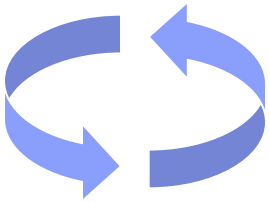
Knowledge Analytics Synergy in Clinical Decision Support



MIE 2012

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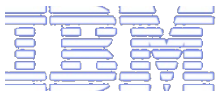
IBM Haifa Research Labs

Machine Learning and Data Mining (MLDM) group

Cli-G group

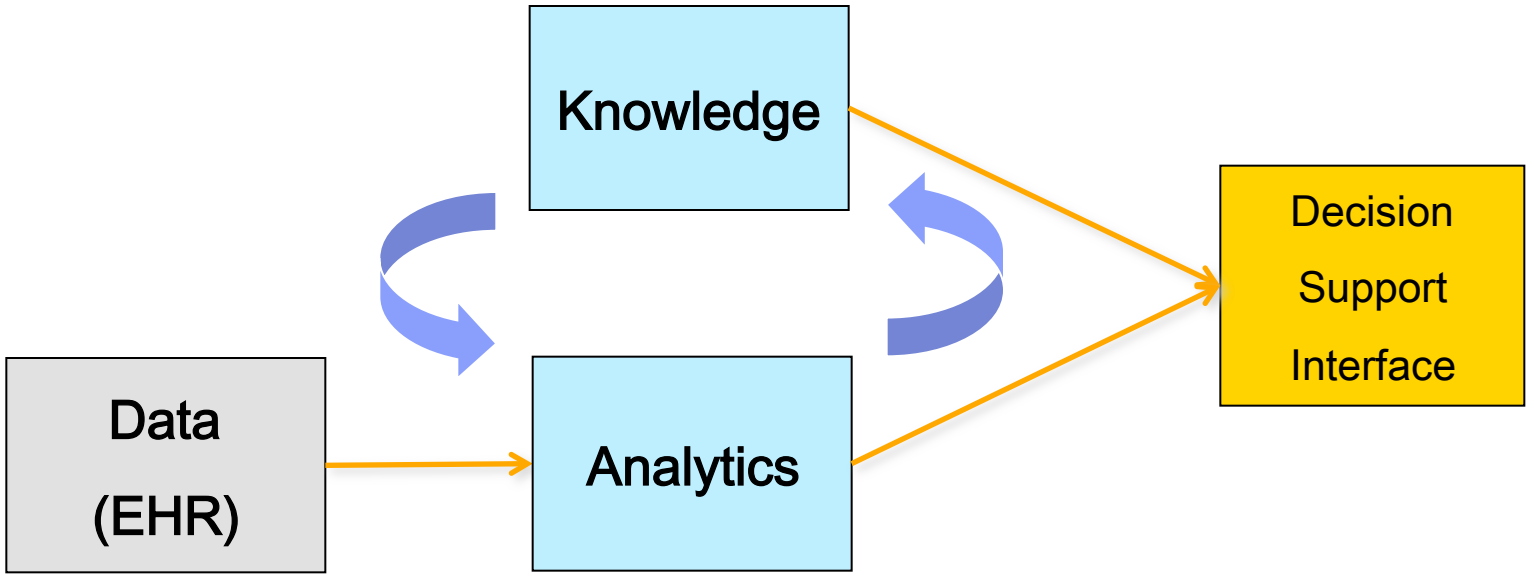


Clinical Genomics IT

Introduction

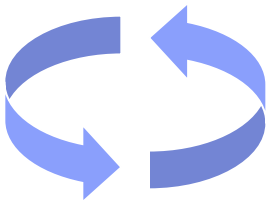
- Clinical Decision Support (CDS) have great potential
  - Improving clinical care
  - Reducing associated costs
- Most existing tools are knowledge-based CDS
  - Clinical trials → Clinical guidelines → simple CDS rules
  - Well established
- Emerging alternative paradigm – analytics-based CDS
  - EHR data → Analytics (Machine Learning) → Statistically-based CDS
  - No need to define/maintain long list of rules
  - Allows to take new "omic" data into account quickly
  - Address groups not participating in clinical trials (co-morbidities, elderly, etc.)

Both paradigms are complementary



- Analytics techniques may benefit from domain knowledge
- Domain knowledge may benefit from analytics

- CDS knowledge-Analytics Synergy (KAS) paradigm



The proposed CDS KAS Paradigm

- Synergistically combine relevant clinical knowledge with analytics applied to EHR data, improving overall CDS quality
- Knowledge and analytics components mutually feed and enhance each other to achieve better results.
- Implemented as part of a generic CDS system – Cli-G
  - Cli-G underlying architecture explicitly supports the KAS paradigm
  - See also Evicase presentation (Wed. 1000, Fermi)

Data examined to demonstrate KAS potential

- 3 cohorts of hypertensive patients:*
  - EPOGH
    - 1,149 patients
    - 15 clinical features
  - IMA_Sardinia
    - 278 patients
    - 45 clinical features
    - Genotype data for 1M SNPs
  - Immidiet
    - 258 patients
    - 45 clinical features
    - Genotype data for 1M SNPs

HYPERGENES
European Network for Genetic-Epidemiological Studies

* http://www.hypergenes.eu/

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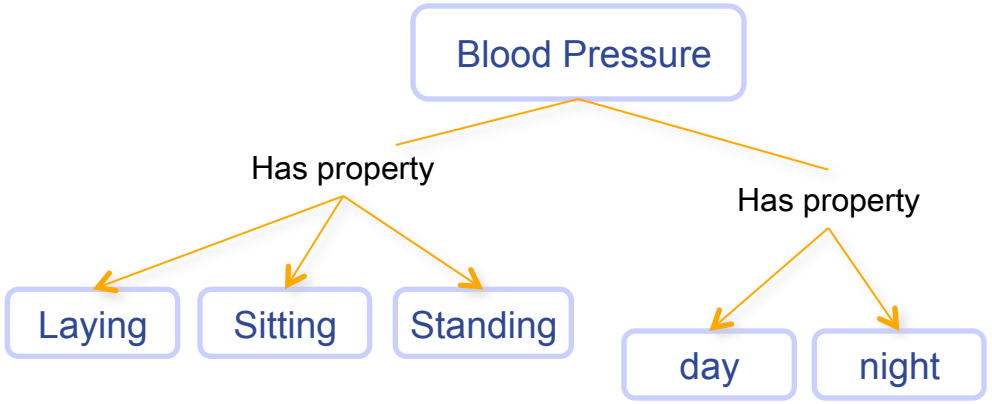
The Knowledge-Management (KM) component

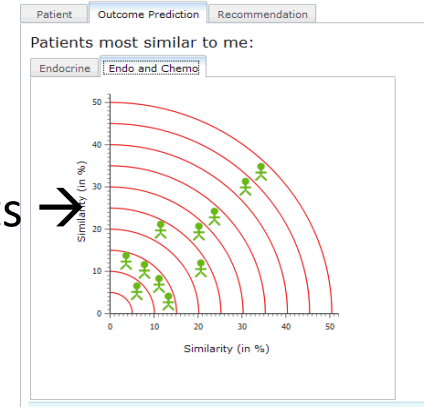
- Represents and streams relevant clinical knowledge to other components.
- Declarative Knowledge (DK)
  - Factual information: hierarchy of concepts with properties and relations

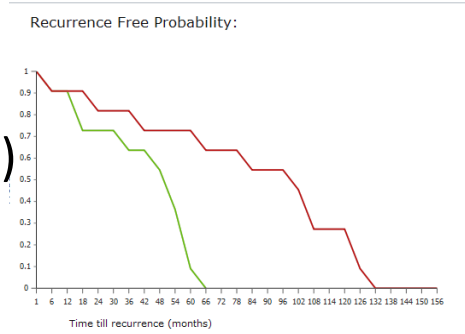


- Procedural Knowledge (PK)
  - The knowledge on how to operate upon the DK concepts
    - Clinical Guidelines
    - Rules defining Deductive Concepts to be added to the DK model; e.g.,
      - Risk Group based on Gender, Weight, Co-morbidities, etc
- May support various CDS applications
  - Guidelines based treatment recommendations
  - Rule-based alerts for adverse-drug events

The Analytics component

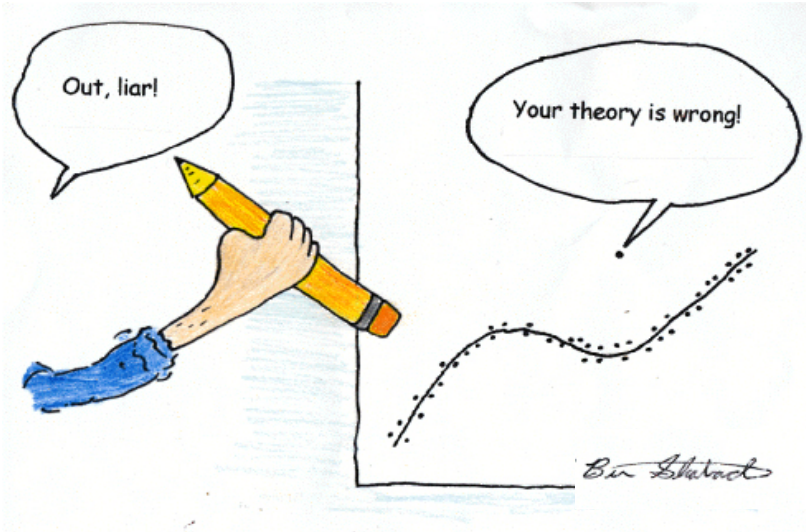
- Encompasses an arsenal of ML algorithms for various CDS tasks
- Feature ranking/selection
  - Automatically highlight clinical features of potential interest to the clinician
- Estimating patient similarity
  - Automatically reveal meaningful groups of similar patients → recommendations at Point Of Care
- Supervised Machine Learning algorithms
  - Predicting most common treatment (IHI 2012)
  - Predicting the outcome of candidate treatment (EuResist)
  - More…

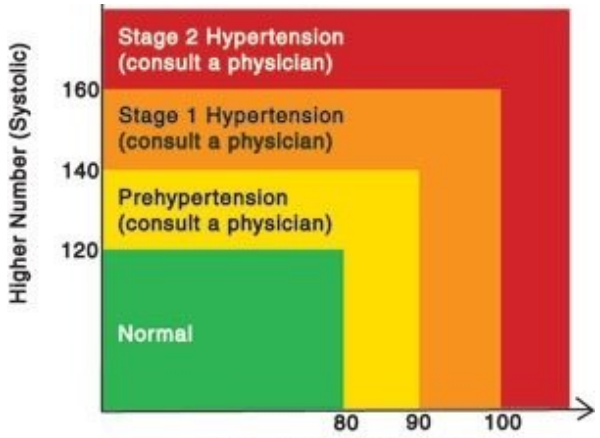




KAS: using KM component to enhance Analytics

- Procedural Knowledge rules for **Data Cleansing**:
  - Outliers / non-valid data removal
    - Remove Height measurements < 140
    - Remove Serum Cretanine > 2
  - Unifying data reported in different scales
    - Serum Insulin: µIU/mL or pmol/L
  - Quantizing continuous data
    - Systolic Blood Pressure:
      - < 120 → Normal
      - 120-139 → Pre Hypertension
      - 140-159 → Stage-1
      - > 160 → Stage-2

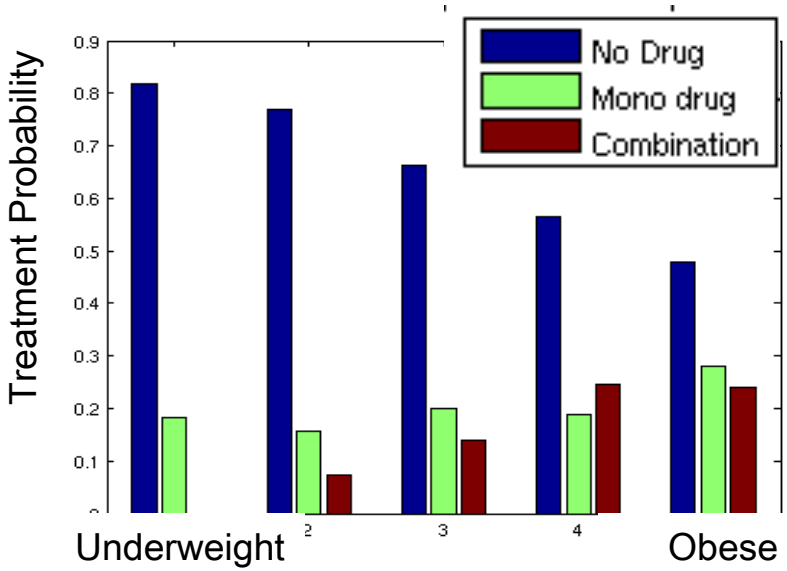




KAS: using KM component to enhance Analytics

- **Data enrichment**
  - Use domain knowledge to pinpoint relevant feature combinations to explore
    - BMI
    - [Serum-Glucose*Serum-Insulin]/25 → HOMAI
    - More...

- Some Deductive Concepts were later identified by feature-ranking as associated with clinicians treatment decision;
  - BMI in the EPOGH cohort → insights regarding treatment-selection process*



* Rinott *et. al* IHI 2011

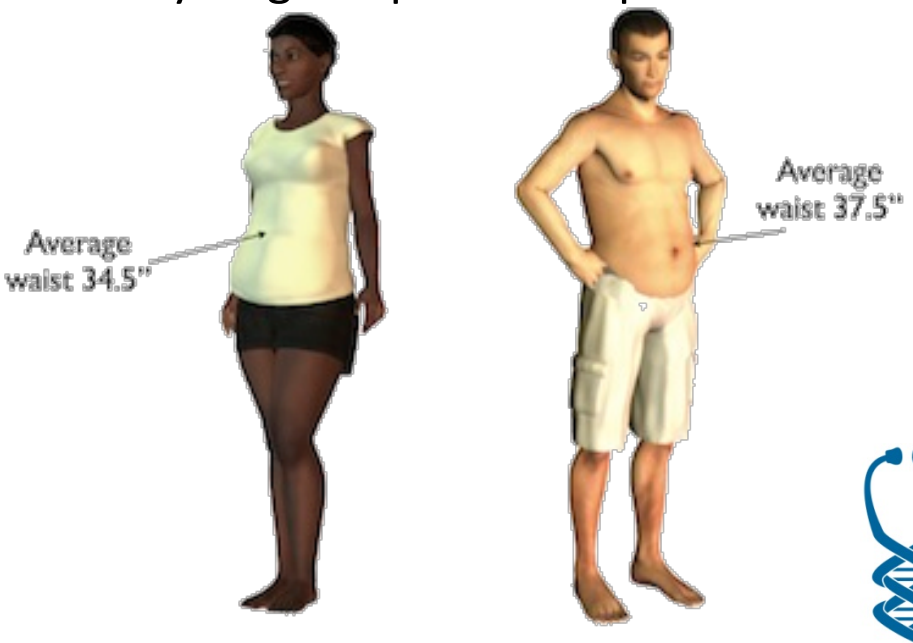
KAS: using KM component to enhance Analytics

- **Data filtering**
  - Use domain knowledge to filter irrelevant features, focusing analytics on important features
    - Find similar patients based on genetic SNP data
    - Using all 1M SNPs available
      - Time costly
      - Low signal to noise ratio
    - Pre-select 5,717 SNPs according to domain knowledge - potentially related to molecular pathways associated with hypertension
      - Reduce run time by more than 2 orders
      - Clustering patient based on similarity results in meaningful clusters

KAS: using Analytics to enhance KM component

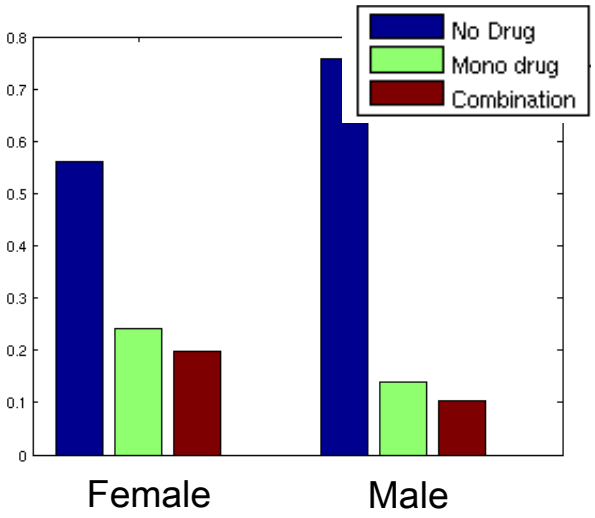
- **Enhancing Declarative Model**
  - EHR often includes free-text data
  - Analytics may reveal the importance of a particular free-text term; e.g.,
    - Drug-name → added to the DK Model

- Deductive Concepts
  - Exploring all feature pairs → Reveal pairs with synergistic predictive power → TBA as Deductive Concepts to the DK model
  - Waist circumference & Gender has synergistic predictive power for selected treatment in EPOGH data



KAS: using Analytics to enhance KM component

- **Enhancing Procedural Knowledge**
  - Reveal clinicians "common practices" → TBA to the PK model → supporting rule-based CDS applications
  - Feature ranking applied to identify features associated with treatment selection
  - Gender found to be significantly associated with treatment selection
  - Gender highlighted in PK model as related to "Common Practices" in "Treatment Selection"

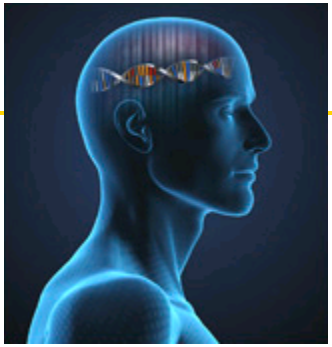


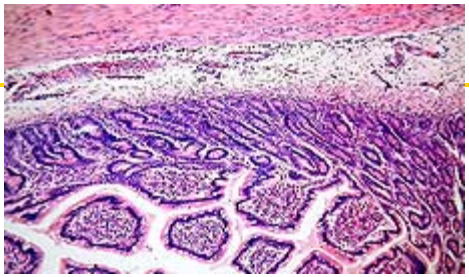
- Guidelines refinement
  - Pinpoint SNPs of potential clinical value to enhance PK and DK → guidelines refinement (Not implemented yet)

Summary

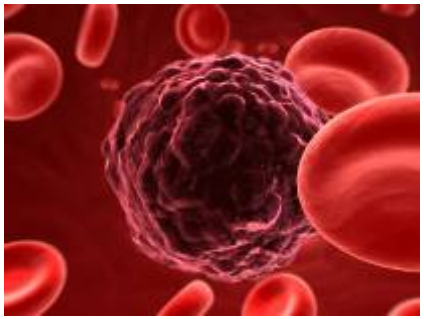
- Presented the Knowledge Analytics Synergy paradigm for CDS
  - Demonstrated via a generic tool (Cli-G) that relies on the KAS Architecture
- Presented concrete examples over clinical and genomic data:
  - Knowledge can enhance Analytics
  - Data-driven analytics can enhance Knowledge
- The synergisytic approach holds great potential for CDS tools

cli-g





Thank You



cli-g

Introduction

- Clinical Decision Support (CDS) have great potential
  - Improving clinical care
  - Reducing associated costs

- Most existing tools are *knowledge-based CDS*
  - Clinical trials → Clinical guidelines → simple CDS rules

- Emerging alternative paradigm – *analytics-based CDS*
  - EHR data → Analytics (Machine Learning) → Statistically-based CDS rules

Results – Analytics enhancement – **Data Filtering**

- Patients were clustered using Patient Similarity defined according to SNP data
  - Emphasizing relative similarity of patients sharing identical rare SNPs
- Similarity estimated from 5,717 SNPs (from 1M) selected by domain knowledge
  - Filtering reduced computation time by more than two orders of magnitude
  - Filtering focused analysis in advance on potentially most relevant SNPs
- Statistical significance of clinical features was estimated in each cluster
  - c10 (30 people)
    - Avg. Systolic BP: 153, vs. 140 in remaining population (P-val 0.004)
  - c5 (23 people)
    - Avg. Triglyceride: 95.3, vs. 132 in remaining population (P-val 0.0002)
  - More…
- → Encouraging results that should be further explored …

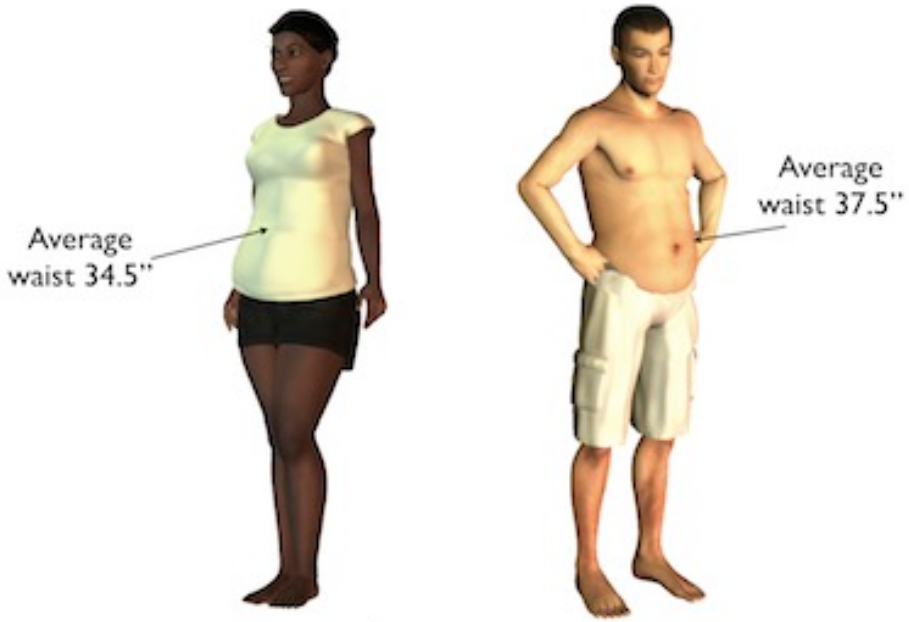
Both paradigms are potentially complementary

- Analytics-based Insights extracted from EHR data may better reflect the relevant population
- Analytics-based CDS require no need to define/maintain long list of rules
- Inherently stochastic statistical signals may better reflect clinical world than deterministic rules
- Being blind to the relevant clinical knowledge is obviously hazardous
  - Contraindications
- Analytics techniques may benefit from domain knowledge

CDS knowledge-Analytics Synergy (KAS) paradigm

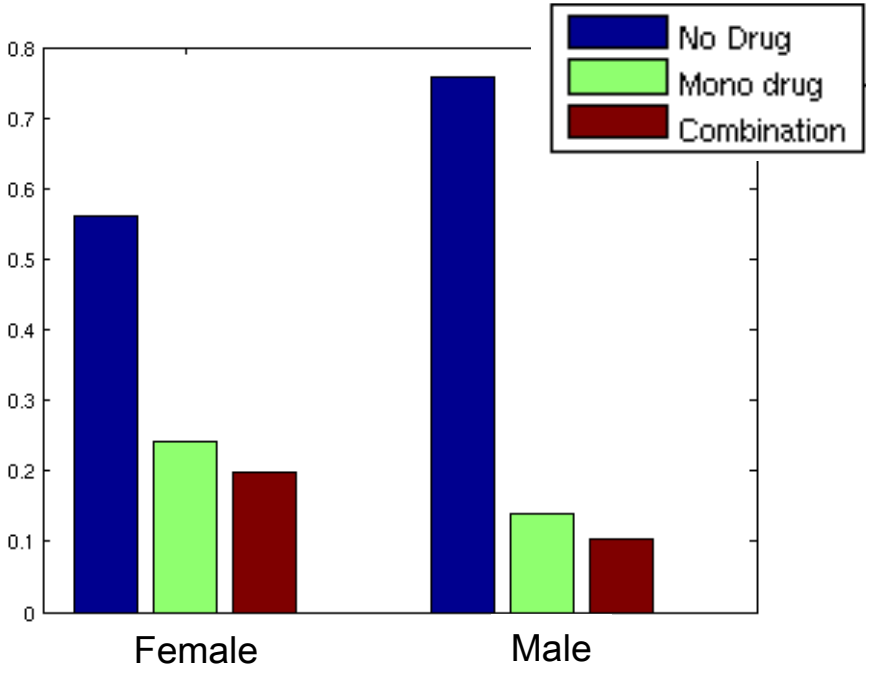
Results – Knowledge enhancement

- Searched for feature-pairs with synergistic predictive power for selected treatment in EPOGH data
  - Several pairs were detected as significantly associated with treatment allocation:
    - Waist circumference & Gender → added to DK model as Deductive Concepts



Results – Knowledge enhancement

- Feature ranking applied to identify features associated with treatment allocation
  - Gender found to be significantly associated with treatment selection
  - → Gender highlighted in PK model as
    - related to "Common Practices" in "Treatment Selection"
  - Relevant reference exist
    - → Accompany analytics-based evidence with pointer to relevant literature…?

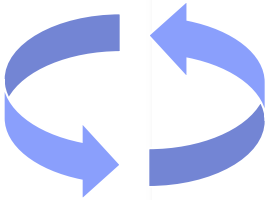


Both paradigms are complementary

- Being blind to the relevant clinical knowledge is obviously hazardous
  - Contraindications
  - Rare conditions
- Analytics techniques may benefit from domain knowledge

- Analytics-based insights may highlight important features not taken into account by current guidelines
- Analytics-based Insights extracted from EHR data may better reflect population
  - Address groups not participating in clinical trials (co-morbidities, elderly, etc.)
  - Consider new genetic information
- Domain knowledge may benefit from analytics

CDS knowledge-Analytics Synergy (KAS) paradigm



KAS CDS High level architecture