Clinical Decision Support

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MASSACHUSETTS GENERAL HOSPITAL
PATHOLOGY

PATHOLOGY
Advancing Diagnosis and Discovery

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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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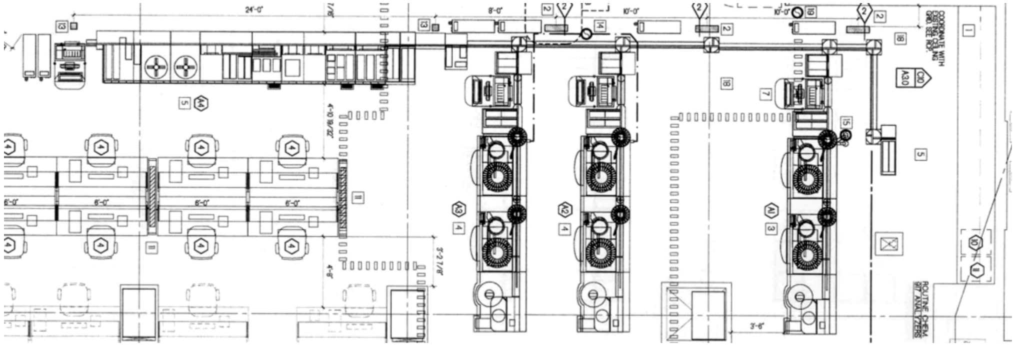
The Need for Informatics

- 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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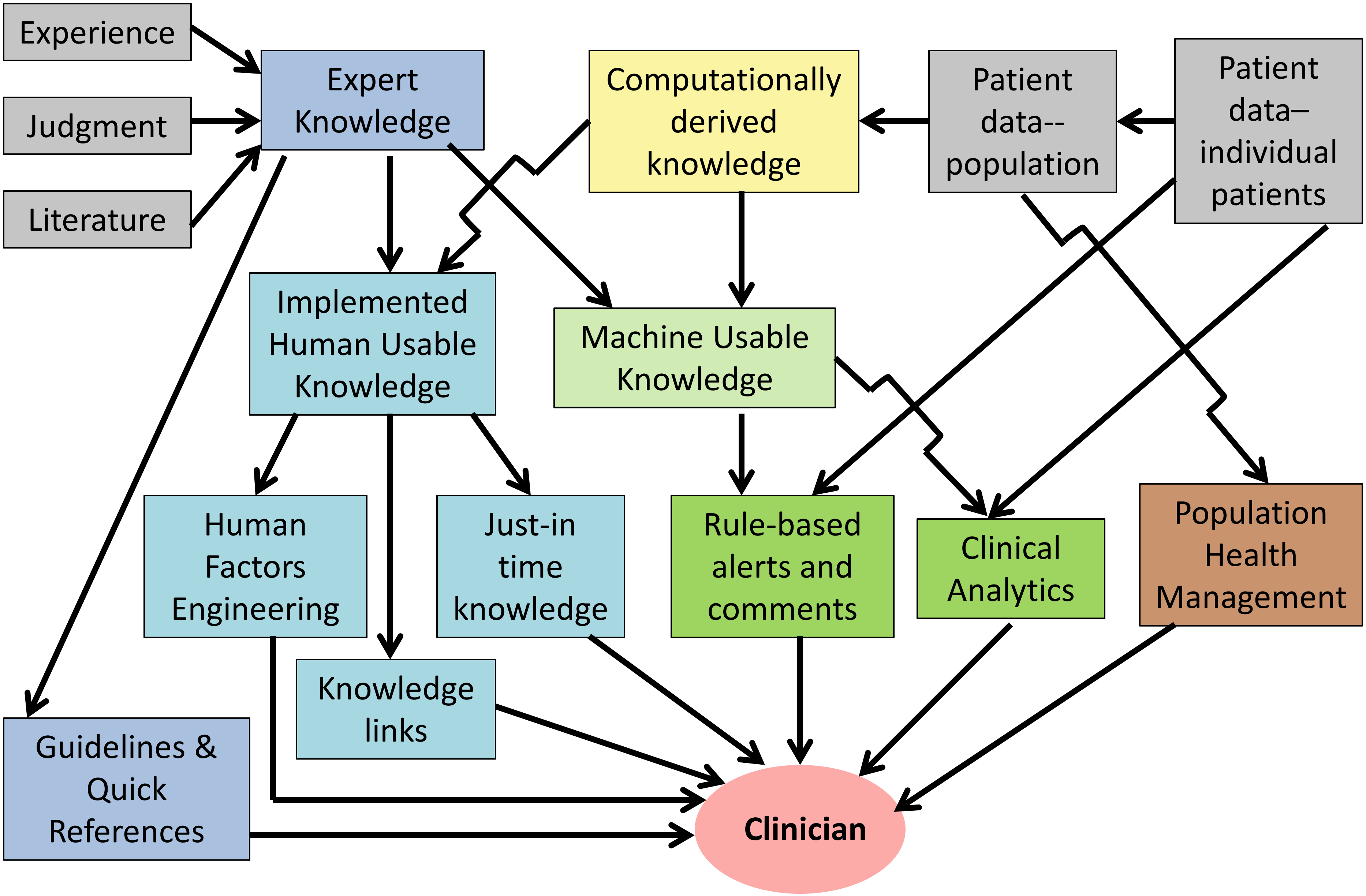
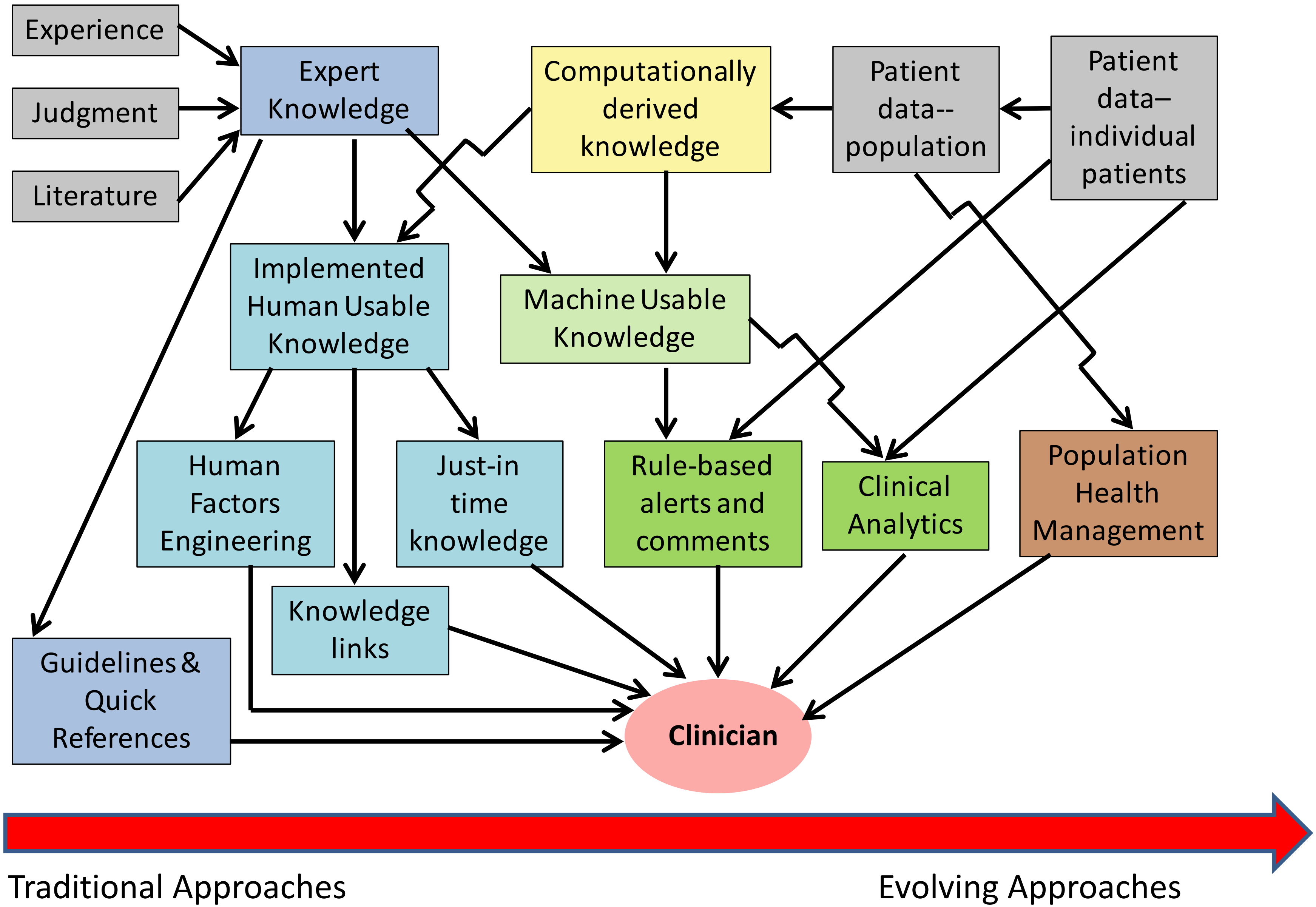
A High Level View of Clinical Decision Support



Evolution of Decision Support



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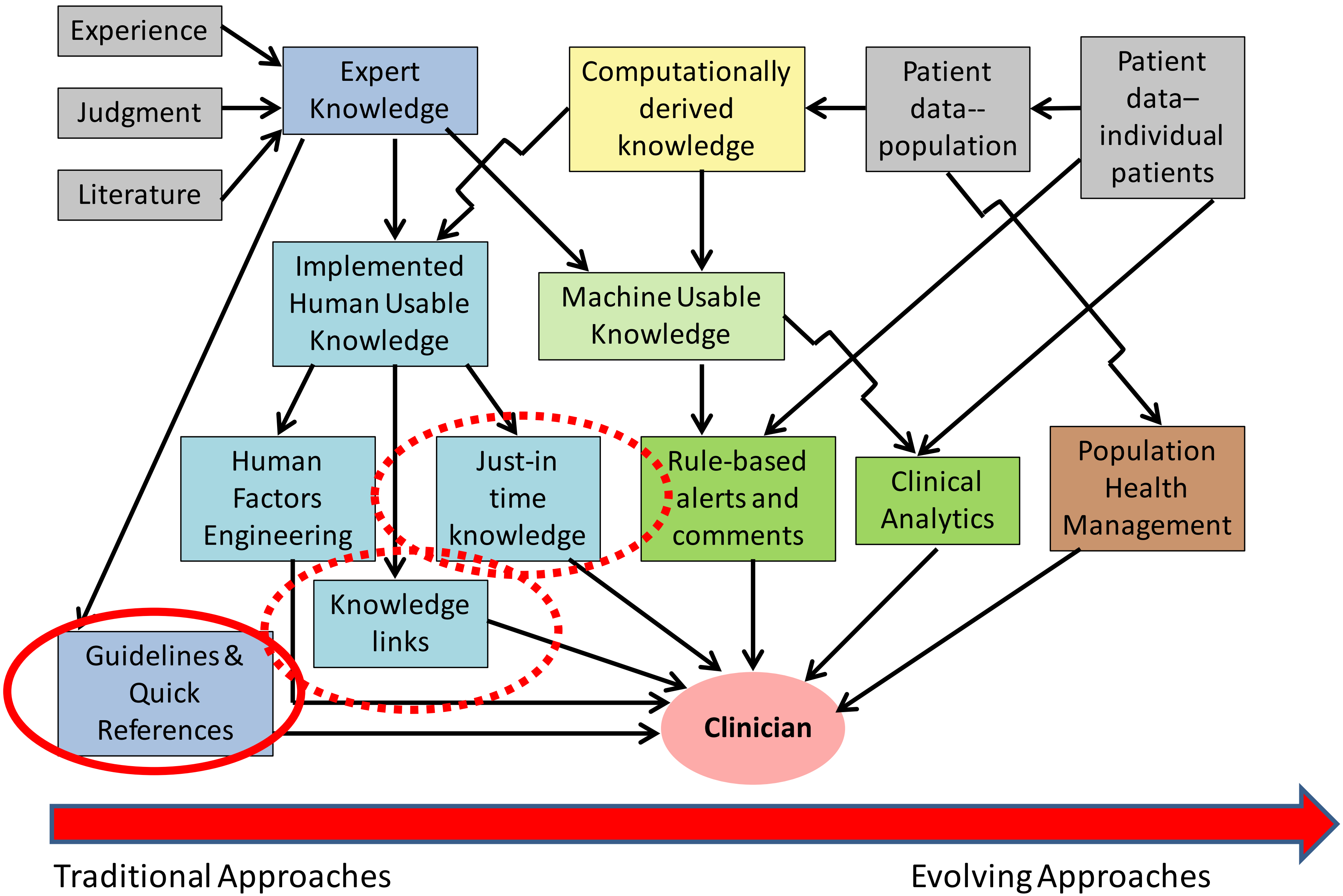

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Patient data–individual patients
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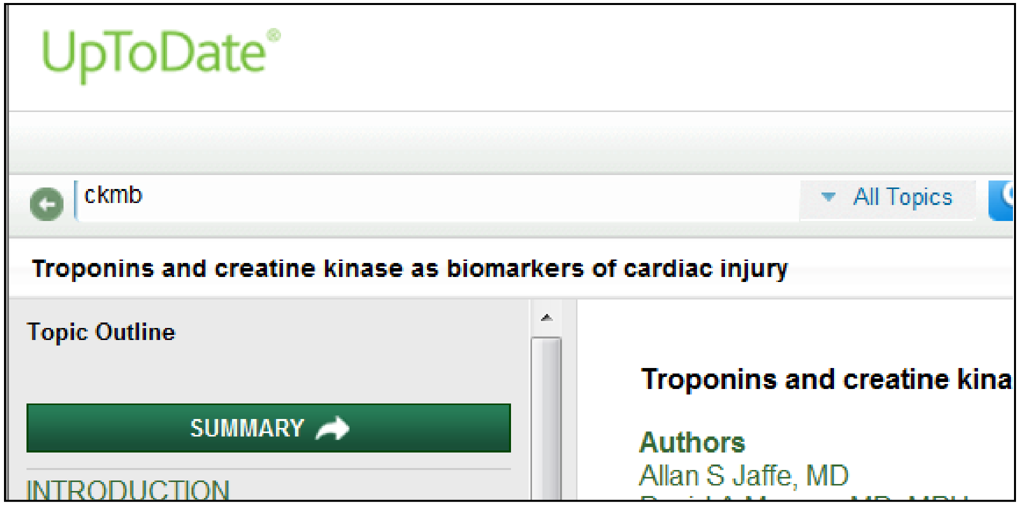
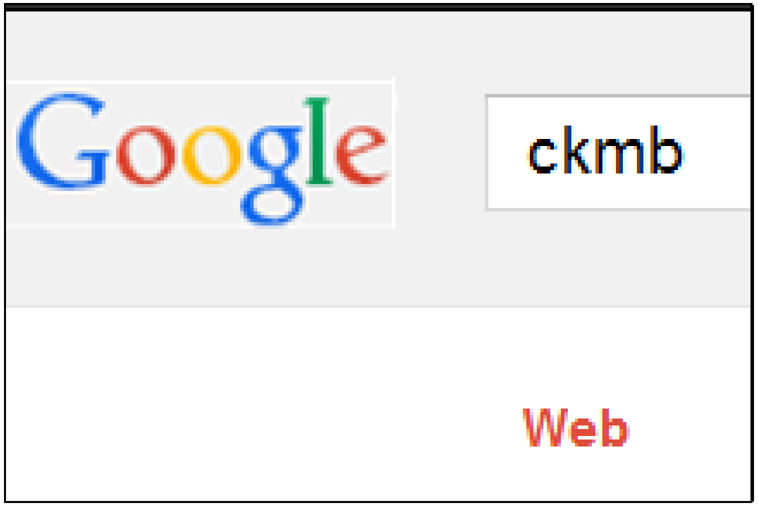
Clinical Analytics
Population Health Management
Knowledge links
Guidelines & Quick References
Clinician
Traditional Approaches
Evolving Approaches

Guidelines & Quick References

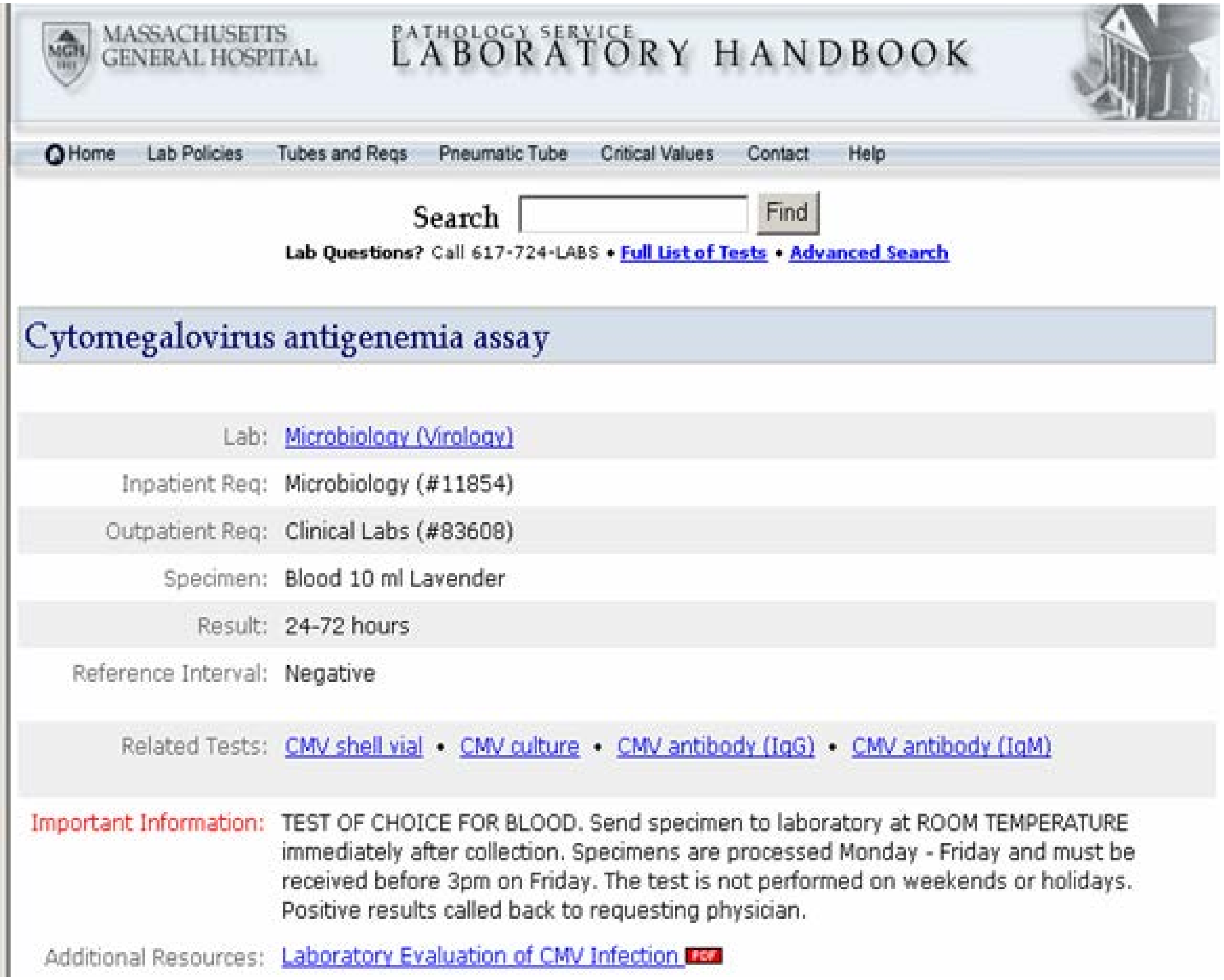


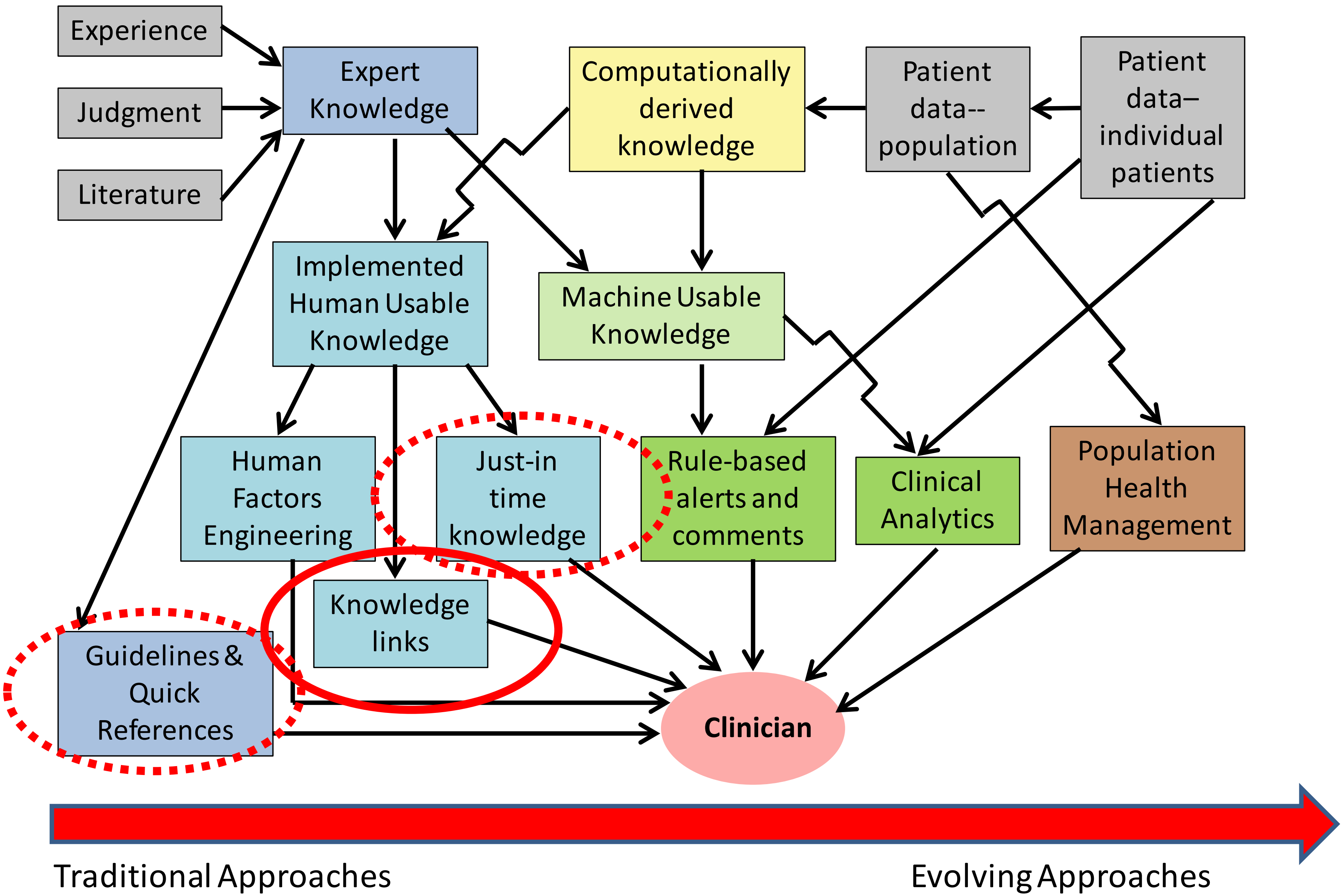


Key Question: What Information Can be Trusted?

Guidelines & Quick References: Laboratory Handbooks

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

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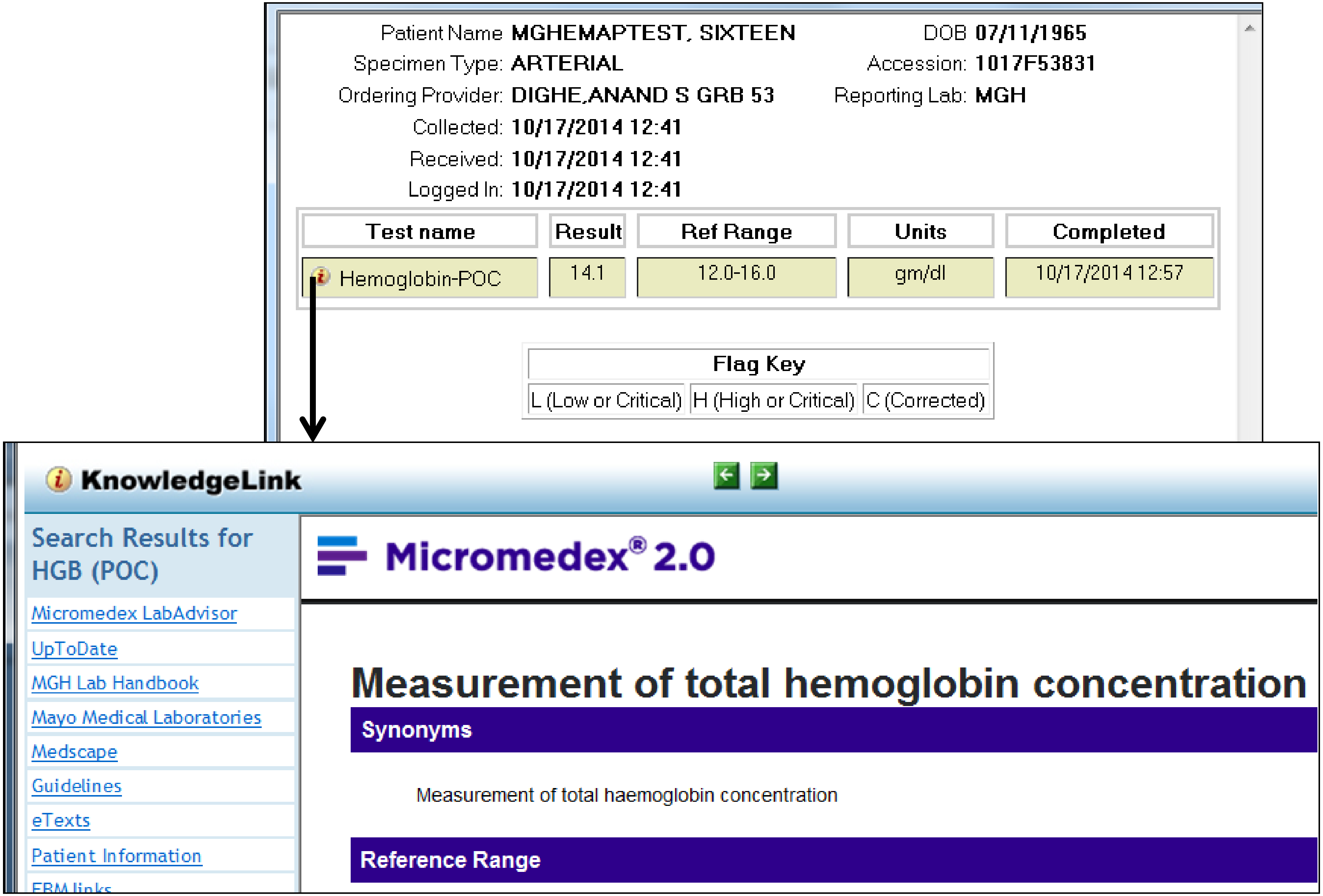

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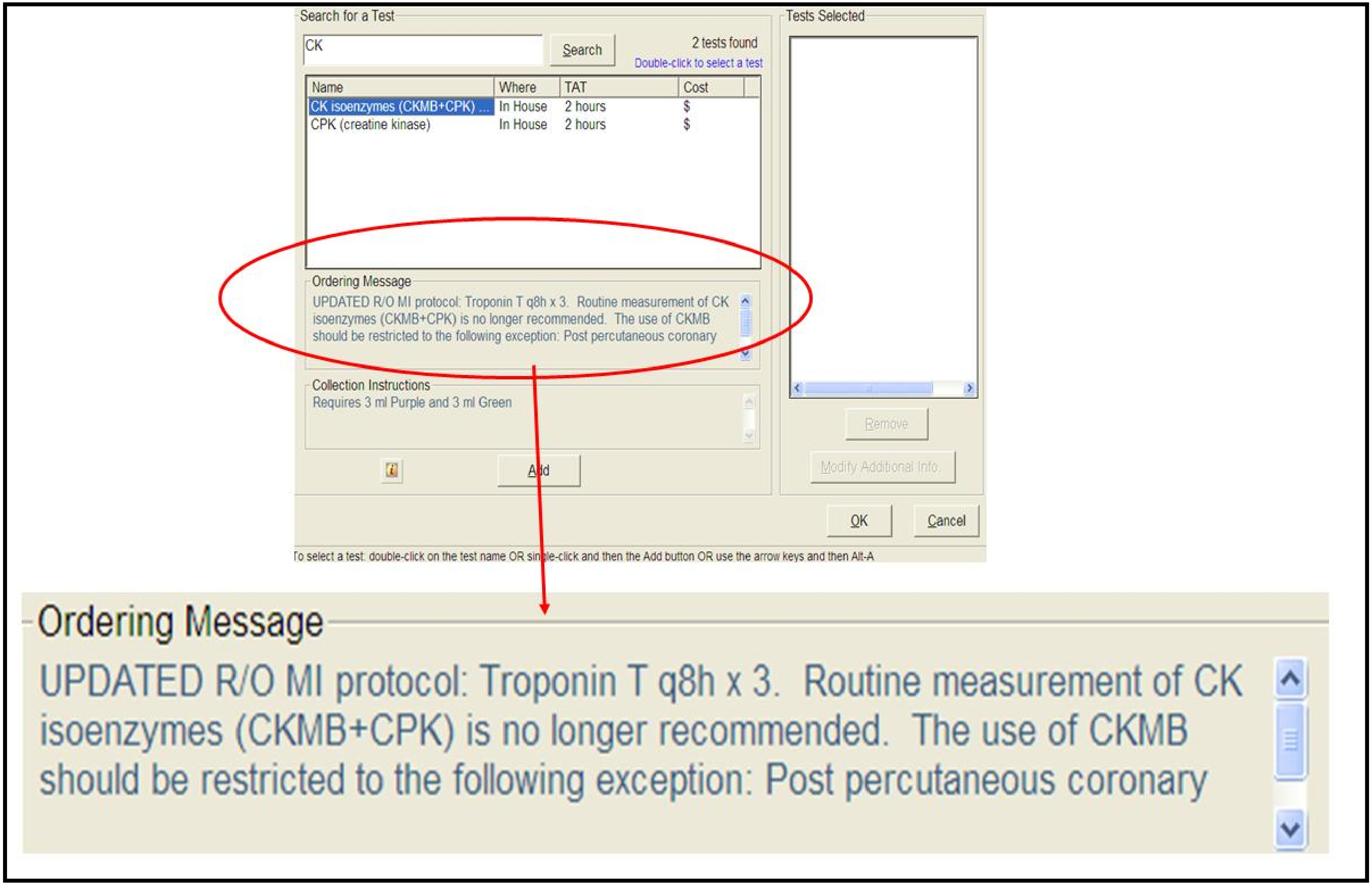
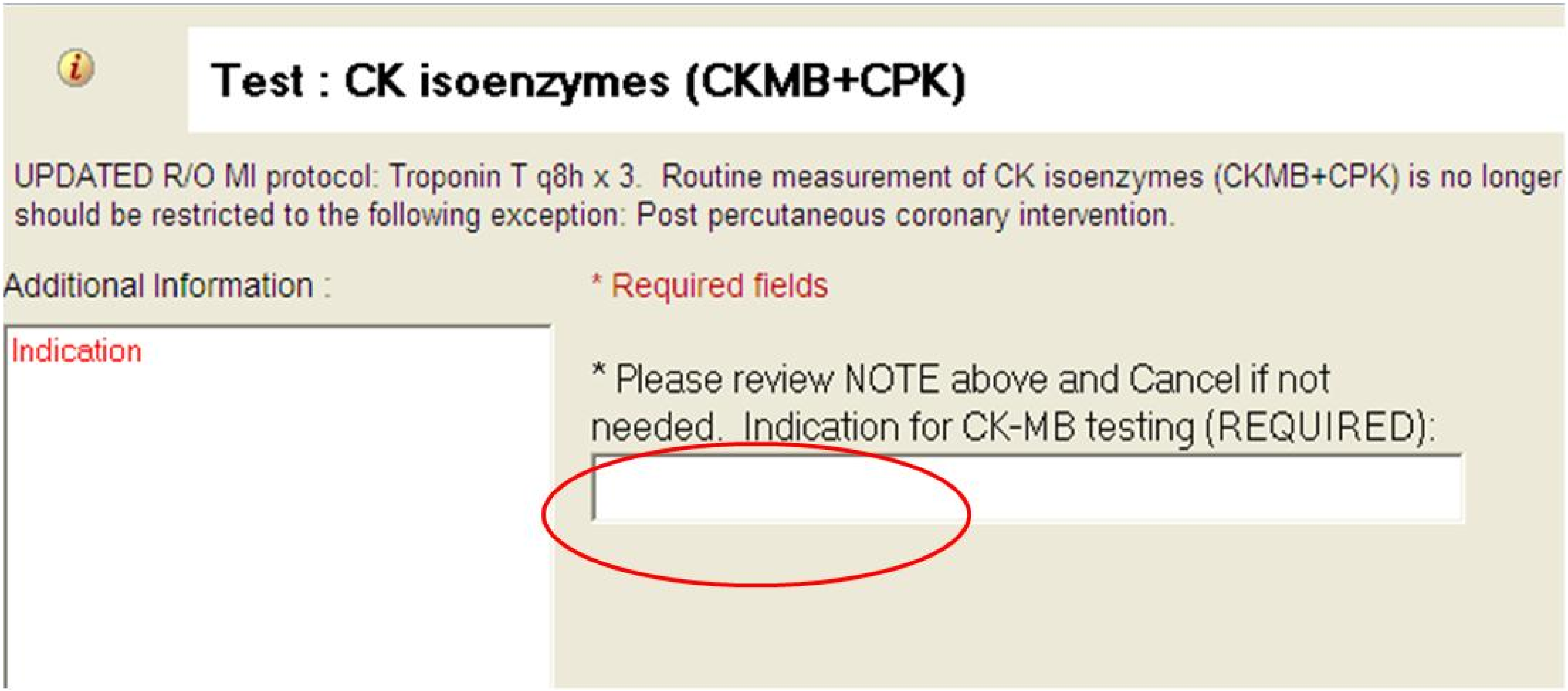
Just-in-time Knowledge Delivery: Non-Interruptive Alerts



Just-in-time Knowledge Delivery: Interruptive Alerts

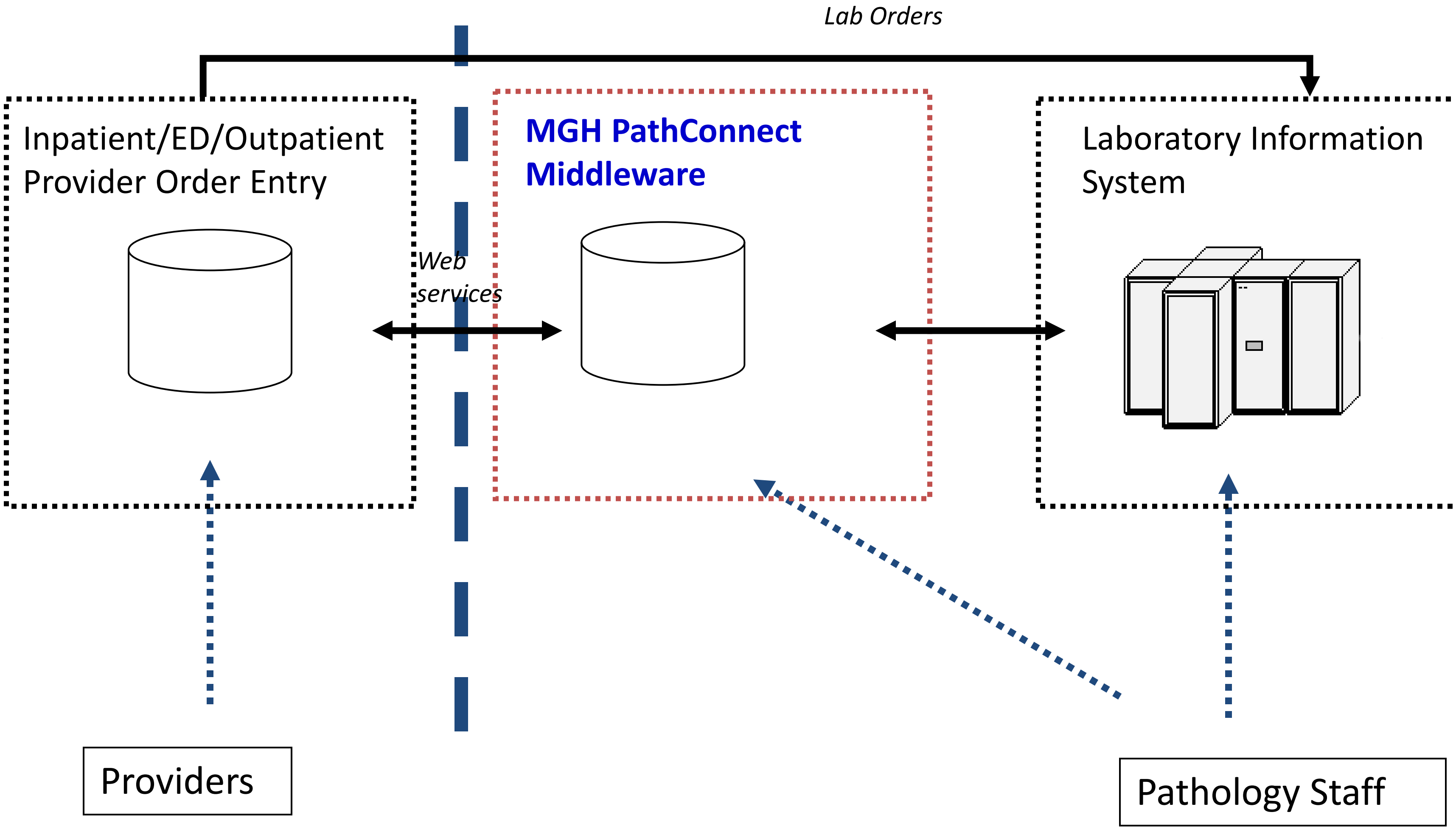


Just-in-time Knowledge Delivery: Knowledge Management Systems, Pathology Portal

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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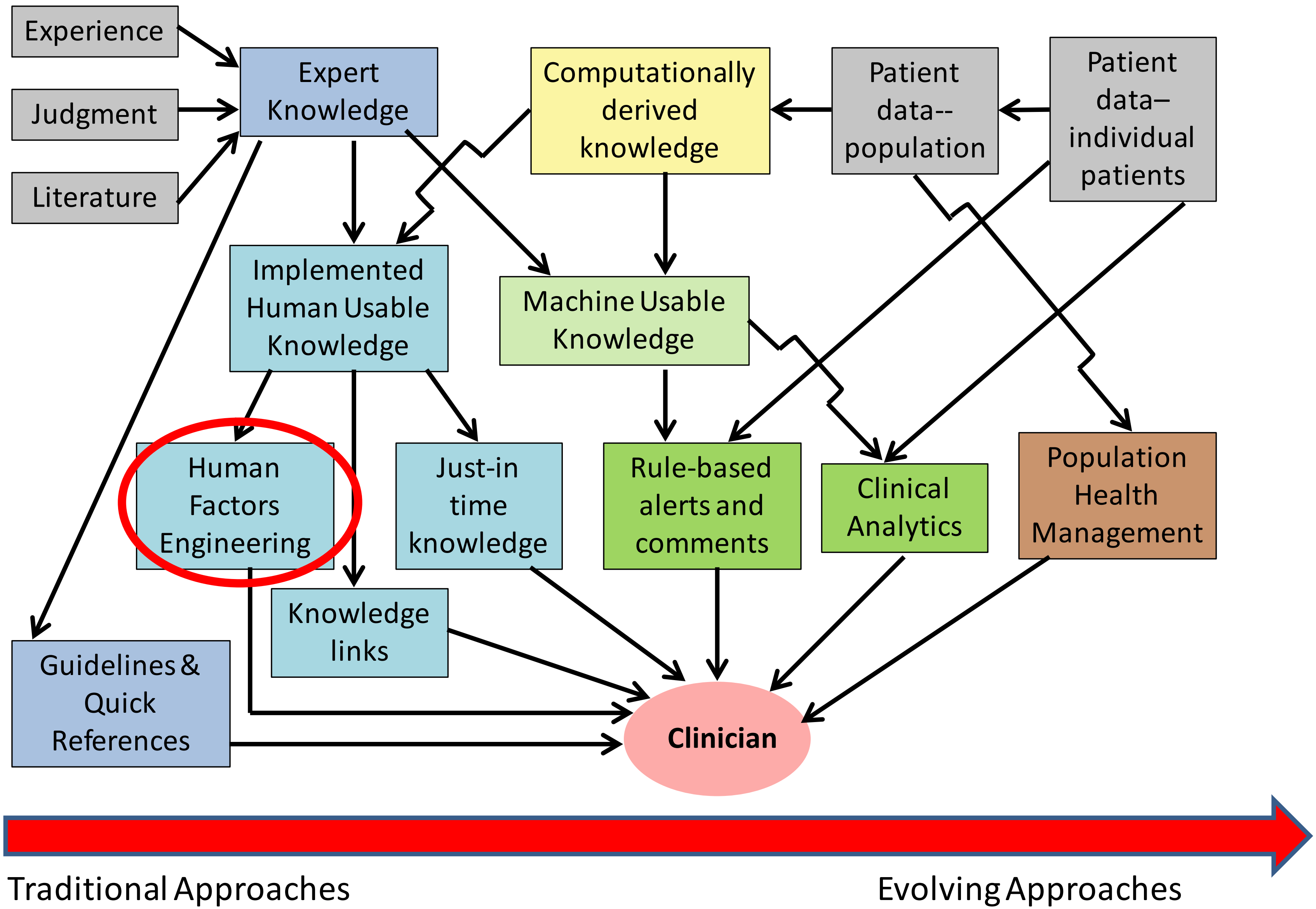
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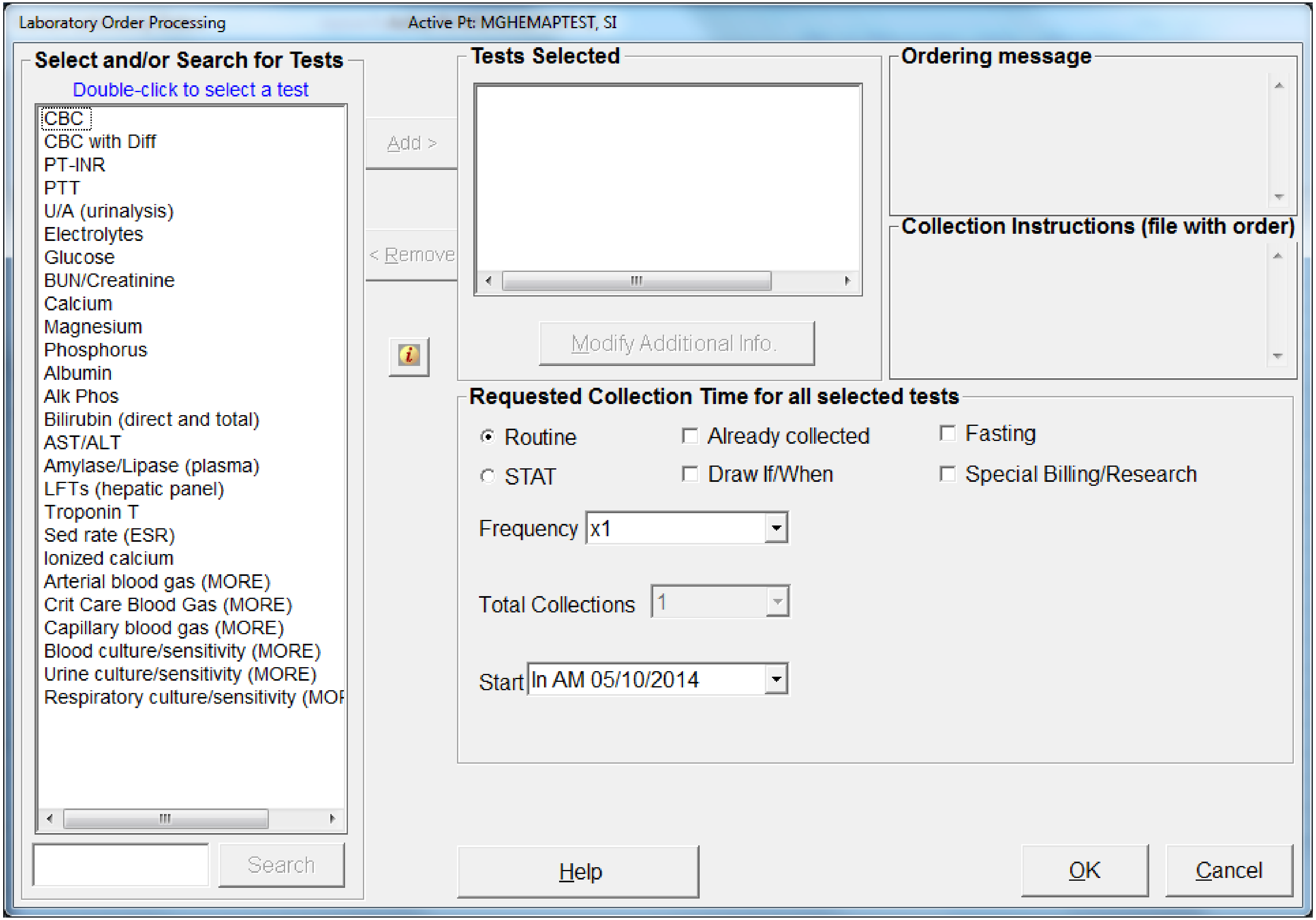
Human Factors Engineering

- Design systems to encourage a particular outcome

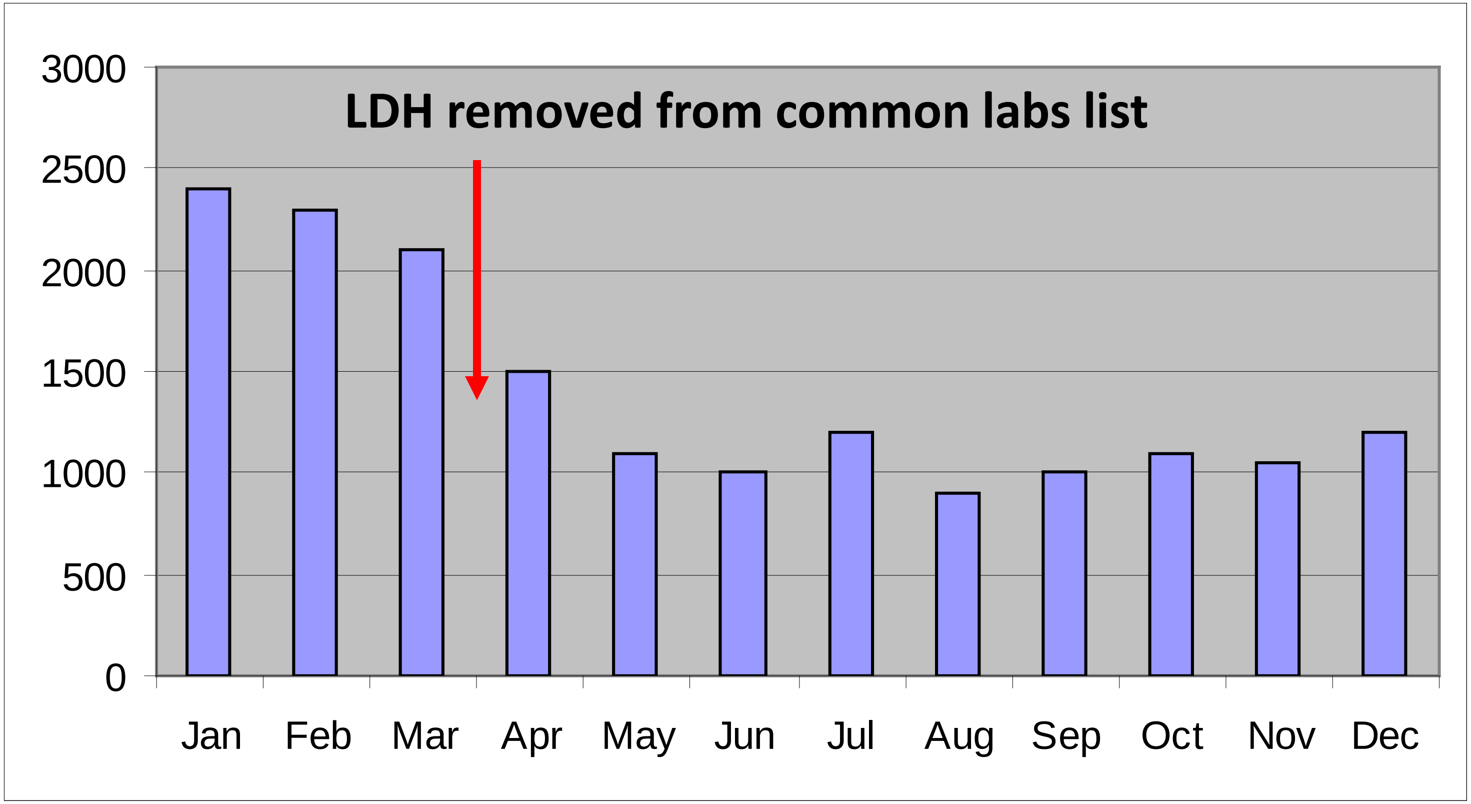
- Examples:
  - Design requisitions, templates or quick picks to include tests that are often appropriate and require specific searchers for uncommonly needed tests (that should usually be used by a specialty)
  - Use “smart” search to guide clinicians toward the correct test

- Guiding principle: Make it easy to do the right thing and hard to the wrong thing

Human Factors Engineering: Example Quick Picks



Human Factors Engineering: Example LDH Quick Pick



Courtesy of Anand Dighe , MD, PhD

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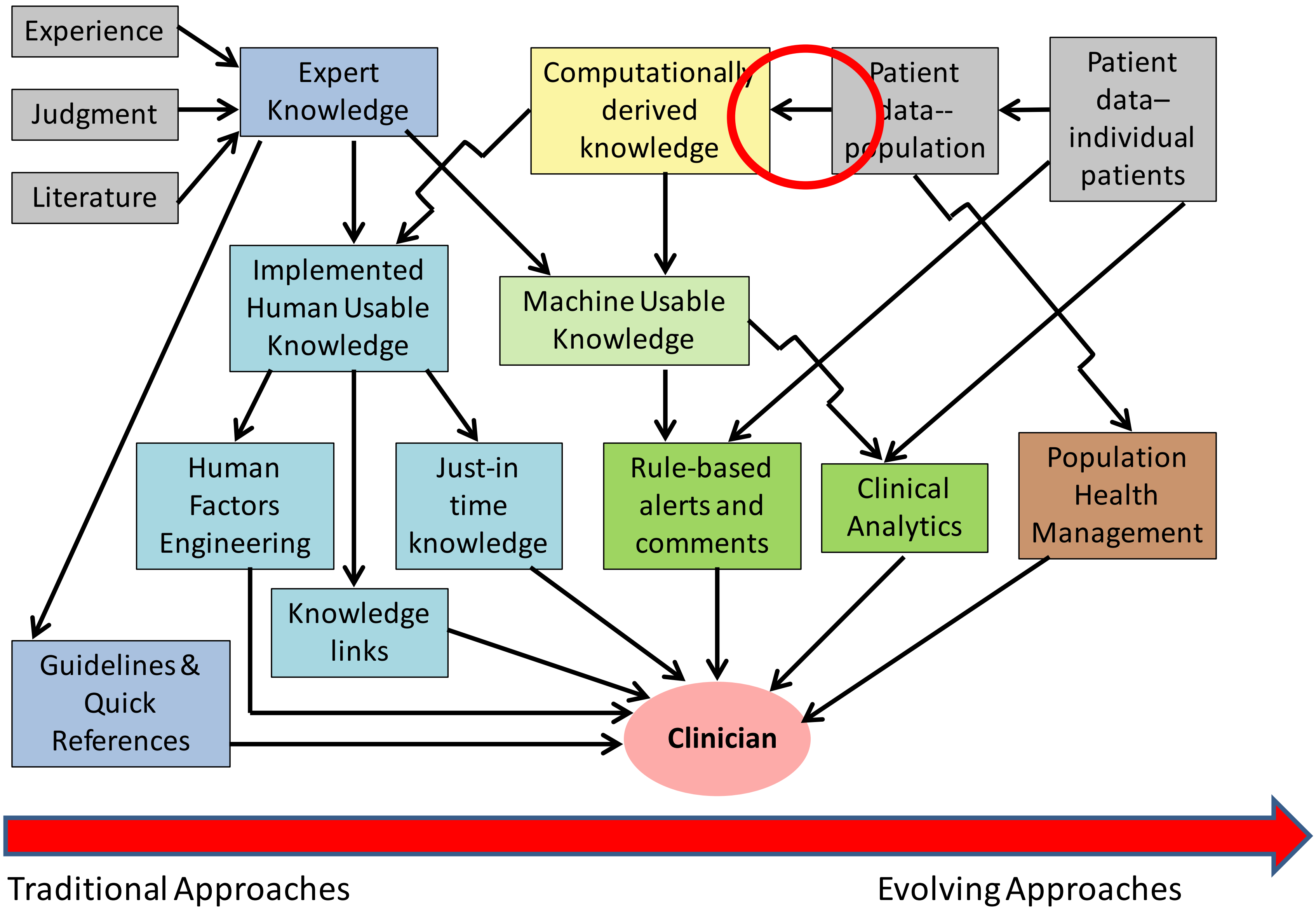
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Traditional Vs. Computational Derivation of Knowledge

- <u>Traditional Knowledge Sources</u>

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

<u>Computational Knowledge Discovery</u>

- 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	•Well established, easily understood •Incorporates clinical intuition •Often easily applied •In the case of well-defined studies, includes high quality evidence	•Can learn from large datasets and potentially identify very subtle patterns •Often comparatively objective •Less expensive than RCTs •Provides opportunities for personalized medicine
Limitations	•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	•May be difficult to understand and apply •Limited by overfitting

Opinion: Need to Integrate both Types of Knowledge

Computational Knowledge Discovery: Machine Learning

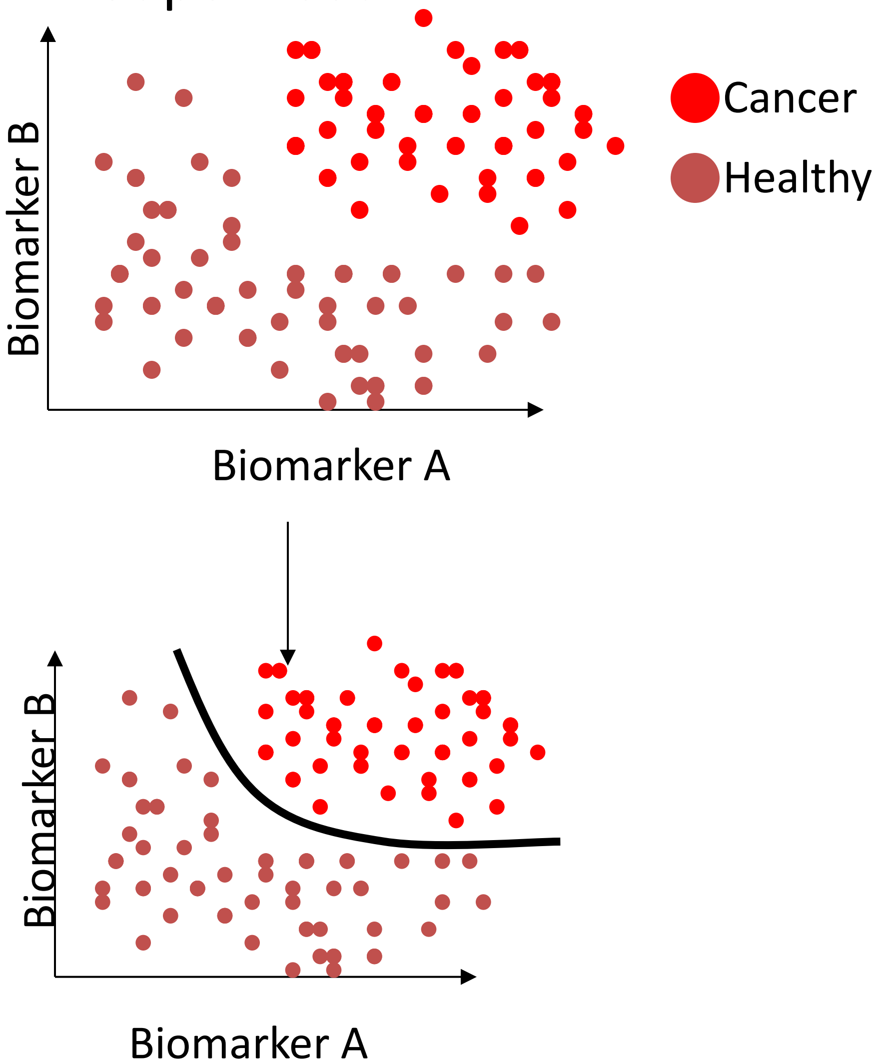
Repository of Patient Data

Machine Learning →

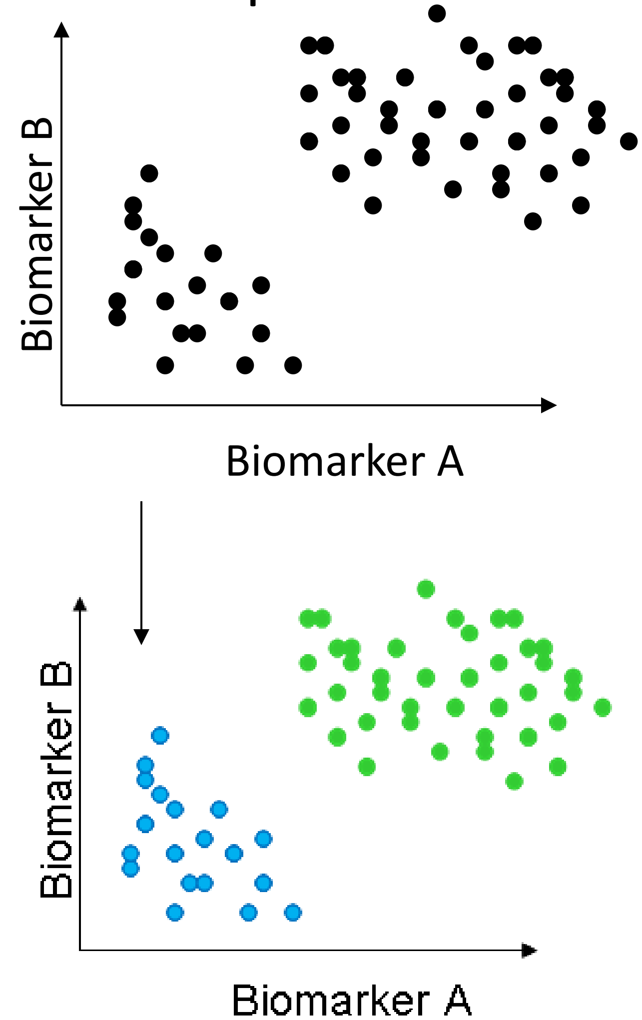
Clinical Knowledge

Computational Derivation of Knowledge: Supervised Vs. Unsupervised Machine Learning

Supervised



Unsupervised



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

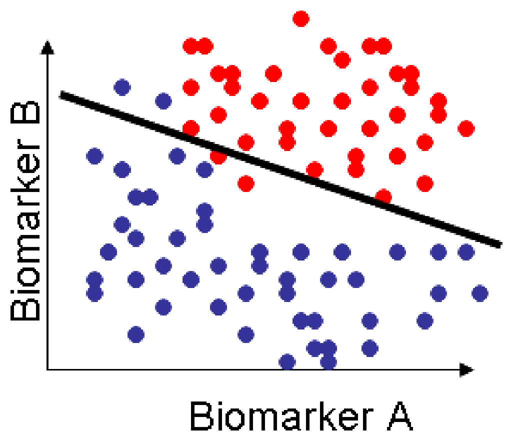
Overfitting and the Red Sox

- 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?**

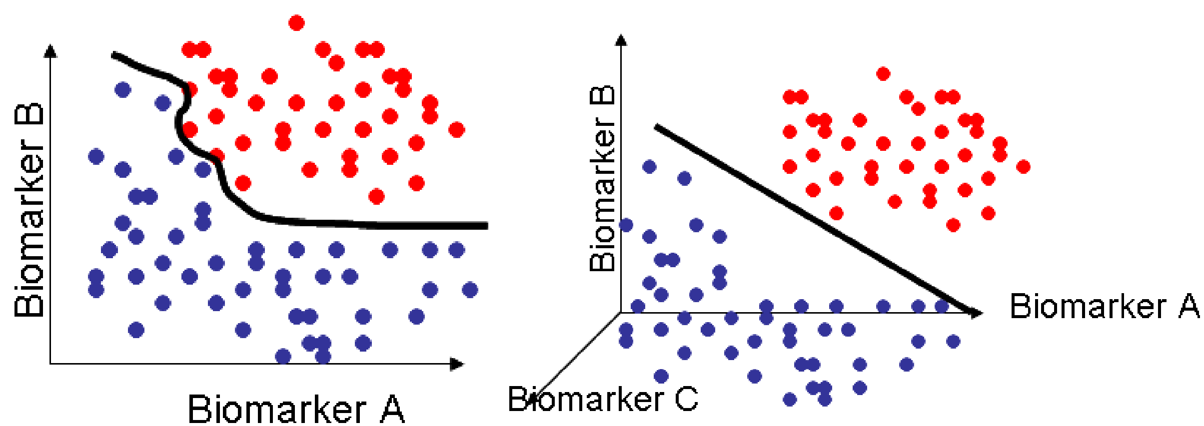
Computational Derivation of Knowledge: Overfitting, An Important Pitfall

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

Simple Model



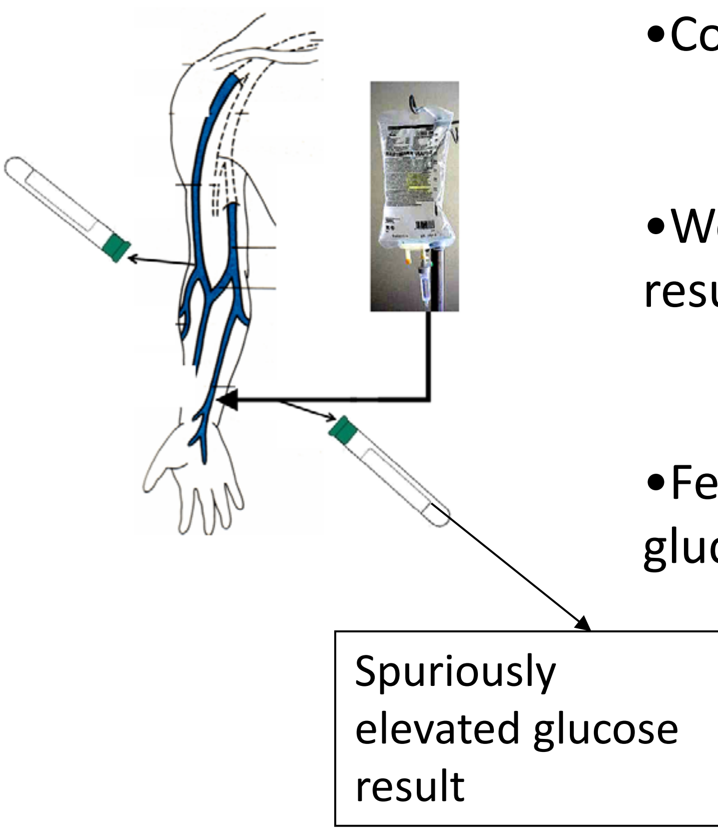
More Complex Models



Computational Derivation of Knowledge: Machine Learning, Sample Methods

- Linear methods
  - Ordinary least squares regression
  - Logistic regression
  - Perceptrons
- Decision trees
  - Recursive portioning 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

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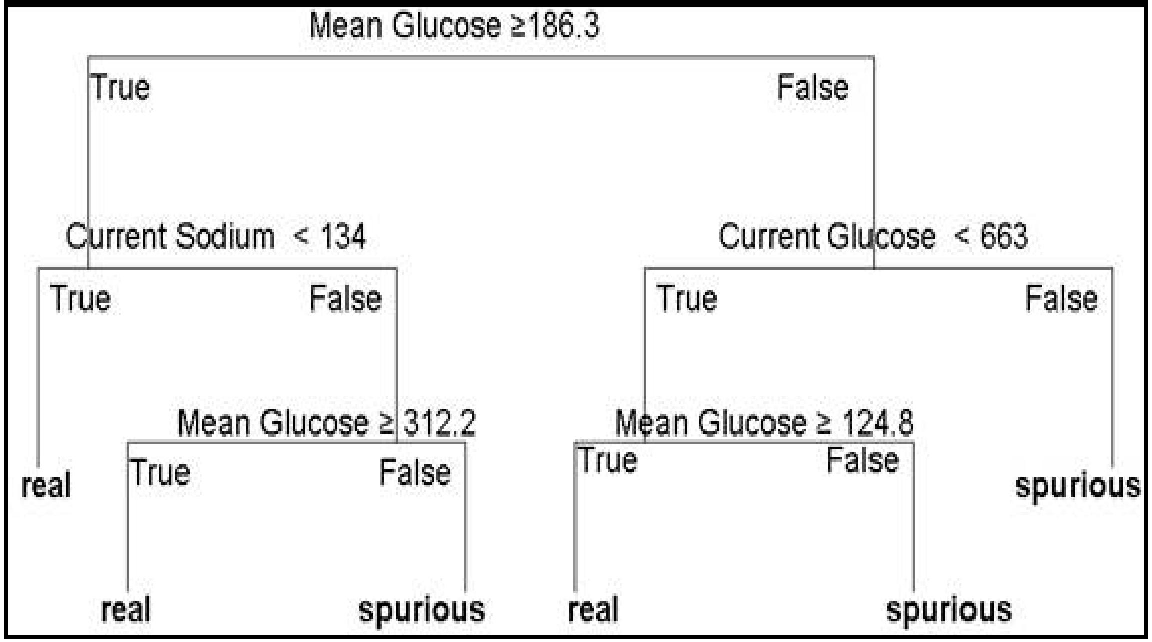
Computational Derivation of Knowledge: Example Spurious Glucose Identification, Results

Tree built Using: Na, K, Cl, Bicarbonate, Anion Gap, Glucose, and 30 day mean glucose



	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%)

Implementation Discussed Later

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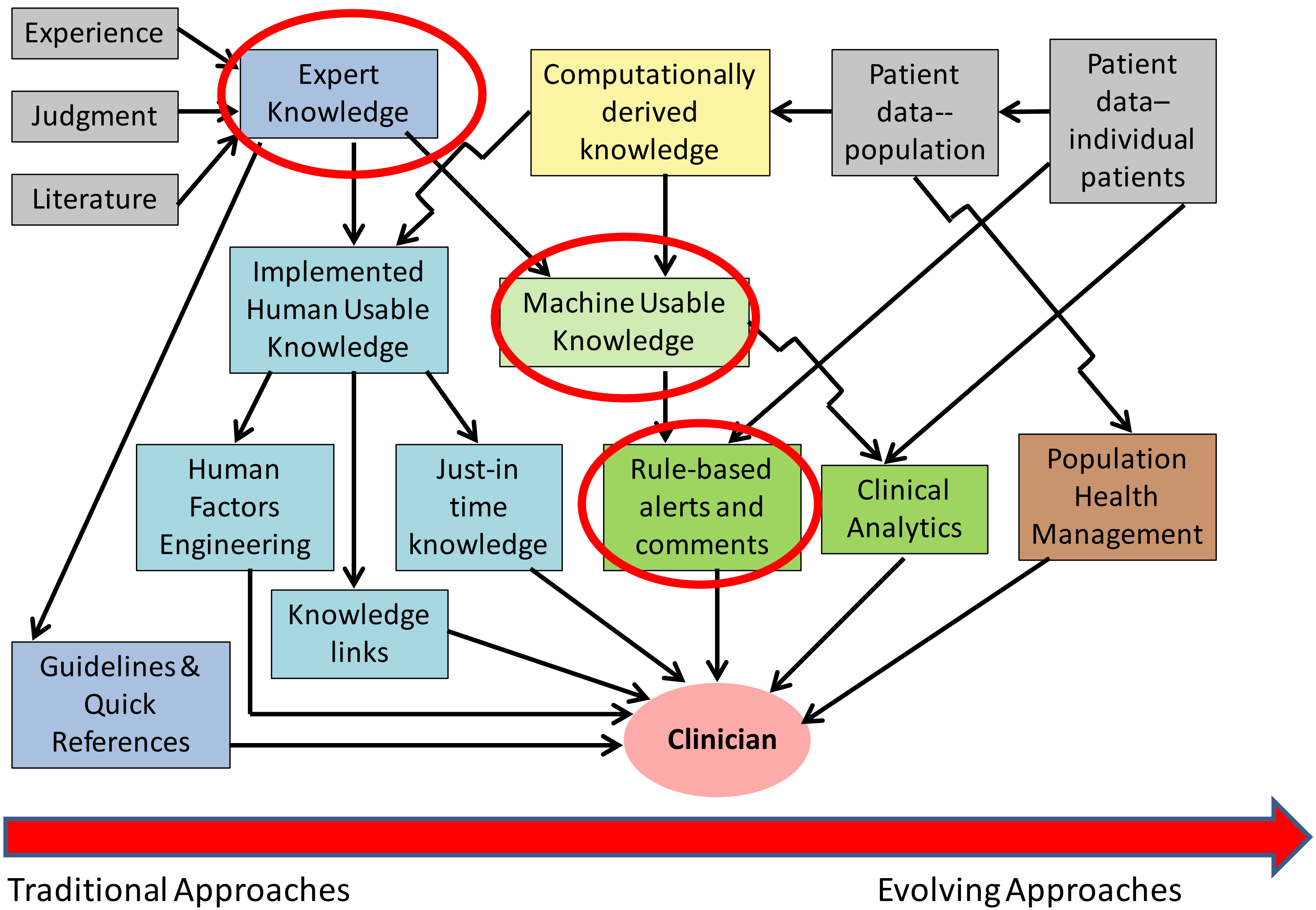
Transforming Expert Knowledge into Rule-based Alerts and Comments



Transforming Expert Knowledge into Rule-based Alerts and Comments

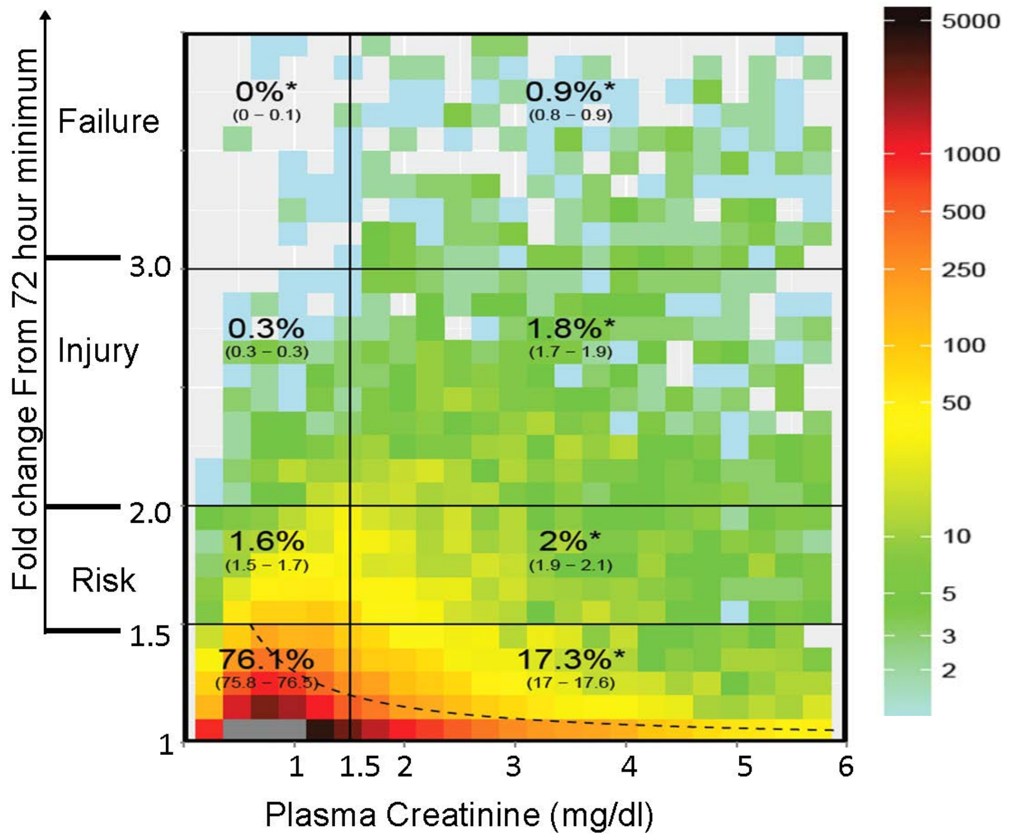
- Knowledge acquisition is only part of the battle
- Implementation of decision support can be a key challenge
- Many health information systems offer opportunities for rule-base alerts, but may still be limited in what rules can be implemented
- Building alerts can be resource intensive

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



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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**

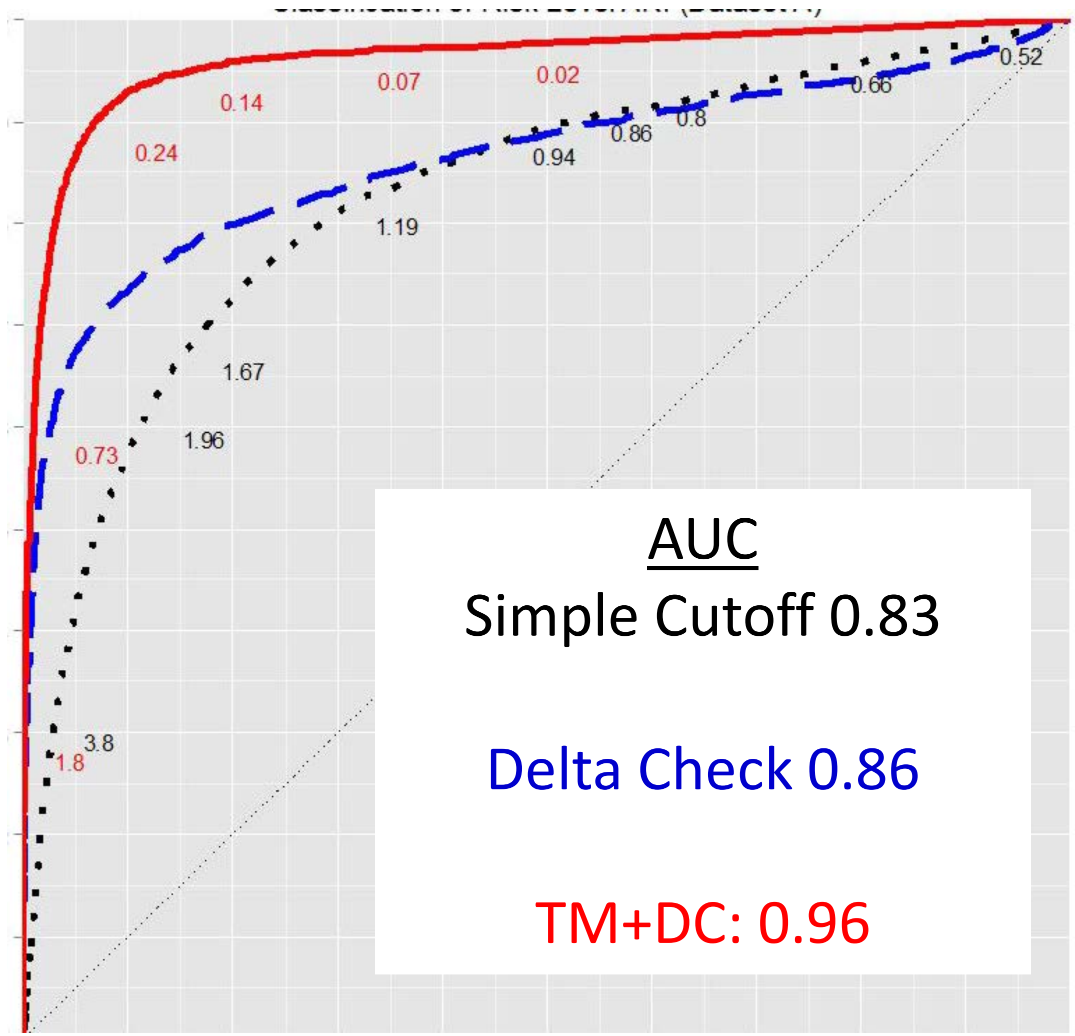
Transforming Expert Knowledge into Rule-based Alerts
Example, Acute Kidney Injury Detection: Tracked Minimums

The tracked minimum is updated to the current creatine 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



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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	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. Result = 35 mL/min/1.73m2

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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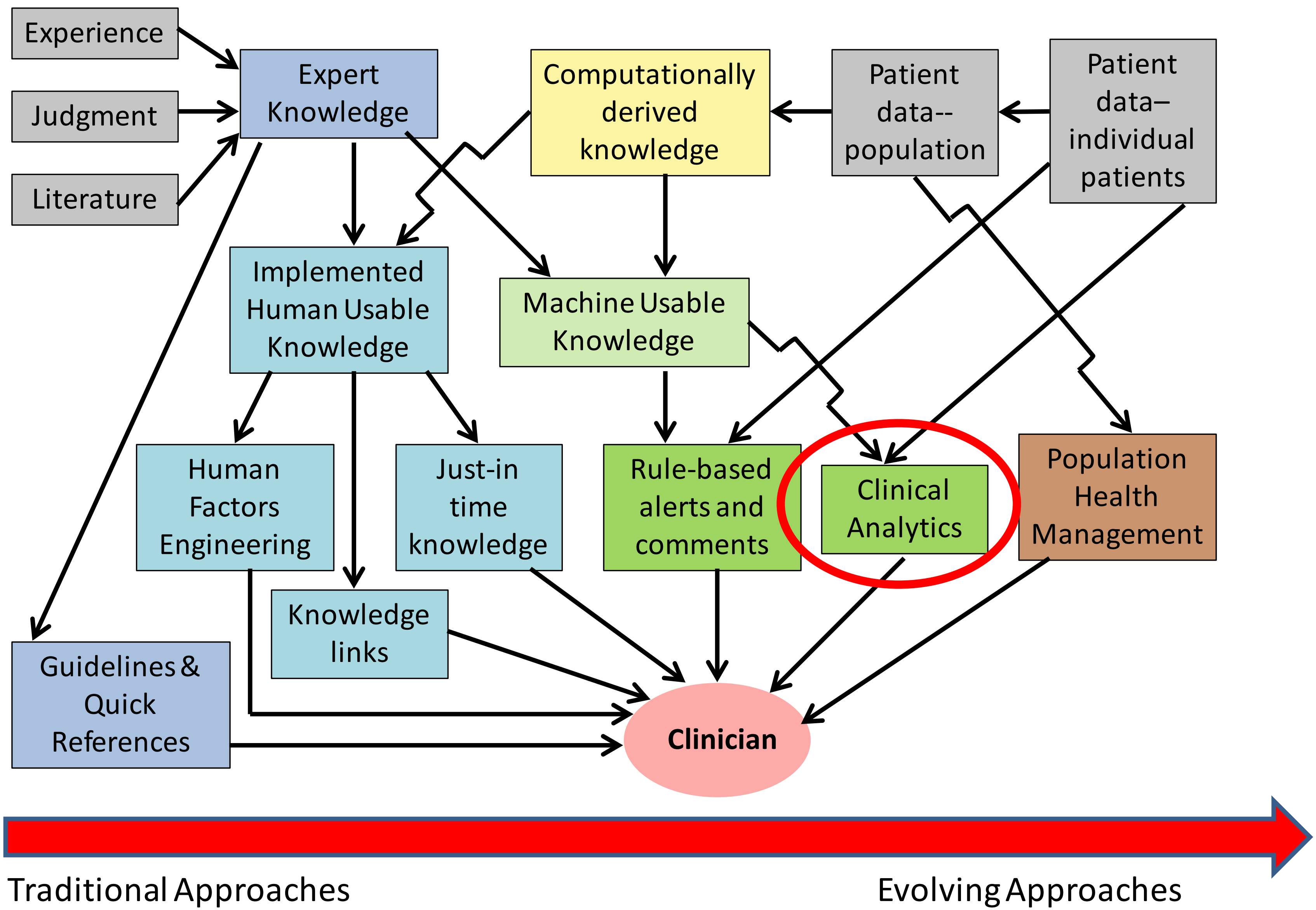
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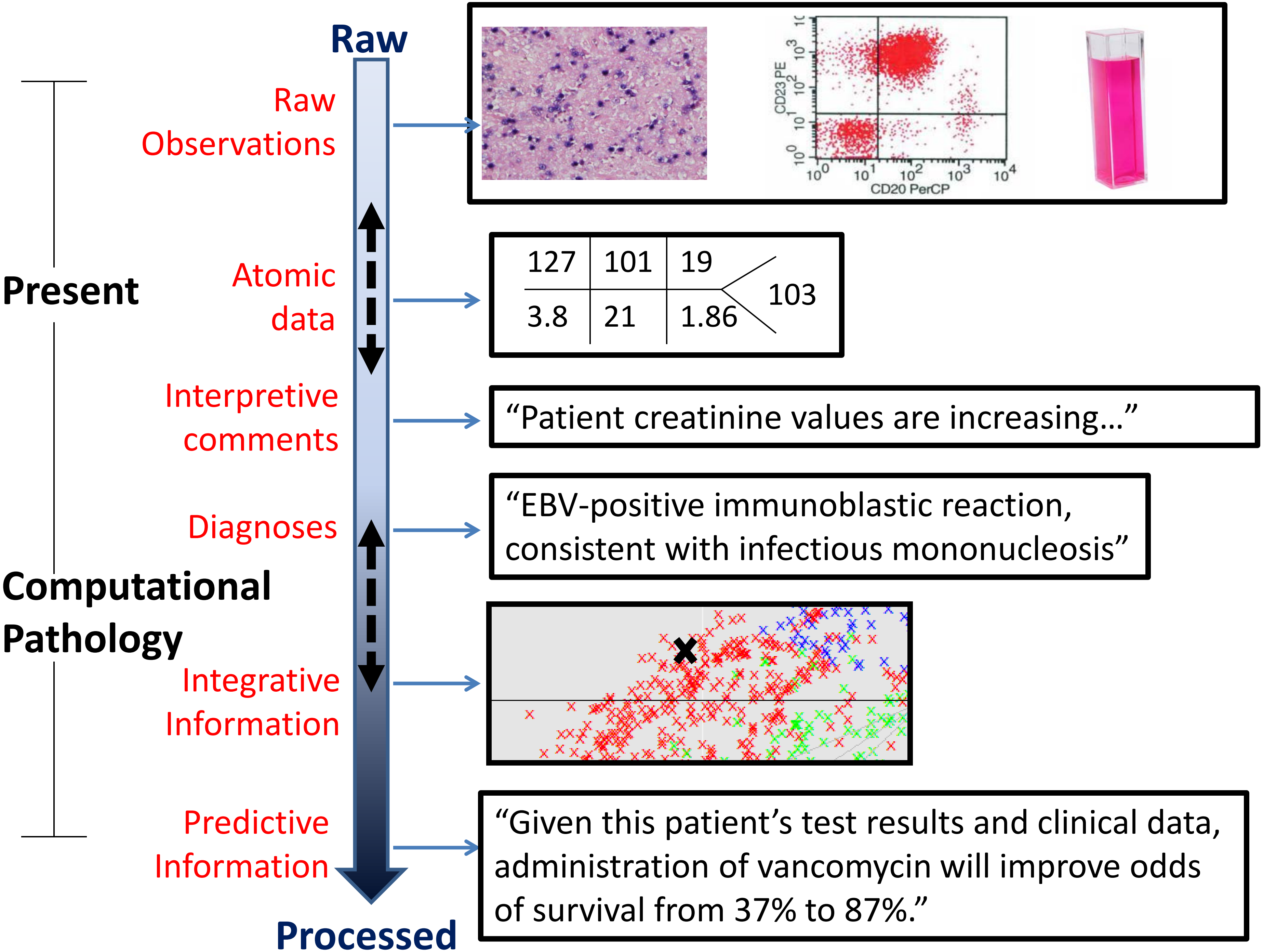
Raw
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Observations
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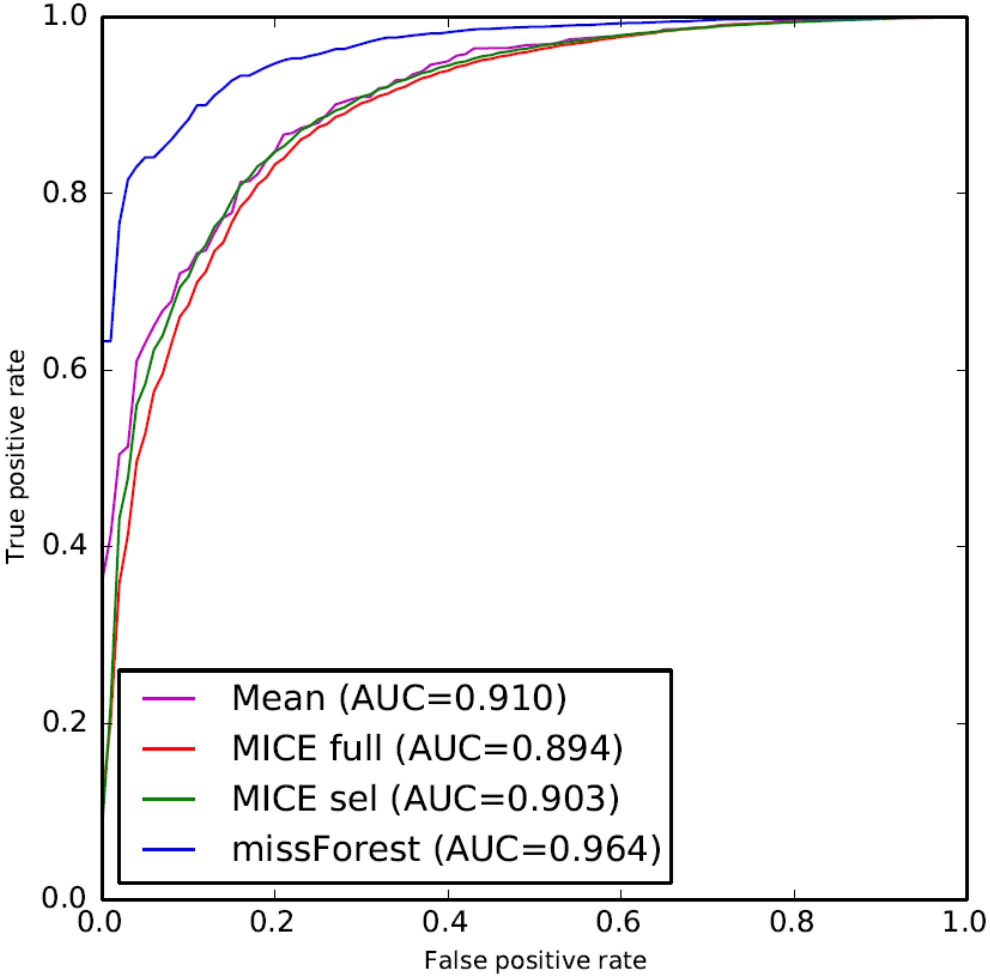
data
Interpretive
comments
Diagnoses
Integrative
Information
Predictive
Information
Processed
CD23 PE
CD20 PerCP
127
101
19
3.8
21
1.86
103
“Patient creatinine values are increasing…”
“EBV-positive immunoblastic reaction, consistent with infectious mononucleosis”
“Given this patient’s test results and 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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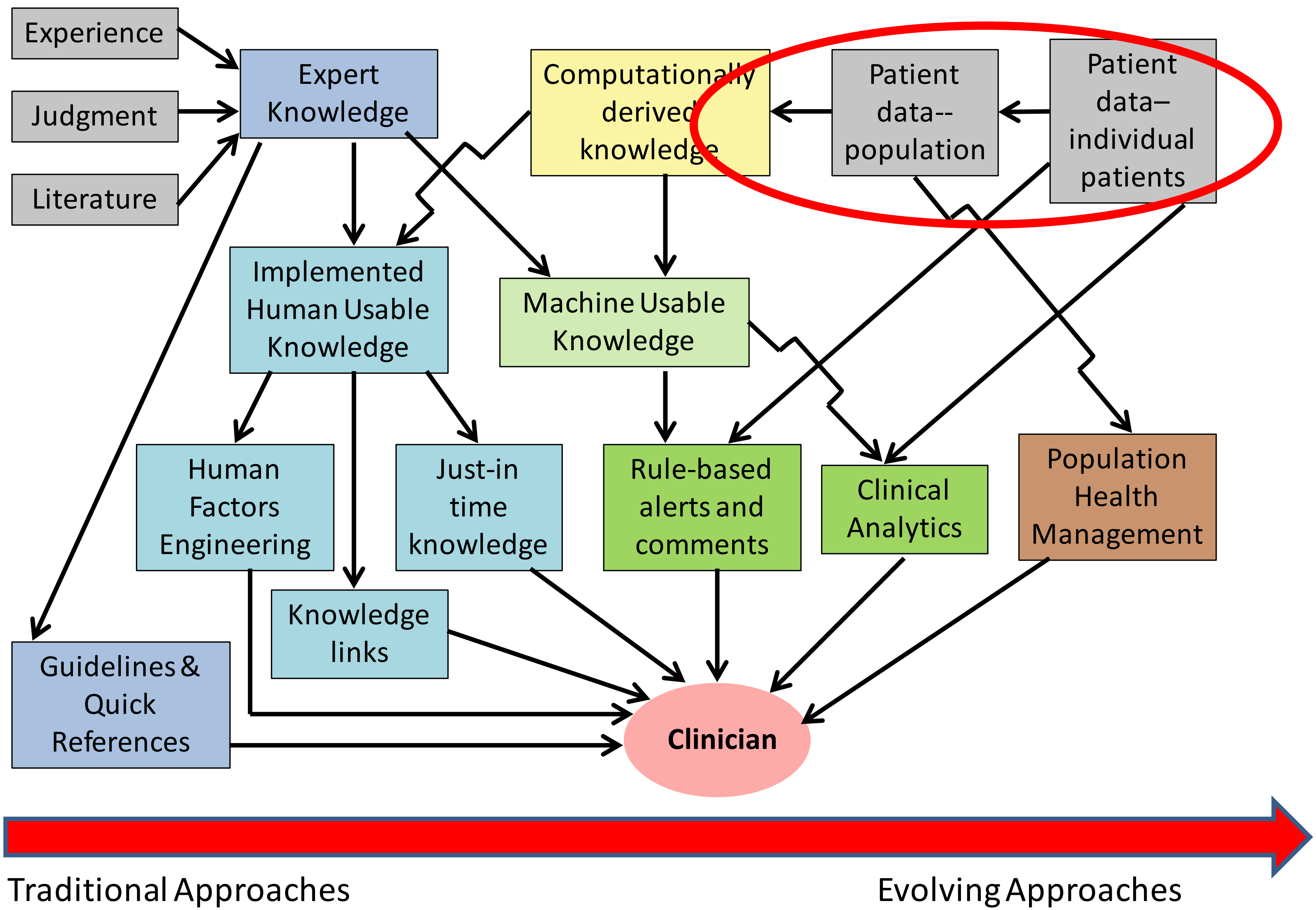
Challenge: Clinical Data Quality



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

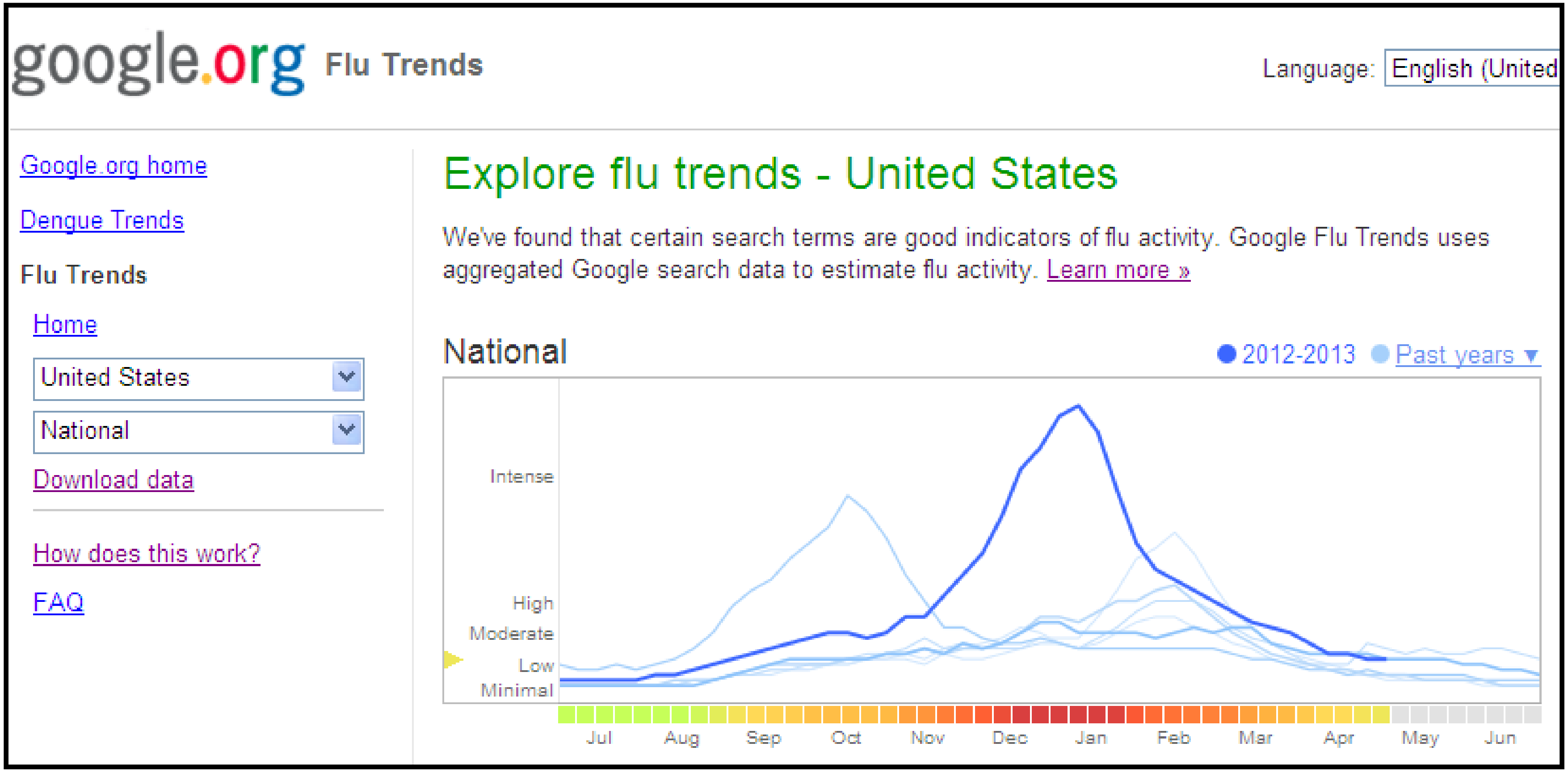
VS.

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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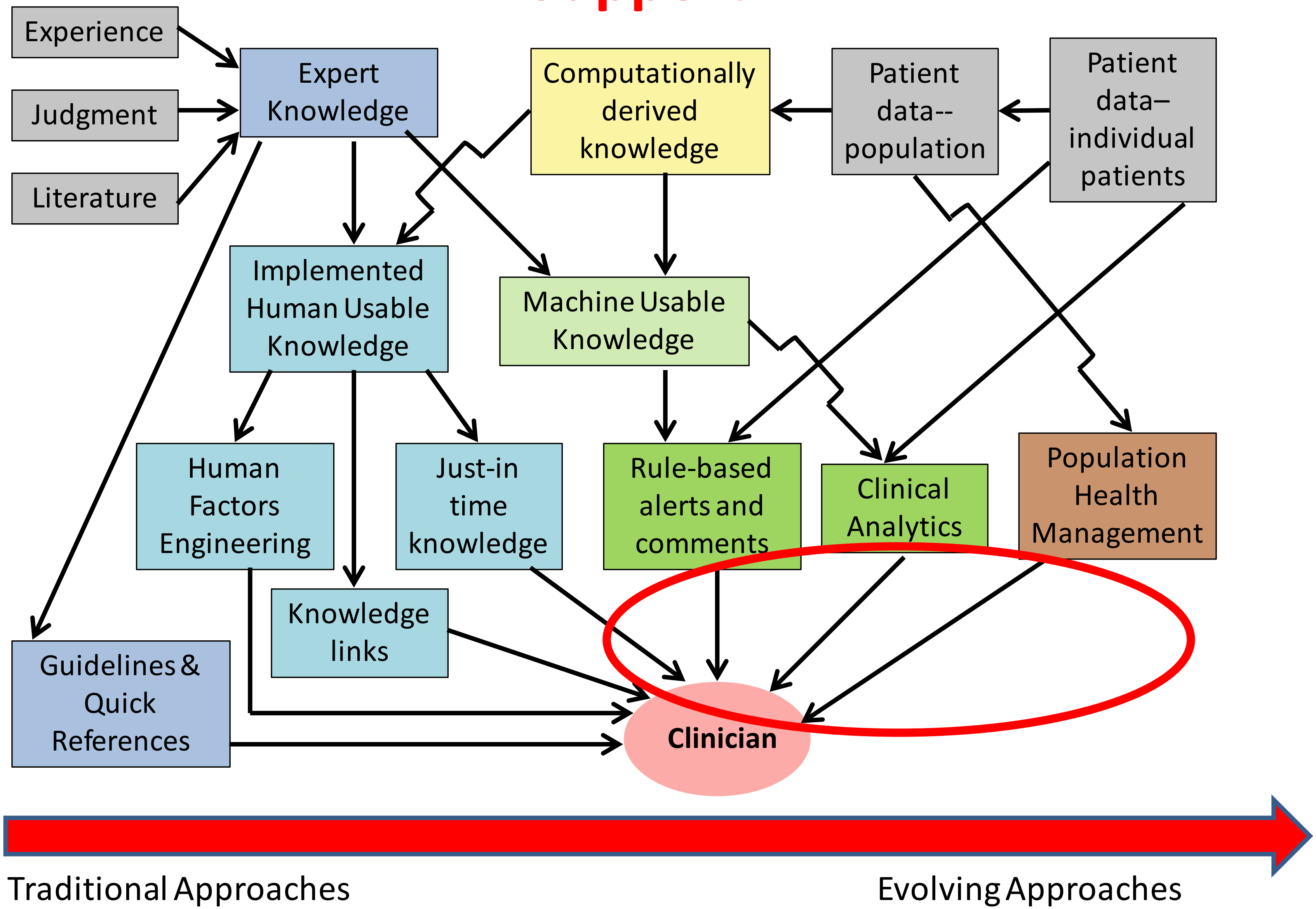
Challenge: Implementation of Evolving Decision Support



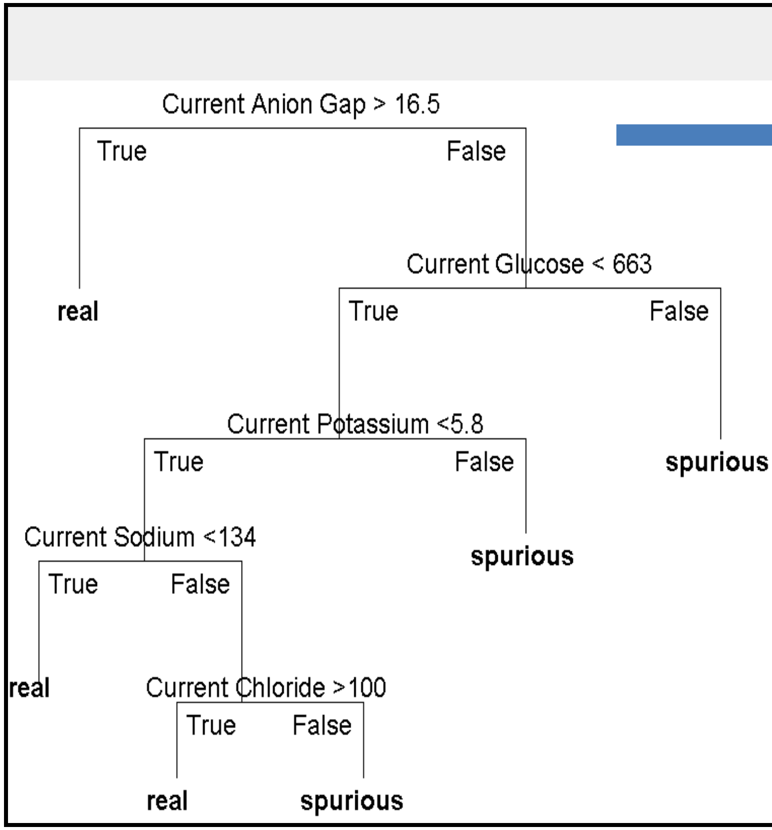
Implementation Challenge

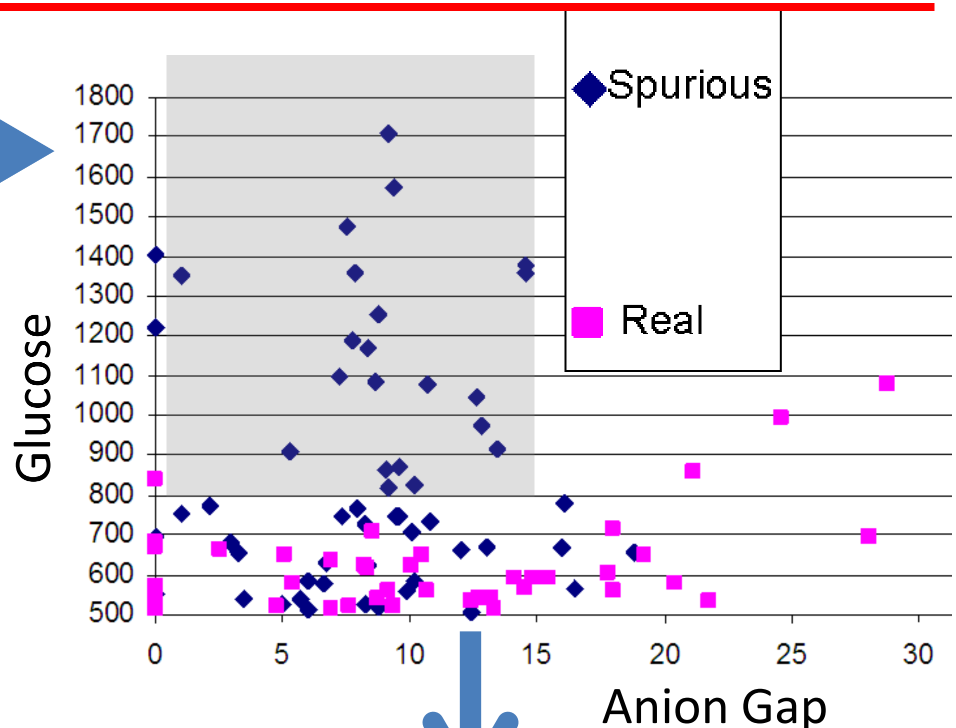
- Even straightforward rule-based alerts can be challenging to implement (e.g. AKI alert)
- But what about decision support based on machine learning algorithm– is it hopeless?

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

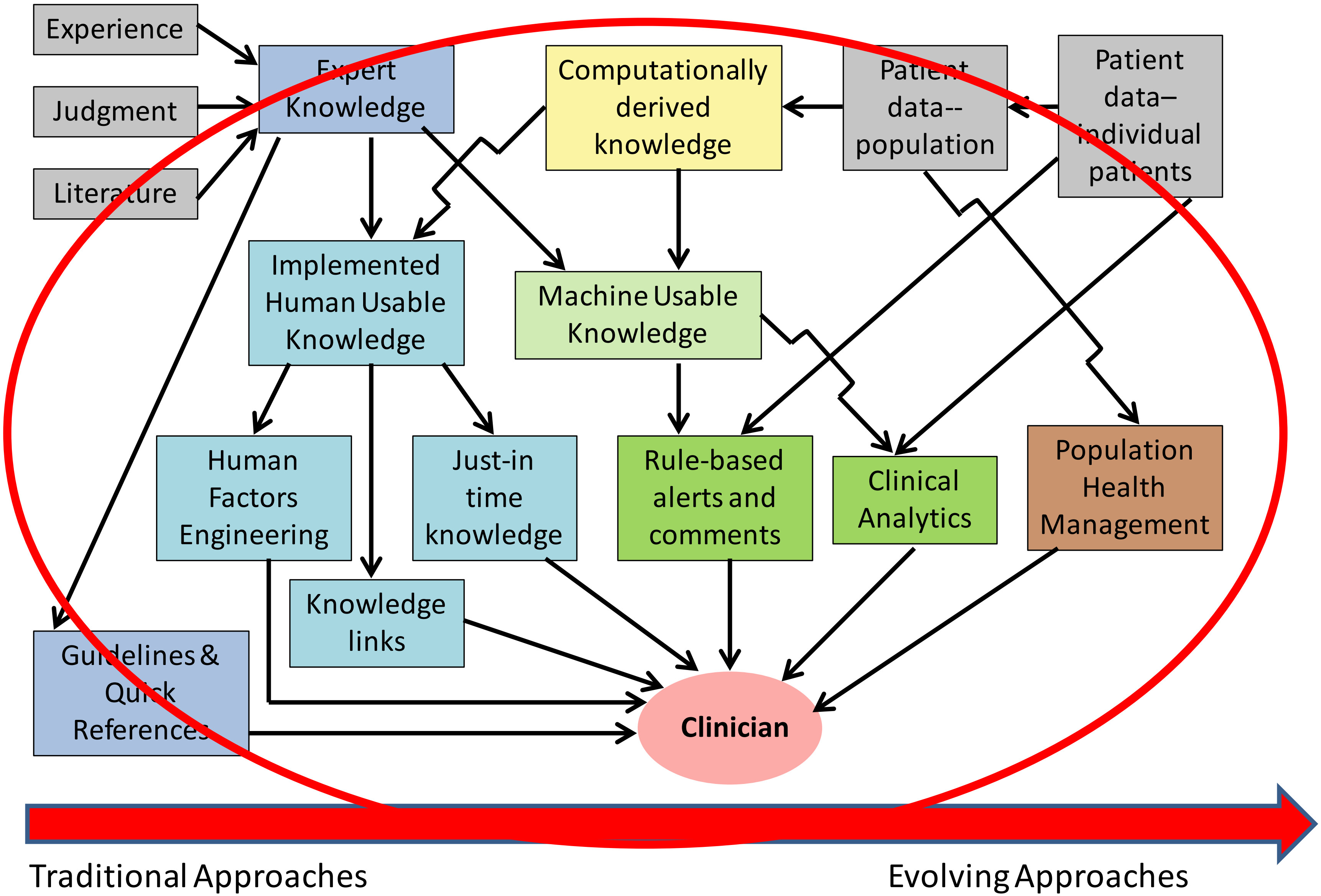
- While some machine learning algorithms can be reduced to implementable rules, others cannot

- 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

Acknowledgements

Many Aspects

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Acute Kidney Injury Alert

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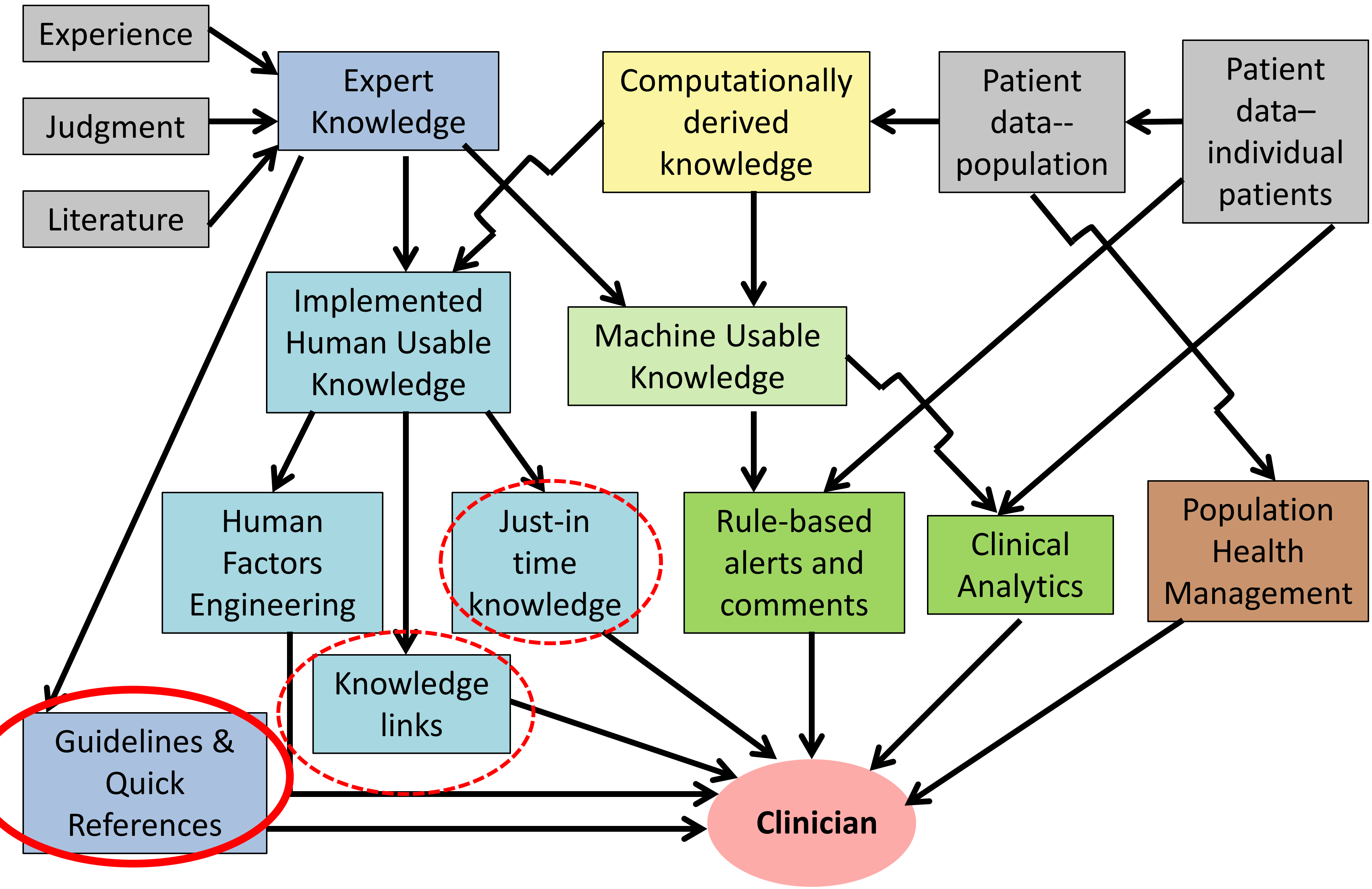
- Hasan Bazari
- Ishir Bhan
- Rosemary Jaromin
- Chris Lofgren

Spurious Glucose Identification

- Craig Mermel

Extra


Experience
Judgment
Literature
Expert Knowledge
Computationally derived knowledge
Patient data--population
Patient data– individual patients
Implemented Human Usable Knowledge
Machine Usable Knowledge
Human Factors Engineering
Just-in time knowledge
Rule-based alerts and comments
Clinical Analytics
Population Health Management
Knowledge links
Guidelines & Quick References
Clinician