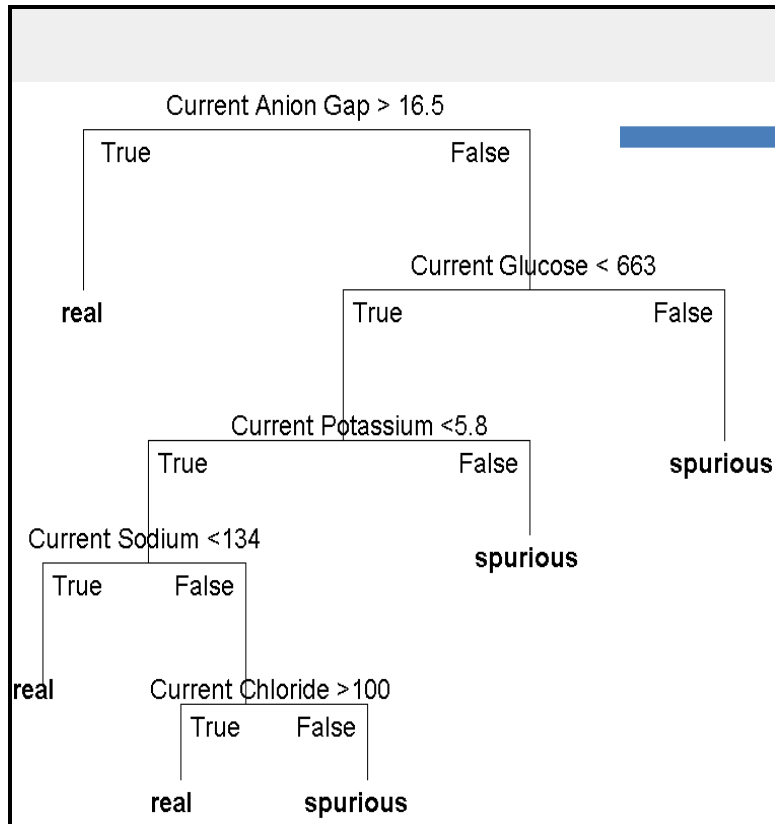
Implementation Challenge

- Even straightforward rule-based alerts can be challenging to implement (e.g. AKI alert)
- But what about decision support based on machine learning algorithm— is it hopeless?

Implementation Challenge: Current Approaches

- Implementation is difficult
- Manual methods → flowcharts with e-mails, etc.
- LIS calculation functionality
- EHR alerts
- Transform statistically-based approaches into rule based one (trees do so automatically)

Implementation Challenge: Current Approaches Example, Spurious Glucose



Glucose > 800 with
anion gap ≤ 15
indicates spurious

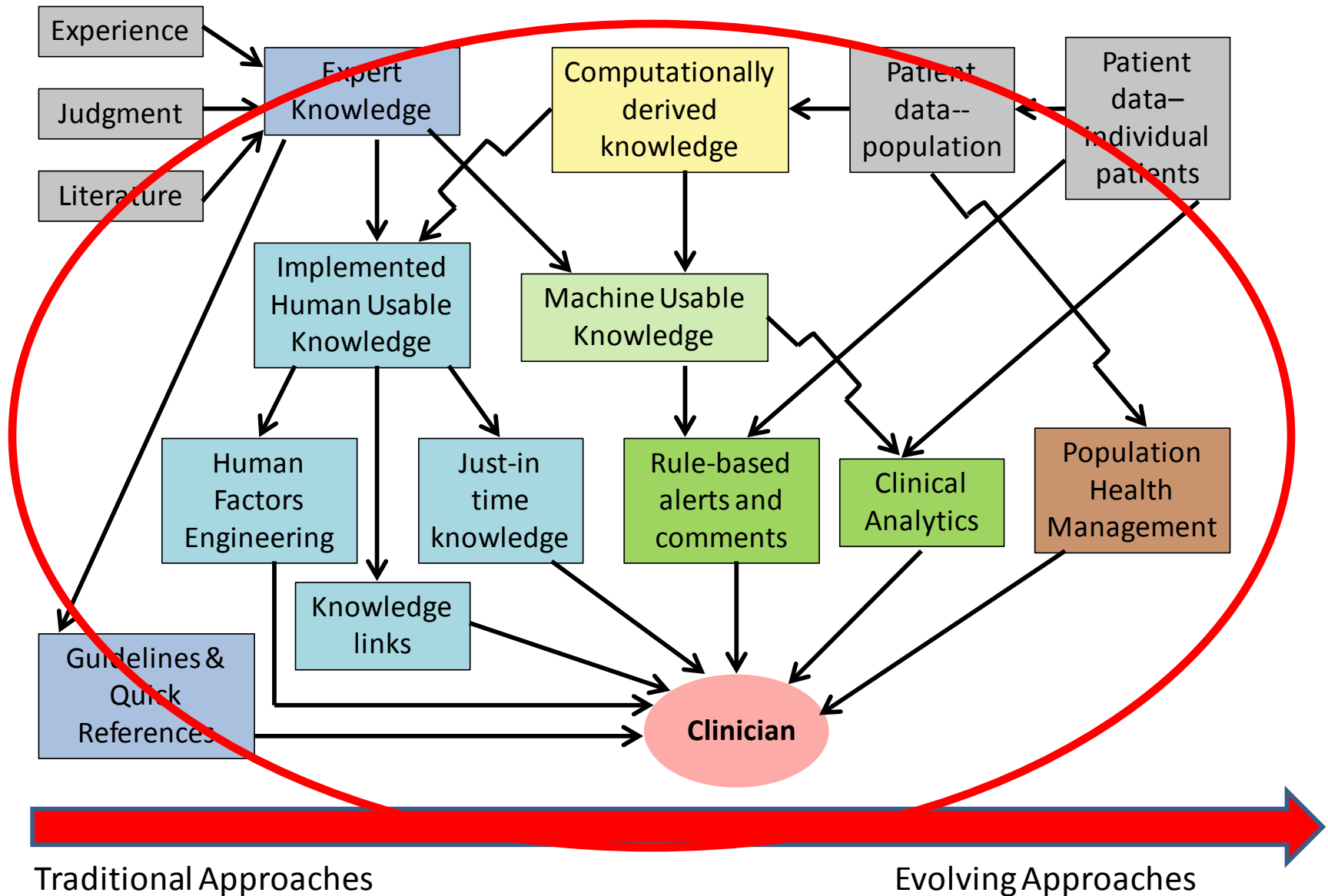
Implementation Challenge: Need for New Technology

- While some machine learning algorithms can be reduced to implementable rules, others cannot
- Highlights a need for new technologic solutions capable of implementing more complex algorithms

Overview

1. Why do we need decision support?
2. A high level view
3. Guidelines and quick refs
4. Just-in-time knowledge delivery
5. Human factors engineering
6. Computational knowledge derivation
7. Transforming expert knowledge into rule-based alerts
8. Computational Pathology—a 3 minute primer
9. **Selected Challenges**
 - a. Clinical data quality
 - b. Implementation—limits of current health IT infrastructure
 - c. **Non-technical infrastructure**

Challenge: Integrated Infrastructure



Integrated Infrastructure Challenge

- Technical
 - What systems will we have for development and implementation?
 - How will we get high quality data?
- Administrative
 - Who signs off?
 - How do we fund?
 - What type of validation is needed?
 - What are the regulatory requirements? (CLIA, FDA, others)
 - What are the risk management implications?
- Educational
 - How should evolving decision support be used to treat patients?
 - Can clinicians trust a black box?
 - If not, how can we make the box transparent?

Summary and Conclusions

- Clinical decision support takes many forms
- New opportunities are emerging to apply computational approaches to knowledge acquisition
- Decision support implementation remains a key challenge
- We need better integrated systems to couple knowledge discovery and curation with decision support implementation

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Spurious Glucose Identification

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Extra

