Hasso Plattner Institut
IT Systems Engineering | Universität Potsdam

Predictive Modelling for Clinical Applications

Harry Freitas da Cruz

Data Management for Digital Health

Summer 2017

Where are we?

Hasso Plattner Institut

Real-world Use Cases

Oncology | Nephrology | Heart Insufficiency | Additional Topics

Data Management & Foundations

Biology Recap

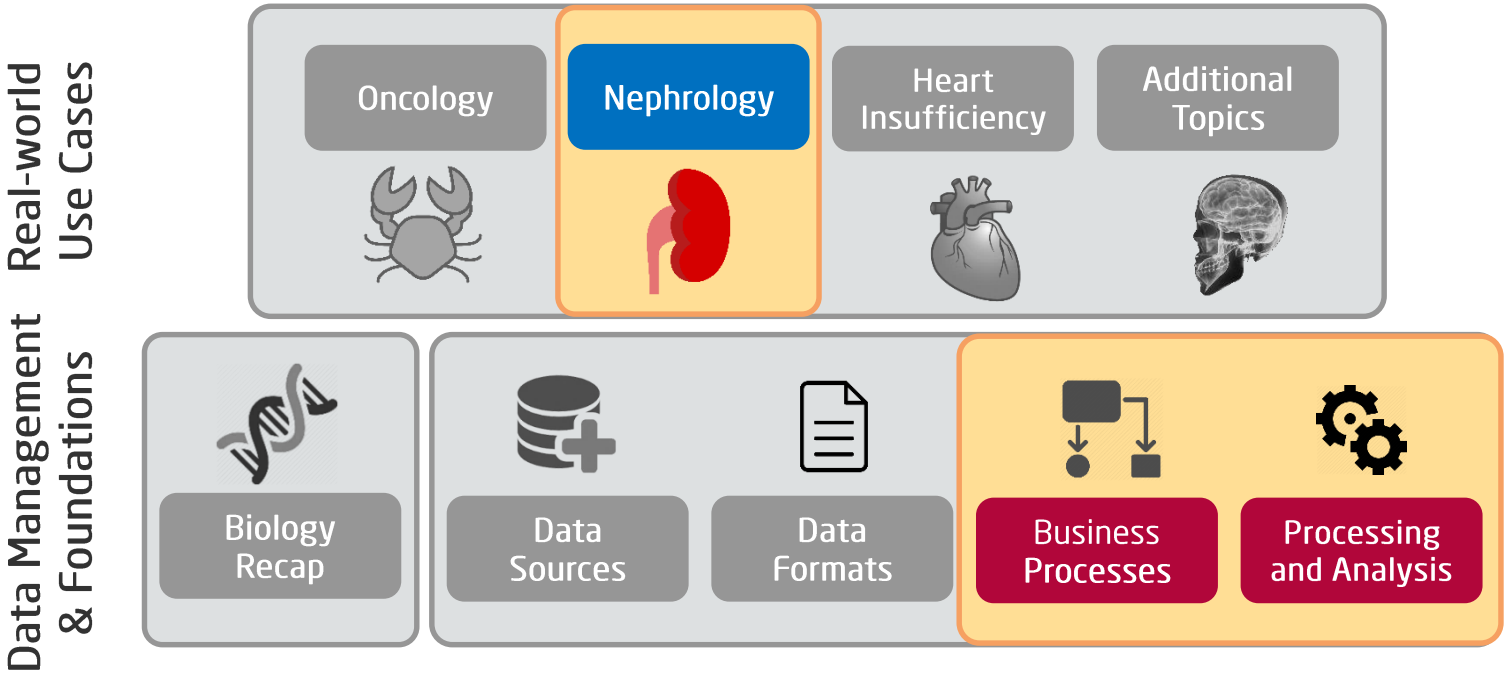
Data Sources

Data Formats

Business Processes

Processing and Analysis

Where are we?


Real-world Use Cases
Oncology
Nephrology
Heart Insufficiency
Additional Topics
Data Management & Foundations
Biology Recap
Data Sources
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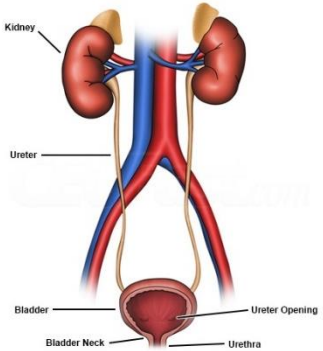
Business Processes
Processing and Analysis

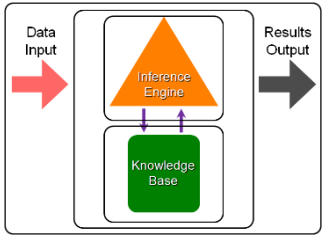
Recap Use Case Nephrology

- The urinary system
- How the kidneys work
- Kidney diseases
- Bayesian networks for AKI
- Machine learning in Nephrology

https://edc2.healthtap.com/ht-staging/user_answer/reference_image/3694/large/Kidney.jpeg



https://ceufast.com/course/urinary-tract-infections-the-unappreciated-giant



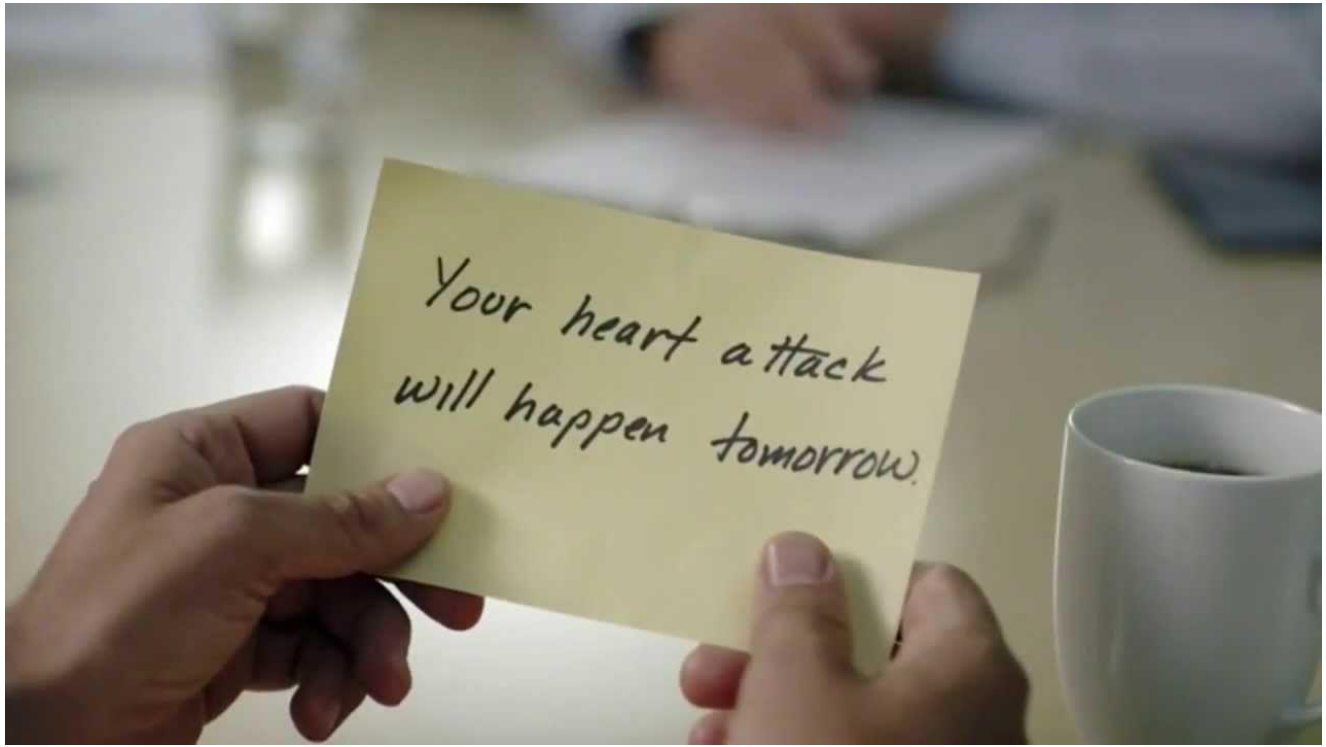
Architecture components of CDSS (Kola, n.d.)

http://sunlightpharmacy.com/wp-content/uploads/2017/03/CKD.jpg

Agenda

- Predictive analytics in healthcare
- Clinical Decision Support Systems (CDSS)
- Clinical Data Repository (CDR)
- Establishing Clinical Prediction Models

Predictive Analytics in Healthcare



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Predictive Analytics in Healthcare

https://i.ytimg.com/vi/xEemneA_qwE/maxresdefault.jpg

Predictive Analytics in Healthcare
Opportunities and Challenges

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Patient safety

Precision medicine

Risk stratification

OPPORTUNITIES

Physician and patient trust

Data standardization

Novel algorithms and tools

CHALLENGES

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https://www.healthcatalyst.com/three-approaches-to-predictive-analytics-in-healthcare

Predictive Analytics in Healthcare
Clinical Decision Making

- Huge variety of clinical (increasingly genomic) data
- Questions to be answered[1]:
  - What disease does this patient have?
  - Should this patient be treated?
  - Should testing be done?
- Accurate, complete, relevant data
- Reliance on pattern recognition and customary practices
- Evidence-based medicine (clinical guidelines)
- Medical errors are frequent

http://www.mii.ucla.edu/images/research/areas/clinical_decision.png

[1] http://www.merckmanuals.com/professional/special-subjects/clinical-decision-making/introduction-to-clinical-decision-making

Clinical Decision Support Systems Definition

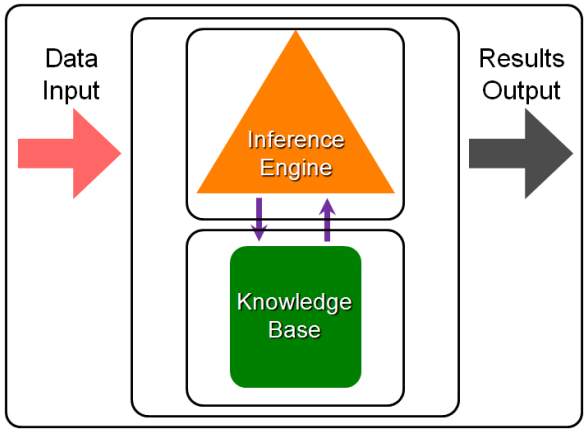
- According to Kabari et al.:

> "Clinical decision support systems (CDSS) provide clinicians, staff, patients, and other individuals with **knowledge** and **person-specific information**, intelligently filtered and presented at **appropriate times**, to enhance health and health care"[1]

[1] L. G. Kabari and E. O. Nwachukwu (2012). Neural Networks and Decision Trees For Eye Diseases Diagnosis, Advances in Expert Systems, Prof. Petrică Vizureanu (Ed.), InTech, DOI: 10.5772/51380.

Clinical Decision Support Systems
Typical Application Scenarios

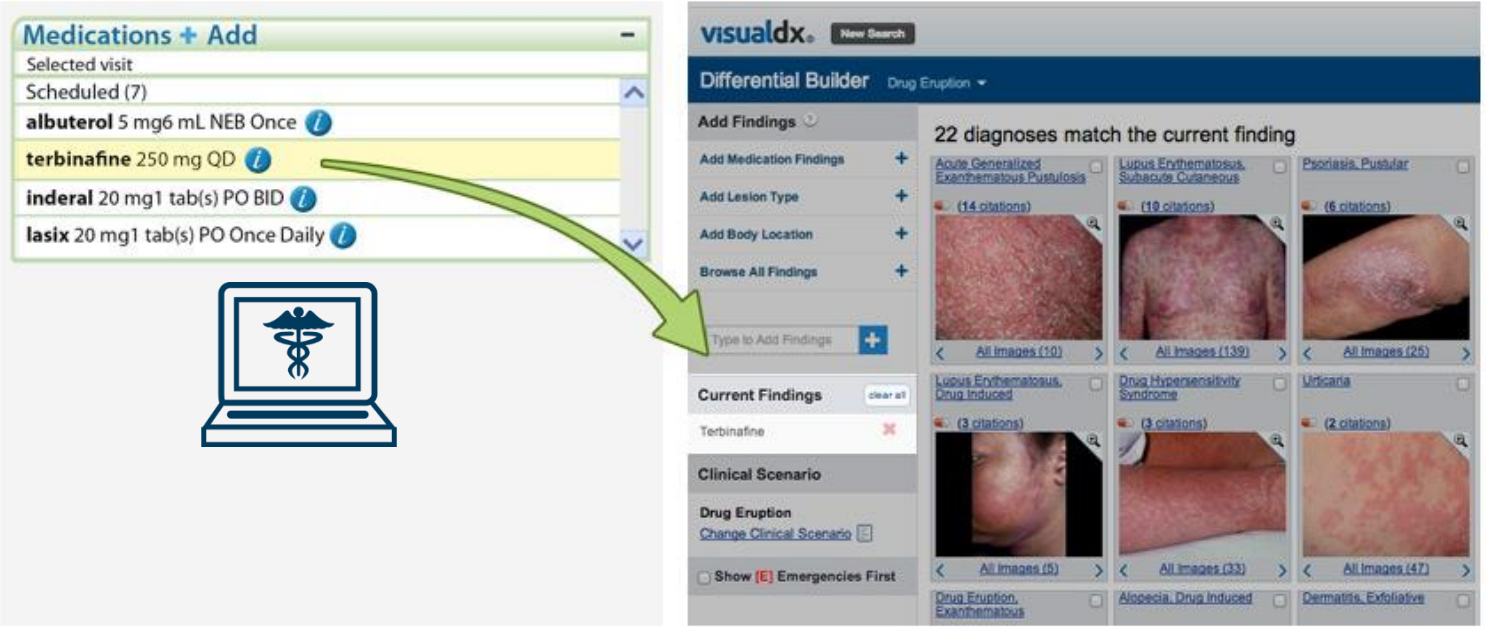
- Usual scenarios
  - Diagnostic support
  - Preventive care
  - Treatment planning / recommendations
- How can this be achieved?
  - Contextual retrieval of highly relevant information
  - Patient-specific reminders and recommendations
  - Organization and presentation of information
- Information logistics / 5 „rights“
  - Information, person, format, channel, time



Architecture components of CDSS (Kola, n.d.)

Berner, E. (2009). Clinical decision support systems: state of the art. AHRQ Publication, (9). Retrieved from https://healthit.ahrq.gov/sites/default/files/docs/page/09-0069-EF_1.pdf

Clinical Decision Support Systems
Contextual Retrieval of Highly Relevant Information



https://www.visualdx.com/benefits/recognize-drug-reactions

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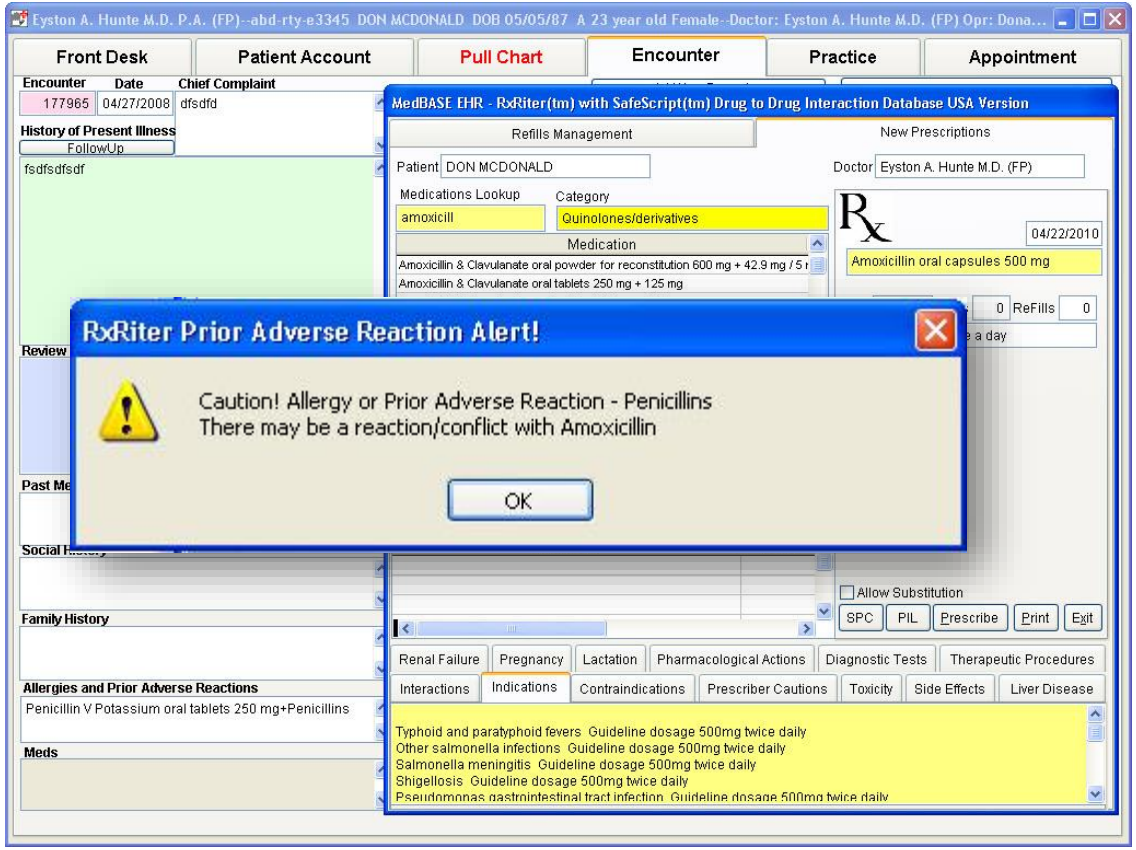
Clinical Decision Support Systems
Patient-specific Reminders and Recommendations

http://www.ehrscreenshots.com/files/2011/10/rxriter001.jpg



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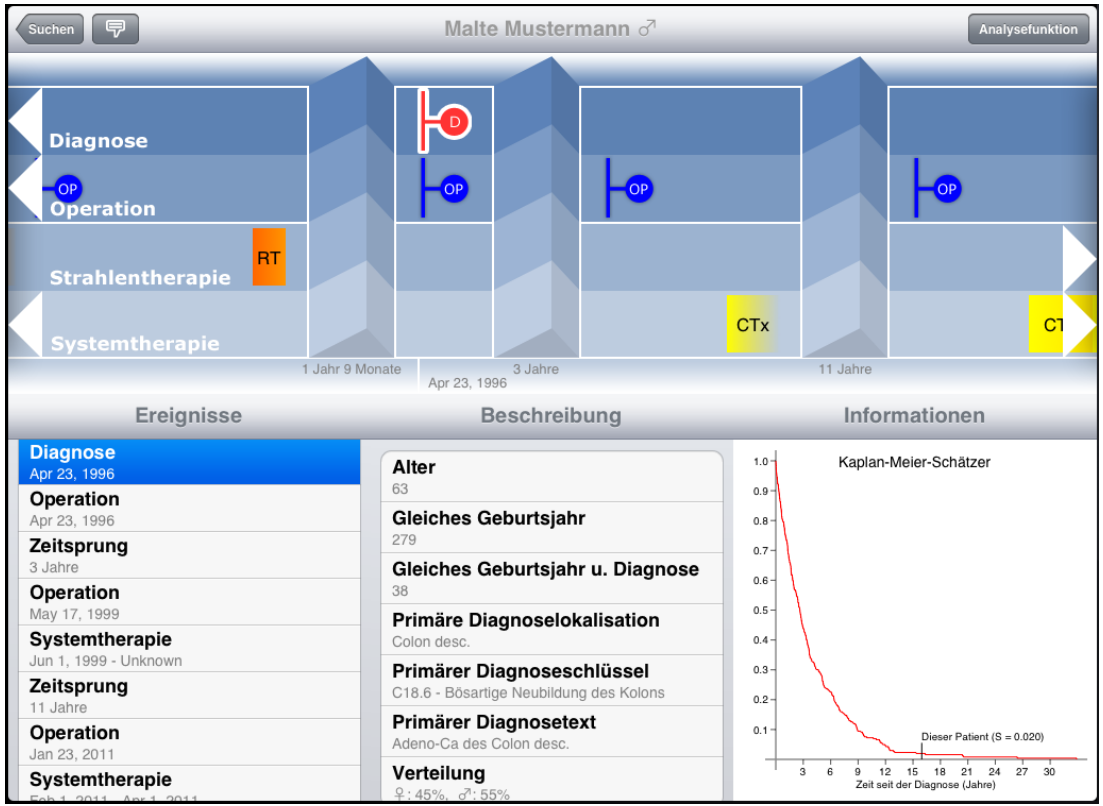
Clinical Decision Support Systems
Organization and Presentation of Information

HANA Oncolyzer



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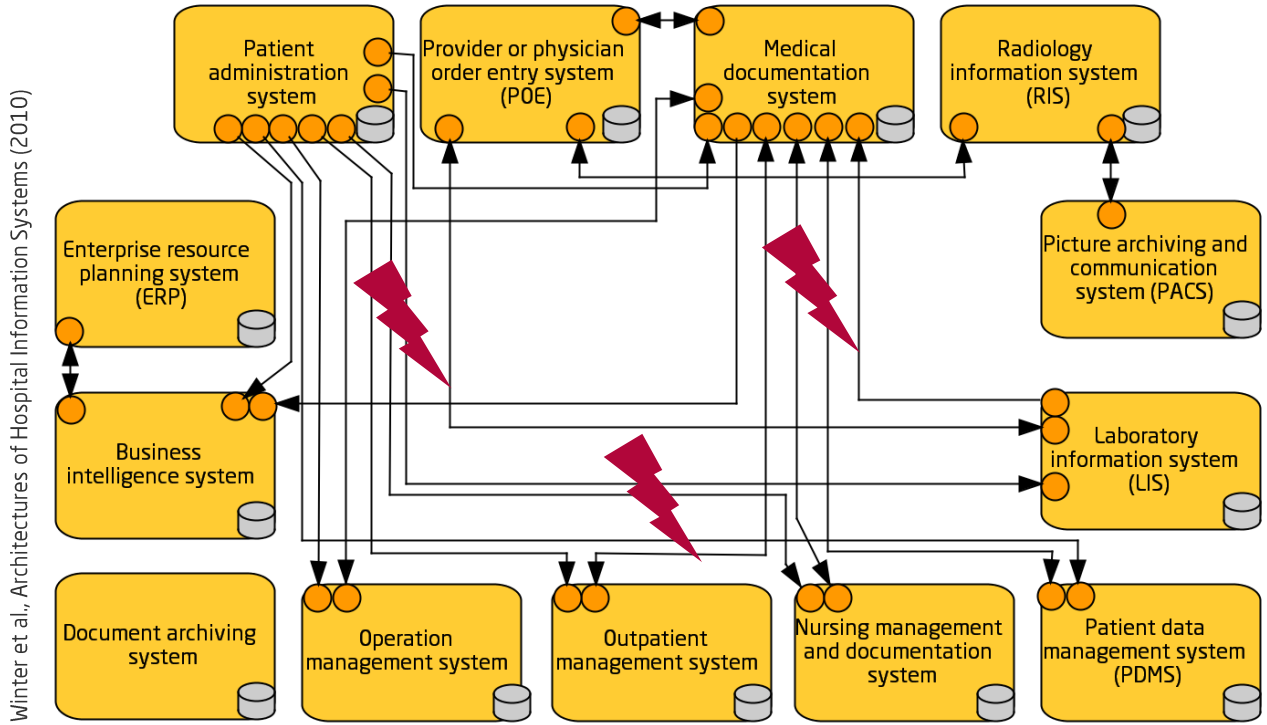
Clinical Data Repository
Heterogeneous Landscape



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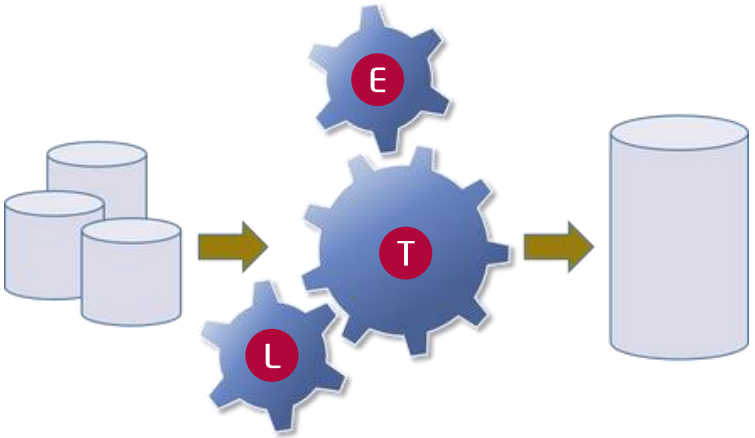
A. Winter, R. Haux, E. Ammenwerth, B. Brigl, N. Hellrung, F. Jahn. Health Information Systems: Architectures and Strategies (2010)

Clinical Data Repository
Challenges and opportunites

- Difficult and costly to develop a general purpose CDR
- Integration of different data sources is a daunting task
- Data inconsistency, redundancies are frequent
- Difficult to adapt to changing needs of users

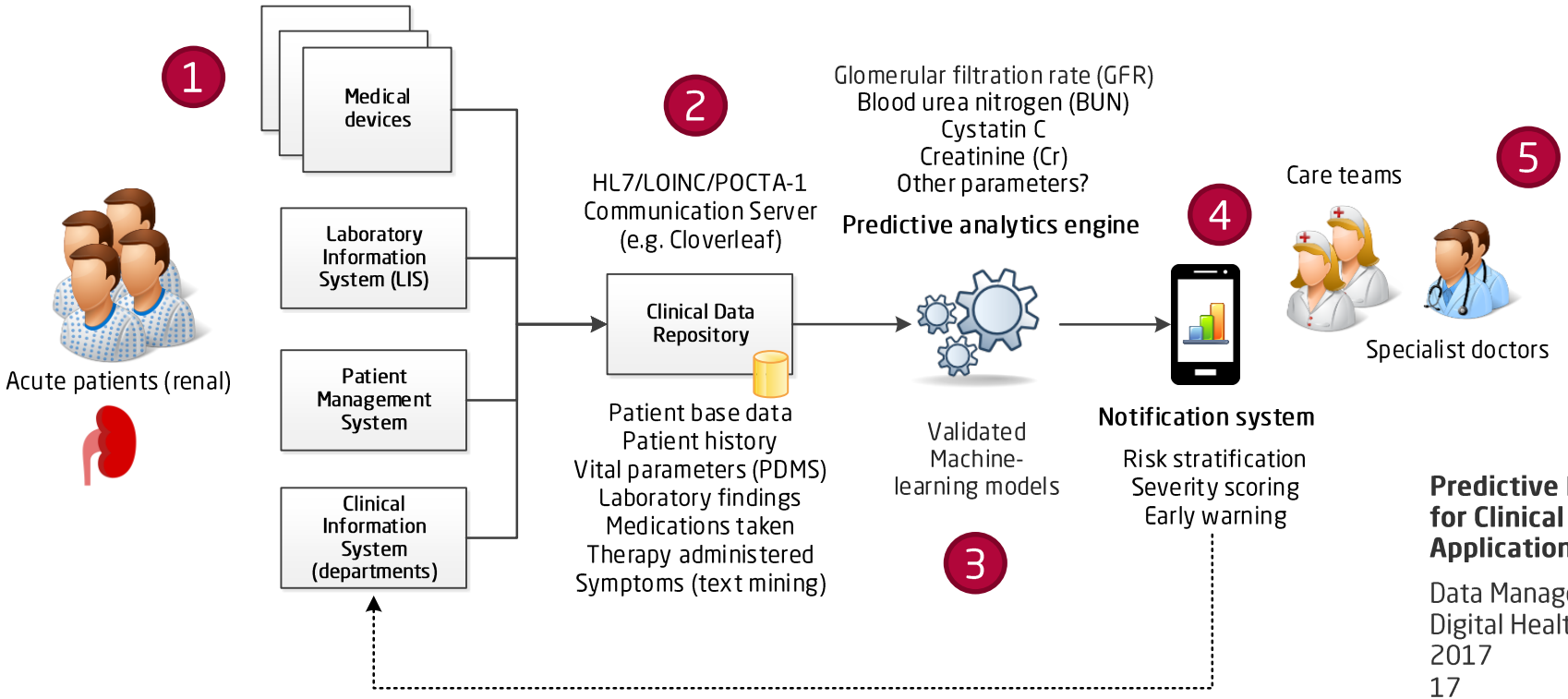
- 360° patient view
- Explore patterns in disease progression and management
- Discover unknown patterns in the data
- Faster hypothesis testing -> Clinical studies



https://discoverbiblog.wordpress.com/2016/11/08/introduction-for-etl/

De Mul, M., Alons, P., van der Velde, P., Konings, I., Bakker, J., & Hazelzet, J. (2012). Development of a clinical data warehouse from an intensive care clinical information system. Computer Methods and Programs in Biomedicine, 105(1), 22–30. http://doi.org/10.1016/j.cmpb.2010.07.002

Clinical Data Repository
Nephrology Use Case (AKI)



H. F. Cruz, Irish Nephrology Society Annual Scientific Meeting (2016)

Predictive Modelling for Clinical Applications

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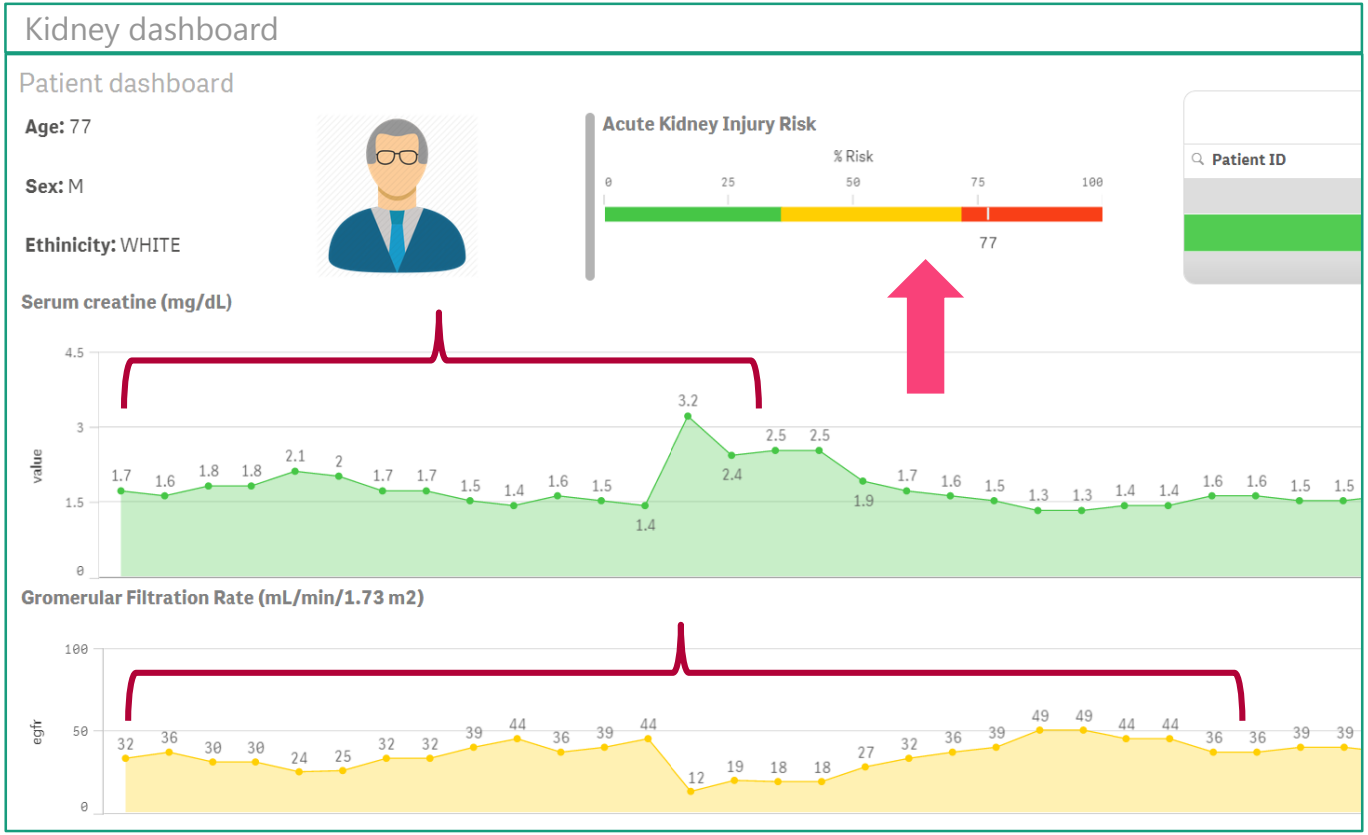
Clinical Data Repository
Nephrology Use Case (AKI): Patient Dashboard



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Predictive Modelling for Clinical Applications

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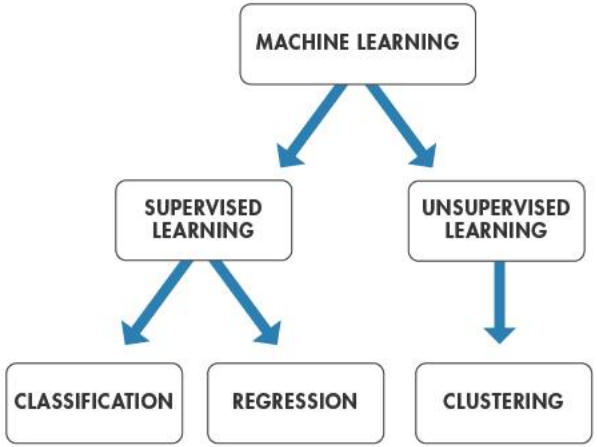
Clinical Prediction Models
Occam's Razor

- Models are an abstraction of reality
- May still be useful depending on the purpose
- Start simple: robust and difficult to break
- As per William of Occam (1287): ontological parsimony
- In diagnostics, not always the case:
  - Hickam's dictum
  - "Patients can have as many diseases as they damn well please"

http://theleanwayconsulting.com/occams-razor-in-business-problem-solving/

Clinical Prediction Models
Supervised or Unsupervised?

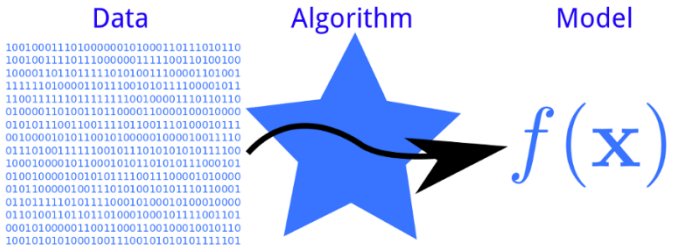
- Supervised learning
  - Labeled data is available
  - Categorical or numerical responses
  - Decision trees, Bayesian nets, ridge regression, etc.
- Unsupervised learning
  - No labeled data
  - Finding hidden patterns in data
  - Hierarchical clustering, k-means, etc.



https://de.mathworks.com/help/stats/machine-learning-in-matlab.html

Clinical Prediction Models
Types of Models

- Classification-based
  - Binary or multi-class
  - Diagnosis, risk stratification, hospital readmission
- Regression-based
  - Optimal drug dosage
  - Treatment plan adjustment
- Survival analysis
  - Time-to-event models
  - Cancer mortality

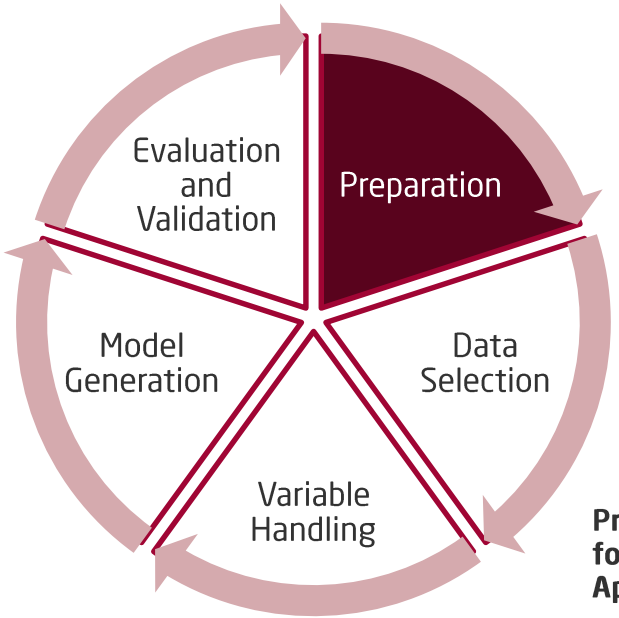


http://phdp.github.io/posts/2013-07-05-dtl.html

Cleophas, T. J., & Zwinderman, A. H. (2013). Machine Learning in Medicine (Vol. 53). Springer Berlin Heidelberg. http://doi.org/10.1017/CBO9781107415324.004

Clinical Prediction Models
Establishing a CPM: Preparation and Dataset Selection

- Step 1: Preparation
  - What is the target outcome?
  - What is the target patient?
  - What is the target user?
- Step 2: Dataset selection
  - Is the data needed available?
  - Is the data representative?
  - What is the validation strategy?



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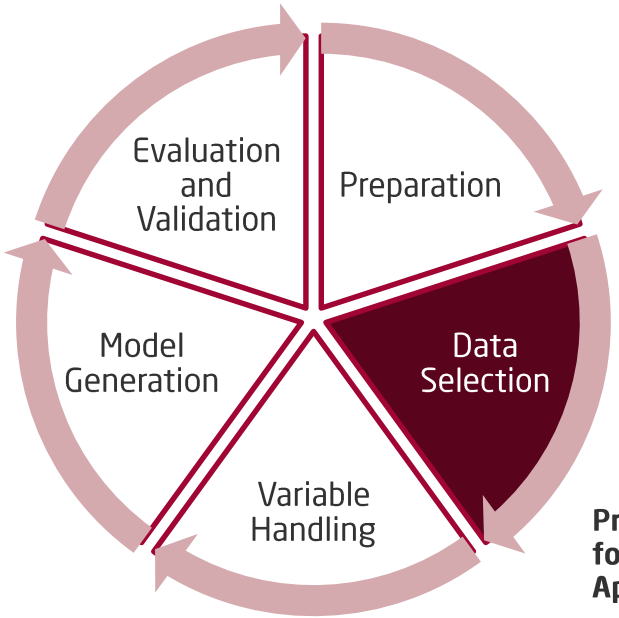

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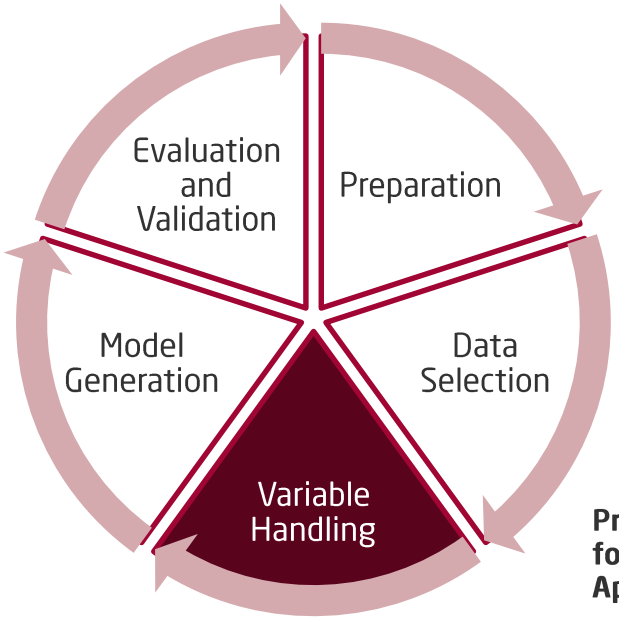
Clinical Prediction Models
Establishing a CPM: Variable Handling

- Expert judgement often necessary
- Previous significant factors should be used
- Avoid predictors that are possible correlated
- Merging categorical variables should be considered
- Scale matters in continuous variables: consistency
- Nominalization often needed for continuous variables
- Consider scale transformation (e.g. log)
- Normalization of values (e.g. from 0-1)
- Identify and handle outliers



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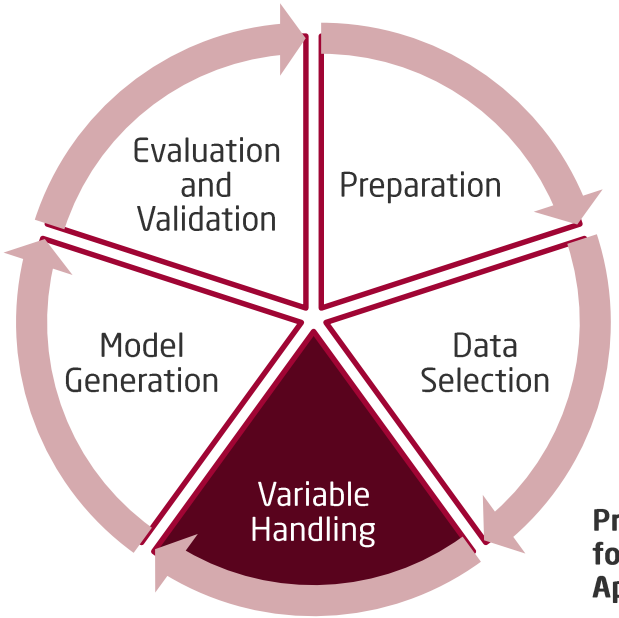
Clinical Prediction Models
Establishing a CPM: Missing Data

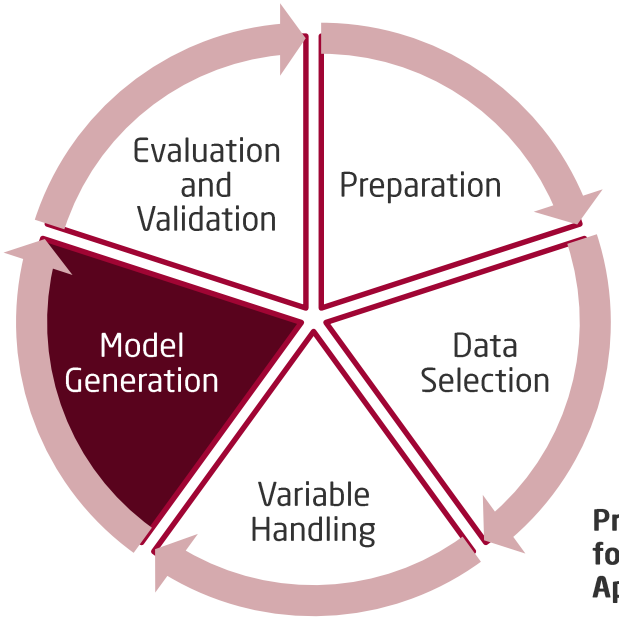
- Leaving out the missing ones: complete case analysis
- Single imputation x multiple imputation
  - Using “other” or “unknown”
  - Averaging occurances, median or mean
- MICE (Multiple Imputation using Chained Equations)
- Regression model from the existing variables



Wells, B. J., Chagin, K. M., Nowacki, A. S., & Kattan, M. W. (2013). Strategies for handling missing data in electronic health record derived data. EGEMS (Washington, DC), 1(3), 1035. http://doi.org/10.13063/2327-9214.1035

Clinical Prediction Models
Establishing a CPM: Model Generation

- Selecting the proper algorithm
- Performing feature selection
  - Backward elimination
  - Stepwise selection
- Trade-offs between goodness of fit and complexity
  - Akeike Information Criterion
  - Bayes Information Criterion
- Perform parameter tuning
  - Optimization of hyperparameters



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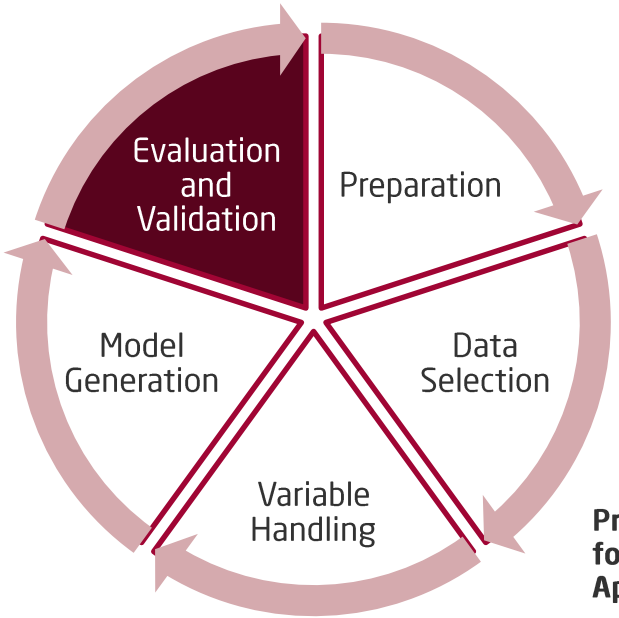
Clinical Prediction Models
Establishing a CPM: Evaluation and Validation

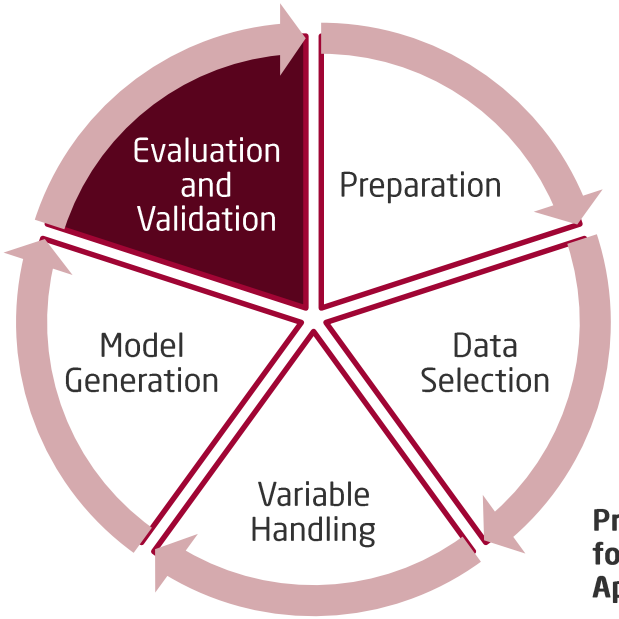
- Internal validation
  - Cross-validation
  - Bootstrapping
- External validation
  - Using a different data source
  - Ensure transportability and generalizability
- Measures of performance
  - ROC Curve
  - R^2, p-values
- True positive rate (TPR) / true negative rate



Clinical Prediction Models
Establishing a CPM: Measures of Performance

Measure
Sensitivity and specificity
Discrimination (ROC/AUC)
Predictive values: positive, negative
Likelihood ratio: positive, negative
Accuracy: Youden index, Brier score
Number needed to treat or screen
Calibration: Calibration plot, Hosmer-Lemeshow test
R^2 statistical significance: p-value (e.g. likelihood ratio test)
Magnitude of association, e.g., β coefficients, odds ratio
Model quality: Akeike IC/ Bayes IC
Net reclassification index and integrated discrimination improvement
Net benefit
Cost-effectiveness

Measures of model performance (Lee 2016)



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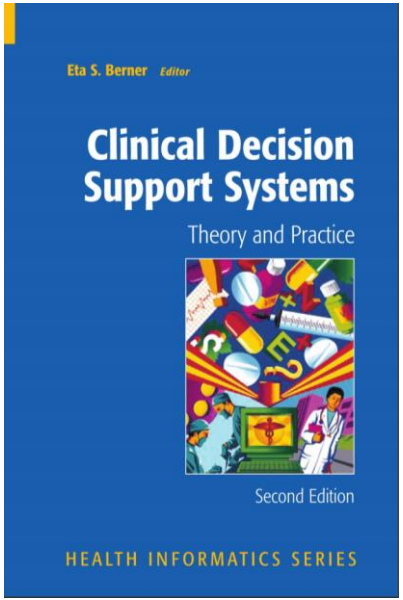
What to Take Home?

- There is lots of potential for health care analytics
- Clinical Decision Support Systems offer a way to tap into that
- Step-by-step process to establishing clinical prediction models
  - Preparation
  - Data selection
  - Model generation
  - Evaluation and validation

To Know More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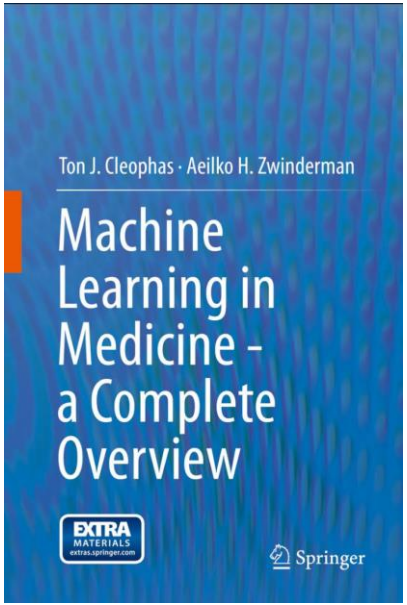
Ton J. Cleophas · Aeilko H. Zwinderman
Machine Learning in Medicine - a Complete Overview
EXTRA MATERIALS
Springer

What's Coming Next?

- Applying the step-by-step process with an example and tool (Rapid Miner)
- Instructions for the exercise